NEUROANATOMY

Prof. Aron Emmi

Central Nervous System Development

Morphogenesis - Histogenesis
Developmental Alterations

G. Klimt – Die Jungfrau

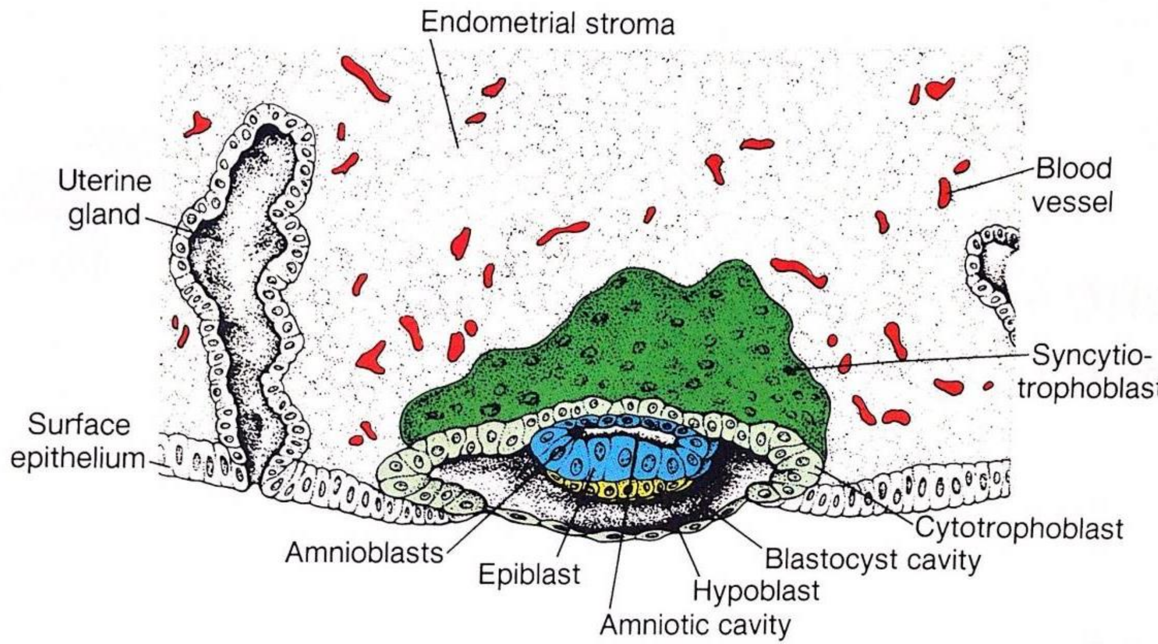


Figure 4.1 A 7.5-day human blastocyst, partially embedded in the endometrial stroma. The trophoblast consists of an inner layer with mononuclear cells, the cytotrophoblast, and an outer layer without distinct cell boundaries, the syncytiotrophoblast. The embryoblast is formed by the epiblast and hypoblast layers. The amniotic cavity appears as a small cleft.

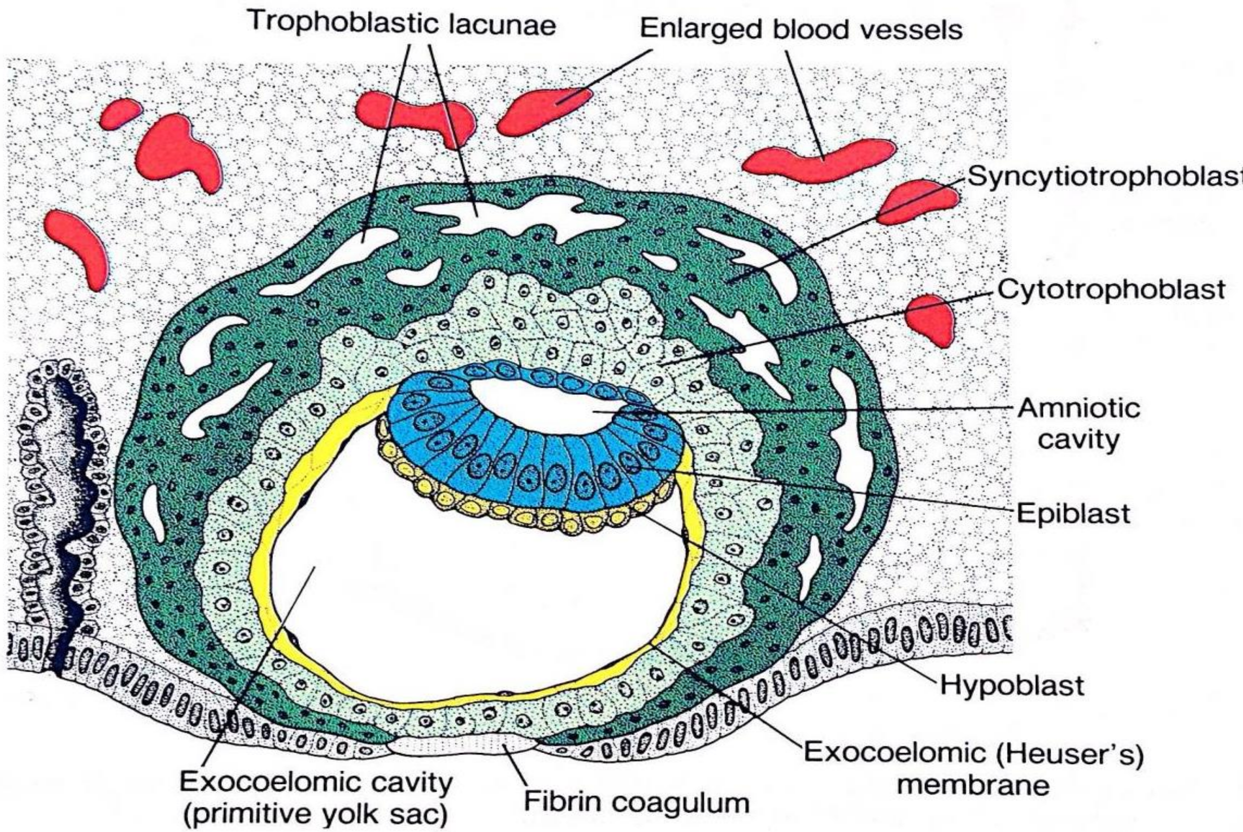


Figure 4.3 A 9-day human blastocyst. The syncytiotrophoblast shows a large number of lacunae. Flat cells form the exocoelomic membrane. The bilaminar disc consists of a layer of columnar epiblast cells and a layer of cuboidal hypoblast cells. The original surface defect is closed by a fibrin coagulum.

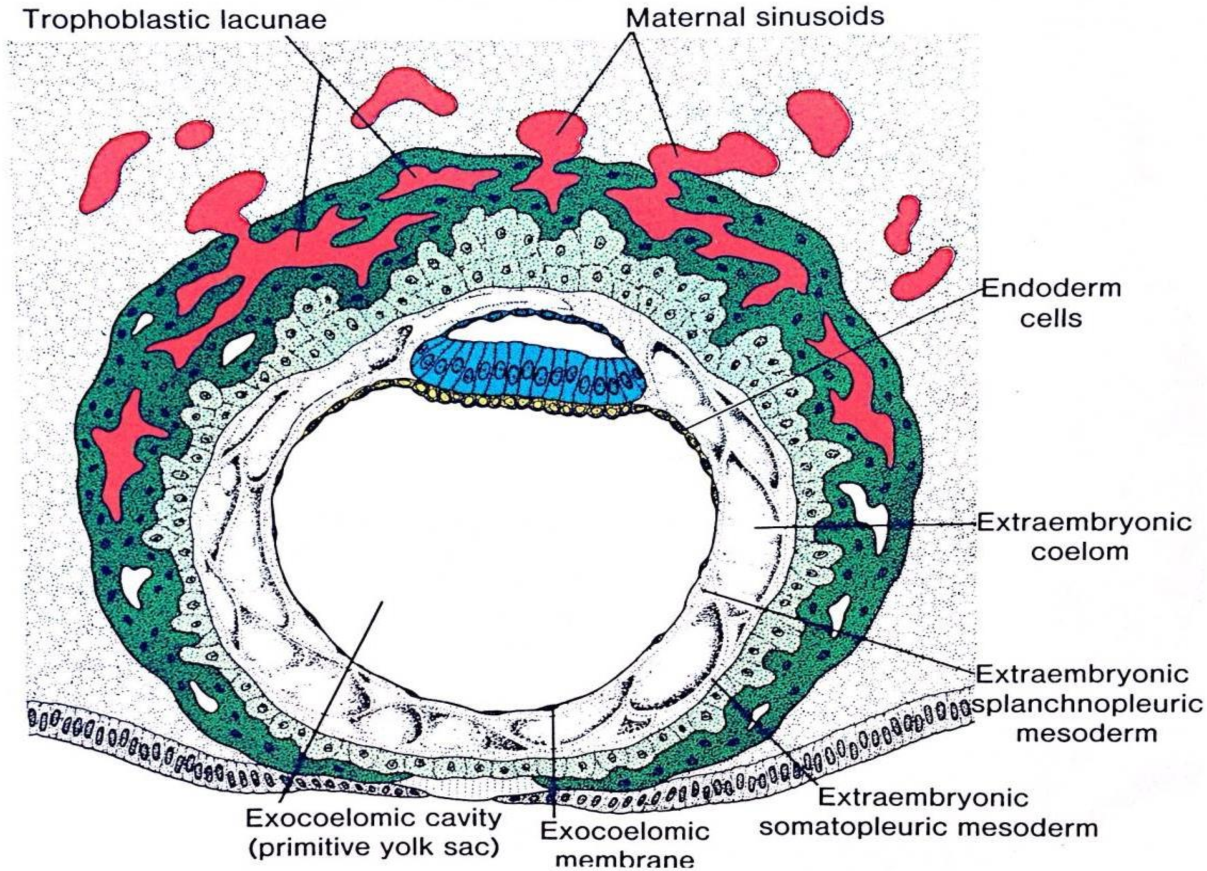


Figure 4.4 Human blastocyst of approximately 12 days. The trophoblastic lacunae at the embryonic pole are in open connection with maternal sinusoids in the endometrial stroma. Extraembryonic mesoderm proliferates and fills the space between the exocoelomic membrane and the inner aspect of the trophoblast.

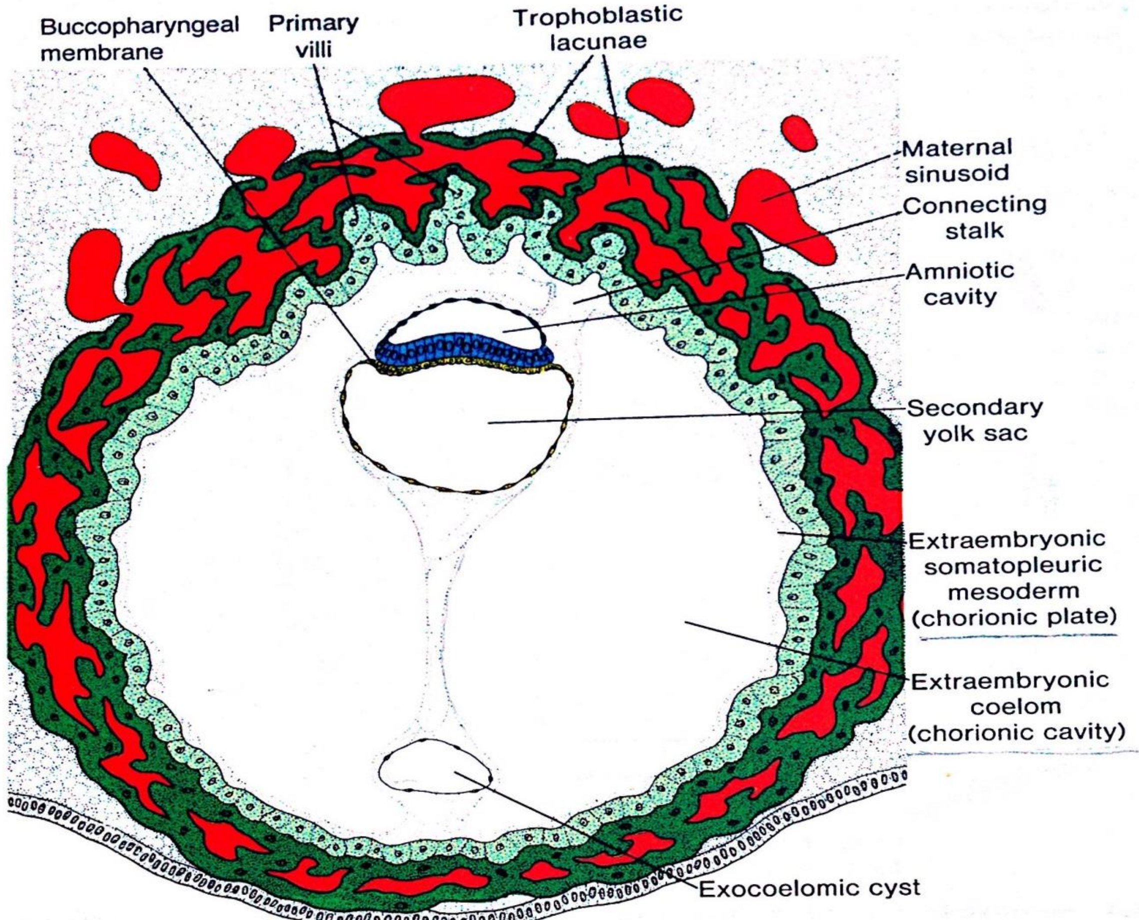


Figure 4.6 A 13-day human blastocyst. Trophoblastic lacunae are present at the embryonic as well as the abembryonic pole, and the uteroplacental circulation has begun. Note the primary villi and the extraembryonic coelom or **chorionic cavity**. The secondary yolk sac is entirely lined with endoderm.

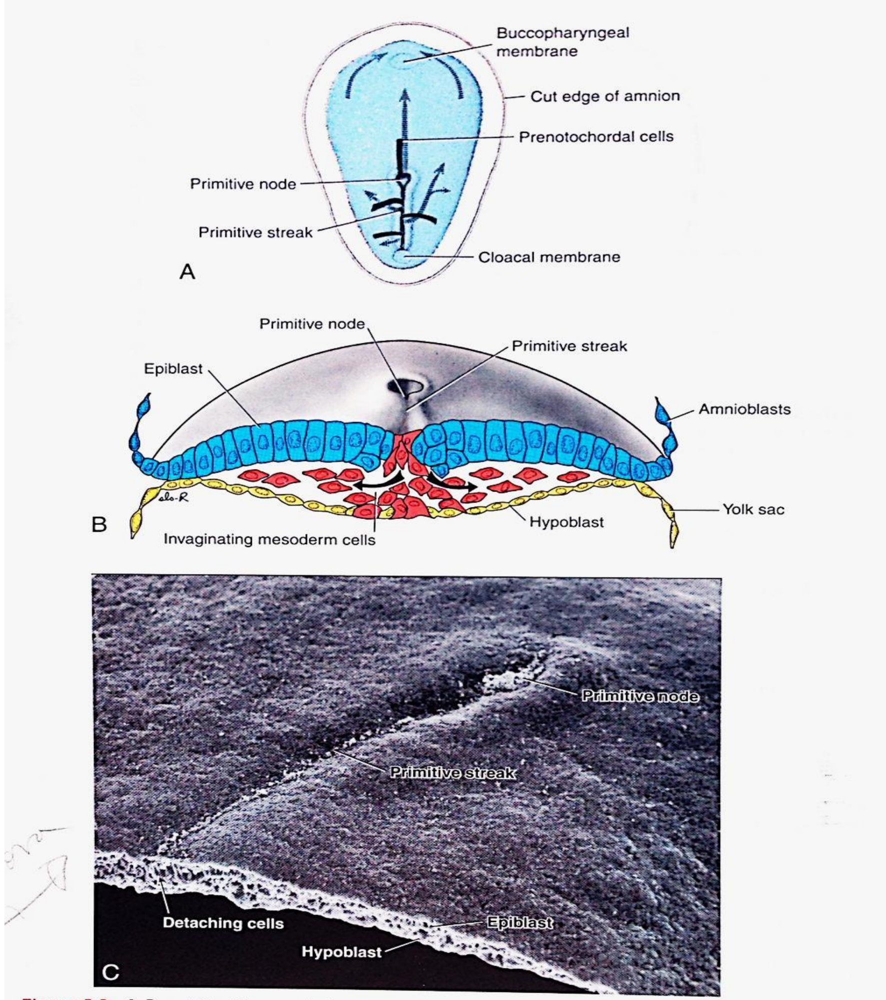


Figure 5.3 **A.** Dorsal side of the germ disc from a 16-day embryo indicating the movement of surface epiblast cells *(solid black lines)* through the primitive streak and node and the subsequent migration of cells between the hypoblast and epiblast *(broken lines)*. **B.** Cross section through the cranial region of the streak at 15 days showing invagination of epiblast cells. The first cells to move inward displace the hypoblast to create the definitive endoderm. Once definitive endoderm is established, inwardly moving epiblast forms mesoderm. **C.** Dorsal view of an embryo showing the primitive node and streak and a cross section through the streak. The view is similar to the cartoon in Figure 5.3*B*; *arrow*, detaching epiblast cells in the primitive streak.

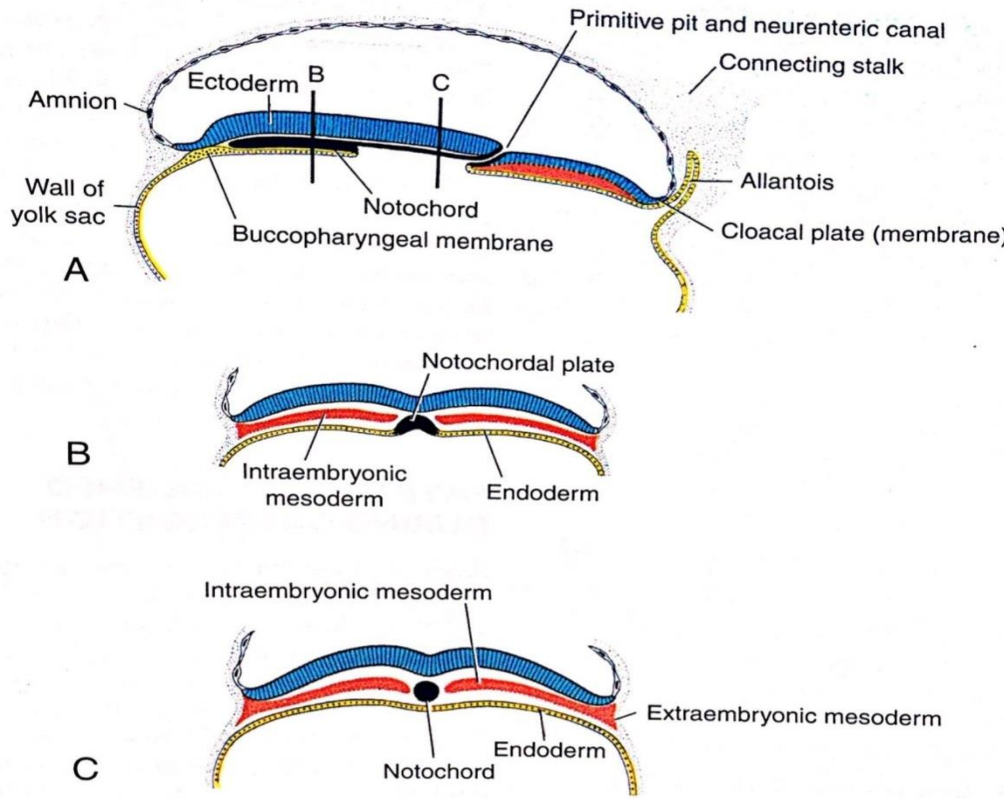


Figure 5.4 Schematic views illustrating formation of the notochord, whereby prenotochordal cells migrate through the primitive streak, become intercalated in the endoderm to form the notochordal plate, and finally detach from the endoderm to form the definitive notochord. Because these events occur in a cranial-to-caudal sequence, portions of the definitive notochord are established in the head region first. **A.** Drawing of a sagittal section through a 17-day embryo. The most cranial portion of the definitive notochord has formed, while prenotochordal cells caudal to this region are intercalated into the endoderm as the notochordal plate. **B.** Schematic cross section through the region of the notochordal plate. Soon the notochordal plate will detach from the endoderm to form the definitive notochord. **C.** Schematic view showing the definitive notochord.

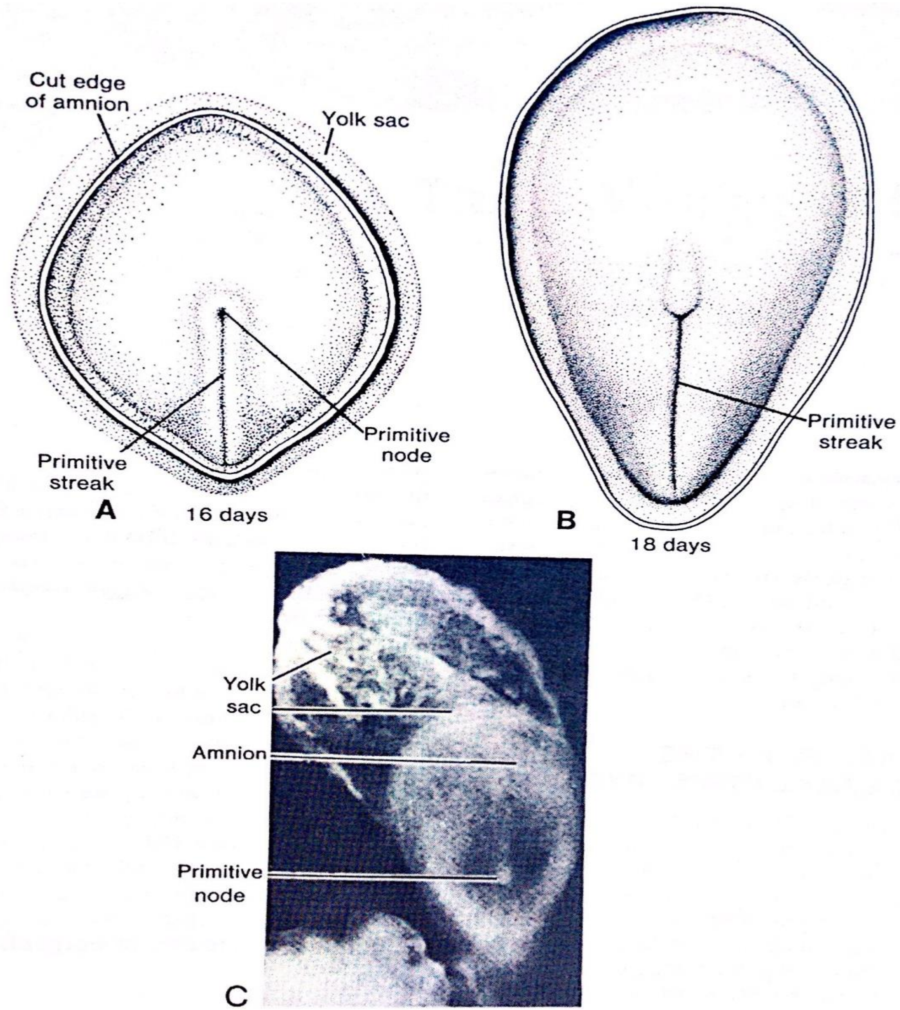


Figure 6.1 **A.** Dorsal view of a 16-day presomite embryo. The primitive streak and primitive node are visible. **B.** Dorsal view of an 18-day presomite embryo. The embryo is pear-shaped, with its cephalic region somewhat broader than its caudal end. **C.** Dorsal view of an 18-day human embryo. Note the primitive node and, extending forward from it, the notochord. The yolk sac has a somewhat mottled appearance. The length of the embryo is 1.25 mm, and the greatest width is 0.68 mm.

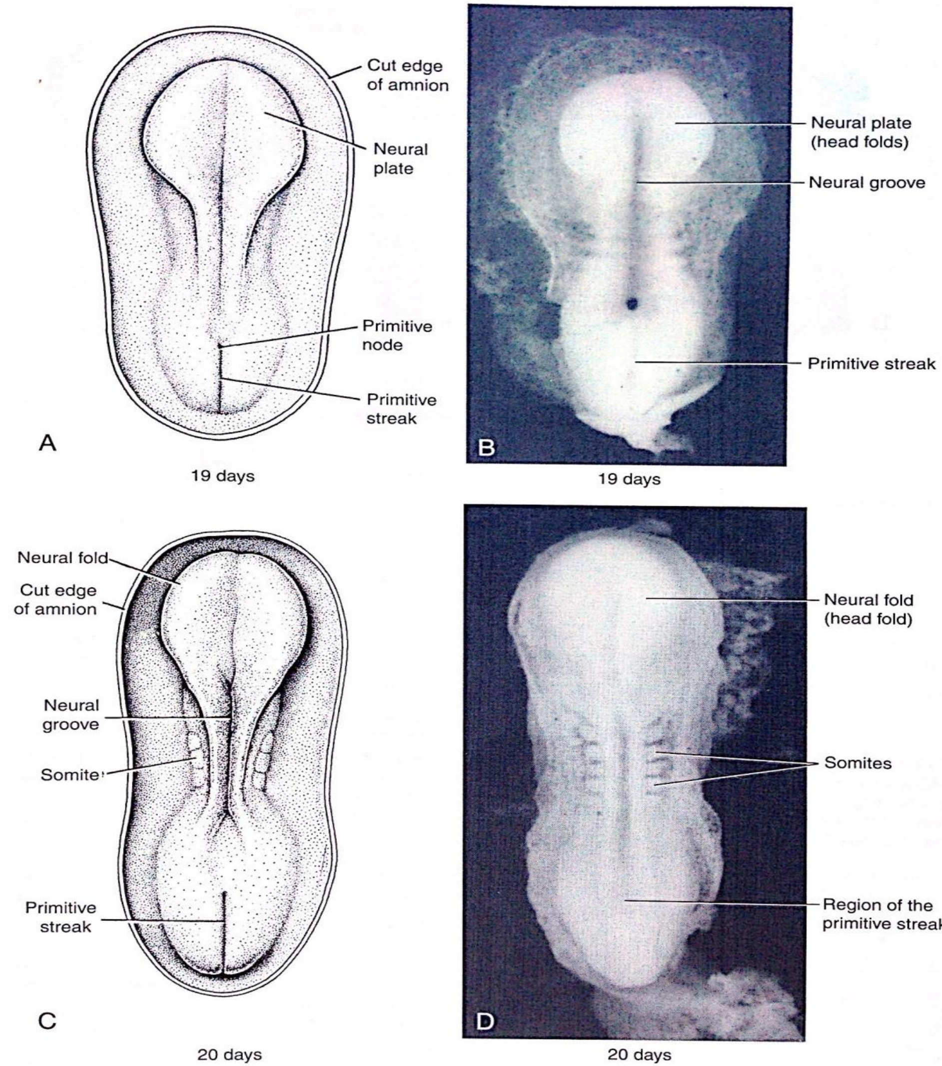


Figure 6.2 **A.** Dorsal view of a late presomite embryo (approximately 19 days). The amnion has been removed, and the neural plate is clearly visible. **B.** Dorsal view of a human embryo at 19 days. **C.** Dorsal view of an embryo at approximately 20 days showing somites and formation of the neural groove and neural folds. **D.** Dorsal view of a human embryo at 20 days.

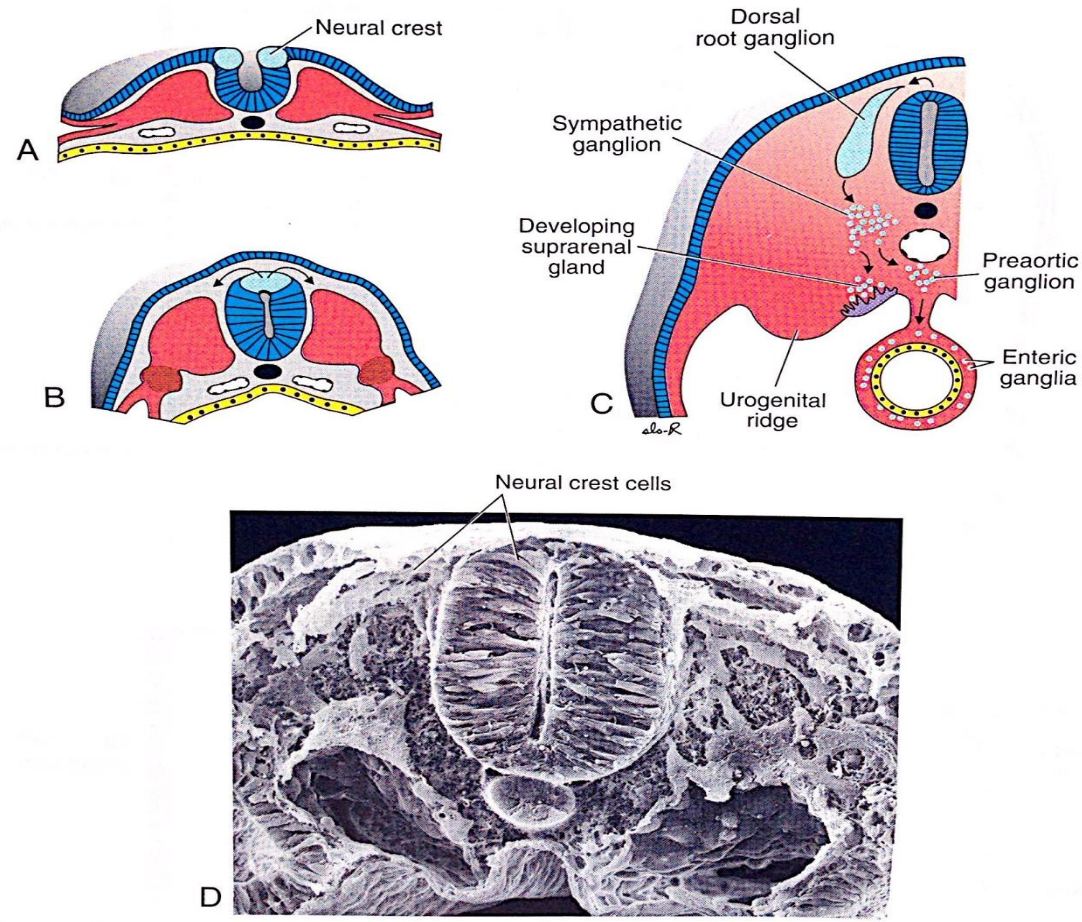


Figure 6.3 Formation and migration of neural crest cells in the spinal cord. **A,B.** Crest cells form at the tips of neural folds and do not migrate away from this region until neural tube closure is complete. **C.** After migration, crest cells contribute to a heterogeneous array of structures, including dorsal root ganglia, sympathetic chain ganglia, adrenal medulla, and other tissues (Table 6.1, p. 72). **D.** In a scanning electron micrograph, crest cells at the top of the closed neural tube can be seen migrating away from this area.

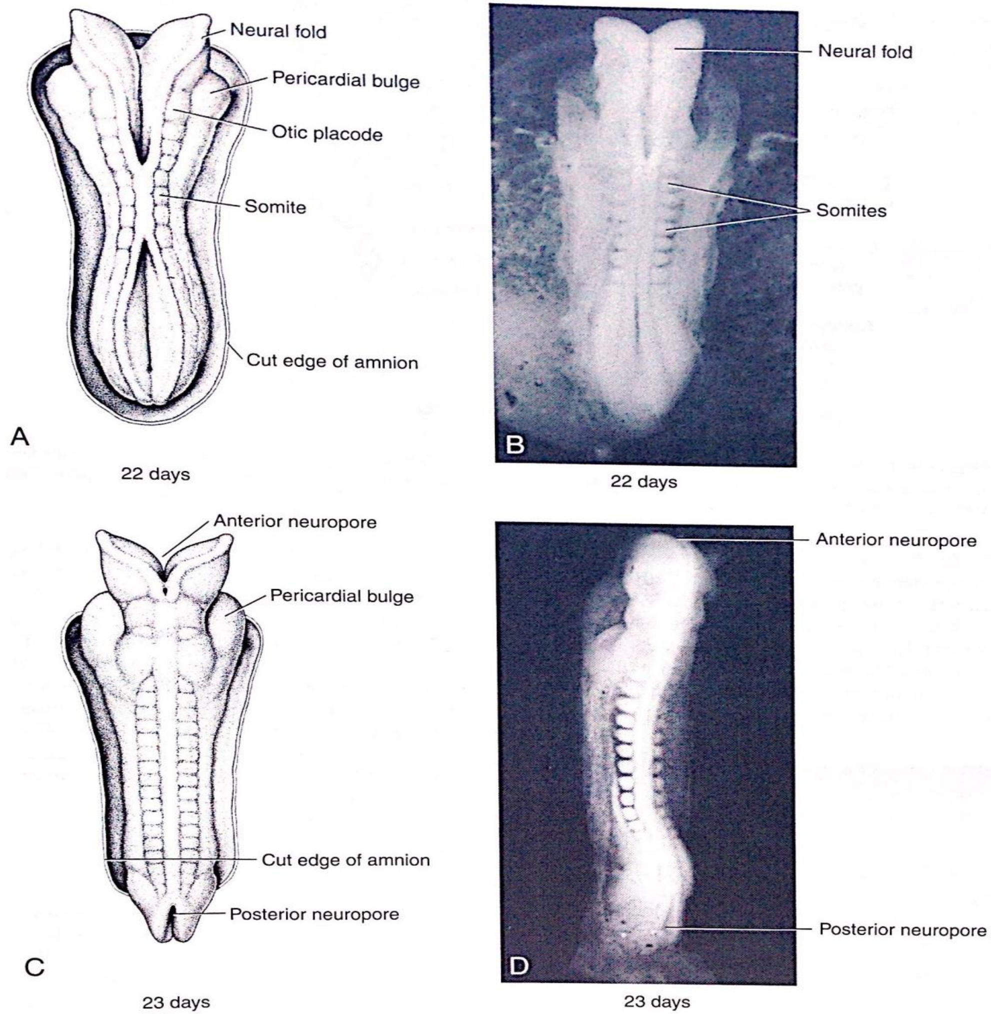


Figure 6.5 **A.** Dorsal view of an embryo at approximately day 22. Seven distinct somites are visible on each side of the neural tube. **B.** Dorsal view of a human embryo at 21 days. **C.** Dorsal view of an embryo at approximately day 23. Note the pericardial bulge on each side of the midline in the cephalic part of the embryo. **D.** Dorsal view of a human embryo at 23 days.

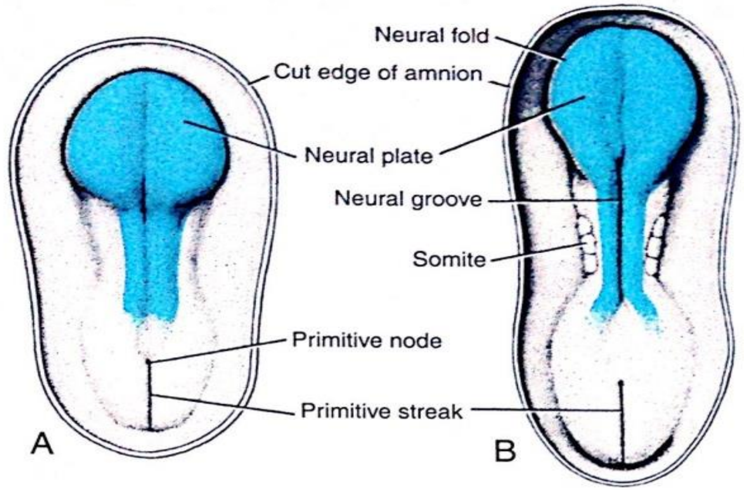


Figure 17.1 **A.** Dorsal view of a late presomite embryo at approximately 18 days. The amnion has been removed, and the neural plate is clearly visible. **B.** Dorsal view at approximately 20 days. Note the somites and the neural groove and neural folds.

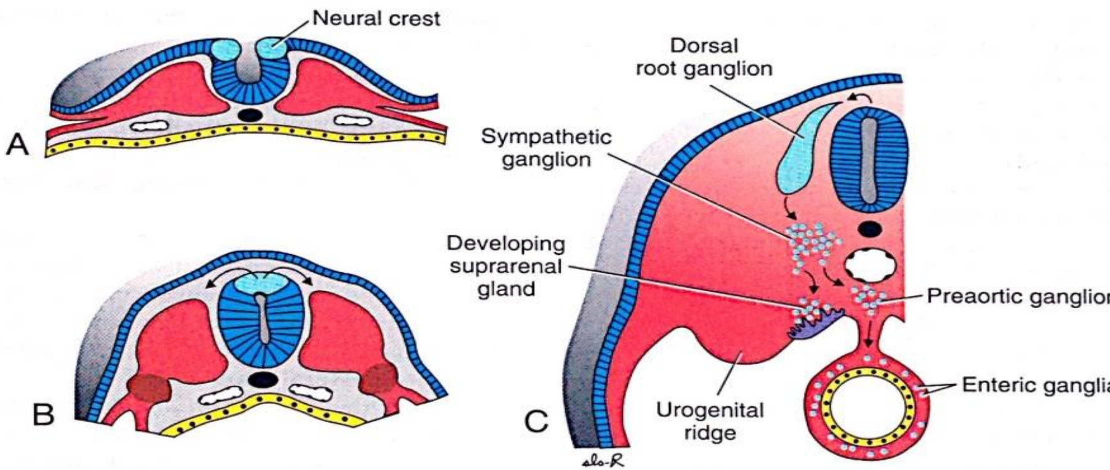
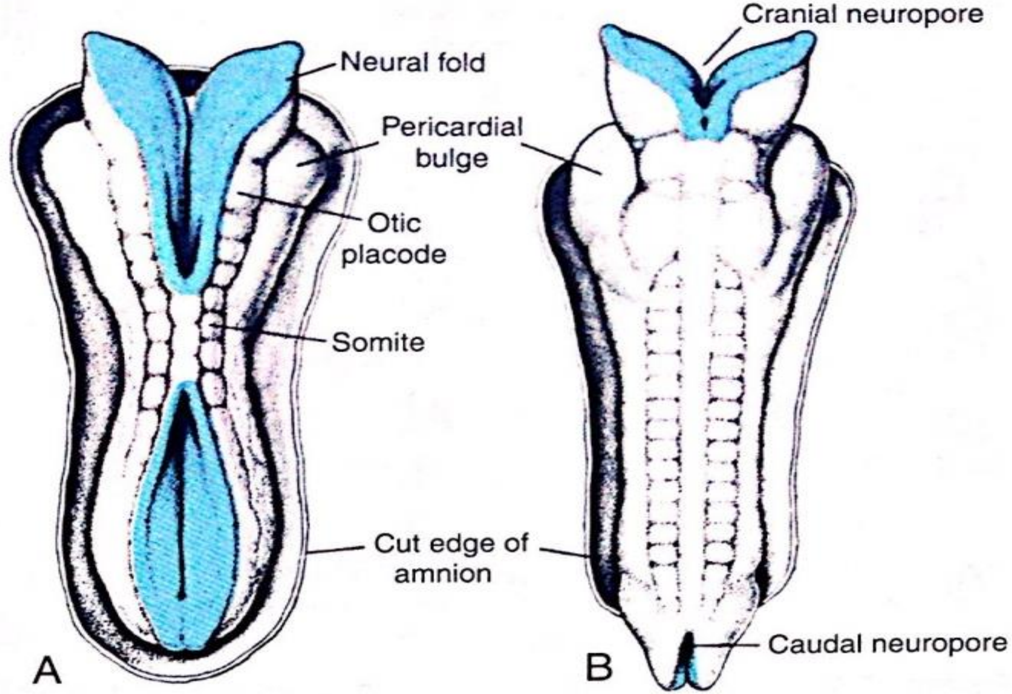


Figure 17.3 **A.** Dorsal view of a human embryo at approximately day 22. Seven distinct somites are visible on each side of the neural tube. **B.** Dorsal view of a human embryo at approximately day 23. The nervous system is in connection with the amniotic cavity through the cranial and caudal neuropores.



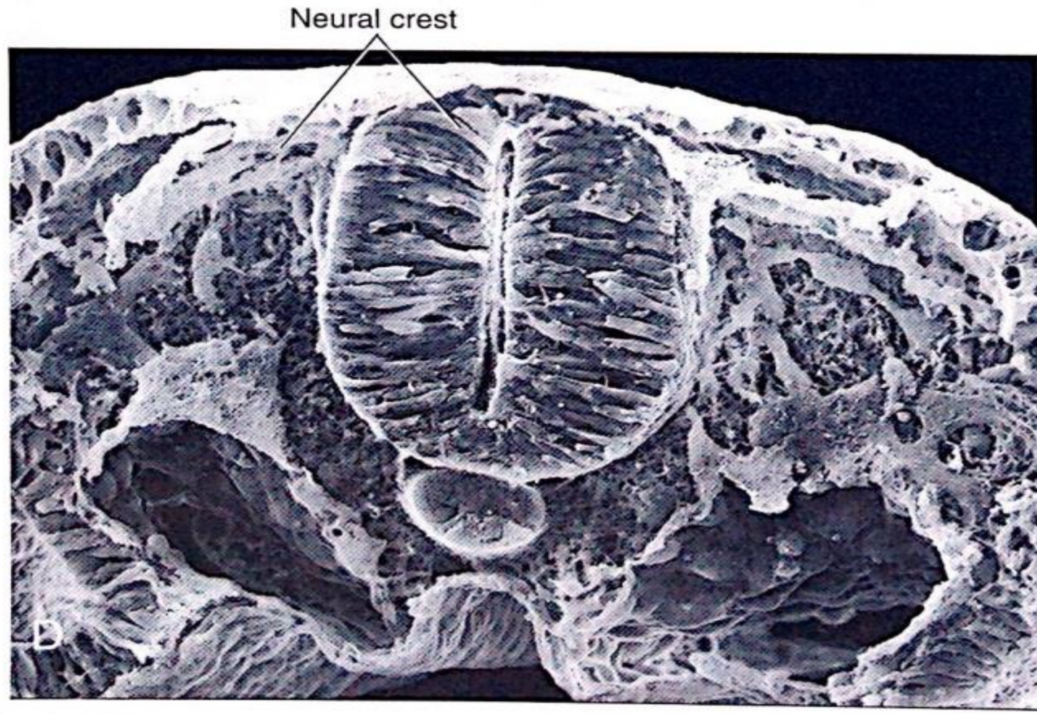
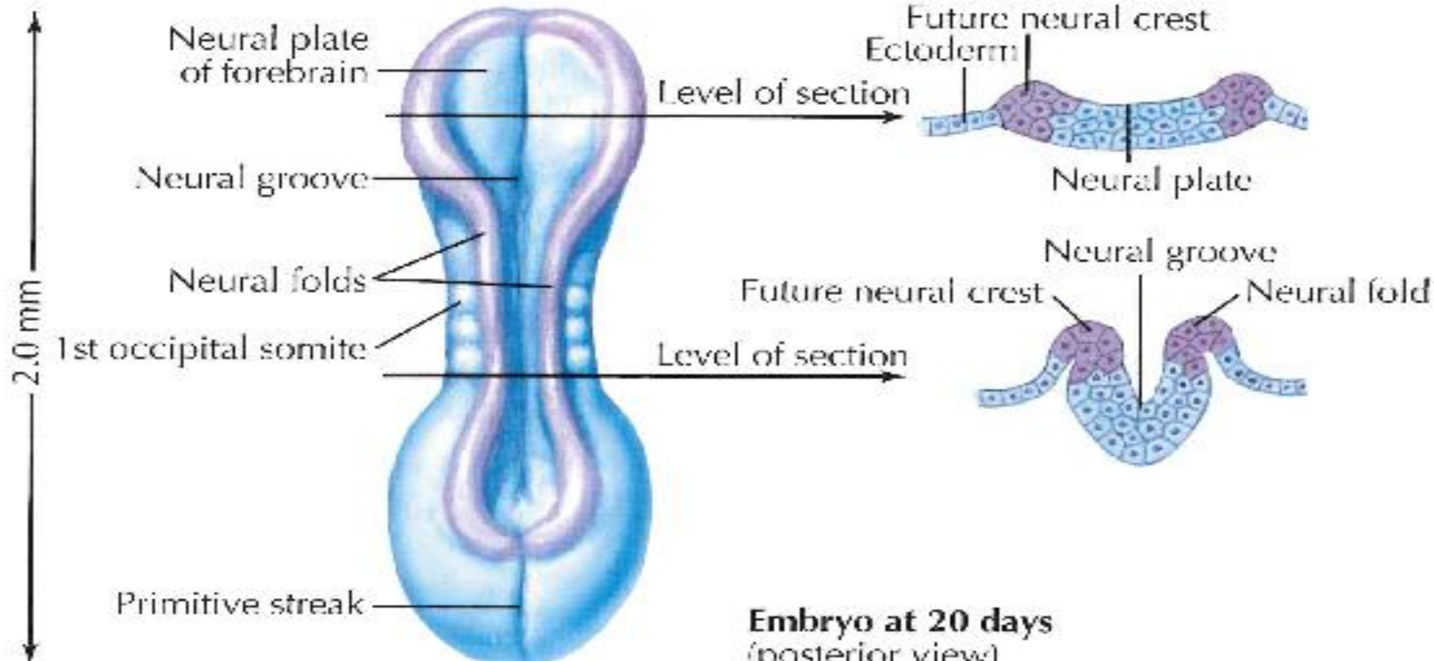
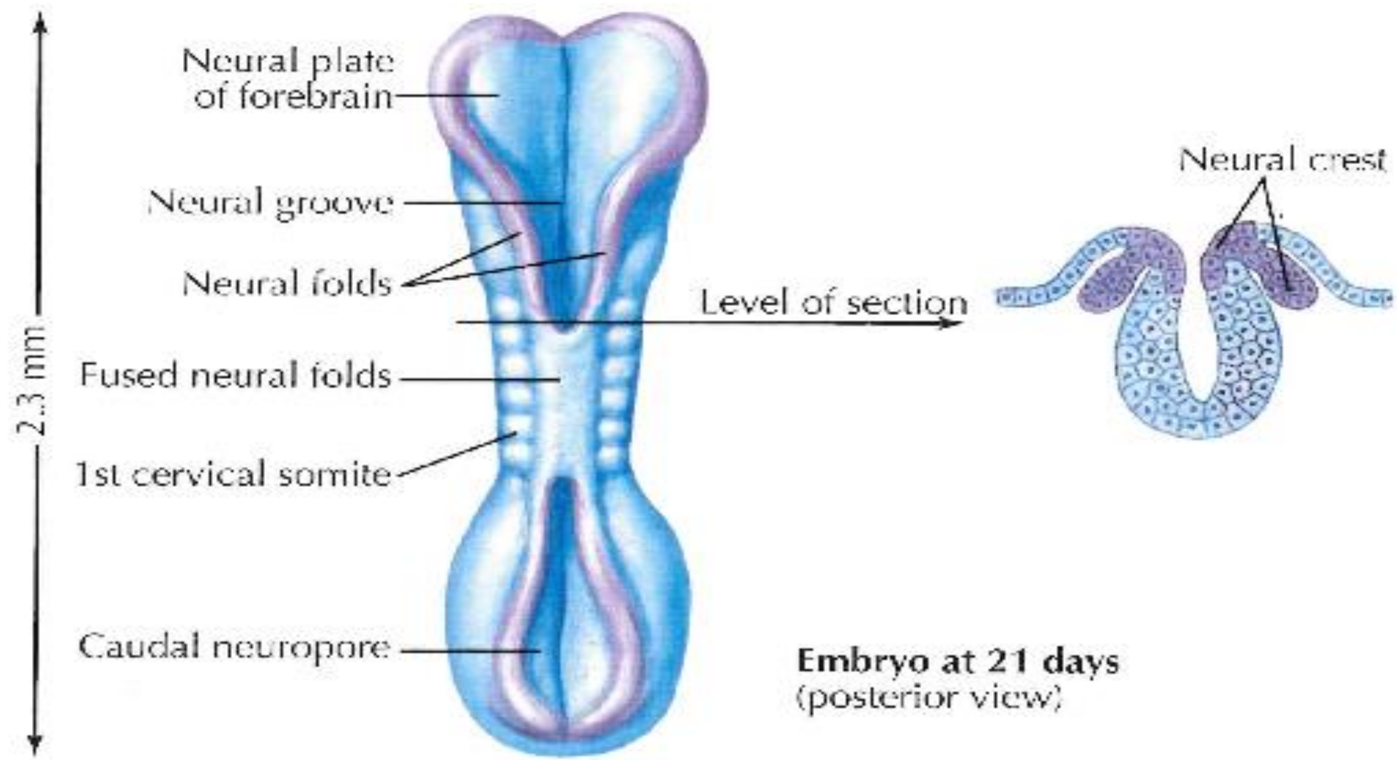


Figure 17.2 **A–C.** Transverse sections through successively older embryos showing formation of the neural groove, neural tube, and neural crest. Cells of the neural crest migrate from the edges of the neural folds and develop into spinal and cranial sensory ganglia **(A–C)**. **D.** Scanning electron micrograph of a chick embryo showing the neural tube and neural crest cells migrating from the dorsal region of the tube (compare with **B** and **C**).

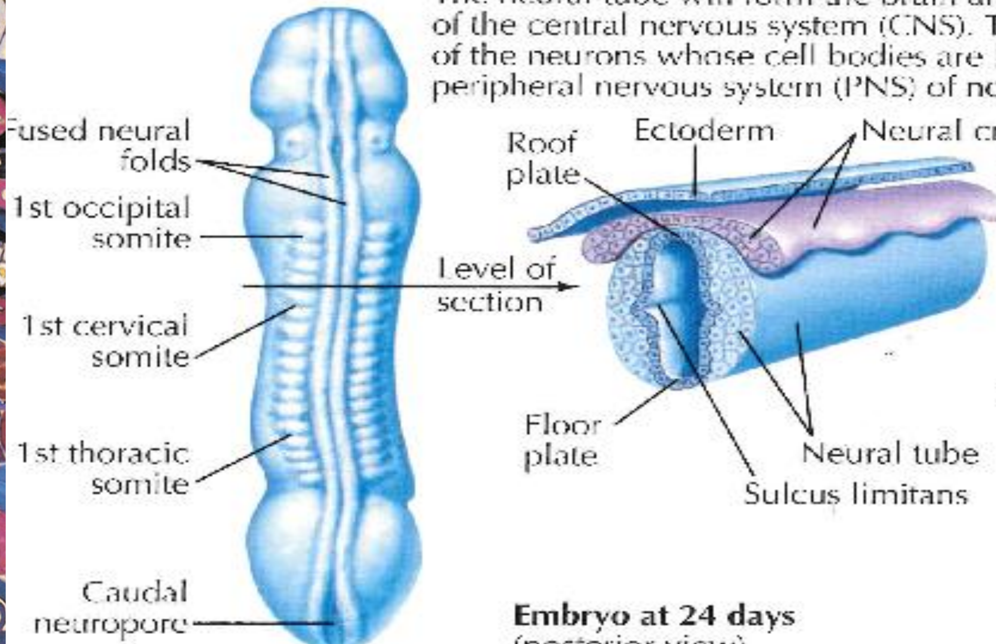


Embryo at 20 days
(posterior view)



Embryo at 21 days
(posterior view)

The neural tube will form the brain and spinal cord, the two components of the central nervous system (CNS). The neural crest will give rise to all of the neurons whose cell bodies are located outside the CNS in the peripheral nervous system (PNS) of nerves, ganglia, and plexuses.



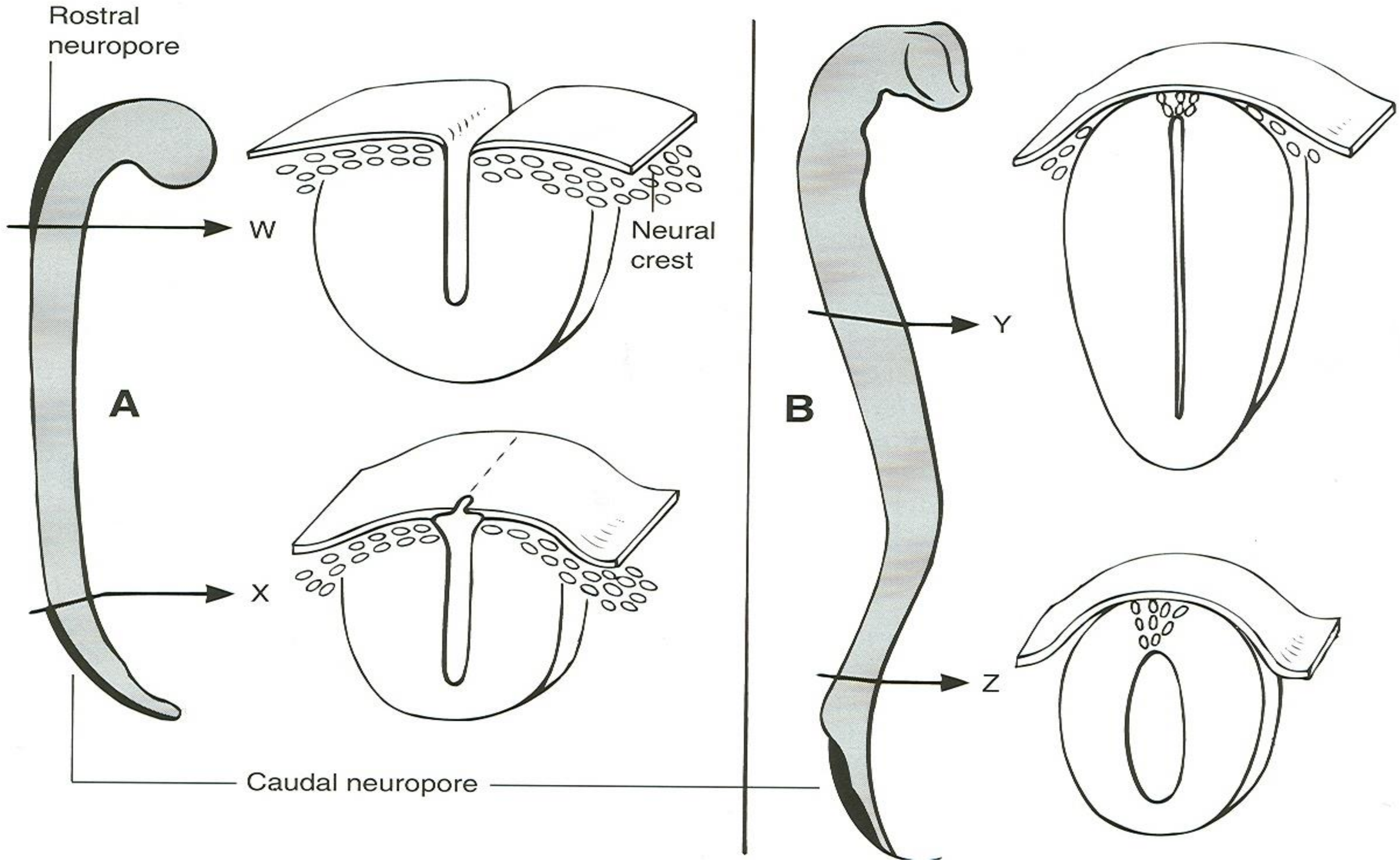
Embryo at 24 days
(posterior view)

Derivatives of the neural tube include

- Neurons of the CNS
- Supporting cells of the CNS
- Somatomotor neurons of the PNS
- Presynaptic autonomic neurons of the PNS

Derivatives of the neural crest include

- Sensory neurons in the PNS
- Postsynaptic autonomic neurons
- Schwann (neurolemma) cells
- Adrenal medulla cells
- Head mesenchyme
- Melanocytes in the skin
- Arachnoid and pia mater of meninges (dura mater from mesoderm)


Rostral neuropore
W
Neural crest
A
X
Caudal neuropore
B
Y
Z

DEVELOPMENT OF THE CNS

- Morphogenesis → Development of CNS Structure
- Histogenesis → Development of CNS Tissue

Figure 17.4 Drawing of a sagittal section through the brain at approximately 27 days of human development. Three brain vesicles represent the forebrain *(F)*, midbrain *(M)*, and hindbrain *(H)*.

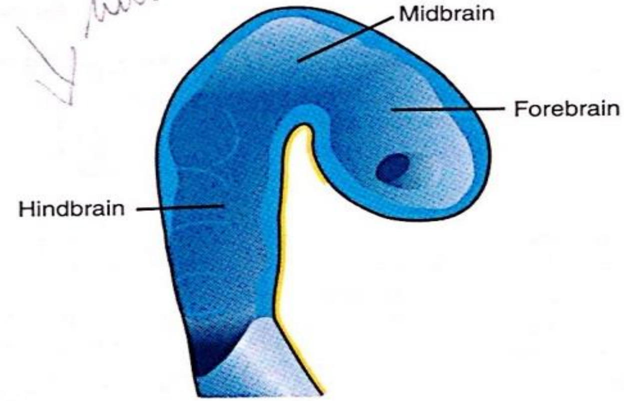
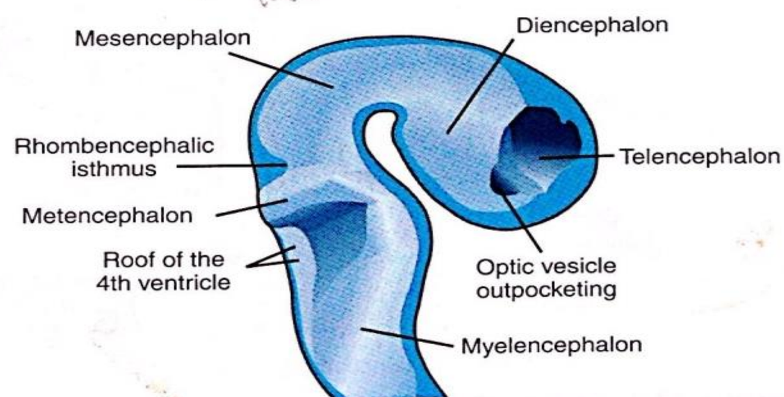


Figure 17.5 Drawing of a sagittal section through the brain approximately 32 days of human development. The three original brain vesicles have segregated into the telencephalon, diencephalon, mesencephalon, metencephalon, and myelencephalon.



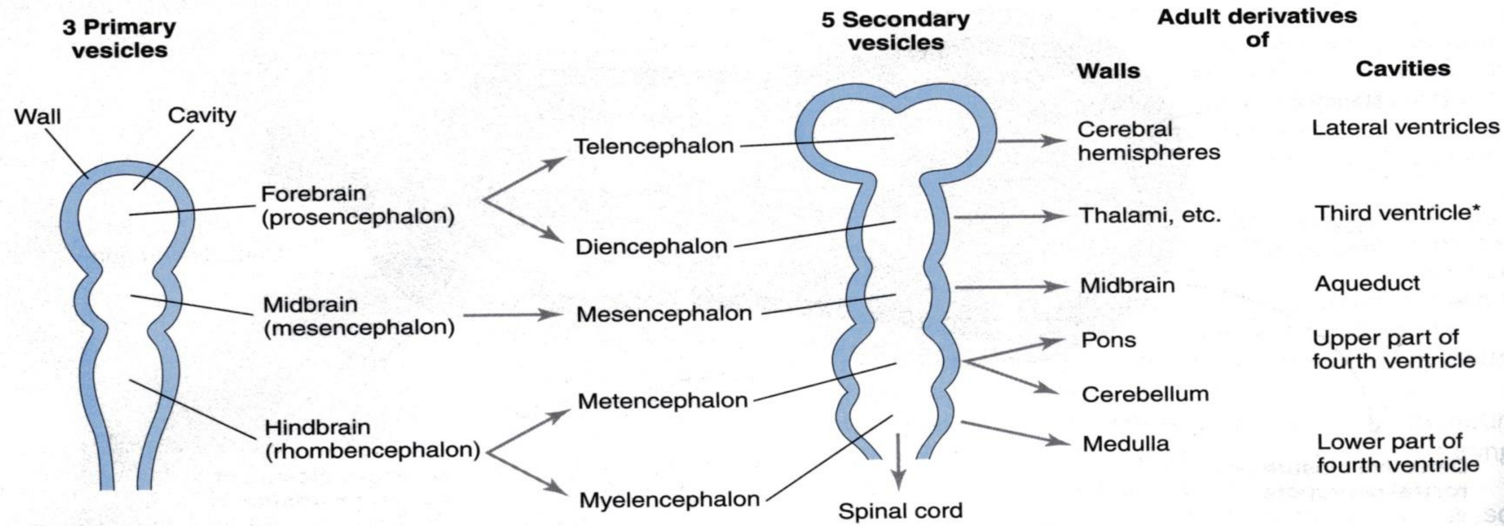
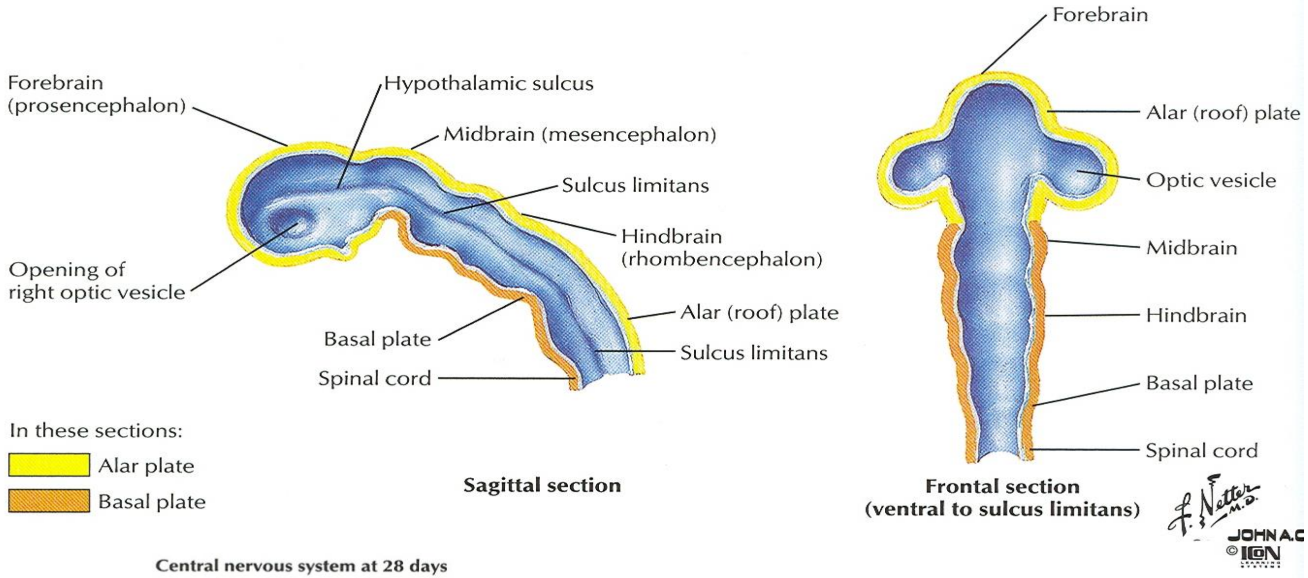
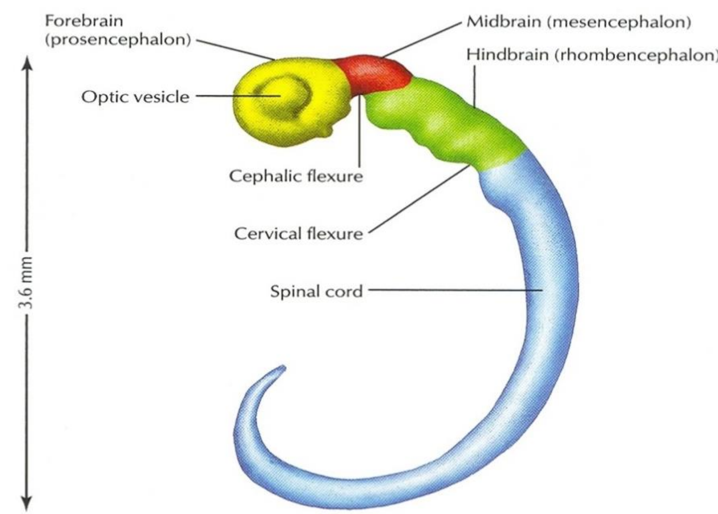
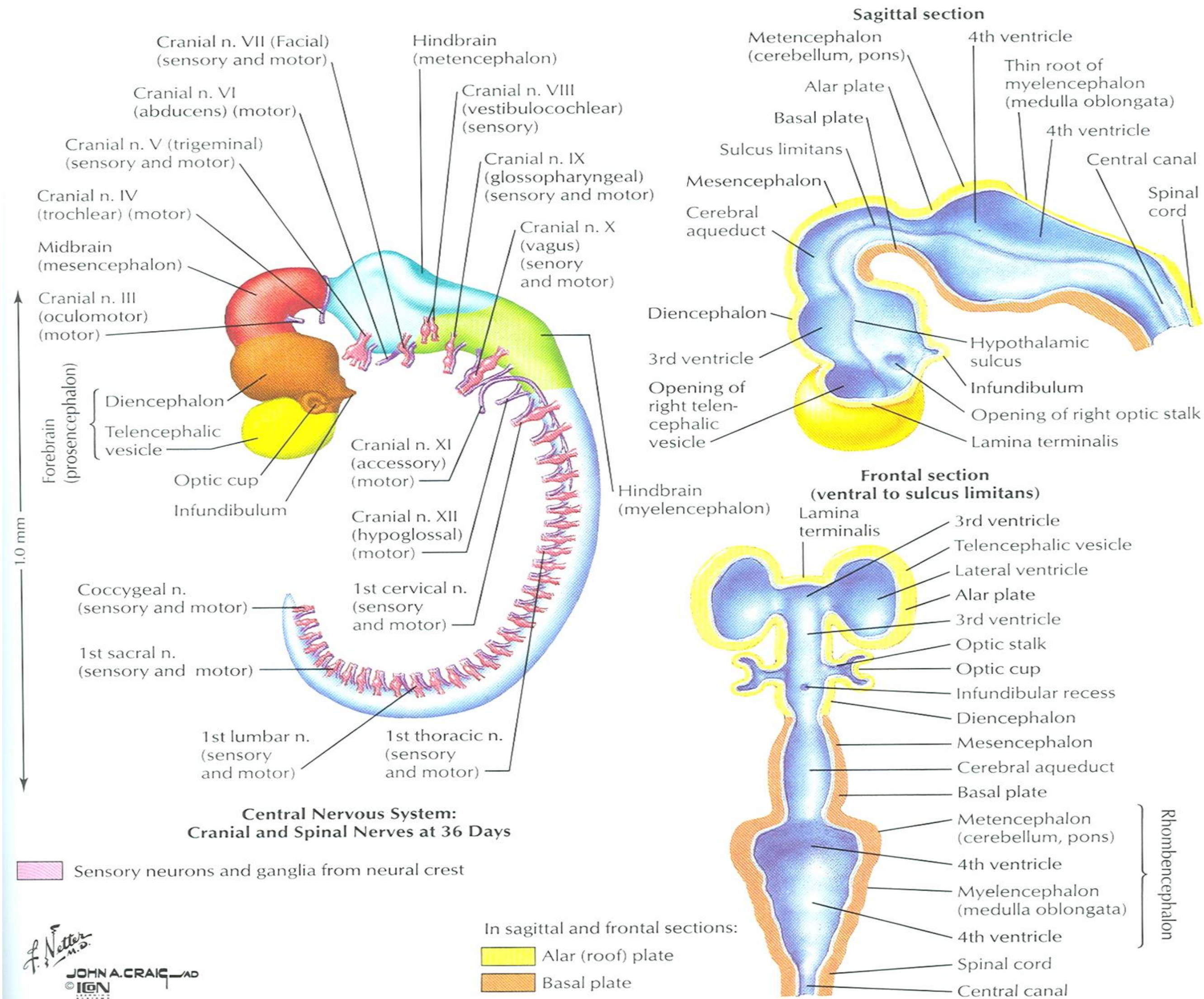


FIGURE 17-20. Diagrammatic sketches of the brain vesicles indicating the adult derivatives of their walls and cavities. *The rostral part of the third ventricle forms from the cavity of the telencephalon; most of this ventricle is derived from the cavity of the diencephalon.

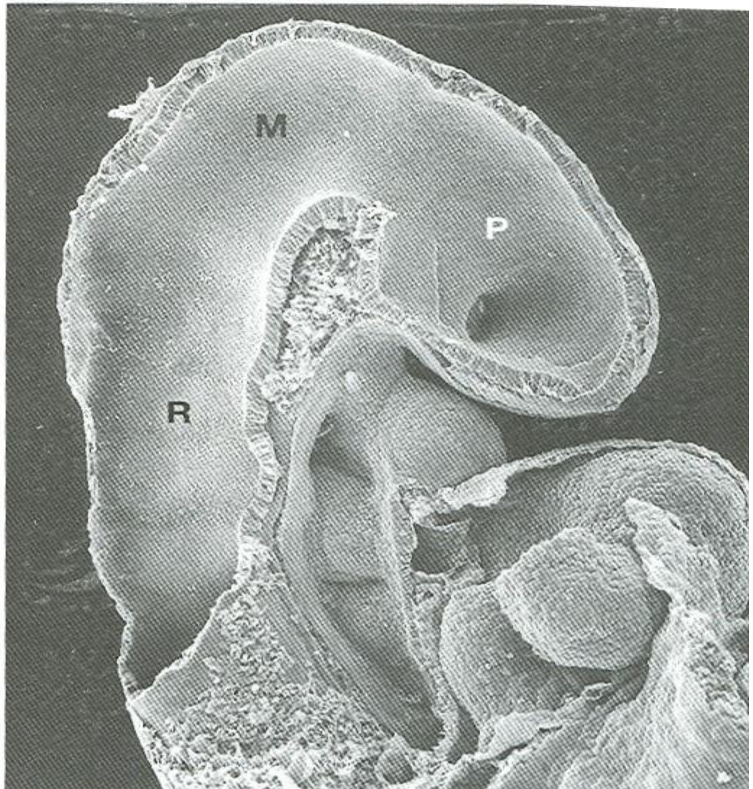


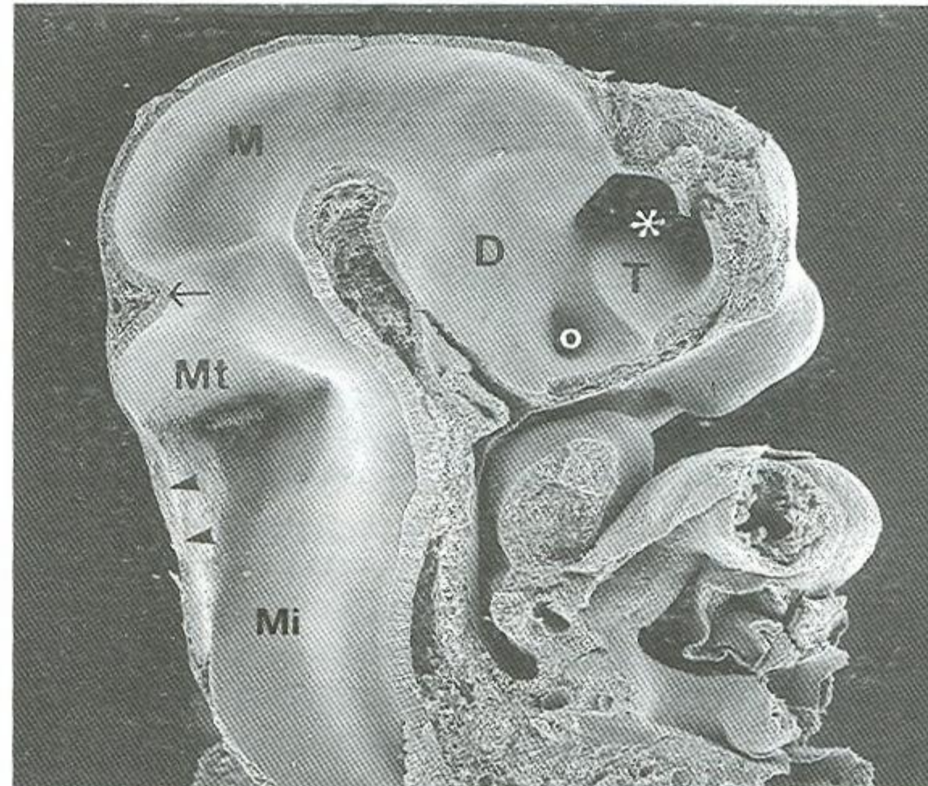
Central nervous system at 28 days

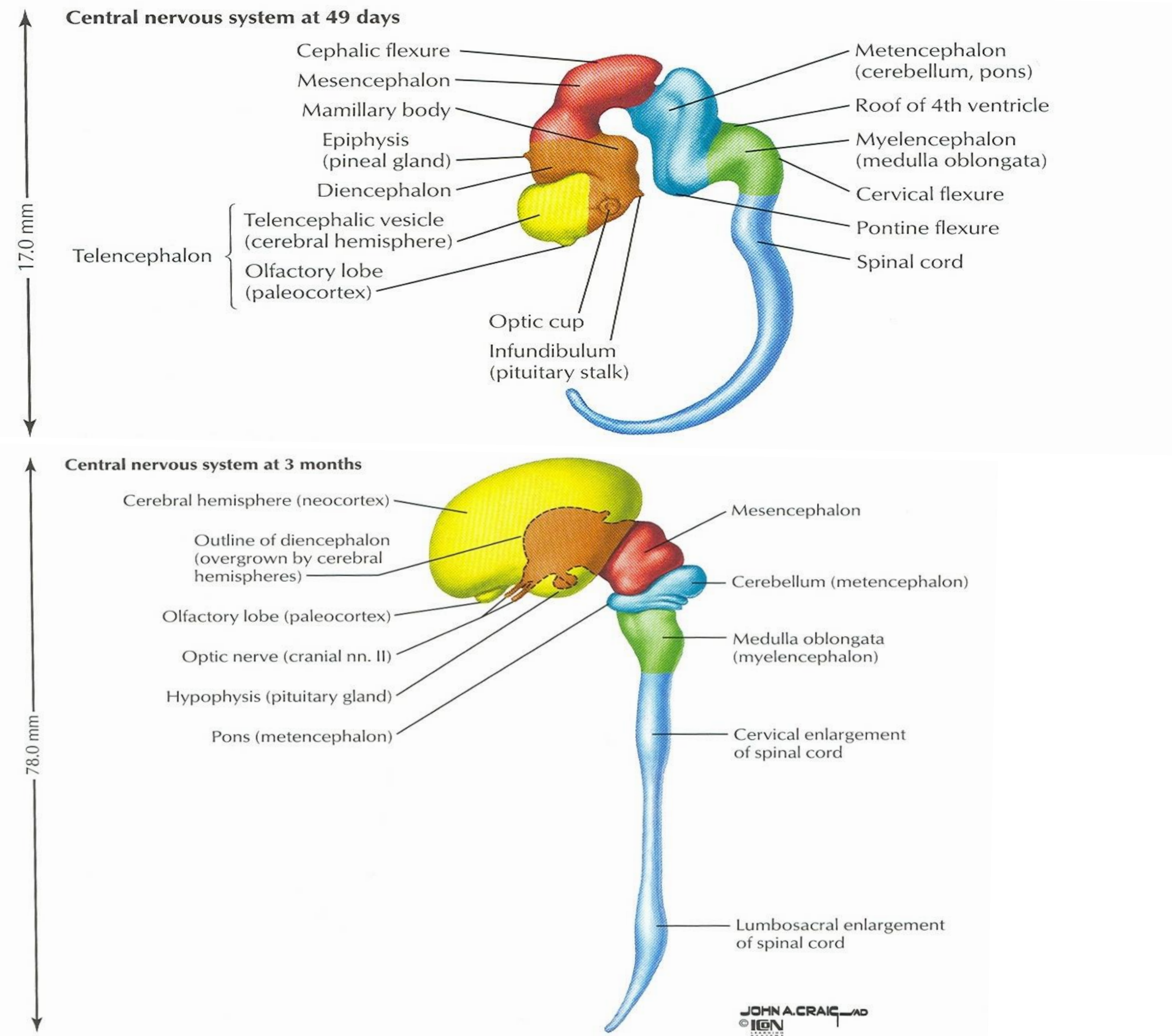




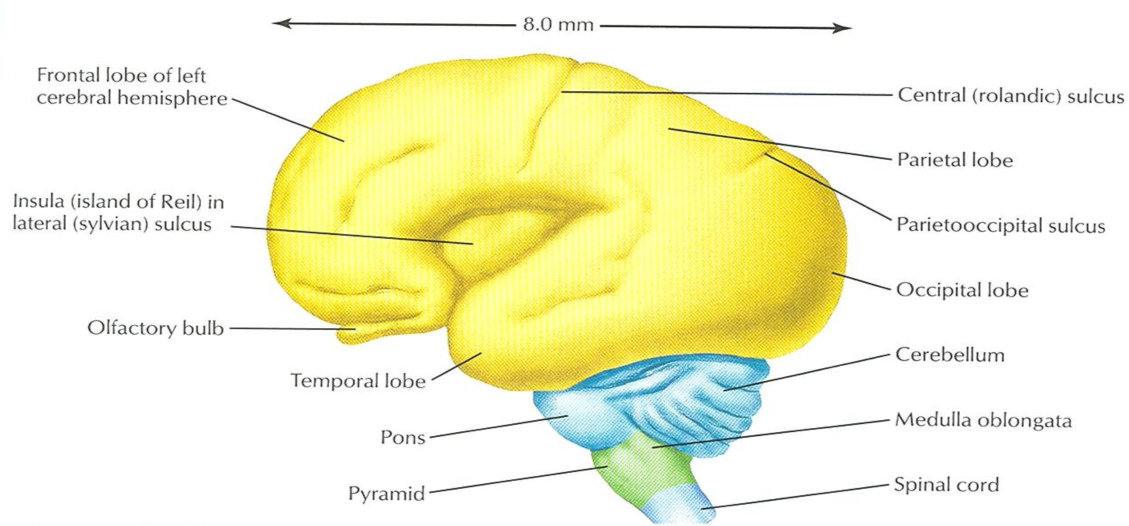
**Central Nervous System:
Cranial and Spinal Nerves at 36 Days**


M
P
R

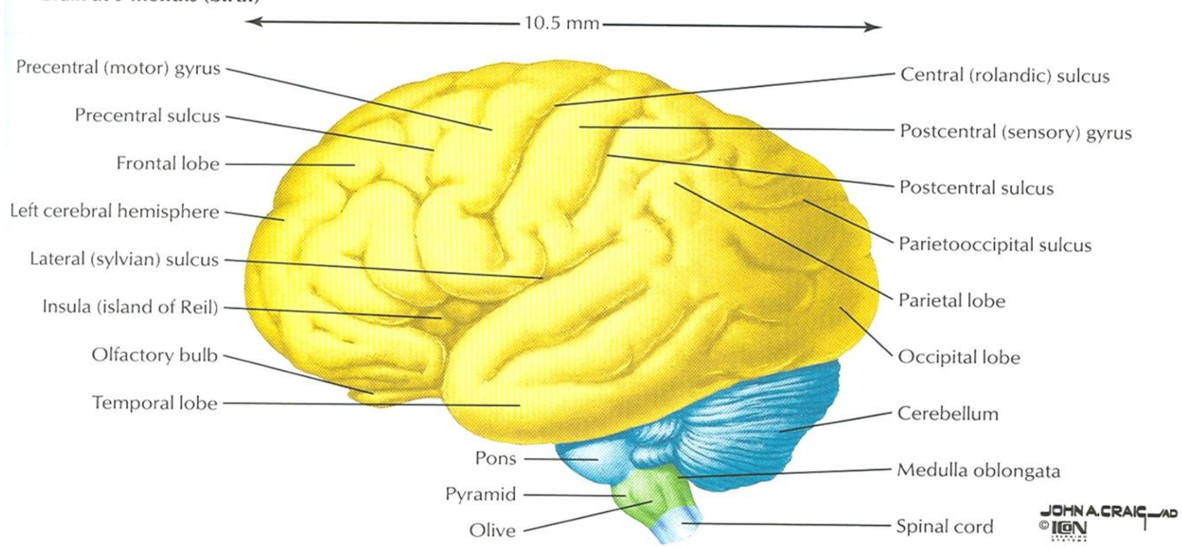

M
D
T
O
Mt
Mi

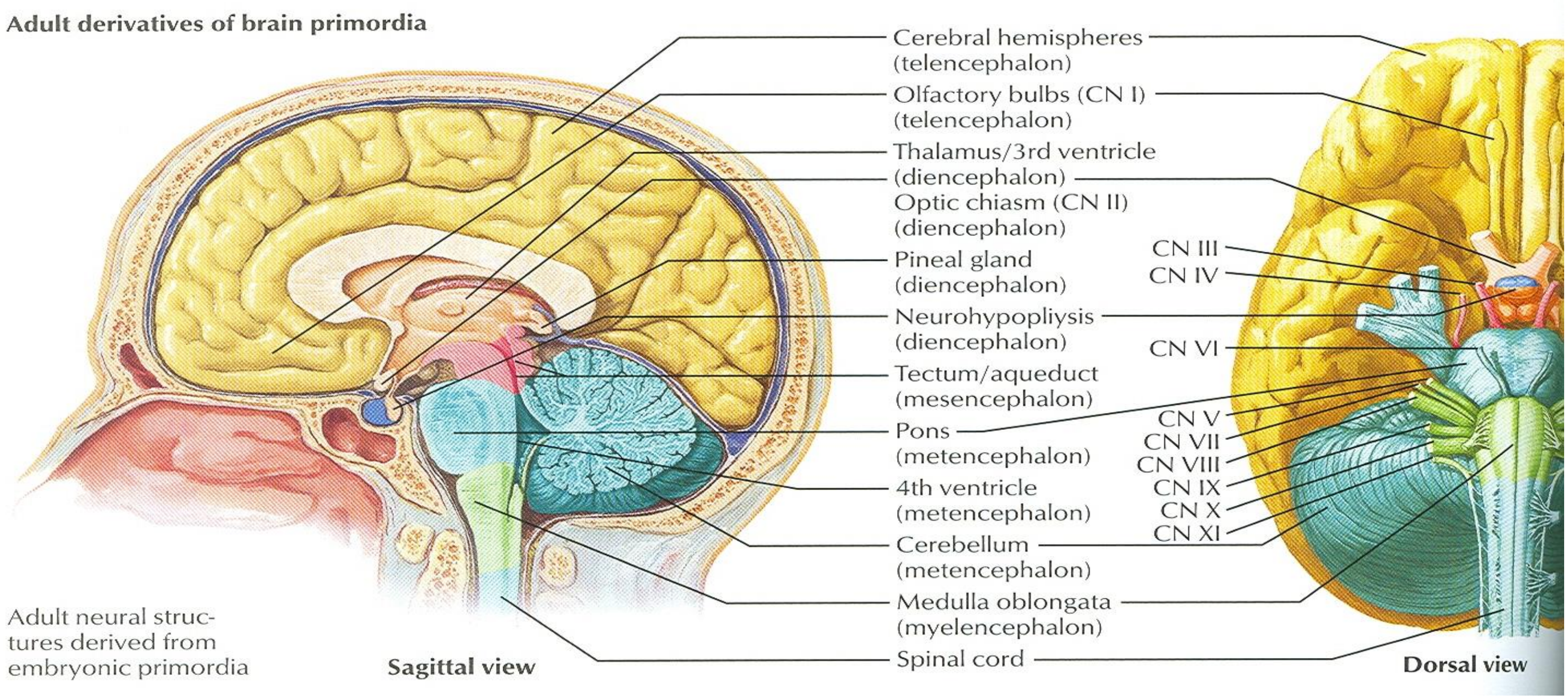

Central nervous system at 49 days
17.0 mm
Cephalic flexure
Mesencephalon
Mamillary body
Epiphysis
(pineal gland)
Diencephalon
Telencephalon
Telencephalic vesicle
(cerebral hemisphere)
Olfactory lobe
(paleocortex)
Optic cup
Infundibulum
(pituitary stalk)
Metencephalon
(cerebellum, pons)
Roof of 4th ventricle
Myelencephalon
(medulla oblongata)
Cervical flexure
Pontine flexure
Spinal cord
Central nervous system at 3 months
78.0 mm
Cerebral hemisphere (neocortex)
Outline of diencephalon
(overgrown by cerebral
hemispheres)
Olfactory lobe (paleocortex)
Optic nerve (cranial nn. II)
Hypophysis (pituitary gland)
Pons (metencephalon)
Mesencephalon
Cerebellum (metencephalon)
Medulla oblongata
(myelencephalon)
Cervical enlargement
of spinal cord
Lumbosacral enlargement
of spinal cord
JOHN A.CRAIG
©ICON

Brain at 6 months



Brain at 9 months (birth)




Adult derivatives of brain primordia
Cerebral hemispheres (telencephalon)
Olfactory bulbs (CN I) (telencephalon)
Thalamus/3rd ventricle (diencephalon)
Optic chiasm (CN II) (diencephalon)
Pineal gland (diencephalon)
Neurohypopliysis (diencephalon)
Tectum/aqueduct (mesencephalon)
Pons (metencephalon)
4th ventricle (metencephalon)
Cerebellum (metencephalon)
Medulla oblongata (myelencephalon)
Spinal cord
CN III
CN IV
CN VI
CN V
CN VII
CN VIII
CN IX
CN X
CN XI
Adult neural structures derived from embryonic primordia
Sagittal view
Dorsal view

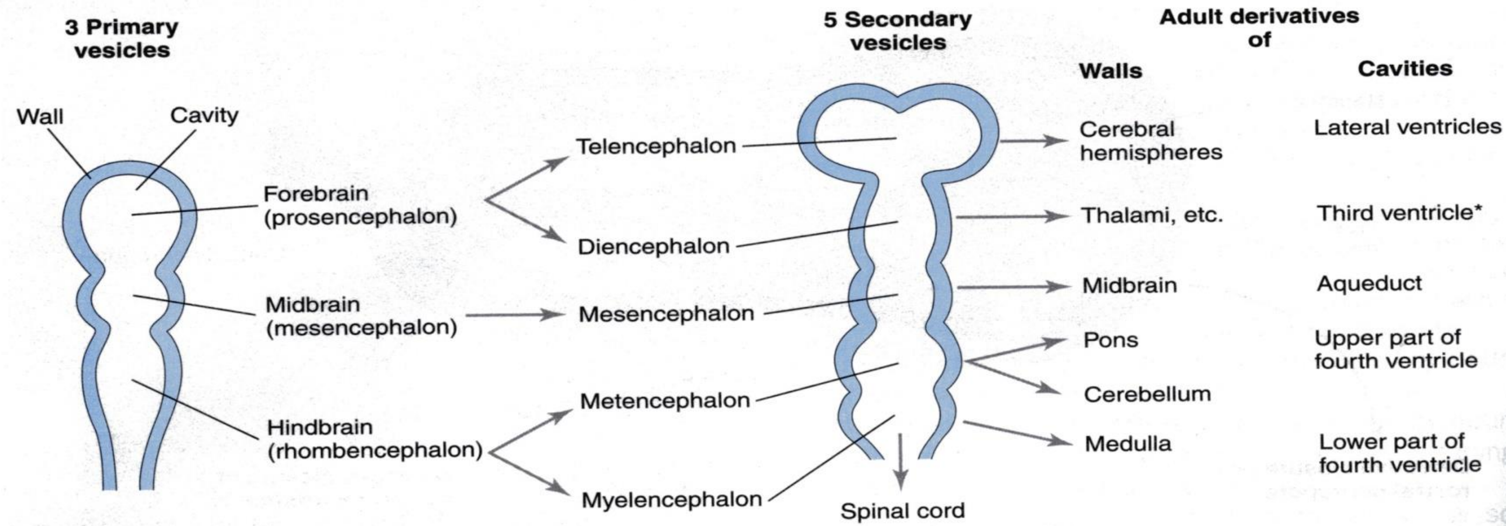
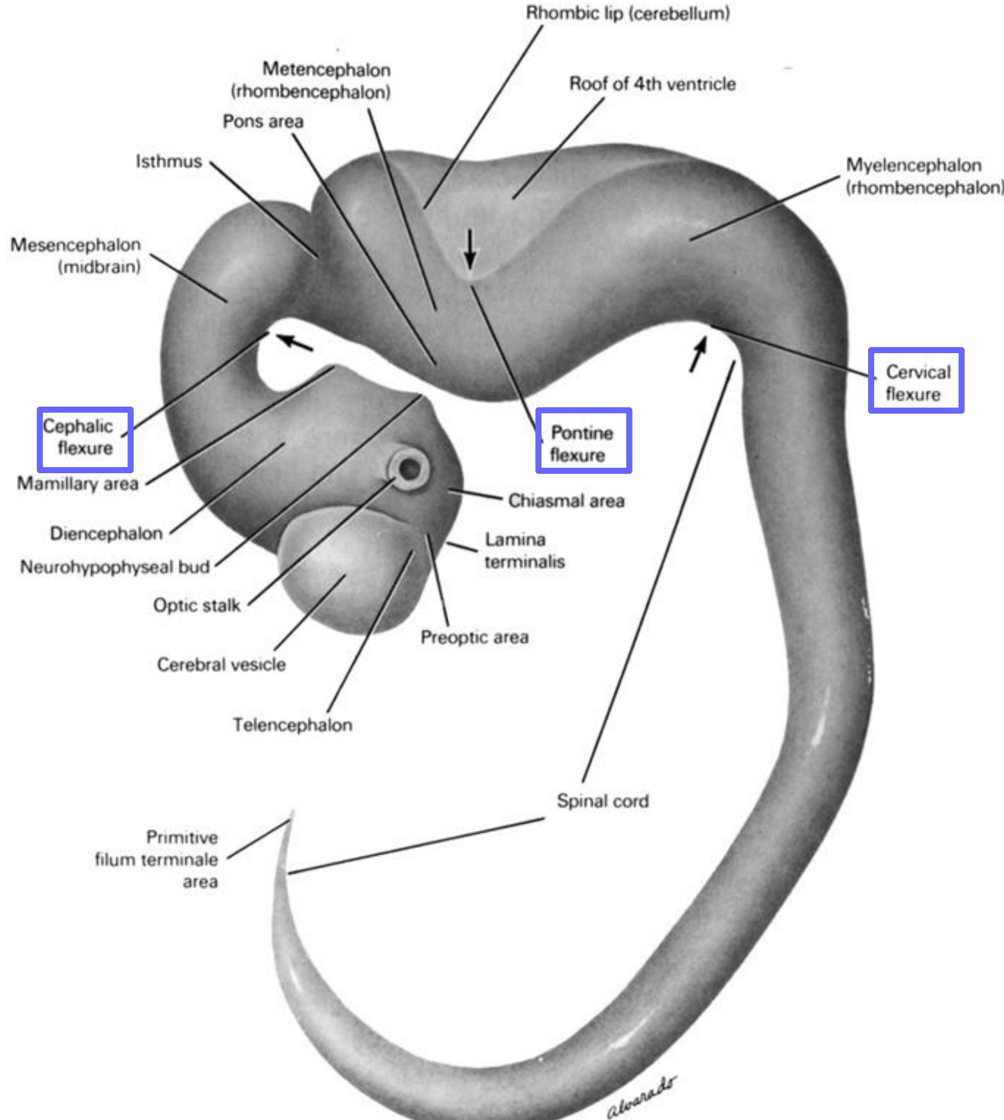


FIGURE 17-20. Diagrammatic sketches of the brain vesicles indicating the adult derivatives of their walls and cavities. *The rostral part of the third ventricle forms from the cavity of the telencephalon; most of this ventricle is derived from the cavity of the diencephalon.



Rhombic lip (cerebellum)
Metencephalon
(rhombencephalon)
Roof of 4th ventricle
Pons area
Isthmus
Myelencephalon
(rhombencephalon)
Mesencephalon
(midbrain)
Cervical
flexure
Cephalic
flexure
Pontine
flexure
Mamillary area
Chiasmal area
Diencephalon
Lamina
terminalis
Neurohypophyseal bud
Optic stalk
Preoptic area
Cerebral vesicle
Telencephalon
Spinal cord
Primitive
filum terminale
area

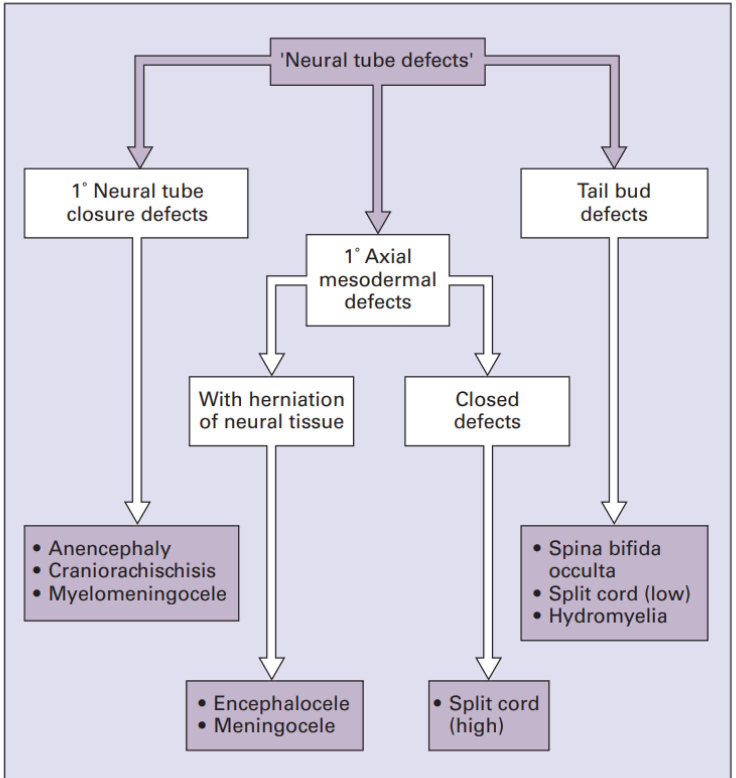
Developmental Alterations

Developmental Alterations

EARLY GESTATION (First 20 Weeks)

- Dysraphic malformations
- Disorders of forebrain induction
- Malformations of cortical development

Dysraphic Malformations

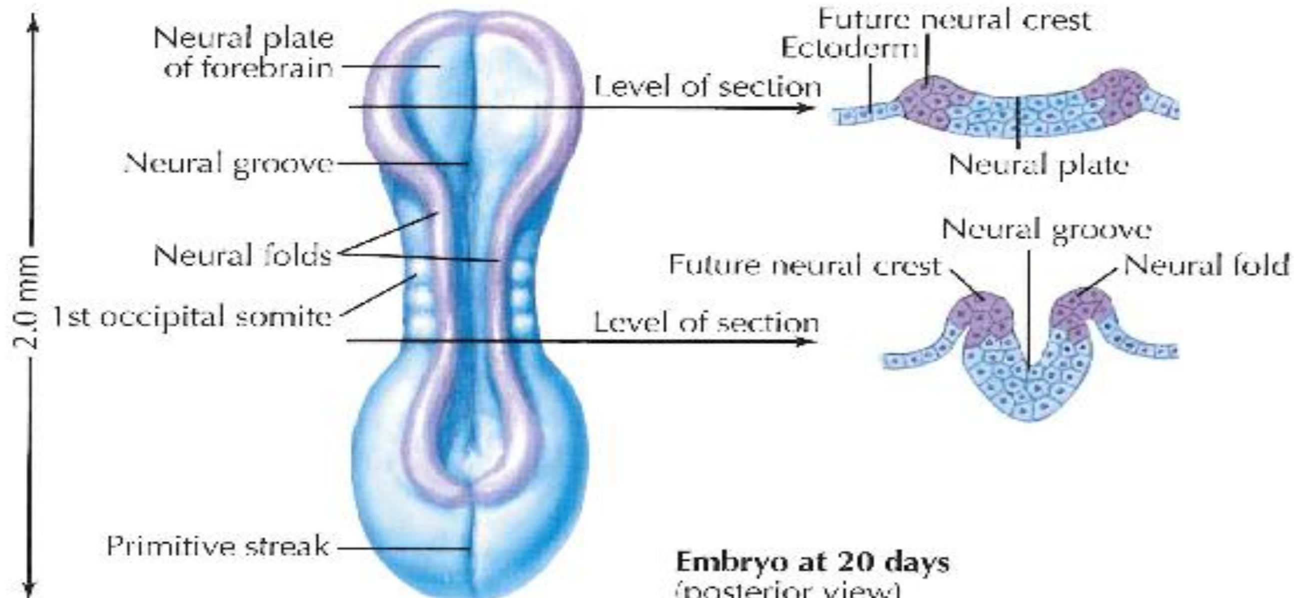


First order neural tube defects
- Anencephaly
- Craniorachischisis
- Myelomeningoecele

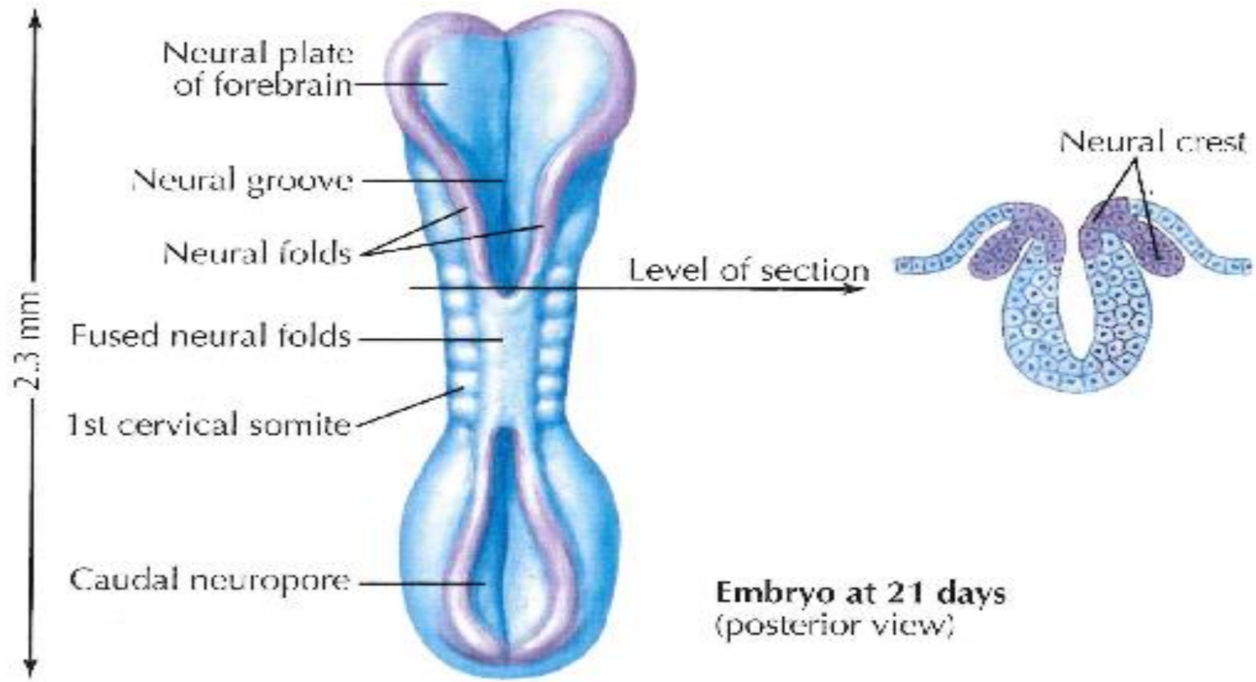
First order axial mesodermal defects
- With tissue herniation (Encephalocele; Meningocele)
- Closed defects

Tail bud defects
- Spina bidifa occulta
- Hydromyelia
- Low Split Cord

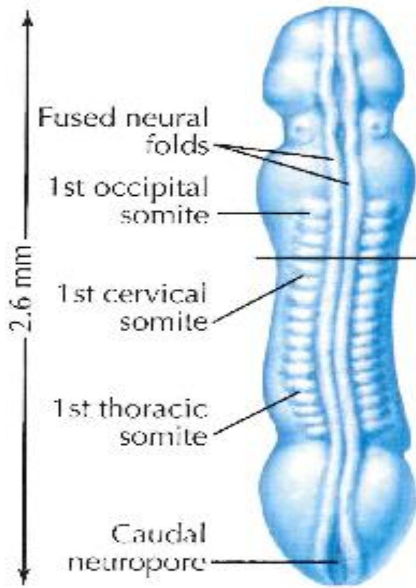
- Rostral neural tube
- Caudal neural tube
- Both



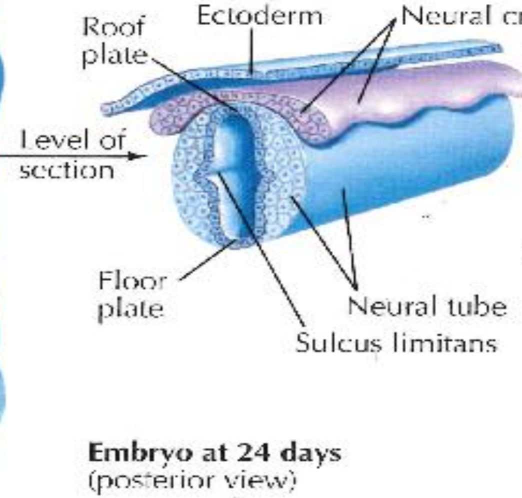
Embryo at 20 days
(posterior view)



Embryo at 21 days
(posterior view)



The neural tube will form the brain and spinal cord, the two components of the central nervous system (CNS). The neural crest will give rise to all of the neurons whose cell bodies are located outside the CNS in the peripheral nervous system (PNS) of nerves, ganglia, and plexuses.

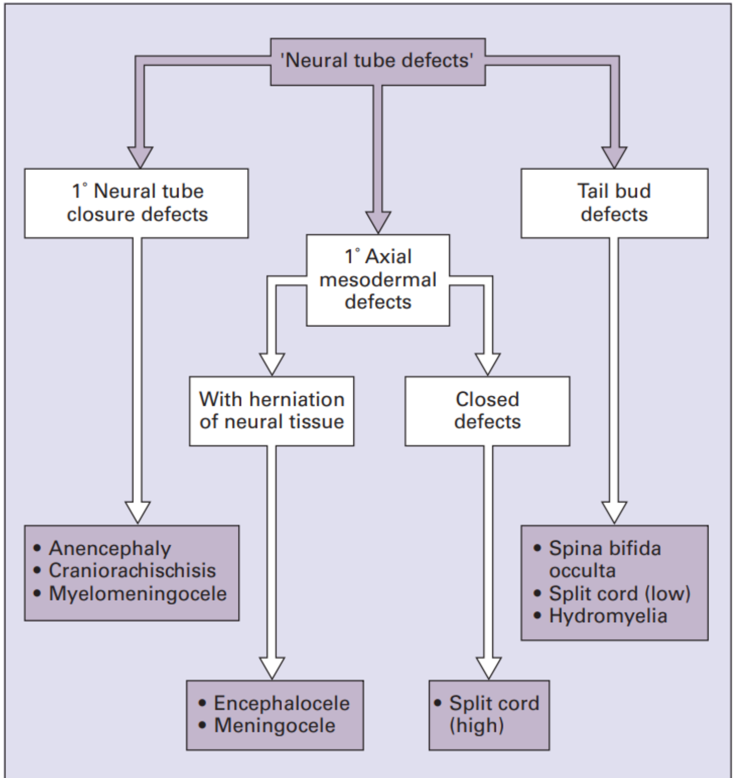


Embryo at 24 days
(posterior view)

Derivatives of the neural tube include
- Neurons of the CNS
- Supporting cells of the CNS
- Somatomotor neurons of the PNS
- Presynaptic autonomic neurons of the PNS

Derivatives of the neural crest include
- Sensory neurons in the PNS
- Postsynaptic autonomic neurons
- Schwann (neurolemma) cells
- Adrenal medulla cells
- Head mesenchyme
- Melanocytes in the skin
- Arachnoid and pia mater of meninges (dura mater from mesoderm)

Dysraphic Malformations



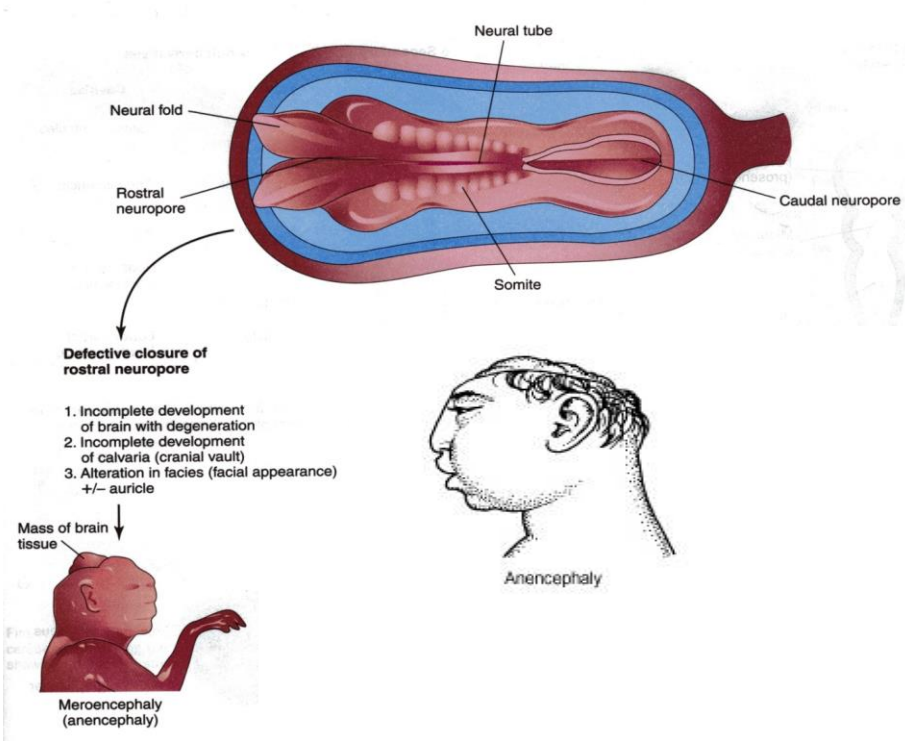
First order neural tube defects
- Anencephaly
- Craniorachischisis
- Myelomeningoecele

First order axial mesodermal defects
- With tissue herniation (Encephalocele; Meningocele)
- Closed defects

Tail bud defects
- Spina bidifa occulta
- Hydromyelia
- Low Split Cord

- Rostral neural tube
- Caudal neural tube
- Both

Anencephaly



ANENCEPHALY

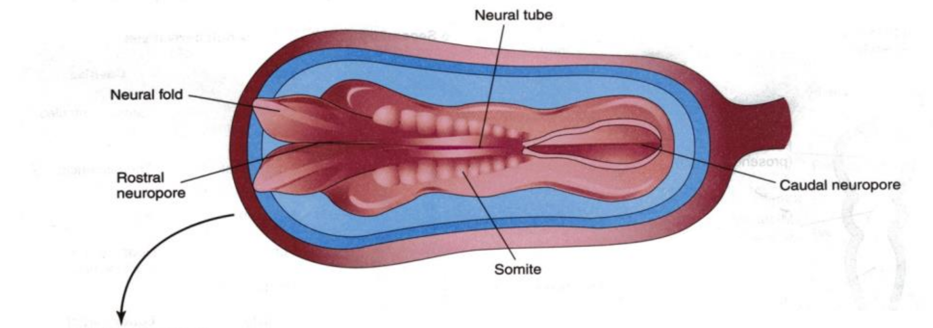
Replacement of most of the intracranial contents by the area cerebrovasculosa.

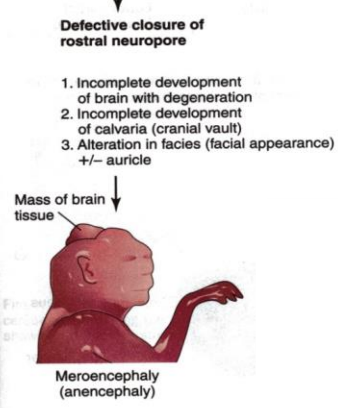
Skull defects include:

- ■ absent or hypoplastic skull vault
- ■ thickened and flat skull base
- ■ shallow orbits so that the eyes protrude

- ❑ Incompatible with life
- ❑ Detected with ultrasound
- ❑ raised α -fetoprotein levels in maternal serum

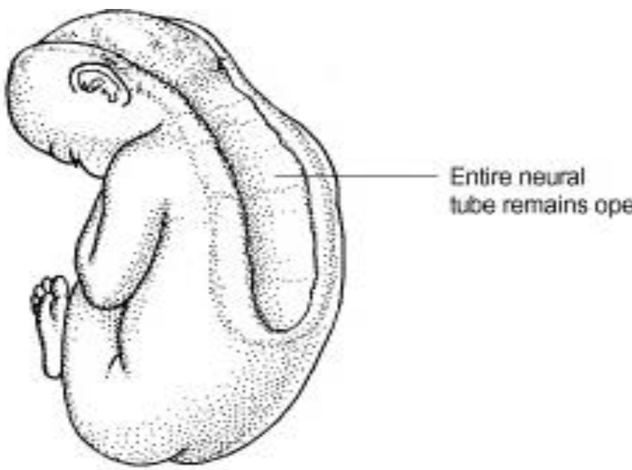
Craniorachischisis





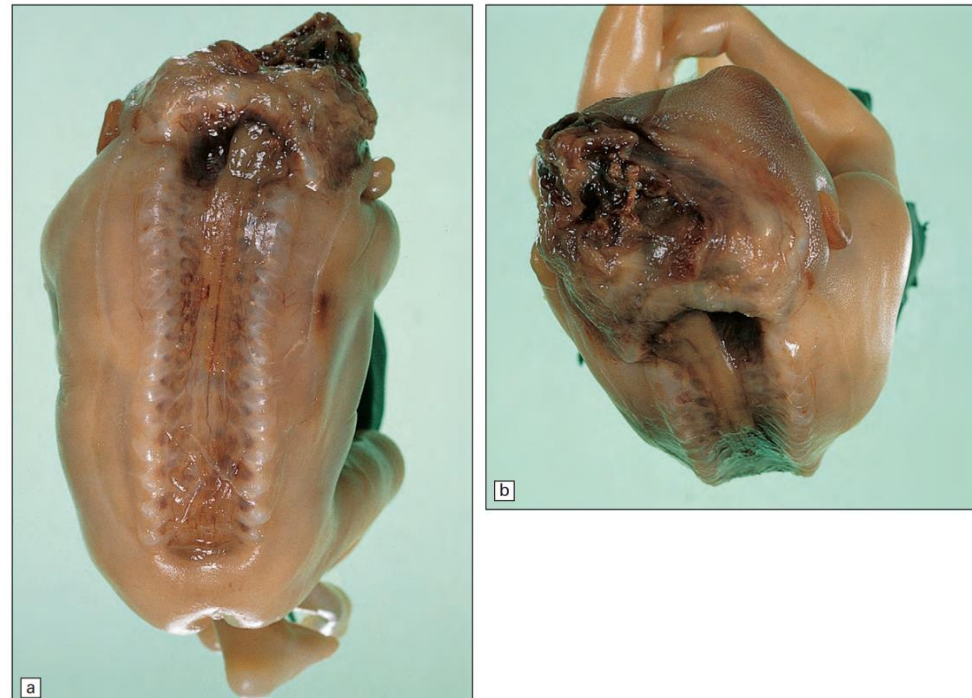
Anencephaly

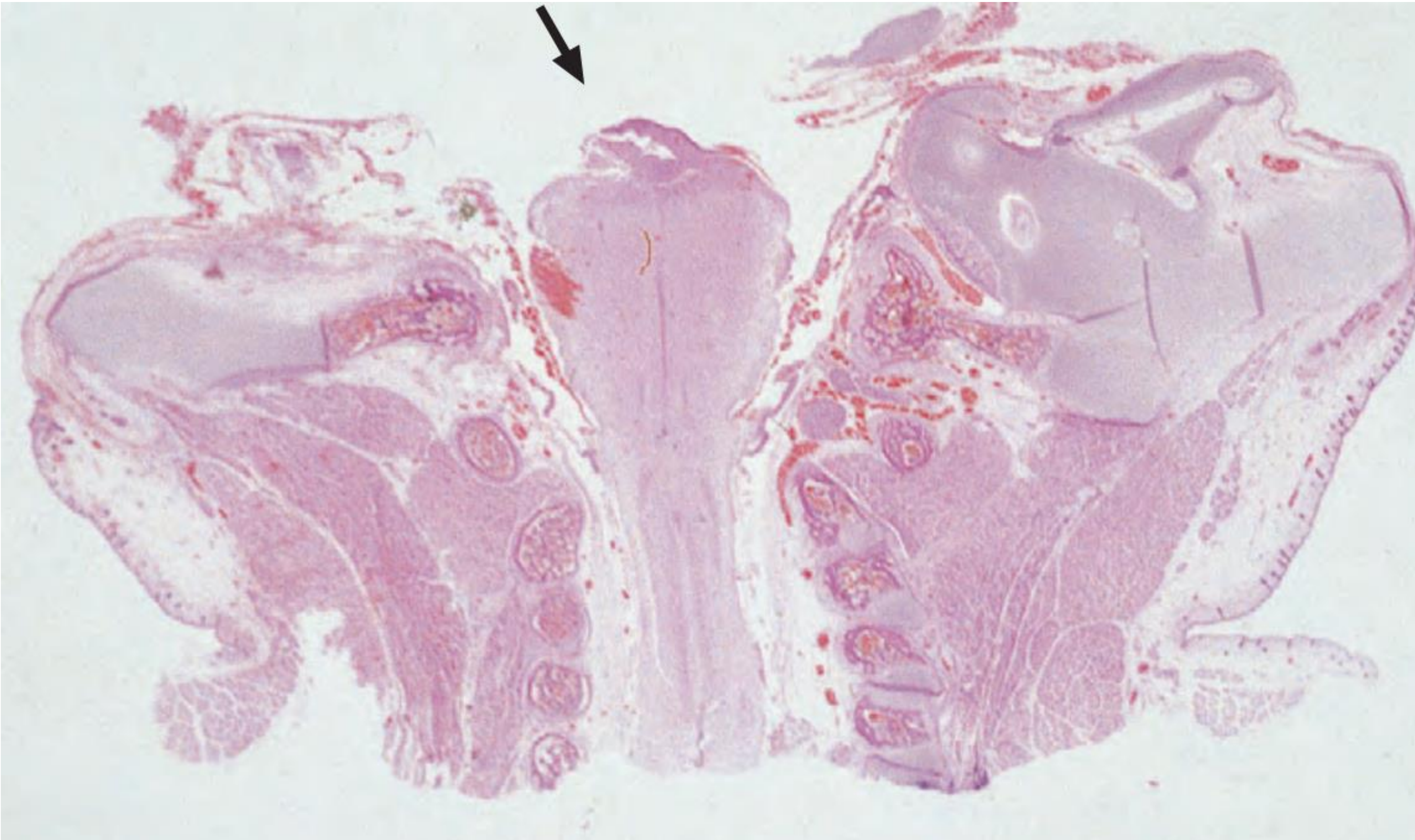
CRANIORACHISCHISIS - RACHISCHISIS



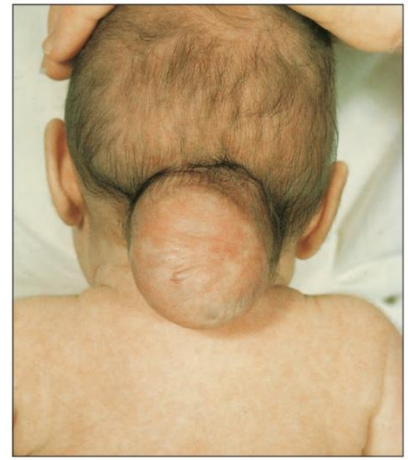
Craniorachischisis

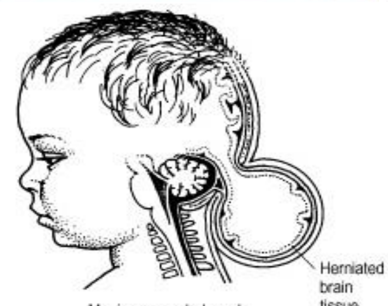
Ancencephaly ~ Craniorachischisis



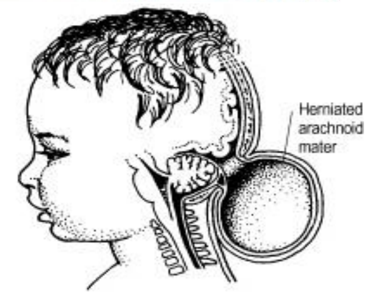


Encephalocele



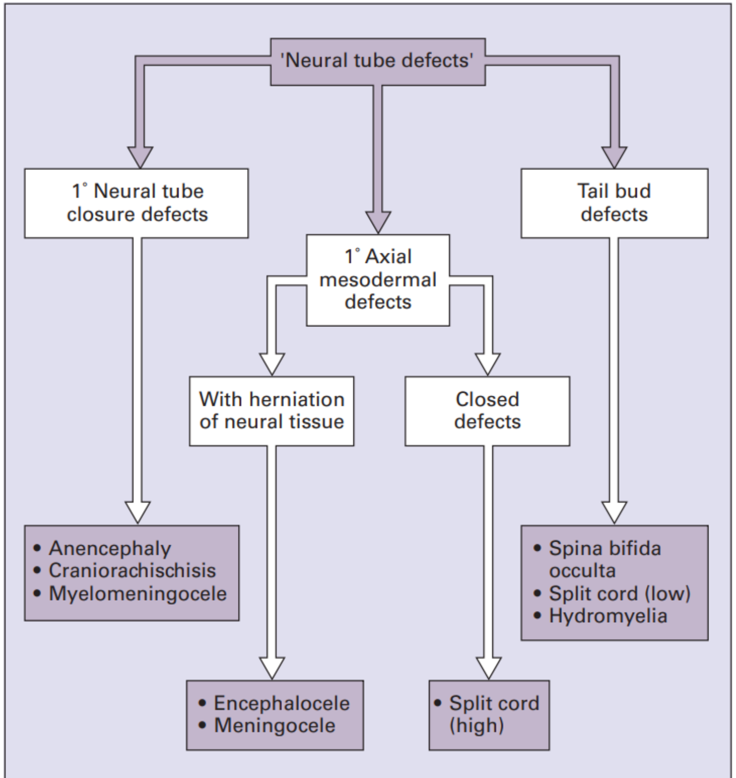


Meningoencephalocoele



Cranial meningocoele

Dysraphic Malformations



First order neural tube defects

- Anencephaly
- Craniorachischisis
- Myelomeningoecele

First order axial mesodermal defects

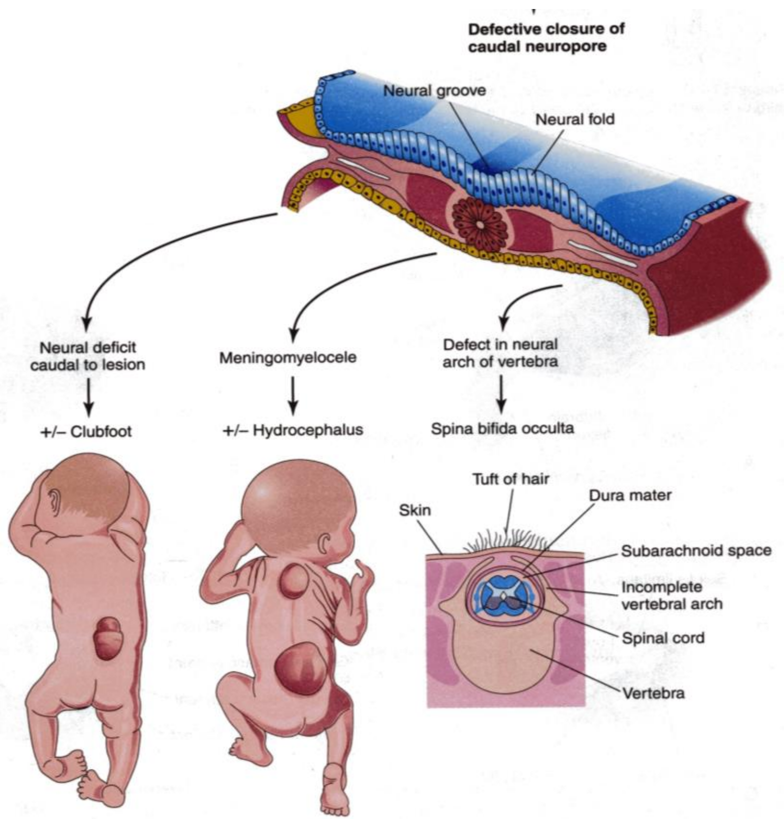
- With tissue herniation (Encephalocele; Meningocele)
- Closed defects

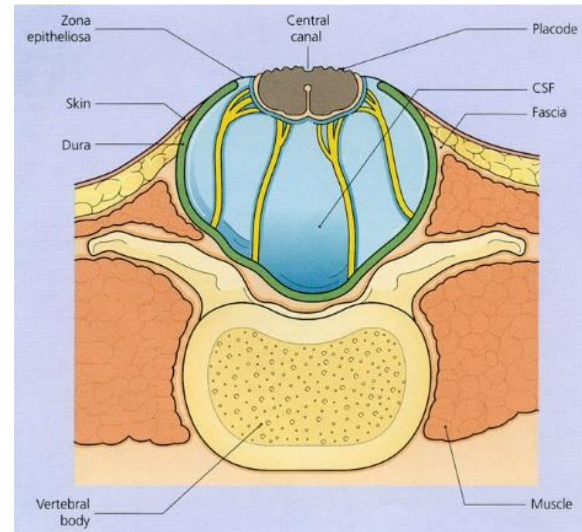
Tail bud defects

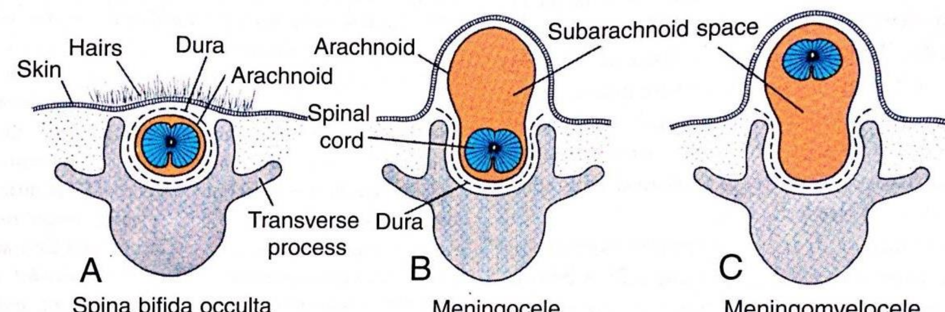
- Spina bidifa occulta
- Hydromyelia
- Low Split Cord

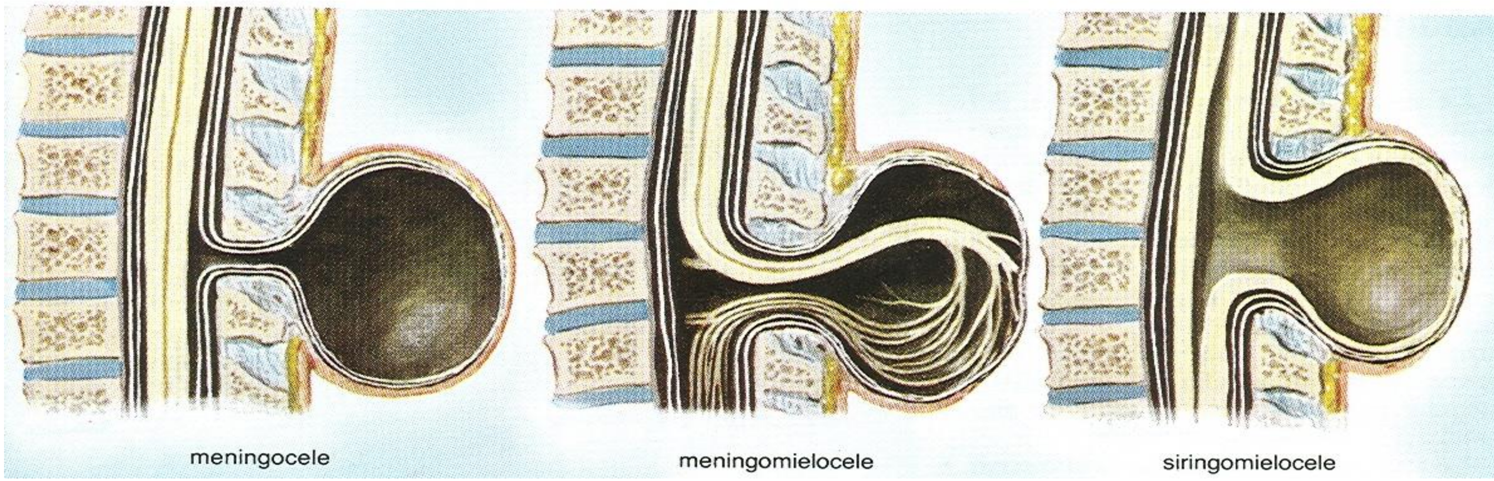
- Rostral neural tube
- Caudal neural tube
- Both

Caudal Neuropore Defects

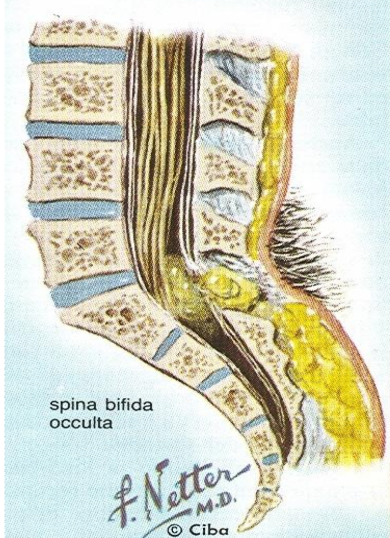




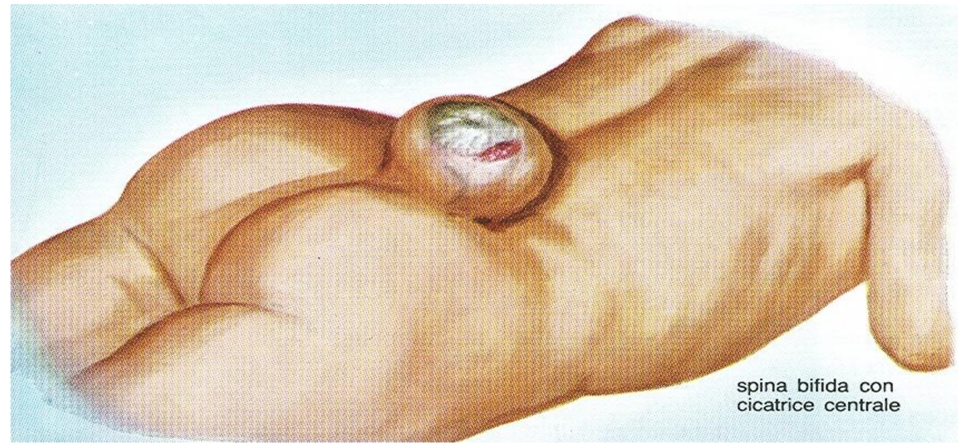



meningocele
meningomielocele
siringomielocele

mielocele



spina bifida
occulta



spina bifida con
cicatrice centrale

a
b
c
d

Developmental Alterations

EARLY GESTATION (First 20 Weeks)

- Dysraphic malformations
- Disorders of forebrain induction
- Malformations of cortical development

Chiari Malformations

Three anatomic types of cerebellar deformity associated with hydrocephalus.

Cerebellar herniation is not secondary to space occupying lesions.

- Chiari Type I
- Chiari Type II (Arnold-Chiari)
- Chiari Type III

Chiari Type I

Herniation of a peg of cerebellar tonsil (min. 5mm) through the foramen magnum in the absence of an intracranial space-occupying lesion or preceding hydrocephalus. No neural tube defect is present.

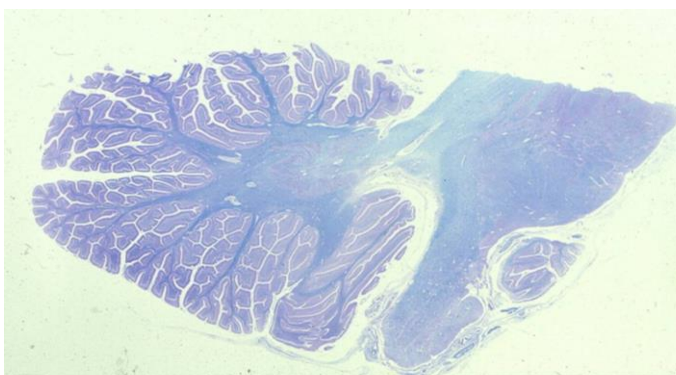
- May be asymptomatic.
- May present in infancy with neck pain, lower cranial nerve palsies, sleep apnea, or sudden unexpected death.
- May present in adulthood with cerebellar ataxia, late-onset **hydrocephalus**, long tract signs, or symptoms and signs of syringomyelia.
- Strongly associated with **syringomyelia** (Chiari type I occurs in 90% of patients with syringomyelia, including familial types).

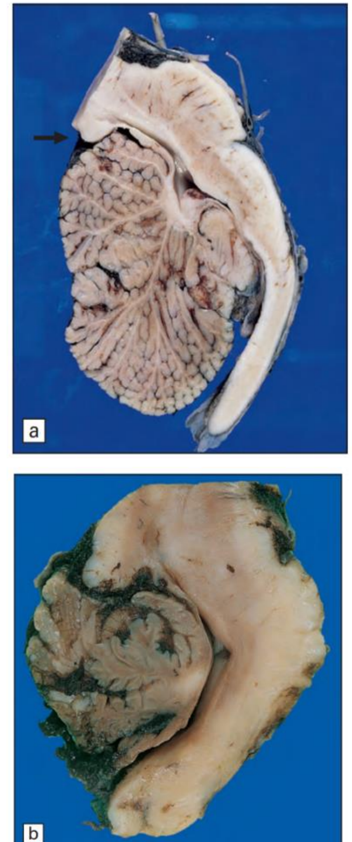
Chiari Type II – Arnold-Chiari

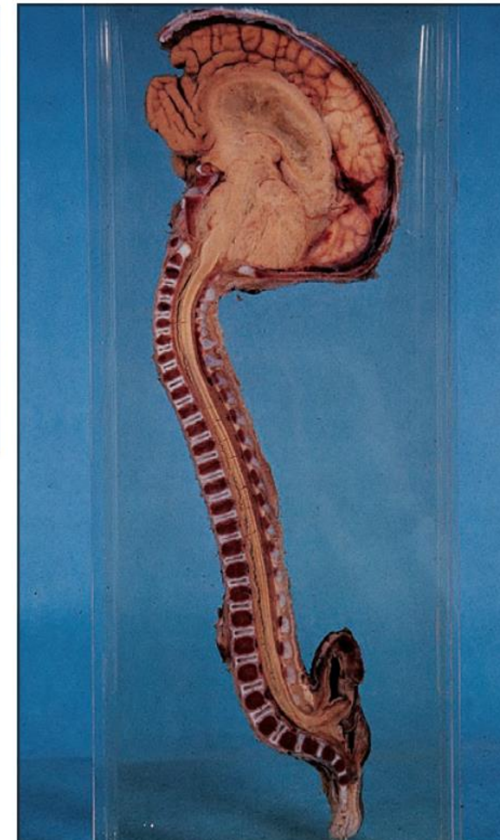
Association of anomalies characterized by a) a neural tube defect, usually a lumbosacral **myelomeningocele (MMC)** b) **abnormalities of the posterior fossa and craniocervical junction** and c) **hydrocephalus**.

It combines herniation of the cerebellar vermis with malformation and downward displacement of the brain stem.

- Almost invariably associated with a lumbosacral myelomeningocele.
- Associated with craniolacunia, a shallow posterior fossa and enlarged foramen magnum, a wide tentorial hiatus and low tentorial insertion, a low torcula, and a short fenestrated falx.
- Accompanied by hydrocephalus at birth in more than 80% of cases







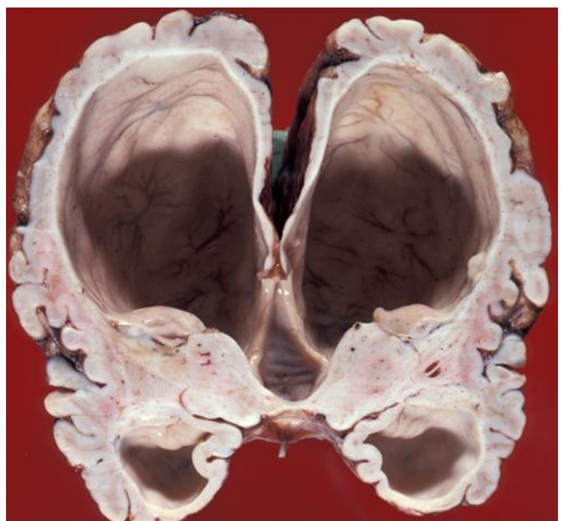
Chiari Type III

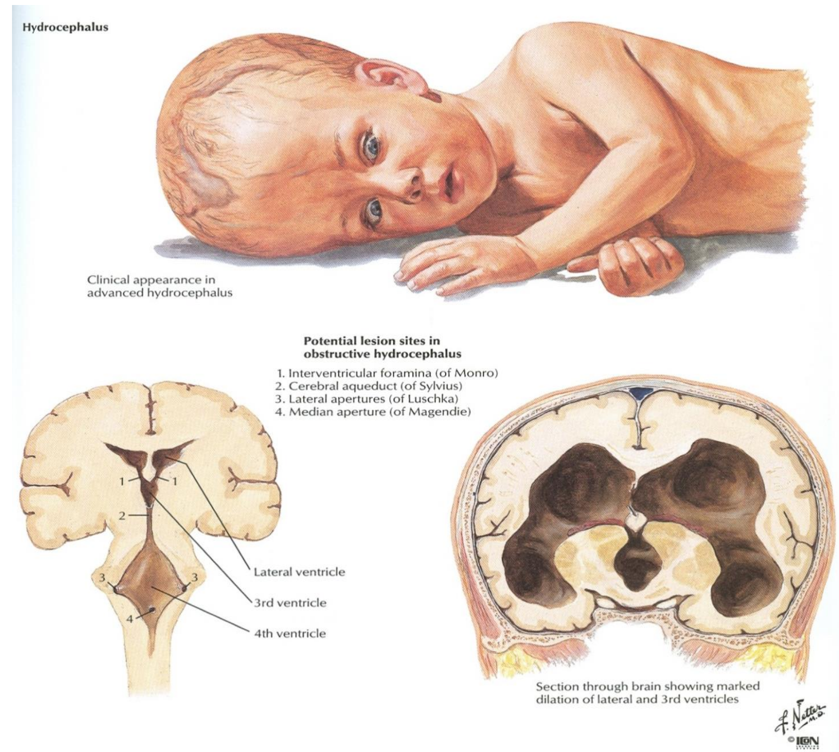
Rare **cerebello-encephalocele** through an occipitocervical or high cervical bony defect. Associated brainstem deformities and spina bifida are similar to type II.

Hydrocephalus

Dilatation of the cerebral ventricles; not a malformation, but **deformation due to increased pressure in the ventricles**. This dilatation has a variety of causes, the common denominator of which is obstruction of CSF flow.

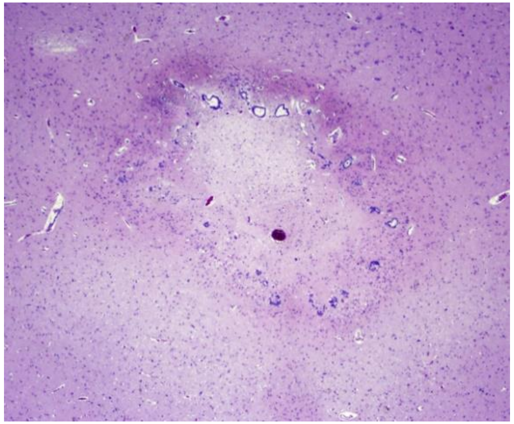
- Hypersecretion of CSF
- **Obstruction of CSF flow**
- Deficitary CSF filtration





OBSTRUCTIVE HYDROCEPHALUS

- Obstruction of the foramina of Monro (colloid cyst, tuberous sclerosis).
- Obstruction of the third ventricle (craniopharyngioma, pilocytic astrocytoma, germ cell tumors).
- Obstruction of the aqueduct (**aqueductal stenosis or atresia**, posterior fossa tumors,).
- Obstruction of the foramina of Luschka or impairment of flow from the fourth ventricle (**Chiari malformations**, Dandy-Walker malformation, meningitis, subarachnoid hemorrhage, posterior fossa tumors).
- Fibrosis of the subarachnoid space (meningitis, subarachnoid hemorrhage, meningeal dissemination of tumors), obliteration of the subarachnoid space by glioneuronal heterotopias in the Walker-Warburg syndrome.

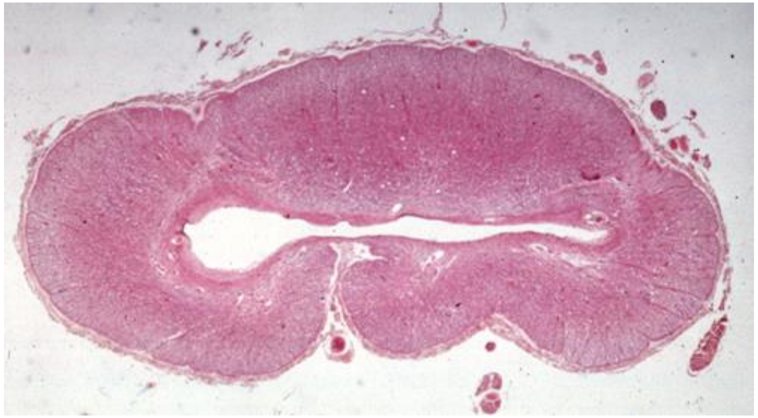


Aqueductal atresia is a disruption that occurs in utero or post-natally. It may be caused by clots from intraventricular bleeding, infection, and other pathologies that cause gliosis and obliterate the aqueduct

Syringomyelia

Tubular cavitation of the spinal cord affecting cervical and upper thoracic segments.

- The cavity is in the central gray matter of the spinal cord.
- Initially it is separate from the central canal, but later, as it enlarges, it may communicate with it.
- **Syringobulbia** is an extension of the cavity from the spinal cord into the medulla.
- The syrinx is lined by glial tissue.
- It contains CSF-like fluid which accumulates progressively under **pressure**, causing **atrophy of gray and white matter of the spinal cord.**



Developmental Alterations

EARLY GESTATION (First 20 Weeks)

- Dysraphic malformations
- Disorders of forebrain induction
- Malformations of cortical development

Disorders of Forebrain Induction

Failures in outgrowth and separation of the **forebrain vesicles** and in the development of the commissures. The hemispheric anomalies are associated with **craniofacial anomalies**.

- Holoprosencephaly
- Agenesis of the corpus callosum

Holoprosencephaly

• Developmental defect of the forebrain (prosencephalon)
• Incomplete separation of the cerebral hemispheres into distinct right and left halves
• Mostly sporadic (occasional familial cases)
• Prevalence: – 1:16,000 live births – 1:250 conceptuses
• Three types:
– **Alobar** (complete): no separation of the telencephalon, single ventricle in a small brain
– **Semilobar** (incomplete): variable degrees of separation of the posterior cerebrum
– **Lobar**: a small focal fusion of the midline with T-shaped or Y-shaped lateral and third ventricles

Holoprosencephaly

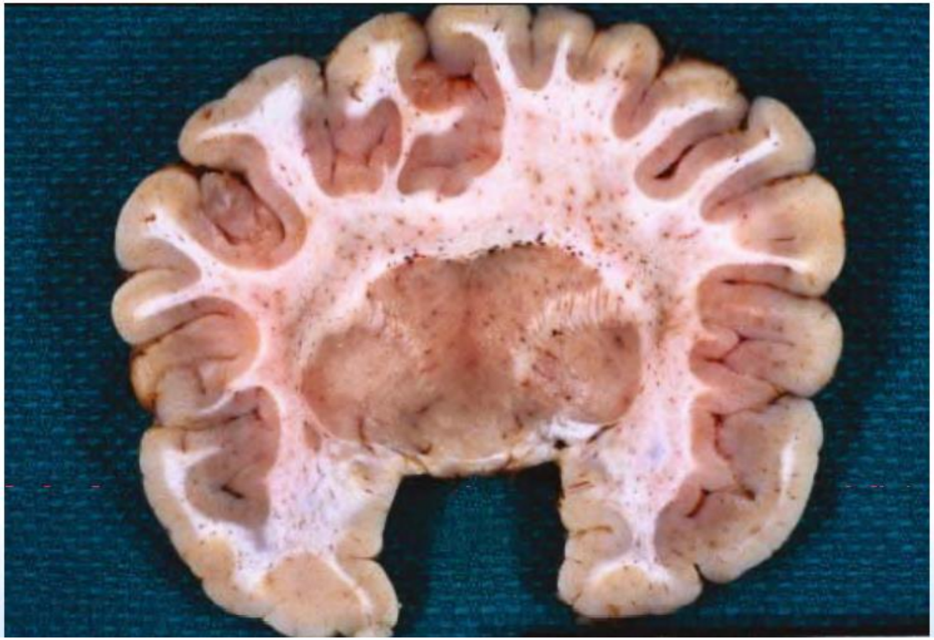
ETIOLOGY

- Material diabetes mellitus
- Infections: toxoplasmosis, syphilis, rubella
- Teratogens: ethanol, retinoic acid, cholesterol synthesis inhibitors
- Genetic factors: – Cytogenetic abnormalities seen in 50% of cases; **Trisomy 13** most frequent

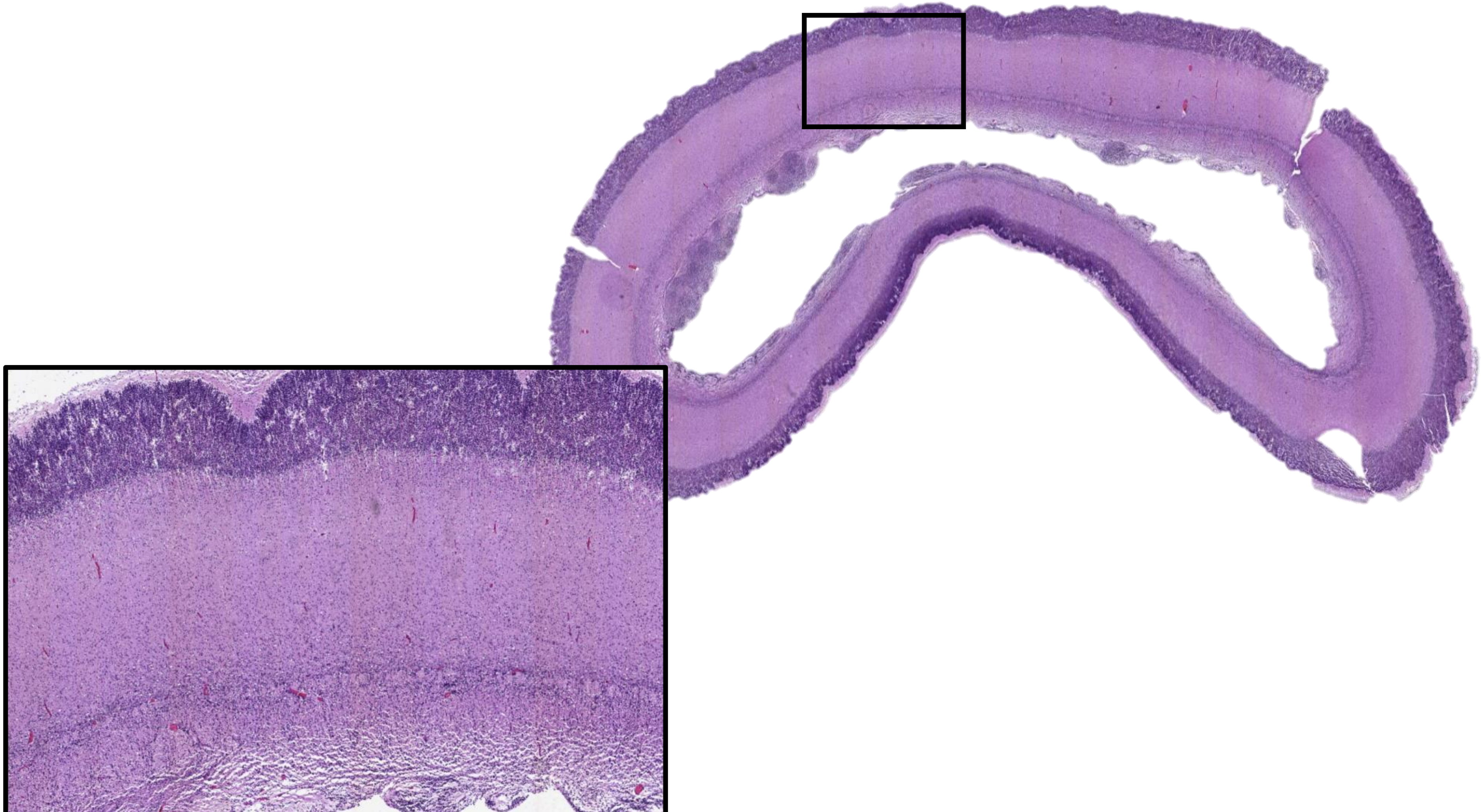
Disease or locus name	CNS malformations involved	Gene	Function of gene product	Chromosome location
Holoprosencephaly (HPE1)	Alobar holoprosencephaly	ND	ND	21q22.3
Holoprosencephaly (HPE2)	Alobar or semi-lobar holoprosencephaly	*SIX3*[1064]	Homologue of sine oculis gene of *Drosophila:* homeobox-containing transcription factor	2p21
Holoprosencephaly (HPE3)	Holoprosencephaly	*SHH* (Sonic hedgehog)[875]	Secreted signalling molecule; neural inducer	7q36
Holoprosencephaly (HPE4)	Holoprosencephaly	*TGIF*[405]	Homeodomain protein functioning as repressor of TGF-β	18p11.3
Holoprosencephaly (HPE5; 13q32 deletion syndrome)	Holoprosencephaly, exencephaly	*ZIC2*[124]	Transcription factor encoded by homologue of odd paired gene of *Drosophila*	13q32
Holoprosencephaly (HPE6)	Holoprosencephaly	ND	ND	2q37.1
Holoprosencephaly (HPE7)	Holoprosencephaly	*PTCH1*[703]	Patched: membrane receptor for Sonic hedgehog protein	9q22.3
Holoprosencephaly (HPE8)	Holoprosencephaly	ND	ND	14q13

Alobar Holoprosencephaly

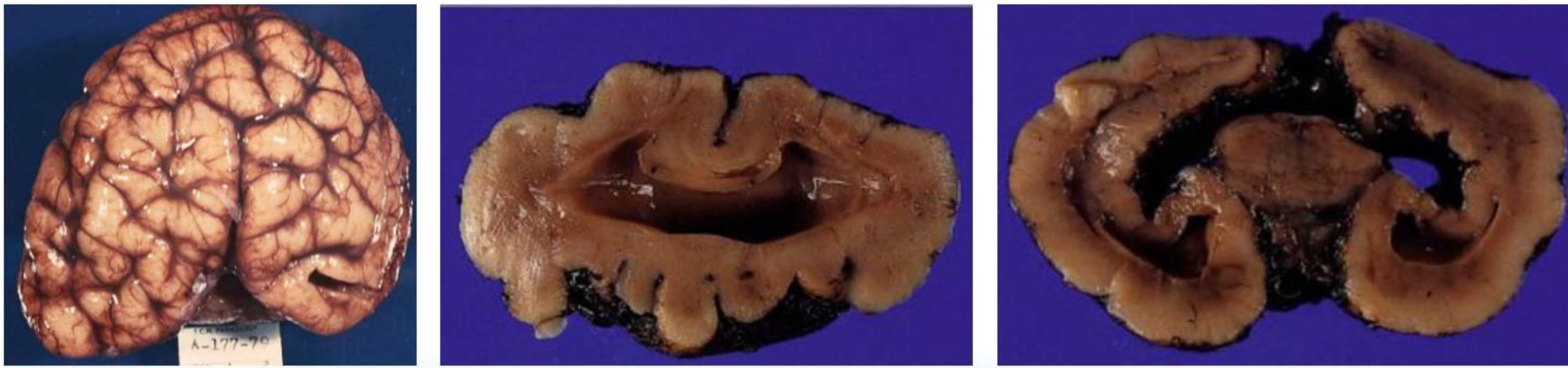
Alobar Holoprosencephaly



■ Neocortical hypoplasia with a relative lack of prefrontal association cortex and excessive allocortex.
■ Cortical disorganization or disturbed neuronal migration such as polymicrogyria, superficial cortical segmentation, prominent perpendicular cords of cells, and more deeply placed aneuronal neuropilic glomerular structures.



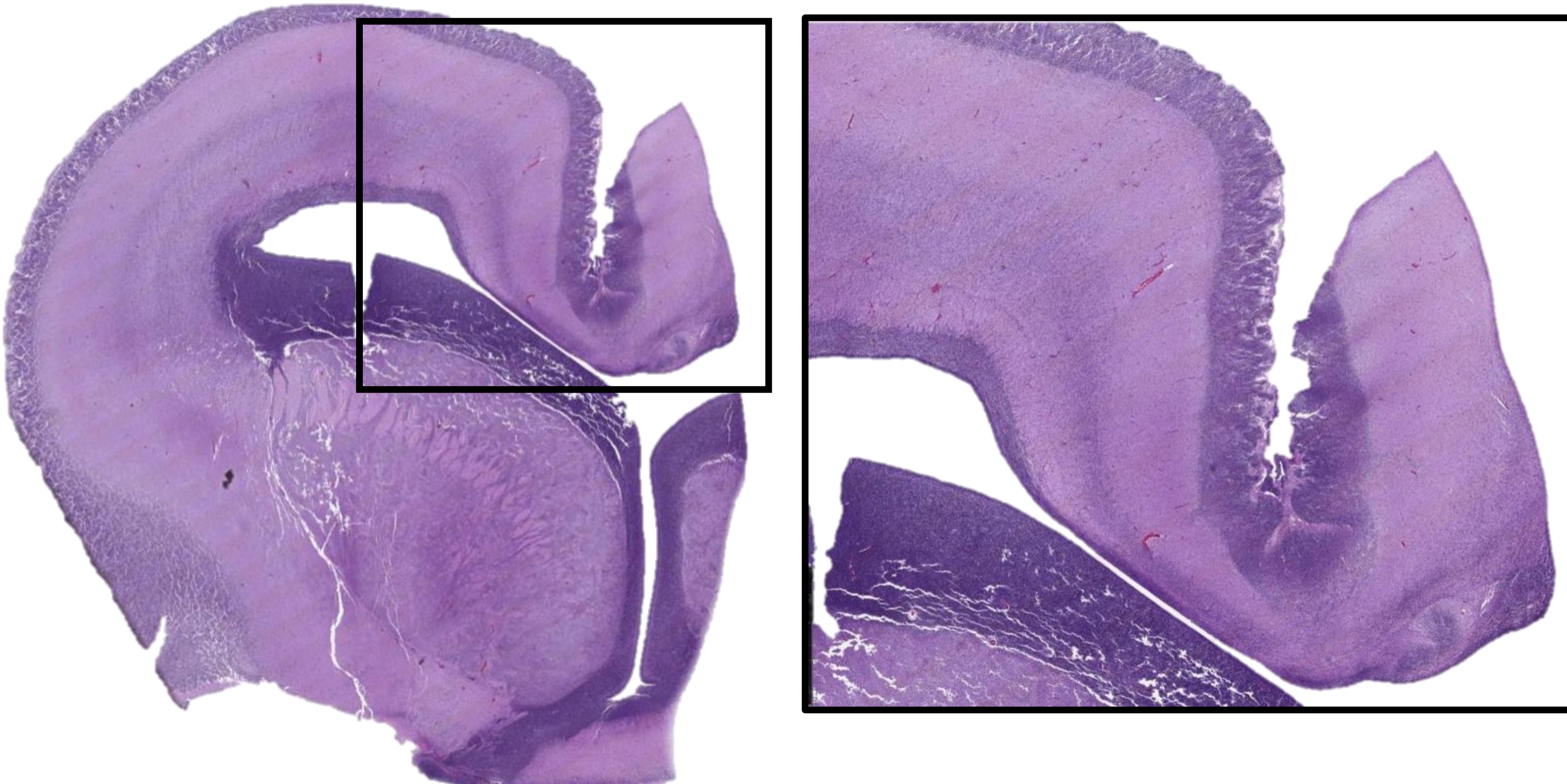
Semilobar Holoprosencephaly



Intermediate between the alobar and lobar forms. There are mild microcephaly, a partly formed shallow interhemispheric fissure, and some lobar structure with rudimentary temporal and occipital horns but continuity of the cortex across the midline. Olfactory structures are usually absent.

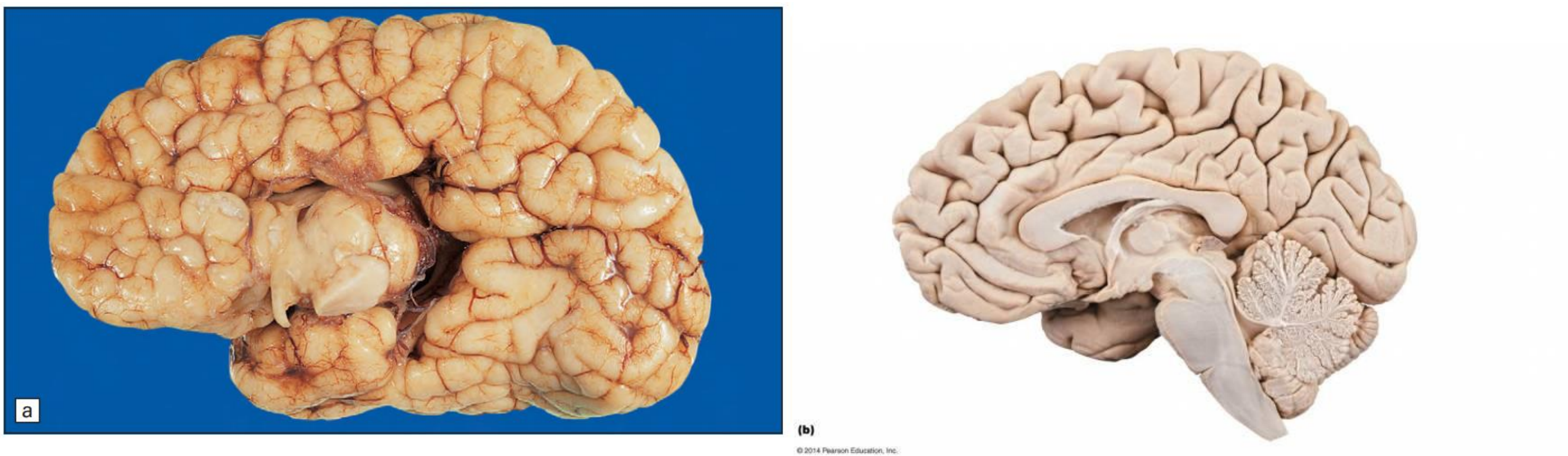
Lobar Holoprosencephaly

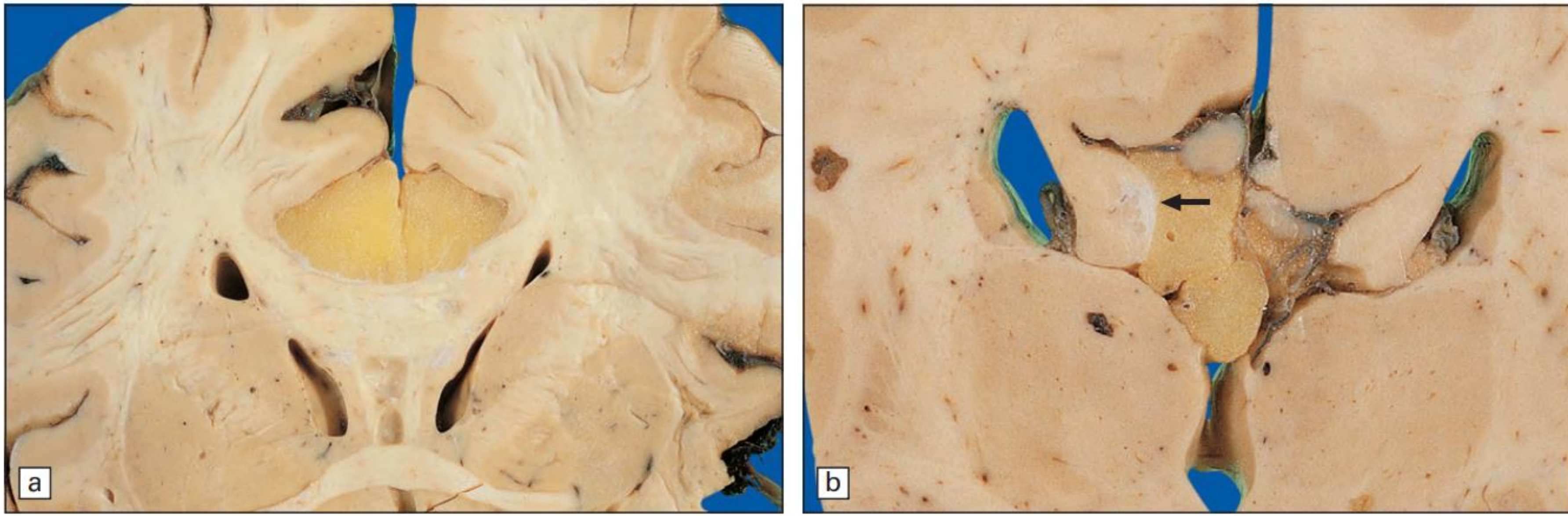
Despite near-normal brain size, normal lobe formation, and separated hemispheres, the cerebral cortex is continuous across the midline, at the frontal pole, or in the orbital region, or above the callosum (cingulosynapsis). Olfactory bulbs and callosum may be absent or hypoplastic. Heterotopic gray matter may be found in the ventricular roof.

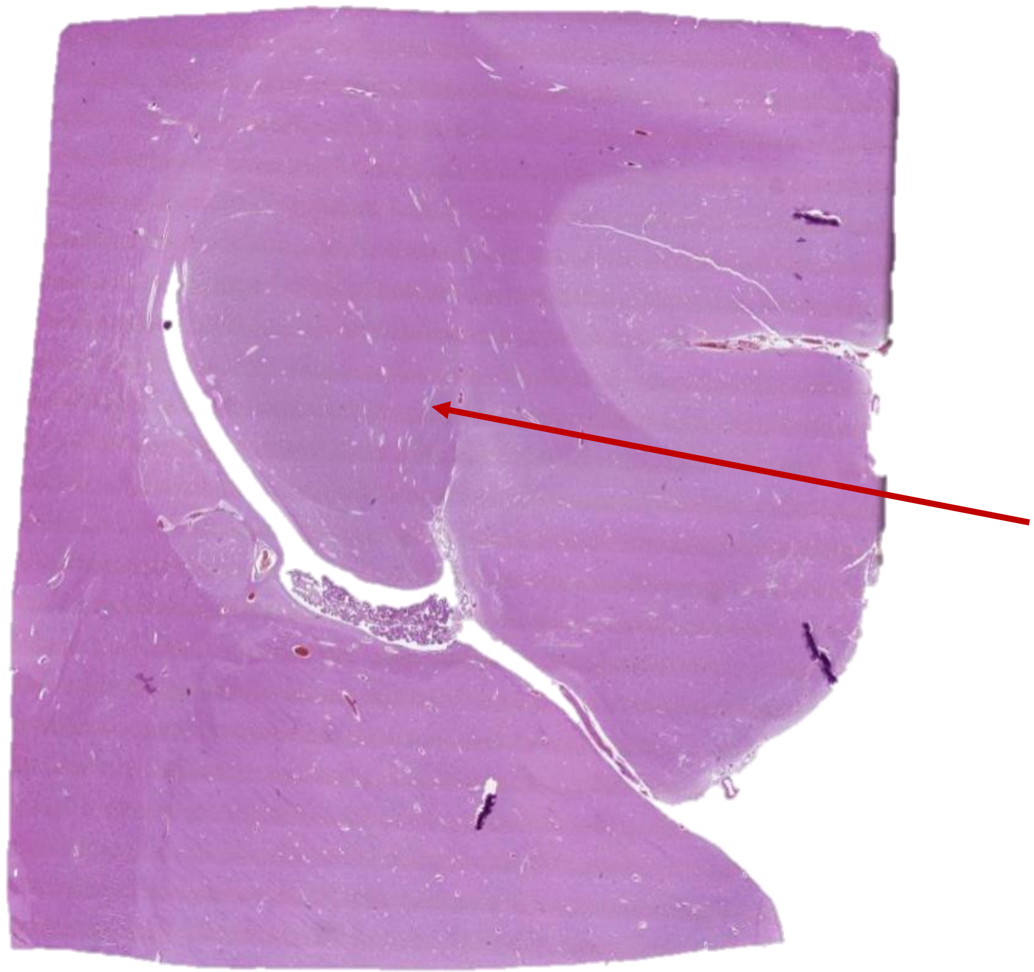


Callosal Agenesia

• Complete (total) and incomplete (partial) types – Partial is usually only missing the splenium
• Isolated (silent clinically or subtle) or seen in association with other malformations (ex. holoprosencephaly)
• Possible pathogenetic mechanisms: – Probst bundle of misdirected fibers – Mechanical defect suggested by hamartoma/ lipoma

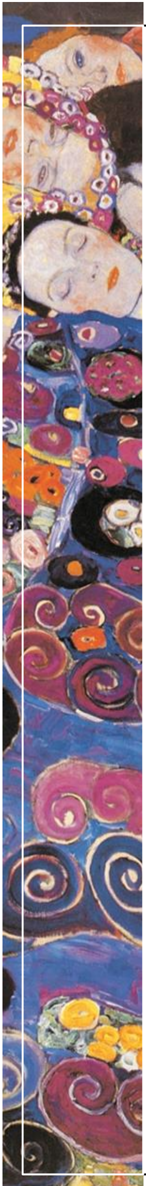


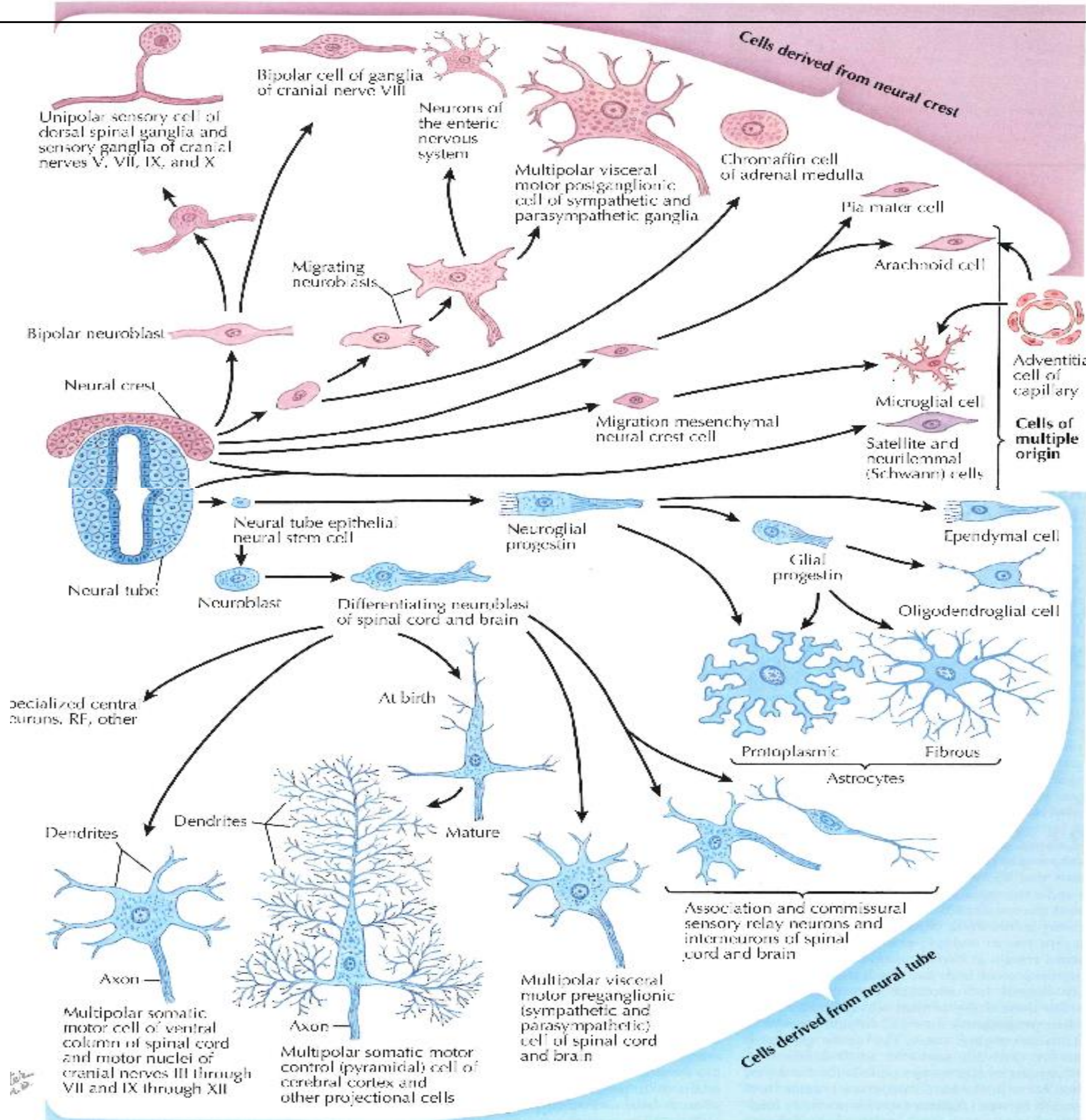

a
b



DEVELOPMENT OF THE CNS

- Morphogenesis → Development of CNS Structure
- Histogenesis → Development of CNS Tissue





Cells derived from neural crest
Unipolar sensory cell of dorsal spinal ganglia and sensory ganglia of cranial nerves V, VII, IX, and X
Bipolar cell of ganglia of cranial nerve VIII
Neurons of the enteric nervous system
Multipolar visceral motor postganglionic cell of sympathetic and parasympathetic ganglia
Chromaffin cell of adrenal medulla
Pia mater cell
Arachnoid cell
Migrating neuroblasts
Bipolar neuroblast
Neural crest
Adventitial cell of capillary
Microglial cell
Migration mesenchymal neural crest cell
Satellite and neurilemmal (Schwann) cells
Cells of multiple origin
Neural tube epithelial neural stem cell
Neuroglial progestin
Ependymal cell
Glial progestin
Oligodendroglial cell
Neural tube
Neuroblast
Differentiating neuroblast of spinal cord and brain
pecialized central eurons, RF, other
At birth
Protoplasmic
Fibrous
Astrocytes
Dendrites
Dendrites
Mature
Axon
Axon
Multipolar somatic motor cell of ventral column of spinal cord and motor nuclei of cranial nerves III through VII and IX through XII
Multipolar somatic motor control (pyramidal) cell of cerebral cortex and other projectional cells
Multipolar visceral motor preganglionic (sympathetic and parasympathetic) cell of spinal cord and brain
Association and commissural sensory relay neurons and interneurons of spinal cord and brain
Cells derived from neural tube

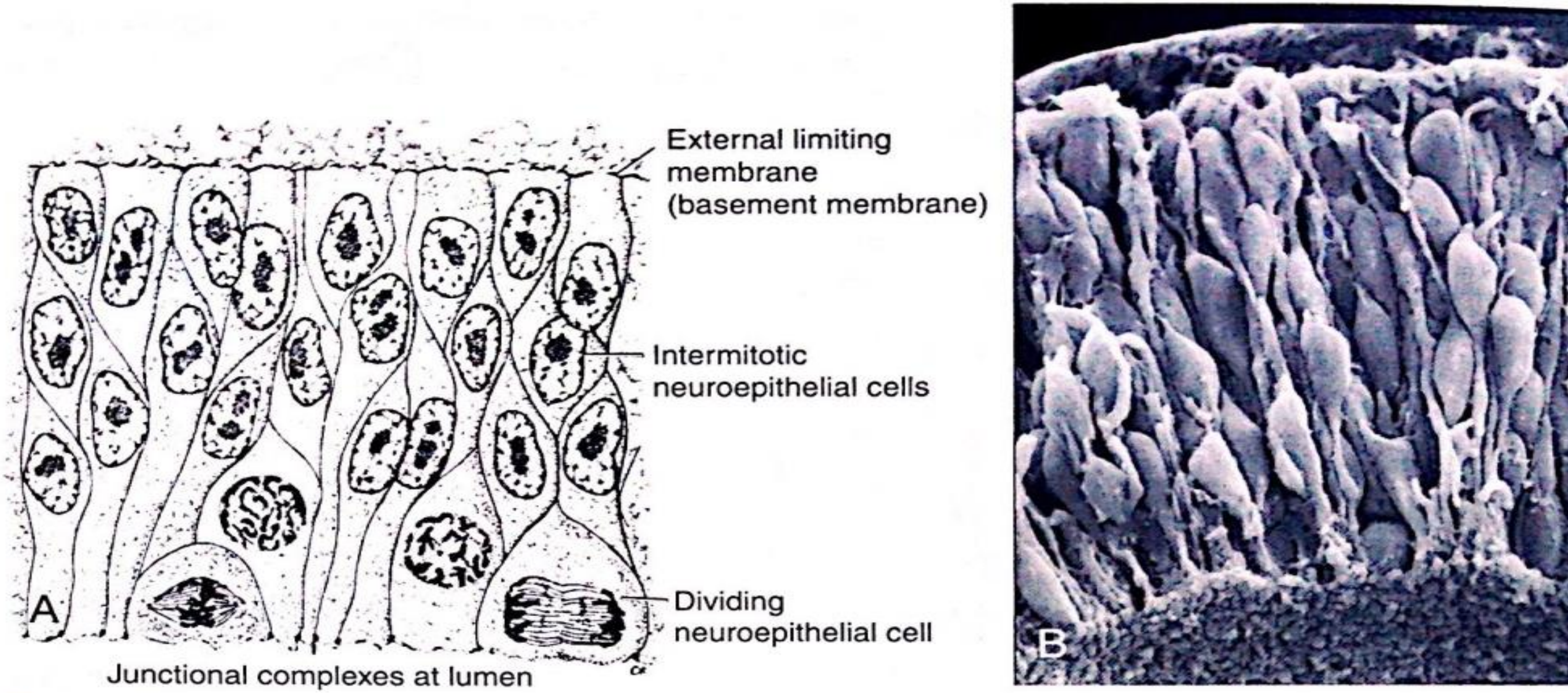


Figure 17.6 **A.** Section of the wall of the recently closed neural tube showing neuroepithelial cells, which form a pseudostratified epithelium extending over the full width of the wall. Note the dividing cells at the lumen of the tube. **B.** Scanning electron micrograph of a section of the neural tube of a chick embryo similar to that in **A.**

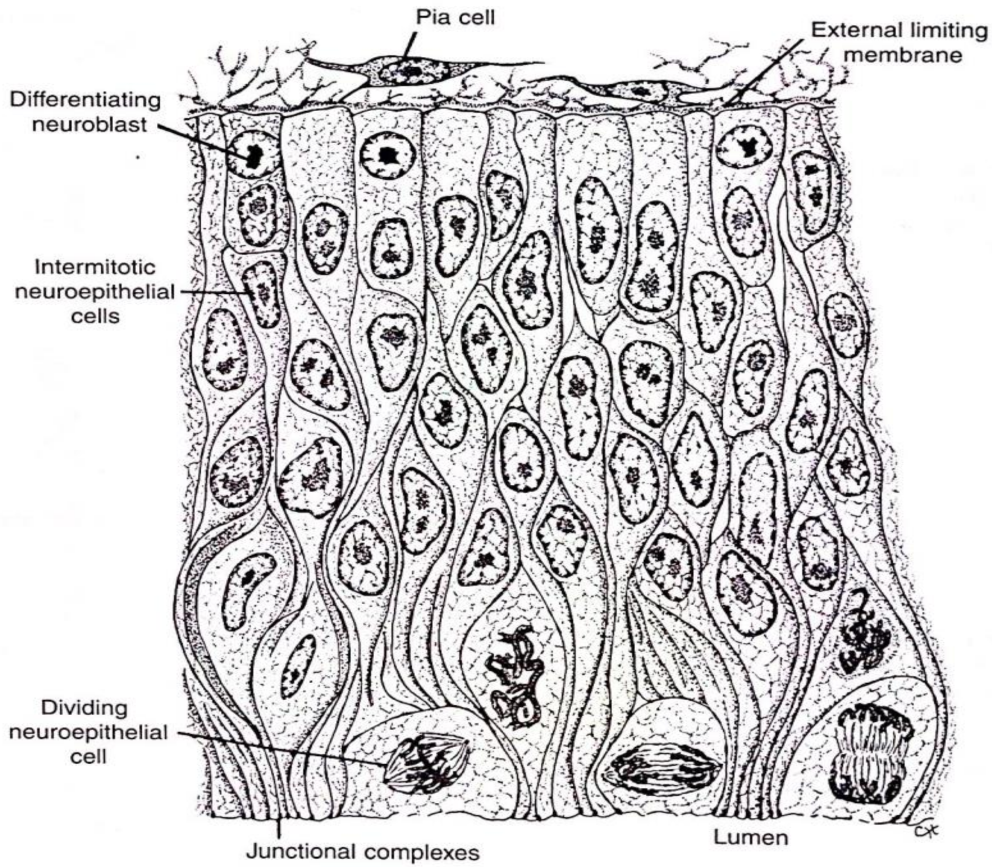
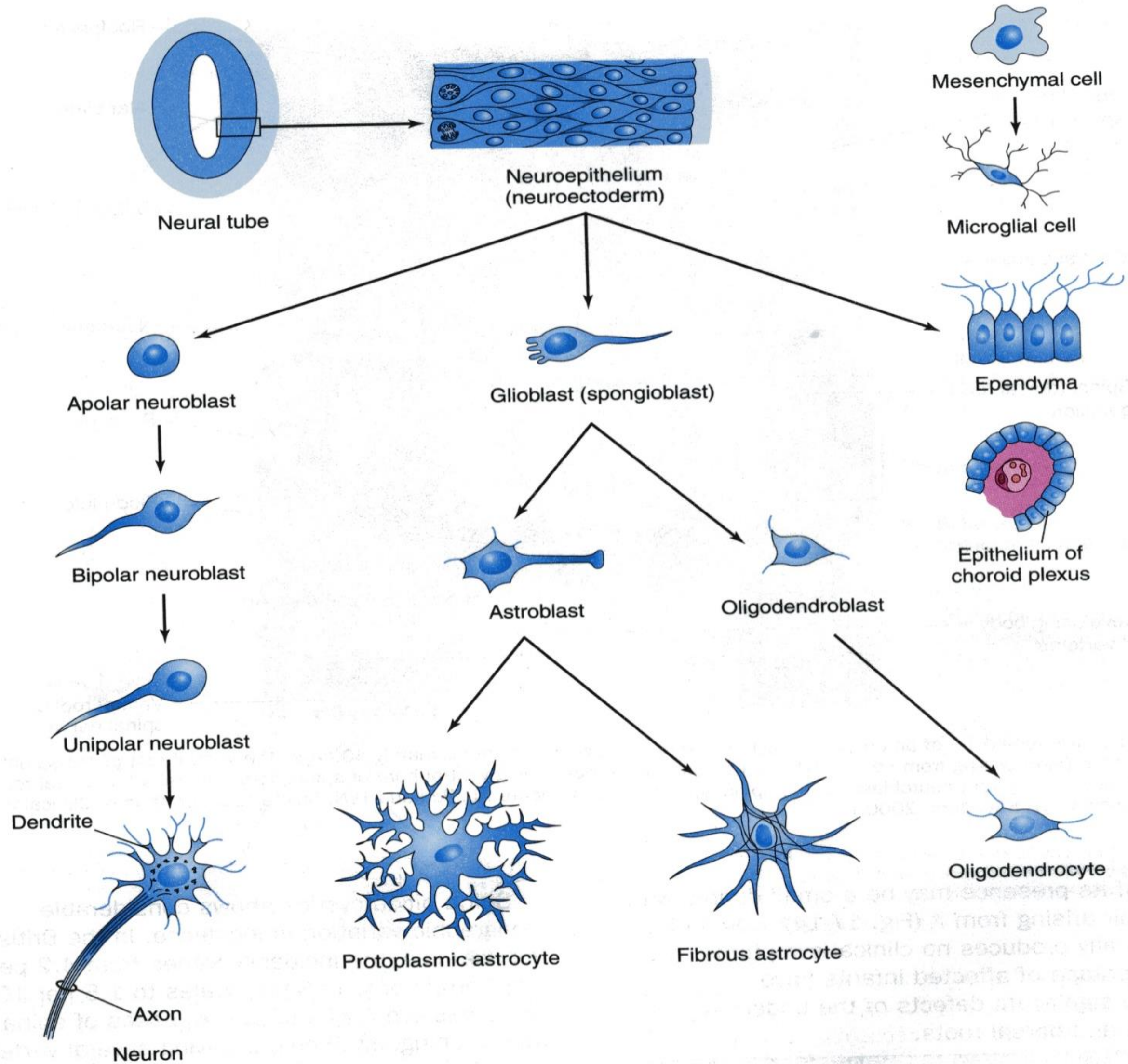


Figure 17.7 Section of the neural tube at a slightly more advanced stage than in Figure 17.6. The major portion of the wall consists of neuroepithelial cells. On the periphery, immediately adjacent to the external limiting membrane, neuroblasts form. These cells, which are produced by the neuroepithelial cells in ever-increasing numbers, will form the mantle layer.



Neural tube
Neuroepithelium
(neuroectoderm)
Mesenchymal cell
Microglial cell
Ependyma
Epithelium of
choroid plexus
Apolar neuroblast
Glioblast (spongioblast)
Bipolar neuroblast
Astroblast
Oligodendroblast
Unipolar neuroblast
Dendrite
Protoplasmic astrocyte
Fibrous astrocyte
Oligodendrocyte
Axon
Neuron

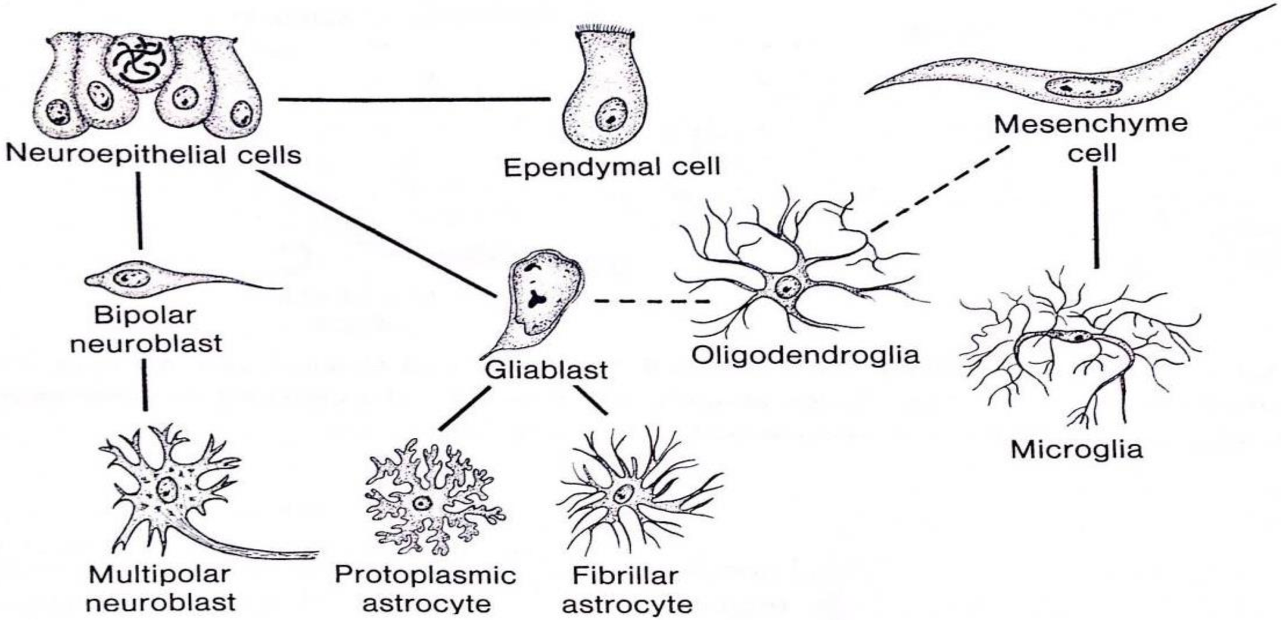


Figure 17.11 Origin of the nerve cell and the various types of glial cells. Neuroblasts, fibrillar and protoplasmic astrocytes, and ependymal cells originate from neuroepithelial cells. Microglia develop from mesenchyme cells. The origin of the oligodendroglia is not clear.

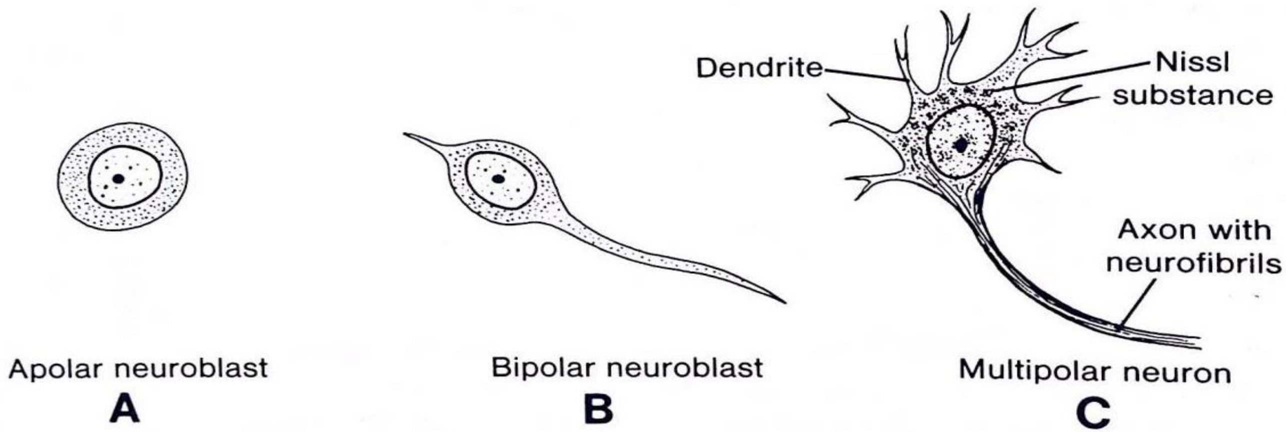
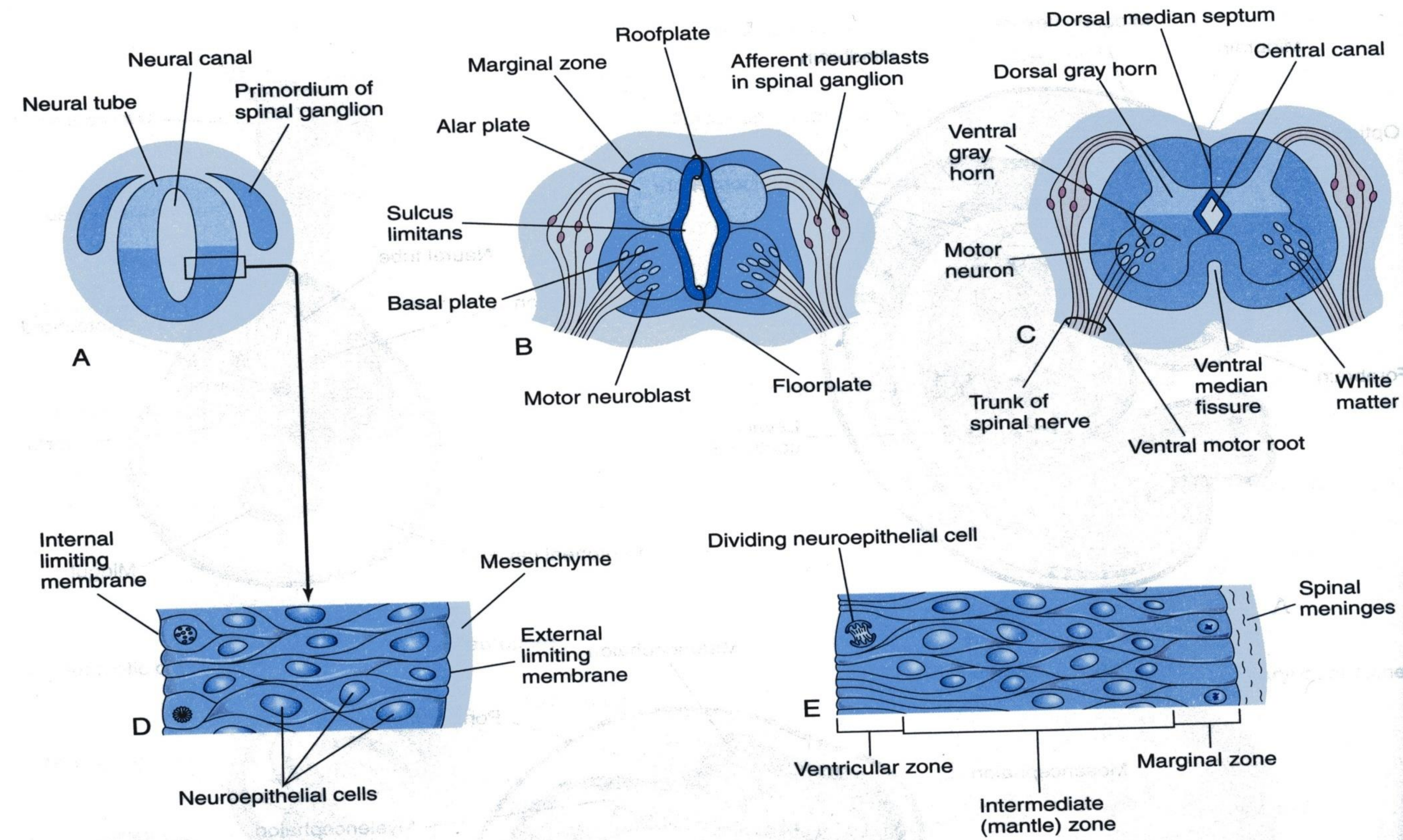


Figure 17.9 Various stages of development of a neuroblast. A neuron is a structural and functional unit consisting of the cell body and all its processes.


Neural canal
Neural tube
Primordium of spinal ganglion
A
Roofplate
Marginal zone
Afferent neuroblasts in spinal ganglion
Alar plate
Sulcus limitans
Basal plate
B
Motor neuroblast
Floorplate
Dorsal median septum
Dorsal gray horn
Central canal
Ventral gray horn
Motor neuron
C
Trunk of spinal nerve
Ventral median fissure
White matter
Ventral motor root
Internal limiting membrane
Mesenchyme
External limiting membrane
D
Neuroepithelial cells
Dividing neuroepithelial cell
Spinal meninges
E
Ventricular zone
Intermediate (mantle) zone
Marginal zone

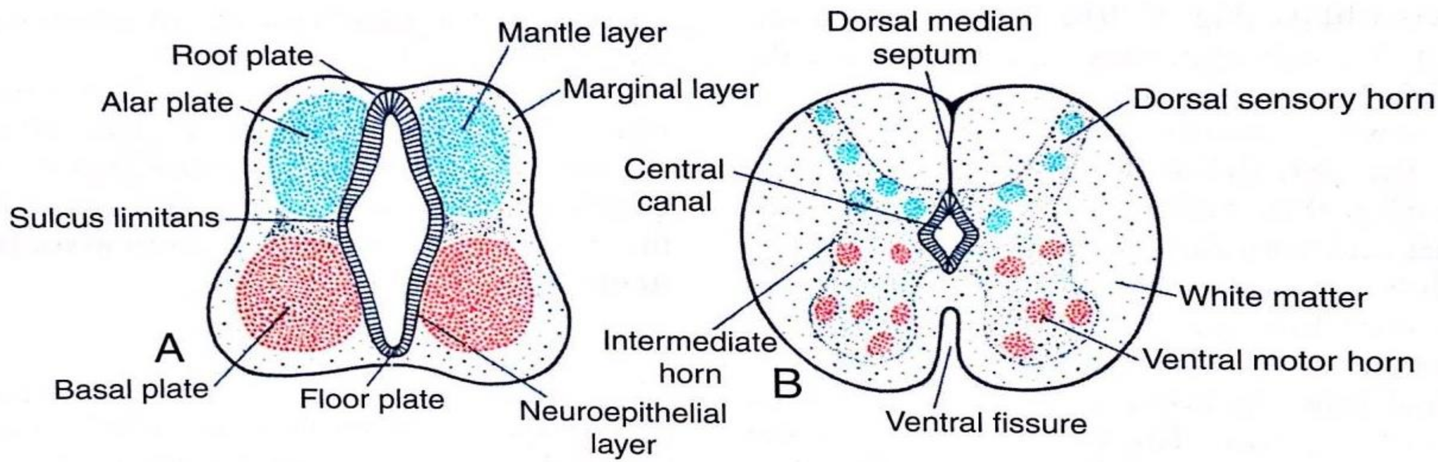


Figure 17.8 **A,B.** Two successive stages in the development of the spinal cord. Note formation of ventral motor and dorsal sensory horns and the intermediate column.

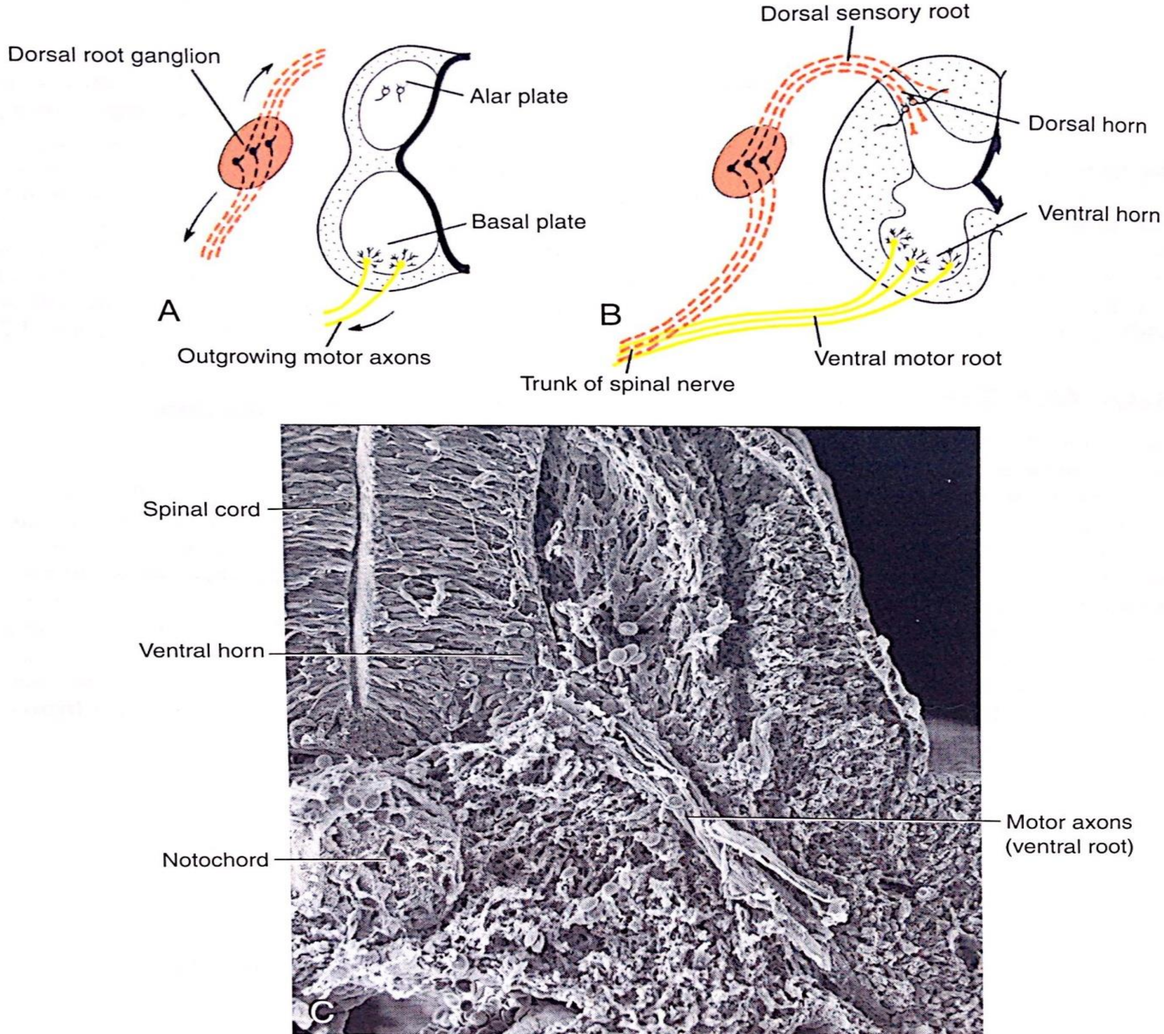


Figure 17.10 **A.** Motor axons growing out from neurons in the basal plate and centrally and peripherally growing fibers of nerve cells in the dorsal root ganglion. **B.** Nerve fibers of the ventral motor and dorsal sensory roots join to form the trunk of the spinal nerve. **C.** Scanning electron micrograph of a cross section through the spinal cord of a chick embryo. The ventral horn and ventral motor root are differentiating.

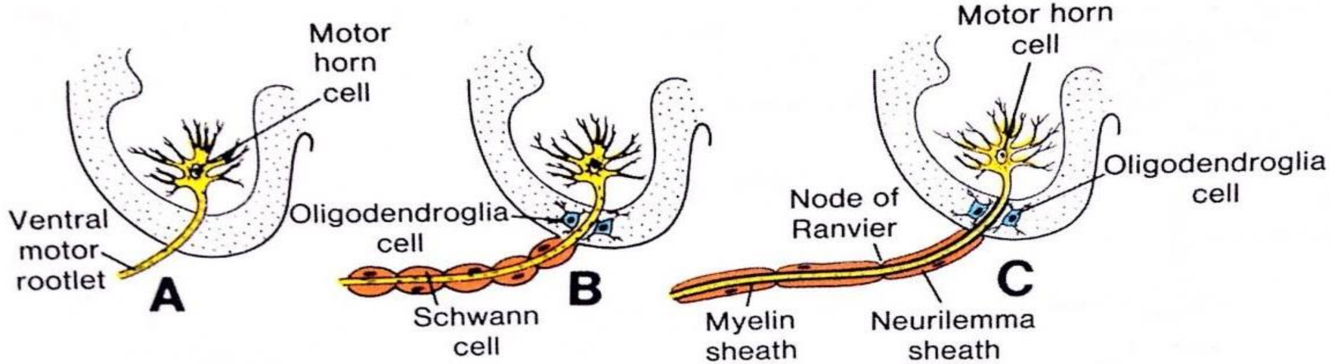


Figure 17.12 **A.** Motor horn cell with naked rootlet. **B.** In the spinal cord, oligodendroglia cells surround the ventral rootlet; outside the spinal cord, Schwann cells begin to surround the rootlet. **C.** In the spinal cord, the myelin sheath is formed by oligodendroglia cells; outside the spinal cord, the sheath is formed by Schwann cells.

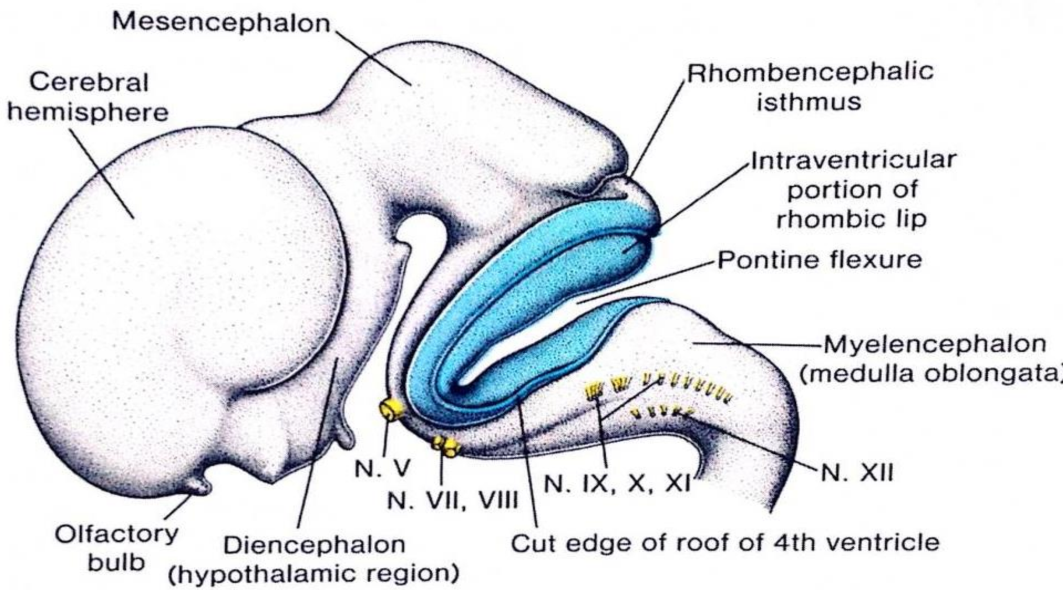


Figure 17.17 Lateral view of the brain vesicles in an 8-week embryo (crown-rump length ~27 mm). The roof plate of the rhombencephalon has been removed to show the intraventricular portion of the rhombic lip. Note the origin of the cranial nerves.

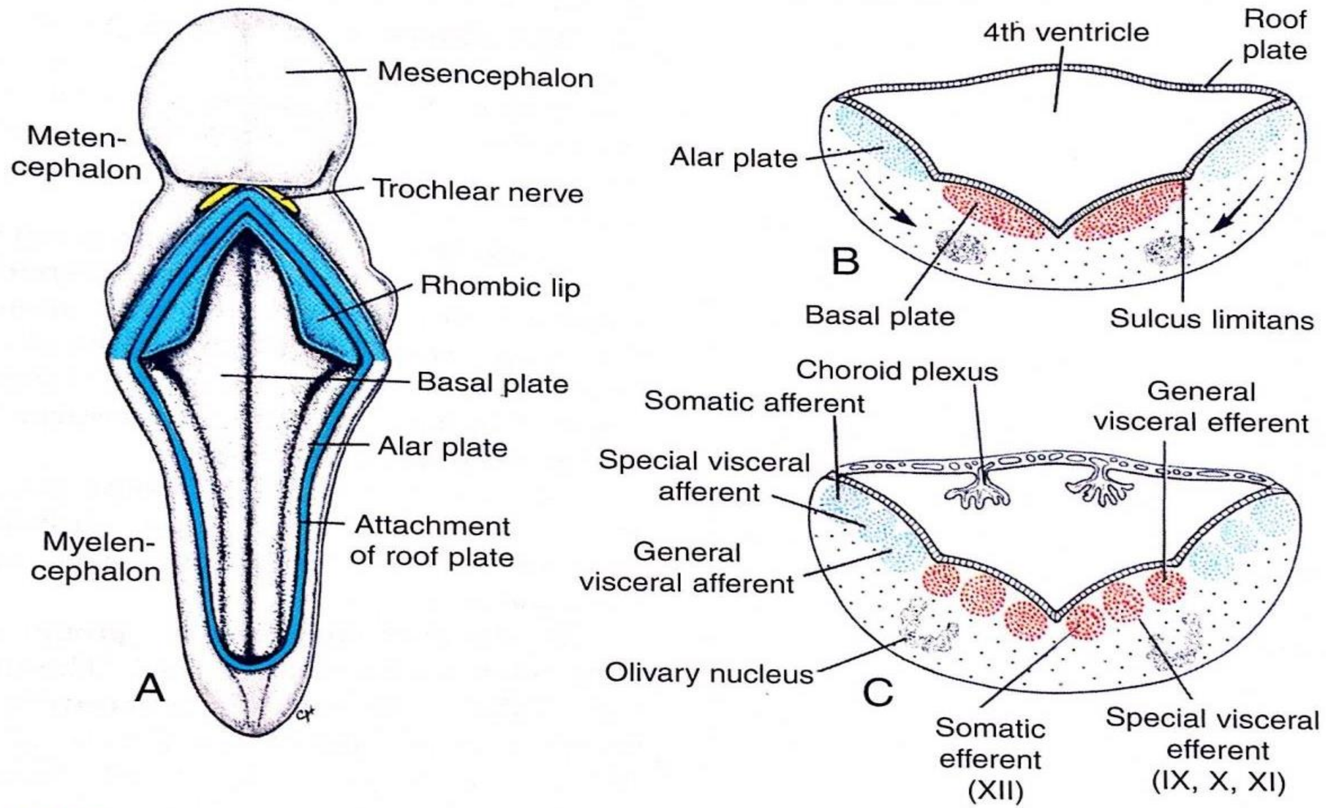


Figure 17.18 **A.** Dorsal view of the floor of the fourth ventricle in a 6-week embryo after removal of the roof plate. Note the alar and basal plates in the myelencephalon. The rhombic lip is visible in the metencephalon. **B,C.** Position and differentiation of the basal and alar plates of the myelencephalon at different stages of development. Note formation of the nuclear groups in the basal and alar plates. *Arrows*, path followed by cells of the alar plate to the olivary nuclear complex. The choroid plexus produces cerebrospinal fluid.

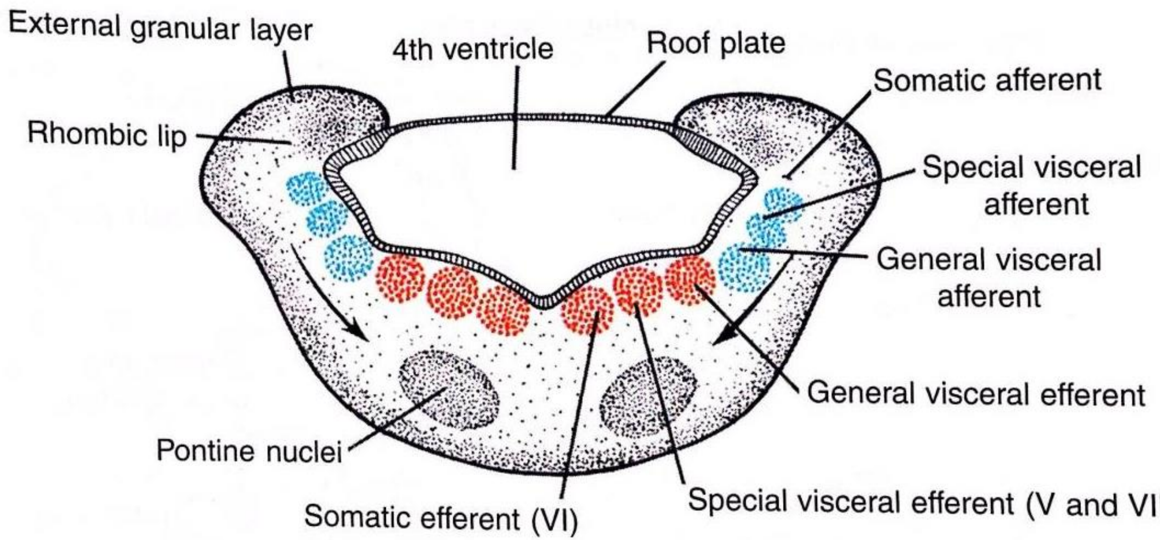


Figure 17.19 Transverse section through the caudal part of the metencephalon. Note the differentiation of the various motor and sensory nuclear areas in the basal and alar plates, respectively, and the position of the rhombic lips, which project partly into the lumen of the fourth ventricle and partly above the attachment of the roof plate. *Arrows*, direction of migration of the pontine nuclei.

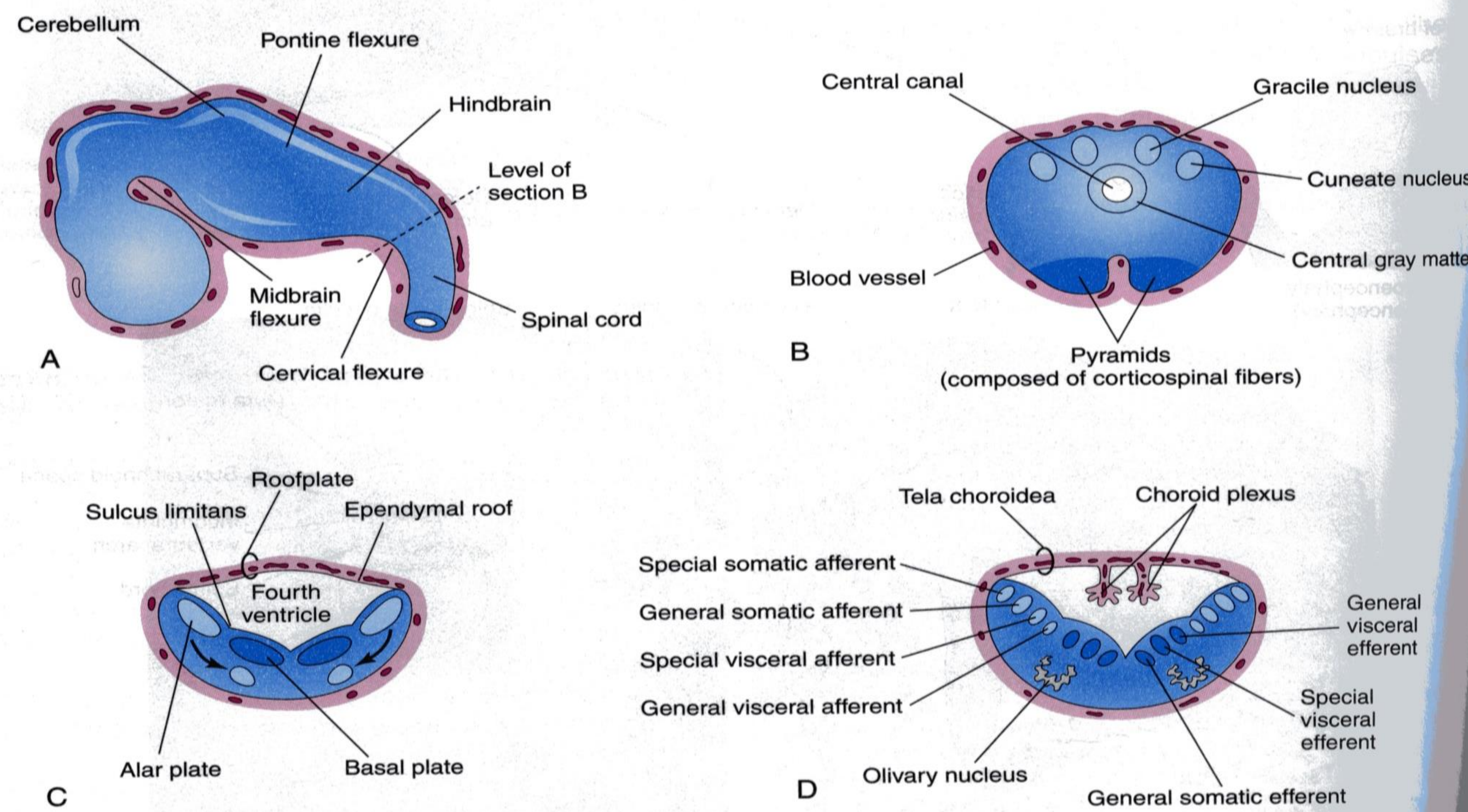


FIGURE 17-21. A, Sketch of the developing brain at the end of the fifth week showing the three primary divisions of the brain and the brain flexures. **B,** Transverse section of the caudal part of the myelencephalon (developing closed part of the medulla). **C** and **D,** Similar sections of the rostral part of the myelencephalon (developing open part of the medulla) showing the position and successive stages of differentiation of the alar and basal plates. The arrows in **C** show the pathway taken by neuroblasts from the alar plates to form the olivary nuclei.

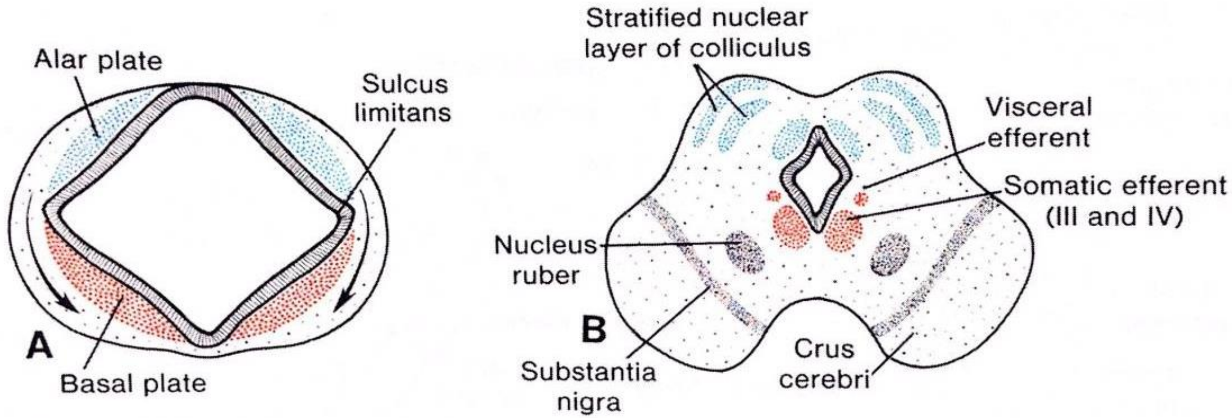


Figure 17.23 **A,B.** Position and differentiation of the basal and alar plates in the mesencephalon at various stages of development. *Arrows* in **A** indicate the path followed by cells of the alar plate to form the nucleus ruber and substantia nigra. Note the various motor nuclei in the basal plate.

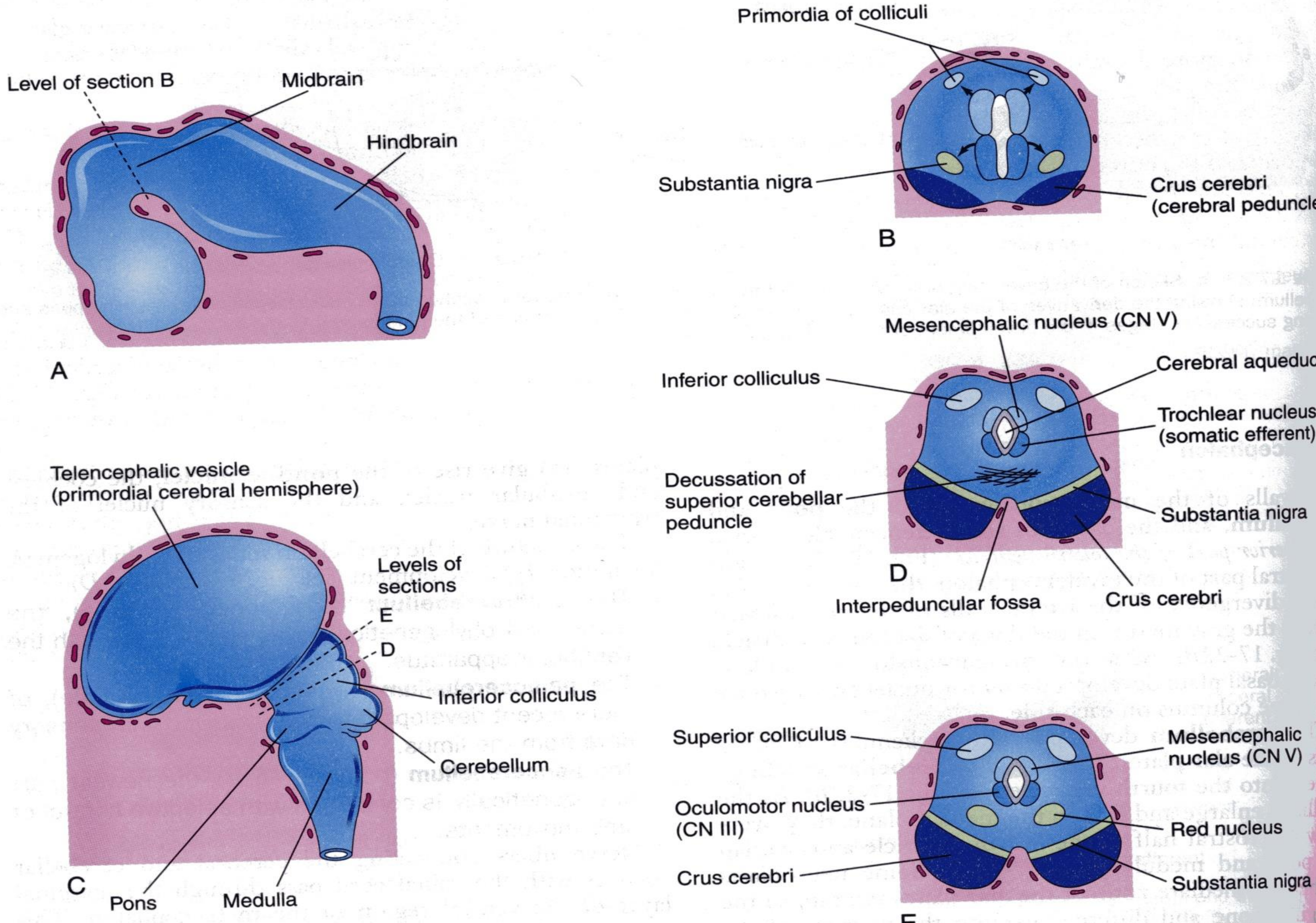


FIGURE 17-23. A, Sketch of the developing brain at the end of the fifth week. **B,** Transverse section of the developing midbrain showing the early migration of cells from the basal and alar plates. **C,** Sketch of the developing brain at 11 weeks. **D** and **E,** Transverse sections of the developing midbrain at the level of the inferior and superior colliculi, respectively. CN, cranial nerve.

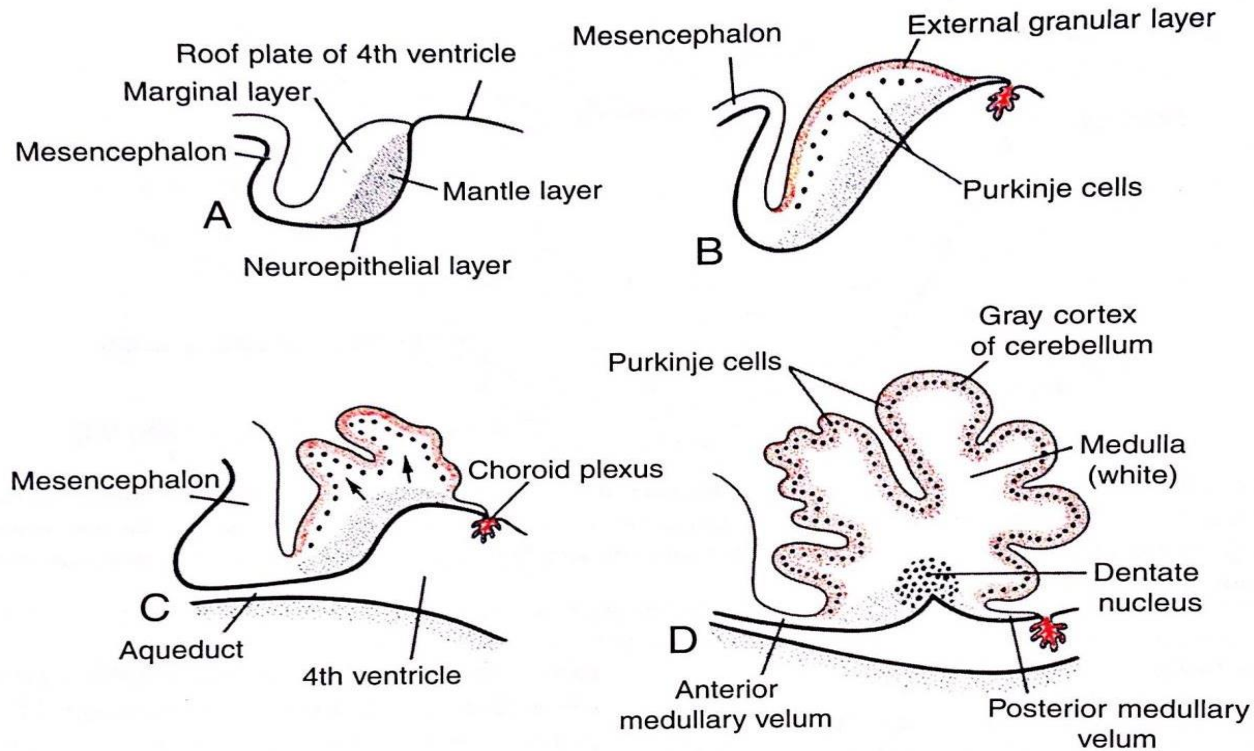


Figure 17.21 Sagittal sections through the roof of the metencephalon showing development of the cerebellum. **A.** 8 weeks (~30 mm). **B.** 12 weeks (70 mm). **C.** 13 weeks. **D.** 15 weeks. Note formation of the external granular layer on the surface of the cerebellar plate **(B,C)**. During later stages, cells of the external granular layer migrate inward to mingle with Purkinje cells and form the definitive cortex of the cerebellum. The dentate nucleus is one of the deep cerebellar nuclei. Note the anterior and posterior velum.

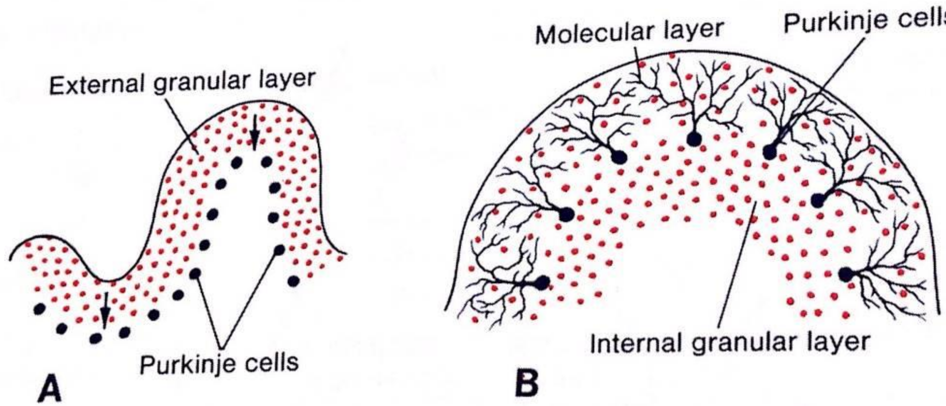
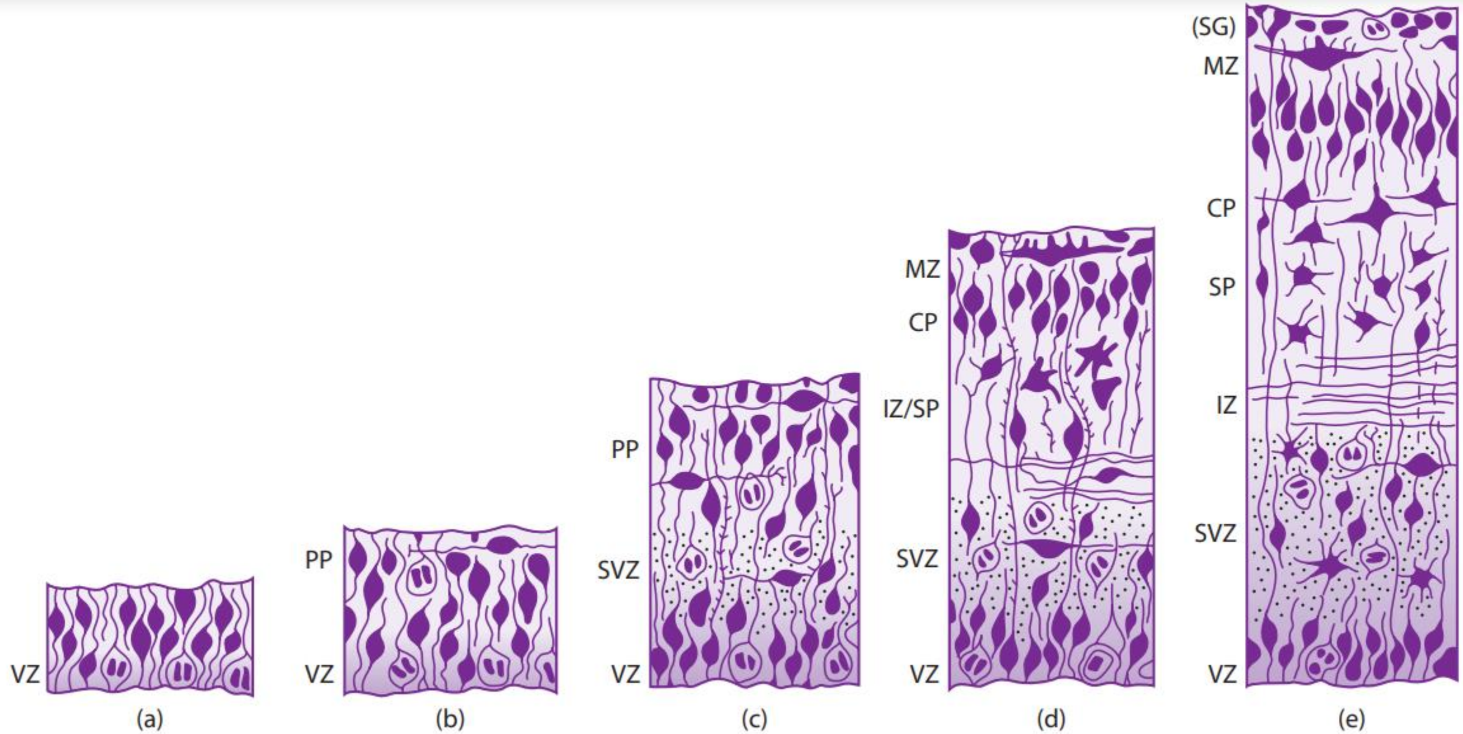
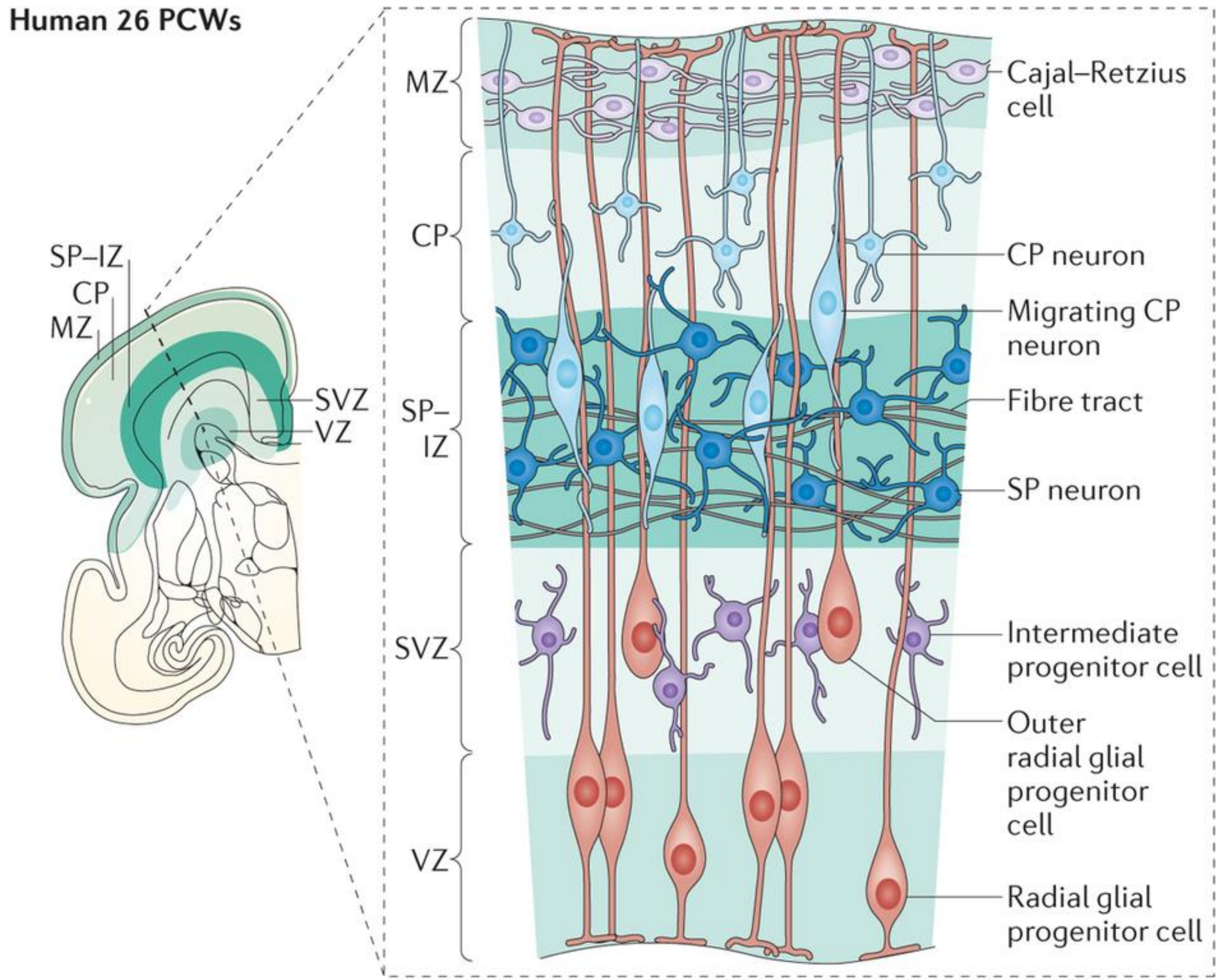


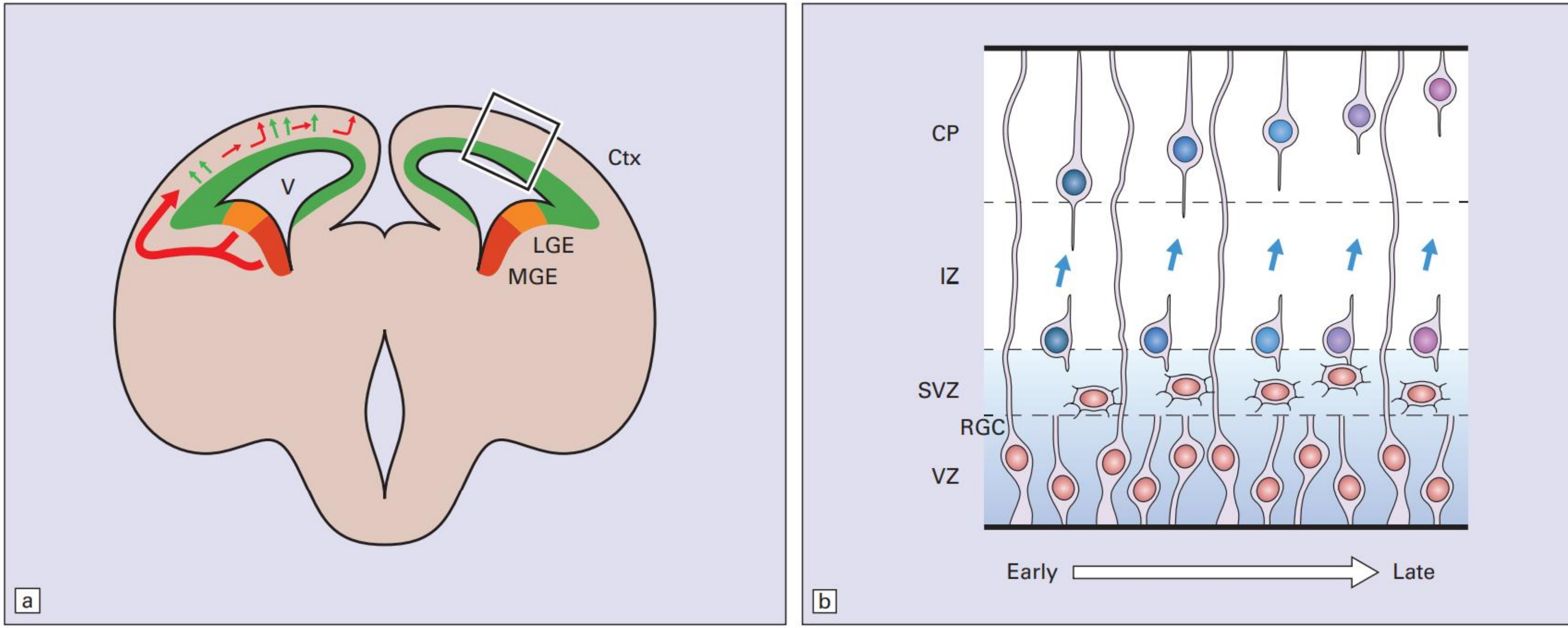
Figure 17.22 Stages in development of the cerebellar cortex. **A.** The external granular layer on the surface of the cerebellum forms a proliferative layer from which granule cells arise. They migrate inward from the surface *(arrows)*. Basket and stellate cells derive from proliferating cells in the cerebellar white matter. **B.** Postnatal cerebellar cortex showing differentiated Purkinje cells, the molecular layer on the surface, and the internal granular layer beneath the Purkinje cells.

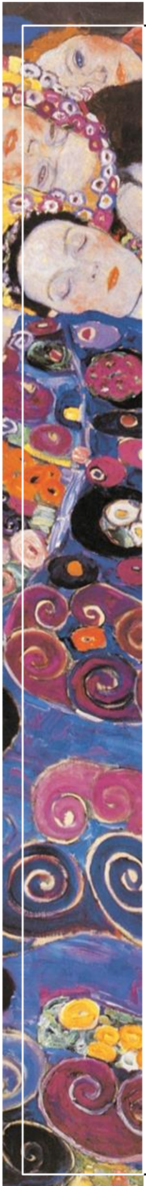


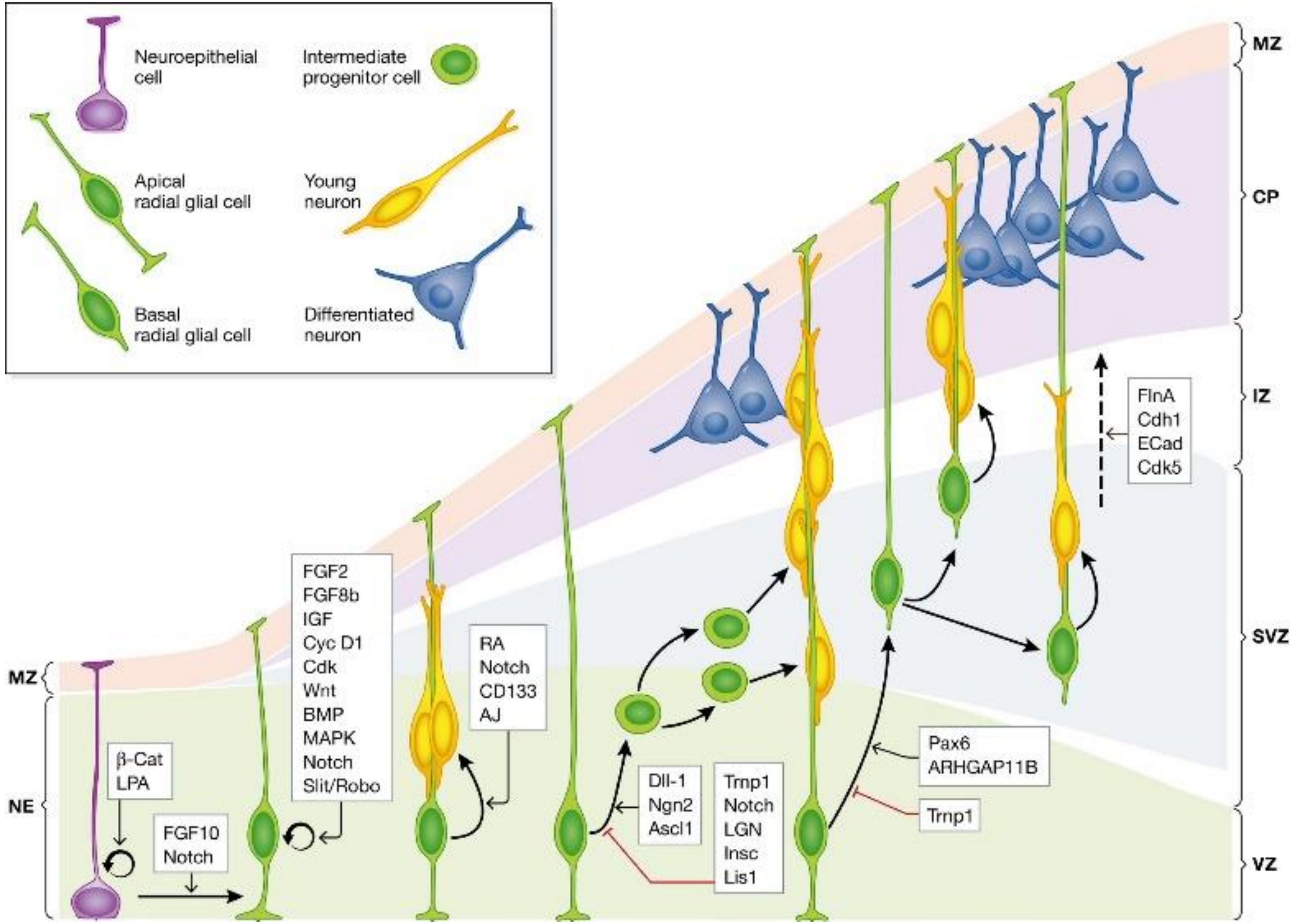
3.4 Neural tube layering during embryonic development. A proposed revision of the Boulder Committee's summary diagram of neocortical development shows the sequence of structural changes in the lateral part of the dorsal telencephalon at the approximate ages of embryonic day (E) 30 **(a)**; E31–E32 **(b)**, E45 **(c)**, E55 **(d)** and gestational week 14 **(e)**. The major layers are cortical plate (CP), intermediate zone (IZ), marginal zone (MZ), subventricular zone (SVZ), subpial granular layer (SG; part of the MZ), and the ventricular zone (VZ). The revised view incorporates transient compartments, including the preplate (PP) and the intermediate and subplate zones (IZ and SP).



Nature Reviews | Neuroscience


V
Ctx
LGE
MGE
a
CP
IZ
SVZ
RGC
VZ
Early
Late
b

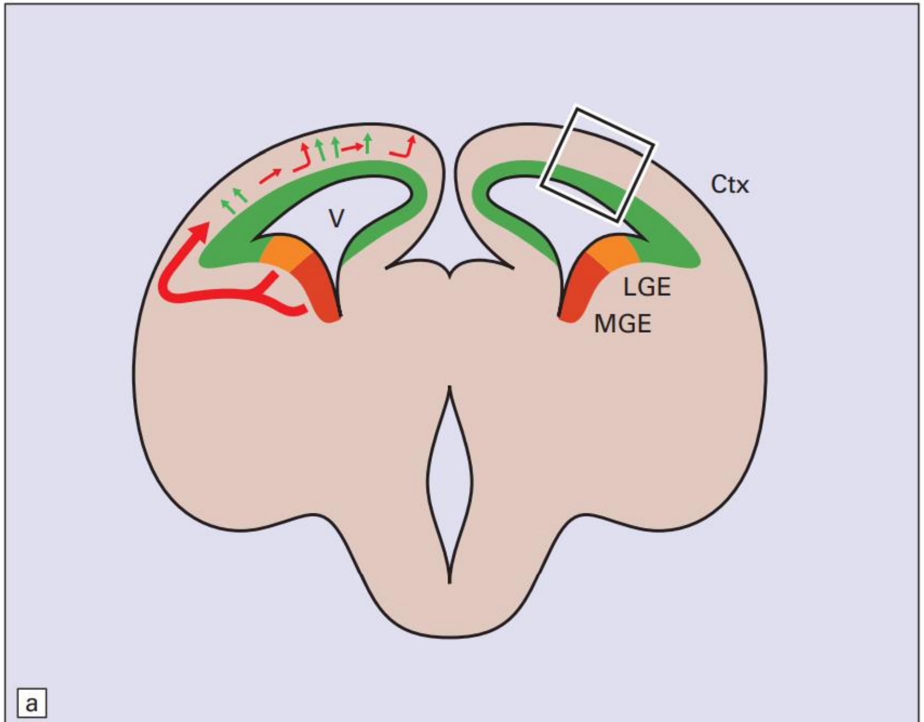


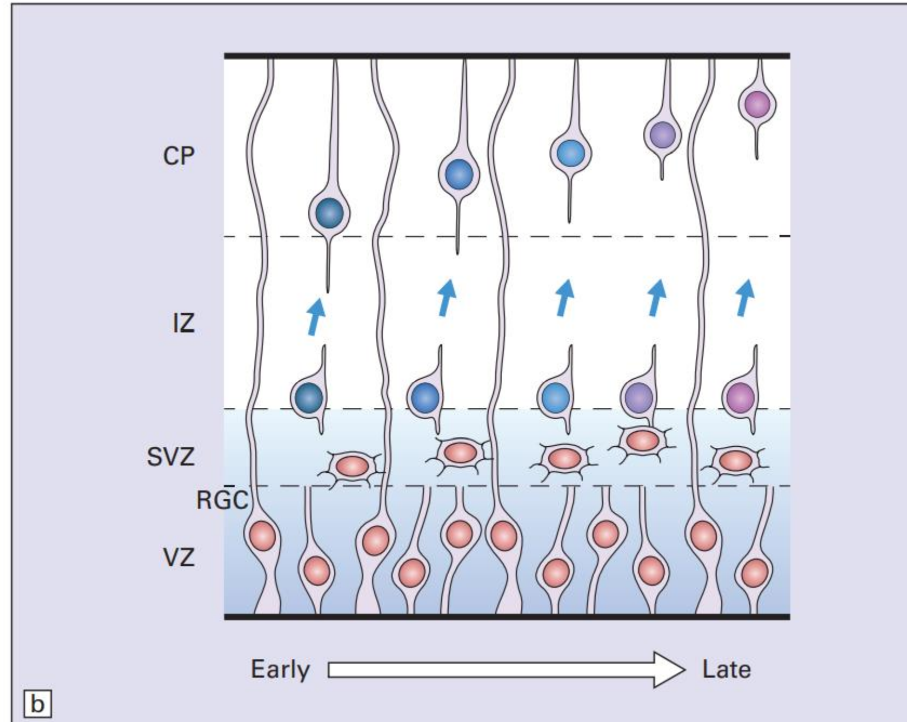

Neuroepithelial cell
Intermediate progenitor cell
Apical radial glial cell
Young neuron
Basal radial glial cell
Differentiated neuron
MZ
CP
IZ
SVZ
VZ
MZ
NE
β-Cat
LPA
FGF10
Notch
FGF2
FGF8b
IGF
Cyc D1
Cdk
Wnt
BMP
MAPK
Notch
Slit/Robo
RA
Notch
CD133
AJ
Dll-1
Ngn2
Ascl1
Trnp1
Notch
LGN
Insc
Lis1
Pax6
ARHGAP11B
Trnp1
FlnA
Cdh1
ECad
Cdk5

EARLY GESTATION (First 20 Weeks)

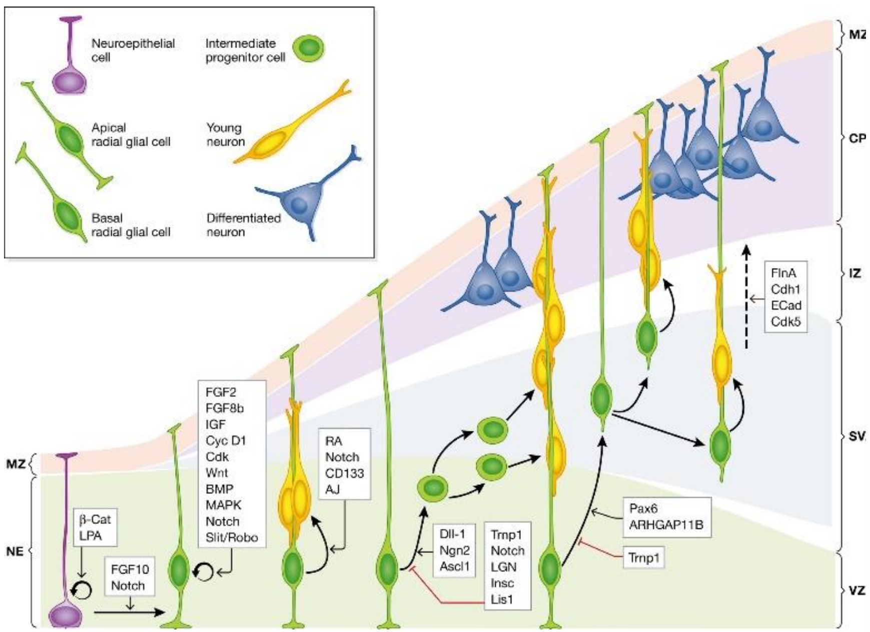
- Dysraphic malformations
- Disorders of forebrain induction
- Malformations of cortical development

Malformations of Cortical Development





Malformations of Cortical Development

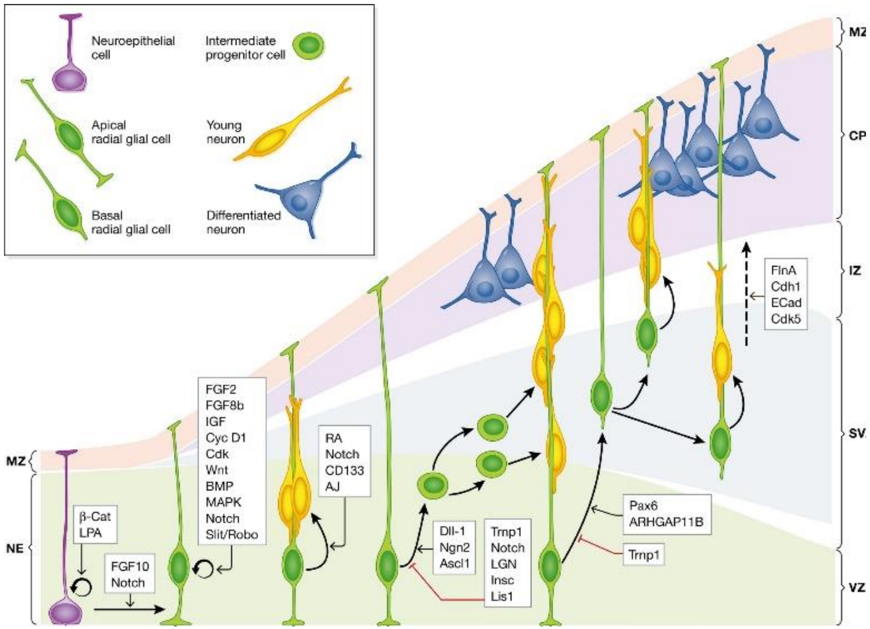


Malformations of cortical development with associated genes and clinical features

Developmental stage	Cortical malformation	Genetic cause	Clinical features
Abnormal neurogenesis			
	Microcephaly	*ASPM*	Mental retardation, not generally associated with epilepsy, autosomal recessive inheritance
		Microcephalin	
		CDK5RAP2	
		CENPJ	
	Hemimegalencephaly	Unknown	Mental retardation, early onset seizures (frequently intractable epilepsy), +/- neurocutaneous syndrome
	Focal cortical dysplasia	Unknown	Most common, focal and generalized Seizures
Abnormal neuronal migration			
	Periventricular heterotopia	*FLNA*	Normal intelligence, adolescent onset seizures, X-linked disorder with male lethality
		ARFGEF2	Mental retardation, microcephaly, autosomal recessive inheritance, rare
	Subcortical band heterotopia	*DCX*	Subcortical band heterotopia in females, mental retardation, epilepsy, X-linked disorder
	Lissencephaly	*LIS1*	Miller-Dieker syndrome (characteristic facial features), autosomal dominant inheritance
		DCX	Lissencephaly in males, X-linked
		TUBA1A	Lissencephaly, clinical features similar those caused by *LIS1* and *DCX*, de novo mutations
		ARX	Associated with ambiguous genitalia, hypothalamic dysfunction, neonatal epilepsy, X-linked disorder
		RELN	Associated with cerebellar hypoplasia, epilepsy, autosomal recessive inheritance
Abnormal arrest in neuronal migration			
	Cobblestone lissencephaly	*Fukutin*	Fukuyama congenital muscular dystrophy
		POMGnT1	Muscle-eye-brain disease
		POMT1	Walker-Warburg Syndrome


pia mater
I
II
III
IV
V
VI
white matter

Malformations of Cortical Development



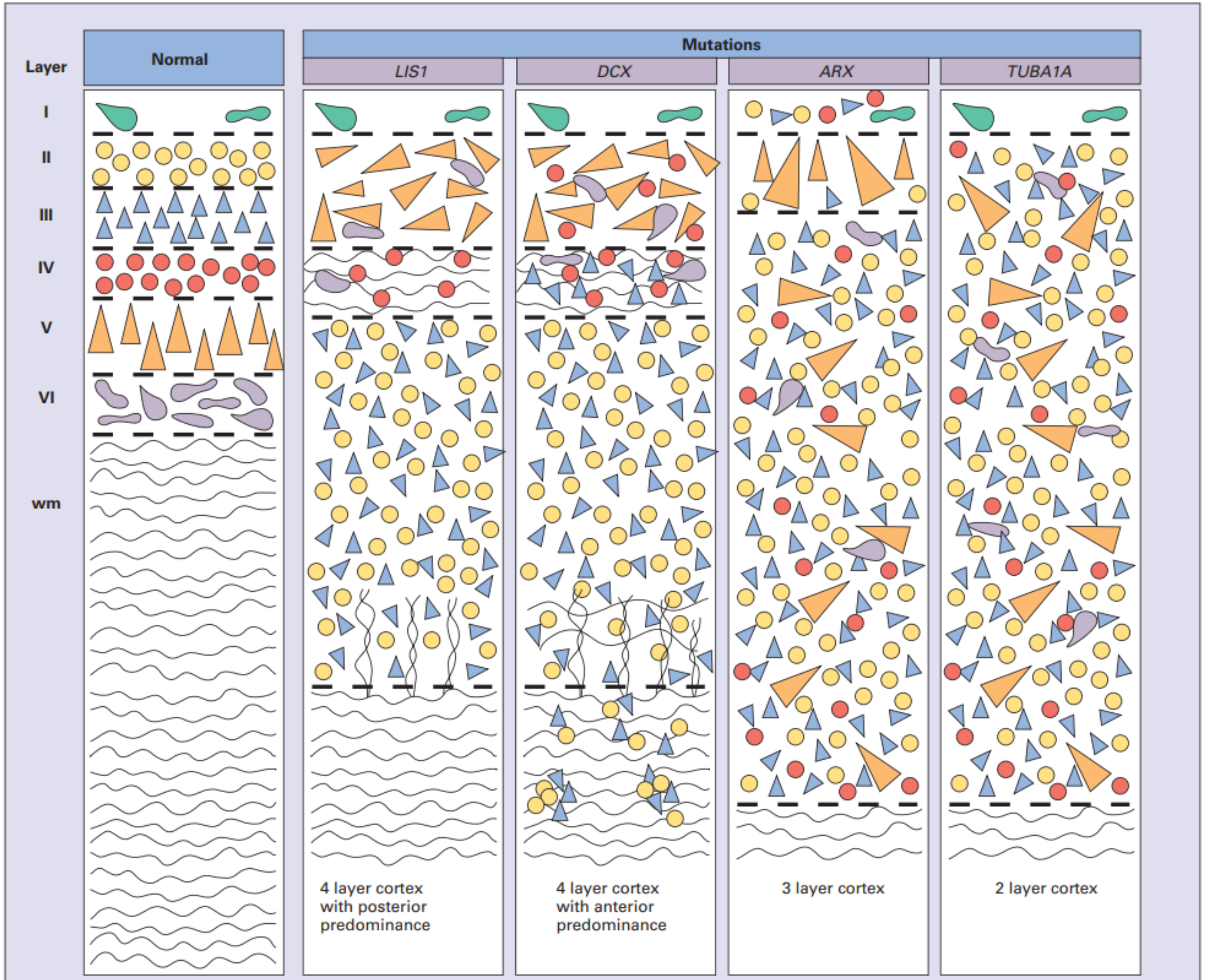
Malformations of cortical development with associated genes and clinical features

Developmental stage	Cortical malformation	Genetic cause	Clinical features
Abnormal neurogenesis			
	Microcephaly	*ASPM*	Mental retardation, not generally associated with epilepsy, autosomal recessive inheritance
		Microcephalin	
		CDK5RAP2	
		CENPJ	
	Hemimegalencephaly	Unknown	Mental retardation, early onset seizures (frequently intractable epilepsy), +/- neurocutaneous syndrome
	Focal cortical dysplasia	Unknown	Most common, focal and generalized Seizures
Abnormal neuronal migration			
	Periventricular heterotopia	*FLNA*	Normal intelligence, adolescent onset seizures, X-linked disorder with male lethality
		ARFGEF2	Mental retardation, microcephaly, autosomal recessive inheritance, rare
	Subcortical band heterotopia	*DCX*	Subcortical band heterotopia in females, mental retardation, epilepsy, X-linked disorder
	Lissencephaly	*LIS1*	Miller-Dieker syndrome (characteristic facial features), autosomal dominant inheritance
		DCX	Lissencephaly in males, X-linked
		TUBA1A	Lissencephaly, clinical features similar those caused by *LIS1* and *DCX*, de novo mutations
		ARX	Associated with ambiguous genitalia, hypothalamic dysfunction, neonatal epilepsy, X-linked disorder
		RELN	Associated with cerebellar hypoplasia, epilepsy, autosomal recessive inheritance
Abnormal arrest in neuronal migration			
	Cobblestone lissencephaly	*Fukutin*	Fukuyama congenital muscular dystrophy
		POMGnT1	Muscle-eye-brain disease
		POMT1	Walker-Warburg Syndrome

Lissencephaly Type I

- Neuronal migration disorder characterized by abnormal gyri
- Varies from agyria to pachygyria
- Severe mental retardation, hypotonia, intractable seizures
- Several genetic types are recognized

Disease	CNS	Gene	Function of product	Chromosome	Mouse model
Lissencephaly (type I): autosomal recessive (Norman-Roberts type)	Lissencephaly with low sloping forehead and prominent nasal bridge	*RELN*	Reelin: extracellular matrix protein produced by Cajal-Retzius cells required for neuronal migration	7q22	*reeler* mutant mouse causes cerebellar and cerebral cortical lamination anomalies
Lissencephaly (type I): Miller-Dieker syndrome, autosomal dominant (haploinsufficiency)	Lissencephaly, cerebral heterotopias, facial dysmorphism	*LIS1* and *14-3-3$^{\varepsilon}$* *YWHAE* ; (contiguous gene deletion)	LIS1: Non-catalytic subunit of brain platelet-activating factor acetyl hydrolase (PAFAH)	17p13.3	Targeted loss of function alleles of *Pafah1b1* gene and *14-3-3$^{\varepsilon}$*
Lissencephaly (type I): isolated lissencephaly sequence (ILS), autosomal dominant	Lissencephaly	*LIS1* deletion alone	LIS1: as above	17p13.3	Targeted loss of function alleles of *Pafah1b1* gene causes neuronal migration disorders
Lissencephaly (type I): X-linked	Lissencephaly with agenesis of corpus callosum in males; subcortical band heterotopia in females	*DCX*	Doublecortin: microtubule-associated protein that interacts with non-receptor tyrosine kinases, including Abl	Xq22.3-q23	suppression of doublecortin expression by RNAi inhibits neuronal migration in rat neocortex
Lissencephaly (type I): X-linked (XLAG)	Lissencephaly with ambiguous genitalia	*ARX*	Aristaless-related homeodomain transcription factor	Xp22.13	Targeted mutation of *Arx*

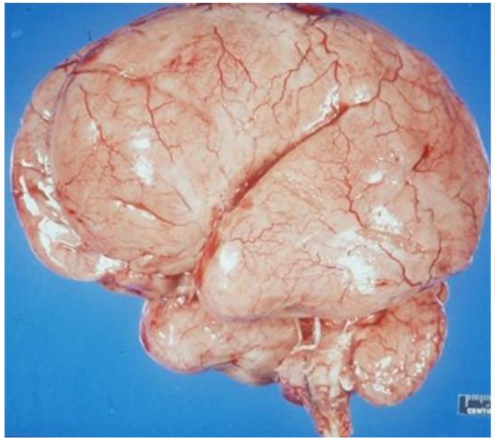

Layer
Normal
Mutations
LIS1
DCX
ARX
TUBA1A
I
II
III
IV
V
VI
wm
4 layer cortex with posterior predominance
4 layer cortex with anterior predominance
3 layer cortex
2 layer cortex

Lissencephaly Type I

Isolated lissencephaly sequence occurs in patients with **deletions of the LIS1 gene**

- **LIS1** encodes the non-catalytic subunit of **platelet activating factor acetyl hydrolase**: Involved in the regulatory pathway for dynein – Important for neuronal migration
- More severe occipital/posterior parietal
- **LIS1 + 14-3-3 GENES** (short arm of chromosome 17): **Miller-Dieker Syndrome** (craniofacial malformations due to 14-3-3; lissencephaly due to LIS1).

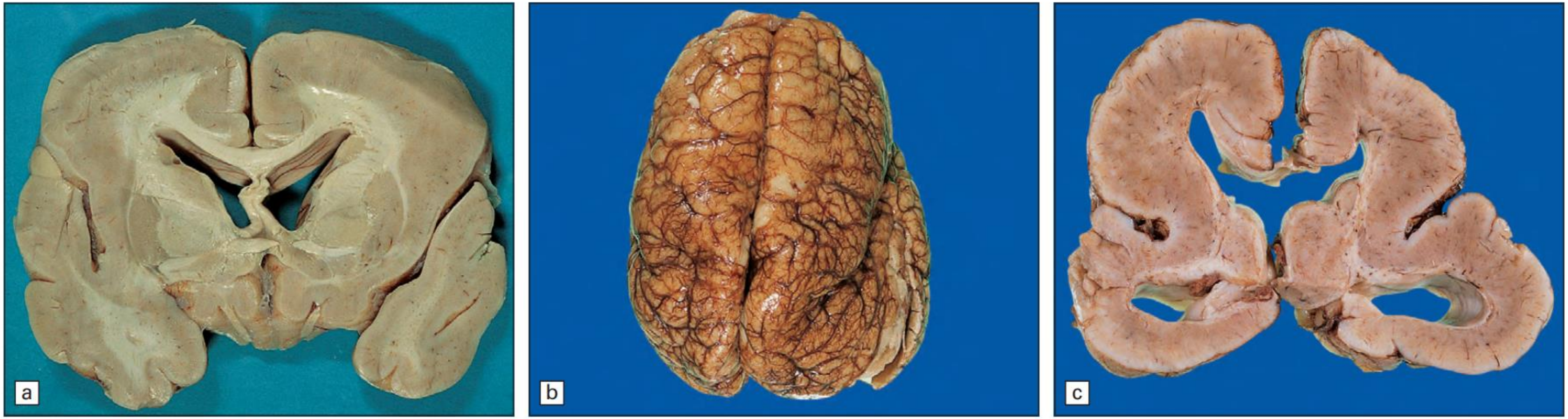
Doublecortin (DCX) gene mutation: X-linked dominant (Xq22); more severe anteriorly; **lissencephaly in males**, subcortical band heterotopia in females (see later).

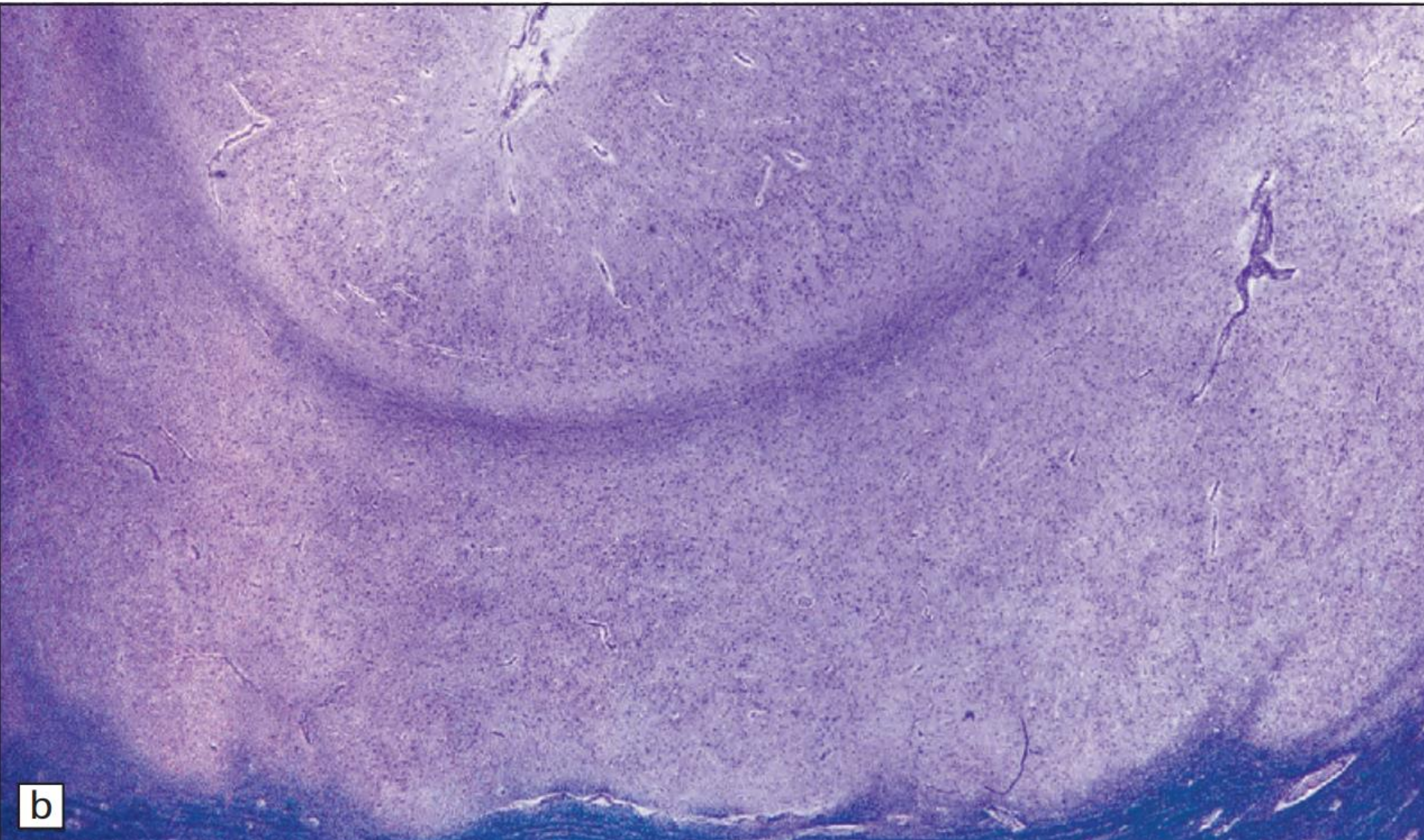


Agyria ~ Pachygyria

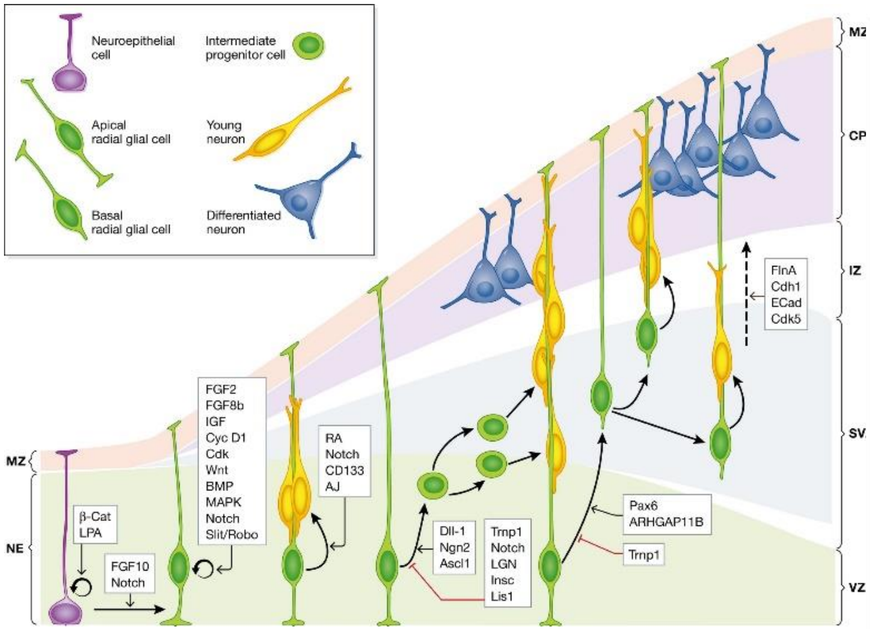
Agyria and pachygyria refer to an absence of gyri and sulci, or reduced numbers of broadened convolutions, respectively, associated both macroscopically and microscopically with a thickened cortical ribbon

- Molecular layer.
- Thin, external neuronal layer.
- Sparsely cellular layer with a tangential myelin fiber plexus.
- A thick, inner neuronal layer, which splits in its deeper zone into columns of cells (lissencephaly type I).
- Posterior–anterior gradient of severity in LIS-I cases
- Anterior–posterior gradient of severity in DCX cases.




b

Malformations of Cortical Development



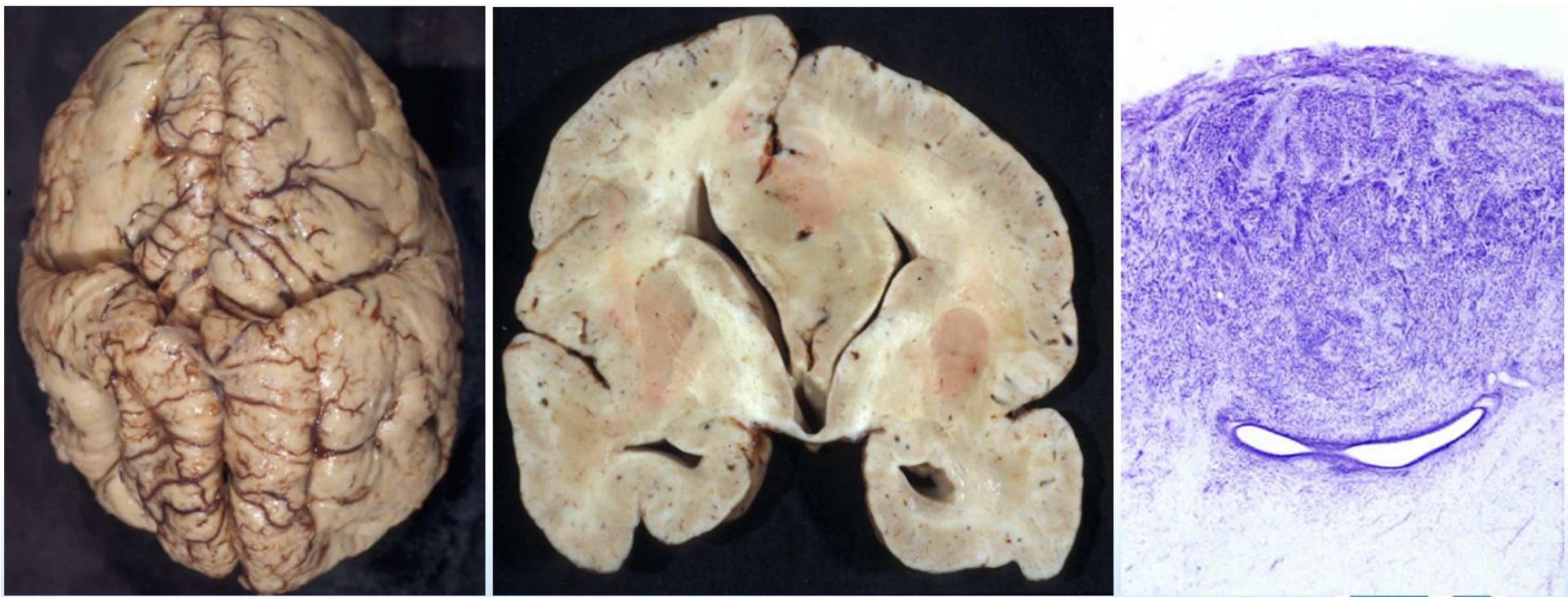
Malformations of cortical development with associated genes and clinical features

Developmental stage	Cortical malformation	Genetic cause	Clinical features
Abnormal neurogenesis			
	Microcephaly	*ASPM*	Mental retardation, not generally associated with epilepsy, autosomal recessive inheritance
		Microcephalin	
		CDK5RAP2	
		CENPJ	
	Hemimegalencephaly	Unknown	Mental retardation, early onset seizures (frequently intractable epilepsy), +/- neurocutaneous syndrome
	Focal cortical dysplasia	Unknown	Most common, focal and generalized Seizures
Abnormal neuronal migration			
	Periventricular heterotopia	*FLNA*	Normal intelligence, adolescent onset seizures, X-linked disorder with male lethality
		ARFGEF2	Mental retardation, microcephaly, autosomal recessive inheritance, rare
	Subcortical band heterotopia	*DCX*	Subcortical band heterotopia in females, mental retardation, epilepsy, X-linked disorder
	Lissencephaly	*LIS1*	Miller-Dieker syndrome (characteristic facial features), autosomal dominant inheritance
		DCX	Lissencephaly in males, X-linked
		TUBA1A	Lissencephaly, clinical features similar those caused by *LIS1* and *DCX*, de novo mutations
		ARX	Associated with ambiguous genitalia, hypothalamic dysfunction, neonatal epilepsy, X-linked disorder
		RELN	Associated with cerebellar hypoplasia, epilepsy, autosomal recessive inheritance
Abnormal arrest in neuronal migration			
	Cobblestone lissencephaly	*Fukutin*	Fukuyama congenital muscular dystrophy
		POMGnT1	Muscle-eye-brain disease
		POMT1	Walker-Warburg Syndrome

Lissencephaly Type II

LISSENCEPHALY TYPE II **(COBBLESTONE)**

- Autosomal recessive
- Cortex unlayered disorganized with cobblestone surface and thickened meninges
- Variable muscular and ocular involvement with CNS disorders (muscle-eye-brain disorders)

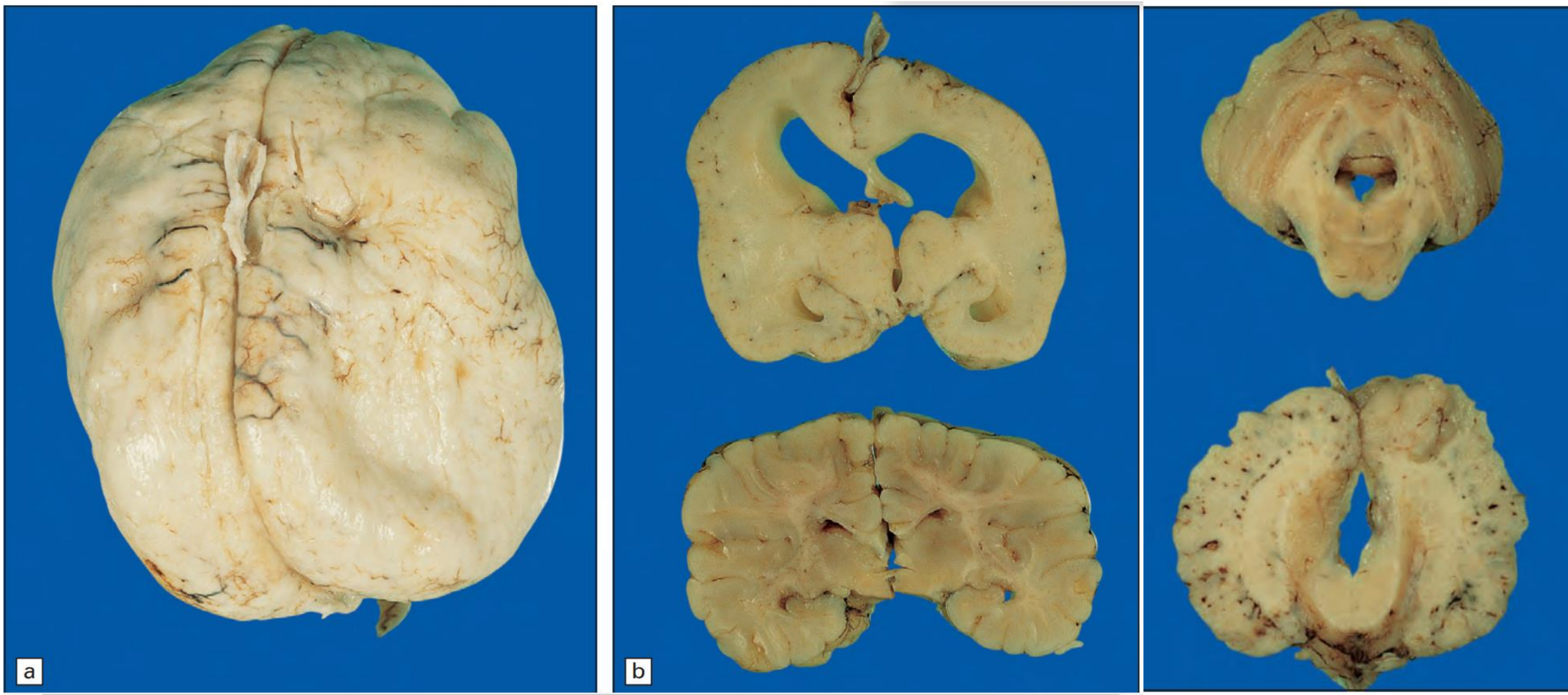


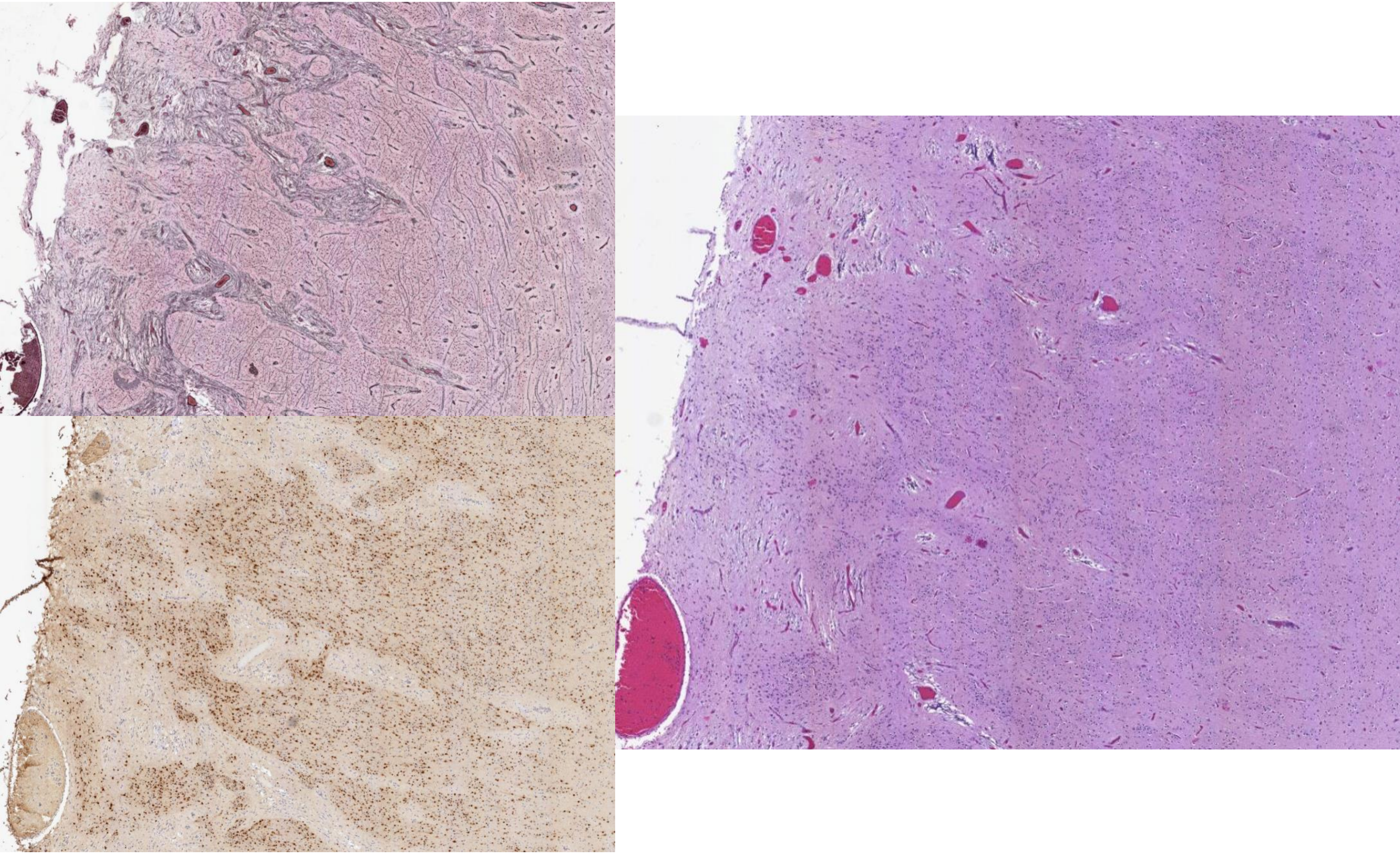
Lissencephaly Type II

Walker–Warburg syndrome
– Also known as HARD+E syndrome (hydrocephalus, agyria, retinal dysplasia, encephalocele) and cerebro-ocular dysplasia–muscular dystrophy syndrome
– **Cobblestone lissencephaly**, **cerebellar dysplasia** and **vermal agenesis**, **hydrocephaly**, occipital **encephalocele**, congenital muscular dystrophy
– Variety of ocular anomalies
– Die in infancy
– Associated with mutations in **POMT1** and **POMT2** genes

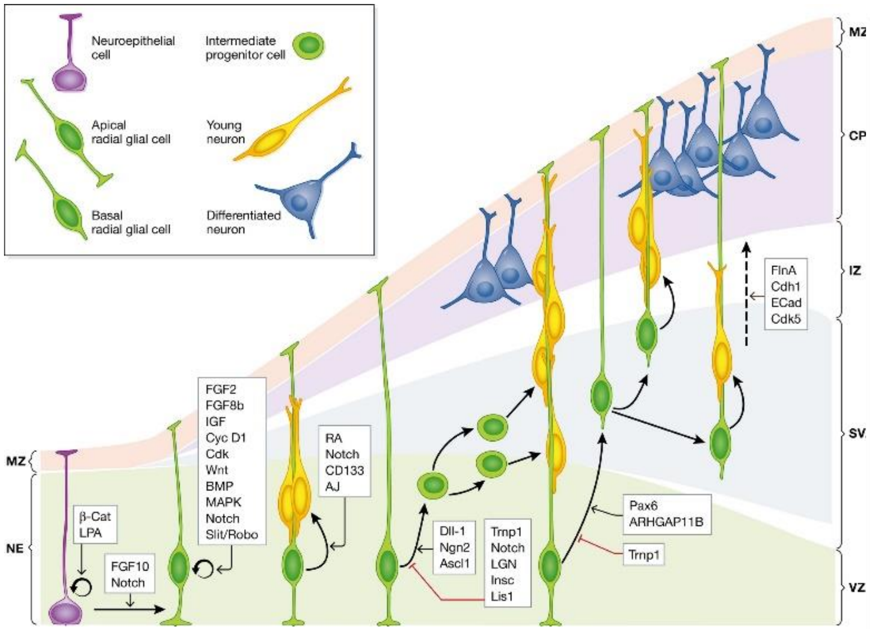
Muscle-Eye-Brain disease
– Generalized muscle weakness, contractures, seizures, eye anomalies, cobblestone lissencephaly
– Associated with mutations in POMGnT1, LARGE, and FKRP

Lissencephaly Type II





Malformations of Cortical Development



Malformations of cortical development with associated genes and clinical features

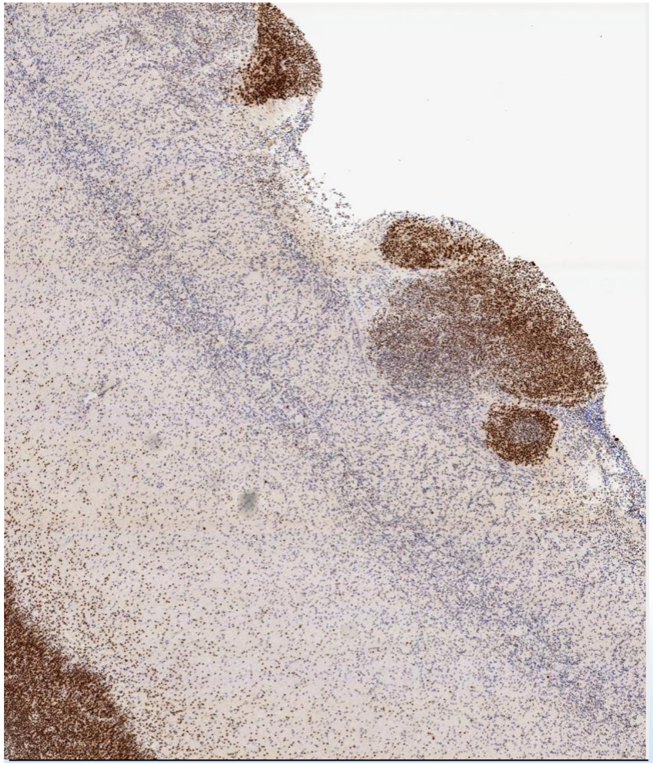
Developmental stage	Cortical malformation	Genetic cause	Clinical features
Abnormal neurogenesis			
	Microcephaly	*ASPM*	Mental retardation, not generally associated with epilepsy, autosomal recessive inheritance
		Microcephalin	
		CDK5RAP2	
		CENPJ	
	Hemimegalencephaly	Unknown	Mental retardation, early onset seizures (frequently intractable epilepsy), +/- neurocutaneous syndrome
	Focal cortical dysplasia	Unknown	Most common, focal and generalized Seizures
Abnormal neuronal migration			
	Periventricular heterotopia	*FLNA*	Normal intelligence, adolescent onset seizures, X-linked disorder with male lethality
		ARFGEF2	Mental retardation, microcephaly, autosomal recessive inheritance, rare
	Subcortical band heterotopia	*DCX*	Subcortical band heterotopia in females, mental retardation, epilepsy, X-linked disorder
	Lissencephaly	*LIS1*	Miller-Dieker syndrome (characteristic facial features), autosomal dominant inheritance
		DCX	Lissencephaly in males, X-linked
		TUBA1A	Lissencephaly, clinical features similar those caused by *LIS1* and *DCX*, de novo mutations
		ARX	Associated with ambiguous genitalia, hypothalamic dysfunction, neonatal epilepsy, X-linked disorder
		RELN	Associated with cerebellar hypoplasia, epilepsy, autosomal recessive inheritance
Abnormal arrest in neuronal migration			
	Cobblestone lissencephaly	*Fukutin*	Fukuyama congenital muscular dystrophy
		POMGnT1	Muscle-eye-brain disease
		POMT1	Walker-Warburg Syndrome

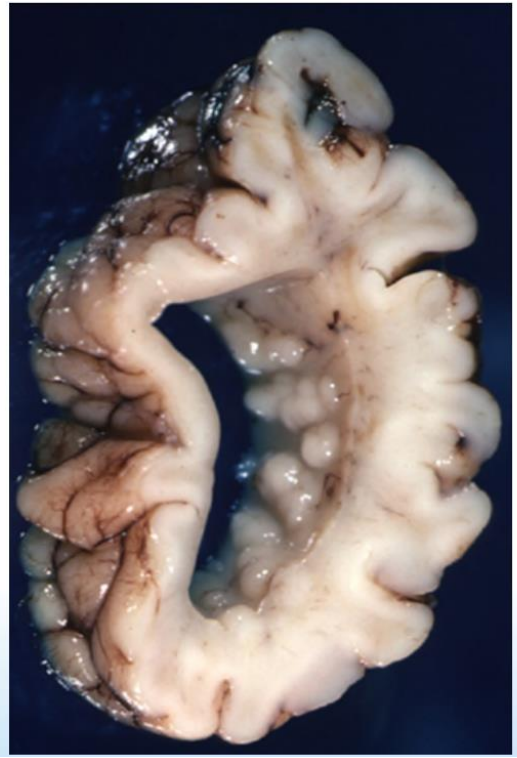
Gray Matter Heterotopia

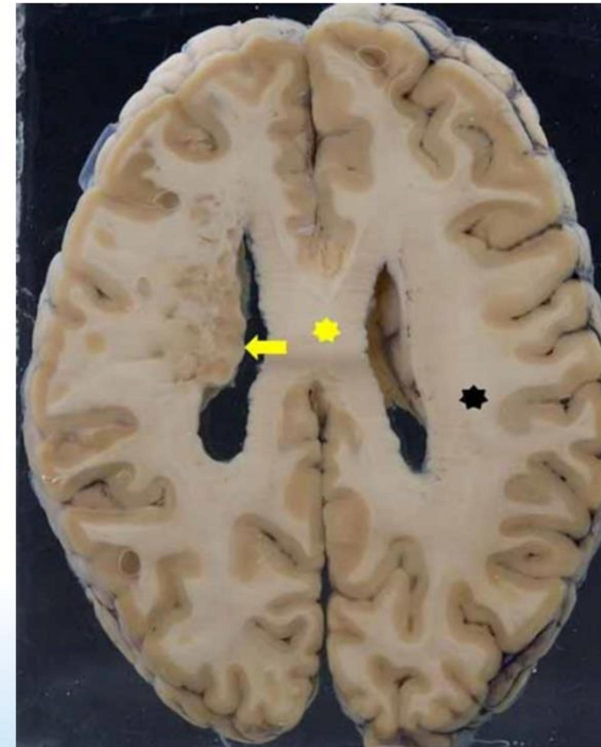
- Clusters of neurons and glia that form a region of gray matter in an abnormal location
- May be single or multiple, line ventricles, in deep white matter, subcortical white matter, leptomeninges
- Overlying cortex can be normal or disrupted
- May have normal intelligence and normal neurologic exam

- **Nodular Heterotopia**
- **Band Subcortical Heterotopia**

Nodular Heterotopia



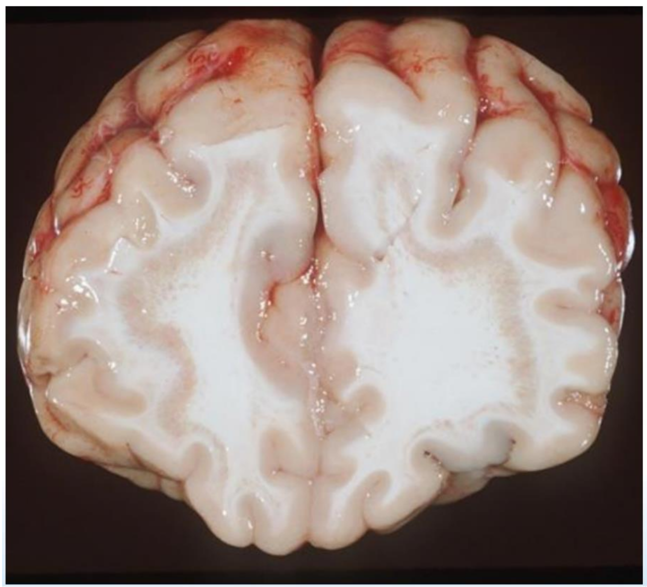


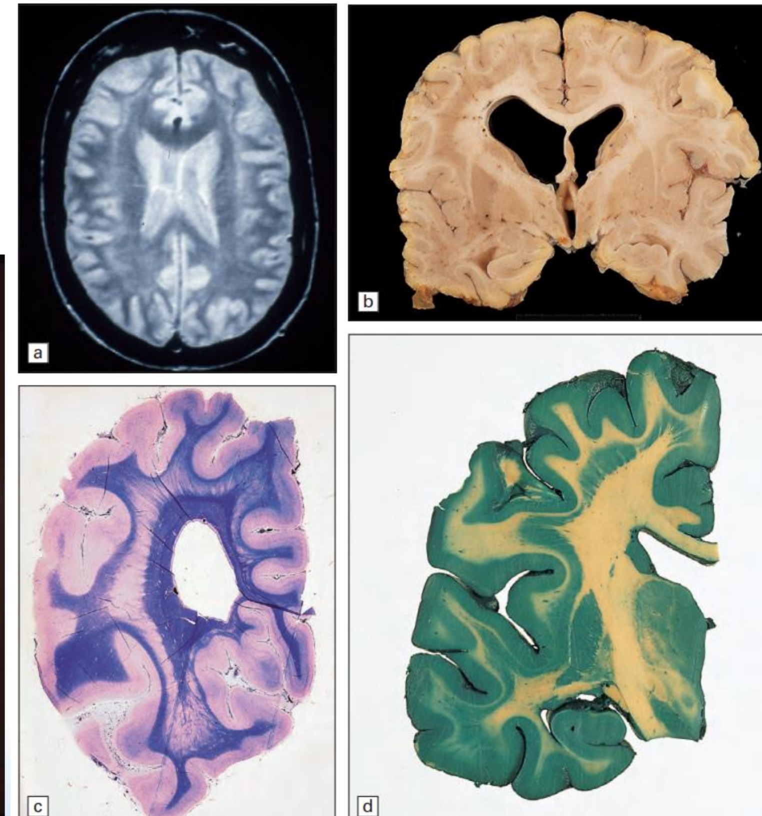


Band Heterotopia

Bilateral bands of heterotopic gray matter in the white matter located between the lateral ventricular walls and the cortex:
– Overlying cortex may be normal or have simplified gyral pattern
– Mild to moderate mental retardation
– Seizures, often with later onset

Mutations of **DCX**
Predominant in females (!)

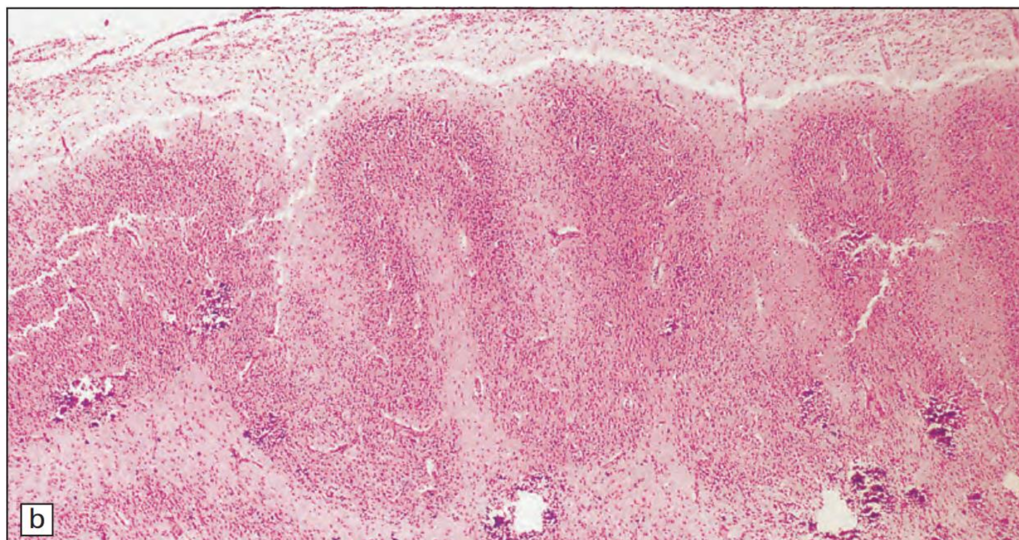




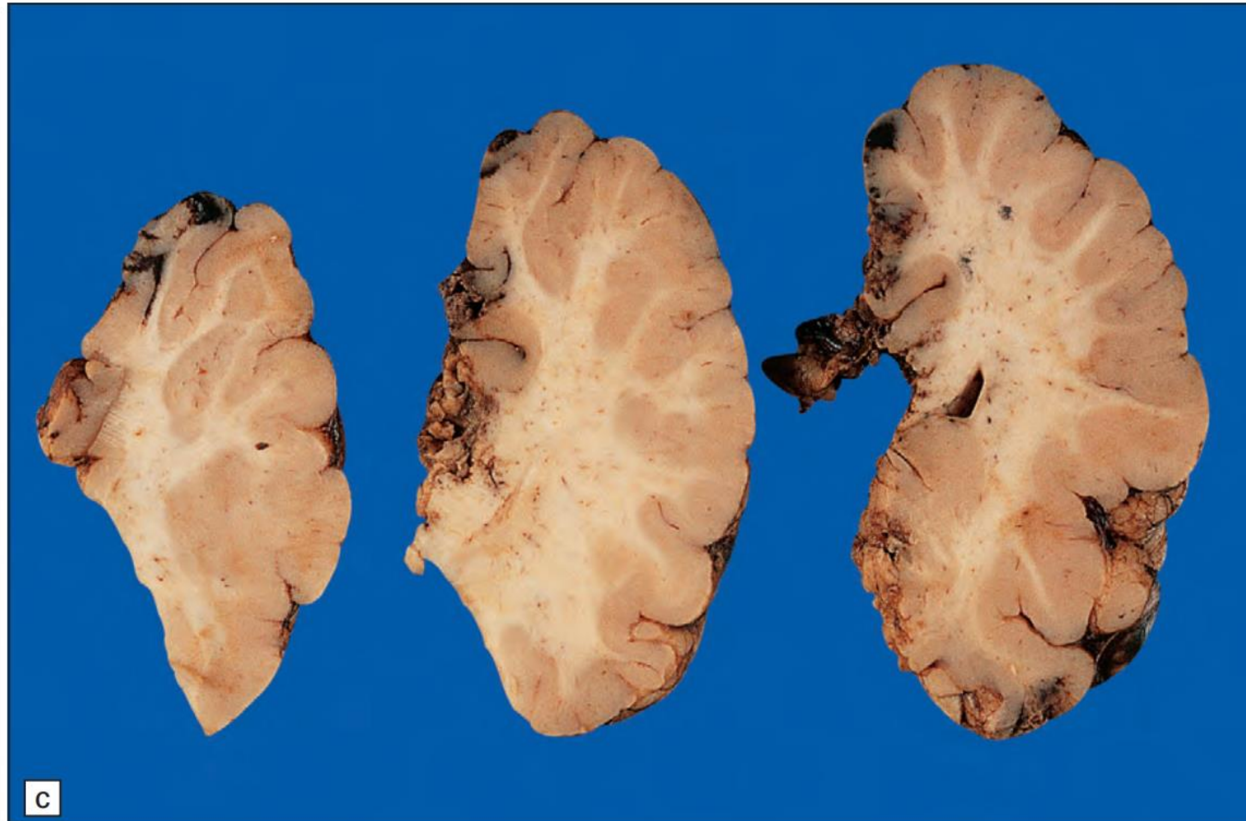
Polymicrogyria

Hyperconvoluted cortical ribbon of miniature, individually thin gyri, which are often fused together or piled on top of one another.

Acquired in the context of **intrauterine ischemia** (including encephaloclastic lesions), twinning, or **intrauterine infection with cytomegalovirus**, varicella–zoster virus, toxoplasmosis, or syphilis.
Can also be familial, associated with metabolic diseases and peroxisomal disorders.



Polymicrogyria

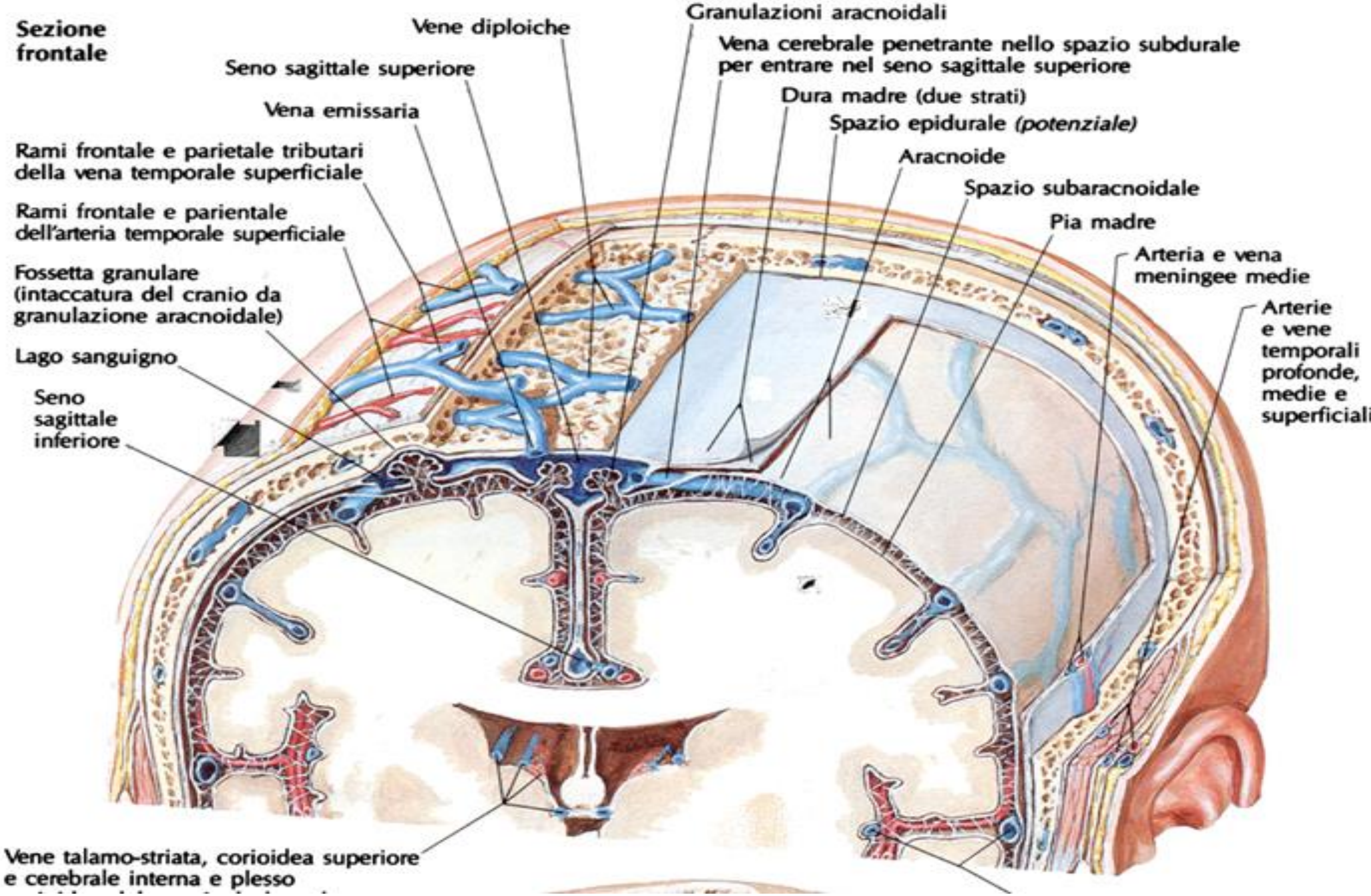


The Meninges

V. Kandisnky – Squares with concentric circles

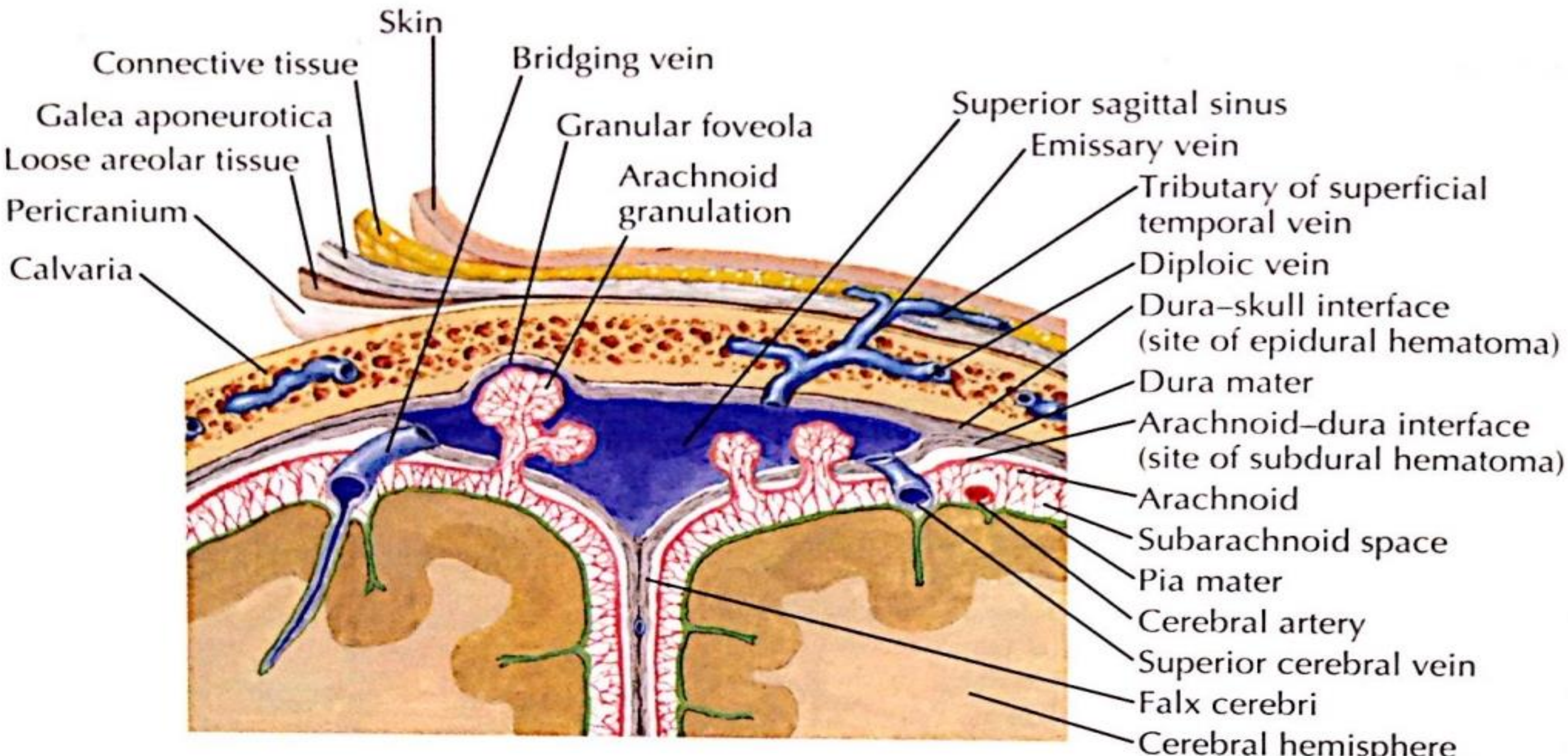

Subarachnoidal Space
Subdural Space
Epidural Space
Dura Mater
Arachnoid
Pia Mater

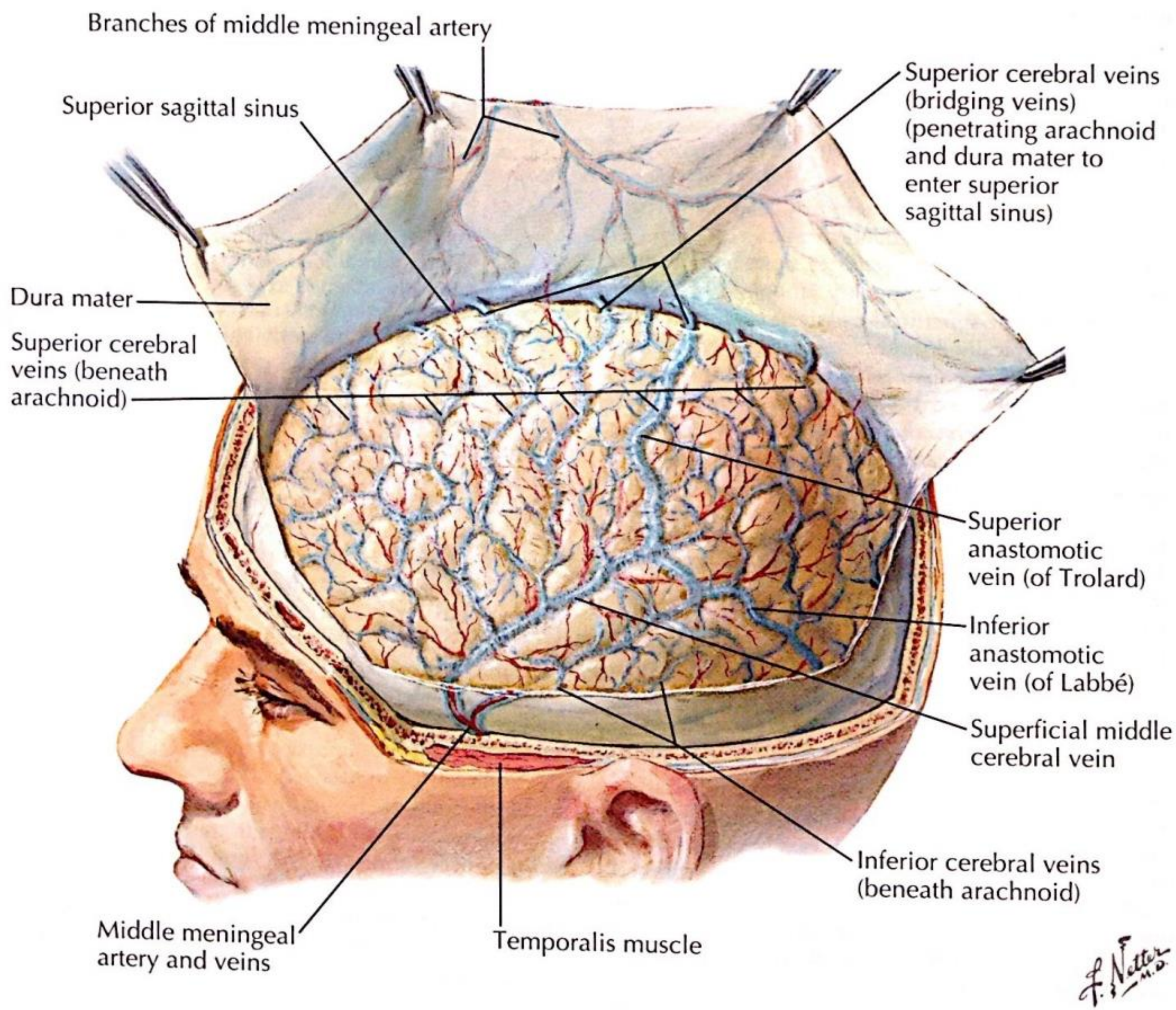
Optic Nerve



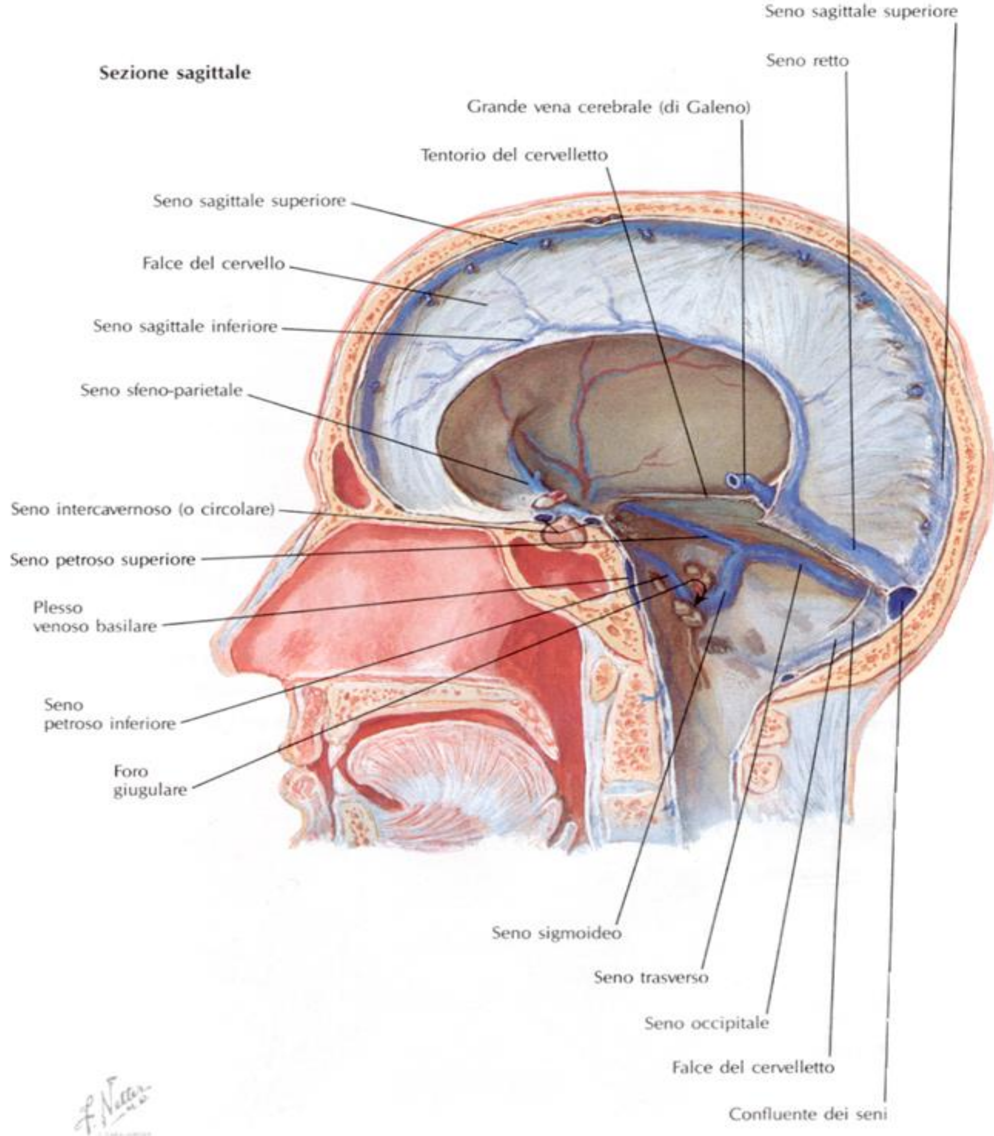
Sezione frontale
Vene diploiche
Granulazioni aracnoidali
Vena cerebrale penetrante nello spazio subdurale per entrare nel seno sagittale superiore
Seno sagittale superiore
Dura madre (due strati)
Vena emissaria
Spazio epidurale *(potenziale)*
Rami frontale e parietale tributari della vena temporale superficiale
Aracnoide
Spazio subaracnoidale
Rami frontale e parientale dell'arteria temporale superficiale
Pia madre
Arteria e vena meningee medie
Fossetta granulare (intaccatura del cranio da granulazione aracnoidale)
Arterie e vene temporali profonde, medie e superficiali
Lago sanguigno
Seno sagittale inferiore
Vene talamo-striata, corioidea superiore e cerebrale interna e plesso

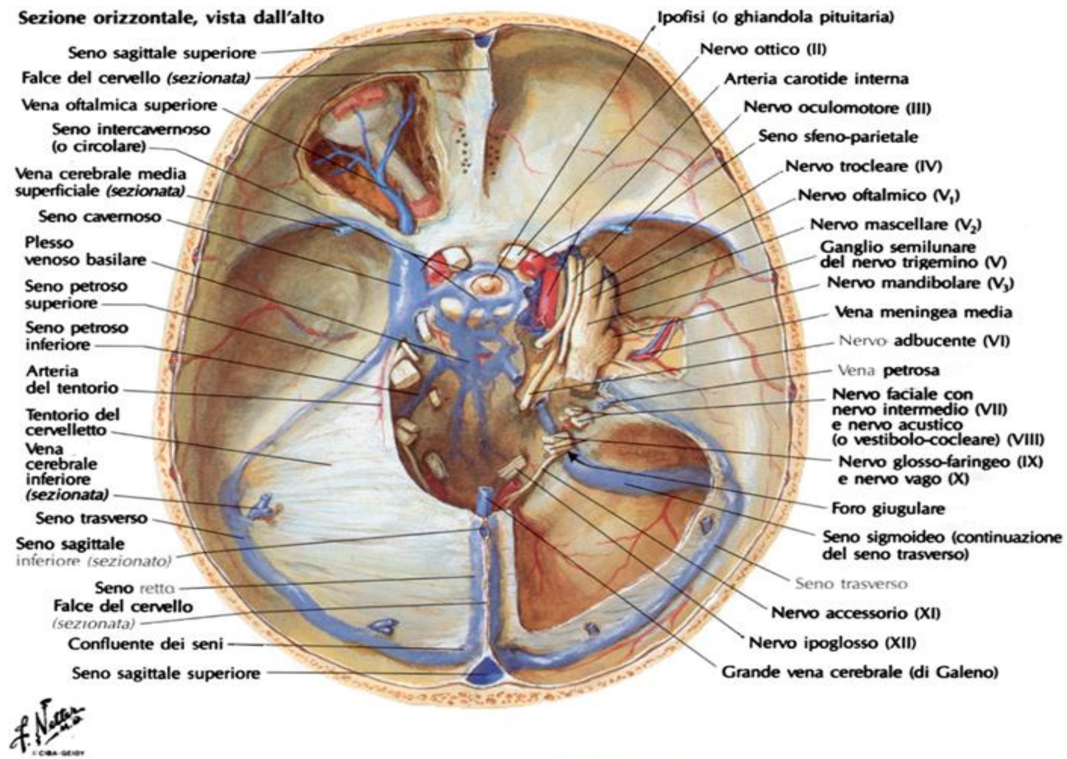
Meninges and Superficial Cerebral Veins



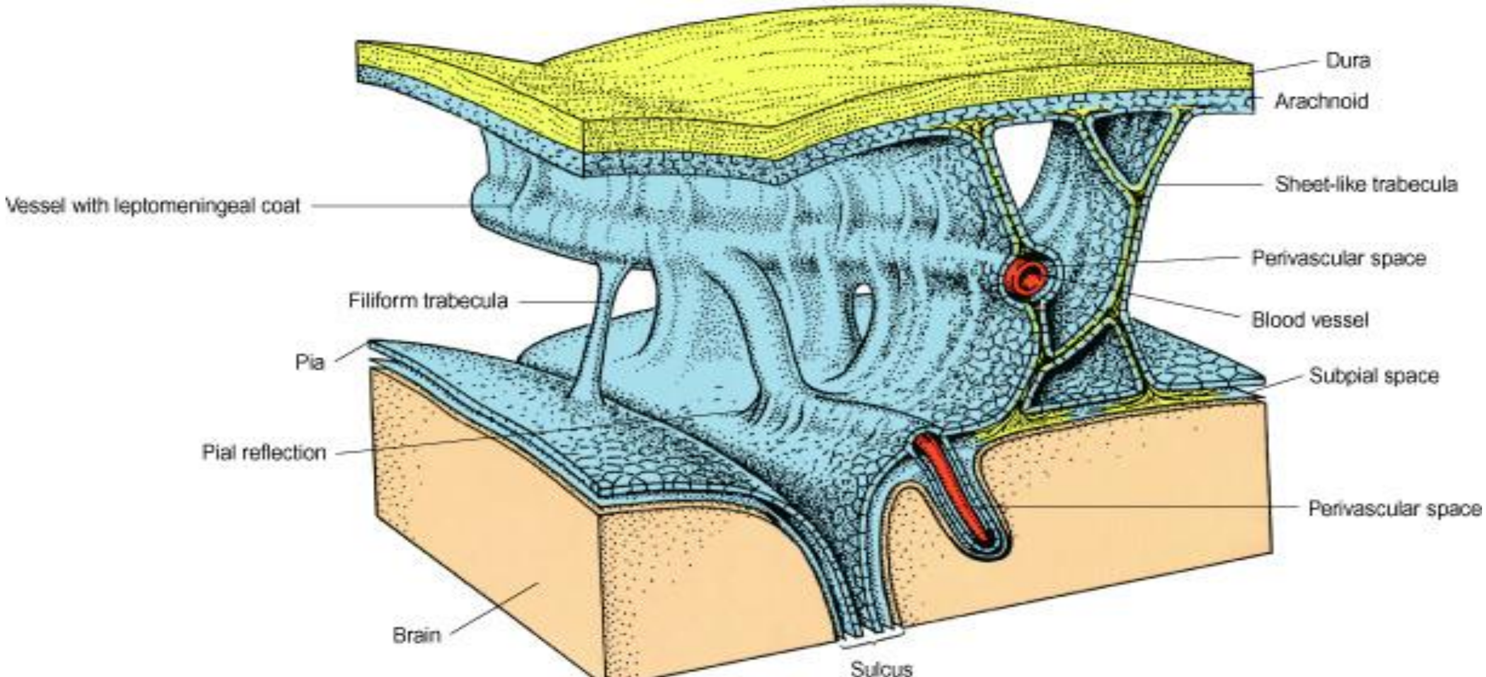

Branches of middle meningeal artery
Superior sagittal sinus
Superior cerebral veins (bridging veins) (penetrating arachnoid and dura mater to enter superior sagittal sinus)
Dura mater
Superior cerebral veins (beneath arachnoid)
Superior anastomotic vein (of Trolard)
Inferior anastomotic vein (of Labbé)
Superficial middle cerebral vein
Inferior cerebral veins (beneath arachnoid)
Middle meningeal artery and veins
Temporalis muscle
F. Netter M.D.

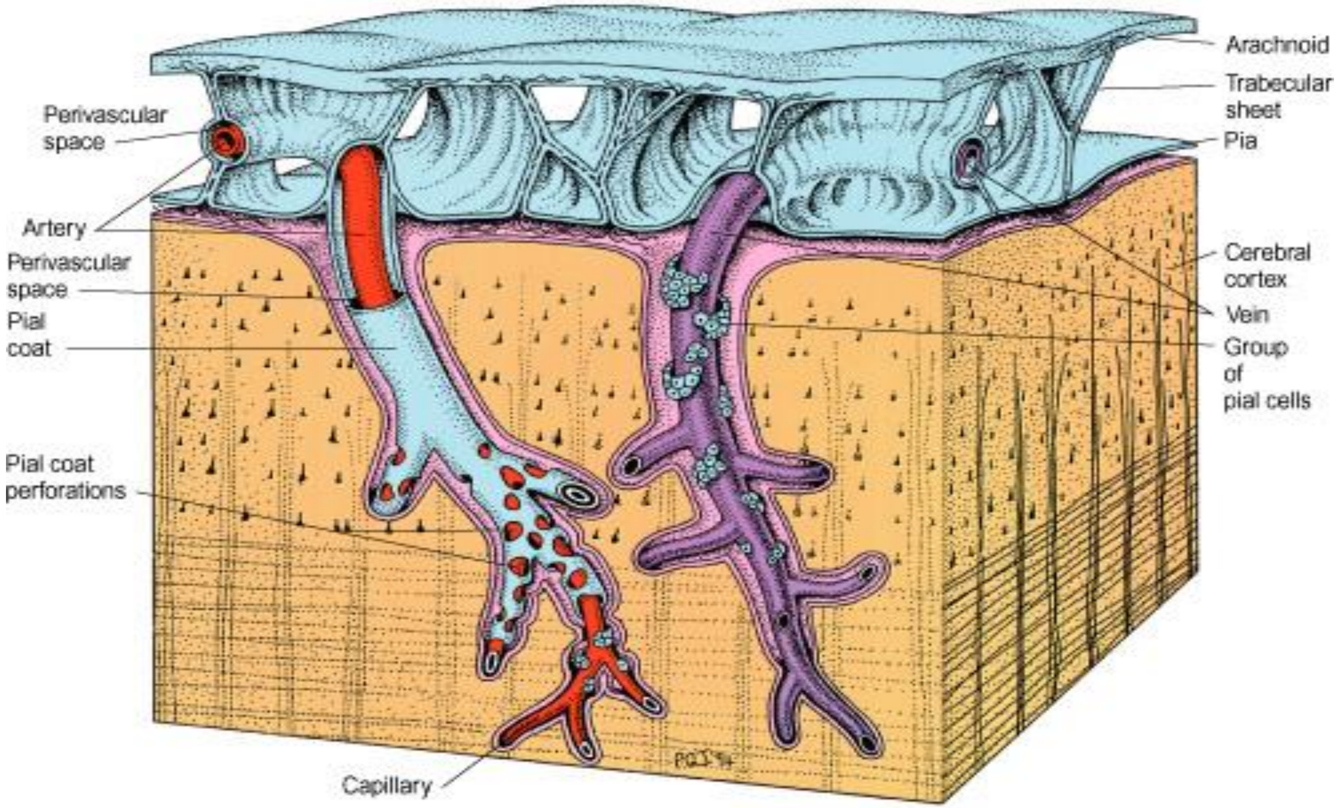
Sezione sagittale



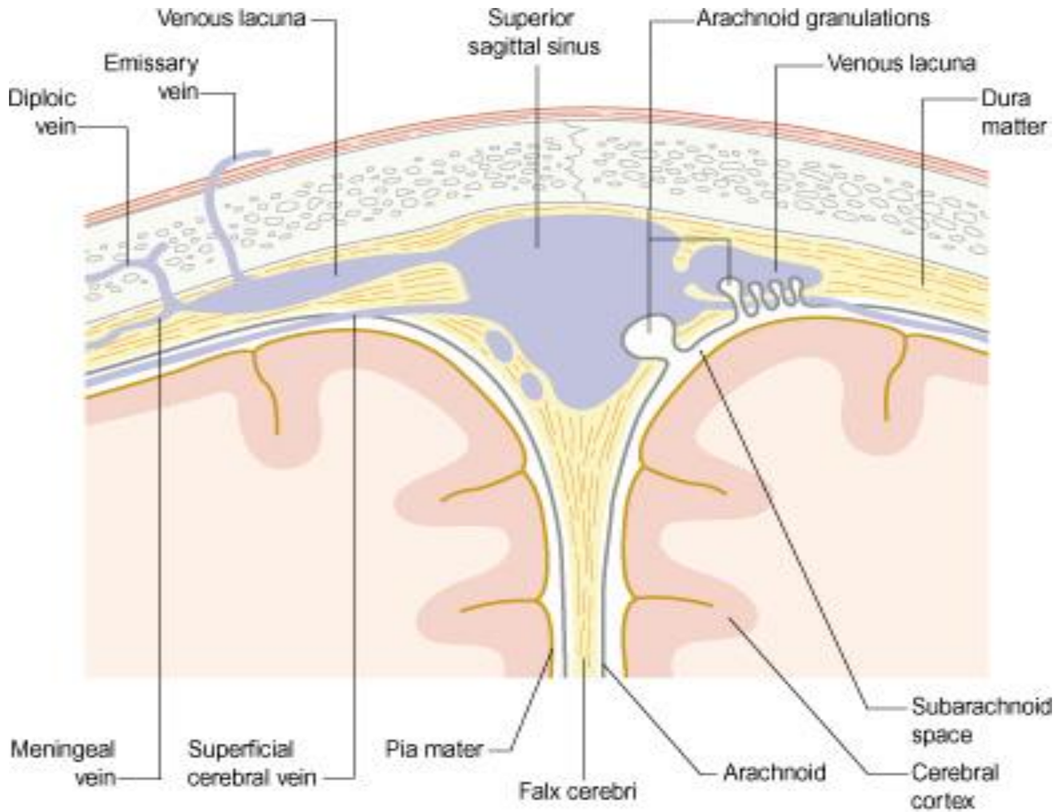


Sezione frontale attraverso i seni cavernosi


Dura
Arachnoid
Sheet-like trabecula
Vessel with leptomeningeal coat
Perivascular space
Filiform trabecula
Blood vessel
Pia
Subpial space
Pial reflection
Perivascular space
Brain
Sulcus



Arachnoid
Trabecular sheet
Pia
Perivascular space
Artery
Perivascular space
Pial coat
Cerebral cortex
Vein
Group of pial cells
Pial coat perforations
Capillary


Venous lacuna
Superior sagittal sinus
Arachnoid granulations
Emissary vein
Venous lacuna
Diploic vein
Dura matter
Meningeal vein
Superficial cerebral vein
Pia mater
Falx cerebri
Arachnoid
Subarachnoid space
Cerebral cortex

CLINICAL CASE 1

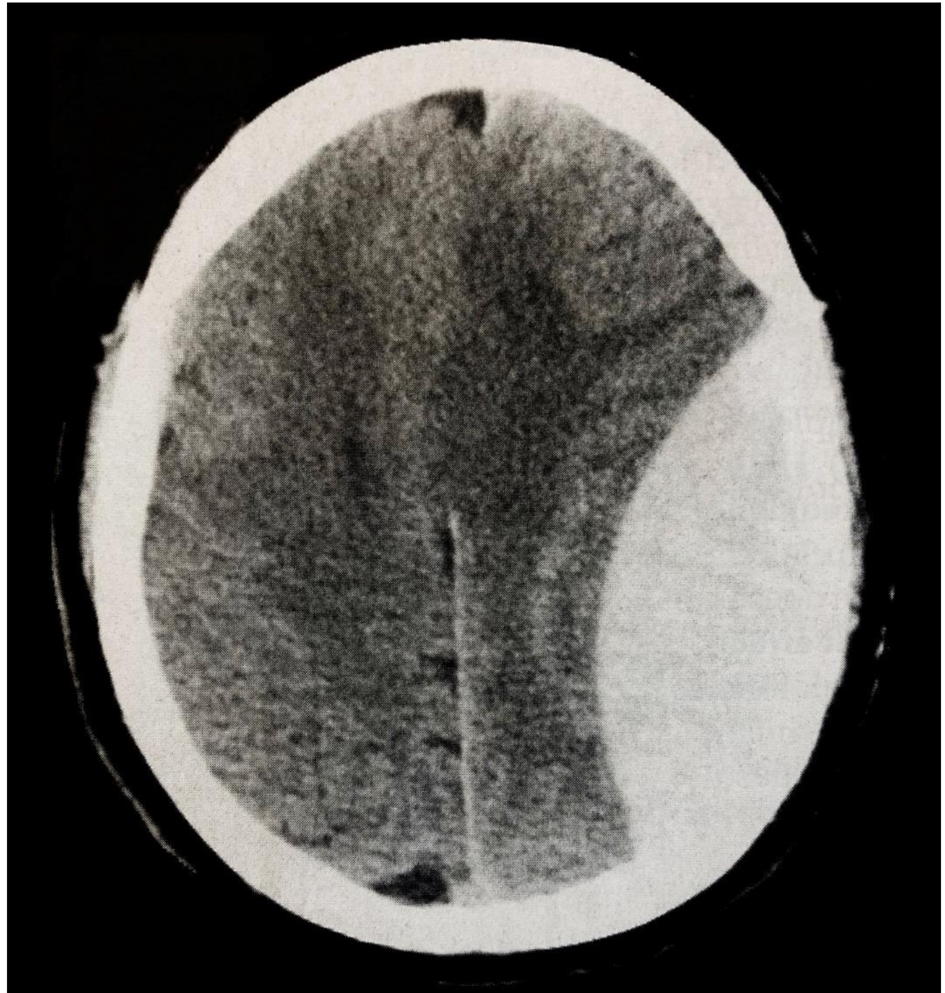
64-year-old Male

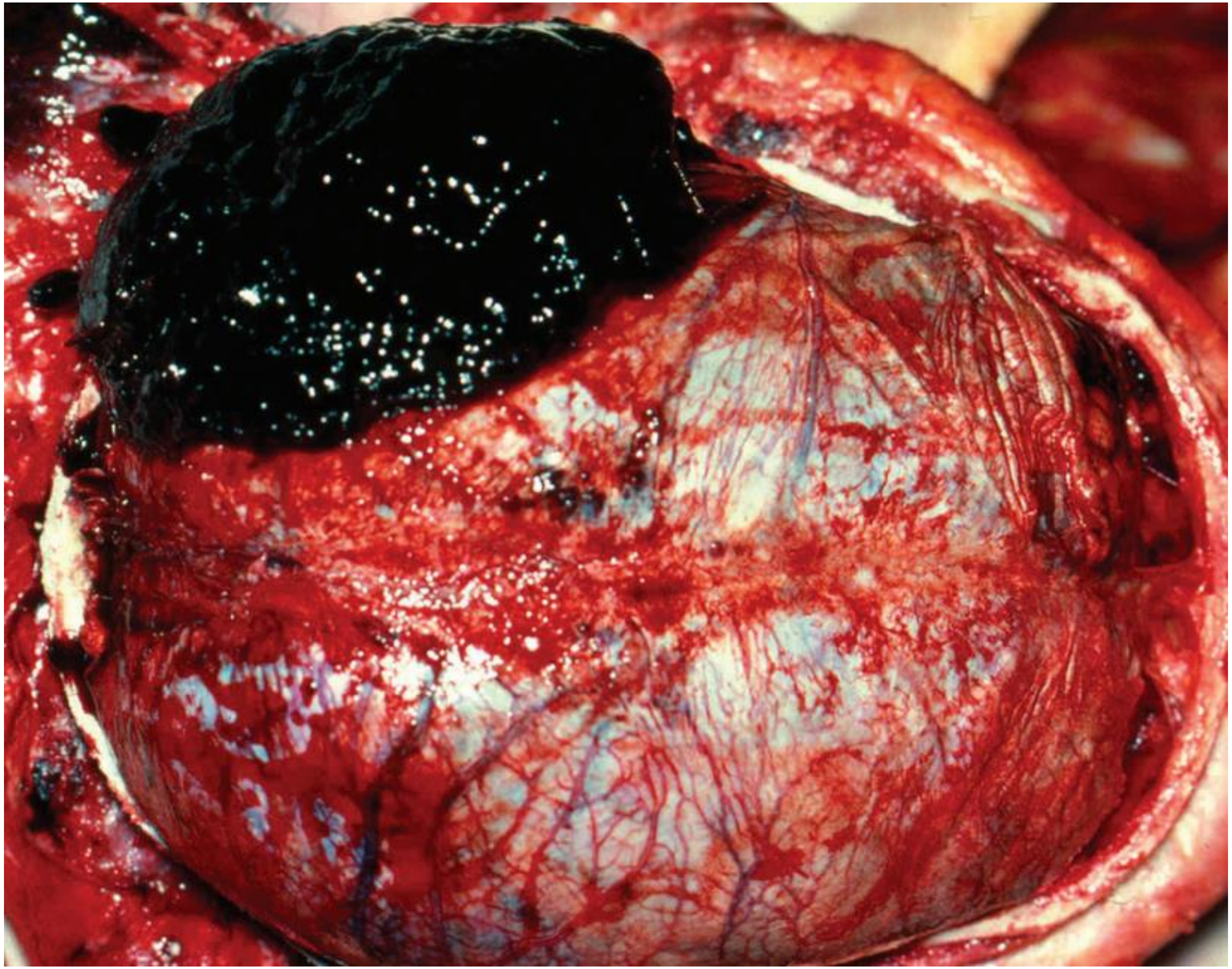
Found unresponsive following head injury. Prior to ER examination, the patient fell down the stairs due to alcohol intoxication.. Reported loss of consciousness for approx. 15 minutes following injury. Refused medical treatment and remained at home. The following morning, the patient was found unresponsive and had vomited during the night; patient was brought to the ER for neurological evaluation.

Physical examination: left forehead abrasion.
Neurological examination: unresponsive to commands, occasional agitated thrashing.
Left pupil not responsive to light. Right arm and leg did not move even in response to painful stimulation.

Where is the site of the lesion?
What’s the likely diagnosis?

CT SCAN





CLINICAL CASE 2

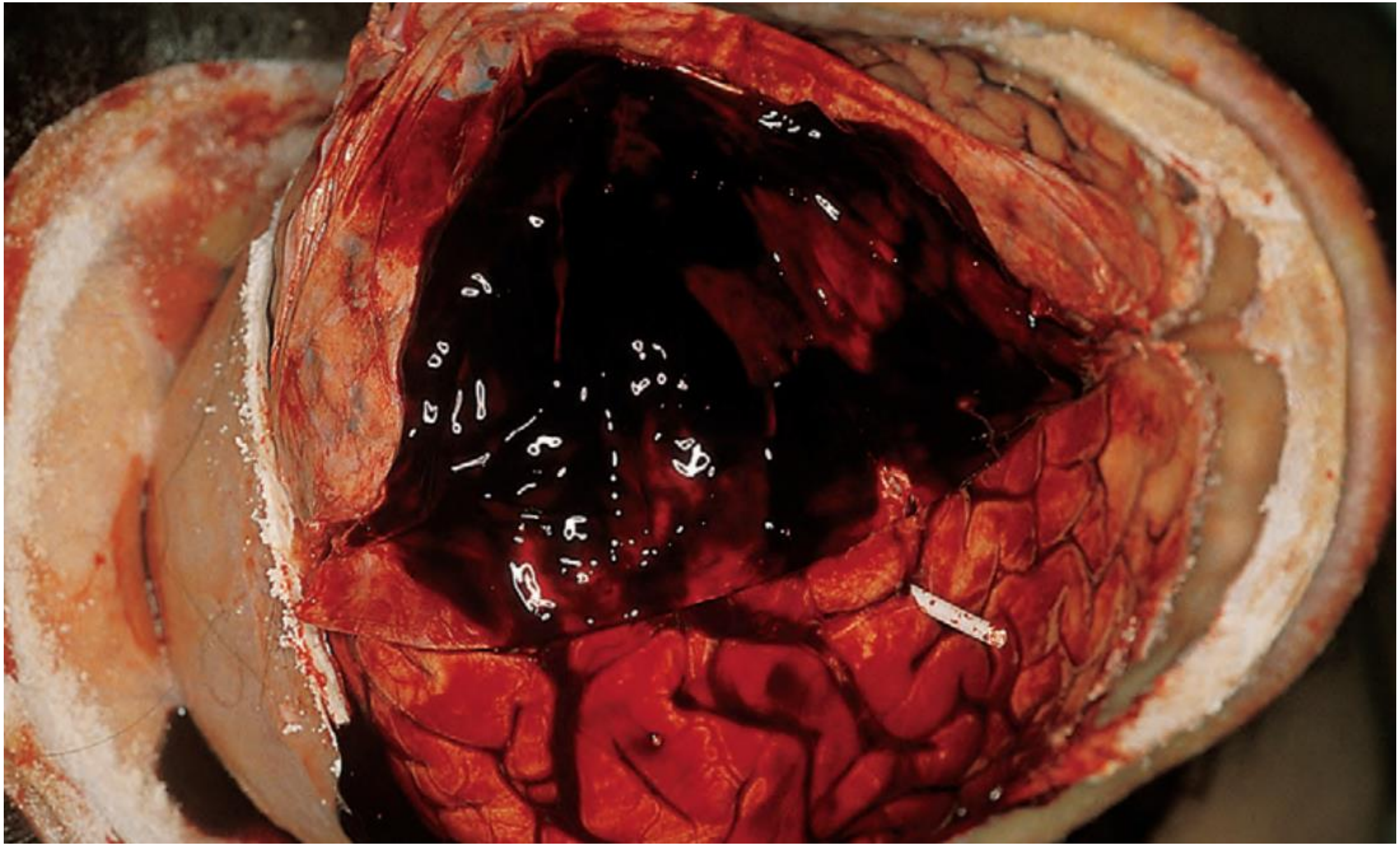
78-year-old Male

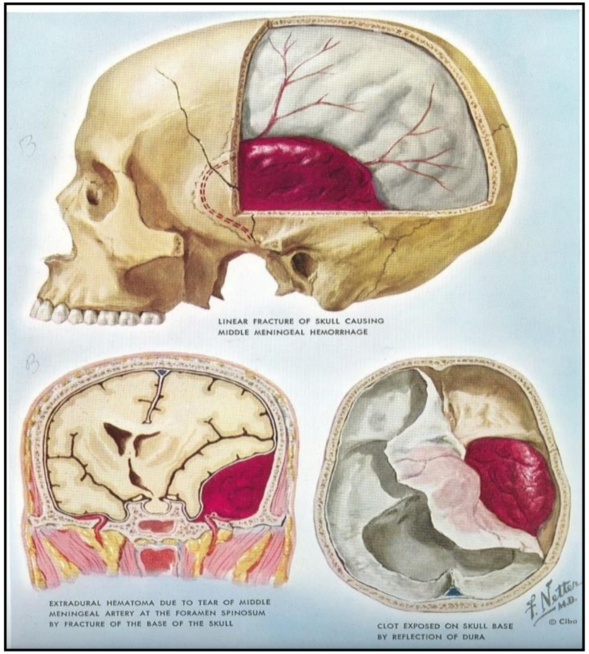
Prior motorbike accident 2 months ago. The patient does not report direct head trauma nor loss of consciousness during the accident. Examination in the ER following the accident evidenced no abnormalities; the patient was dismissed and sent home.
Ever since, the patient started complaining of generalized fatigue, right-sided headaches, worsening over the last month. The patient reports gait instability due to left leg weakness.

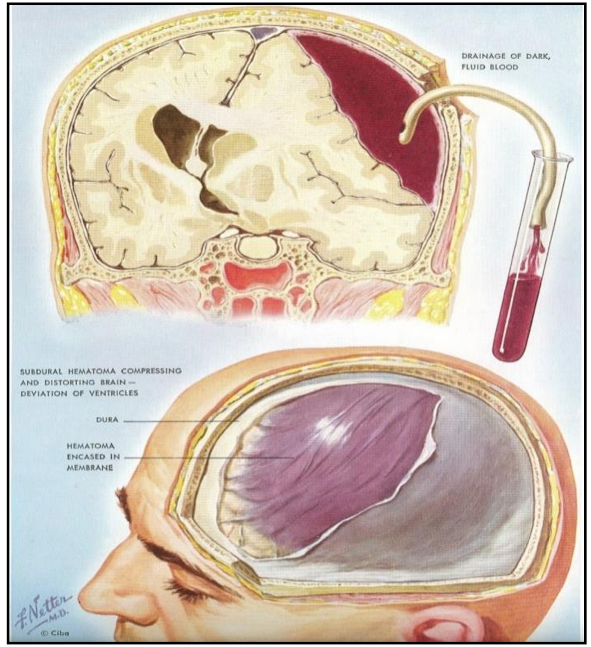
Neurological examination:
Alert and oriented, fluent speech.
Intact visual fields, extinction on the left to double simultaneous stimulation.
Mild left hemiparesis.
Normal reflexes.

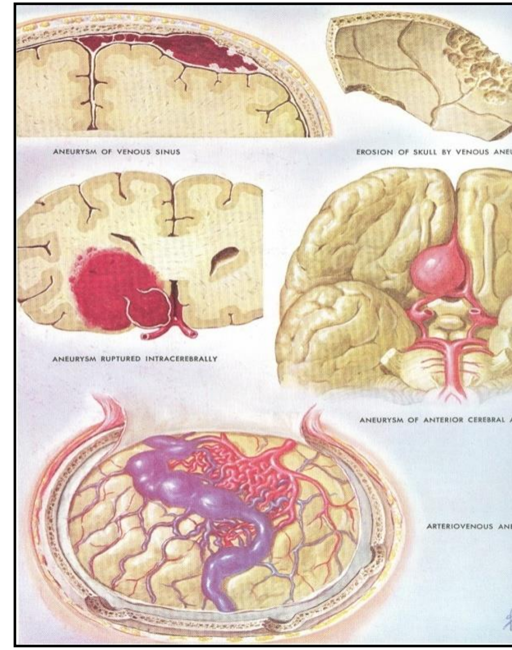
Where is the site of the lesion?
What’s the likely diagnosis?

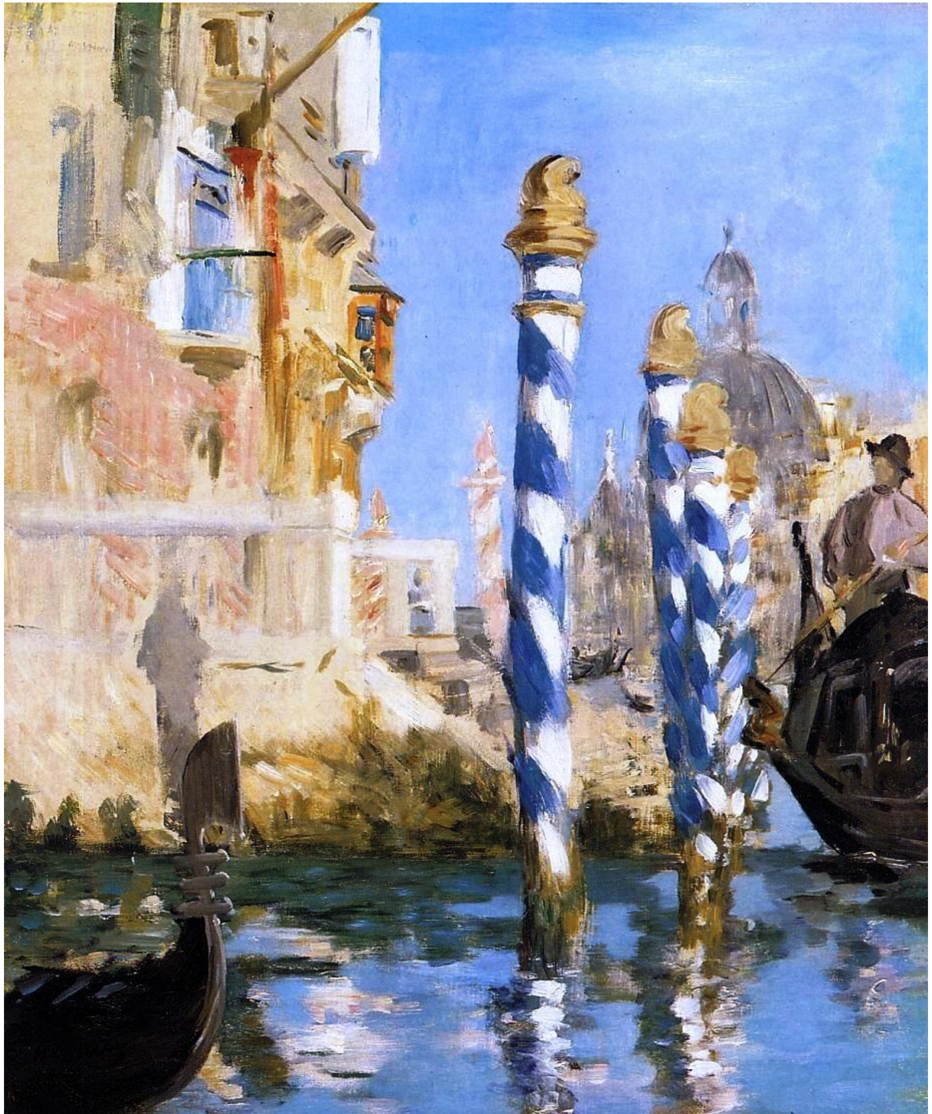
CT SCAN




LINEAR FRACTURE OF SKULL CAUSING
MIDDLE MENINGEAL HEMORRHAGE
EXTRADURAL HEMATOMA DUE TO TEAR OF MIDDLE
MENINGEAL ARTERY AT THE FORAMEN SPINOSUM
BY FRACTURE OF THE BASE OF THE SKULL
CLOT EXPOSED ON SKULL BASE
BY REFLECTION OF DURA
F. Netter M.D.
© Ciba

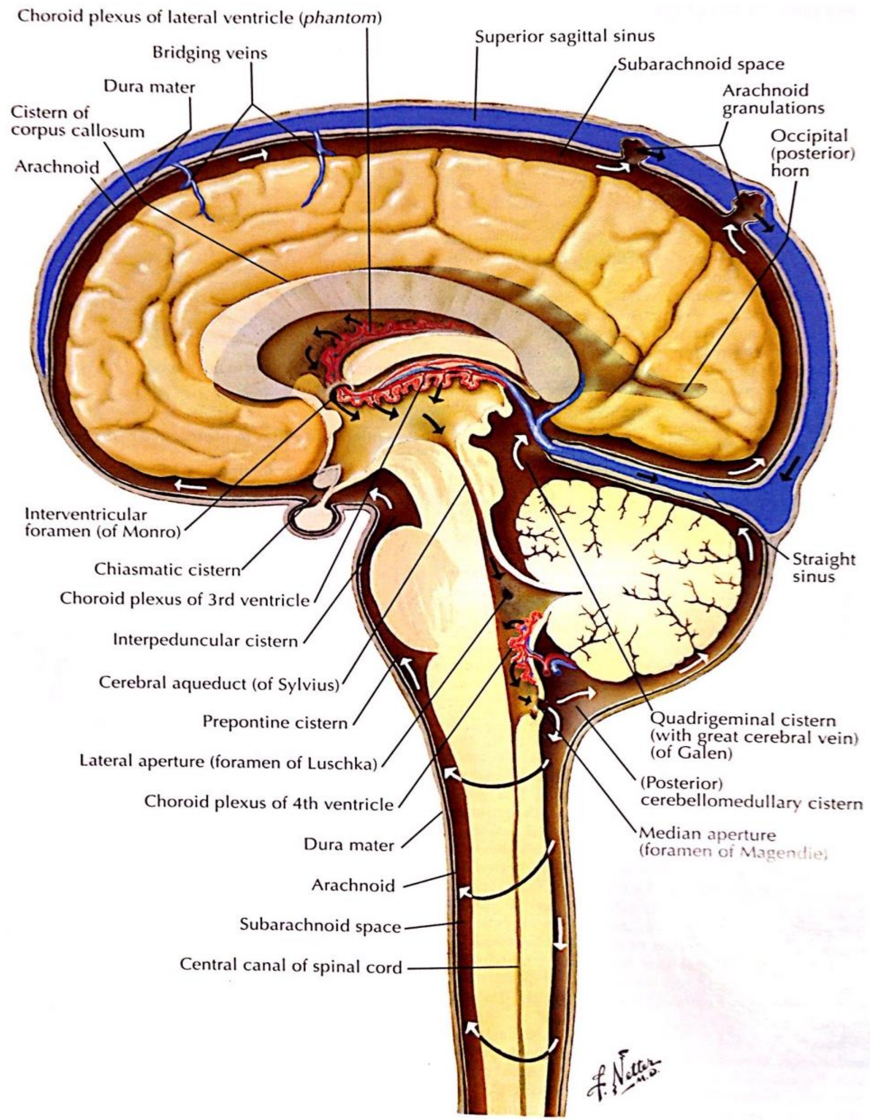

DRAINAGE OF DARK,
FLUID BLOOD
SUBDURAL HEMATOMA COMPRESSING
AND DISTORTING BRAIN —
DEVIATION OF VENTRICLES
DURA
HEMATOMA
ENCASED IN
MEMBRANE
F. Netter M.D.
© Ciba

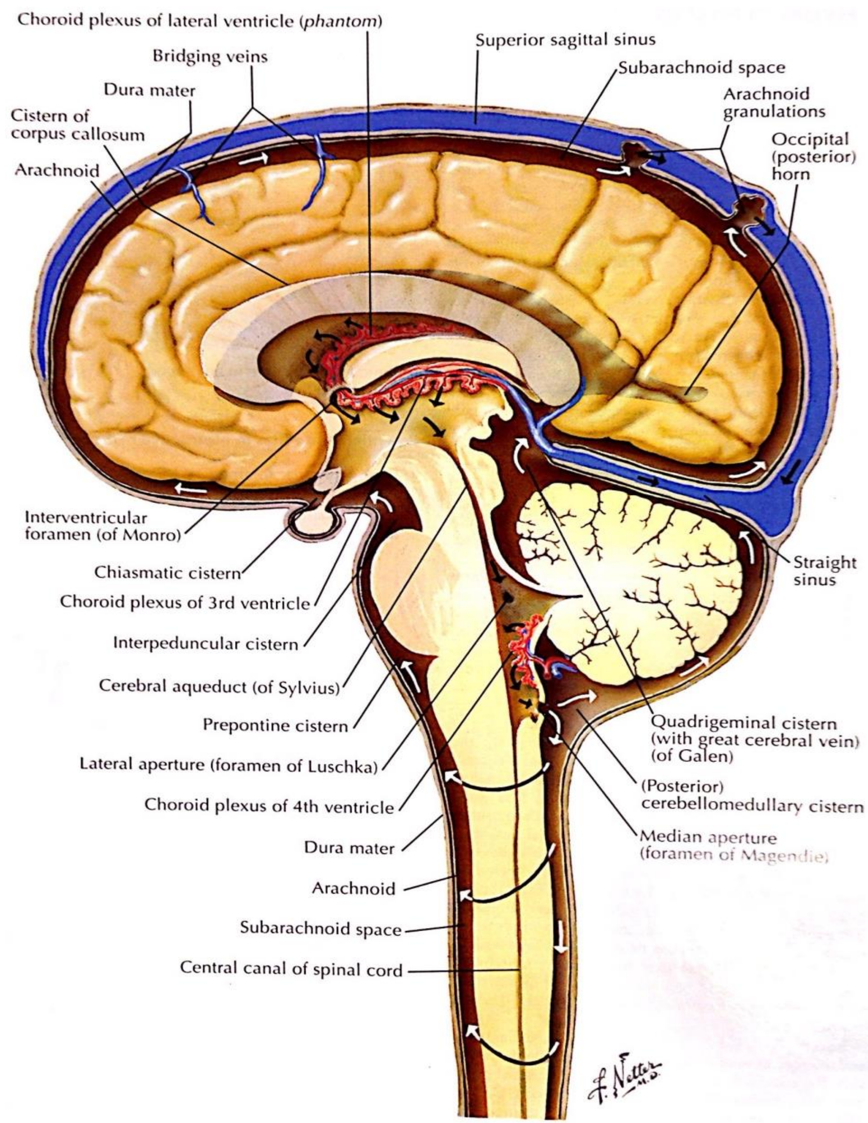

ANEURYSM OF VENOUS SINUS
EROSION OF SKULL BY VENOUS ANEURYS
ANEURYSM RUPTURED INTRACEREBRALLY
ANEURYSM OF ANTERIOR CEREBRAL ARTE
ARTERIOVENOUS ANEURY

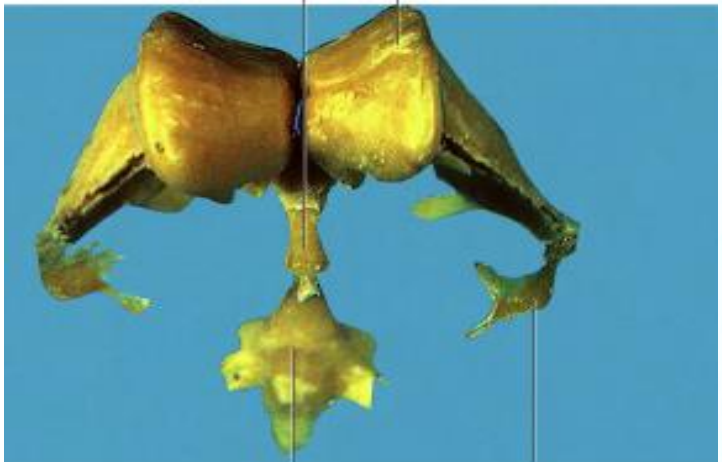


The Ventricular Sytem

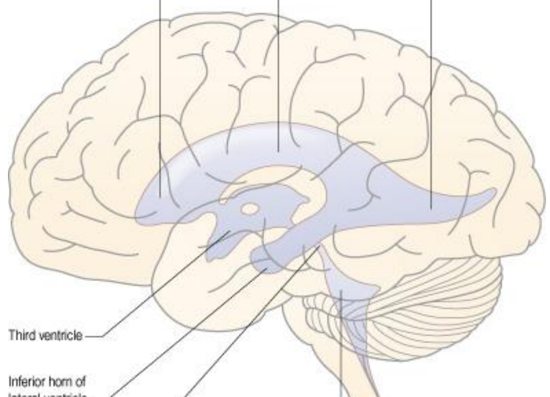
E. Manet – The Grand Canal

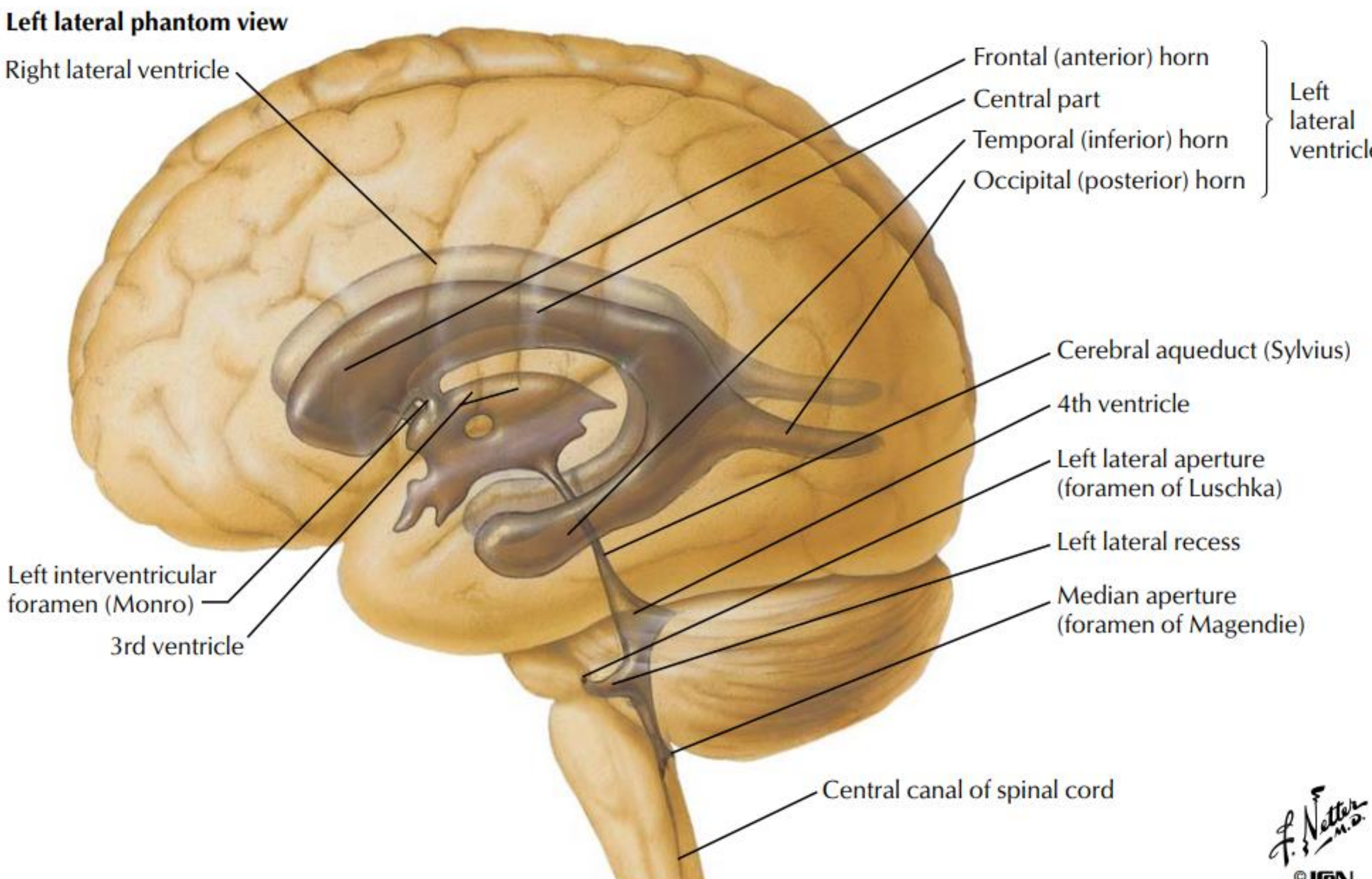

Choroid plexus of lateral ventricle (phantom)
Bridging veins
Dura mater
Cistern of corpus callosum
Arachnoid
Superior sagittal sinus
Subarachnoid space
Arachnoid granulations
Occipital (posterior) horn
Interventricular foramen (of Monro)
Chiasmatic cistern
Choroid plexus of 3rd ventricle
Interpeduncular cistern
Cerebral aqueduct (of Sylvius)
Prepontine cistern
Lateral aperture (foramen of Luschka)
Choroid plexus of 4th ventricle
Dura mater
Arachnoid
Subarachnoid space
Central canal of spinal cord
Straight sinus
Quadrigeminal cistern (with great cerebral vein) (of Galen)
(Posterior) cerebellomedullary cistern
Median aperture (foramen of Magendie)
F. Netter M.D.


Choroid plexus of lateral ventricle (phantom)
Bridging veins
Dura mater
Cistern of corpus callosum
Arachnoid
Superior sagittal sinus
Subarachnoid space
Arachnoid granulations
Occipital (posterior) horn
Interventricular foramen (of Monro)
Chiasmatic cistern
Choroid plexus of 3rd ventricle
Interpeduncular cistern
Cerebral aqueduct (of Sylvius)
Prepontine cistern
Lateral aperture (foramen of Luschka)
Choroid plexus of 4th ventricle
Dura mater
Arachnoid
Subarachnoid space
Central canal of spinal cord
Straight sinus
Quadrigeminal cistern (with great cerebral vein) (of Galen)
(Posterior) cerebellomedullary cistern
Median aperture (foramen of Magendie)
F. Netter M.D.

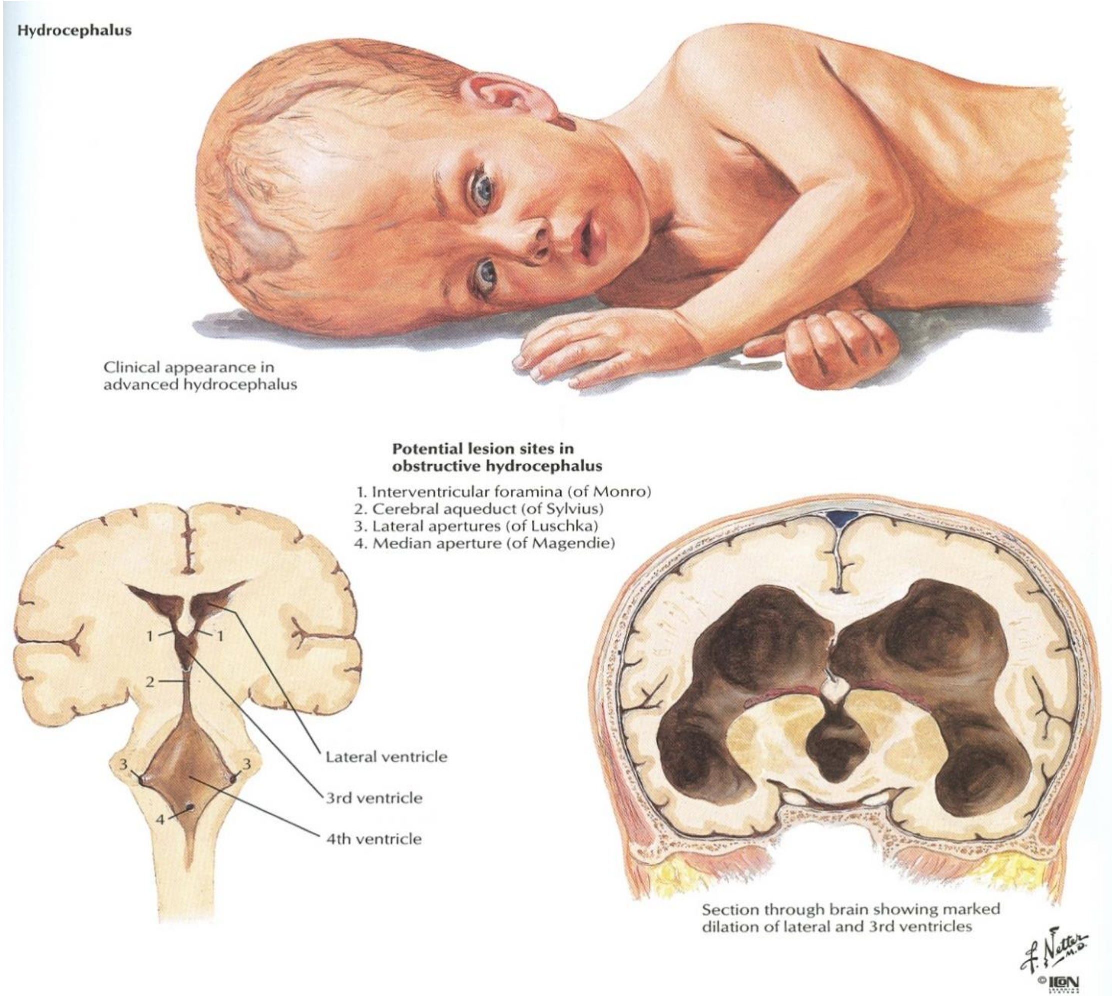

Cerebral aqueduct
Body of lateral ventricle
Fourth ventricle
Inferior horn of lateral ventricle


Anterior horn of lateral ventricle
Body of lateral ventricle
Posterior horn of lateral ventricle
Interventricular foramen
Third ventricle
Inferior horn of lateral ventricle
Cerebral aqueduct
Fourth ventricle

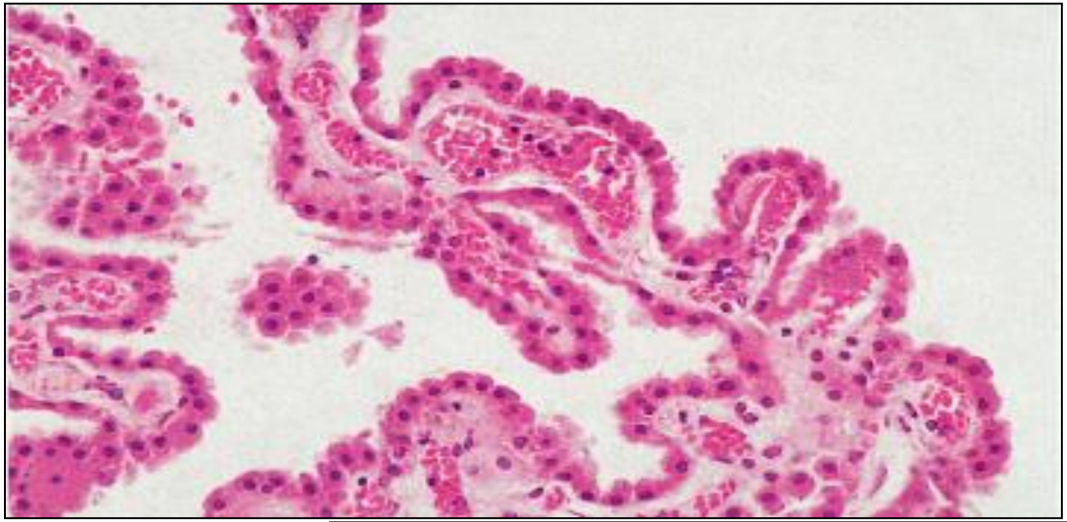

Anterior horn of lateral ventricle
Body of lateral ventricle
Posterior horn of lateral ventricle
Third ventricle
Inferior horn of lateral ventricle
Cerebral aqueduct
Fourth ventricle



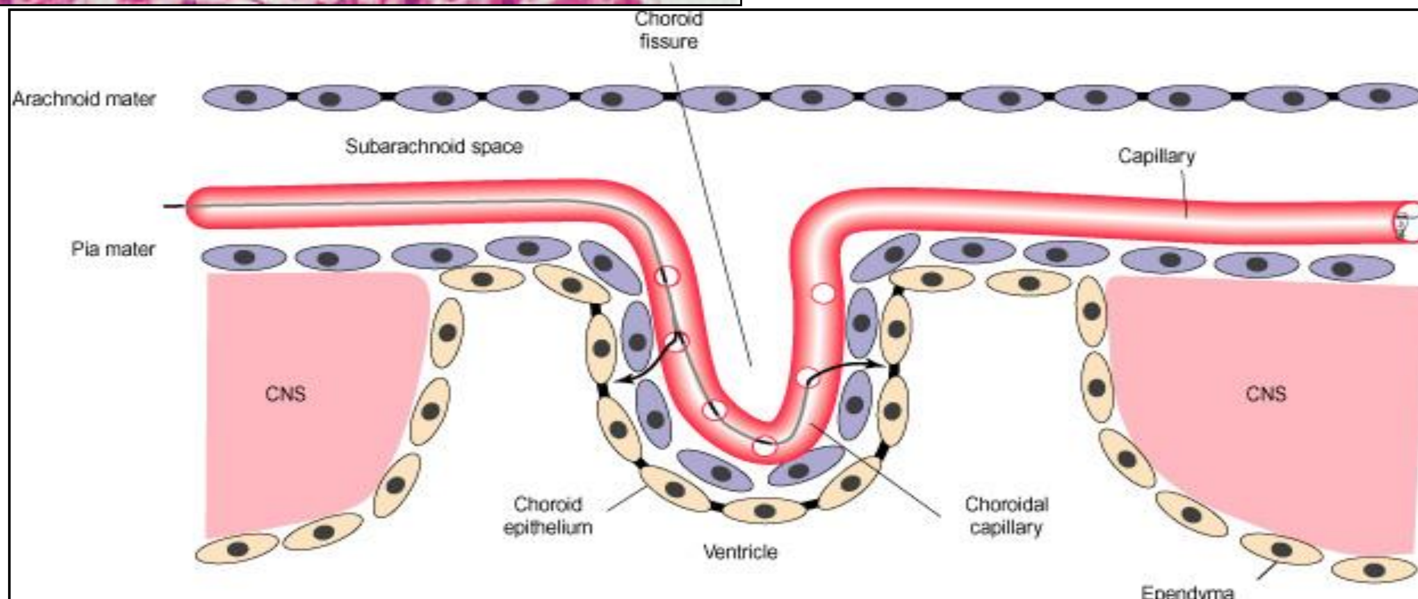
Left lateral phantom view
Right lateral ventricle
Frontal (anterior) horn
Central part
Temporal (inferior) horn
Occipital (posterior) horn
Left lateral ventricle
Cerebral aqueduct (Sylvius)
4th ventricle
Left lateral aperture (foramen of Luschka)
Left lateral recess
Median aperture (foramen of Magendie)
Left interventricular foramen (Monro)
3rd ventricle
Central canal of spinal cord
F. Netter M.D.
© ICON

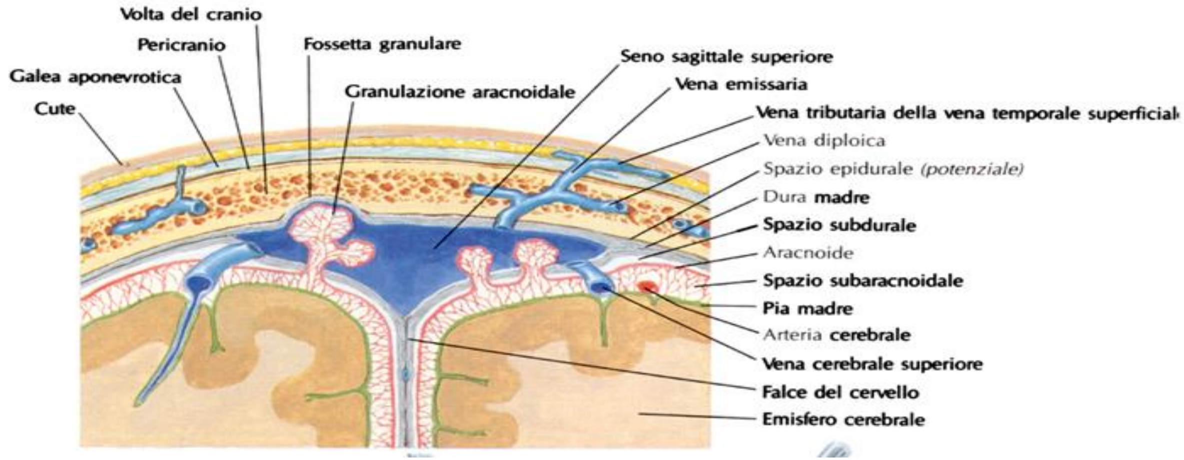

Hydrocephalus
Clinical appearance in advanced hydrocephalus
Potential lesion sites in obstructive hydrocephalus
1. Interventricular foramina (of Monro)
2. Cerebral aqueduct (of Sylvius)
3. Lateral apertures (of Luschka)
4. Median aperture (of Magendie)
1
1
2
3
3
4
Lateral ventricle
3rd ventricle
4th ventricle
Section through brain showing marked dilation of lateral and 3rd ventricles
F. Netter M.D.
© ICON

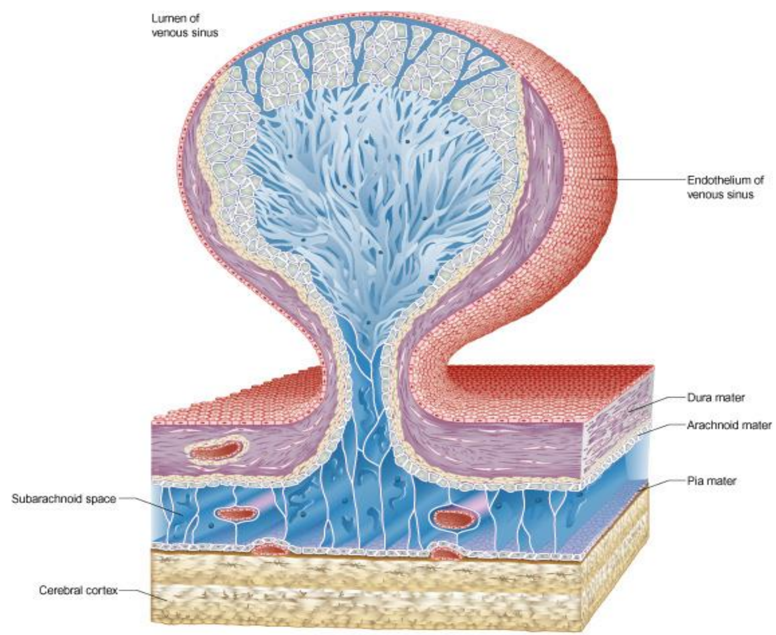
Ciliated cuboidal ependymal cells lining the central canal of the spinal cord.

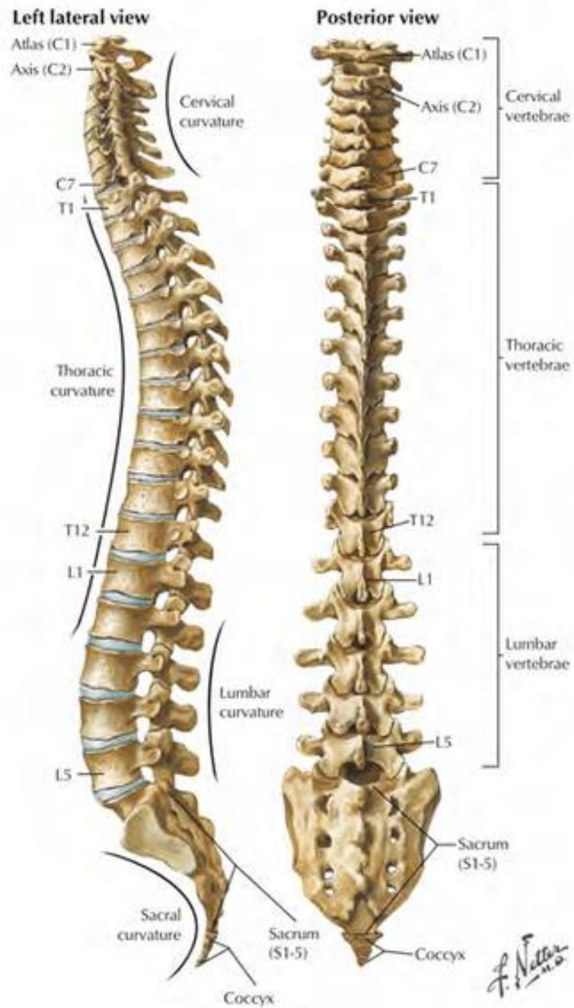


Choroid plexus within a ventricle

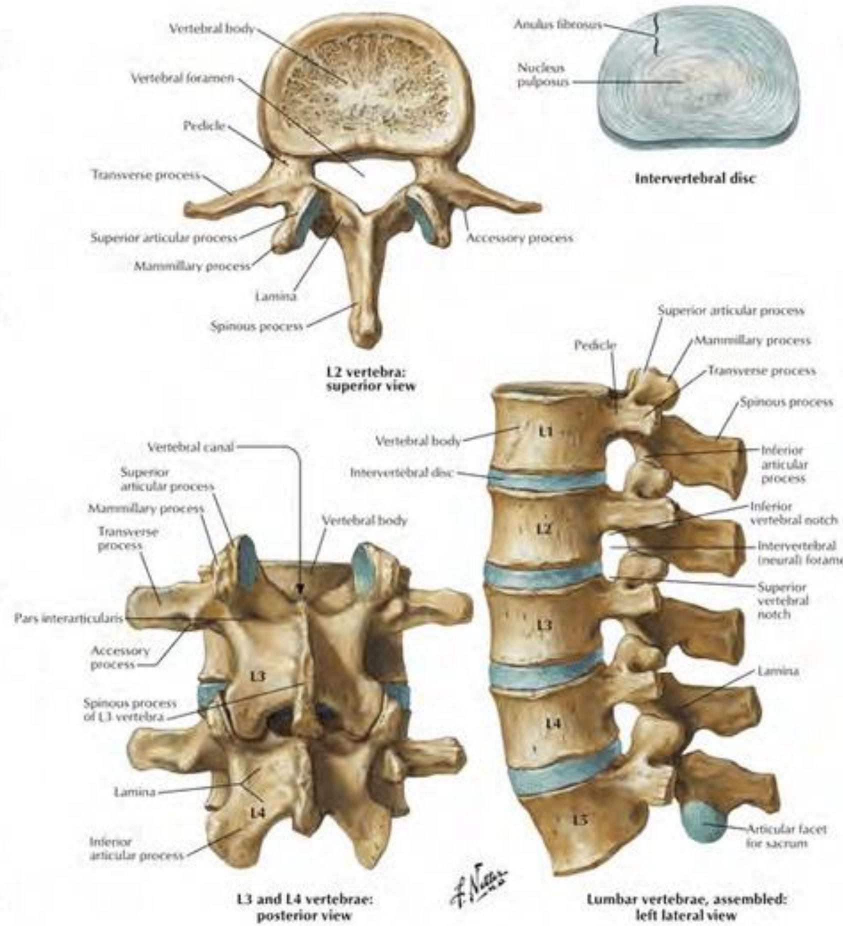



Volta del cranio
Pericranio
Fossetta granulare
Galea aponevrotica
Granulazione aracnoidale
Cute
Seno sagittale superiore
Vena emissaria
Vena tributaria della vena temporale superficial
Vena diploica
Spazio epidurale (potenziale)
Dura madre
Spazio subdurale
Aracnoide
Spazio subaracnoidale
Pia madre
Arteria cerebrale
Vena cerebrale superiore
Falce del cervello
Emisfero cerebrale


Lumen of venous sinus
Endothelium of venous sinus
Dura mater
Arachnoid mater
Pia mater
Subarachnoid space
Cerebral cortex

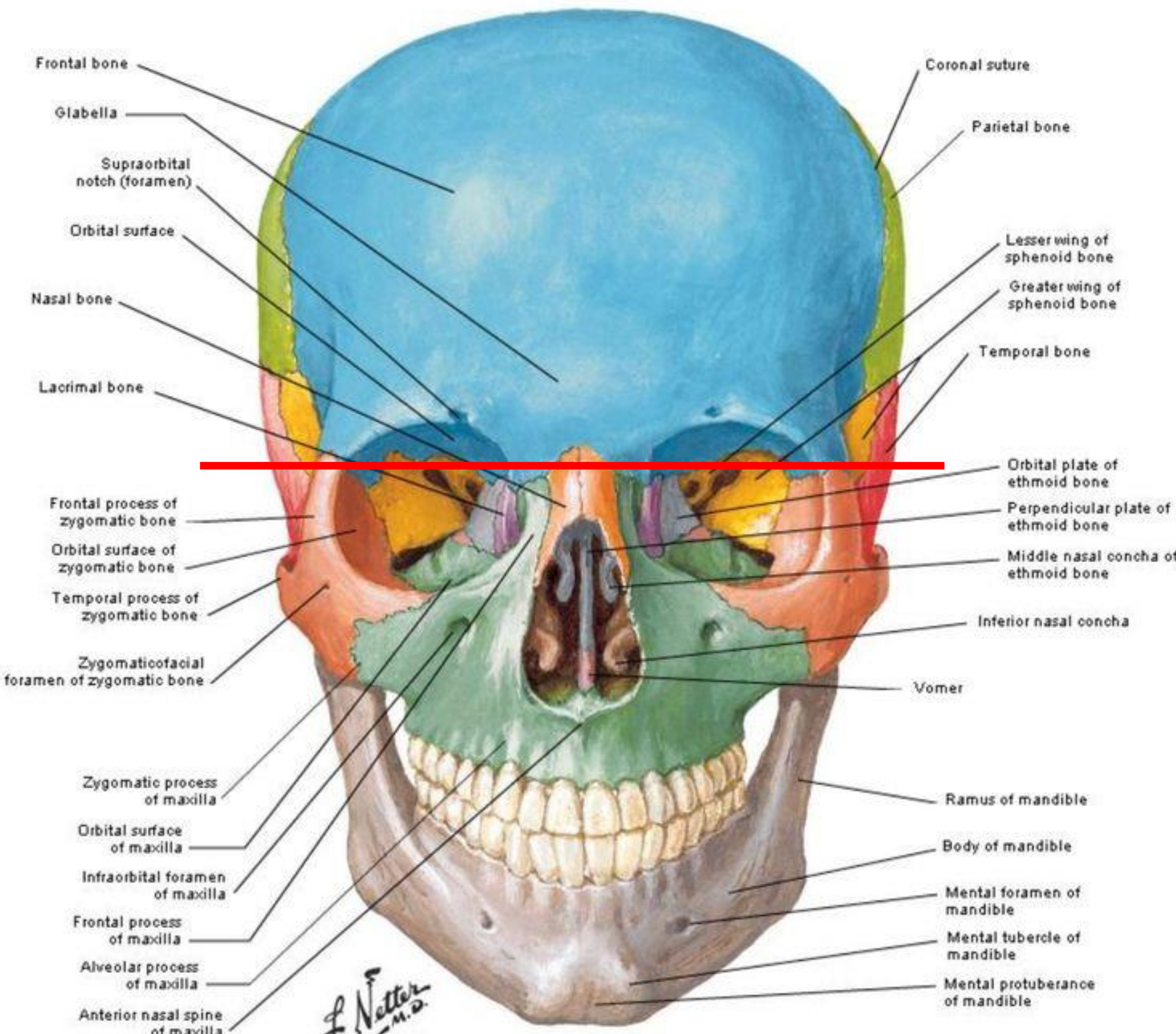

Left lateral view
Atlas (C1)
Axis (C2)
Cervical curvature
C7
T1
Thoracic curvature
T12
L1
Lumbar curvature
L5
Sacral curvature
Sacrum (S1-5)
Coccyx
Posterior view
Atlas (C1)
Axis (C2)
C7
T1
T12
L1
L5
Cervical vertebrae
Thoracic vertebrae
Lumbar vertebrae
Sacrum (S1-5)
Coccyx

(a)

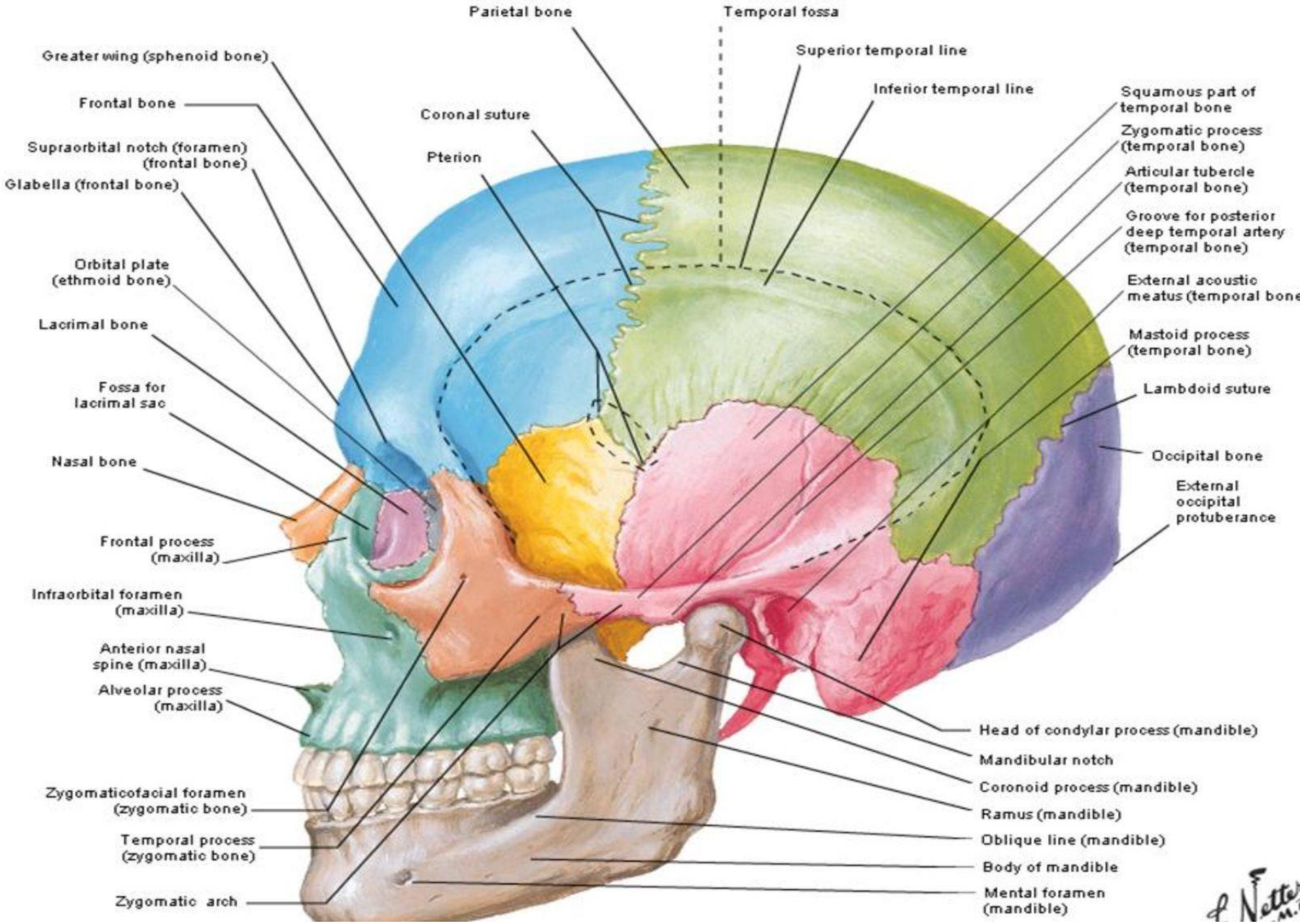

Vertebral body
Vertebral foramen
Pedicle
Transverse process
Superior articular process
Mammillary process
Lamina
Spinous process
Accessory process
L2 vertebra: superior view
Anulus fibrosus
Nucleus pulposus
Intervertebral disc
Vertebral canal
Superior articular process
Mammillary process
Transverse process
Vertebral body
Pars interarticularis
Accessory process
Spinous process of L3 vertebra
Lamina
Inferior articular process
L3
L4
L3 and L4 vertebrae: posterior view
Superior articular process
Pedicle
Mammillary process
Transverse process
Spinous process
Vertebral body
Intervertebral disc
Inferior articular process
Inferior vertebral notch
Intervertebral (neural) foramen
Superior vertebral notch
Lamina
Articular facet for sacrum
L1
L2
L3
L4
L5
Lumbar vertebrae, assembled: left lateral view

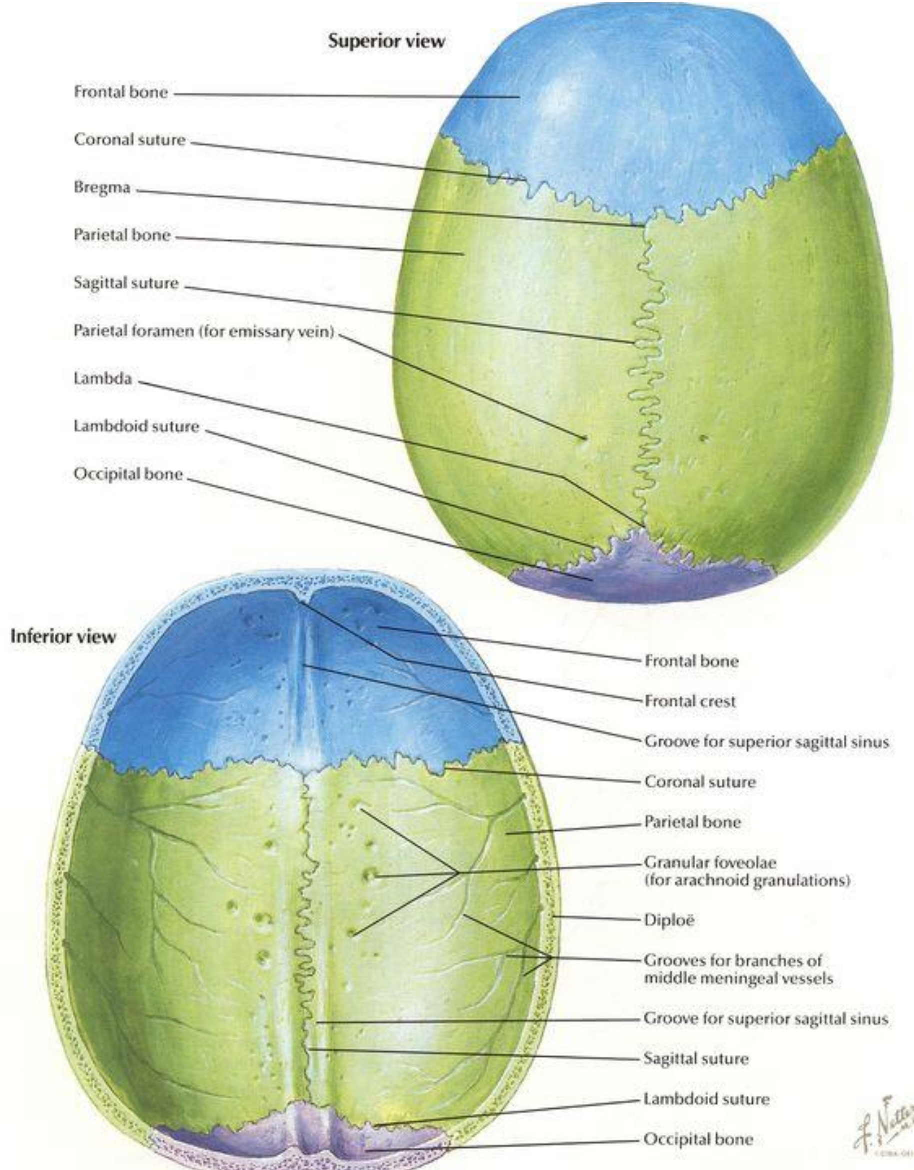
(b)

Skull: Anterior View

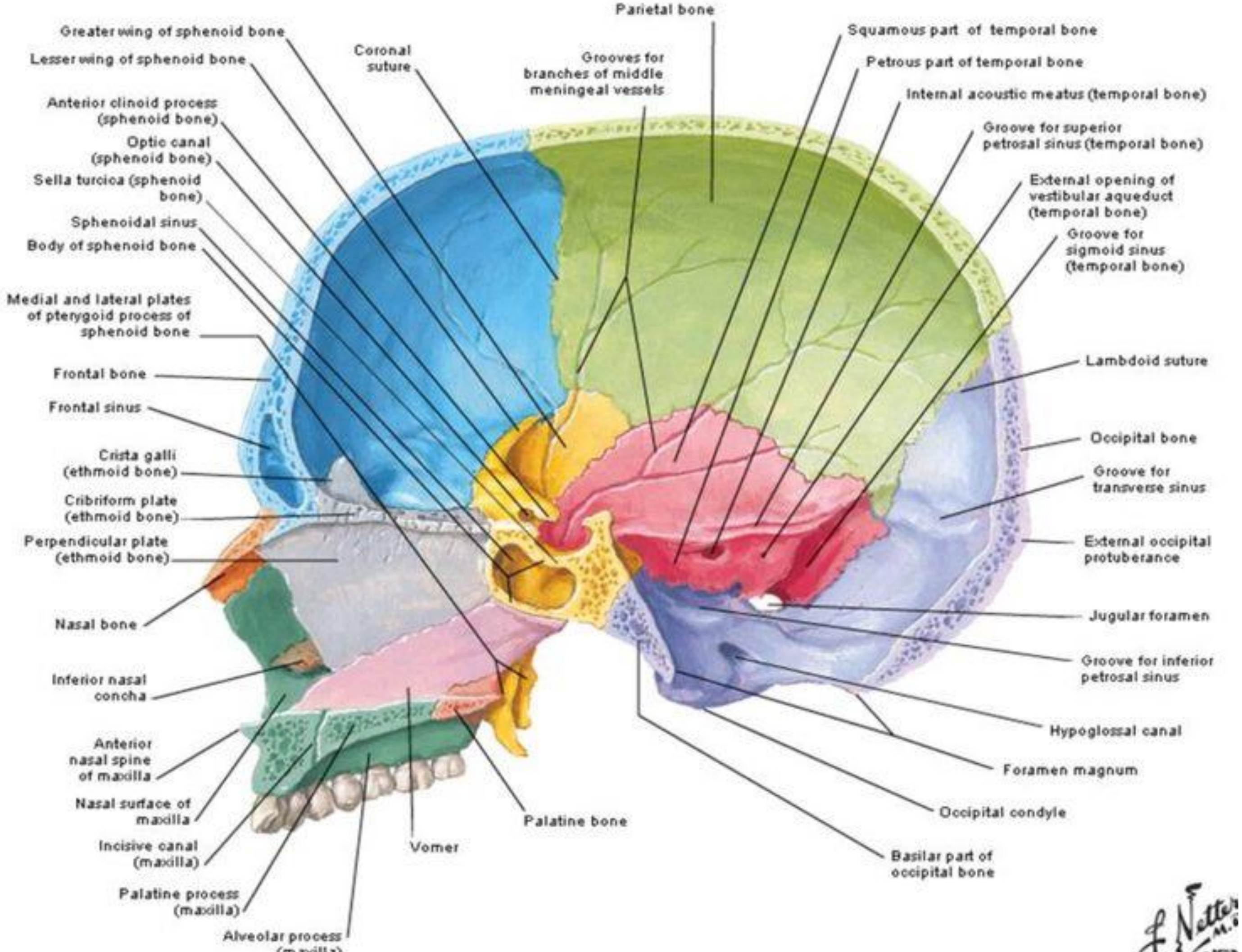


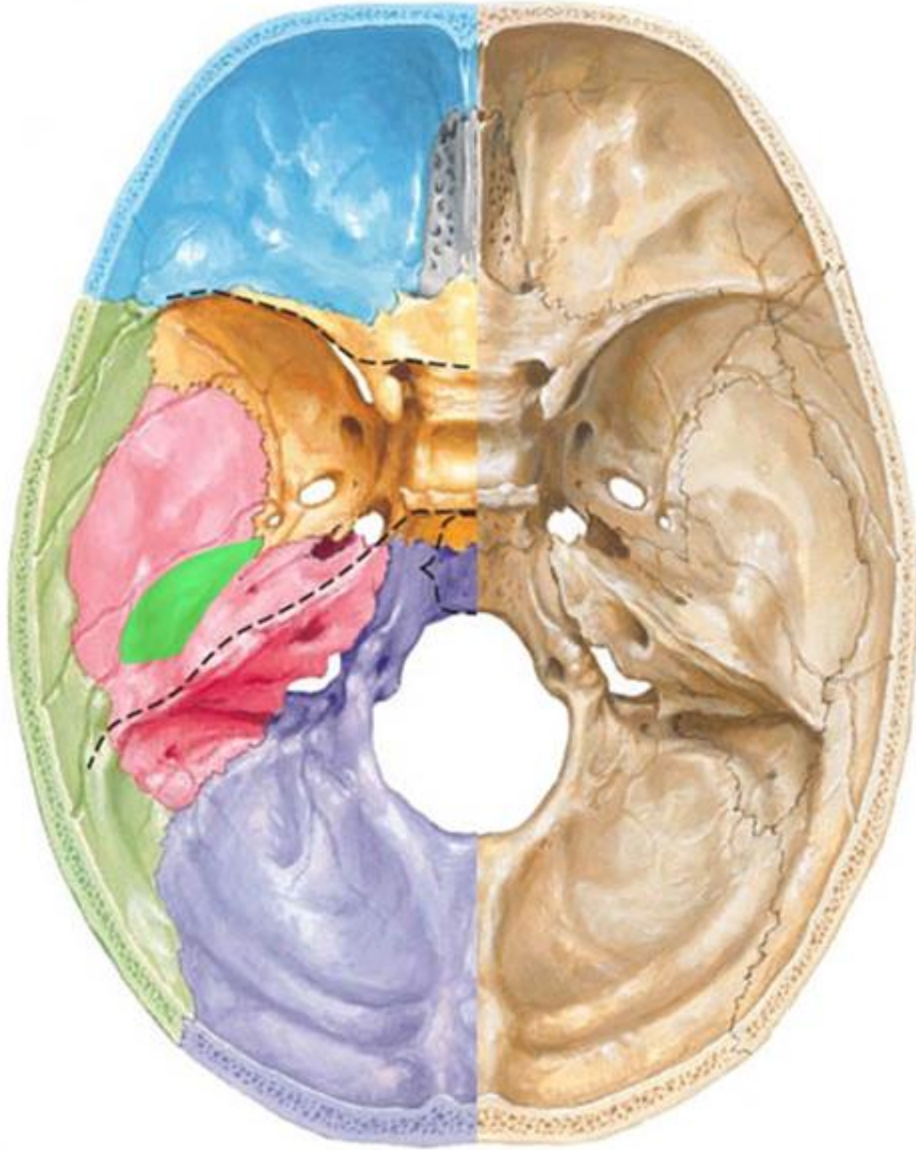
Skull
Lateral View

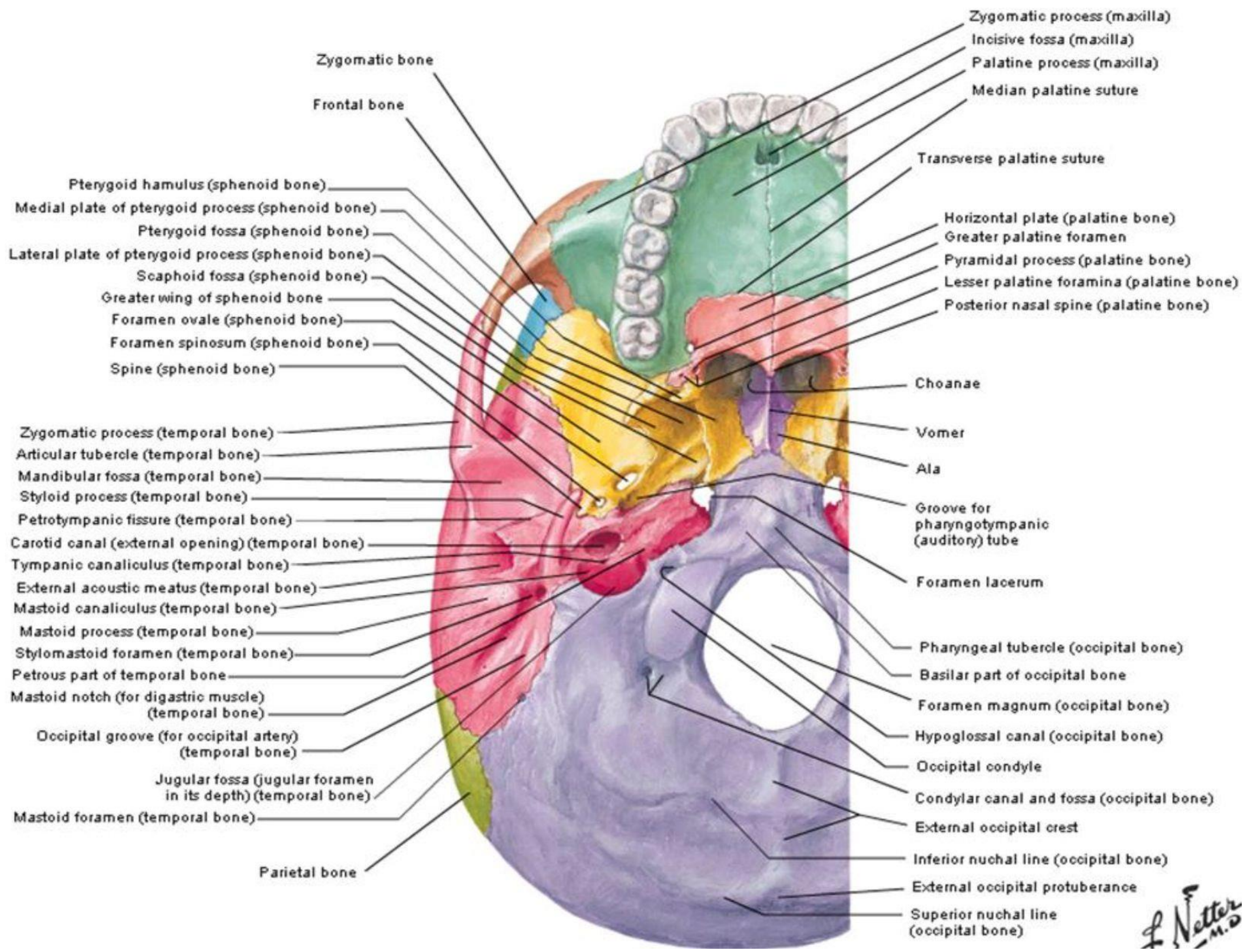



Superior view
Frontal bone
Coronal suture
Bregma
Parietal bone
Sagittal suture
Parietal foramen (for emissary vein)
Lambda
Lambdoid suture
Occipital bone
Inferior view
Frontal bone
Frontal crest
Groove for superior sagittal sinus
Coronal suture
Parietal bone
Granular foveolae
(for arachnoid granulations)
Diploë
Grooves for branches of
middle meningeal vessels
Groove for superior sagittal sinus
Sagittal suture
Lambdoid suture
Occipital bone

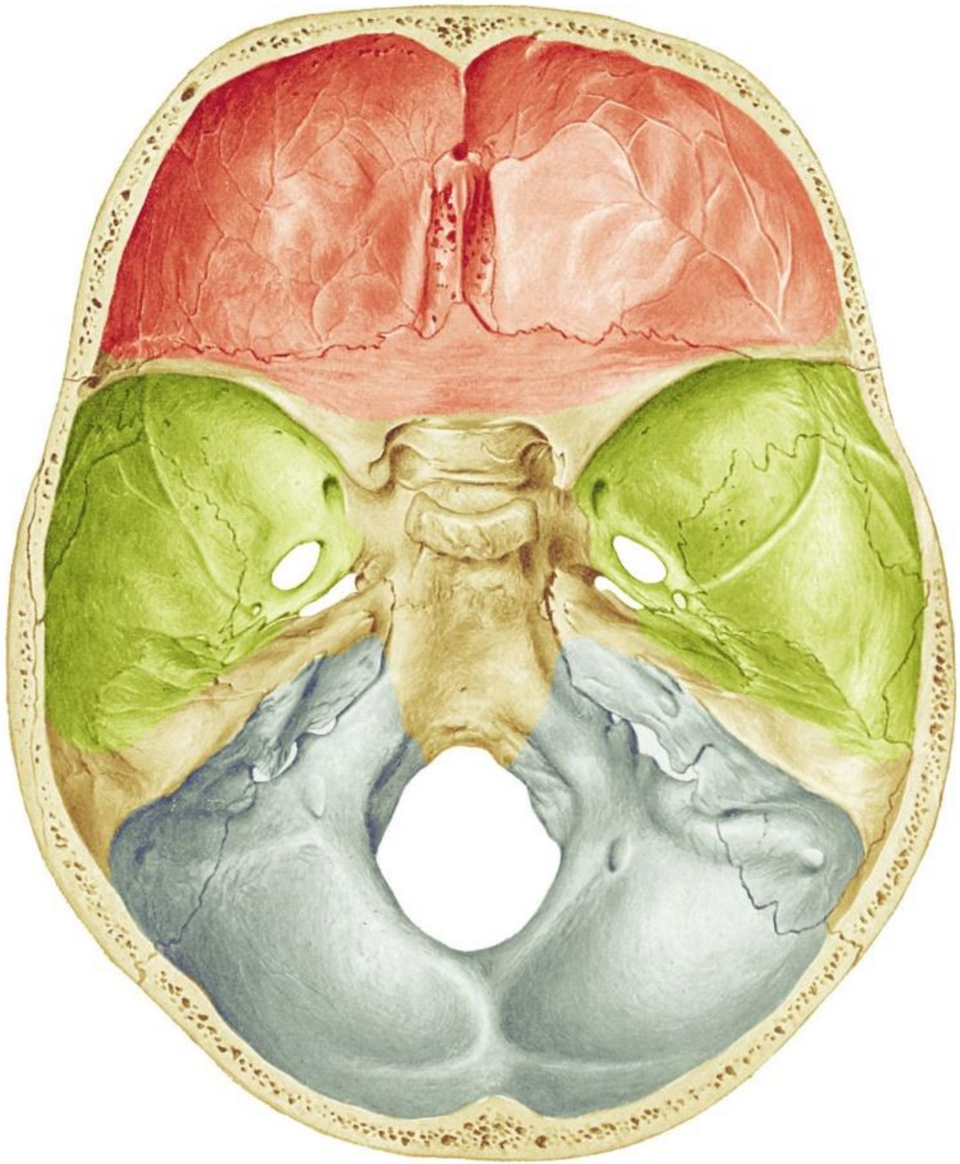
Skull
Midsagittal Section

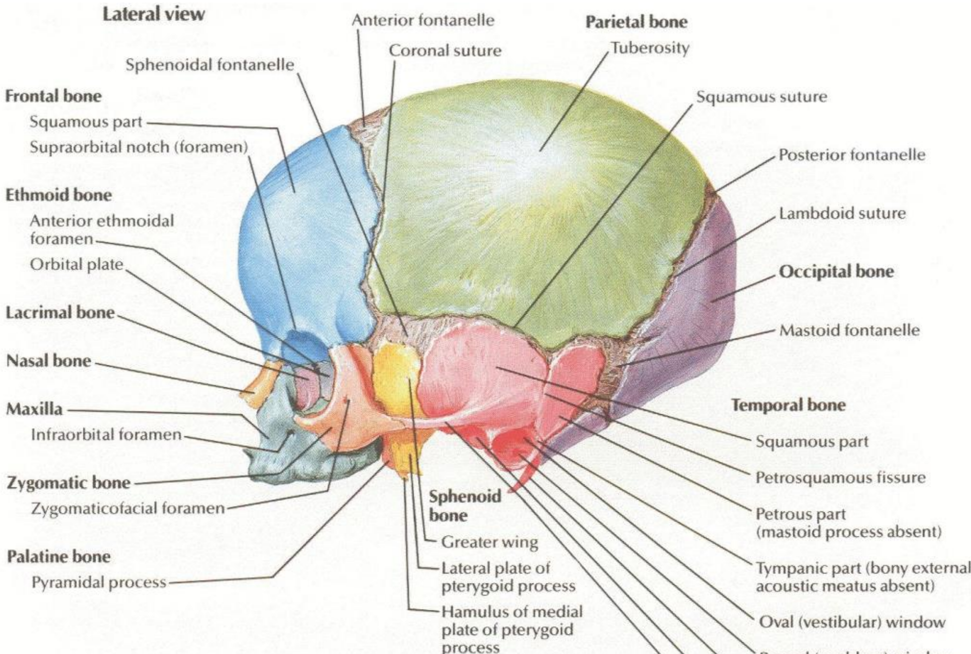


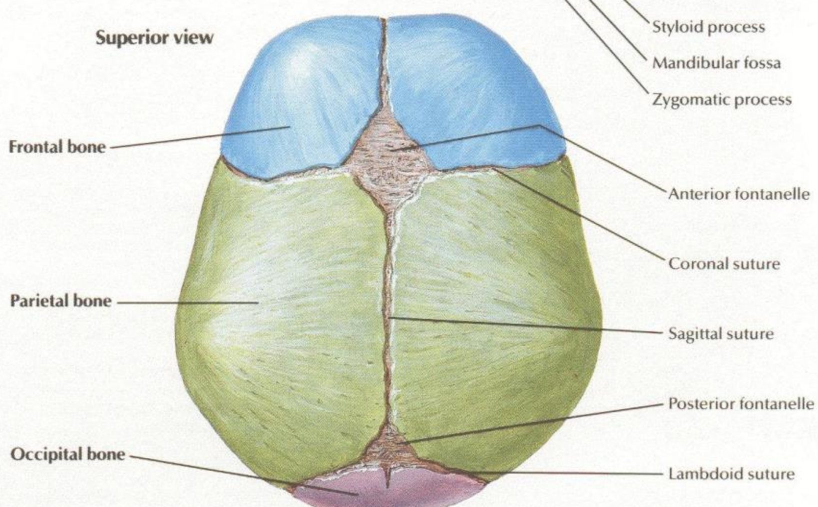




Zygomatic process (maxilla)
Incisive fossa (maxilla)
Palatine process (maxilla)
Median palatine suture
Transverse palatine suture
Horizontal plate (palatine bone)
Greater palatine foramen
Pyramidal process (palatine bone)
Lesser palatine foramina (palatine bone)
Posterior nasal spine (palatine bone)
Choanae
Vomer
Ala
Groove for pharyngotympanic (auditory) tube
Foramen lacerum
Pharyngeal tubercle (occipital bone)
Basilar part of occipital bone
Foramen magnum (occipital bone)
Hypoglossal canal (occipital bone)
Occipital condyle
Condylar canal and fossa (occipital bone)
External occipital crest
Inferior nuchal line (occipital bone)
External occipital protuberance
Superior nuchal line (occipital bone)
Zygomatic bone
Frontal bone
Pterygoid hamulus (sphenoid bone)
Medial plate of pterygoid process (sphenoid bone)
Pterygoid fossa (sphenoid bone)
Lateral plate of pterygoid process (sphenoid bone)
Scaphoid fossa (sphenoid bone)
Greater wing of sphenoid bone
Foramen ovale (sphenoid bone)
Foramen spinosum (sphenoid bone)
Spine (sphenoid bone)
Zygomatic process (temporal bone)
Articular tubercle (temporal bone)
Mandibular fossa (temporal bone)
Styloid process (temporal bone)
Petrotympanic fissure (temporal bone)
Carotid canal (external opening) (temporal bone)
Tympanic canaliculus (temporal bone)
External acoustic meatus (temporal bone)
Mastoid canaliculus (temporal bone)
Mastoid process (temporal bone)
Stylomastoid foramen (temporal bone)
Petrous part of temporal bone
Mastoid notch (for digastric muscle) (temporal bone)
Occipital groove (for occipital artery) (temporal bone)
Jugular fossa (jugular foramen in its depth) (temporal bone)
Mastoid foramen (temporal bone)
Parietal bone
F. Netter M.D.




Lateral view
Anterior fontanelle
Coronal suture
Parietal bone
Tuberosity
Sphenoidal fontanelle
Frontal bone
Squamous part
Supraorbital notch (foramen)
Squamous suture
Posterior fontanelle
Ethmoid bone
Anterior ethmoidal foramen
Orbital plate
Lambdoid suture
Occipital bone
Lacrimal bone
Mastoid fontanelle
Nasal bone
Maxilla
Temporal bone
Infraorbital foramen
Squamous part
Zygomatic bone
Petrosquamous fissure
Zygomaticofacial foramen
Sphenoid bone
Petrous part (mastoid process absent)
Greater wing
Palatine bone
Pyramidal process
Lateral plate of pterygoid process
Tympanic part (bony external acoustic meatus absent)
Hamulus of medial plate of pterygoid process
Oval (vestibular) window
Round (cochlear) window
Styloid process
Mandibular fossa
Zygomatic process

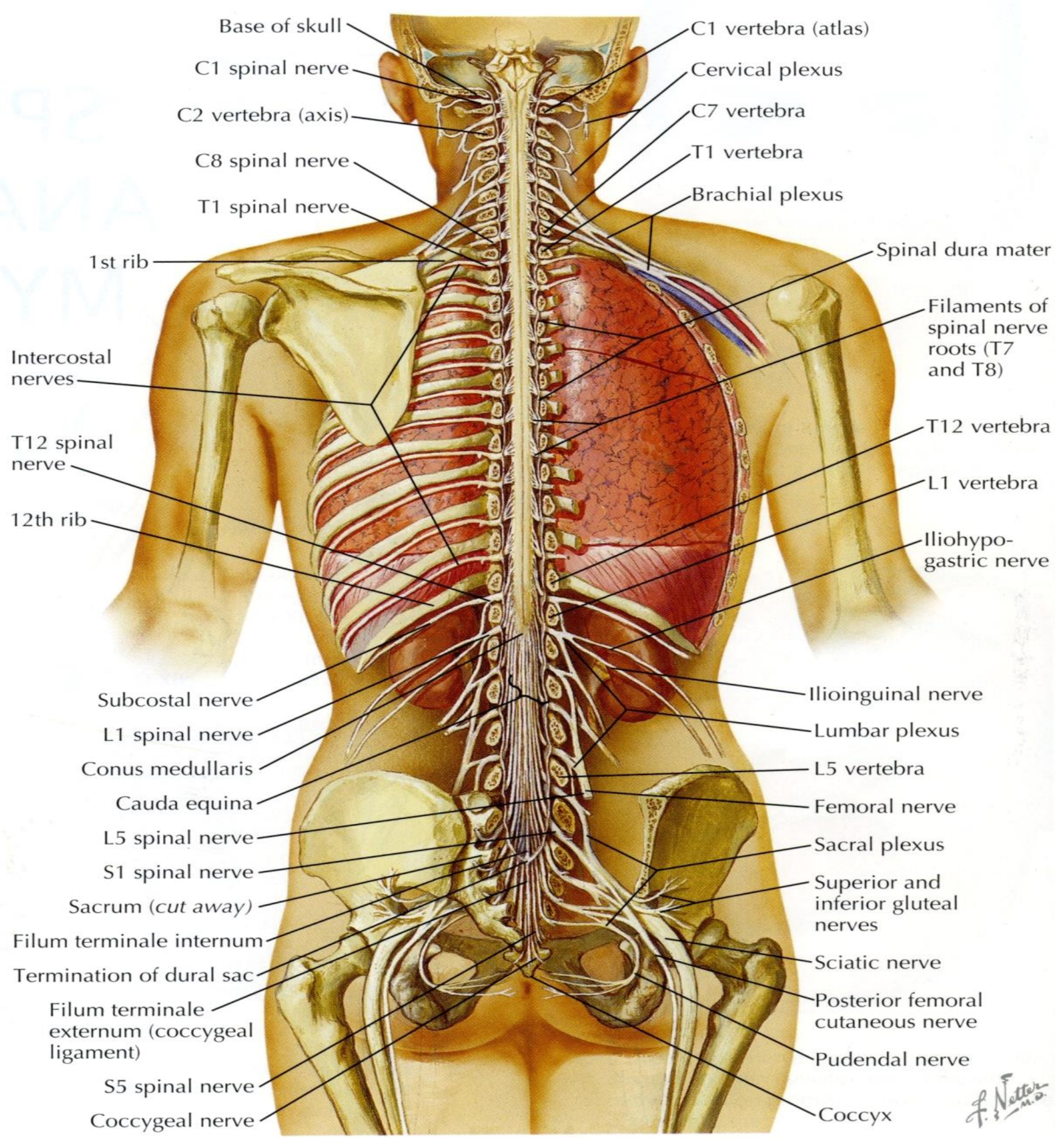

Superior view
Frontal bone
Anterior fontanelle
Coronal suture
Parietal bone
Sagittal suture
Posterior fontanelle
Occipital bone
Lambdoid suture

The Spinal Cord

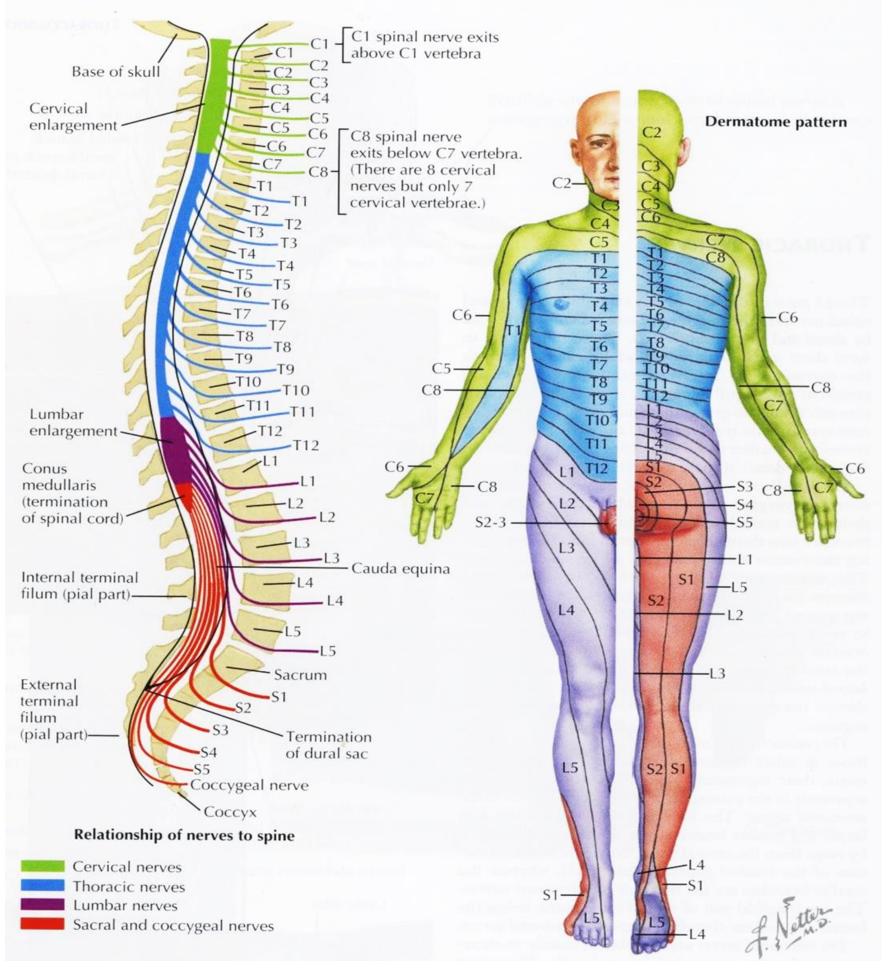
P. Brueghel – The tower of Babel

The
Spinal Cord

P. Brueghel – The tower of Babel



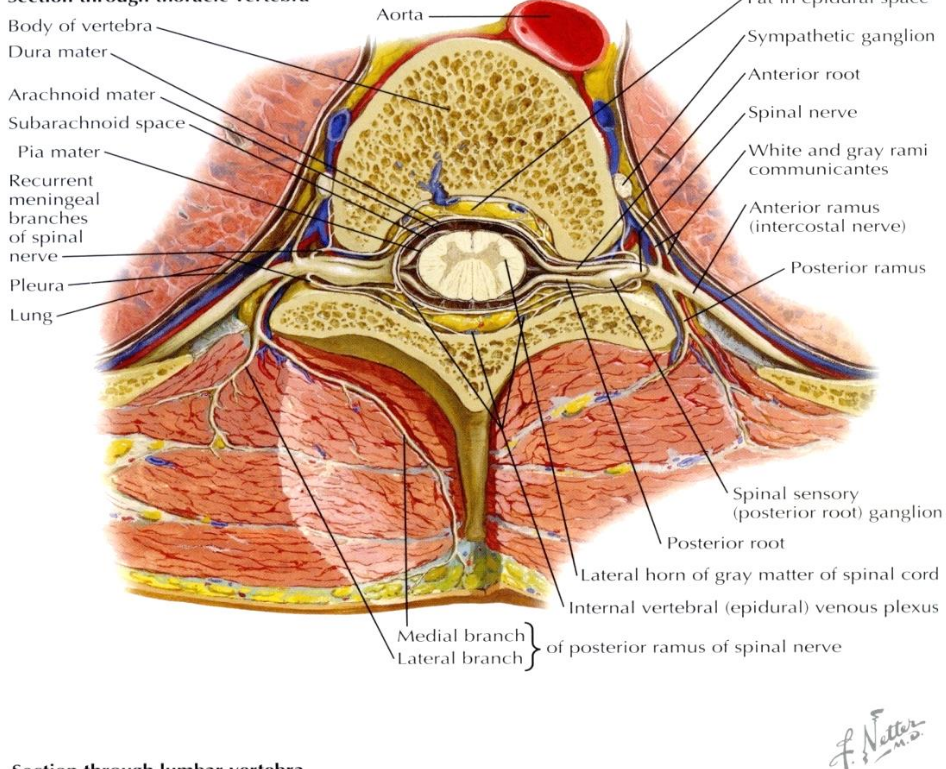
Base of skull
C1 spinal nerve
C2 vertebra (axis)
C8 spinal nerve
T1 spinal nerve
1st rib
Intercostal nerves
T12 spinal nerve
12th rib
Subcostal nerve
L1 spinal nerve
Conus medullaris
Cauda equina
L5 spinal nerve
S1 spinal nerve
Sacrum (cut away)
Filum terminale internum
Termination of dural sac
Filum terminale externum (coccygeal ligament)
S5 spinal nerve
Coccygeal nerve
C1 vertebra (atlas)
Cervical plexus
C7 vertebra
T1 vertebra
Brachial plexus
Spinal dura mater
Filaments of spinal nerve roots (T7 and T8)
T12 vertebra
L1 vertebra
Iliohypogastric nerve
Ilioinguinal nerve
Lumbar plexus
L5 vertebra
Femoral nerve
Sacral plexus
Superior and inferior gluteal nerves
Sciatic nerve
Posterior femoral cutaneous nerve
Pudendal nerve
Coccyx
F. Netter M.D.



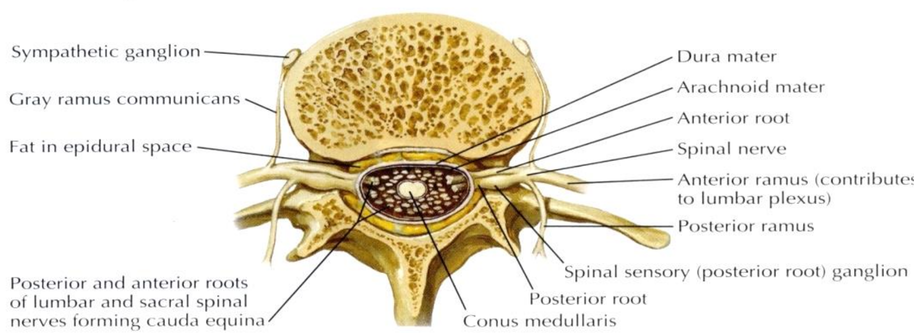
Levels of principal dermatomes

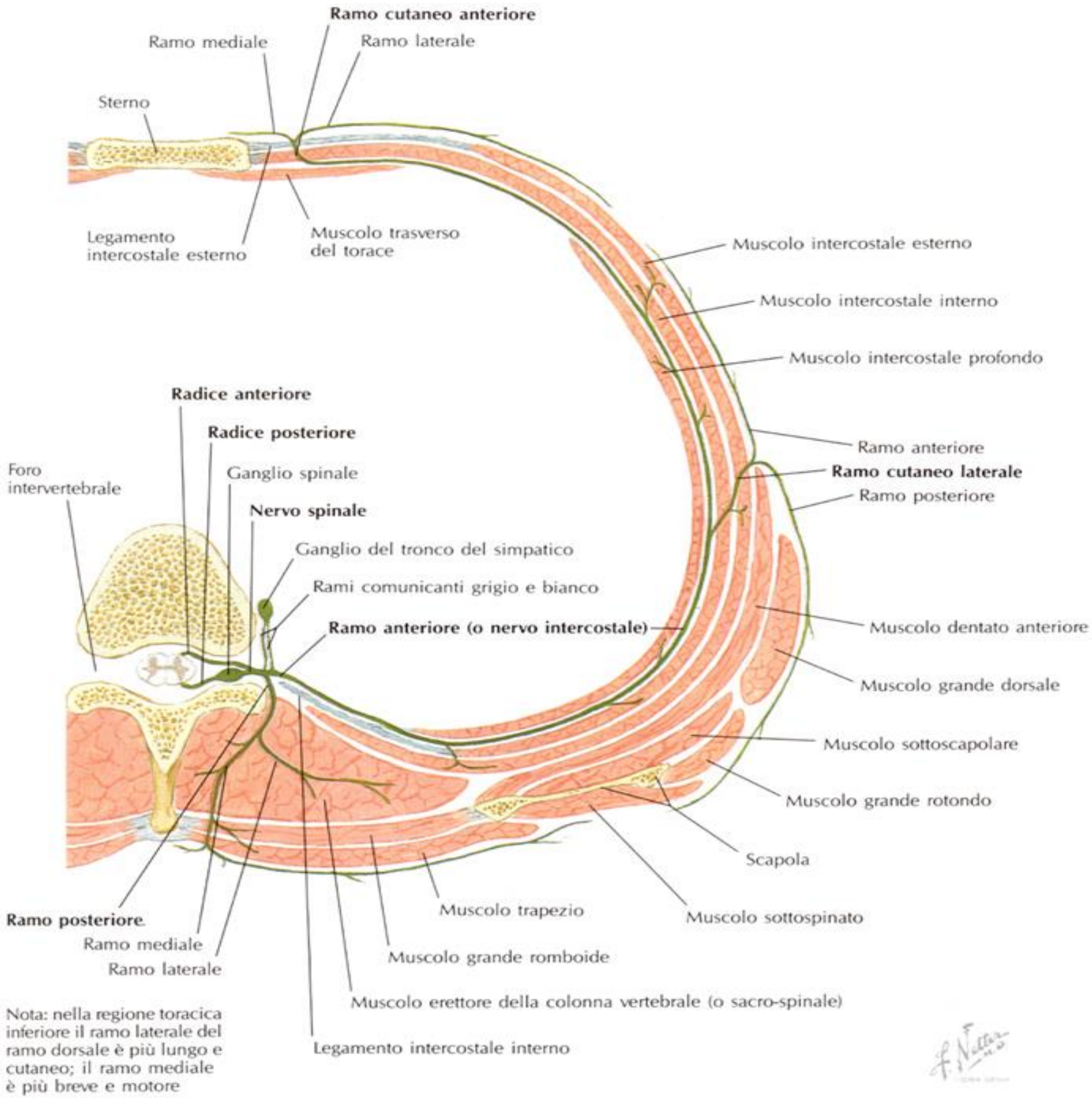
C5	Clavicles	**T10**	Level of umbilicus
C5, 6, 7	Lateral parts of upper limbs	**T12**	Inguinal or groin regions
C8; T1	Medial sides of upper limbs	**L1, 2, 3, 4**	Anterior and inner surfaces of lower limbs
C6	Thumb	**L4, 5; S1**	Foot
C6, 7, 8	Hand	**L4**	Medial side of great toe
C8	Ring and little fingers	**L5; S1, 2**	Outer and posterior sides of lower limbs
T4	Level of nipples	**S1**	Lateral margin of foot and little toe
		S2, 3, 4	Perineum

Section through thoracic vertebra

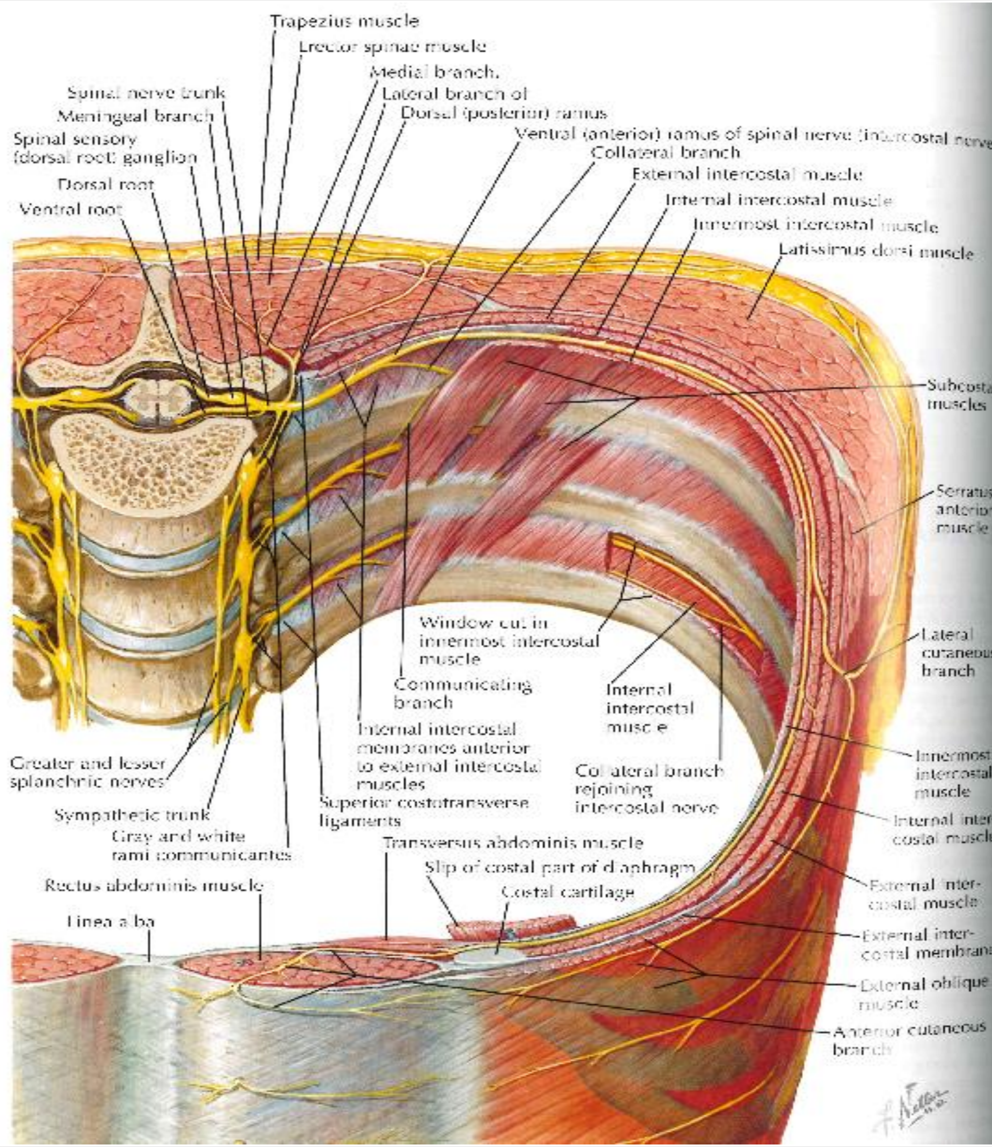


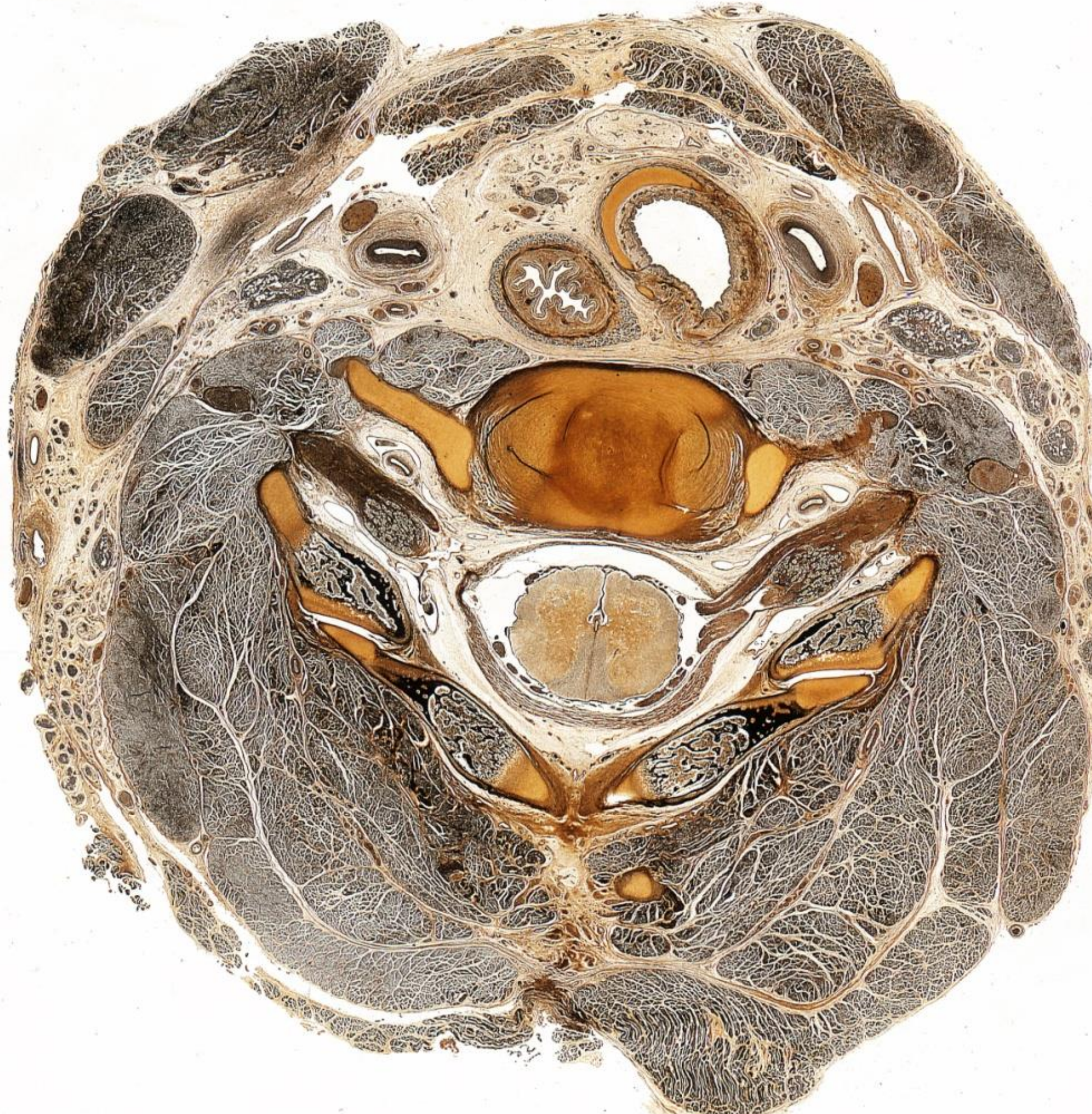
Section through lumbar vertebra



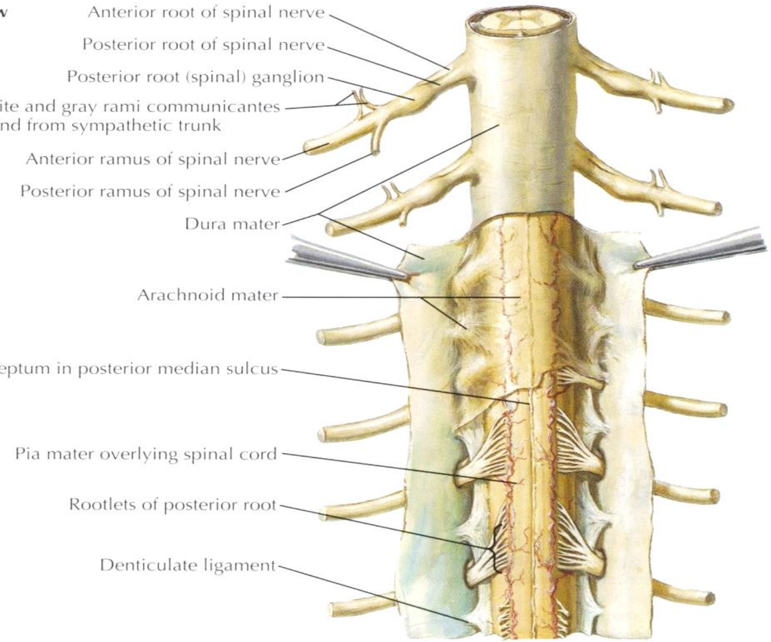


Ramo cutaneo anteriore
Ramo mediale
Ramo laterale
Sterno
Legamento intercostale esterno
Muscolo trasverso del torace
Muscolo intercostale esterno
Muscolo intercostale interno
Muscolo intercostale profondo
Radice anteriore
Radice posteriore
Foro intervertebrale
Ganglio spinale
Nervo spinale
Ganglio del tronco del simpatico
Rami comunicanti grigio e bianco
Ramo anteriore (o nervo intercostale)
Ramo anteriore
Ramo cutaneo laterale
Ramo posteriore
Muscolo dentato anteriore
Muscolo grande dorsale
Muscolo sottoscapolare
Muscolo grande rotondo
Scapola
Muscolo sottospinato
Muscolo trapezio
Muscolo grande romboide
Muscolo erettore della colonna vertebrale (o sacro-spinale)
Legamento intercostale interno
Ramo posteriore
Ramo mediale
Ramo laterale
Nota: nella regione toracica inferiore il ramo laterale del ramo dorsale è più lungo e cutaneo; il ramo mediale è più breve e motore

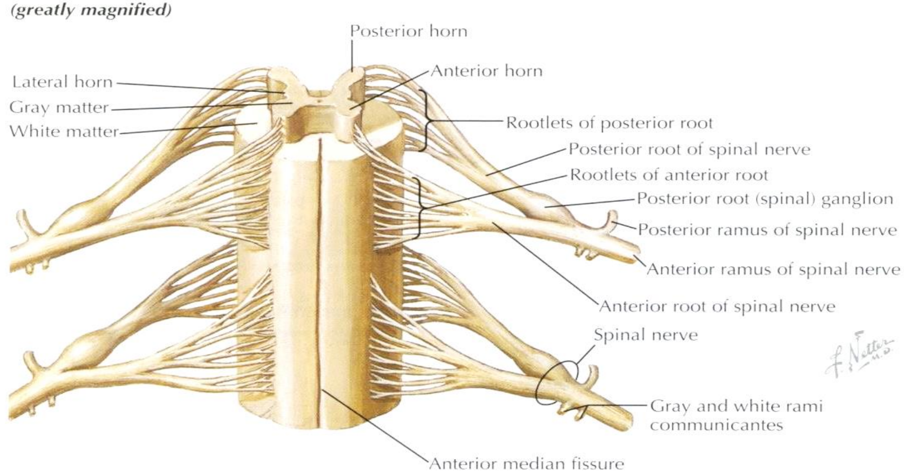

Trapezius muscle
Erector spinae muscle
Medial branch,
Lateral branch of
Dorsal (posterior) ramus
Ventral (anterior) ramus of spinal nerve (intercostal nerve)
Collateral branch
External intercostal muscle
Internal intercostal muscle
Innermost intercostal muscle
Latissimus dorsi muscle
Spinal nerve trunk
Meningeal branch
Spinal sensory
(dorsal root) ganglion
Dorsal root
Ventral root
Subcostal
muscles
Serratus
anterior
muscle
Lateral
cutaneous
branch
Window cut in
innermost intercostal
muscle
Communicating
branch
Internal
intercostal
muscle
Internal intercostal
membranes anterior
to external intercostal
muscles
Collateral branch
rejoining
intercostal nerve
Greater and lesser
splanchnic nerves
Superior costotransverse
ligaments
Sympathetic trunk
Gray and white
rami communicantes
Innermost
intercostal
muscle
Internal inter-
costal muscle
Transversus abdominis muscle
Slip of costal part of diaphragm
Costal cartilage
Rectus abdominis muscle
Linea alba
External inter-
costal muscle
External inter-
costal membrane
External oblique
muscle
Anterior cutaneous
branch



Posterior view



Membranes removed: anterior view
(greatly magnified)



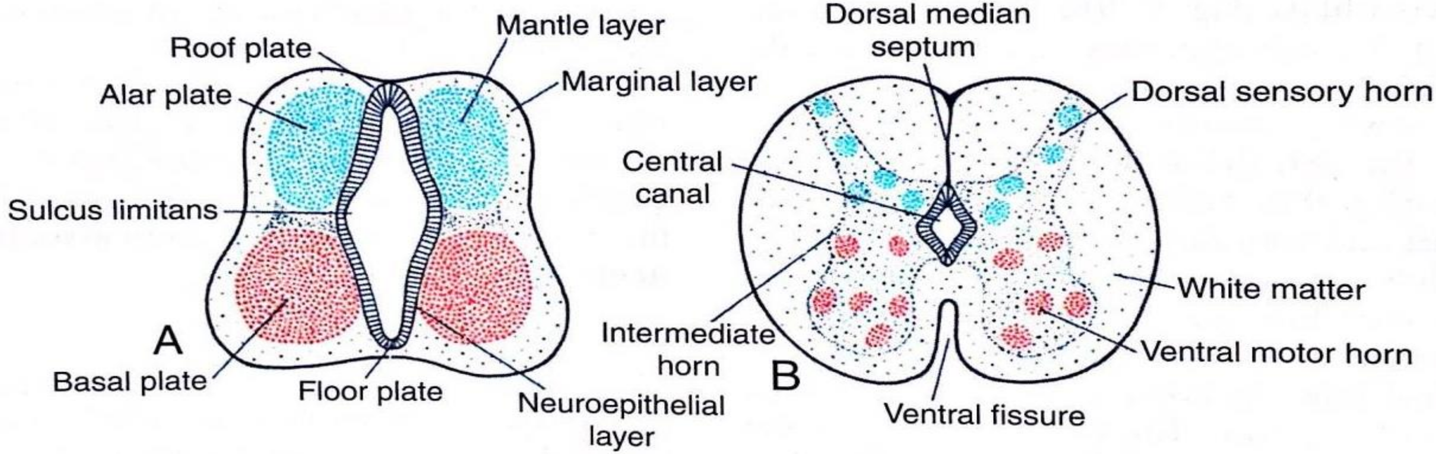


Figure 17.8 **A,B.** Two successive stages in the development of the spinal cord. Note formation of ventral motor and dorsal sensory horns and the intermediate column.

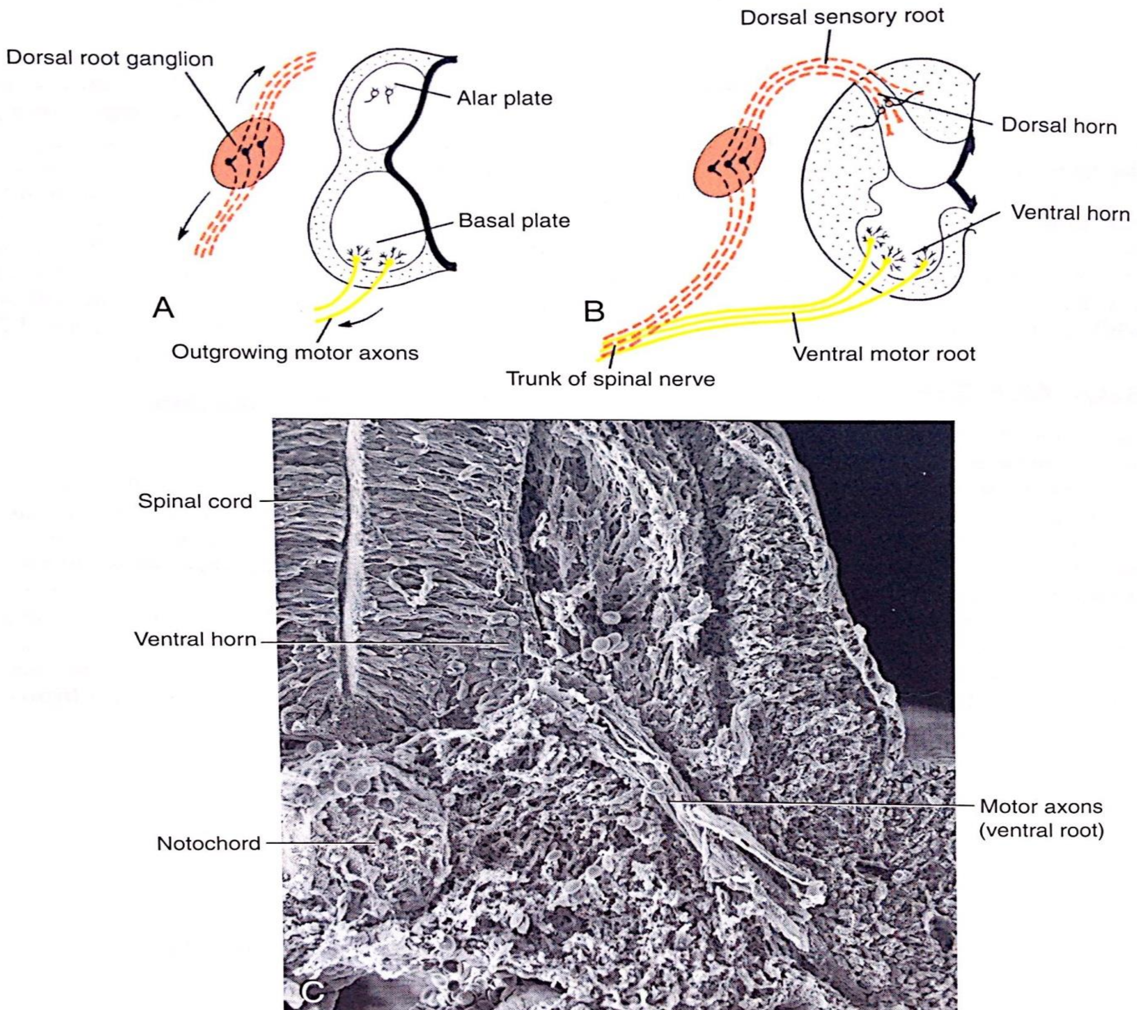


Figure 17.10 **A.** Motor axons growing out from neurons in the basal plate and centrally and peripherally growing fibers of nerve cells in the dorsal root ganglion. **B.** Nerve fibers of the ventral motor and dorsal sensory roots join to form the trunk of the spinal nerve. **C.** Scanning electron micrograph of a cross section through the spinal cord of a chick embryo. The ventral horn and ventral motor root are differentiating.

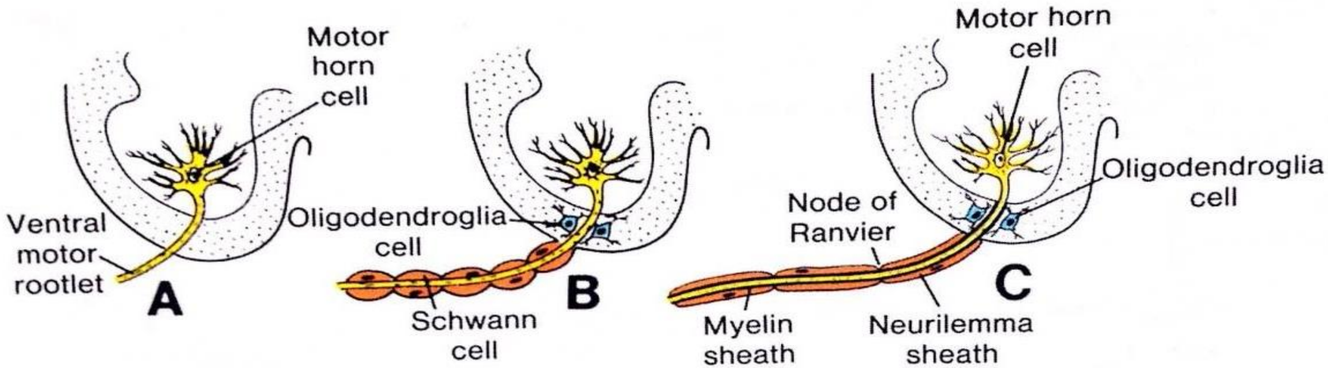
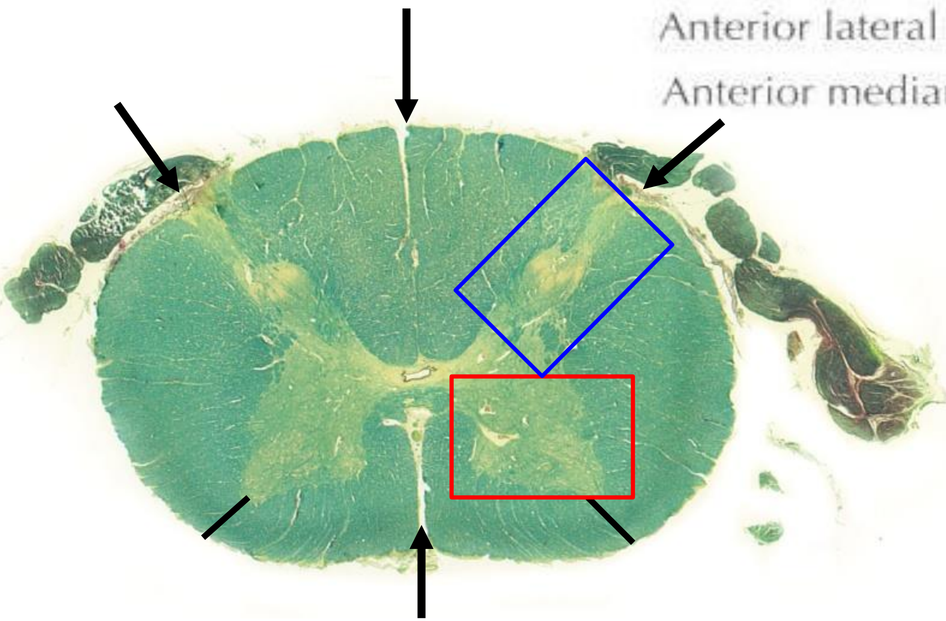
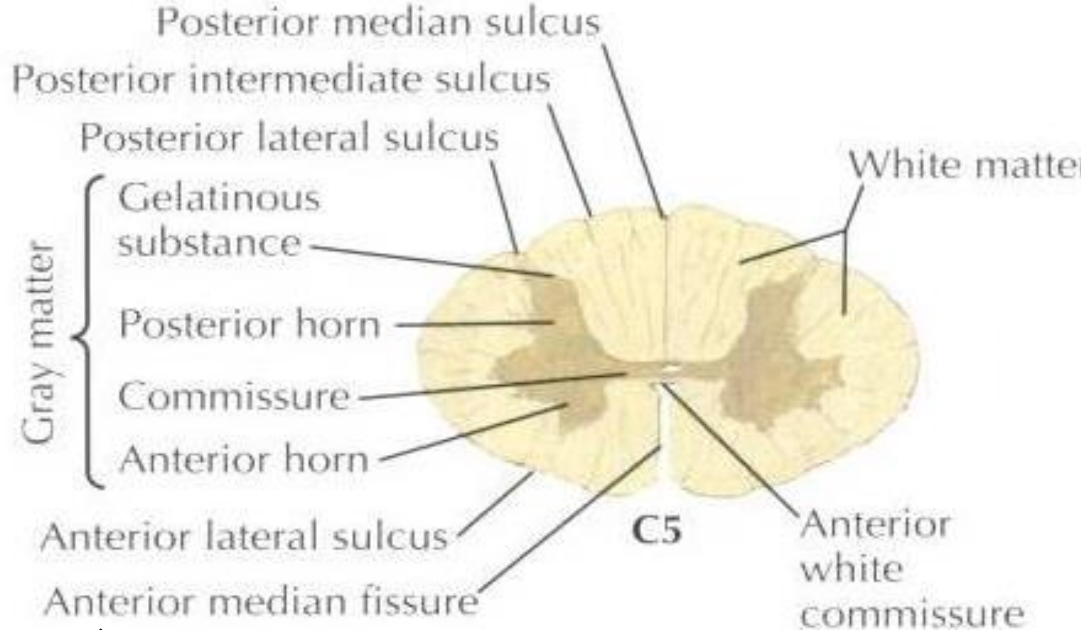
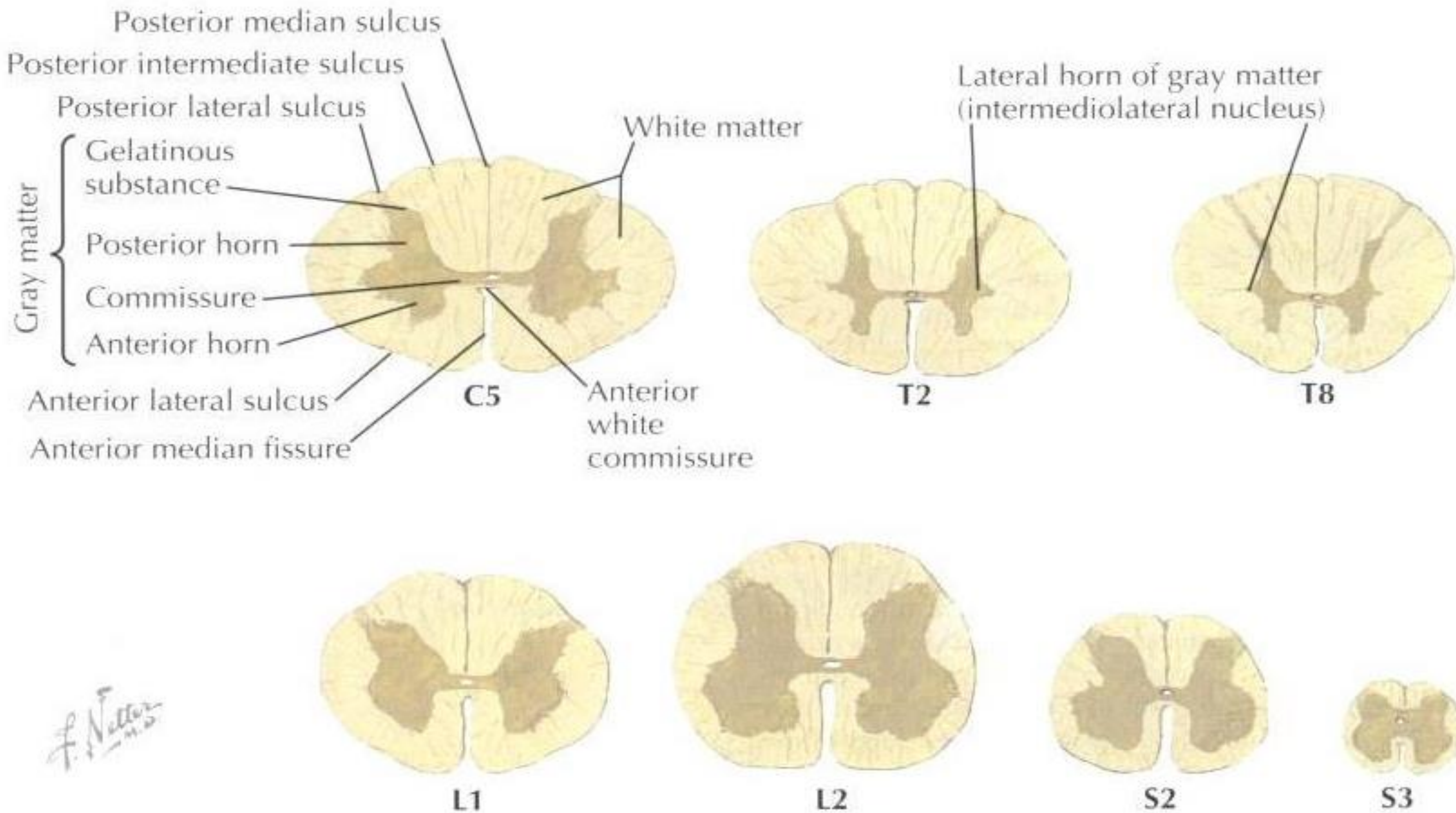


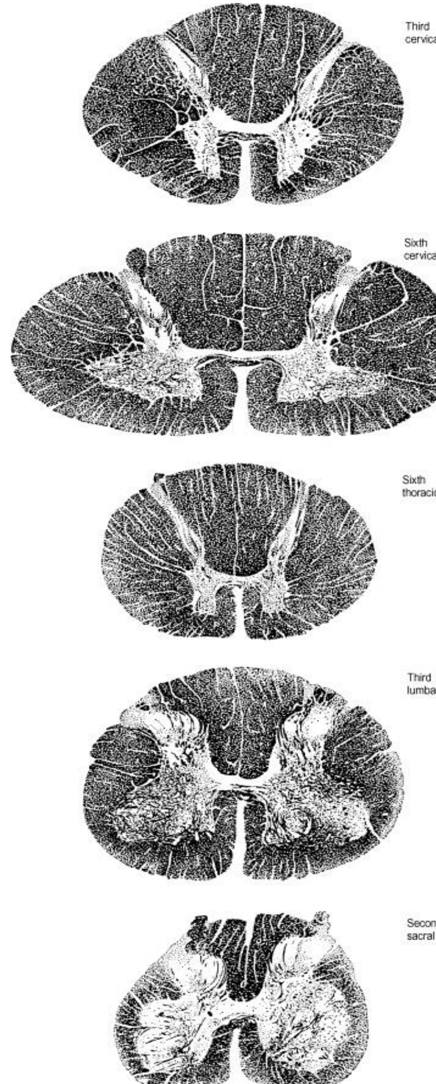
Figure 17.12 **A.** Motor horn cell with naked rootlet. **B.** In the spinal cord, oligodendroglia cells surround the ventral rootlet; outside the spinal cord, Schwann cells begin to surround the rootlet. **C.** In the spinal cord, the myelin sheath is formed by oligodendroglia cells; outside the spinal cord, the sheath is formed by Schwann cells.

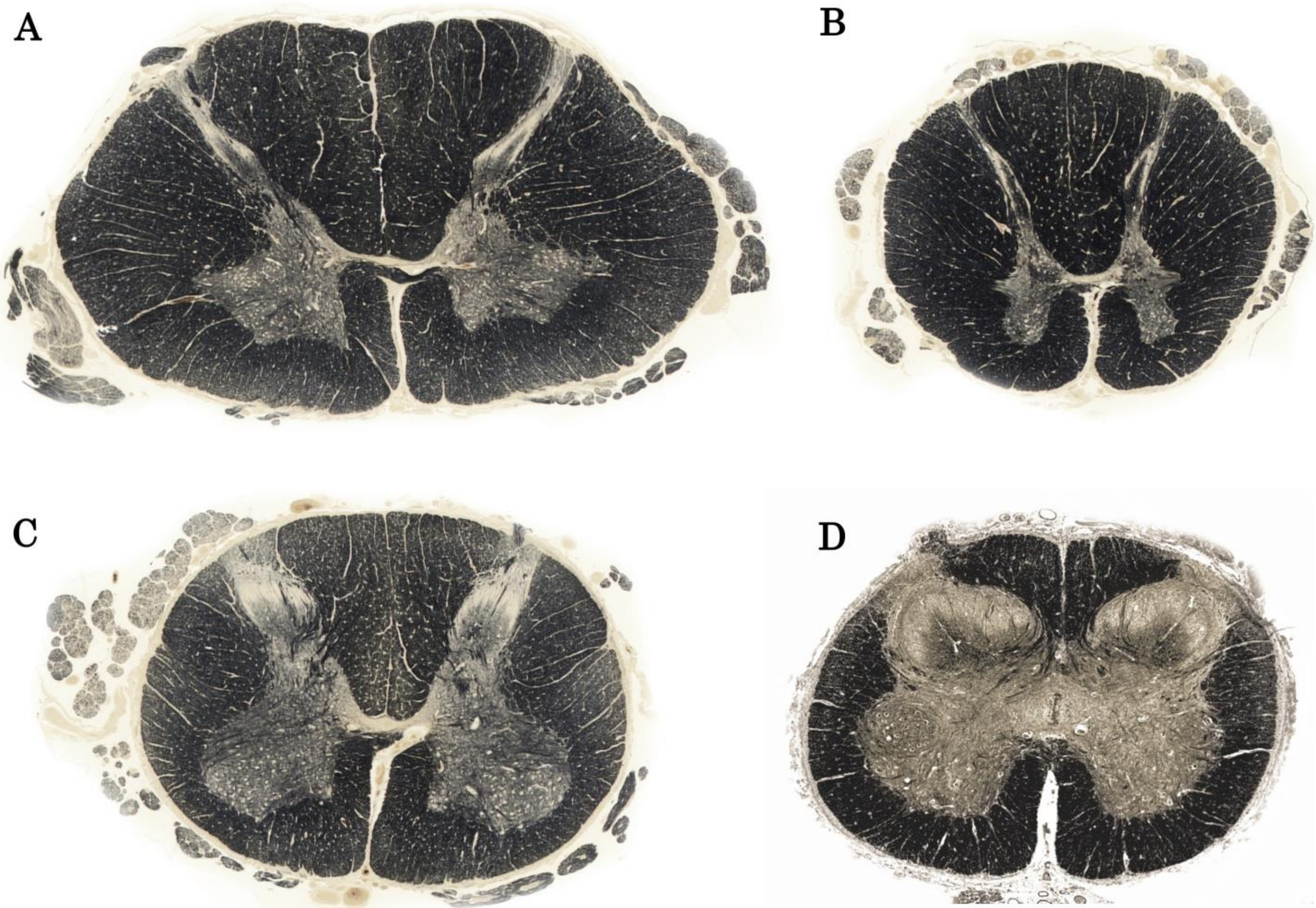



Posterior median sulcus
Posterior intermediate sulcus
Posterior lateral sulcus
Gray matter
Gelatinous substance
Posterior horn
Commissure
Anterior horn
White matter
Anterior lateral sulcus
Anterior median fissure
C5
Anterior white commissure

Sections through spinal cord at various levels

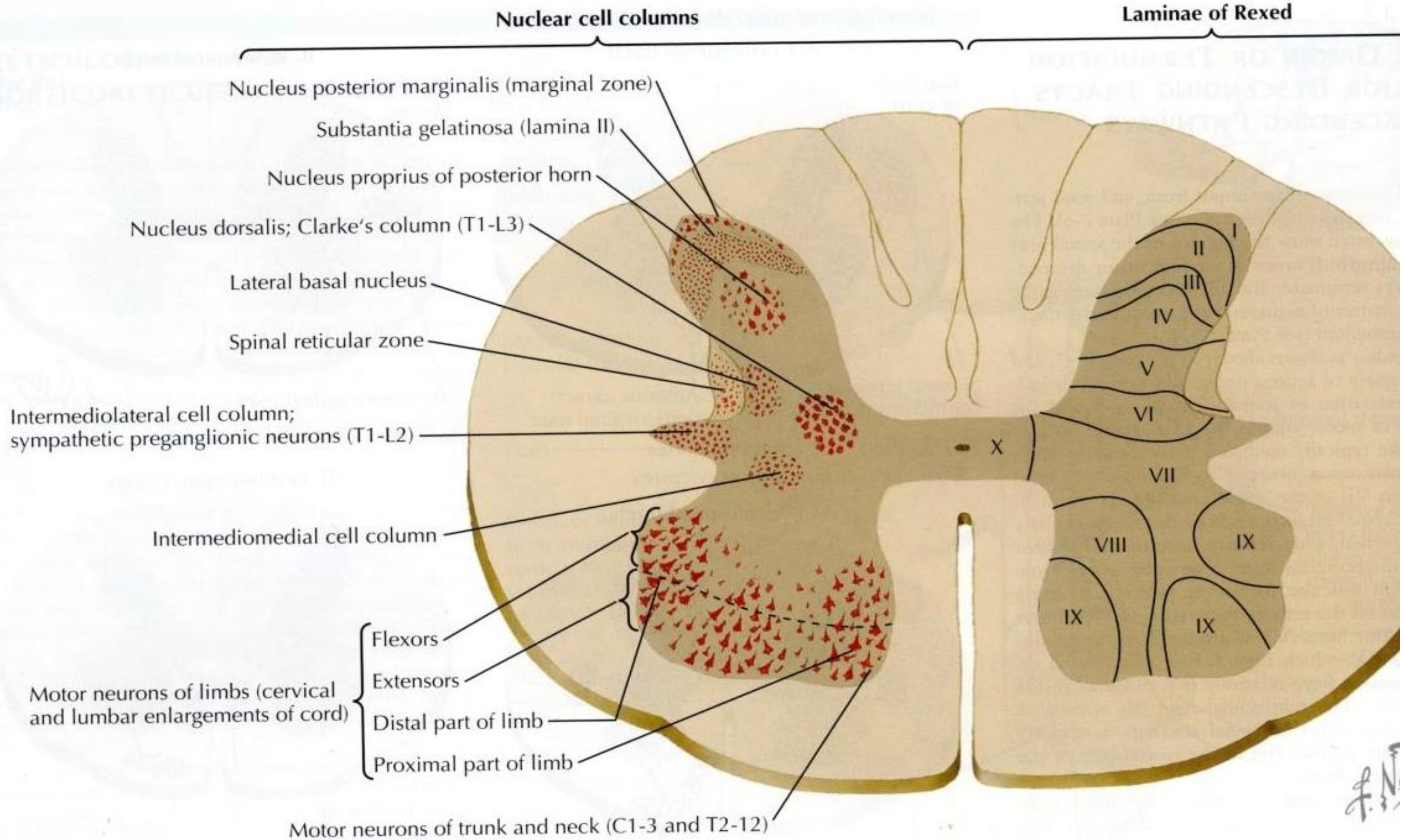



Third
cervical
Sixth
cervical
Sixth
thoracic
Third
lumbar
Second
sacral


A
B
C
D

SPINAL CORD SERIAL SECTIONS

https://pathpresenter.net/#/public/display?token=bca1eaba


Nuclear cell columns
Laminae of Rexed
Nucleus posterior marginalis (marginal zone)
Substantia gelatinosa (lamina II)
Nucleus proprius of posterior horn
Nucleus dorsalis; Clarke's column (T1-L3)
Lateral basal nucleus
Spinal reticular zone
Intermediolateral cell column;
sympathetic preganglionic neurons (T1-L2)
Intermediomedial cell column
Flexors
Extensors
Motor neurons of limbs (cervical
and lumbar enlargements of cord)
Distal part of limb
Proximal part of limb
Motor neurons of trunk and neck (C1-3 and T2-12)
I
II
III
IV
V
VI
VII
VIII
IX
IX
IX
IX
X

SPINAL CORD NISSL

https://pathpresenter.net/#/public/display?token=01011230

SPINAL CORD SILVER

https://pathpresenter.net/#/public/display?token=12ceaaa7

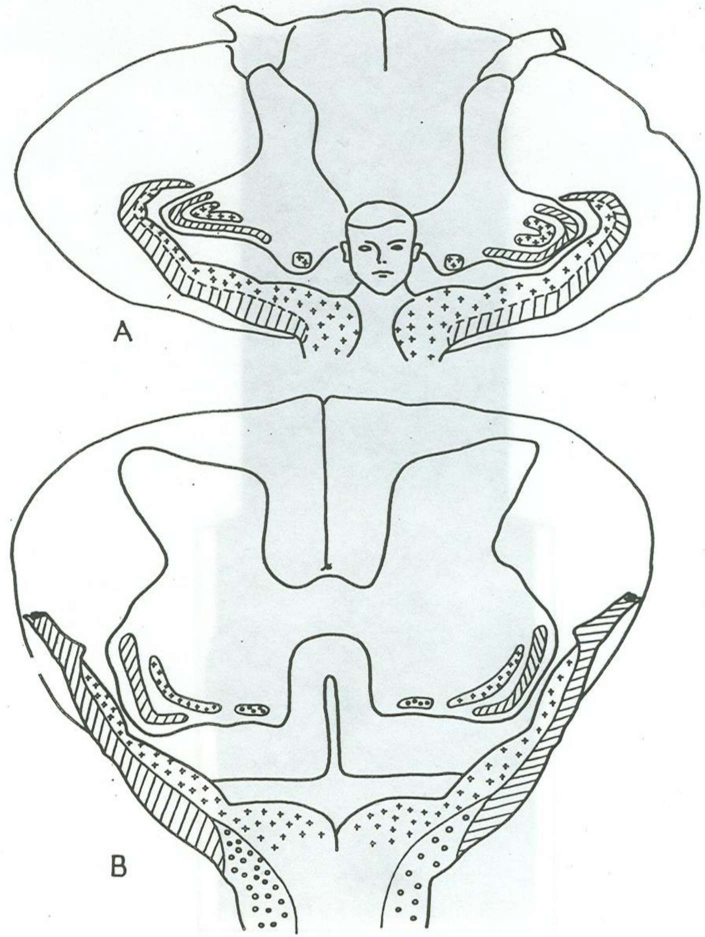


FIG. 16. — *Figure schématique faisant ressortir au niveau des renflements médullaires cervicaux et lombaires les correspondances entre les groupements de motoneurones et les muscles innervés* (d'après CROSBY et coll. [4] et DELMAS [5], modifié).

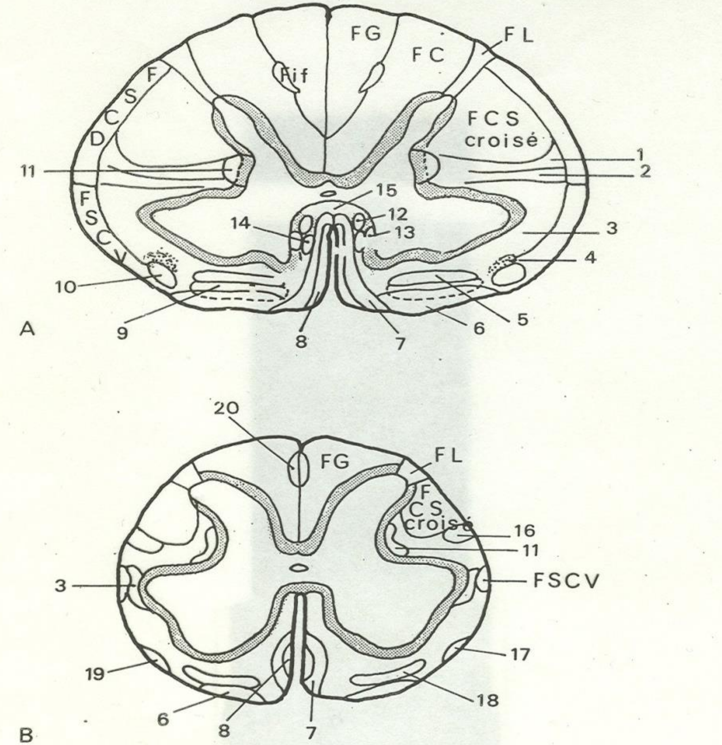
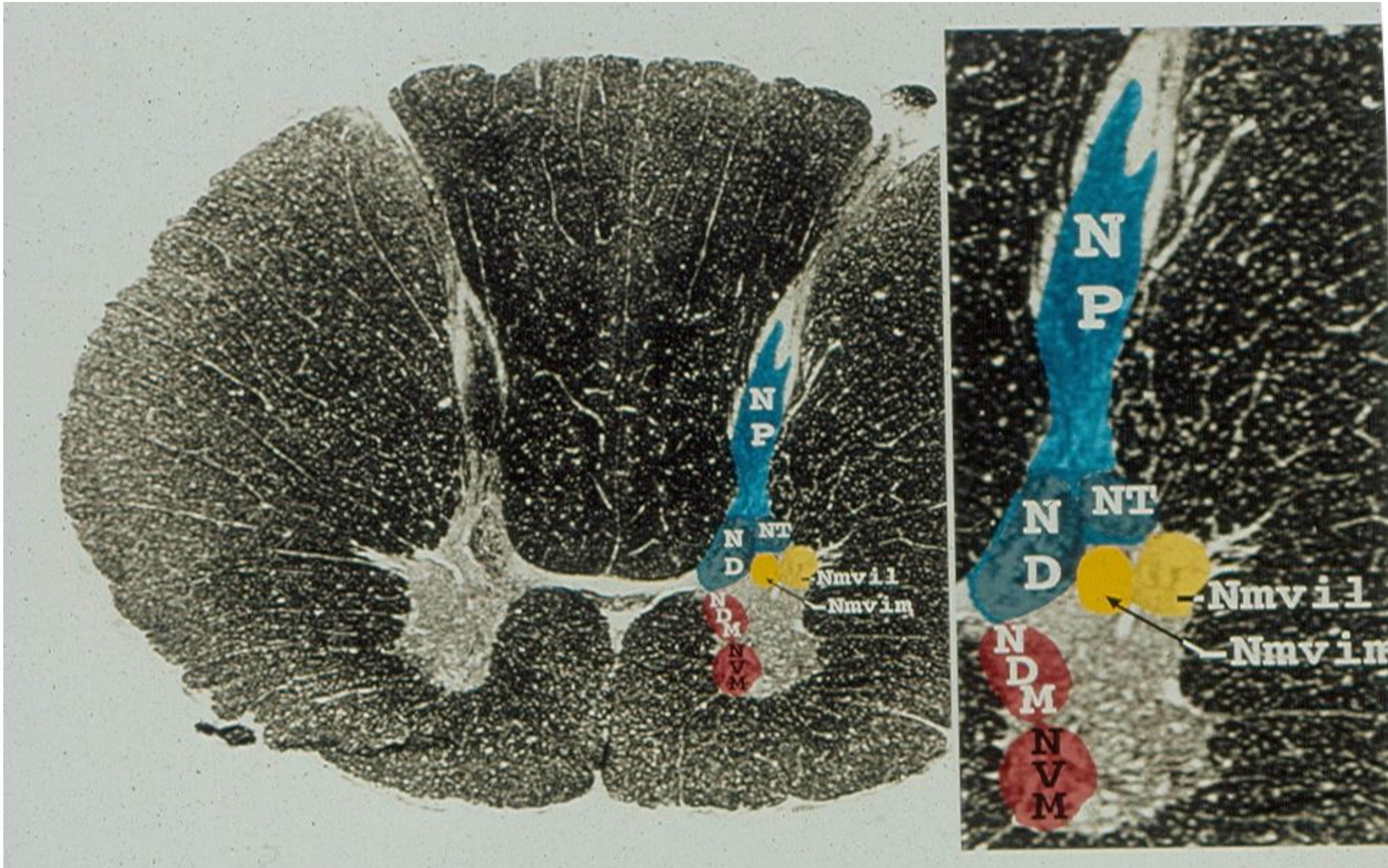
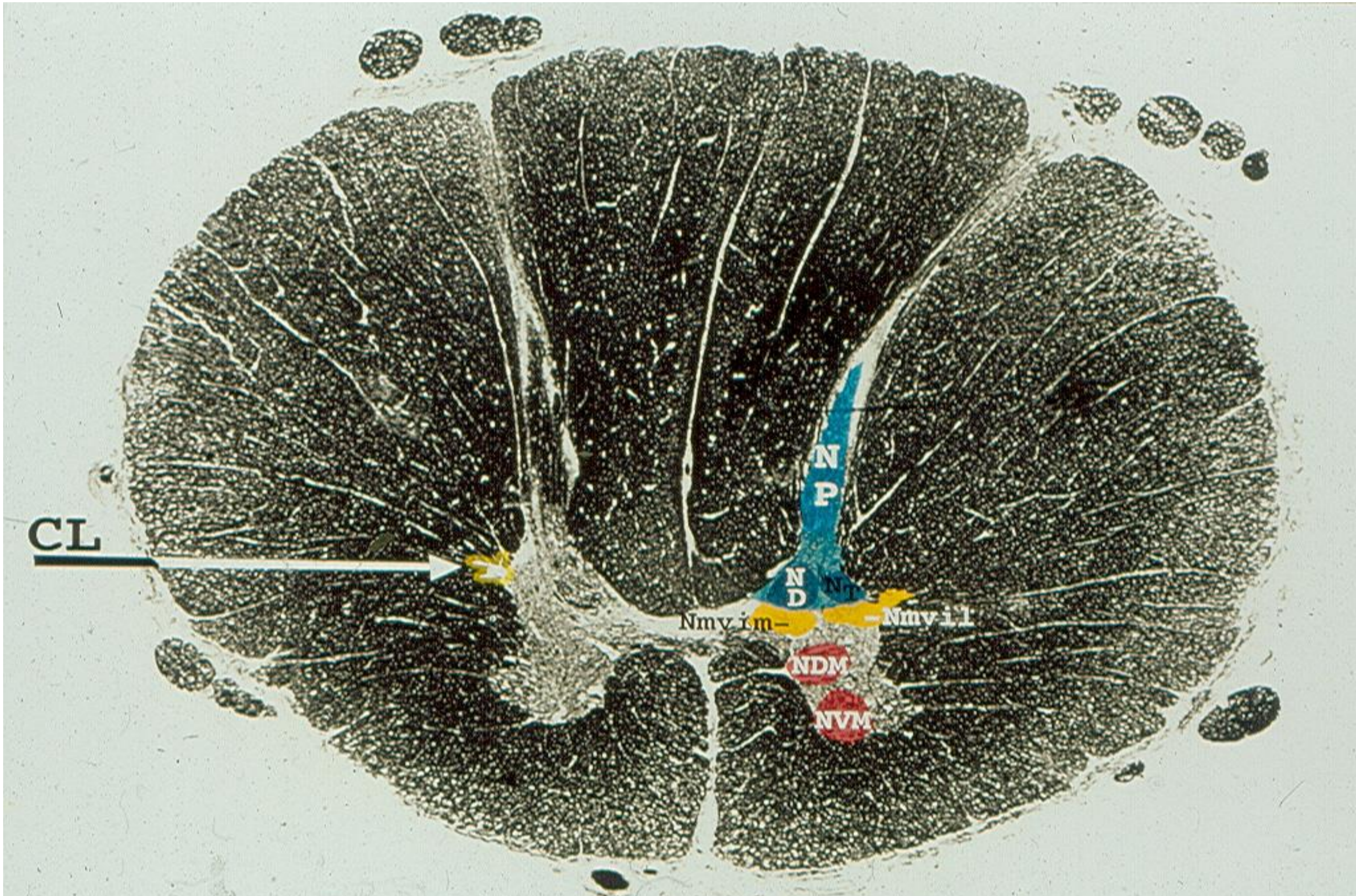


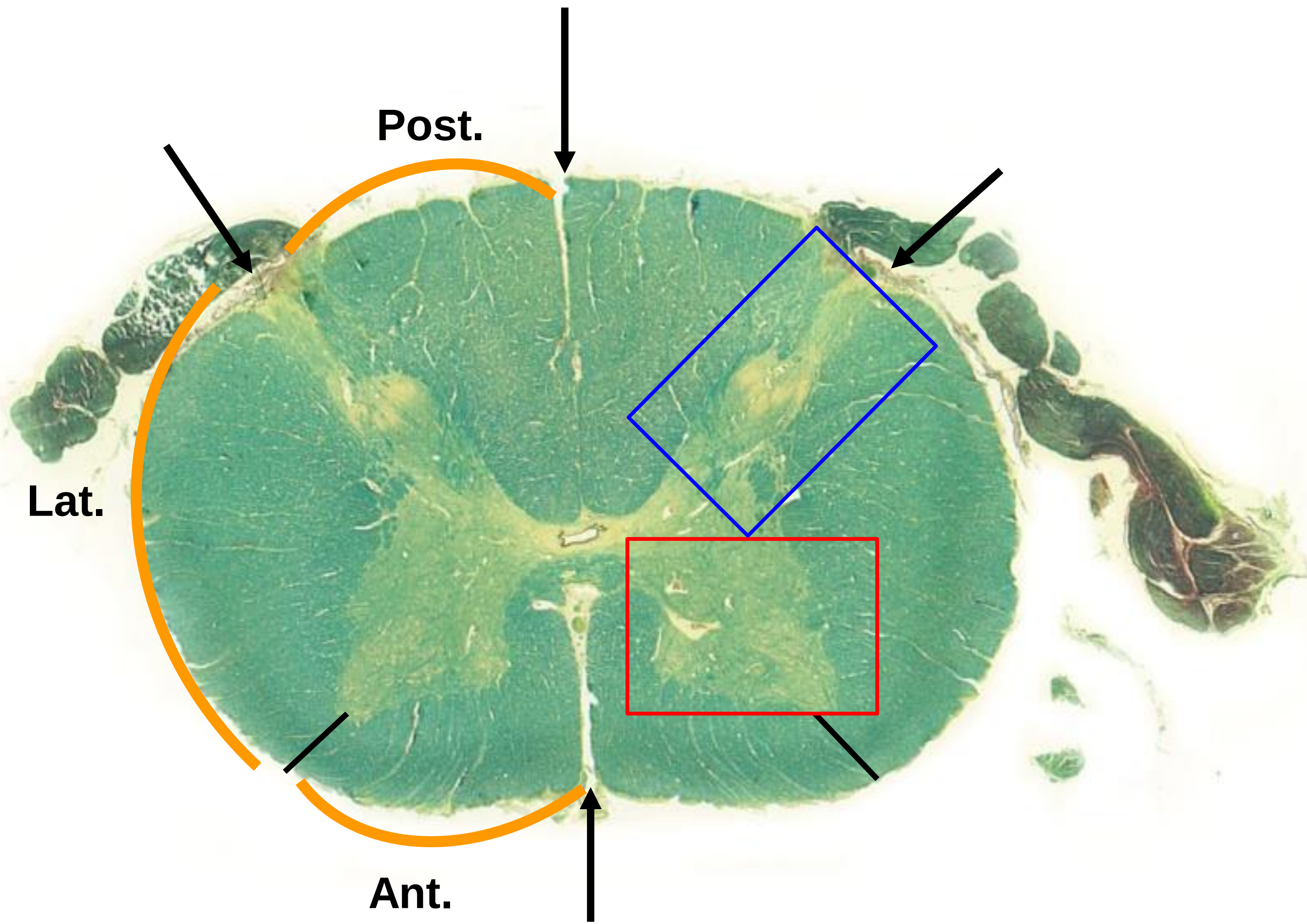
Fig. 19. — *Disposition schématique des principaux faisceaux ascendants et descendants médullaires au niveau des renflements cervicaux* (A) *et lombaires* (B) *chez l'Homme* (d'après Crosby et coll. [4] légèrement modifié).

1, F. rubro-tegmento-spinal ; 2, F. tecto-tegmento-spinal latéral ; 3, F. spino-thalamique latéral + F. spino-tectal ; 4, F. réticulo-spinal ventro-latéral ; 5, F. vestibulo-spinal latéral ; 6, F. spino-thalamique ventral ; 7, F. cortico-spinal direct ; 8, F. sulco-marginal ; 9, F. réticulo-spinal ventral ; 10, F. olivo-spinal + F. spino-olivaire ; 11, F. réticulo-spinal latéral ; 12, F. longitudinal médian ; 13, F. réticulo-spinal médian ; 14, F. tecto-spinal médian ; 15, commissure blanche ventrale ; 16, F. tegmento-spinal ; 17, F. cérébello-spinal ; 18, F. vestibulo-spinal latéral ; 19, F. spino-olivaire ; 20, F. septo-marginal ; F. G, F. gracilis (de Goll) ; F. C, F. cunéiforme (de Burdach) ; F. C. S. croisé, F. cortico-spinal croisé ; F. L, F. de Lissauer ; F. S. C. V., F. spino-cérébelleux ventral ; F. S. C. D., F. spino-cérébelleux dorsal + F. spino-vestibulaire ; F. i. f., F. interfasciculaire.
La bande pointillée entourant la moelle grise correspond à la localisation de l'ensemble des voies propriospinales.

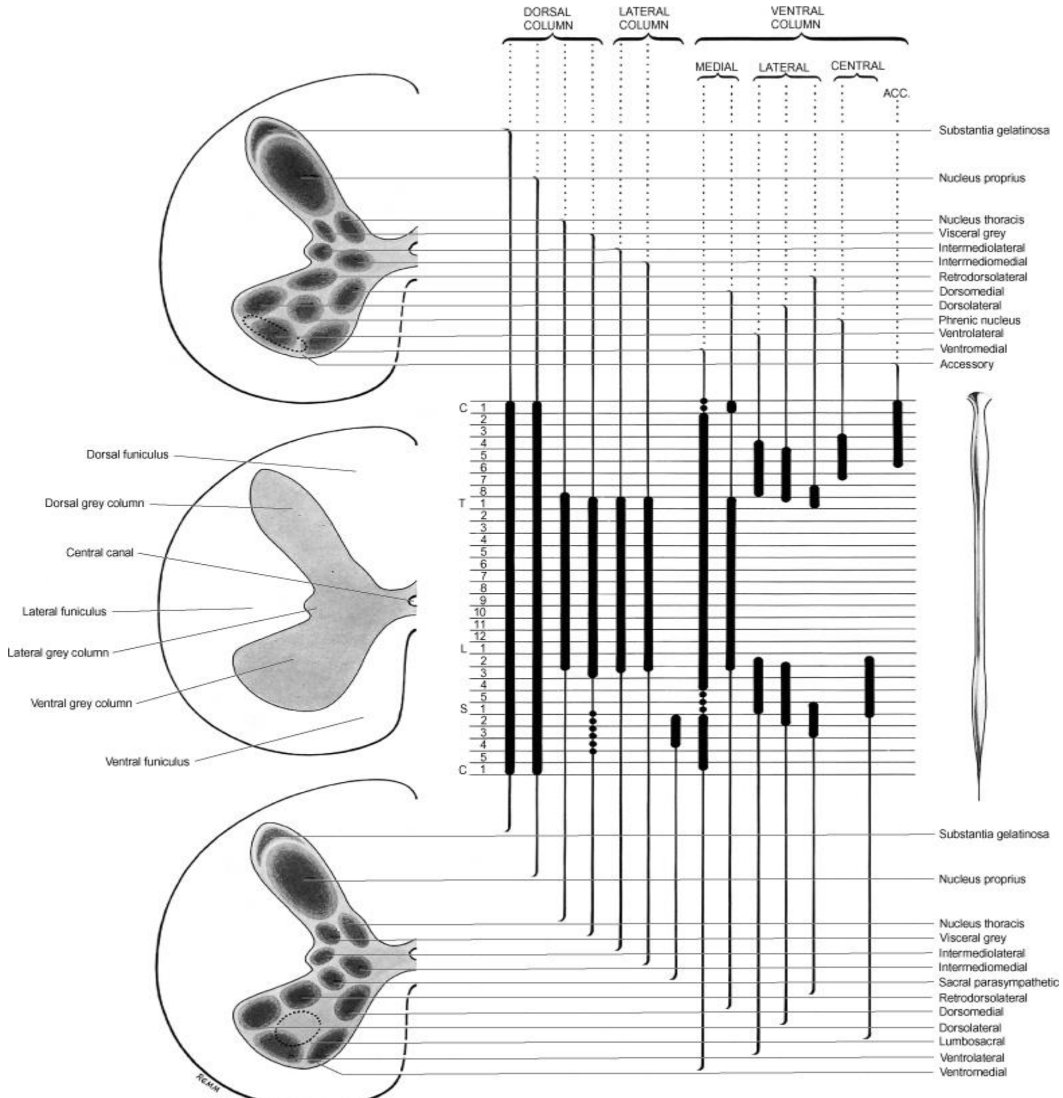


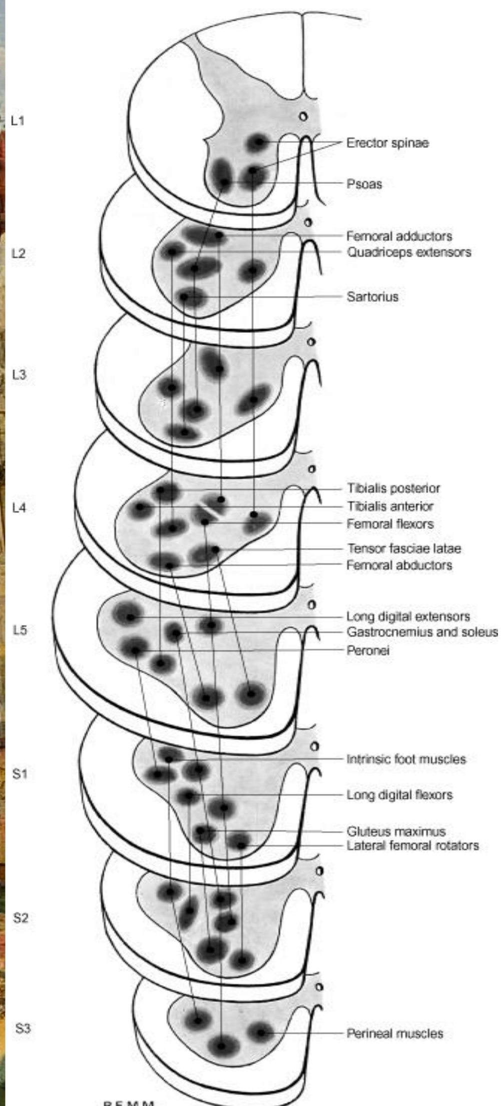
NP
NT
ND
Nmvil
Nmvim
NDM
NVM
NP
NT
ND
Nmvil
Nmvim
NDM
NVM

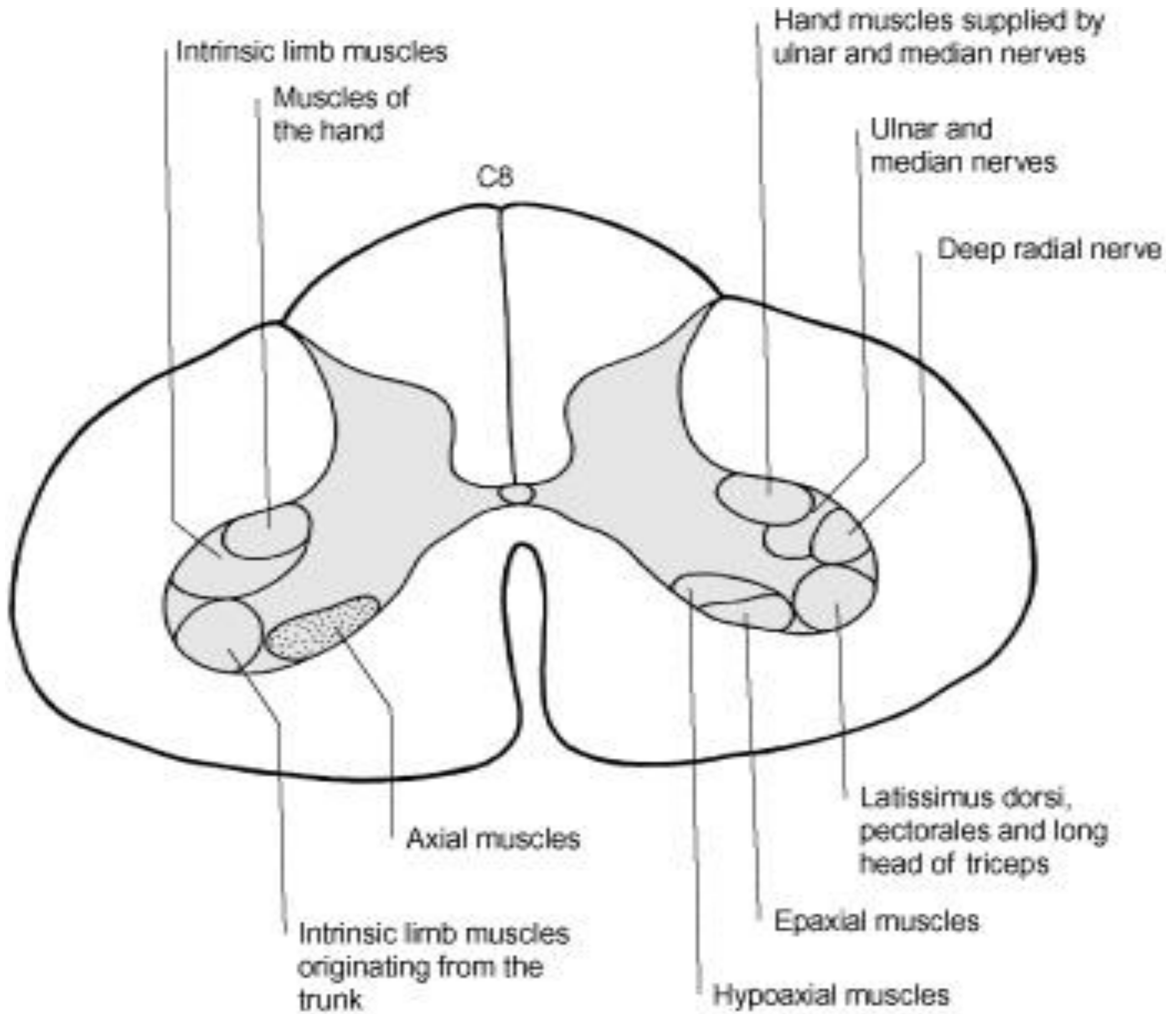

CL
NP
ND
Nmv im-
-Nmv il
NDM
NVM



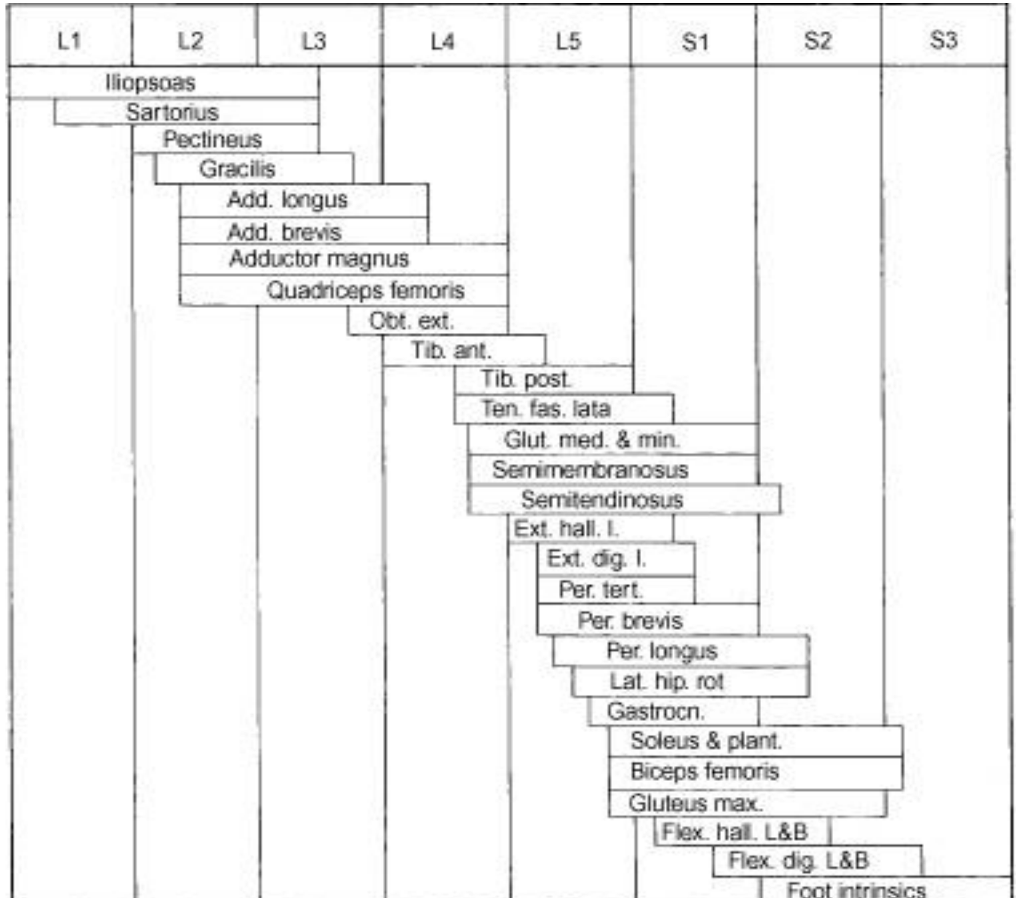
Post.
Lat.
Ant.


DORSAL COLUMN
LATERAL COLUMN
VENTRAL COLUMN
MEDIAL
LATERAL
CENTRAL
ACC.
Substantia gelatinosa
Nucleus proprius
Nucleus thoracis
Visceral grey
Intermediolateral
Intermediomedial
Retrodorsolateral
Dorsomedial
Dorsolateral
Phrenic nucleus
Ventrolateral
Ventromedial
Accessory
Dorsal funiculus
Dorsal grey column
Central canal
Lateral funiculus
Lateral grey column
Ventral grey column
Ventral funiculus
C 1 2 3 4 5 6 7 8
T 1 2 3 4 5 6 7 8 9 10 11 12
L 1 2 3 4 5
S 1 2 3 4 5
C 1
Substantia gelatinosa
Nucleus proprius
Nucleus thoracis
Visceral grey
Intermediolateral
Intermediomedial
Sacral parasympathetic
Retrodorsolateral
Dorsomedial
Dorsolateral
Lumbosacral
Ventrolateral
Ventromedial


L1
L2
L3
L4
L5
S1
S2
S3
Erector spinae
Psoas
Femoral adductors
Quadriceps extensors
Sartorius
Tibialis posterior
Tibialis anterior
Femoral flexors
Tensor fasciae latae
Femoral abductors
Long digital extensors
Gastrocnemius and soleus
Peronei
Intrinsic foot muscles
Long digital flexors
Gluteus maximus
Lateral femoral rotators
Perineal muscles
R.E.M.M.



Intrinsic limb muscles
Muscles of the hand
C8
Hand muscles supplied by ulnar and median nerves
Ulnar and median nerves
Deep radial nerve
Latissimus dorsi, pectorales and long head of triceps
Epaxial muscles
Hypoaxial muscles
Axial muscles
Intrinsic limb muscles originating from the trunk



L1
L2
L3
L4
L5
S1
S2
S3
Iliopsoas
Sartorius
Pectineus
Gracilis
Add. longus
Add. brevis
Adductor magnus
Quadriceps femoris
Obt. ext.
Tib. ant.
Tib. post.
Ten. fas. lata
Glut. med. & min.
Semimembranosus
Semitendinosus
Ext. hall. l.
Ext. dig. l.
Per. tert.
Per. brevis
Per. longus
Lat. hip. rot
Gastrocn.
Soleus & plant.
Biceps femoris
Gluteus max.
Flex. hall. L&B
Flex. dig. L&B
Foot intrinsics

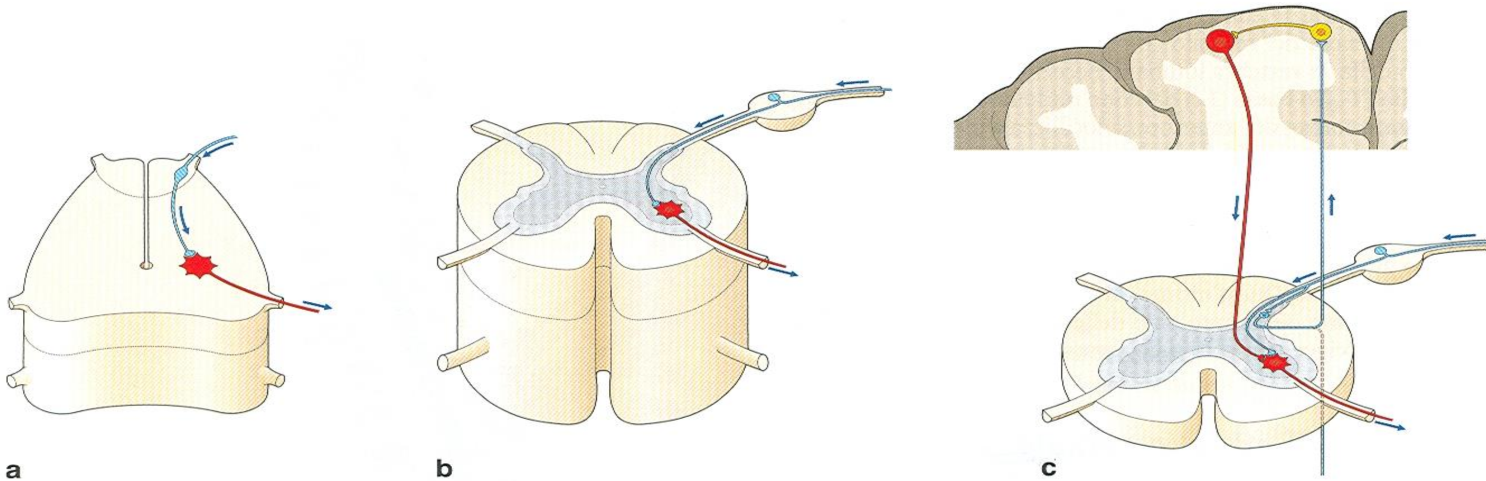
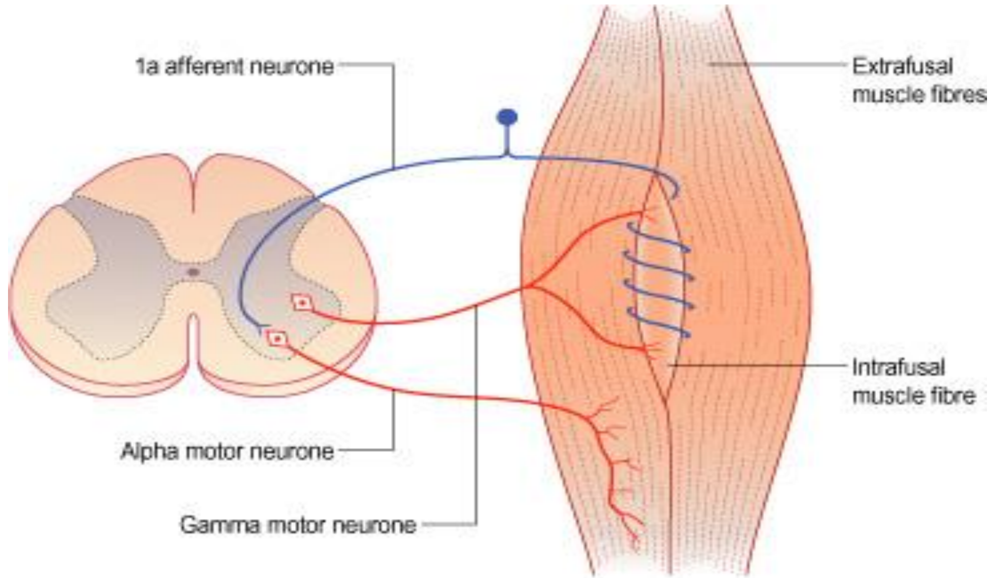
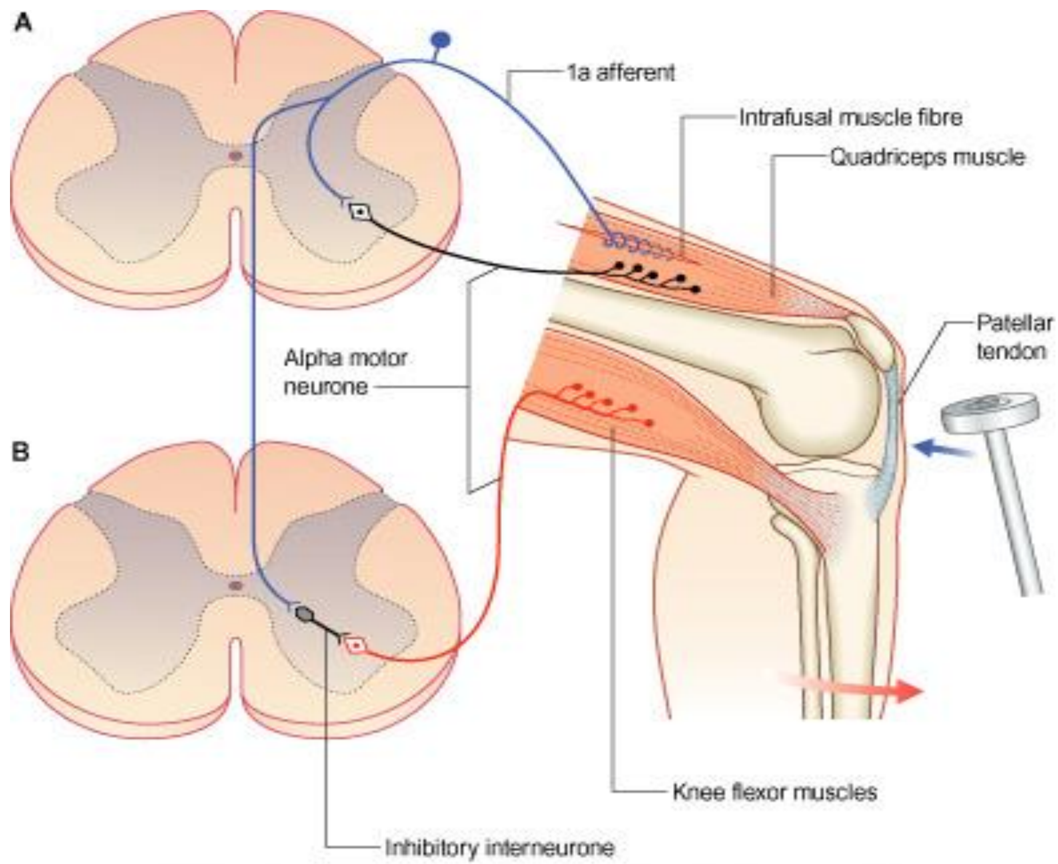
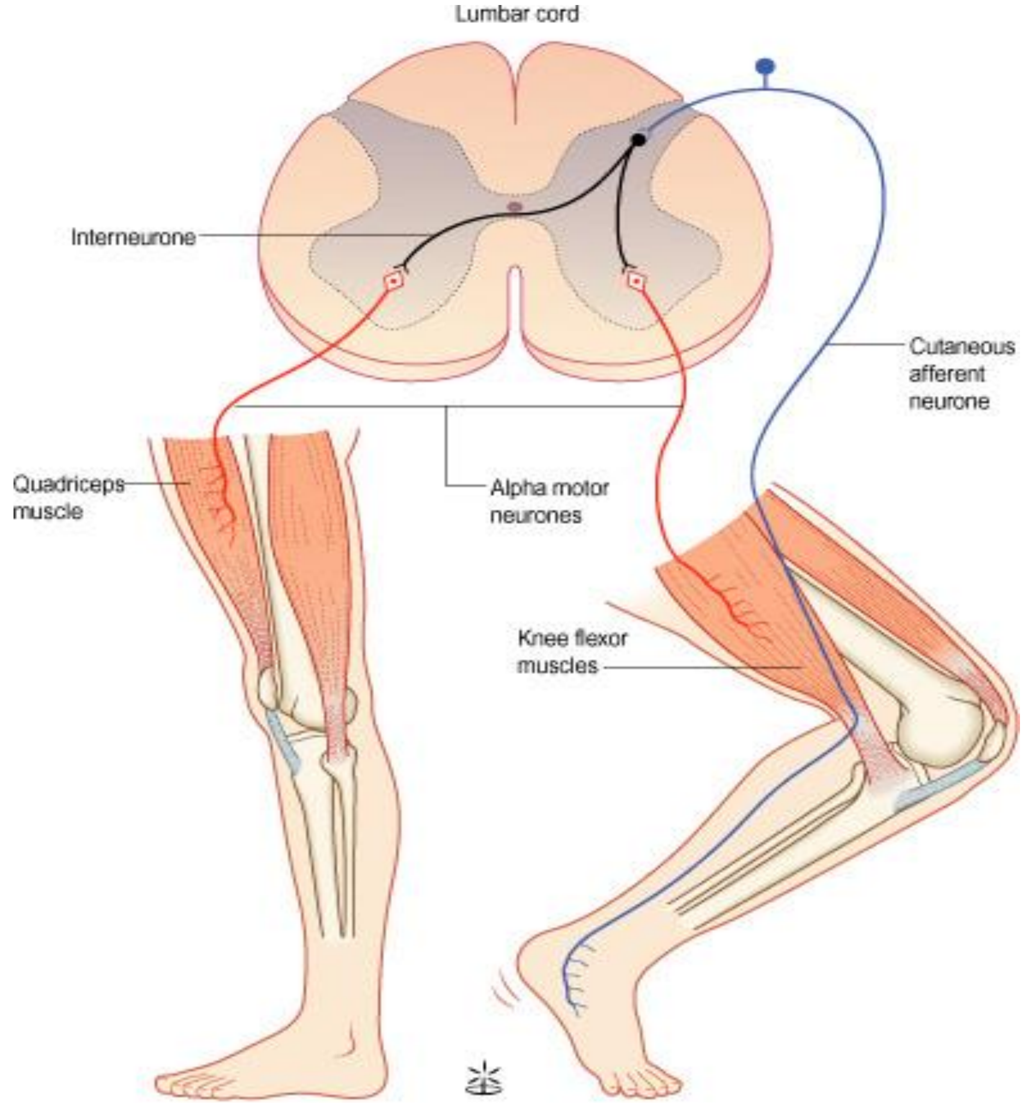
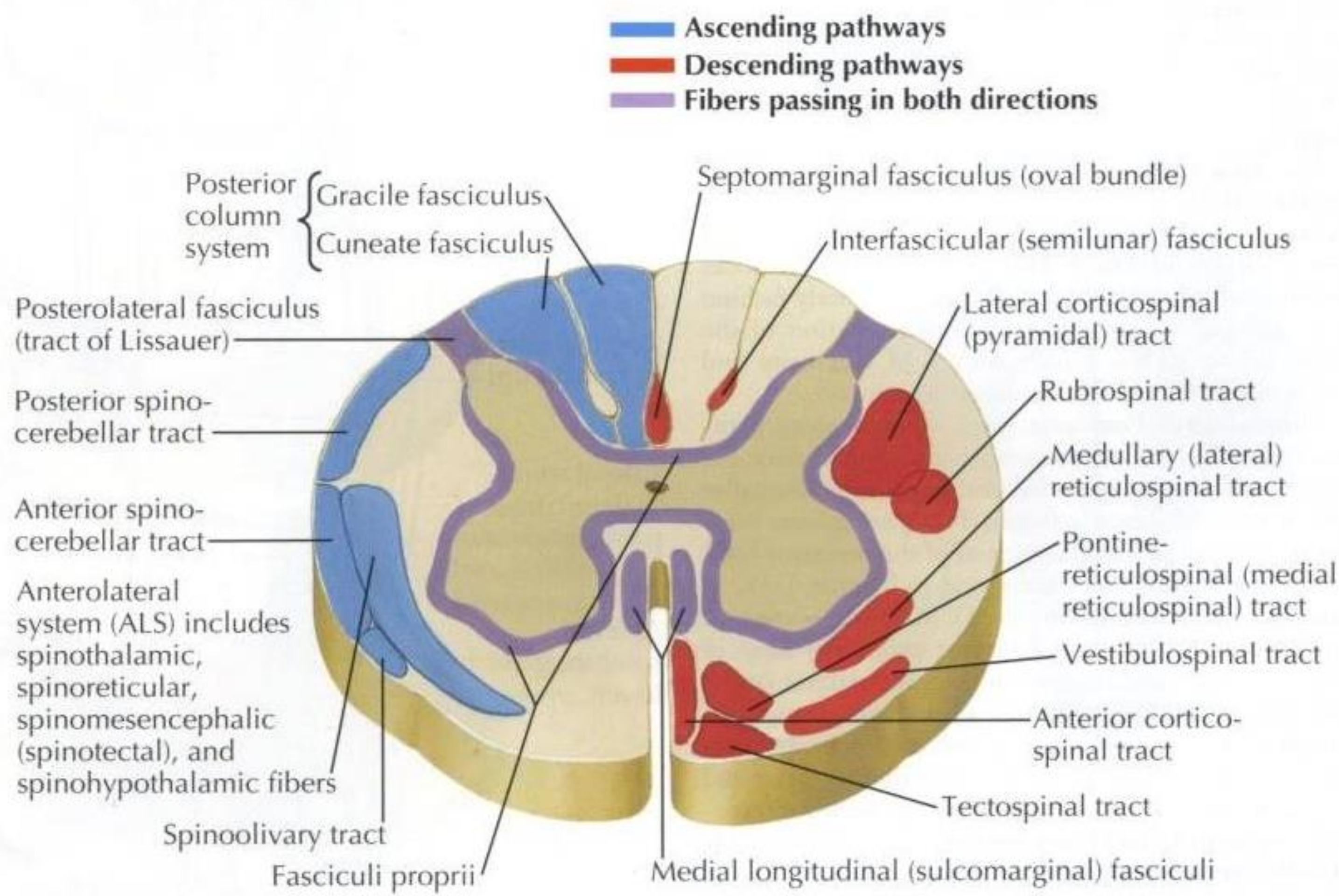


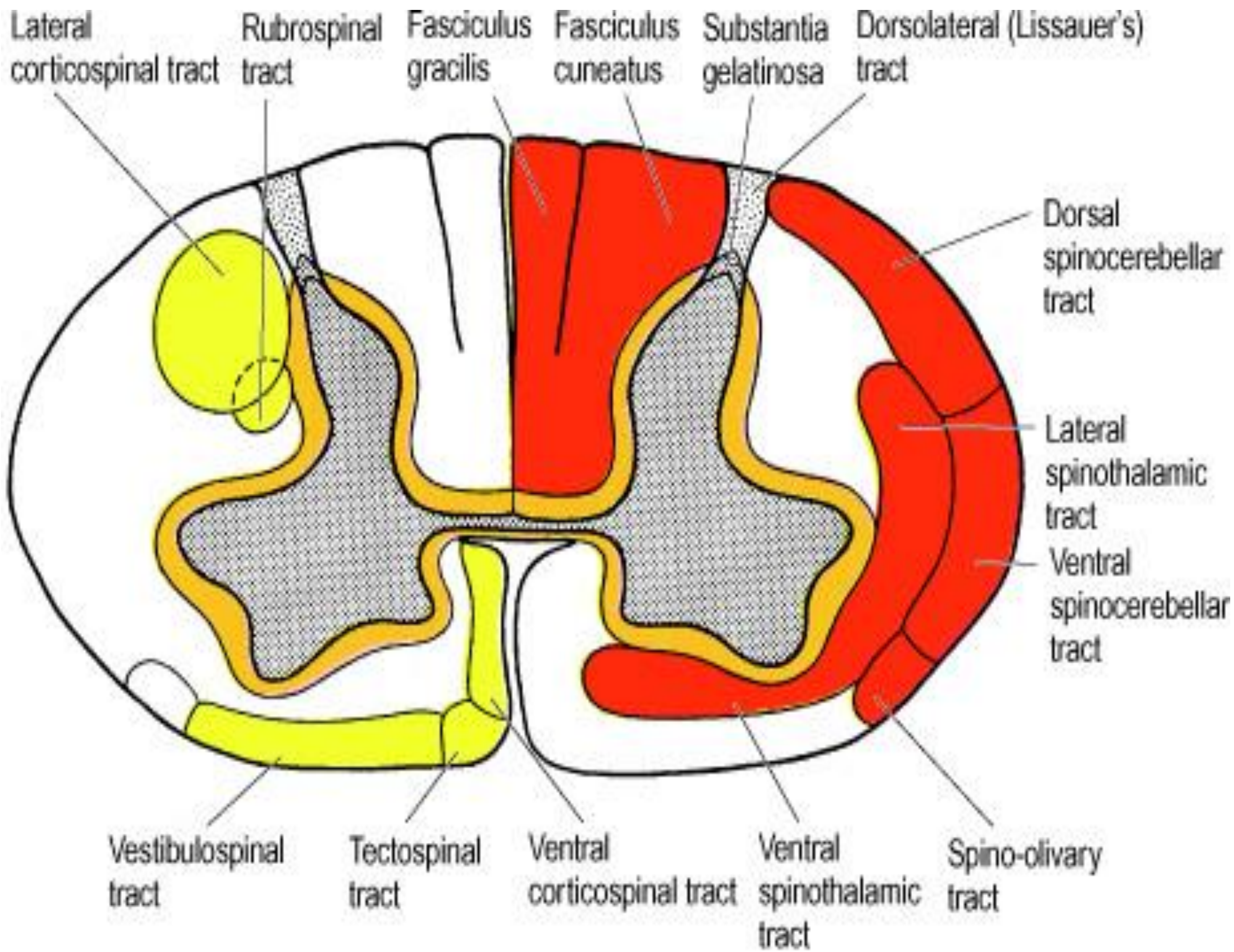
Figura 14.30 - Rappresentazione schematica dei rapporti che si stabiliscono tra neuroni sensitivi (**blu**) e neuroni di moto (**rosso**) in organizzazioni nervose centralizzate. **a**, Nei Cefalocordati, gli elementi sensitivi e quelli effettori sono localizzati nell'asse nervoso; **b**, nei Vertebrati, il protoneurone sensitivo ha sede al di fuori del nevrasse, in formazioni chiamate gangli; **c**, archi riflessi orizzontali a disposizione segmentaria e archi verticali in cui si riconoscono linee di collegamento ascendenti e discendenti.


1a afferent neurone
Extrafusal muscle fibres
Intrafusal muscle fibre
Alpha motor neurone
Gamma motor neurone

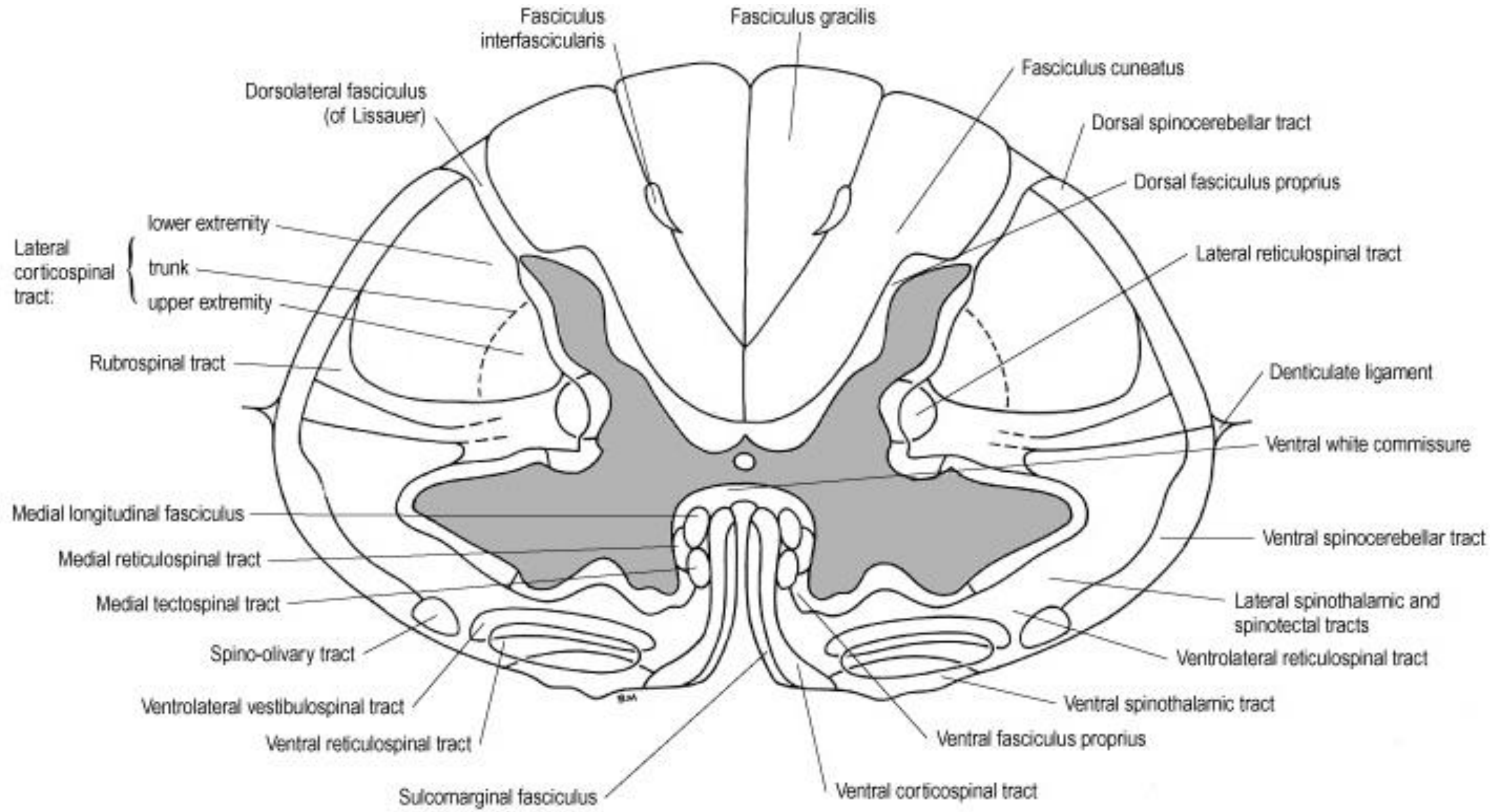

A
B
1a afferent
Intrafusal muscle fibre
Quadriceps muscle
Patellar
tendon
Alpha motor
neurone
Knee flexor muscles
Inhibitory interneurone

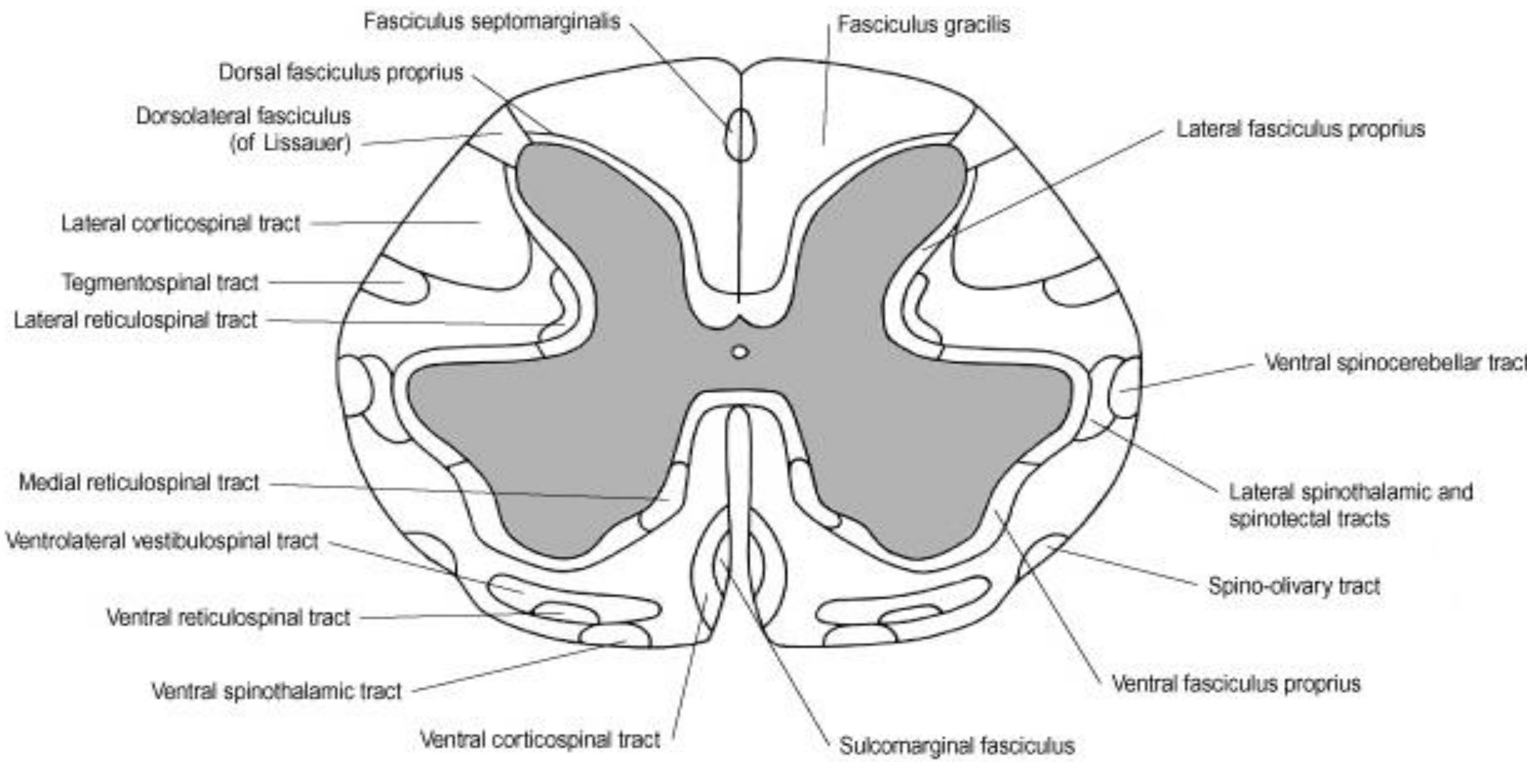

Lumbar cord
Interneurone
Cutaneous
afferent
neurone
Quadriceps
muscle
Alpha motor
neurones
Knee flexor
muscles

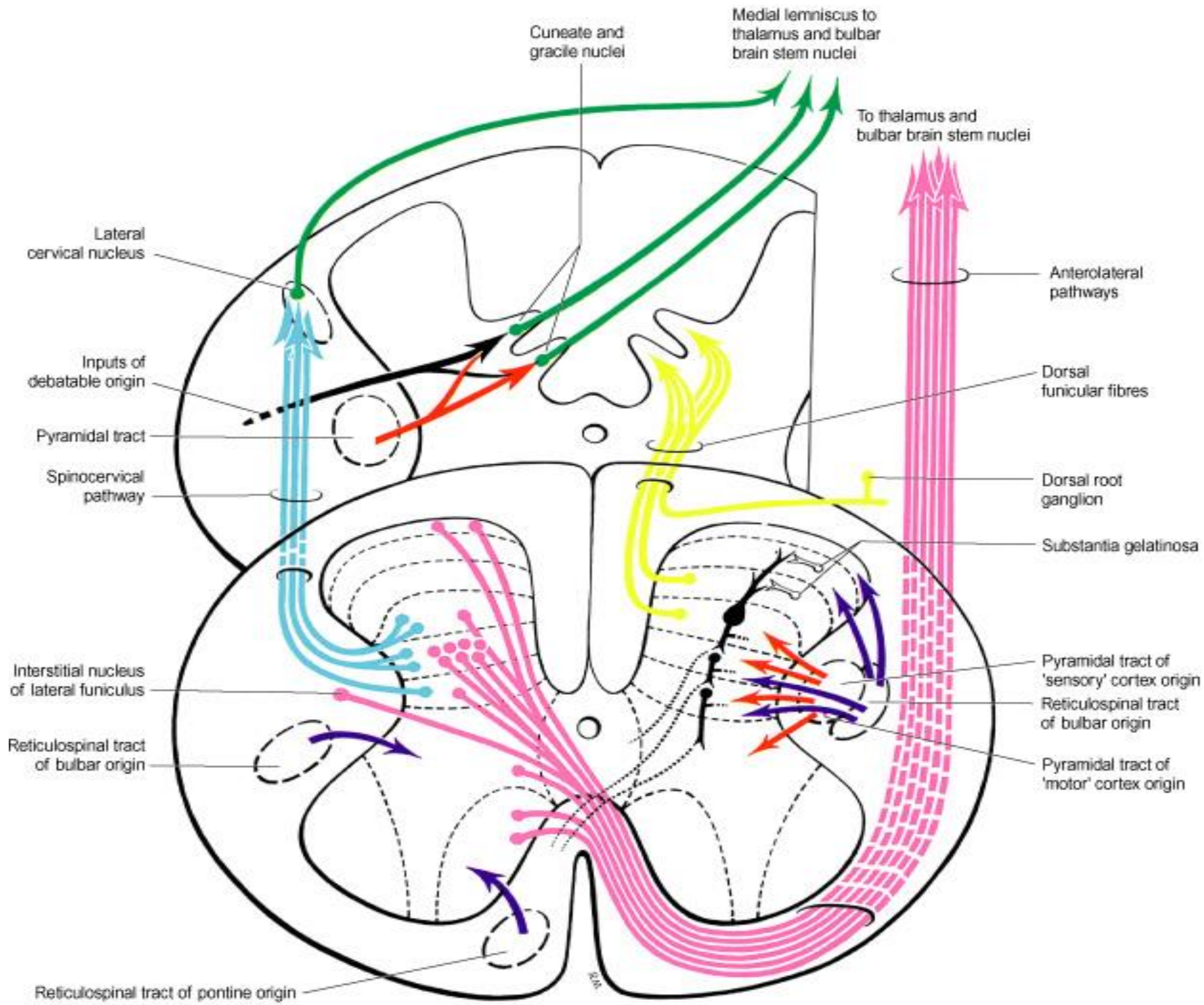

Ascending pathways
Descending pathways
Fibers passing in both directions
Posterior column system
Gracile fasciculus
Cuneate fasciculus
Septomarginal fasciculus (oval bundle)
Interfascicular (semilunar) fasciculus
Posterolateral fasciculus (tract of Lissauer)
Lateral corticospinal (pyramidal) tract
Rubrospinal tract
Posterior spino-cerebellar tract
Medullary (lateral) reticulospinal tract
Anterior spino-cerebellar tract
Pontine-reticulospinal (medial reticulospinal) tract
Anterolateral system (ALS) includes spinothalamic, spinoreticular, spinomesencephalic (spinotectal), and spinohypothalamic fibers
Vestibulospinal tract
Anterior cortico-spinal tract
Tectospinal tract
Spinoolivary tract
Fasciculi proprii
Medial longitudinal (sulcomarginal) fasciculi



Lateral corticospinal tract
Rubrospinal tract
Fasciculus gracilis
Fasciculus cuneatus
Substantia gelatinosa
Dorsolateral (Lissauer's) tract
Dorsal spinocerebellar tract
Lateral spinothalamic tract
Ventral spinocerebellar tract
Vestibulospinal tract
Tectospinal tract
Ventral corticospinal tract
Ventral spinothalamic tract
Spino-olivary tract


Fasciculus interfascicularis
Fasciculus gracilis
Fasciculus cuneatus
Dorsolateral fasciculus (of Lissauer)
Dorsal spinocerebellar tract
Dorsal fasciculus proprius
Lateral corticospinal tract:
lower extremity
trunk
upper extremity
Lateral reticulospinal tract
Rubrospinal tract
Denticulate ligament
Ventral white commissure
Medial longitudinal fasciculus
Ventral spinocerebellar tract
Medial reticulospinal tract
Medial tectospinal tract
Lateral spinothalamic and spinotectal tracts
Spino-olivary tract
Ventrolateral reticulospinal tract
Ventrolateral vestibulospinal tract
Ventral spinothalamic tract
Ventral reticulospinal tract
Ventral fasciculus proprius
Sulcomarginal fasciculus
Ventral corticospinal tract

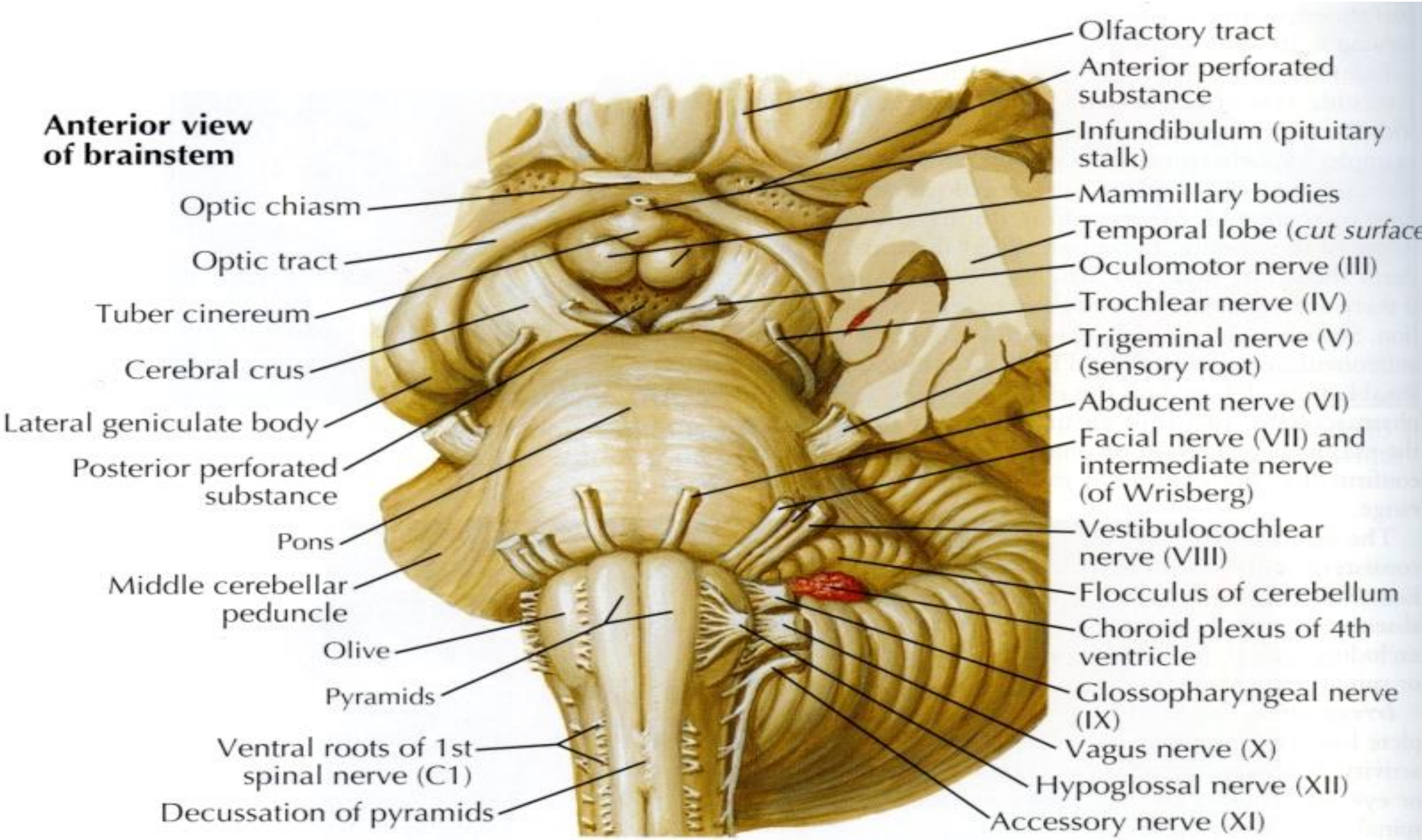

Fasciculus septomarginalis
Fasciculus gracilis
Dorsal fasciculus proprius
Dorsolateral fasciculus (of Lissauer)
Lateral fasciculus proprius
Lateral corticospinal tract
Tegmentospinal tract
Lateral reticulospinal tract
Ventral spinocerebellar tract
Medial reticulospinal tract
Lateral spinothalamic and spinotectal tracts
Ventrolateral vestibulospinal tract
Spino-olivary tract
Ventral reticulospinal tract
Ventral spinothalamic tract
Ventral fasciculus proprius
Ventral corticospinal tract
Sulcomarginal fasciculus

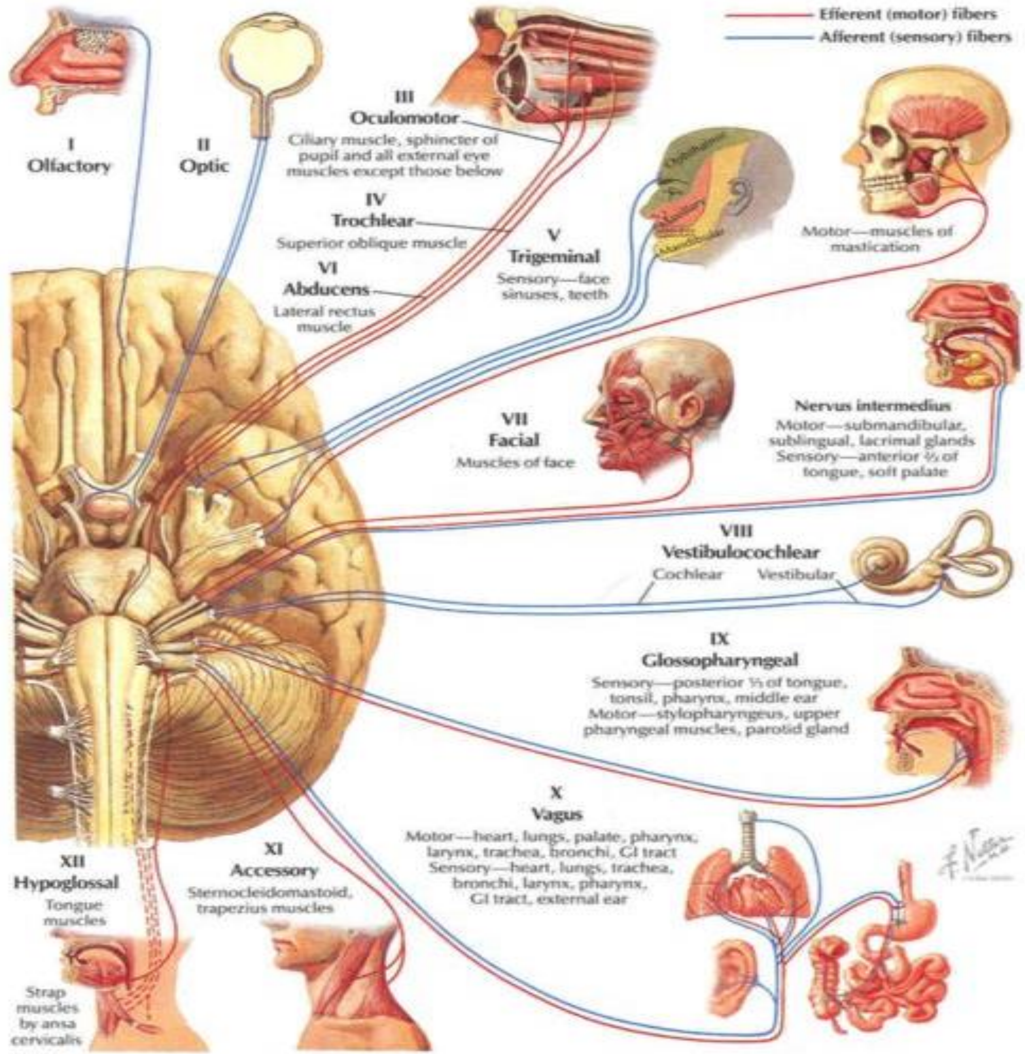


Cuneate and gracile nuclei
Medial lemniscus to thalamus and bulbar brain stem nuclei
To thalamus and bulbar brain stem nuclei
Lateral cervical nucleus
Inputs of debatable origin
Pyramidal tract
Spinocervical pathway
Anterolateral pathways
Dorsal funicular fibres
Dorsal root ganglion
Substantia gelatinosa
Pyramidal tract of 'sensory' cortex origin
Reticulospinal tract of bulbar origin
Pyramidal tract of 'motor' cortex origin
Interstitial nucleus of lateral funiculus
Reticulospinal tract of bulbar origin
Reticulospinal tract of pontine origin

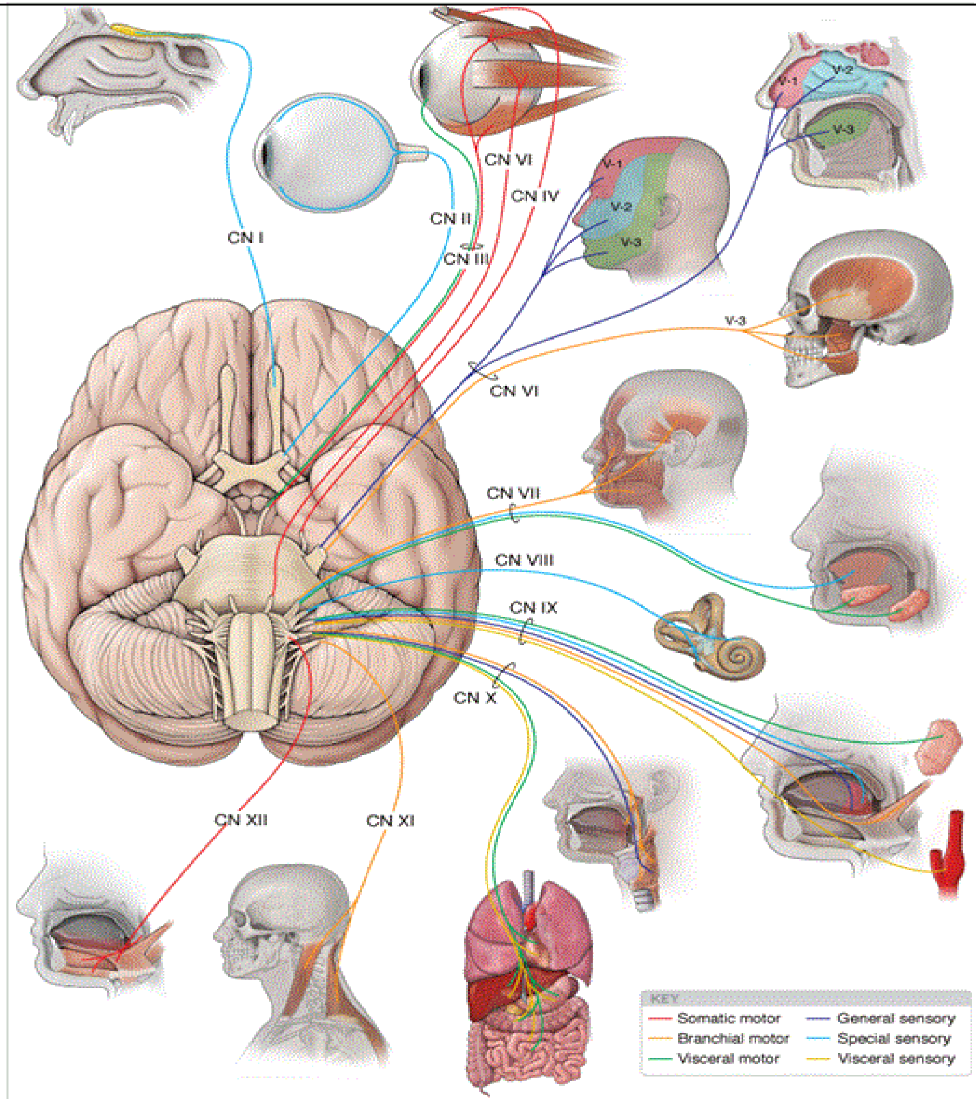
The Brainstem

V. Van Gogh – Mulberry Tree

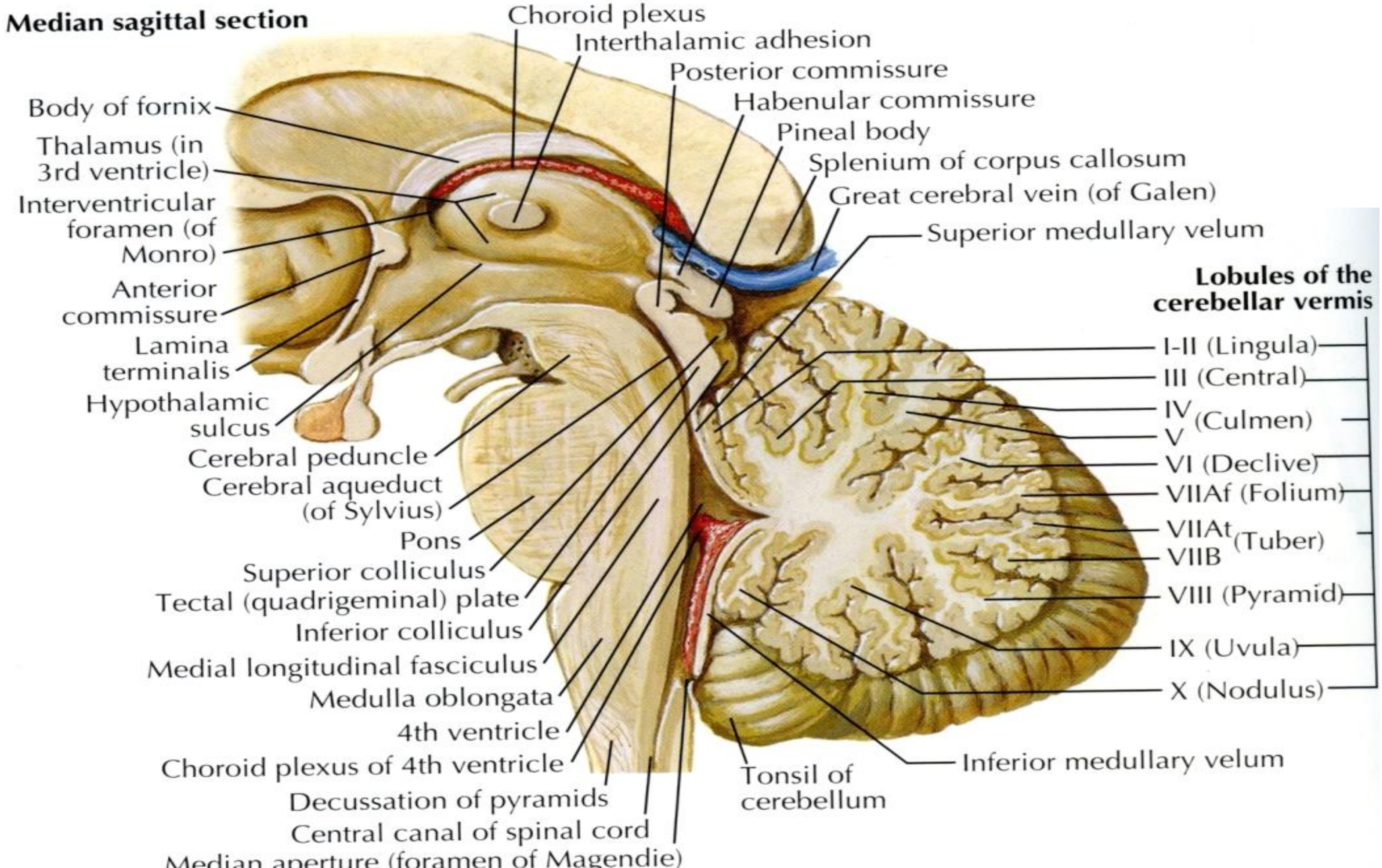

Anterior view
of brainstem
Optic chiasm
Optic tract
Tuber cinereum
Cerebral crus
Lateral geniculate body
Posterior perforated
substance
Pons
Middle cerebellar
peduncle
Olive
Pyramids
Ventral roots of 1st
spinal nerve (C1)
Decussation of pyramids
Olfactory tract
Anterior perforated
substance
Infundibulum (pituitary
stalk)
Mammillary bodies
Temporal lobe (cut surface)
Oculomotor nerve (III)
Trochlear nerve (IV)
Trigeminal nerve (V)
(sensory root)
Abducent nerve (VI)
Facial nerve (VII) and
intermediate nerve
(of Wrisberg)
Vestibulocochlear
nerve (VIII)
Flocculus of cerebellum
Choroid plexus of 4th
ventricle
Glossopharyngeal nerve
(IX)
Vagus nerve (X)
Hypoglossal nerve (XII)
Accessory nerve (XI)



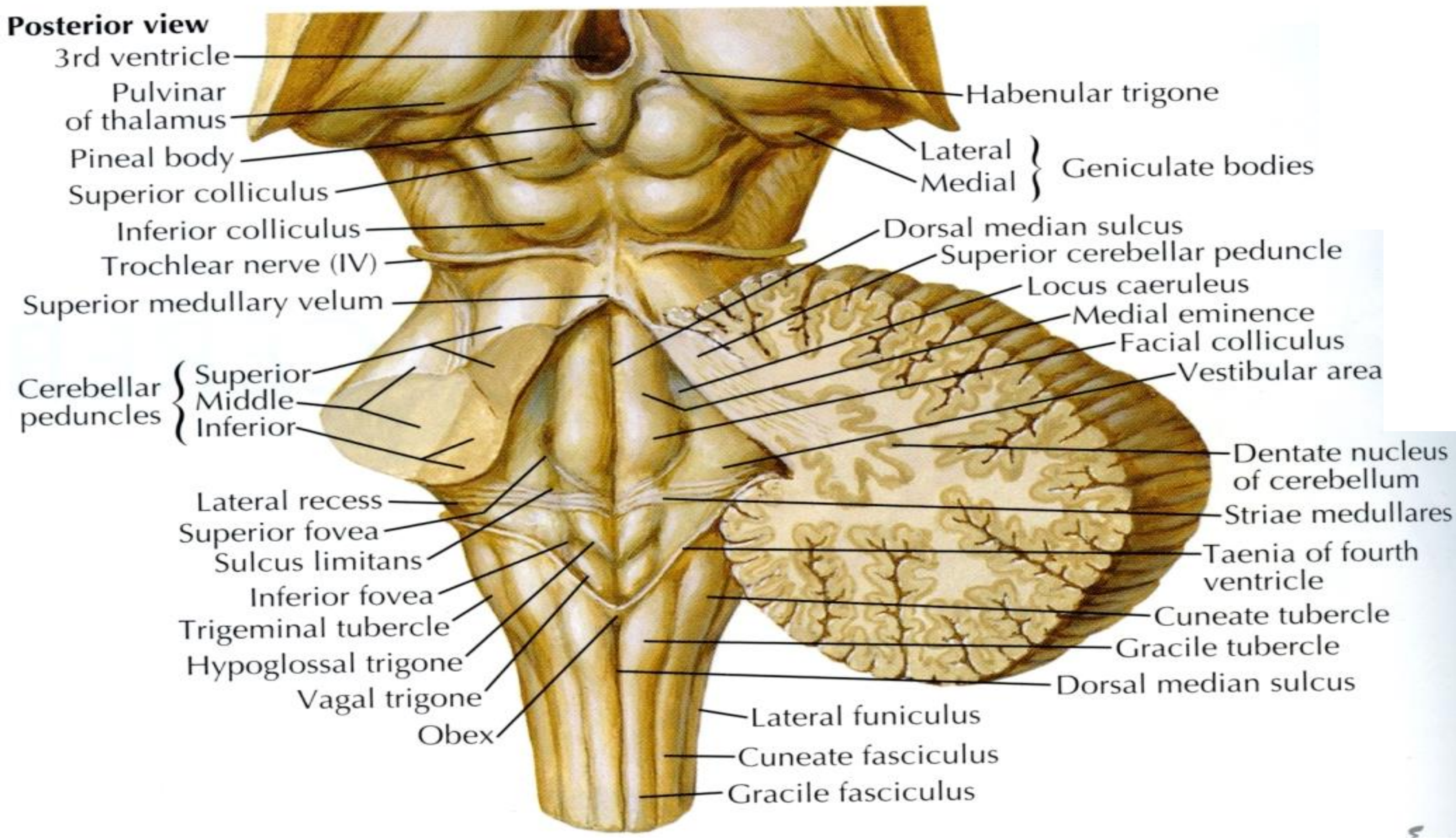
Efferent (motor) fibers
Afferent (sensory) fibers
I
Olfactory
II
Optic
III
Oculomotor
Ciliary muscle, sphincter of pupil and all external eye muscles except those below
IV
Trochlear
Superior oblique muscle
VI
Abducens
Lateral rectus muscle
V
Trigeminal
Sensory—face sinuses, teeth
Ophthalmic
Maxillary
Mandibular
Motor—muscles of mastication
VII
Facial
Muscles of face
Nervus intermedius
Motor—submandibular, sublingual, lacrimal glands
Sensory—anterior ⅔ of tongue, soft palate
VIII
Vestibulocochlear
Cochlear
Vestibular
IX
Glossopharyngeal
Sensory—posterior ⅓ of tongue, tonsil, pharynx, middle ear
Motor—stylopharyngeus, upper pharyngeal muscles, parotid gland
X
Vagus
Motor—heart, lungs, palate, pharynx, larynx, trachea, bronchi, GI tract
Sensory—heart, lungs, trachea, bronchi, larynx, pharynx, GI tract, external ear
XI
Accessory
Sternocleidomastoid, trapezius muscles
XII
Hypoglossal
Tongue muscles
Strap muscles by ansa cervicalis

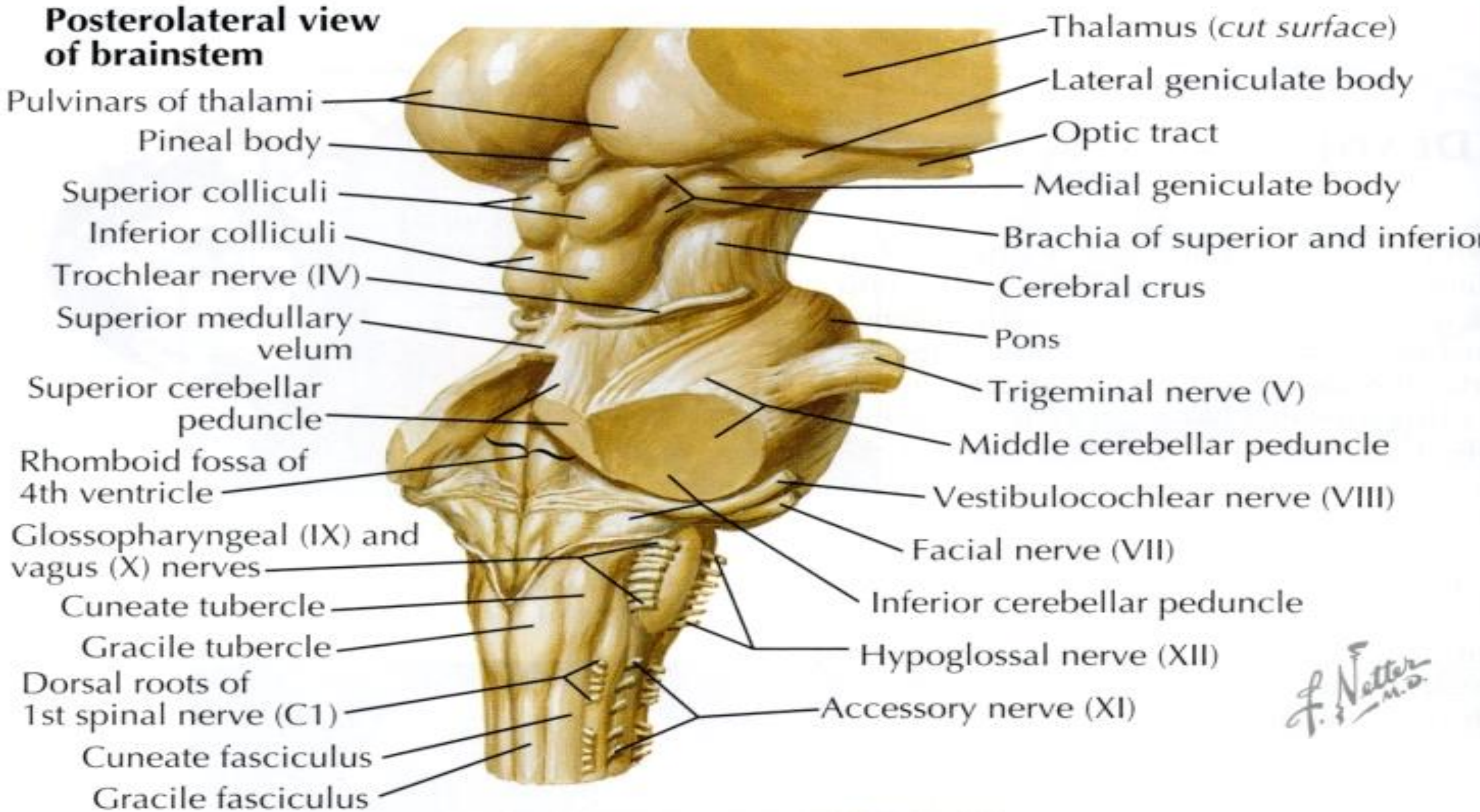


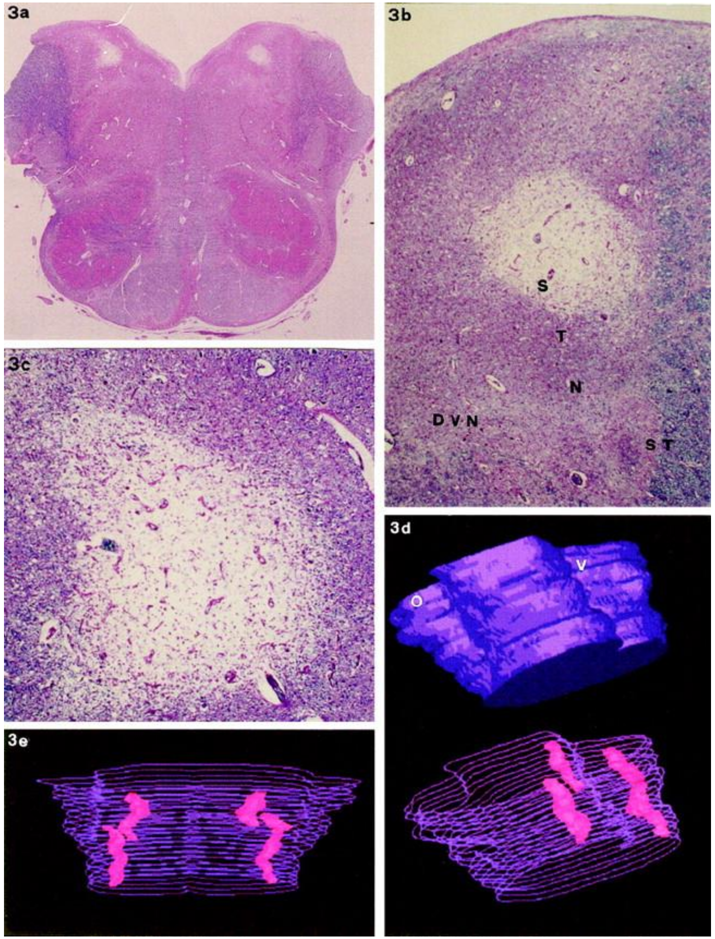
Source: Morton DA, Foreman KB, Albertine KH: *The Big Picture: Gross Anatomy*: www.accessmedicine.com

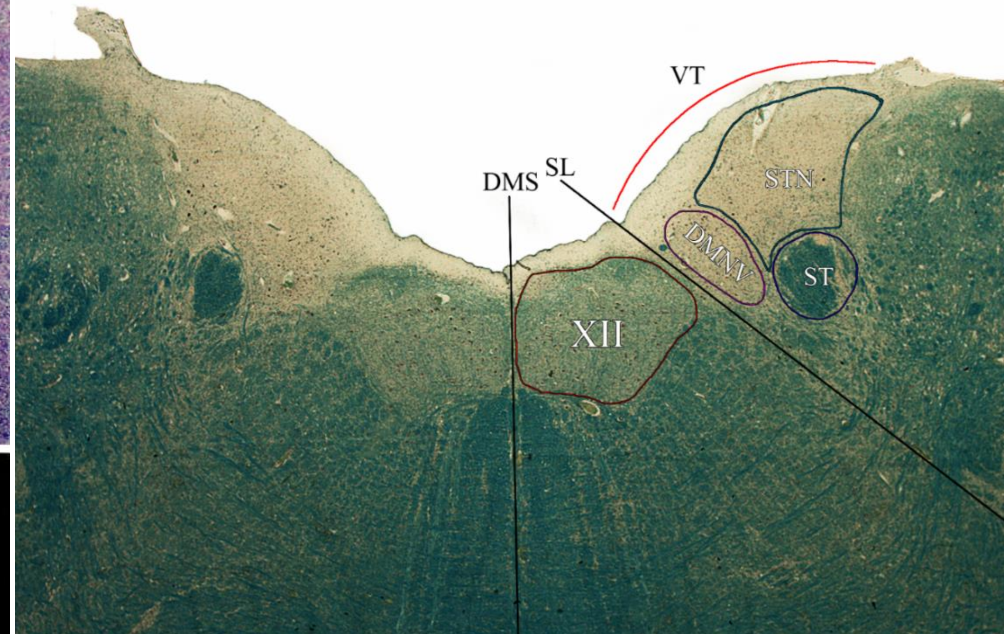


Median sagittal section
Choroid plexus
Interthalamic adhesion
Posterior commissure
Habenular commissure
Pineal body
Splenium of corpus callosum
Great cerebral vein (of Galen)
Superior medullary velum
Body of fornix
Thalamus (in 3rd ventricle)
Interventricular foramen (of Monro)
Anterior commissure
Lamina terminalis
Hypothalamic sulcus
Cerebral peduncle
Cerebral aqueduct (of Sylvius)
Pons
Superior colliculus
Tectal (quadrigeminal) plate
Inferior colliculus
Medial longitudinal fasciculus
Medulla oblongata
4th ventricle
Choroid plexus of 4th ventricle
Decussation of pyramids
Central canal of spinal cord
Median aperture (foramen of Magendie)
Tonsil of cerebellum
Inferior medullary velum
Lobules of the cerebellar vermis
I-II (Lingula)
III (Central)
IV
V
(Culmen)
VI (Declive)
VIIAf (Folium)
VIIAt
VIIB
(Tuber)
VIII (Pyramid)
IX (Uvula)
X (Nodulus)

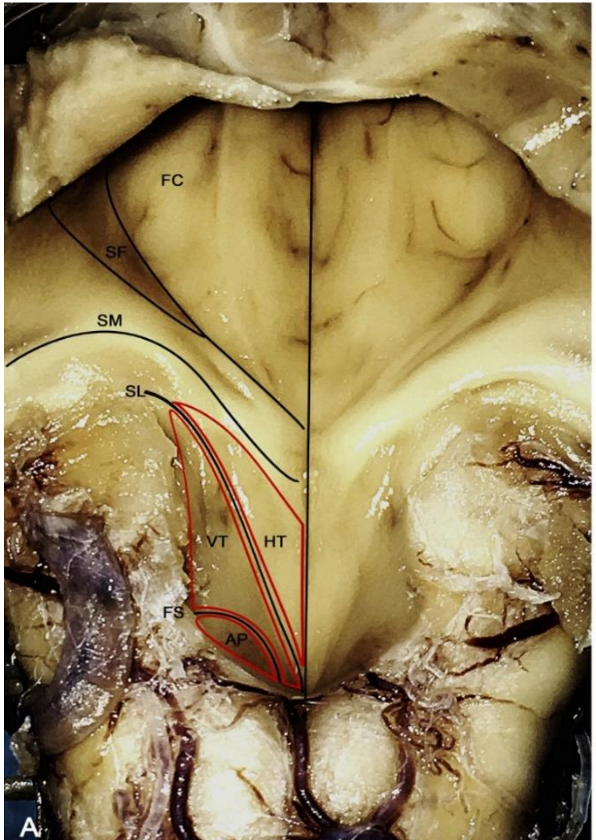

Posterior view
3rd ventricle
Pulvinar of thalamus
Pineal body
Superior colliculus
Inferior colliculus
Trochlear nerve (IV)
Superior medullary velum
Cerebellar peduncles
Superior
Middle
Inferior
Lateral recess
Superior fovea
Sulcus limitans
Inferior fovea
Trigeminal tubercle
Hypoglossal trigone
Vagal trigone
Obex
Habenular trigone
Lateral
Medial
Geniculate bodies
Dorsal median sulcus
Superior cerebellar peduncle
Locus caeruleus
Medial eminence
Facial colliculus
Vestibular area
Dentate nucleus of cerebellum
Striae medullares
Taenia of fourth ventricle
Cuneate tubercle
Gracile tubercle
Dorsal median sulcus
Lateral funiculus
Cuneate fasciculus
Gracile fasciculus

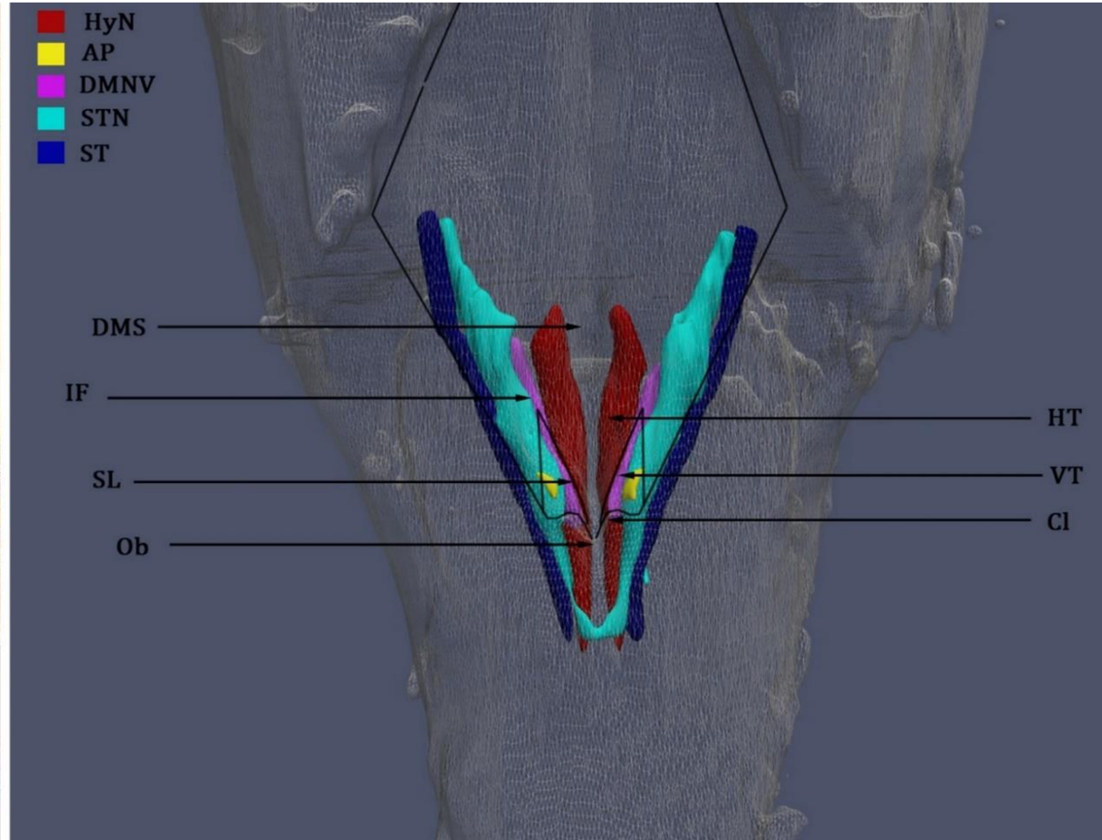

Posterolateral view of brainstem
Pulvinars of thalami
Pineal body
Superior colliculi
Inferior colliculi
Trochlear nerve (IV)
Superior medullary velum
Superior cerebellar peduncle
Rhomboid fossa of 4th ventricle
Glossopharyngeal (IX) and vagus (X) nerves
Cuneate tubercle
Gracile tubercle
Dorsal roots of 1st spinal nerve (C1)
Cuneate fasciculus
Gracile fasciculus
Thalamus (cut surface)
Lateral geniculate body
Optic tract
Medial geniculate body
Brachia of superior and inferior
Cerebral crus
Pons
Trigeminal nerve (V)
Middle cerebellar peduncle
Vestibulocochlear nerve (VIII)
Facial nerve (VII)
Inferior cerebellar peduncle
Hypoglossal nerve (XII)
Accessory nerve (XI)
F. Netter M.D.





De Caro et al., 2000
Emmi et al., 2020





3D Reconstruction of the Morpho-Functional Topography of the Human Vagal Trigone

Aron Emmi†, Andrea Porzionato†, Martina Contran, Enrico De Rose, Veronica Macchi* and Raffaele De Caro

Department of Neuroscience, Institute of Human Anatomy, University of Padua, Padua, Italy

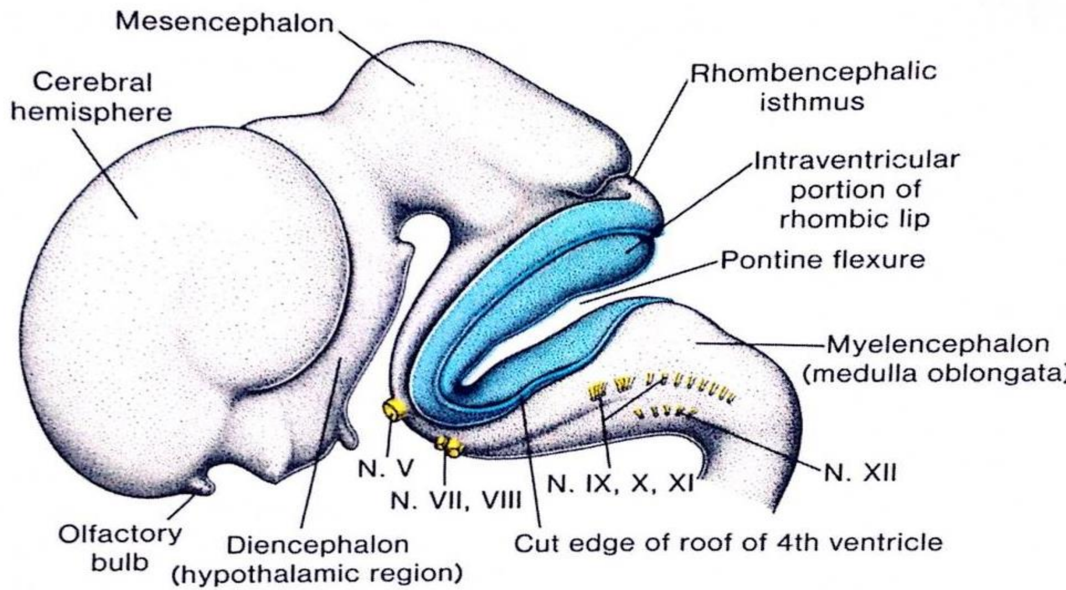


Figure 17.17 Lateral view of the brain vesicles in an 8-week embryo (crown-rump length ~27 mm). The roof plate of the rhombencephalon has been removed to show the intraventricular portion of the rhombic lip. Note the origin of the cranial nerves.

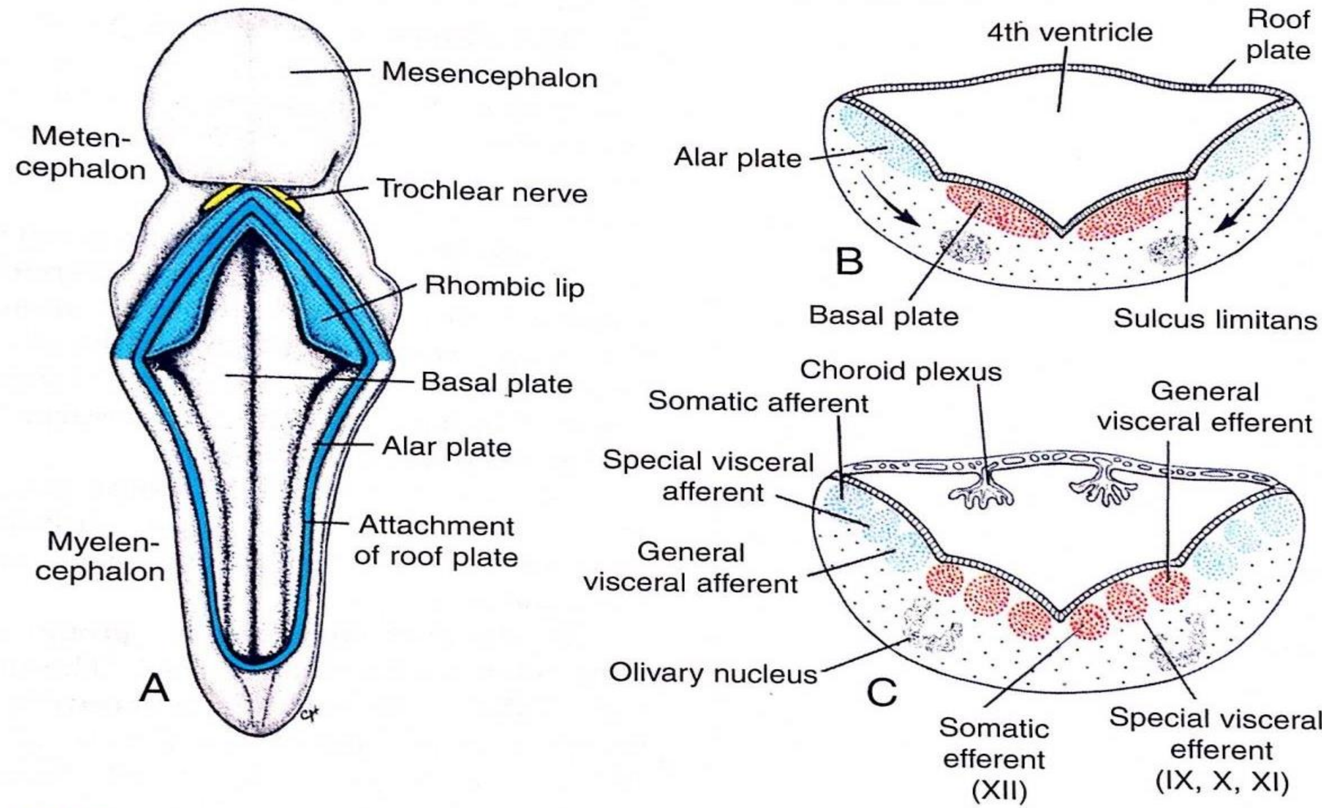


Figure 17.18 **A.** Dorsal view of the floor of the fourth ventricle in a 6-week embryo after removal of the roof plate. Note the alar and basal plates in the myelencephalon. The rhombic lip is visible in the metencephalon. **B,C.** Position and differentiation of the basal and alar plates of the myelencephalon at different stages of development. Note formation of the nuclear groups in the basal and alar plates. *Arrows*, path followed by cells of the alar plate to the olivary nuclear complex. The choroid plexus produces cerebrospinal fluid.

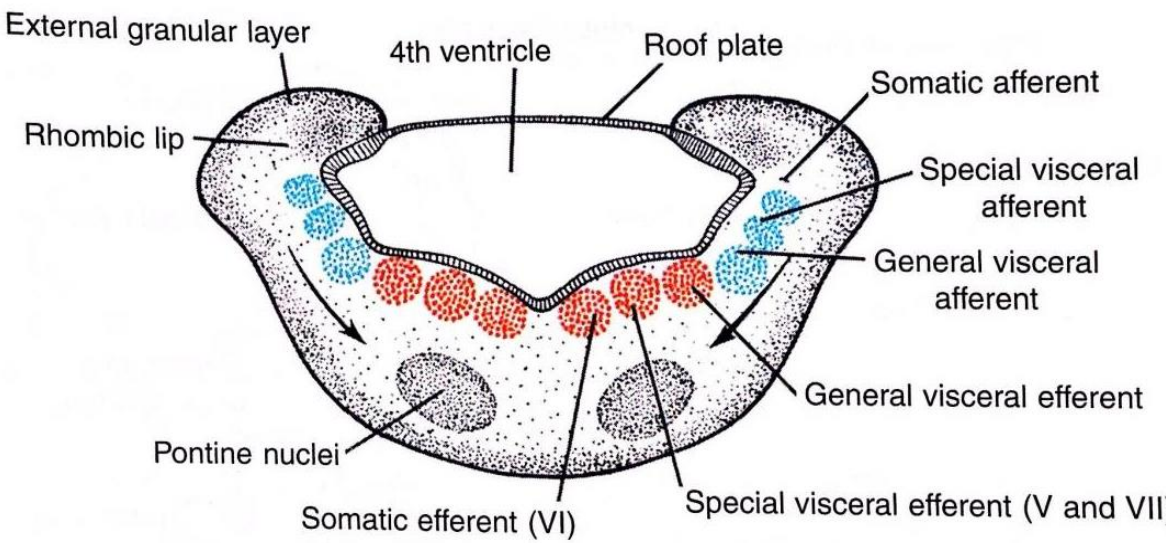
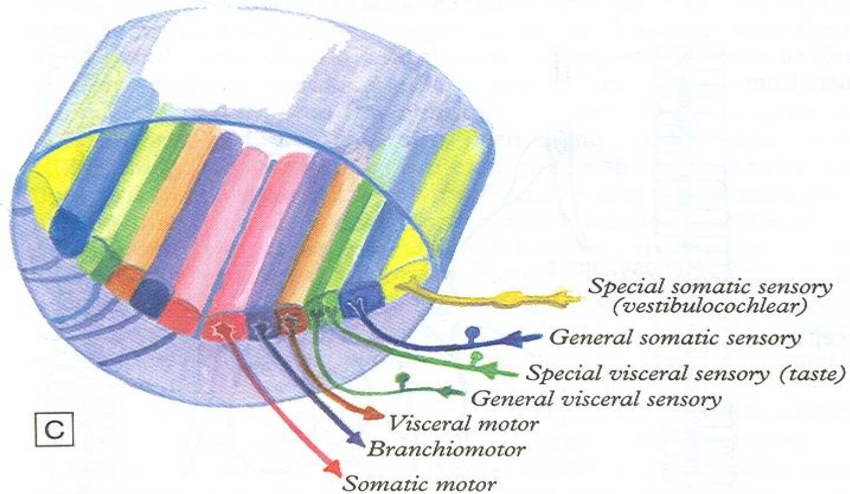
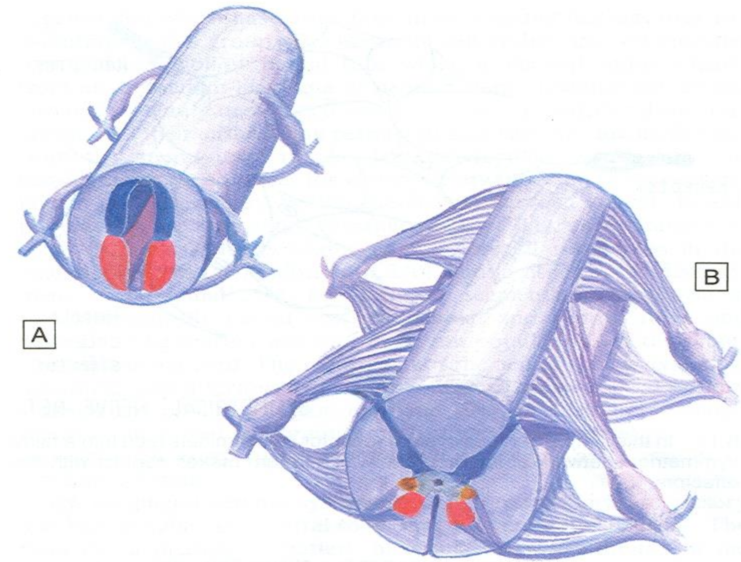


Figure 17.19 Transverse section through the caudal part of the metencephalon. Note the differentiation of the various motor and sensory nuclear areas in the basal and alar plates, respectively, and the position of the rhombic lips, which project partly into the lumen of the fourth ventricle and partly above the attachment of the roof plate. *Arrows*, direction of migration of the pontine nuclei.



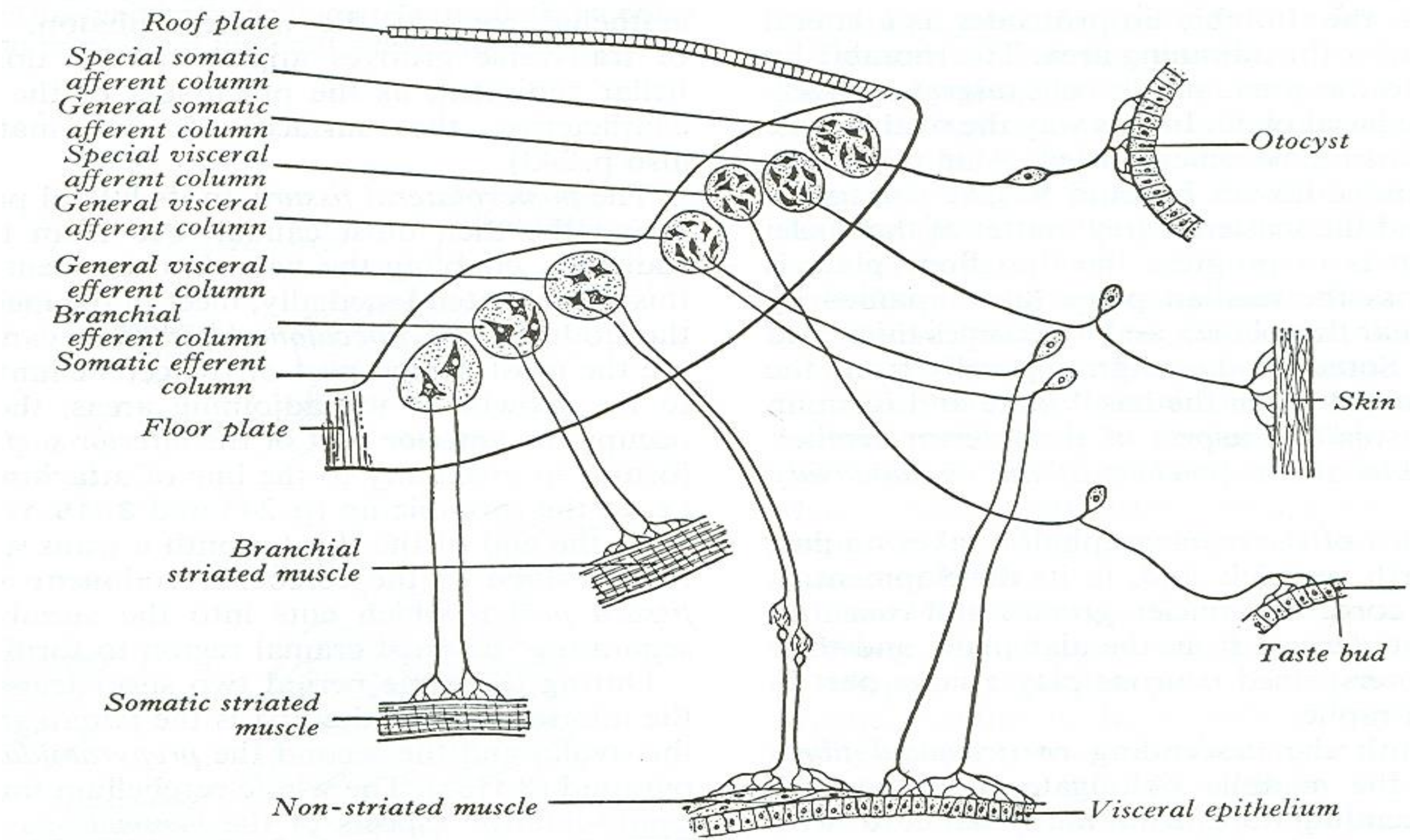


8.13 Schema showing the arrangement of sensory and motor columns in the spinal cord and brain stem.

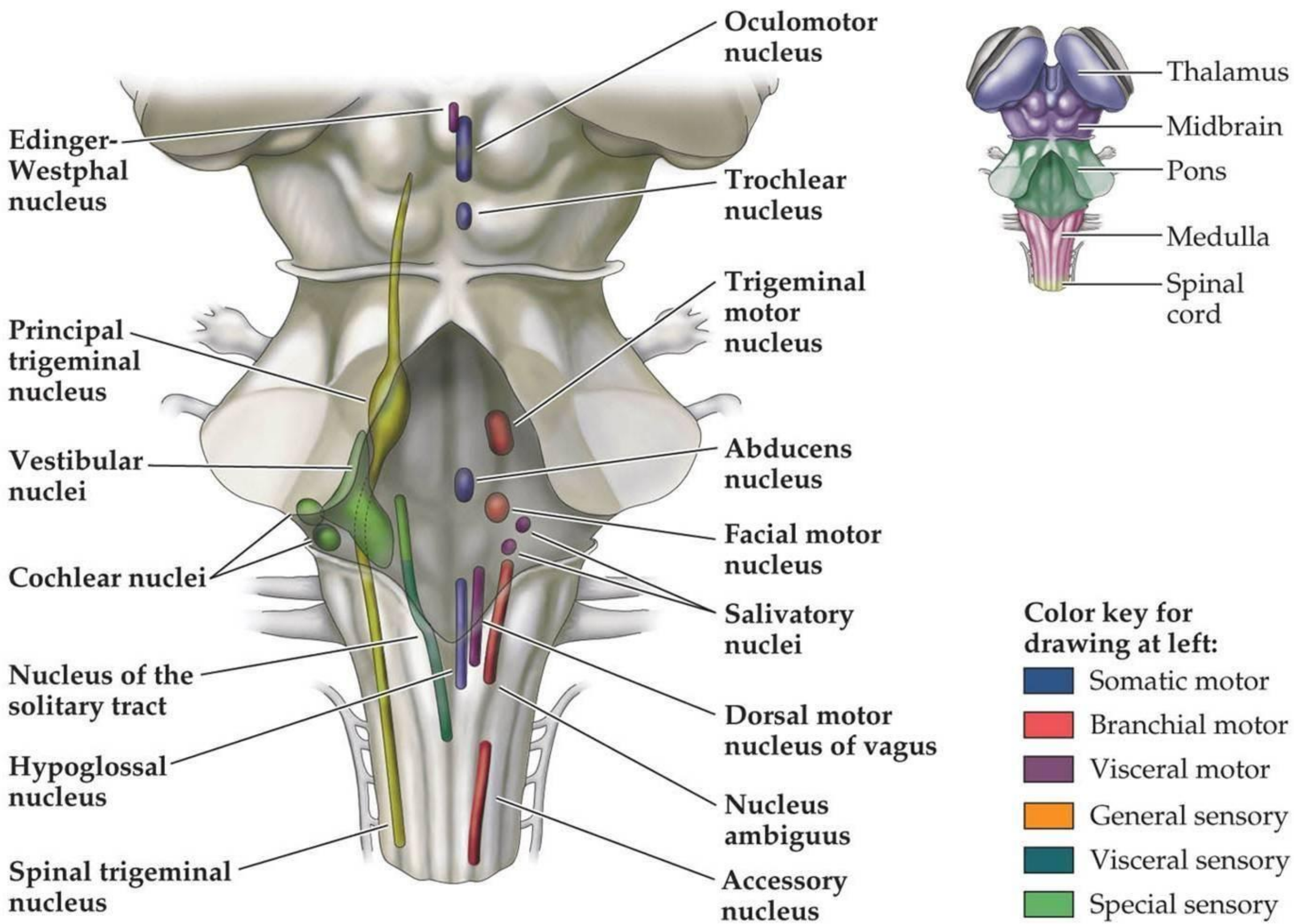
A shows the organization of the primitive spinal cord with a dorsal sensory column (blue), a ventral column (red), and segmentally arranged dorsal and ventral nerve roots.

B depicts the arrangement of adult spinal cord serving the thorax and lumbar region, with sensory and somatic motor columns colour coded in the same way, and an additional intermediate (lateral) visceral motor column (brown).

C indicates the arrangement of multiple longitudinal columns in the brain-stem, where the motor column is now subdivided into three, and the sensory column into four. For further information about the embryological aspects of the early nervous system see p. 217 and **3**.3.



Roof plate
Special somatic afferent column
General somatic afferent column
Special visceral afferent column
General visceral afferent column
General visceral efferent column
Branchial efferent column
Somatic efferent column
Floor plate
Branchial striated muscle
Somatic striated muscle
Non-striated muscle
Otocyst
Skin
Taste bud
Visceral epithelium



NEUROSCIENCE, Third Edition, Figure A2

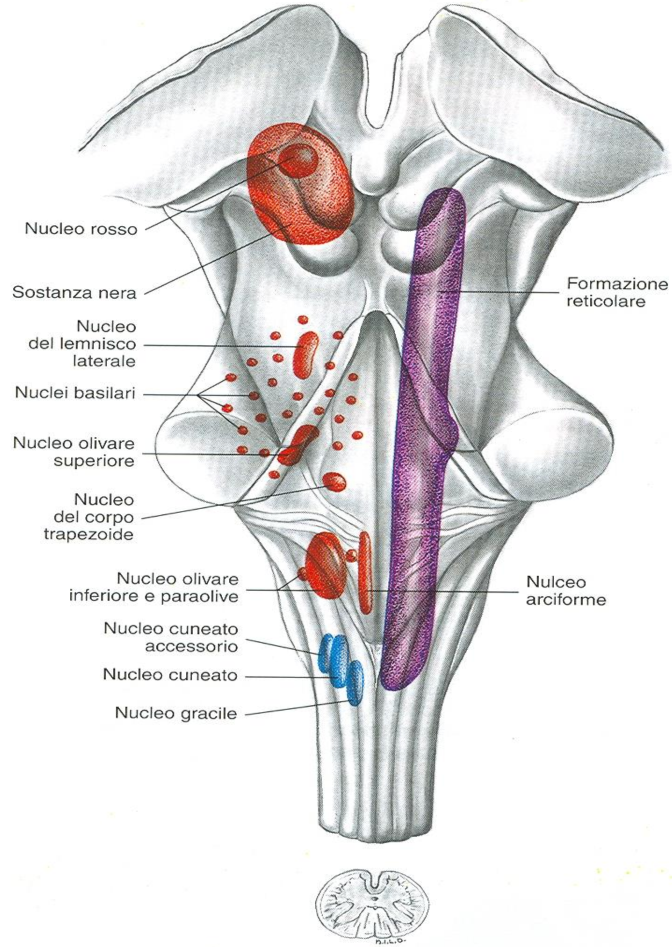
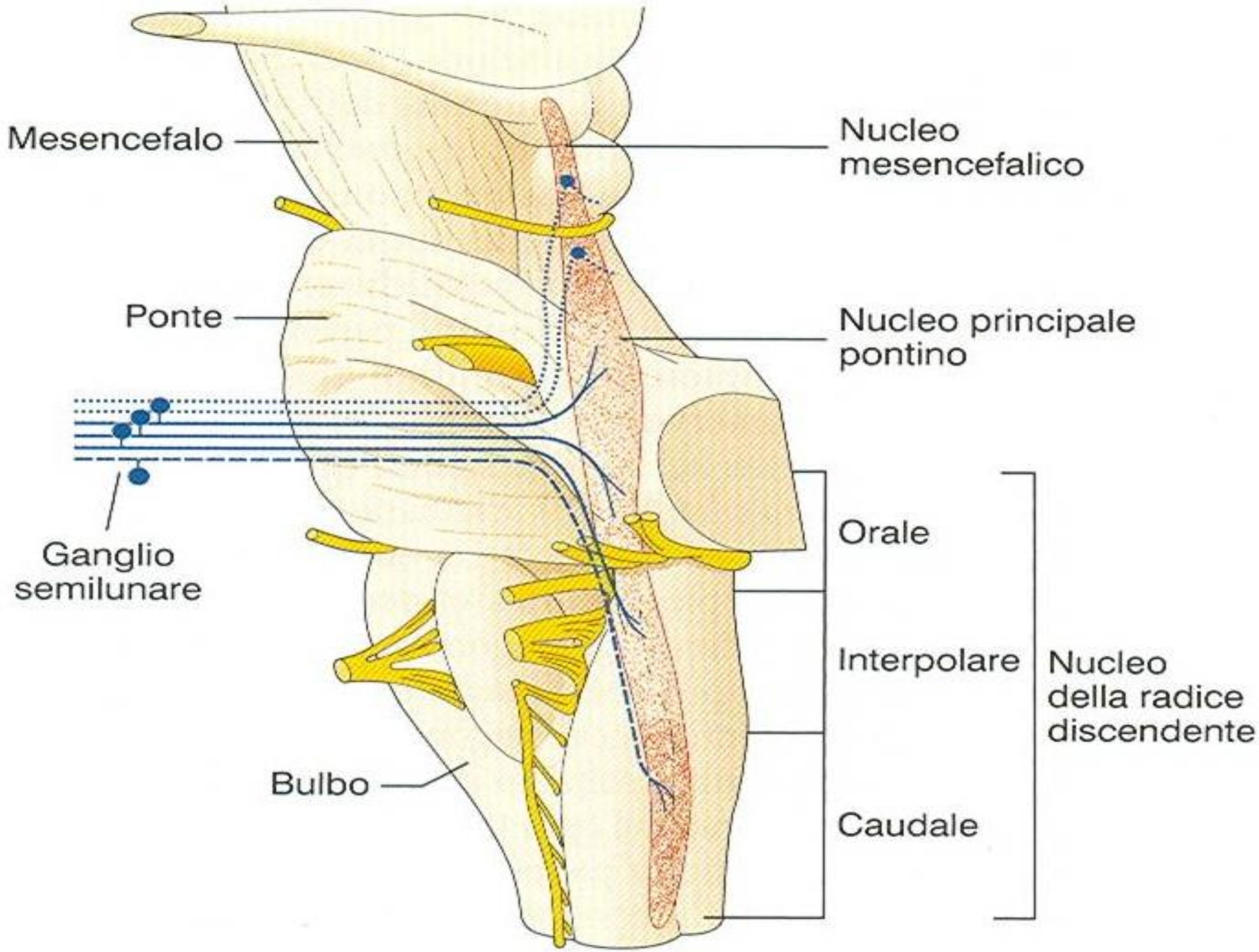
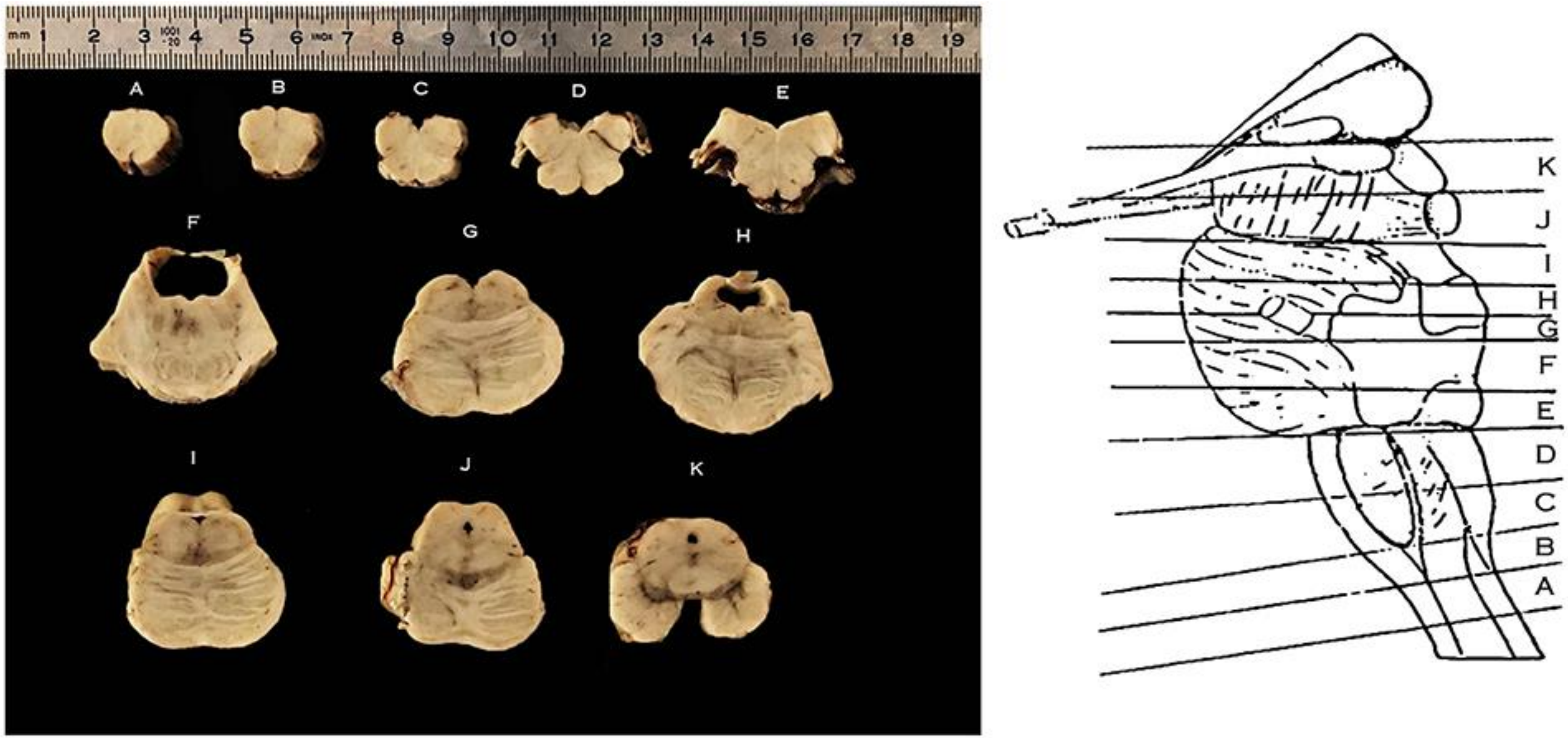


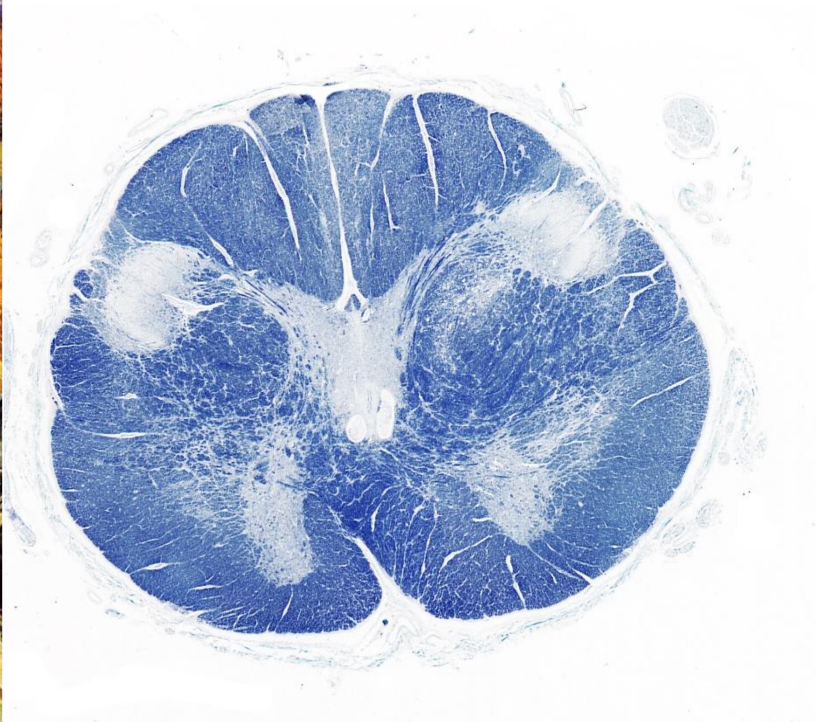
Figura 14.52 - Nuclei propri del tronco encefalico visti in una ricostruzione tridimensionale. I nuclei gracile e cuneato sono indicati in **blu** e sono intercalati sulla principale via della sensibilità generale, la via spinobulbotalamocorticale. Dal nucleo cuneato accessorio prendono origine fibre cuneocerebellari. Si rileva l'estensione della formazione reticolare in tutti e tre i segmenti del tronco encefalico.

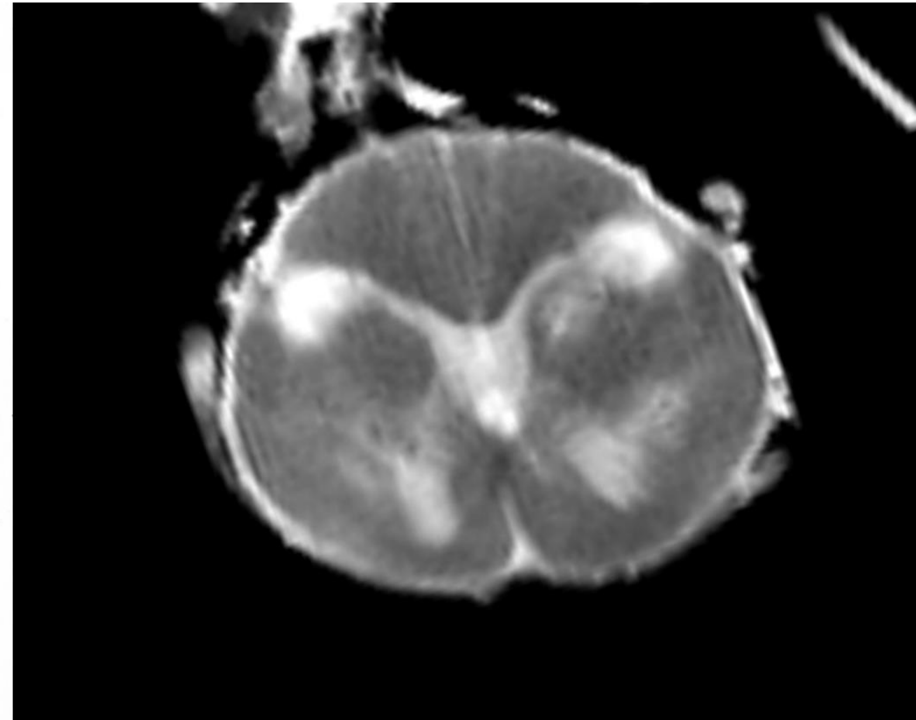

Mesencefalo
Nucleo
mesencefalico
Ponte
Nucleo principale
pontino
Ganglio
semilunare
Orale
Interpolare
Nucleo
della radice
discendente
Caudale
Bulbo

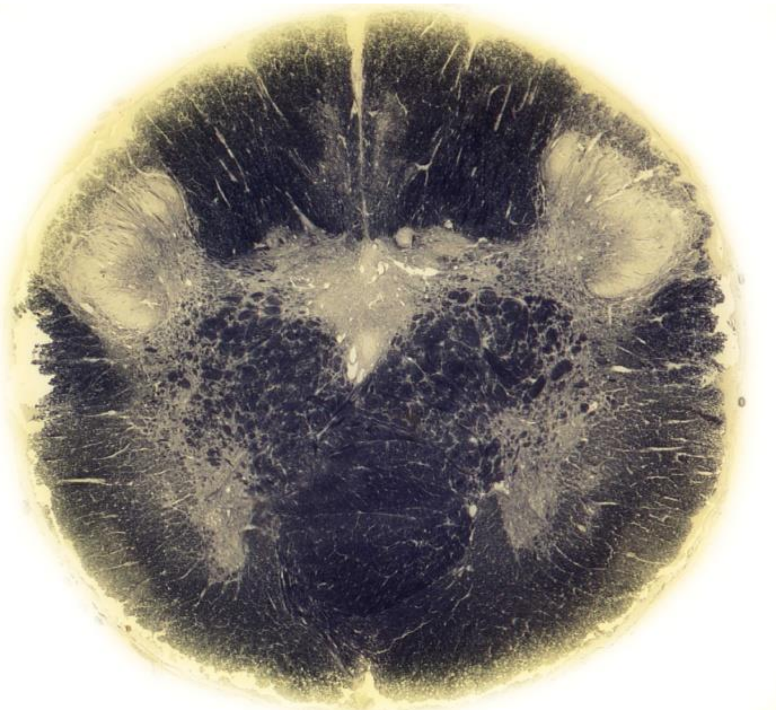

A
B
C
D
E
F
G
H
I
J
K

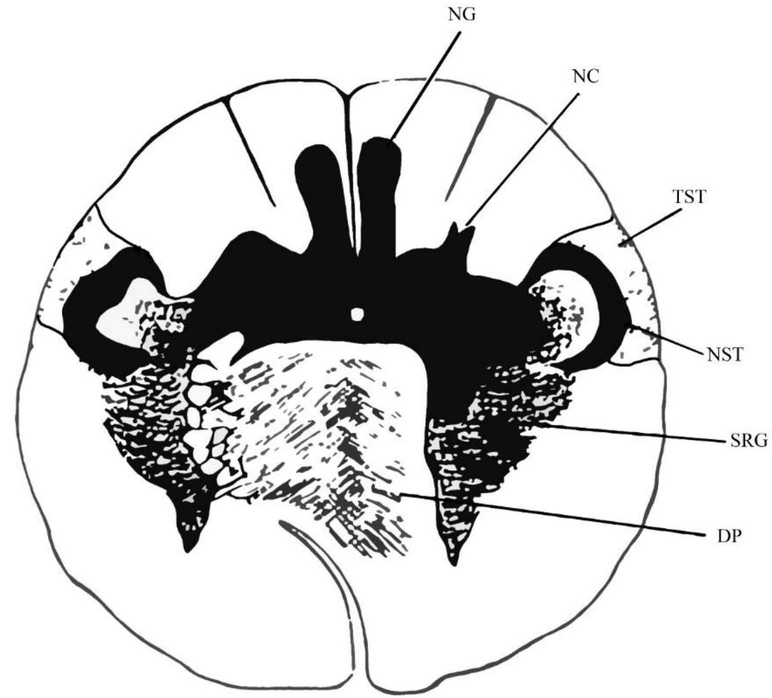
Medulla (lower) 1

https://pathpresenter.net/#/public/display?token=e41bb6dd



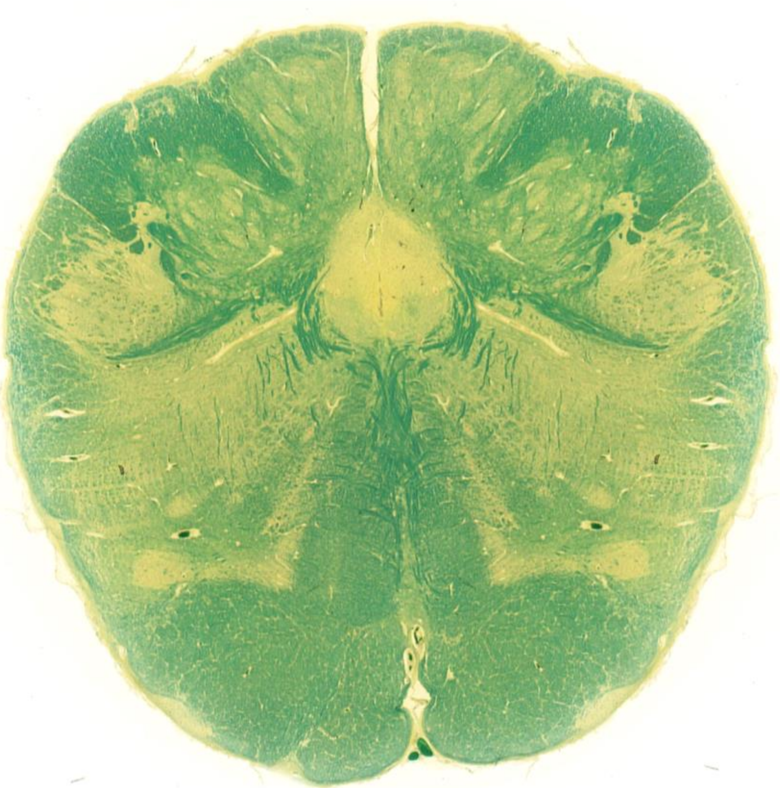


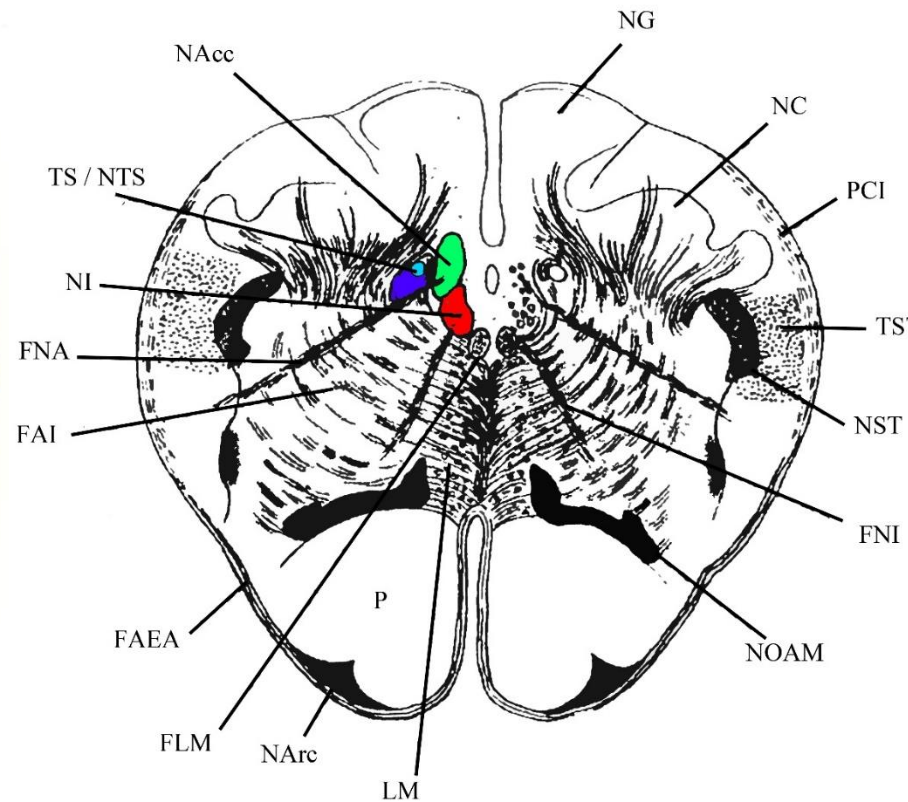



NG
NC
TST
NST
SRG
DP

Medulla (lower) 2

https://pathpresenter.net/#/public/display?token=9e80a680




NAcc
NG
NC
TS / NTS
PCI
NI
TST
FNA
FAI
NST
FNI
FAEA
P
NOAM
FLM
NArc
LM

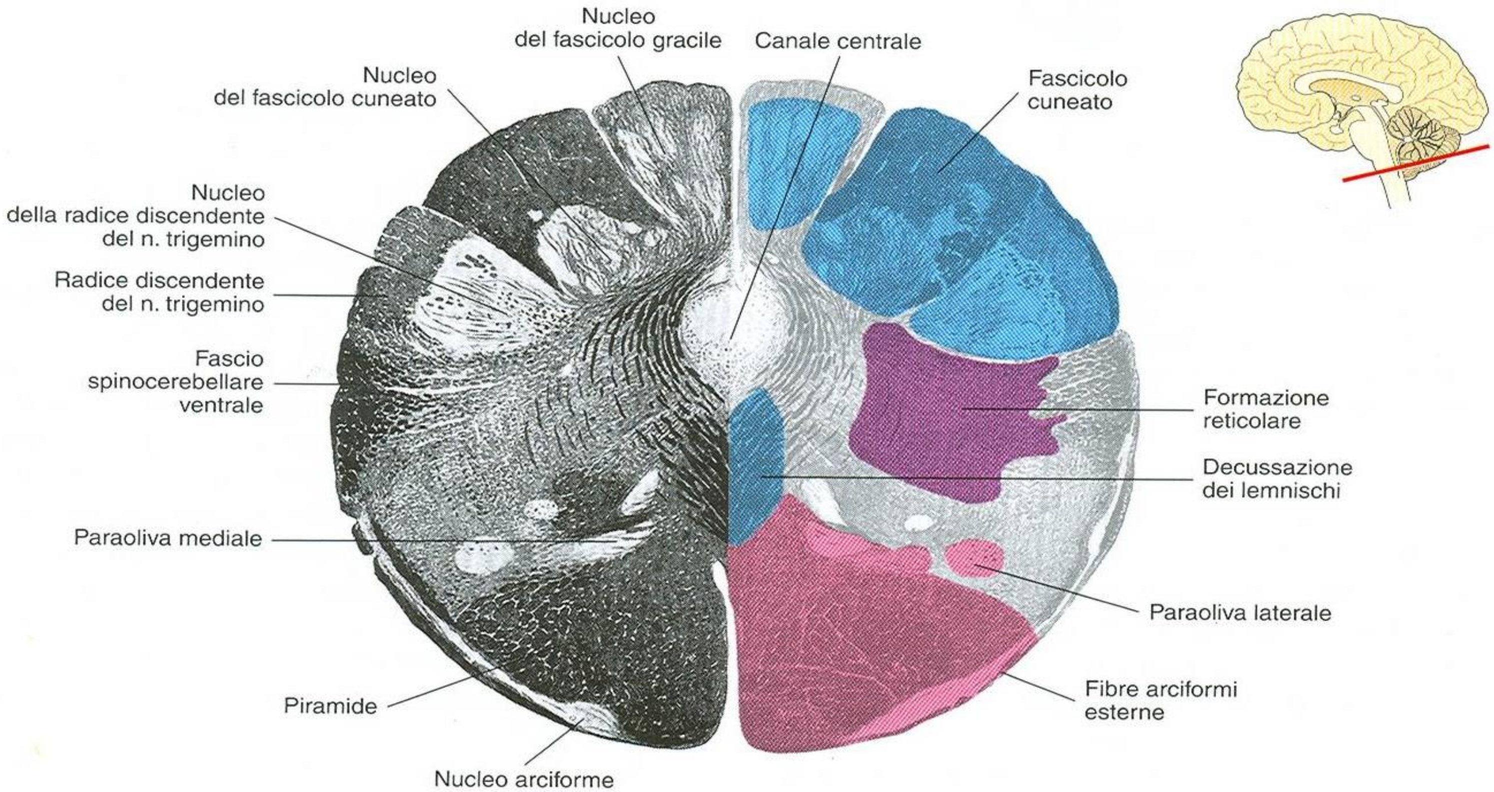
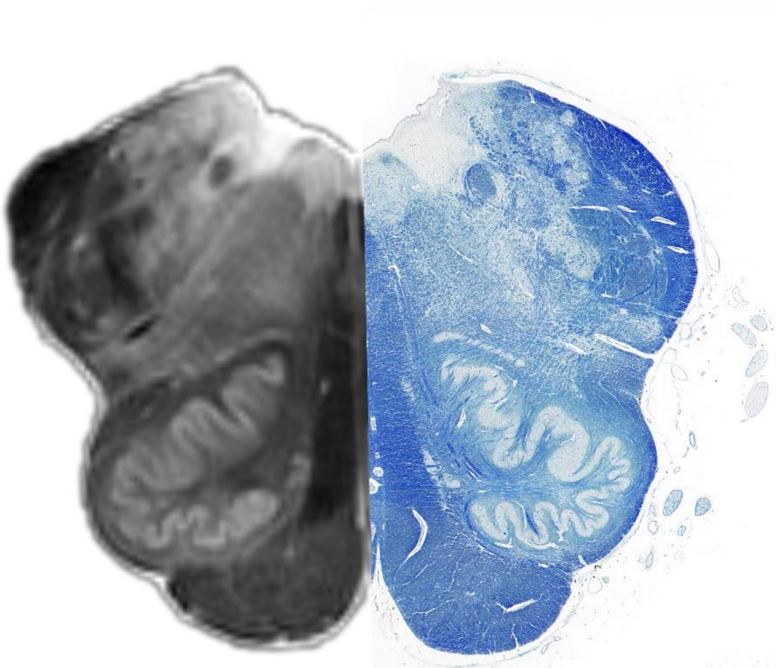
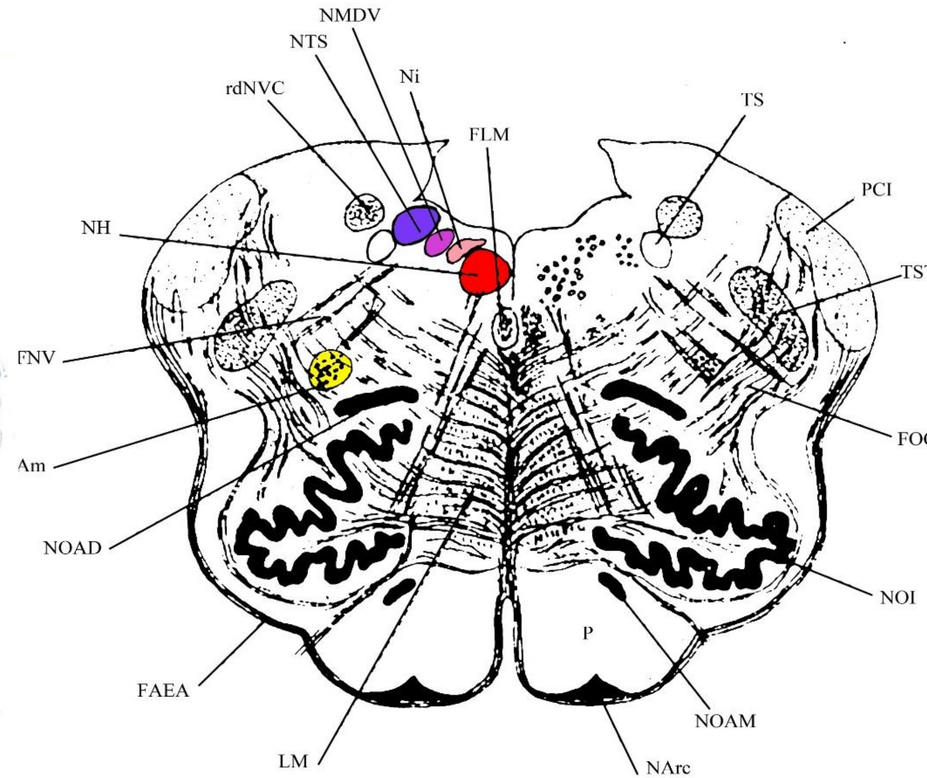


Figura 14.55 - Conformazione interna della porzione inferiore del bulbo in una sezione trasversa colorata per la dimostrazione della mielina. Le vie appaiono in **nero**, i centri in **bianco**. La sezione coglie la decussazione del lemnisco mediale ventralmente alla quale si trovano le piramidi. Nella parte destra le vie e i nuclei motorî sono evidenziati in **rosso**, le vie e i nuclei sensitivi in **blu**, la formazione reticolare in **viola**.

Medulla (upper)

https://pathpresenter.net/#/public/display?token=f8c8c313




NMDV
NTS
Ni
rdNVC
TS
FLM
PCI
NH
TST
FNV
FOC
Am
NOAD
NOI
P
FAEA
NOAM
LM
NArc

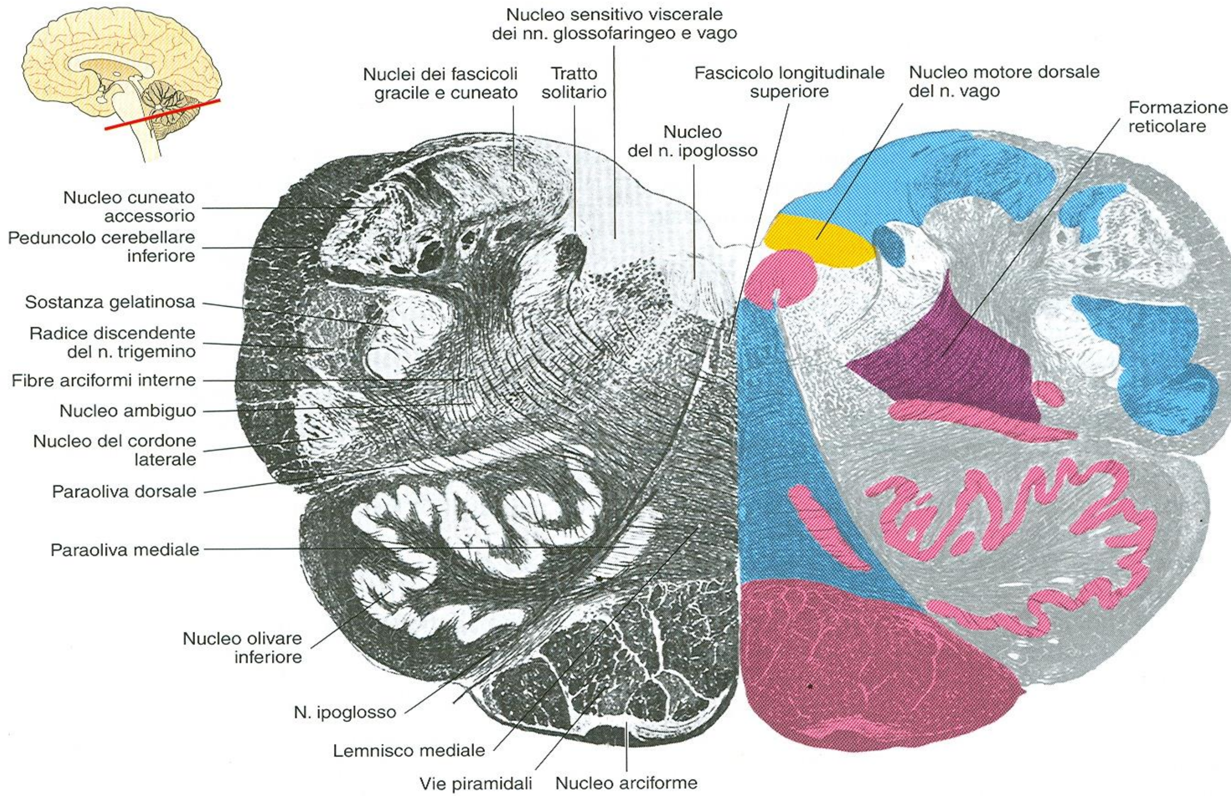
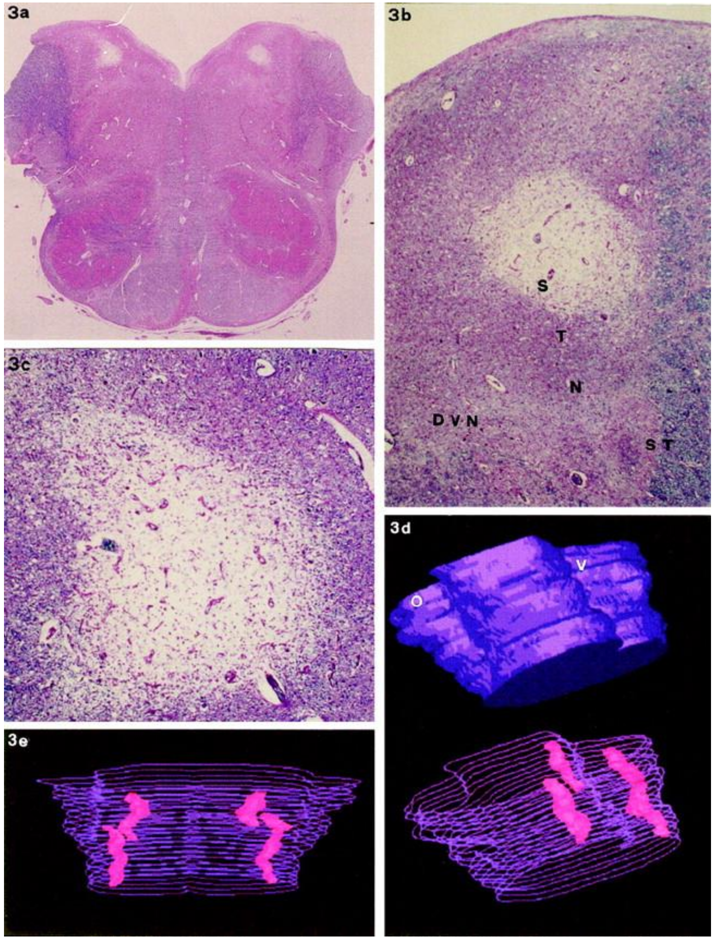
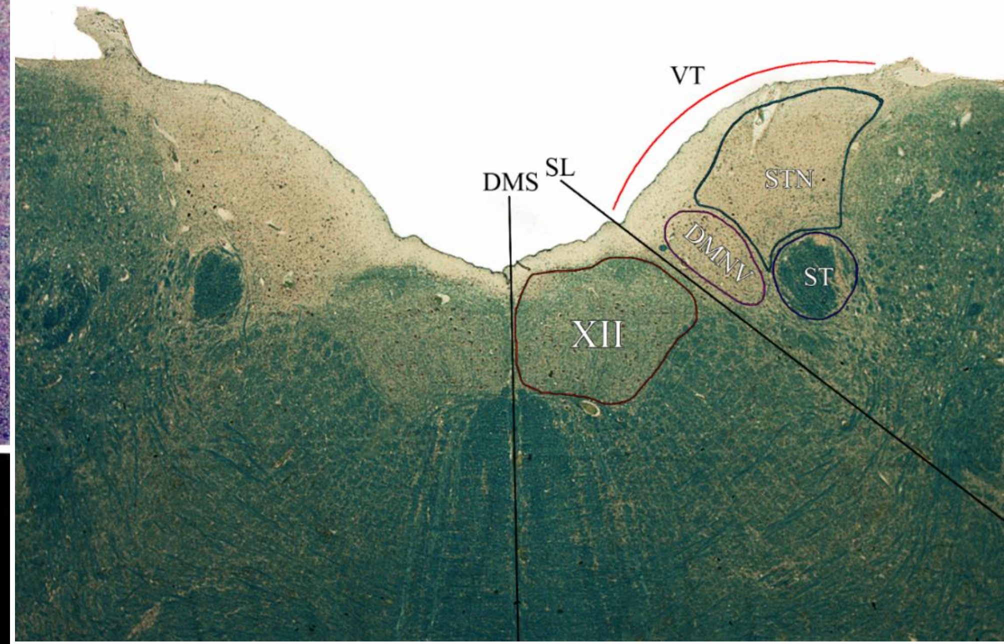
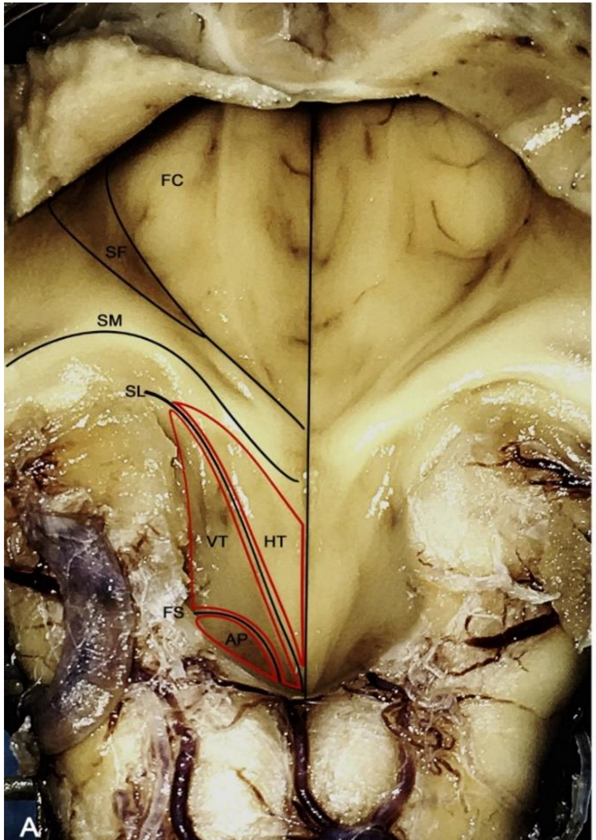


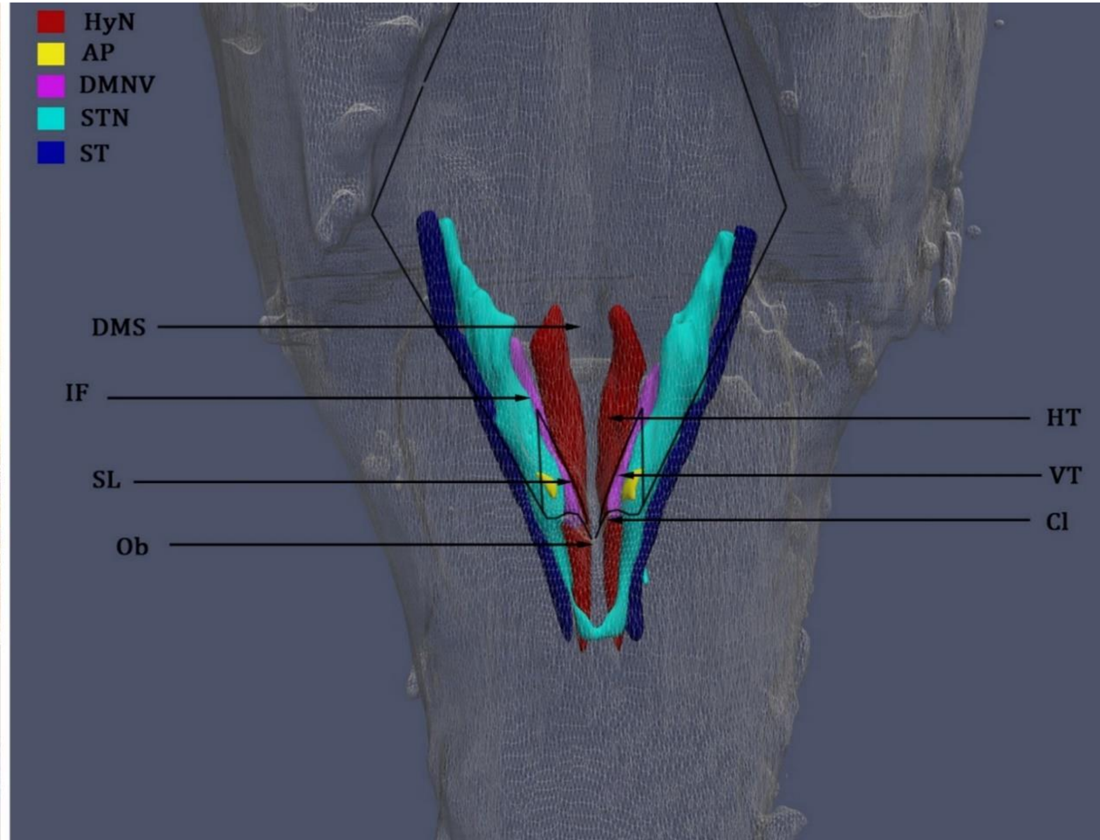
Figura 14.56 - Conformazione interna della porzione superiore del bulbo in una sezione trasversa colorata per la dimostrazione della mielina. Le vie appaiono in **nero**, i centri in **bianco**. La sezione coglie la parte bulbare del pavimento del IV ventricolo e passa per le piramidi e le olive. Nella parte destra le vie e i nuclei motorî sono evidenziati in **rosso**, le vie e i nuclei sensitivi in **blu**, i nuclei parasimpatici in **giallo**, la formazione reticolare in **viola**.





De Caro et al., 2000
Emmi et al., 2020

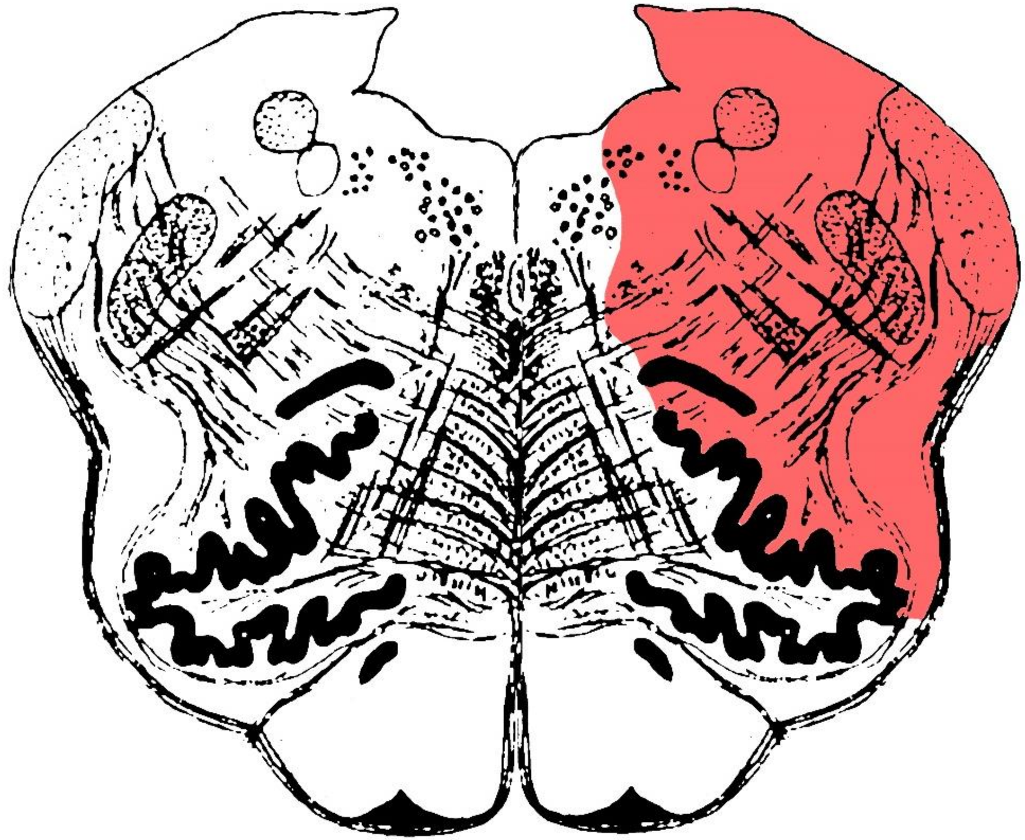


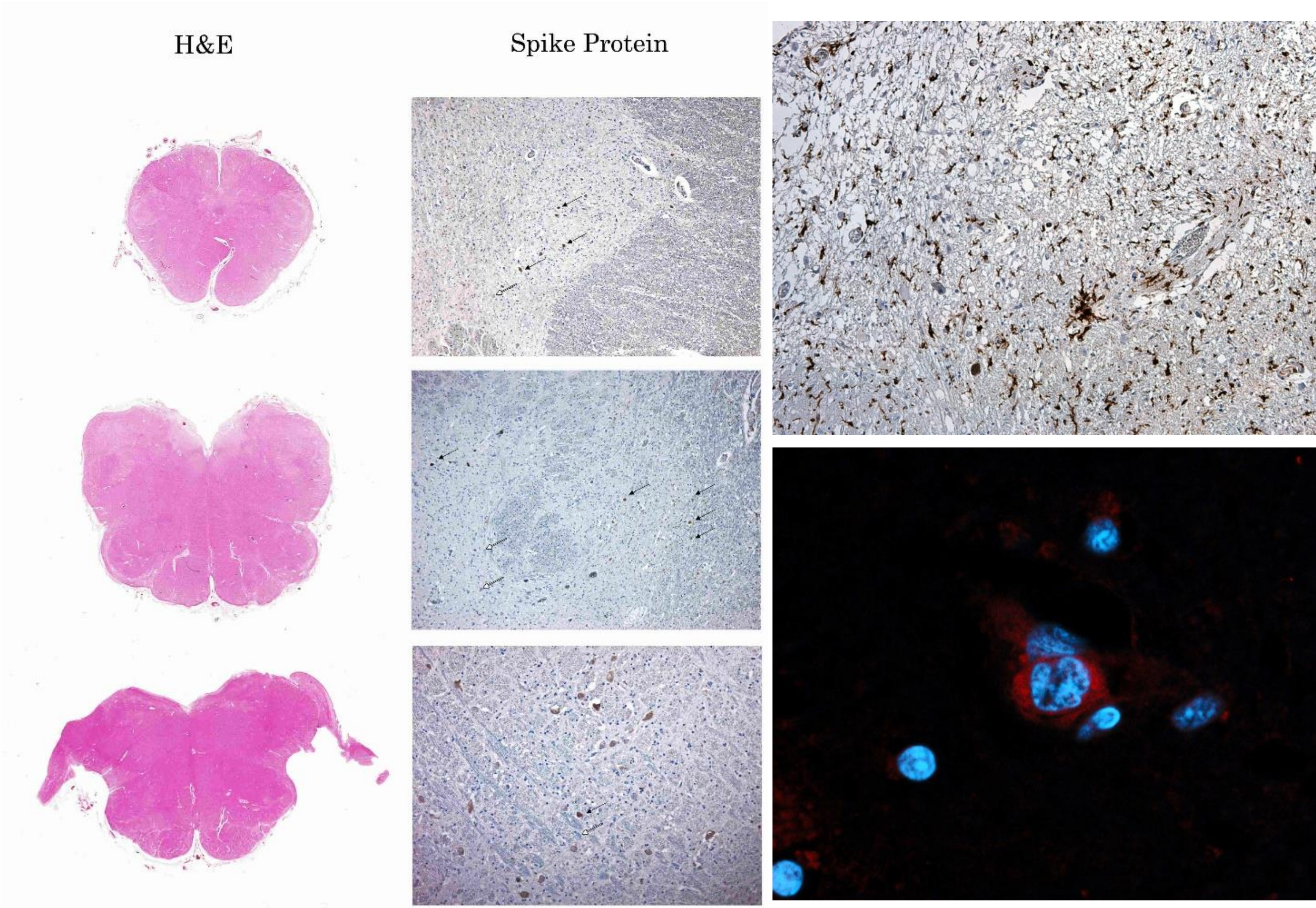


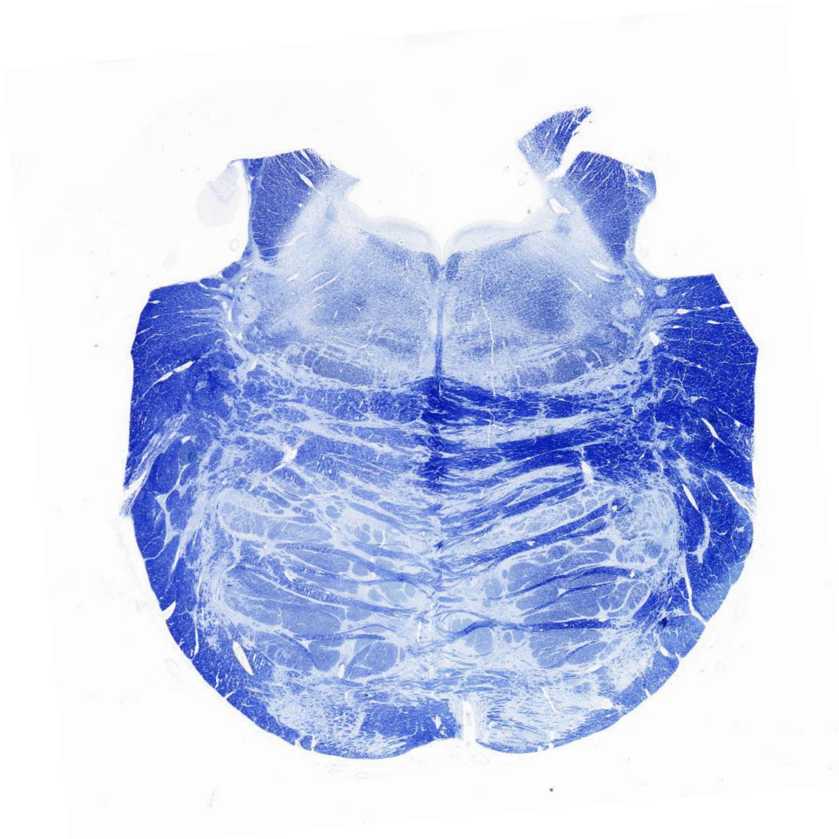
3D Reconstruction of the Morpho-Functional Topography of the Human Vagal Trigone

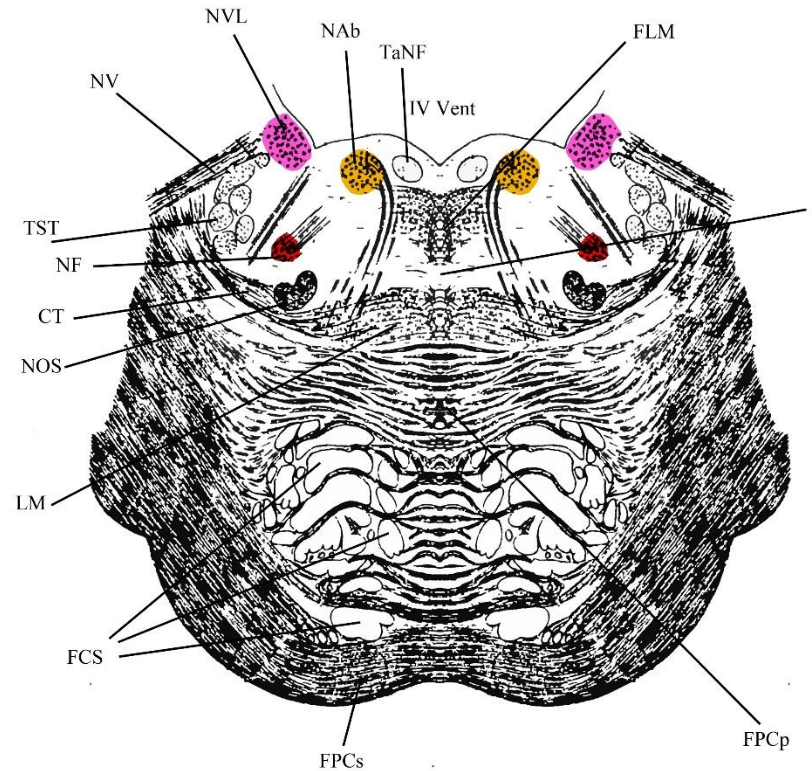
Aron Emmi†, Andrea Porzionato†, Martina Contran, Enrico De Rose, Veronica Macchi* and Raffaele De Caro

Department of Neuroscience, Institute of Human Anatomy, University of Padua, Padua, Italy




H&E
Spike Protein




NVL
NAb
FLM
TaNF
NV
IV Vent
TST
R
NF
CT
NOS
LM
FCS
FPCp
FPCs

https://pathpresenter.net/public/display?token=bf3d748f

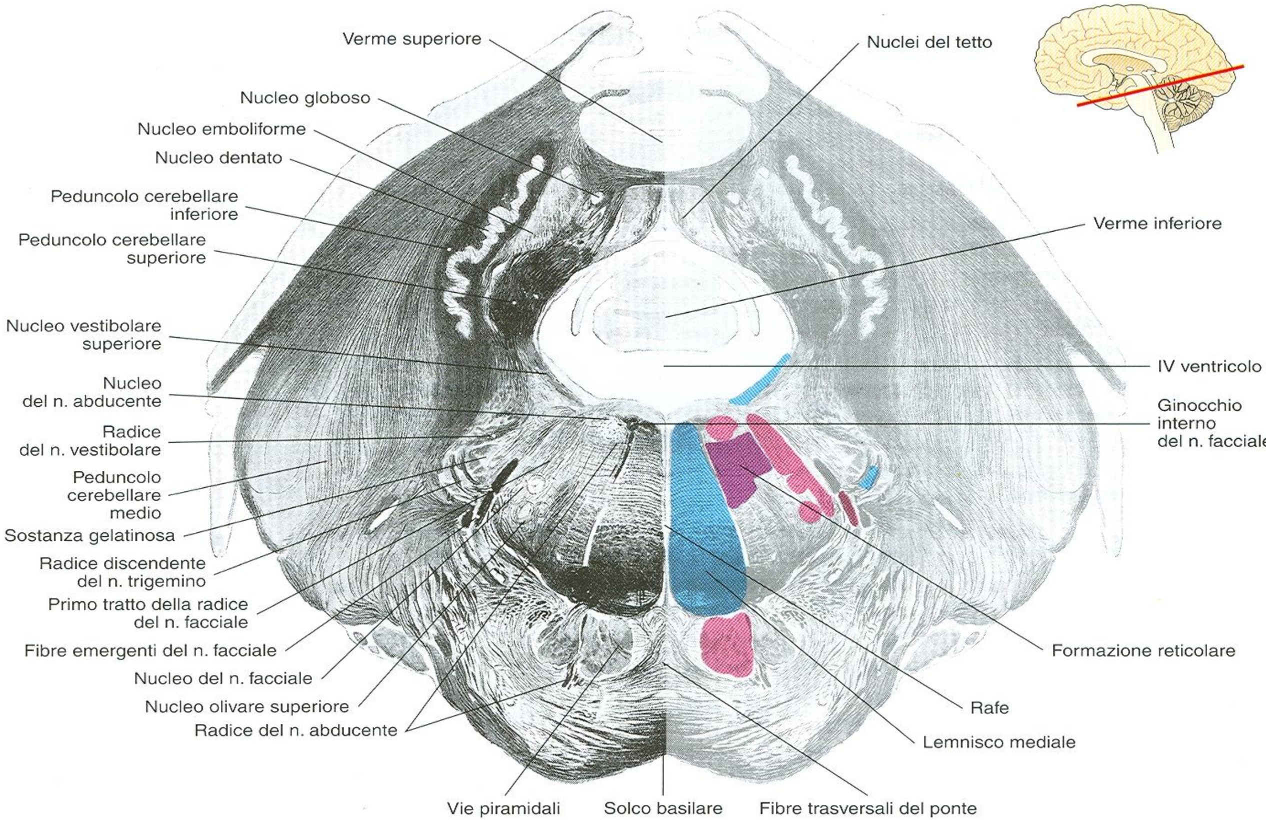
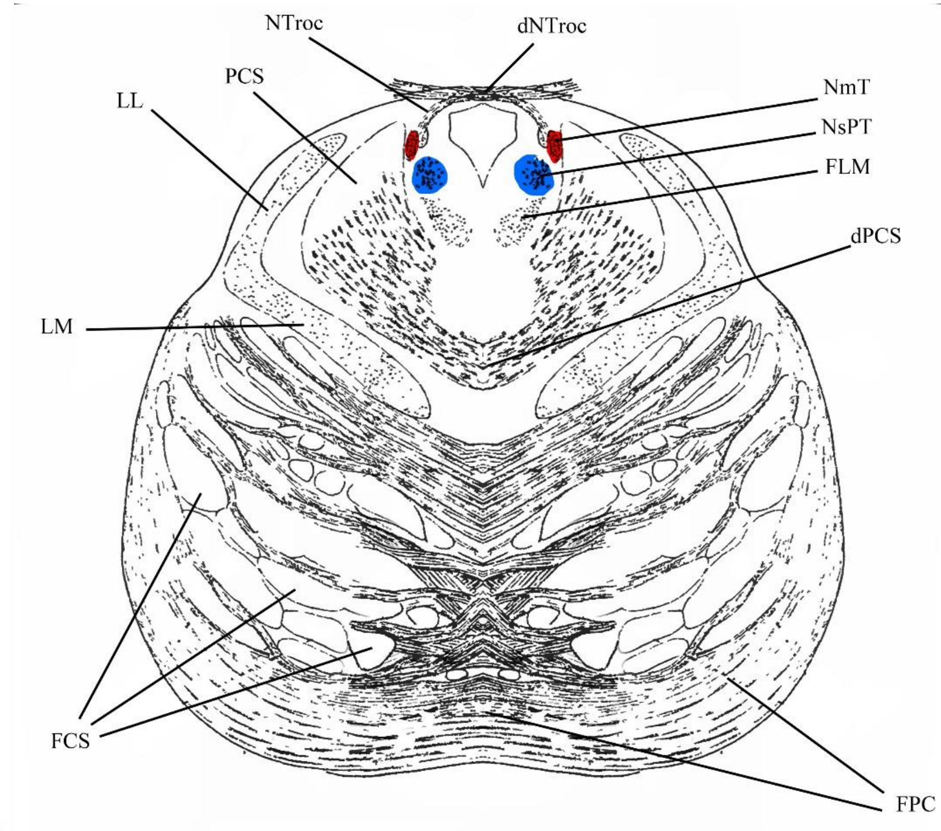


Figura 14.57 - Conformazione interna del ponte in una sezione trasversa colorata per la dimostrazione della mielina. Le vie appaiono in **nero**, i centri in **bianco**. È netta la distinzione del piede rispetto al tegmento. Le vie piramidali si trovano innanzi alle fibre del lemnisco mediale. Nel tegmento sono situati numerosi nuclei propri e di nervi encefalici. Dorsalmente e lateralmente al ponte si apprezzano formazioni grigie appartenenti al cervelletto. Nella parte destra le vie e i nuclei motorî sono evidenziati in **rosso**, le vie e i nuclei sensitivi in **blu**, la formazione reticolare in **viola**.


NTroc
dNTroc
PCS
LL
NmT
NsPT
FLM
dPCS
LM
FCS
FPC

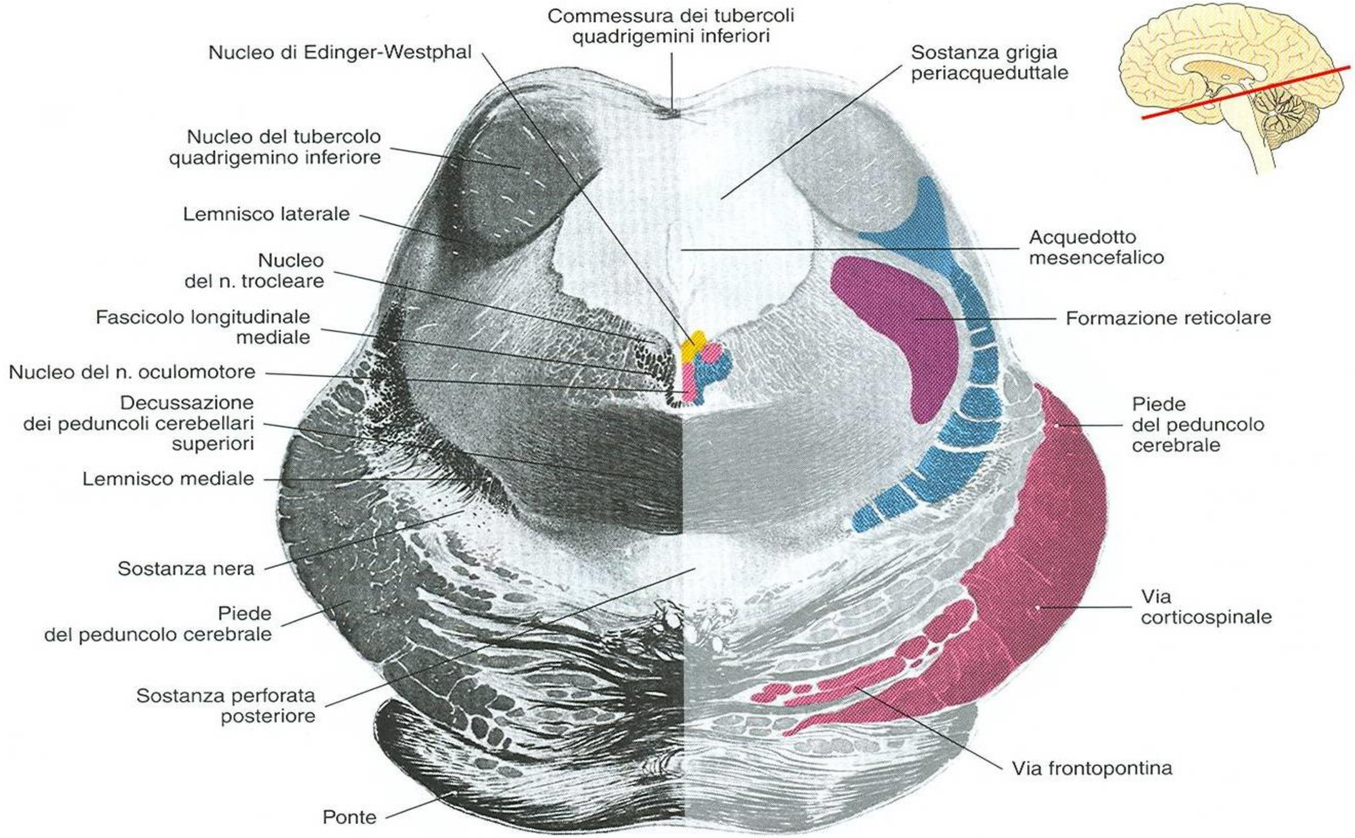
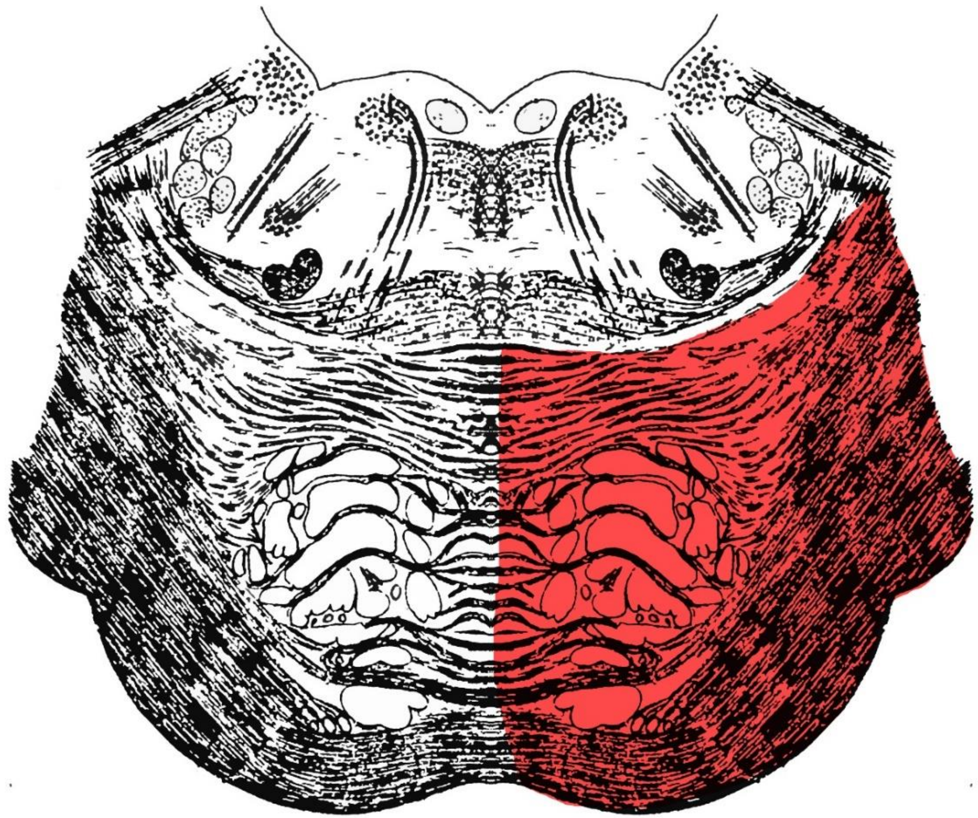
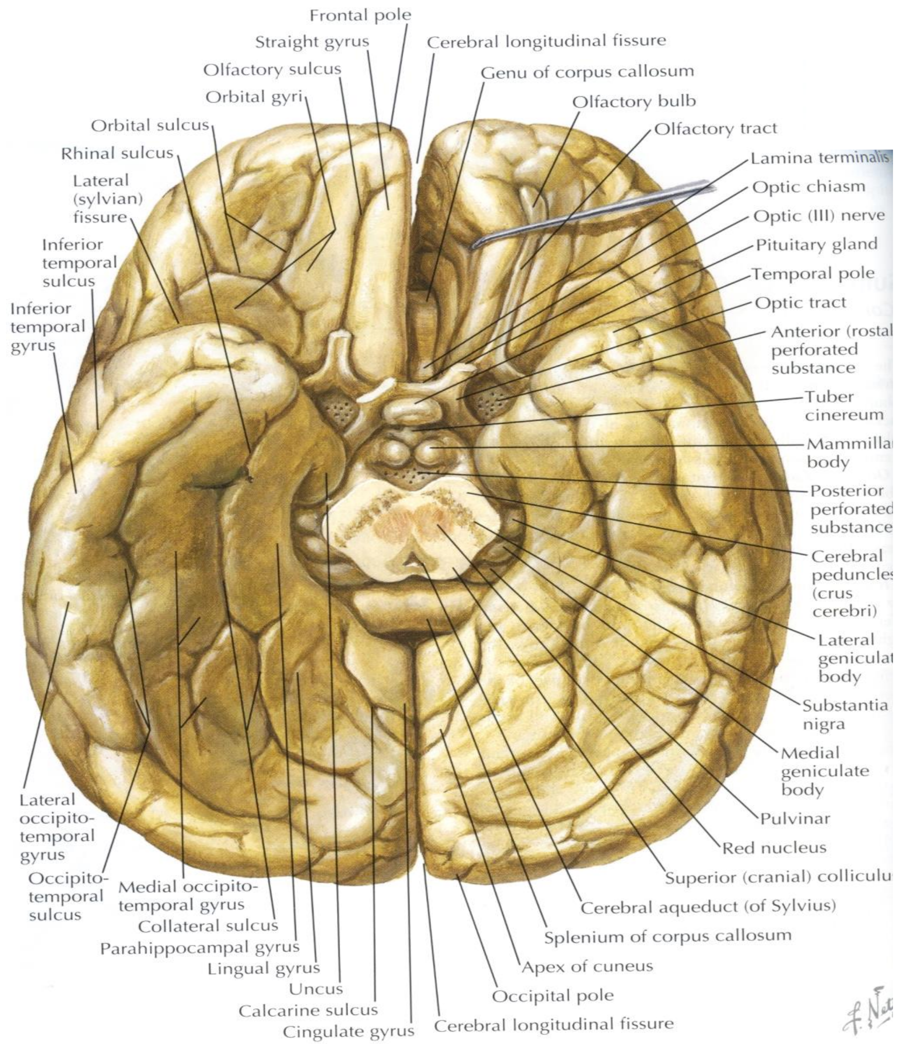
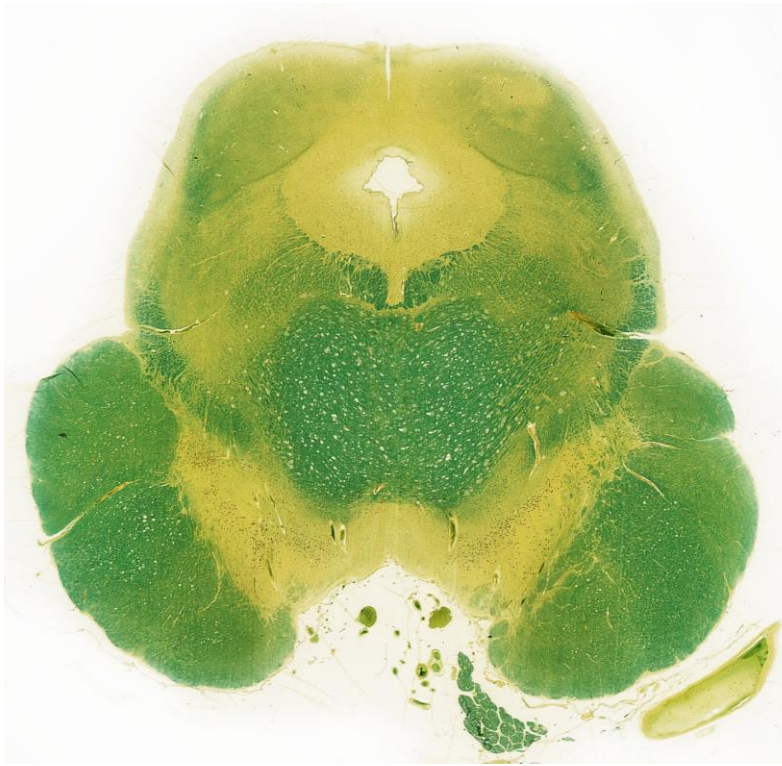


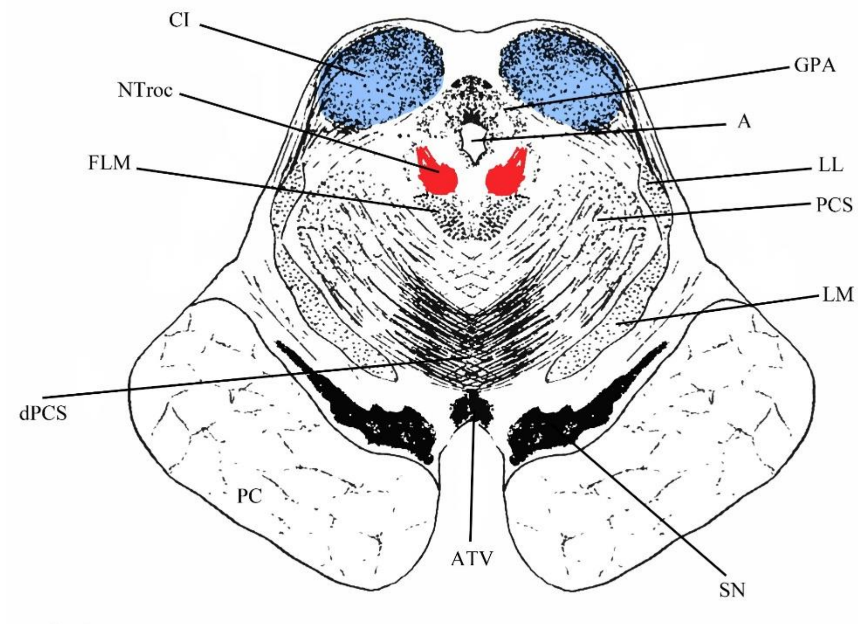
Figura 14.58 - Conformazione interna del mesencefalo in una sezione trasversa colorata per la dimostrazione della mielina. Le vie appaiono in **nero**, i centri in **bianco**. La sezione passa per i tubercoli quadrigemini inferiori e coglie anche una piccola parte del margine superiore del ponte che sormonta i peduncoli cerebrali. È netta la distinzione tra piede e tegmento a opera della sostanza nera. Nella parte destra le vie e i nuclei motorî sono evidenziati in **rosso**, le vie e i nuclei sensitivi in **blu**, i nuclei parasimpatici in **giallo**, la formazione reticolare in **viola**.

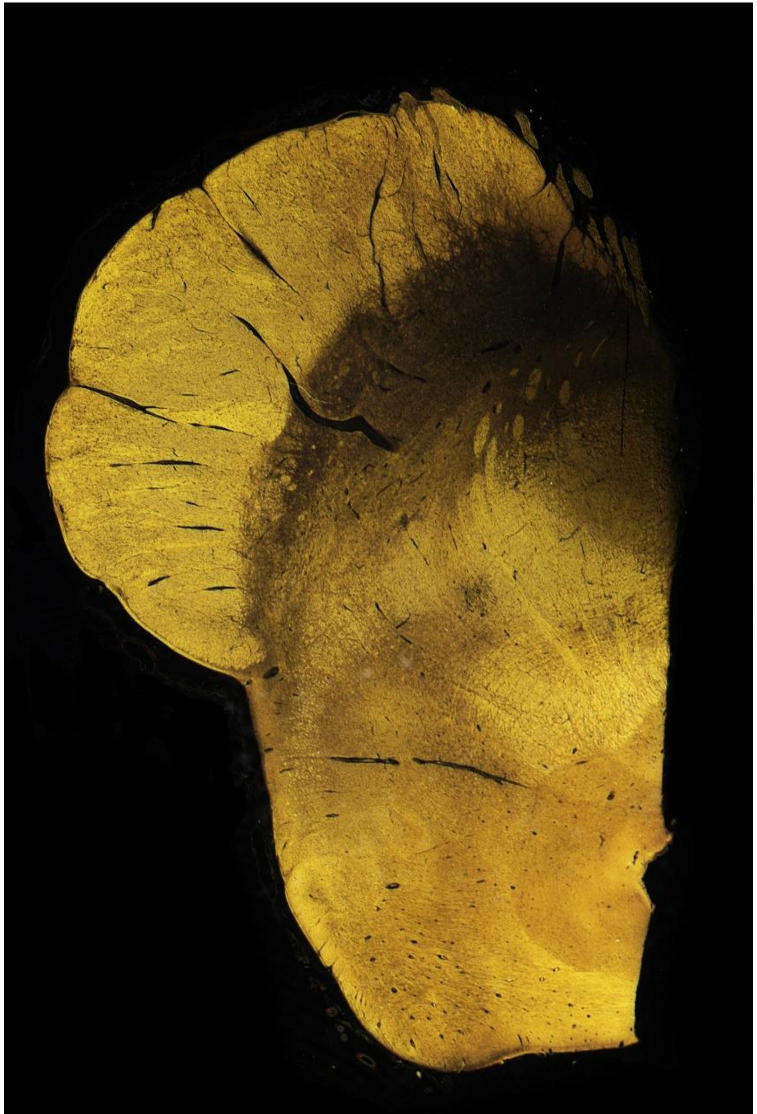


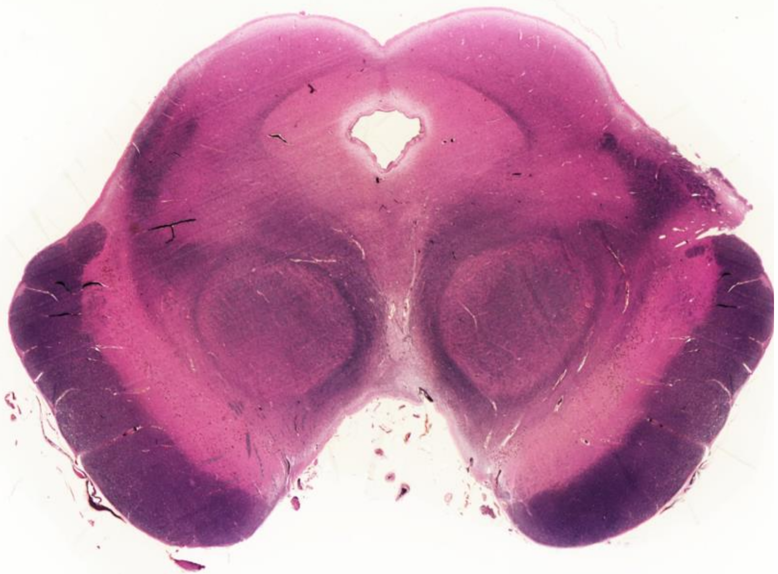
Inferior Surface of Brain

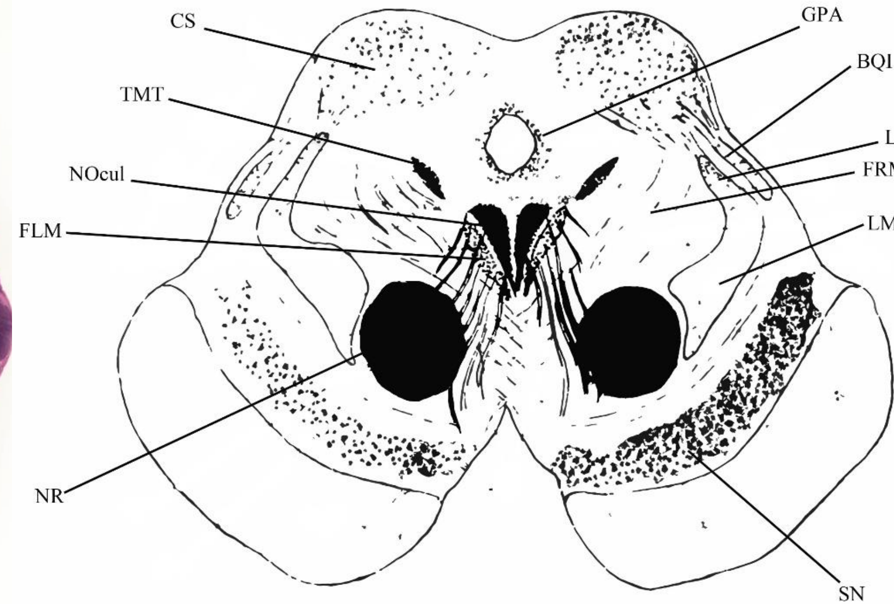


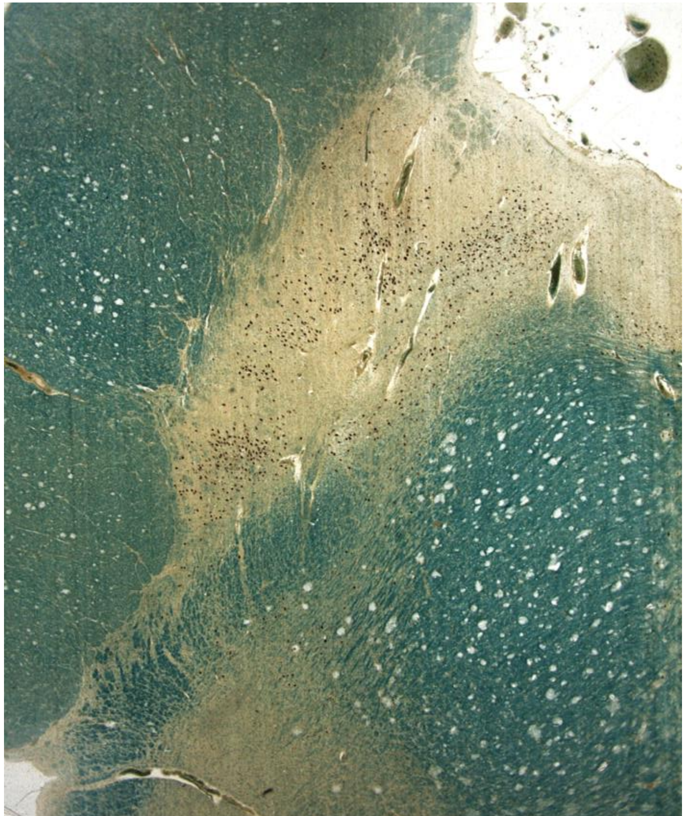


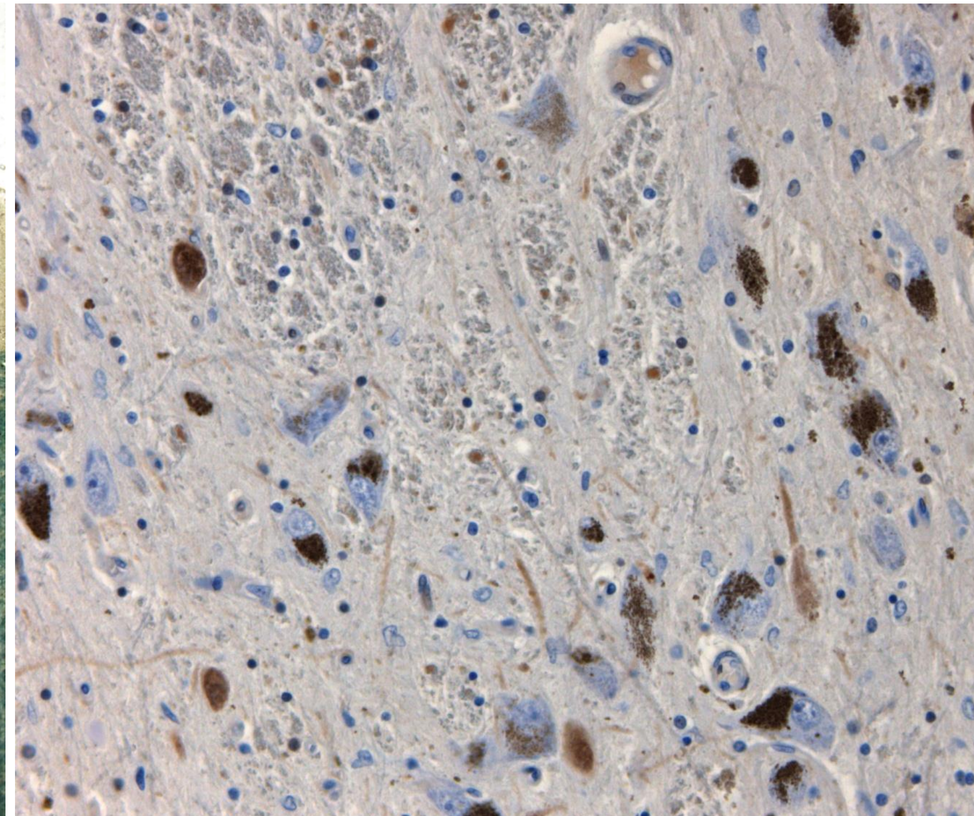

CI
GPA
NTroc
A
FLM
LL
PCS
LM
dPCS
PC
ATV
SN



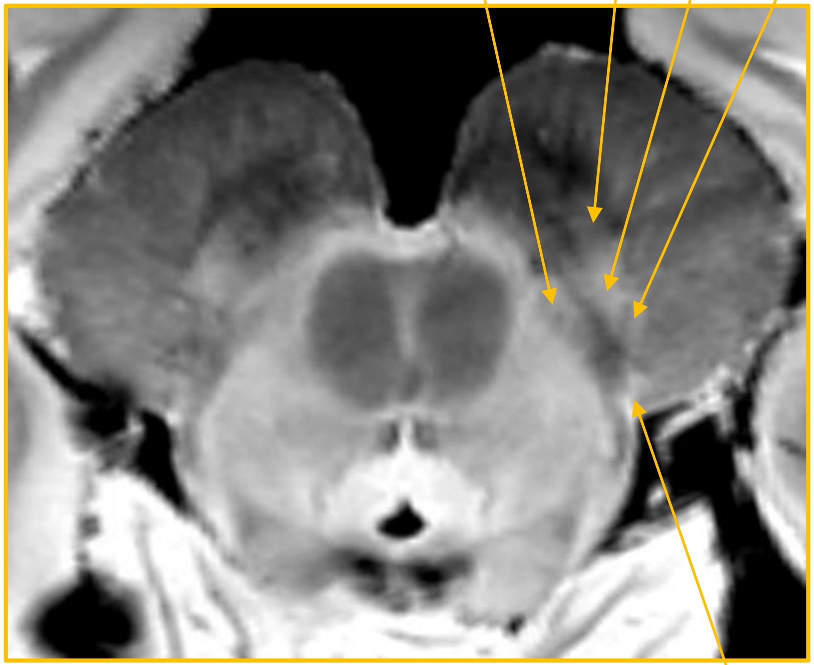



CS
GPA
BQI
TMT
LL
FRM
NOcul
FLM
LM
NR
SN

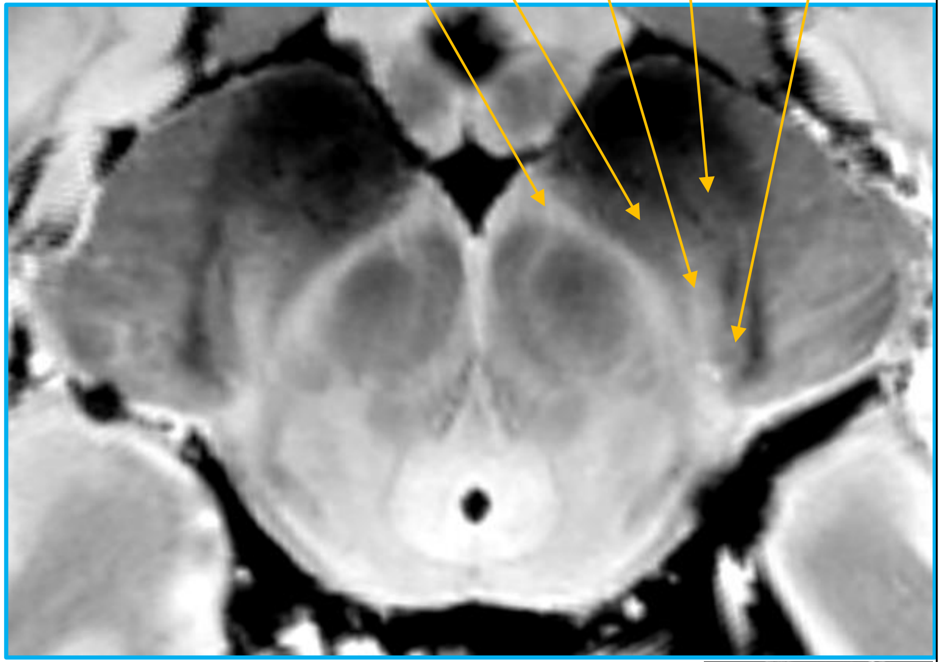




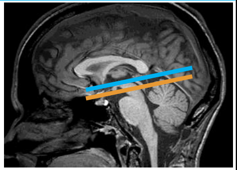
MESENCEPHALON



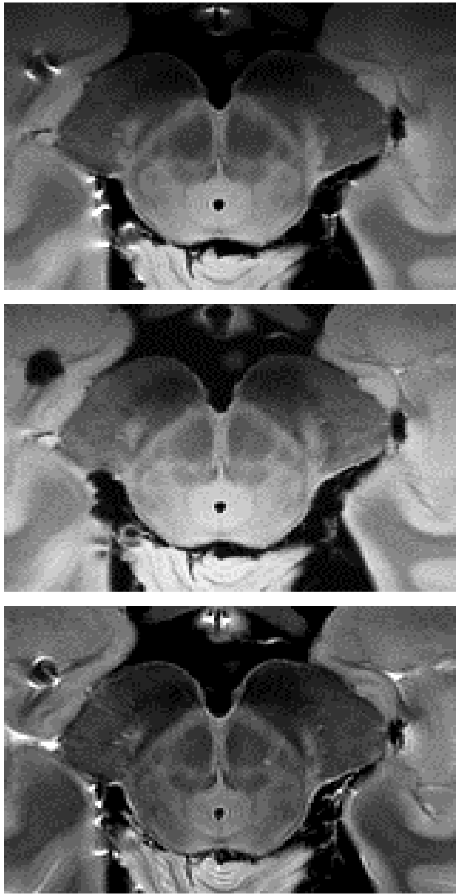
Caudal Section (SCP)

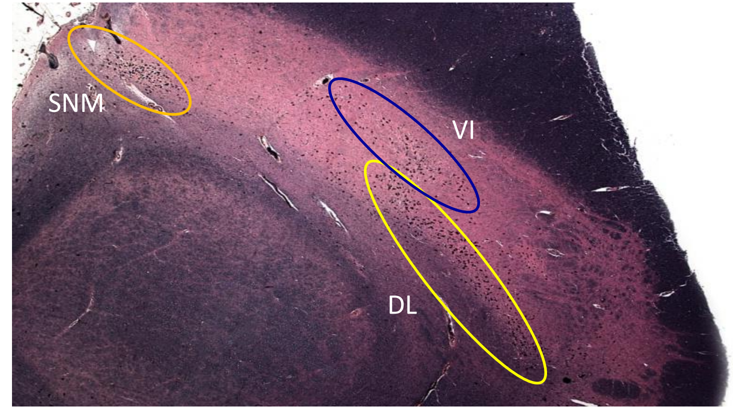


Rostral Section (RN)

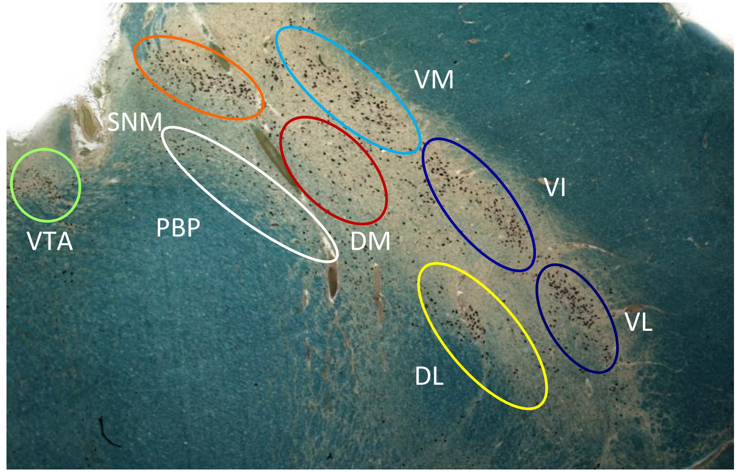


SUBSTANTIA NIGRA

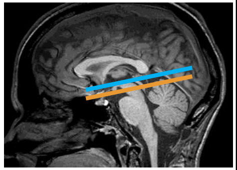




Rostral Section (RN)



Caudal Section (SCP)



Reticular Formation of the Brainstem

- The reticular formation is made of aggregates of neurons of various forms and dimensions and by a system of projection fibers with a diffuse organization.

- The dendrites are disposed in bundles forming an intricated net, through which the ascending and descending fibers pass.

Reticular Formation of the Brainstem

- Philogenetically ancient, even though primitive organisms present a coexisting diffuse and organized system.

Reticular Formation of the Brainstem

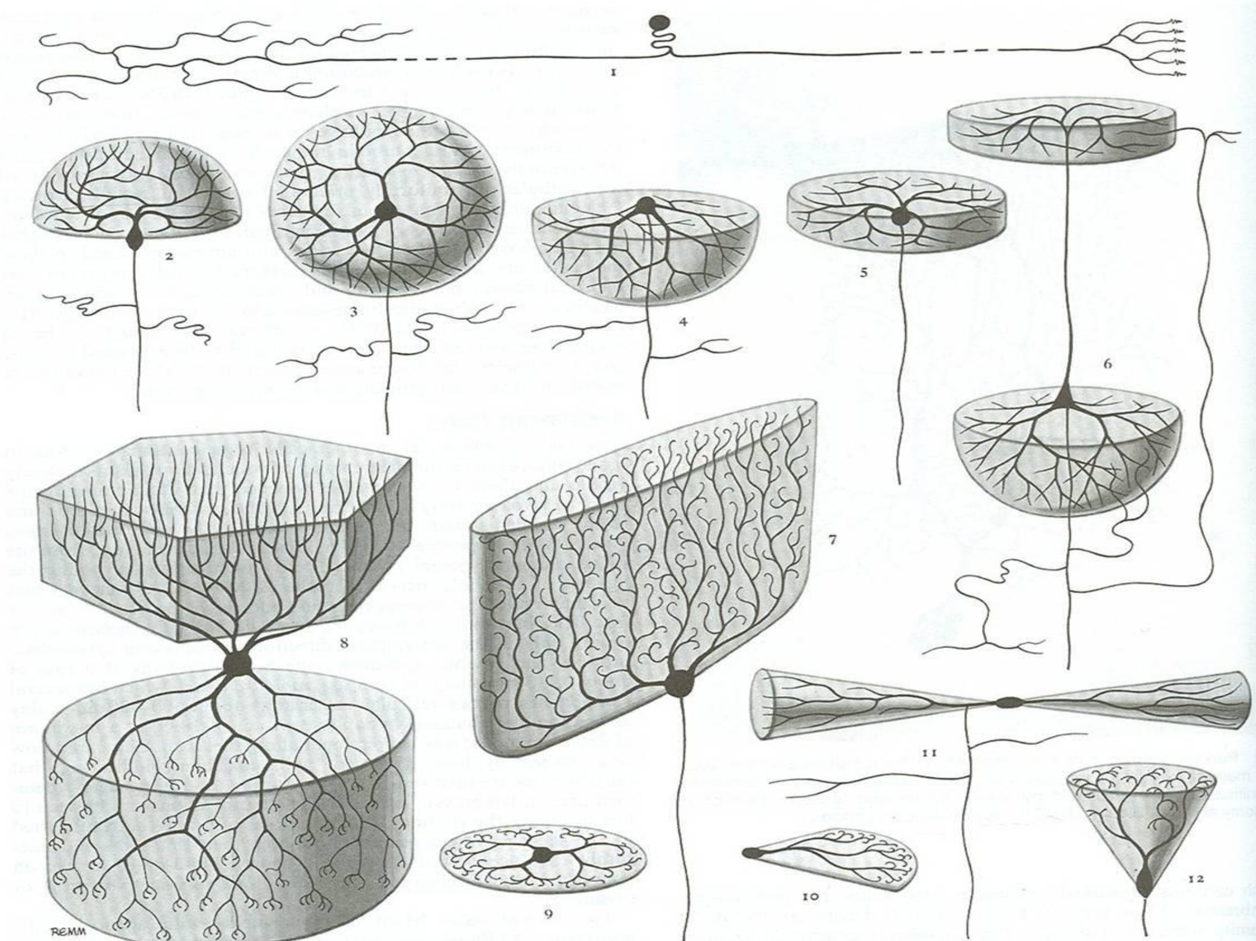
- Localized deeply within the brainstem.
- Diffuse connectivity,
  with direct and decussating projection systems.
- Somatic and visceral functions.

Reticular Formation
Dendritic configuration

- Isodendritic: long dendrites which extend along the main axis of the brainstem, on the transverse plane. (*the most common type in the reticular formation*)

- Idiodendritic: A single dendritic tree with short dendrites which curve towards the periphery of the nuclei of the reticular formation.

- Allodendritic: many short dendrites with reiterating path.



8.33 Scheme showing pattern variations of neuronal geometry: (1) unipolar, sensory ganglionic neuron; (2) bipolar neuron; (3) stellate (isodendritic) neuron, with (4), (5), and (11) which are modifications of this pattern; (6) pyramidal neuron with an apical and a series of basal dendrites and recurrent axon collaterals from the cerebral cortex; (7) Purkinje neur from the cerebellar cortex (see **8**.32); (8) Golgi neuron from the cerebell cortex; (9) and (10) amacrine cells lacking axons; (12) glomerular neur (mitral cell) from the olfactory bulb, showing recurved dendritic tips.

Reticular Formation of the Brainstem

- Chemoarchitectural organization of neuronal nuclei:

    Grup A: noradrenergic e dopaminergic

    Grup B: serotoninergic

    Grup C: adrenergic

    Grup Ch: colinergic

Reticular Formation
Anatomical Subdivision in columns

- <u>Median</u>: large neurons (serotoninergic)

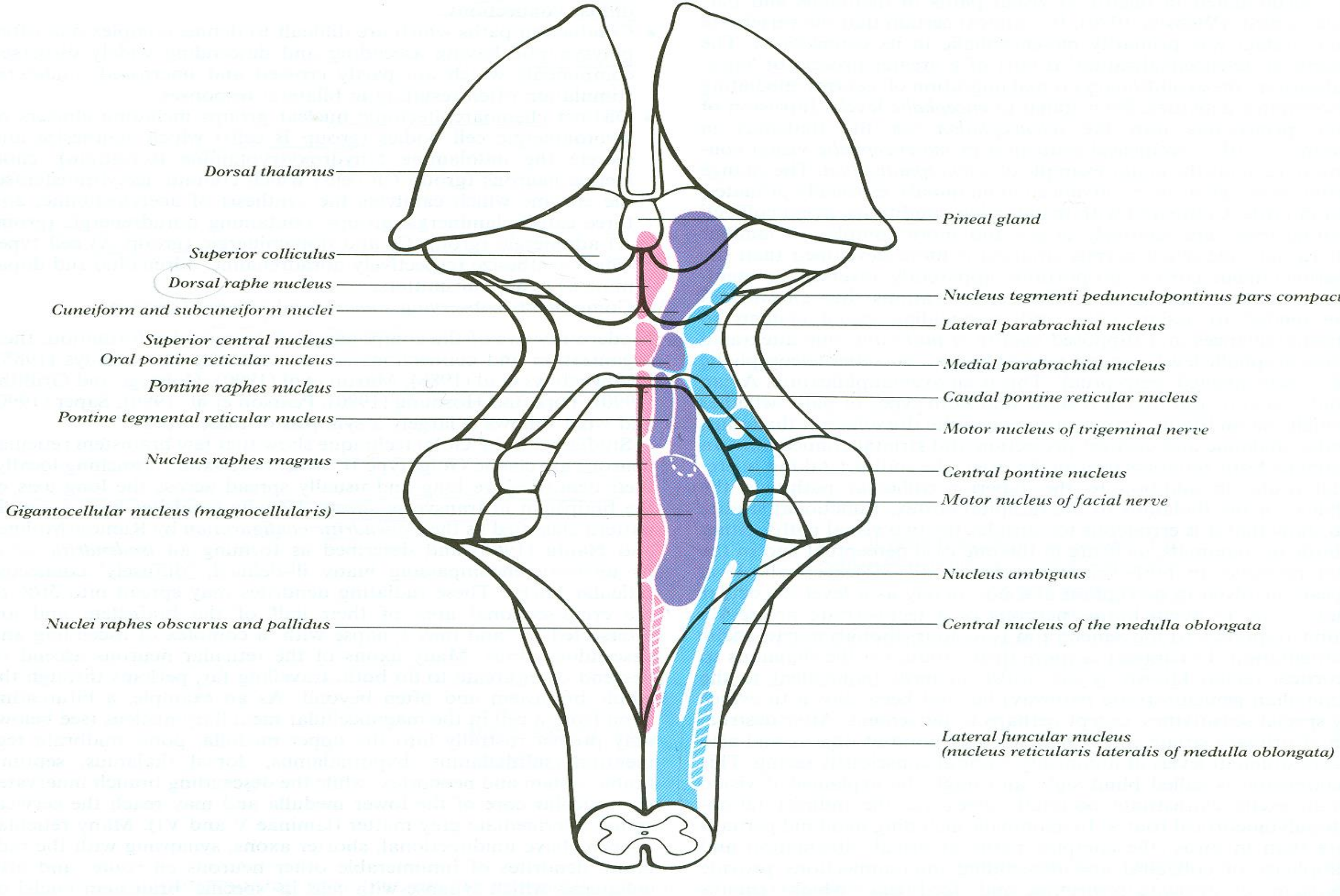
  Raphe nuclei

- <u>Medial</u>: large neurons

  Gigantocellular neurons

- <u>Lateral</u>: medium sized and small neurons

  Grey reticular substance of the pontine tegmentum


Dorsal thalamus
Pineal gland
Superior colliculus
Dorsal raphe nucleus
Cuneiform and subcuneiform nuclei
Nucleus tegmenti pedunculopontinus pars compact
Lateral parabrachial nucleus
Superior central nucleus
Oral pontine reticular nucleus
Medial parabrachial nucleus
Pontine raphes nucleus
Caudal pontine reticular nucleus
Pontine tegmental reticular nucleus
Motor nucleus of trigeminal nerve
Nucleus raphes magnus
Central pontine nucleus
Motor nucleus of facial nerve
Gigantocellular nucleus (magnocellularis)
Nucleus ambiguus
Nuclei raphes obscurus and pallidus
Central nucleus of the medulla oblongata
Lateral funcular nucleus
(nucleus reticularis lateralis of medulla oblongata)

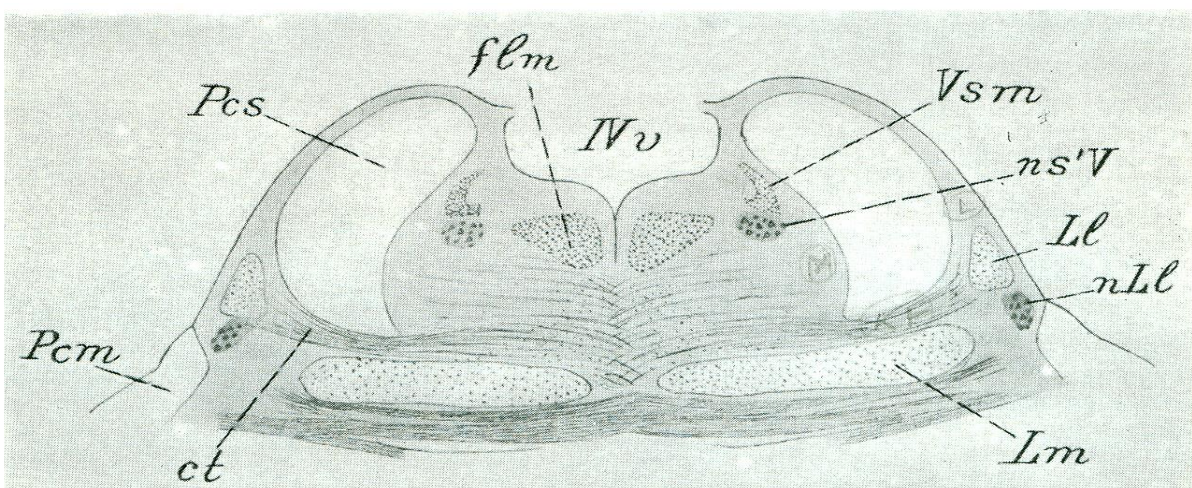
Grey reticular substance of the lateral pontine tegmentum

Parabrachial Nuclei: -medial

-lateral

-ventral (of Kölliker-Fuse)

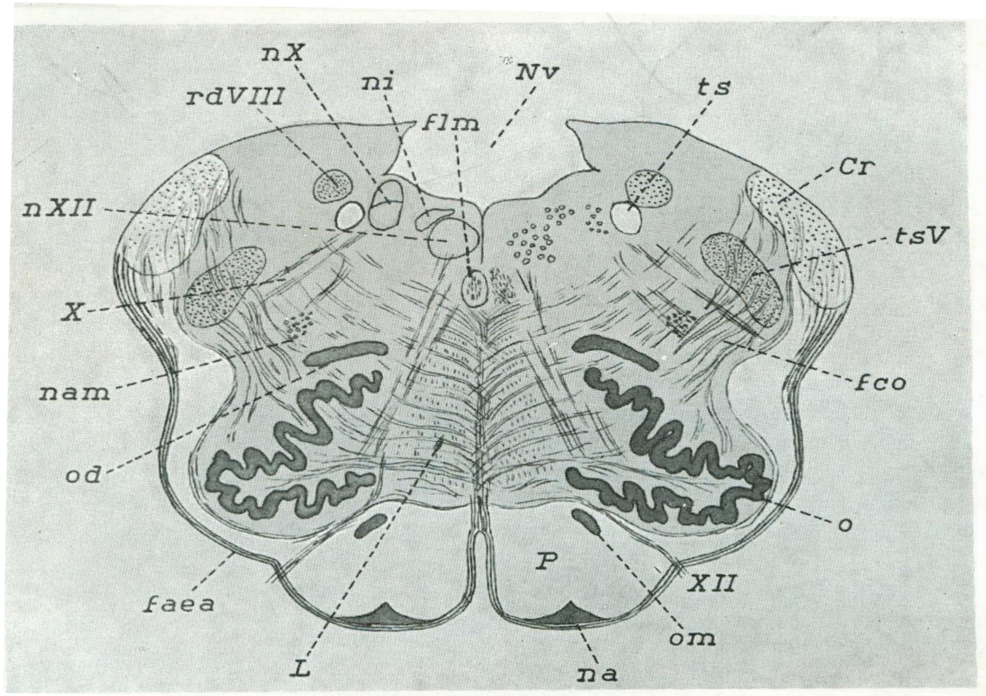
Pneumotaxic center



Bötzinger Nucleus

Stimulation of inhalation

Ventrally to the nucleus ambiguus.

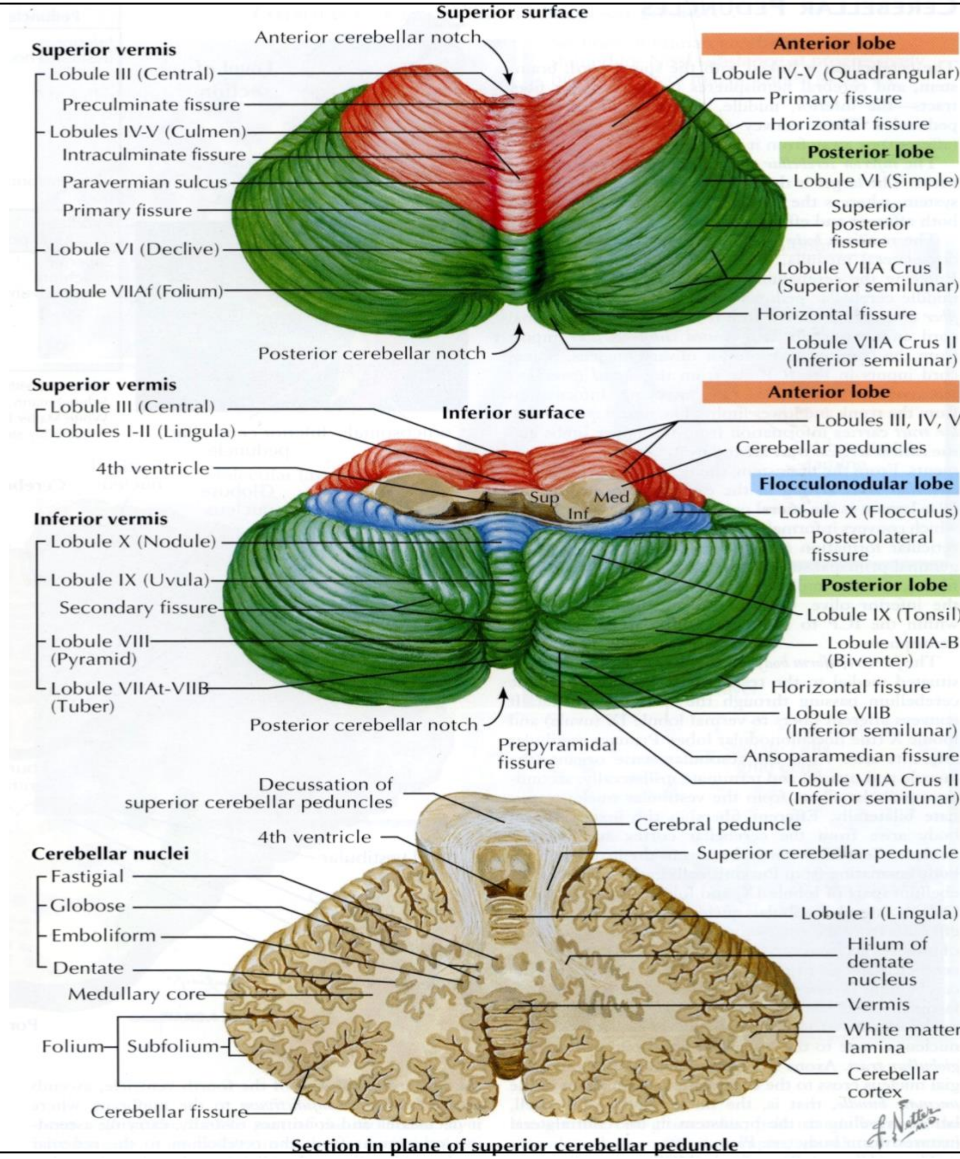


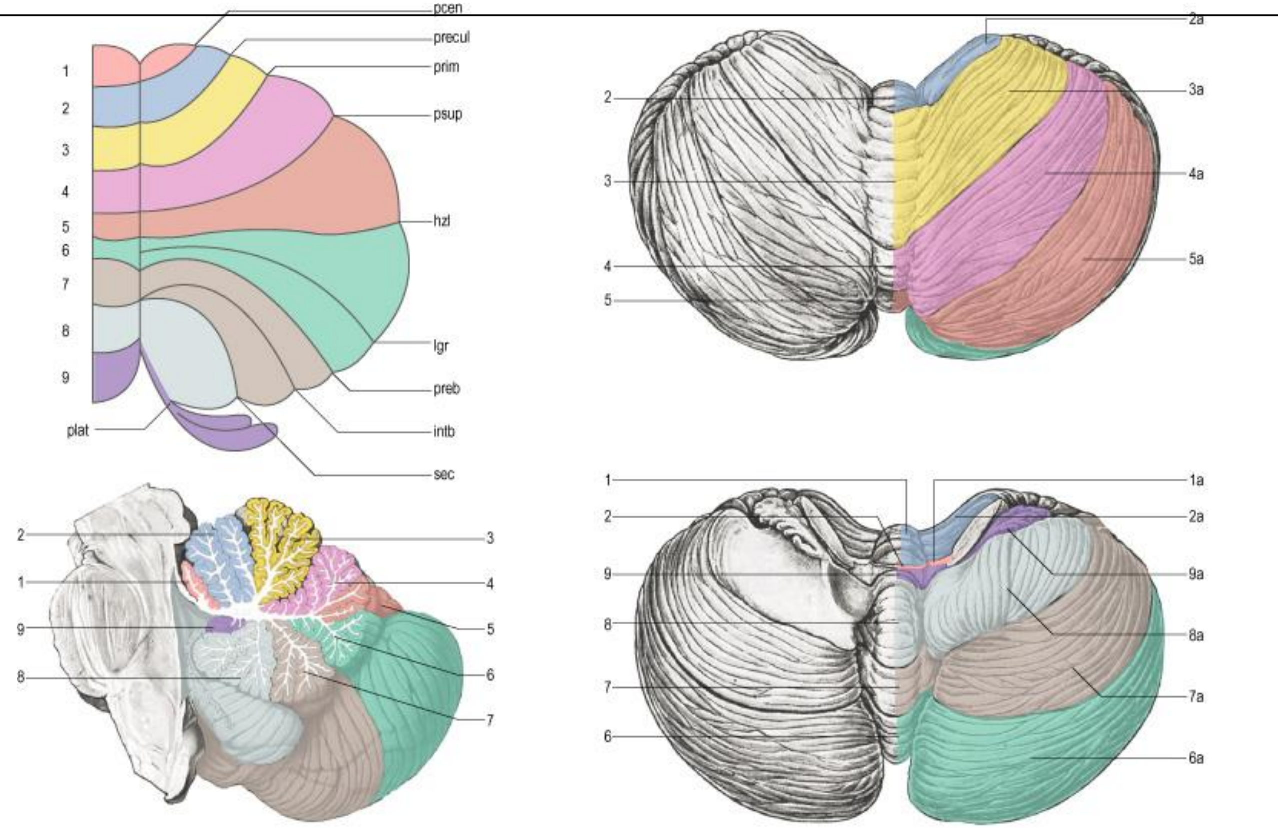
The Cerebellum

F. Von Stuck – Circle Dancing

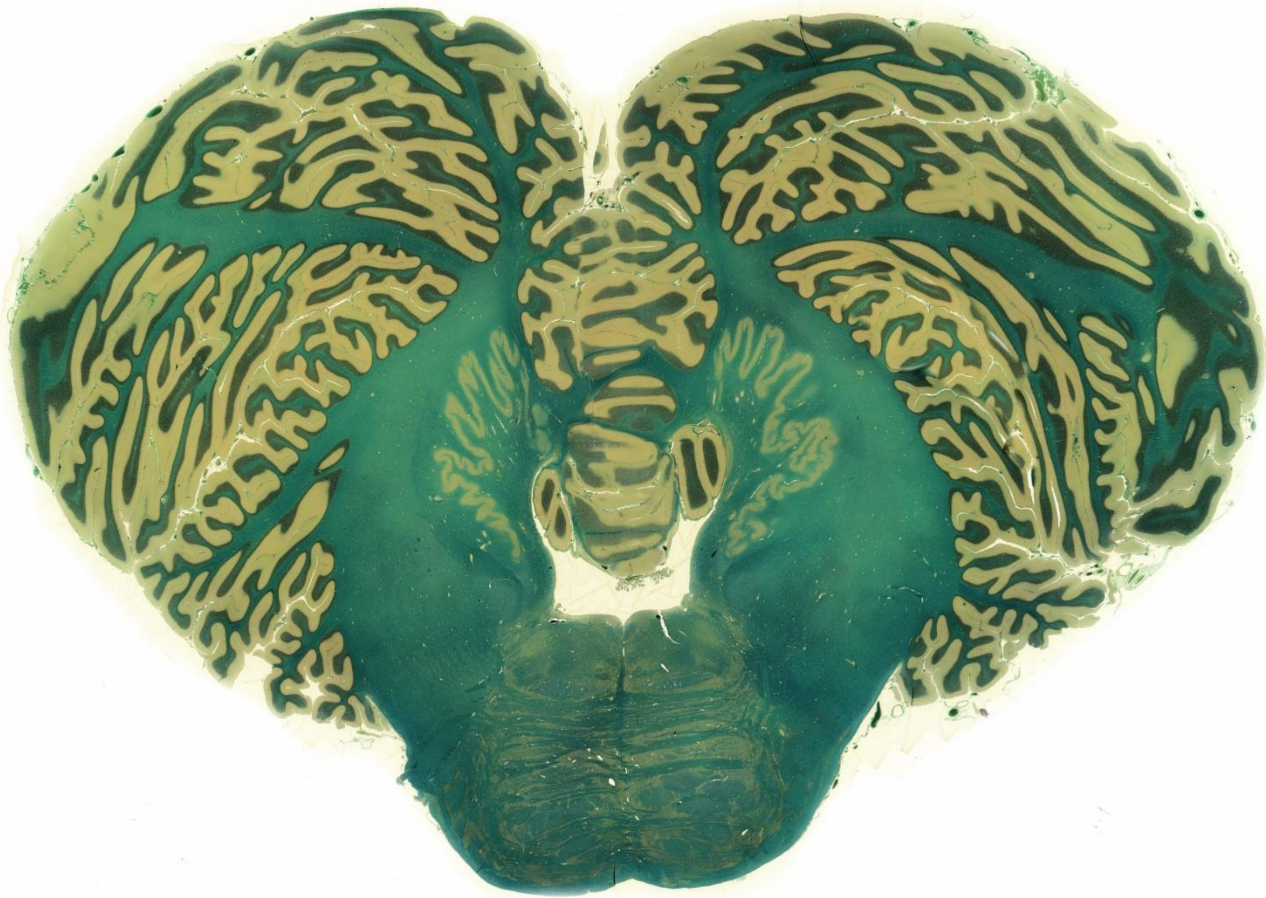
The Cerebellum

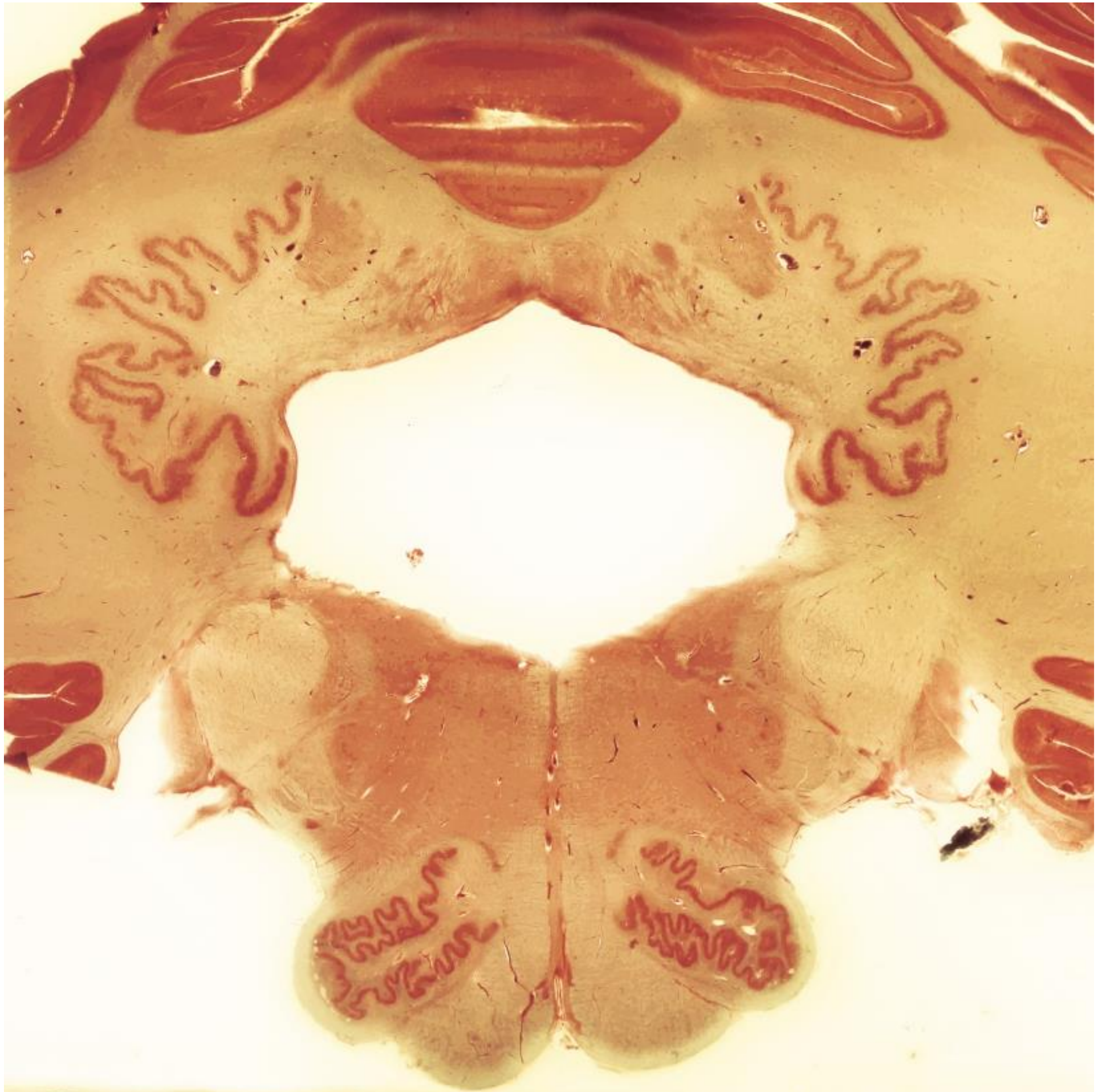
F. Von Stuck – Circle Dancing


Superior surface
Anterior cerebellar notch
Superior vermis
Lobule III (Central)
Preculminate fissure
Lobules IV-V (Culmen)
Intraculminate fissure
Paravermian sulcus
Primary fissure
Lobule VI (Declive)
Lobule VIIAf (Folium)
Anterior lobe
Lobule IV-V (Quadrangular)
Primary fissure
Horizontal fissure
Posterior lobe
Lobule VI (Simple)
Superior posterior fissure
Lobule VIIA Crus I (Superior semilunar)
Horizontal fissure
Lobule VIIA Crus II (Inferior semilunar)
Posterior cerebellar notch
Superior vermis
Lobule III (Central)
Lobules I-II (Lingula)
Inferior surface
4th ventricle
Sup
Med
Inf
Inferior vermis
Lobule X (Nodule)
Lobule IX (Uvula)
Secondary fissure
Lobule VIII (Pyramid)
Lobule VIIAt-VIIB (Tuber)
Posterior cerebellar notch
Anterior lobe
Lobules III, IV, V
Cerebellar peduncles
Flocculonodular lobe
Lobule X (Flocculus)
Posterolateral fissure
Posterior lobe
Lobule IX (Tonsil)
Lobule VIIIA-B (Biventer)
Horizontal fissure
Lobule VIIB (Inferior semilunar)
Prepyramidal fissure
Ansoparamedian fissure
Lobule VIIA Crus II (Inferior semilunar)
Decussation of superior cerebellar peduncles
4th ventricle
Cerebellar nuclei
Fastigial
Globose
Emboliform
Dentate
Medullary core
Folium
Subfolium
Cerebellar fissure
Cerebral peduncle
Superior cerebellar peduncle
Lobule I (Lingula)
Hilum of dentate nucleus
Vermis
White matter lamina
Cerebellar cortex
Section in plane of superior cerebellar peduncle

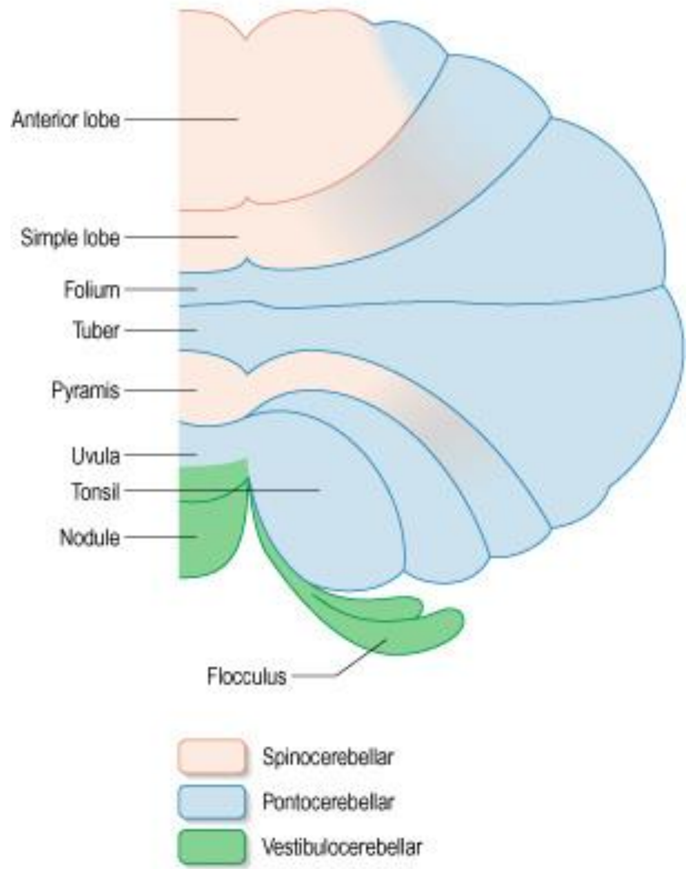


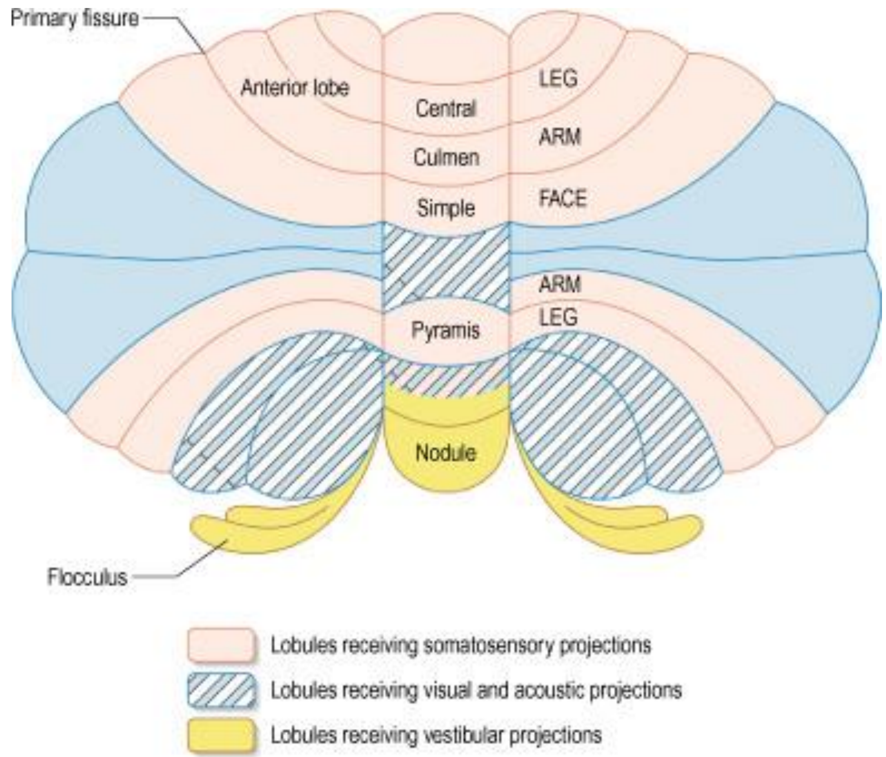
Anterior lobe	**Posterior lobe**	**Flocculonodular lobe**	**Fissures**	**Wings**
1 Lingula	4 Simple	9 Nodule	pcen precentral	1a Wing of lingula
2 Central	5 Folium		precul preculminate	2a Wing of central lobule
3 Culmen	6 Tuber		prim primary	3a Anterior quadrangular lobule
	7 Pyramis		psup posterior superior	4a Posterior quadrangular lobule
	8 Uvula		hzl horizontal	5a Superior semilunar lobule
			lgr lunogracile	6a Inferior semilunar lobule
			preb prebiventral	7a Biventral lobule
			intb intrabiventral	8a Tonsil of cerebellum
			sec secondary	9a Flocculus
			plat posterolateral	



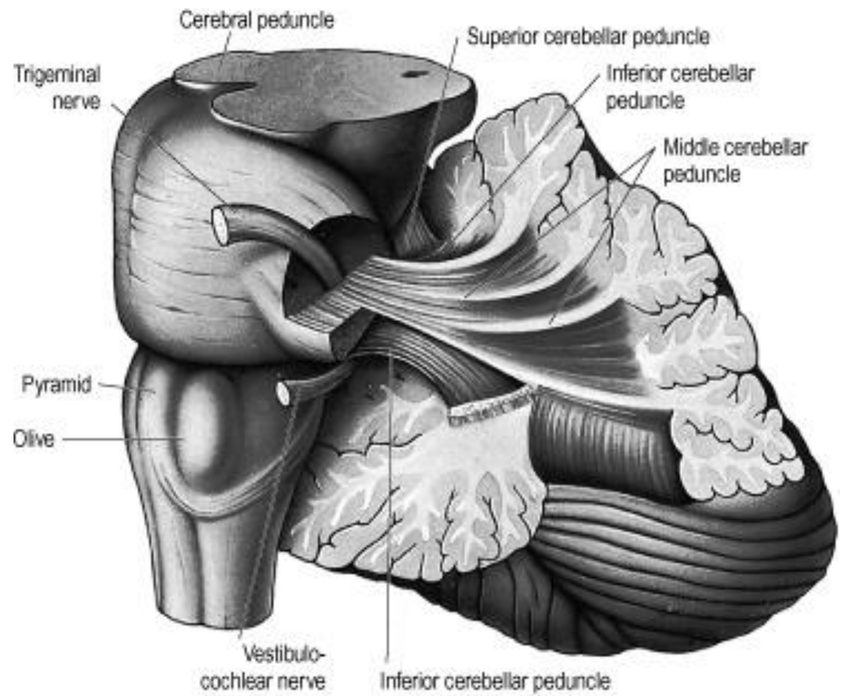


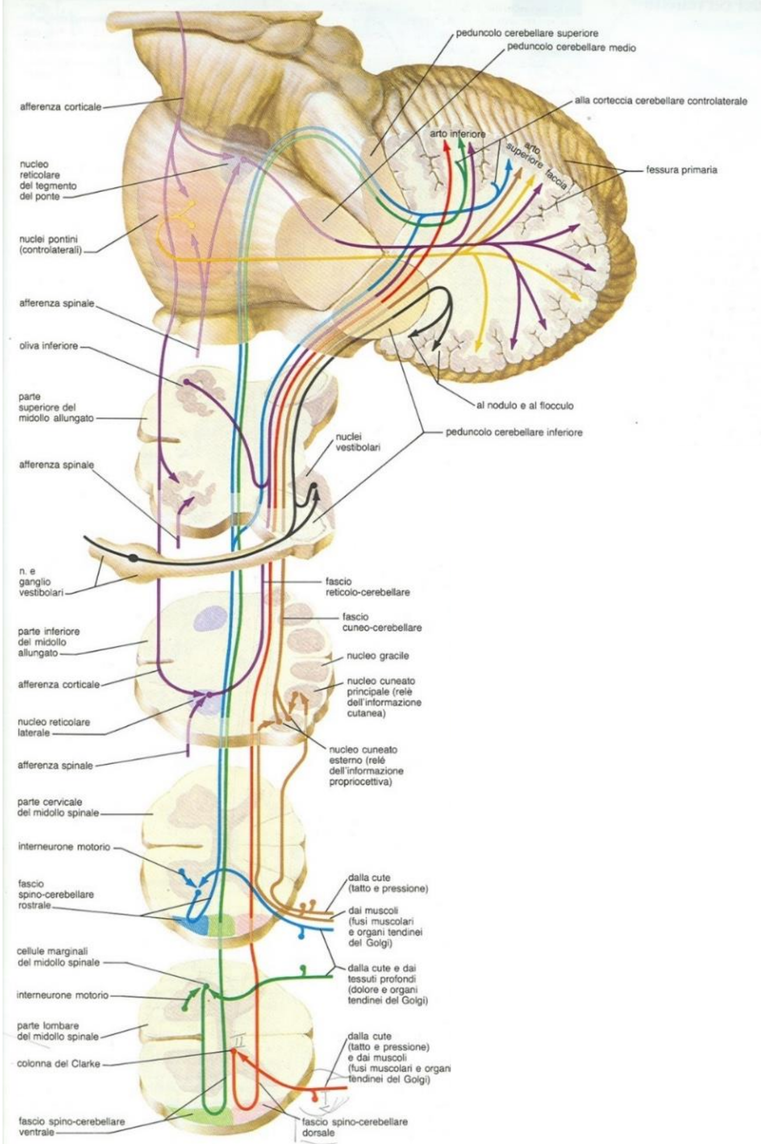
A


Anterior lobe
Simple lobe
Folium
Tuber
Pyramis
Uvula
Tonsil
Nodule
Flocculus
Spinocerebellar
Pontocerebellar
Vestibulocerebellar



Primary fissure
Anterior lobe
Central
Culmen
Simple
LEG
ARM
FACE
ARM
LEG
Pyramis
Nodule
Flocculus
Lobules receiving somatosensory projections
Lobules receiving visual and acoustic projections
Lobules receiving vestibular projections


Cerebral peduncle
Superior cerebellar peduncle
Trigeminal nerve
Inferior cerebellar peduncle
Middle cerebellar peduncle
Pyramid
Olive
Vestibulo-cochlear nerve
Inferior cerebellar peduncle

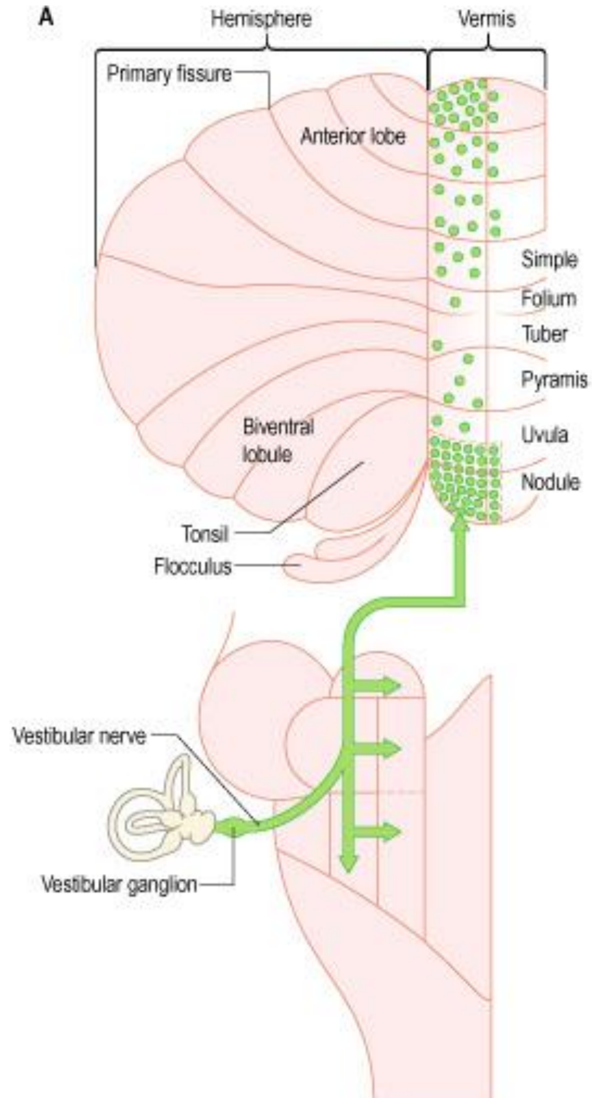


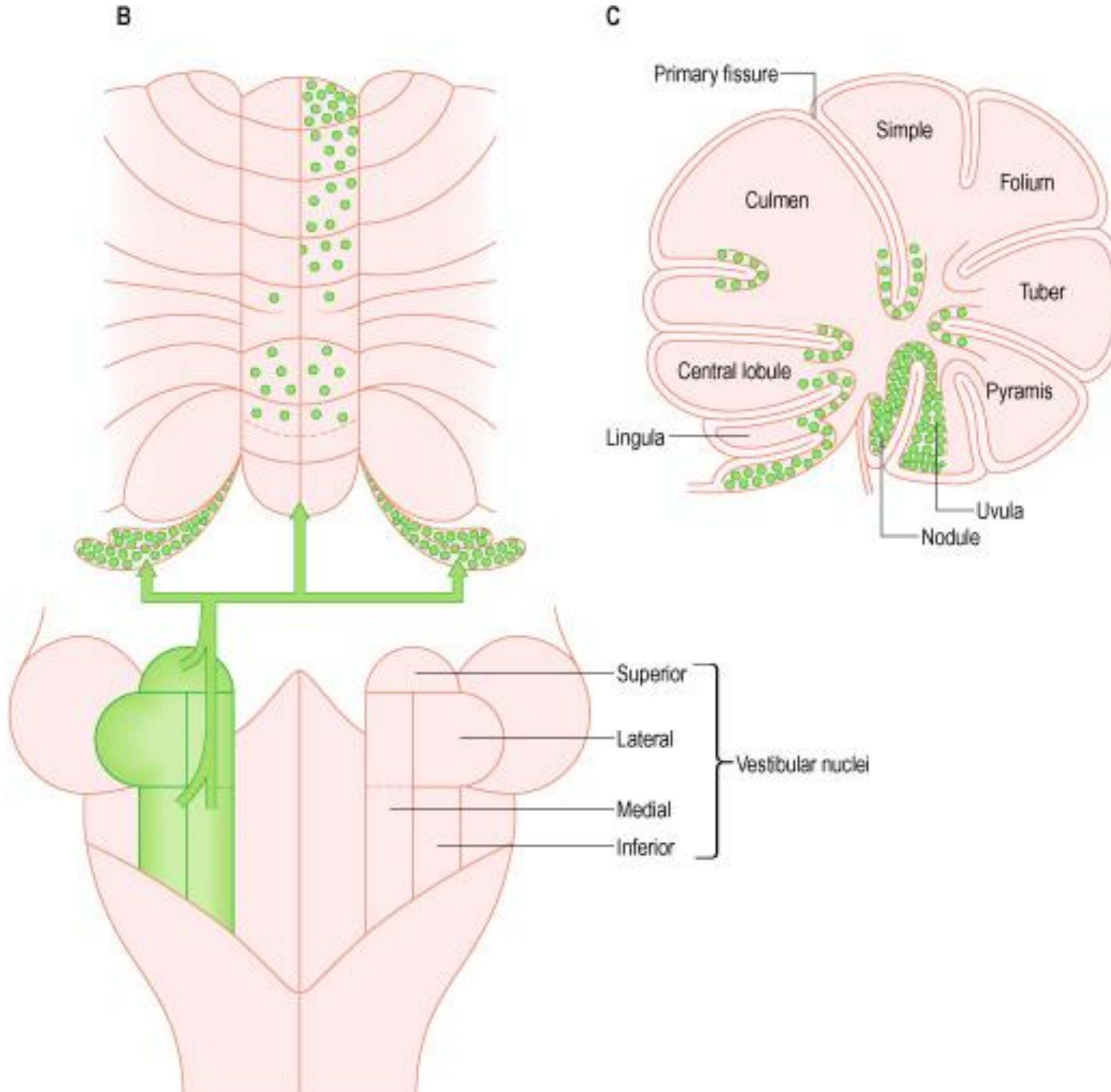
Cerebellar Afferences

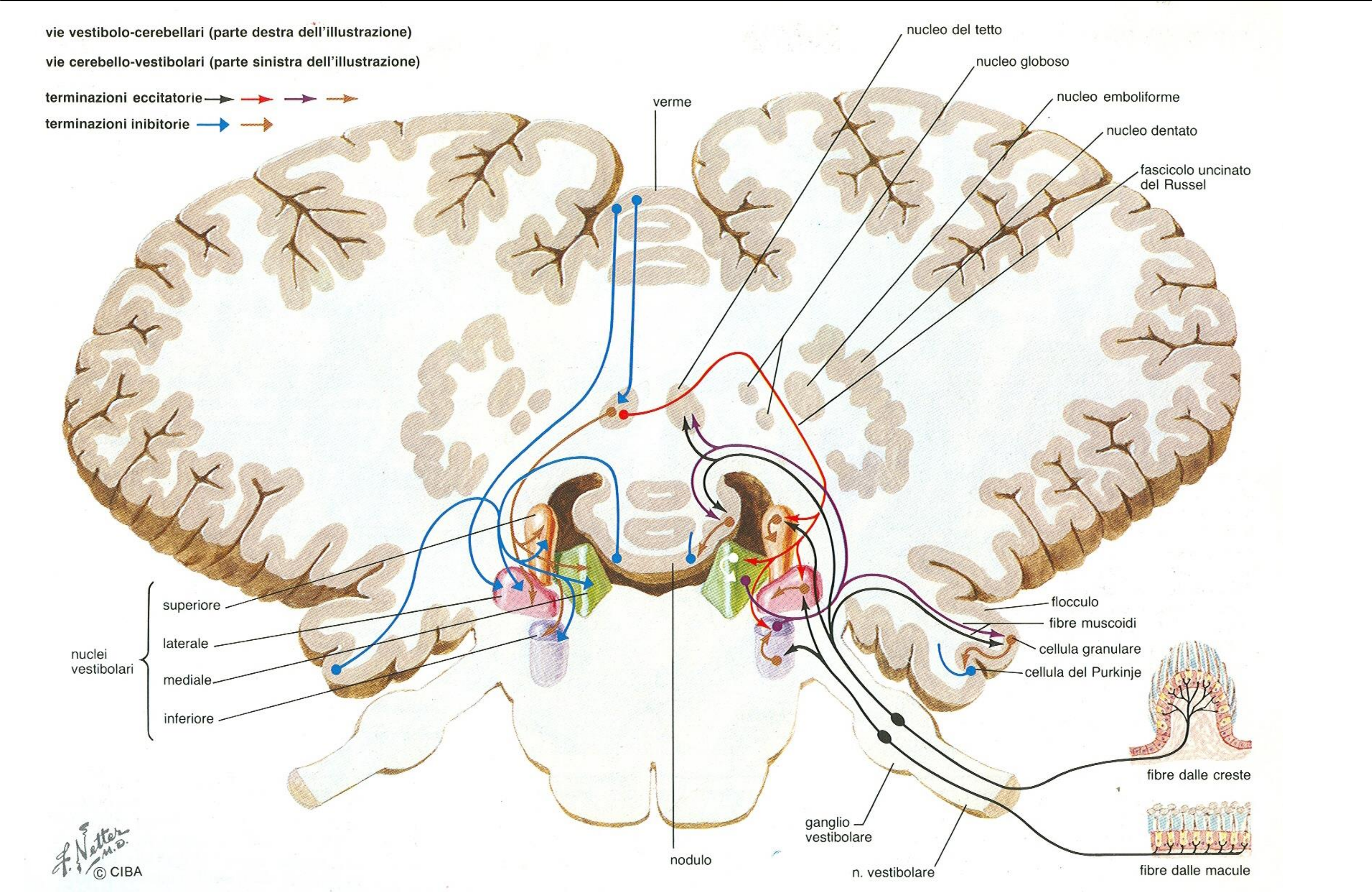
- Vestibulo-cerebellar
- Spino-cerebellar
- Cortico-Ponto-cerebellar
- Olivo-cerebellar

Cerebellar Efferences

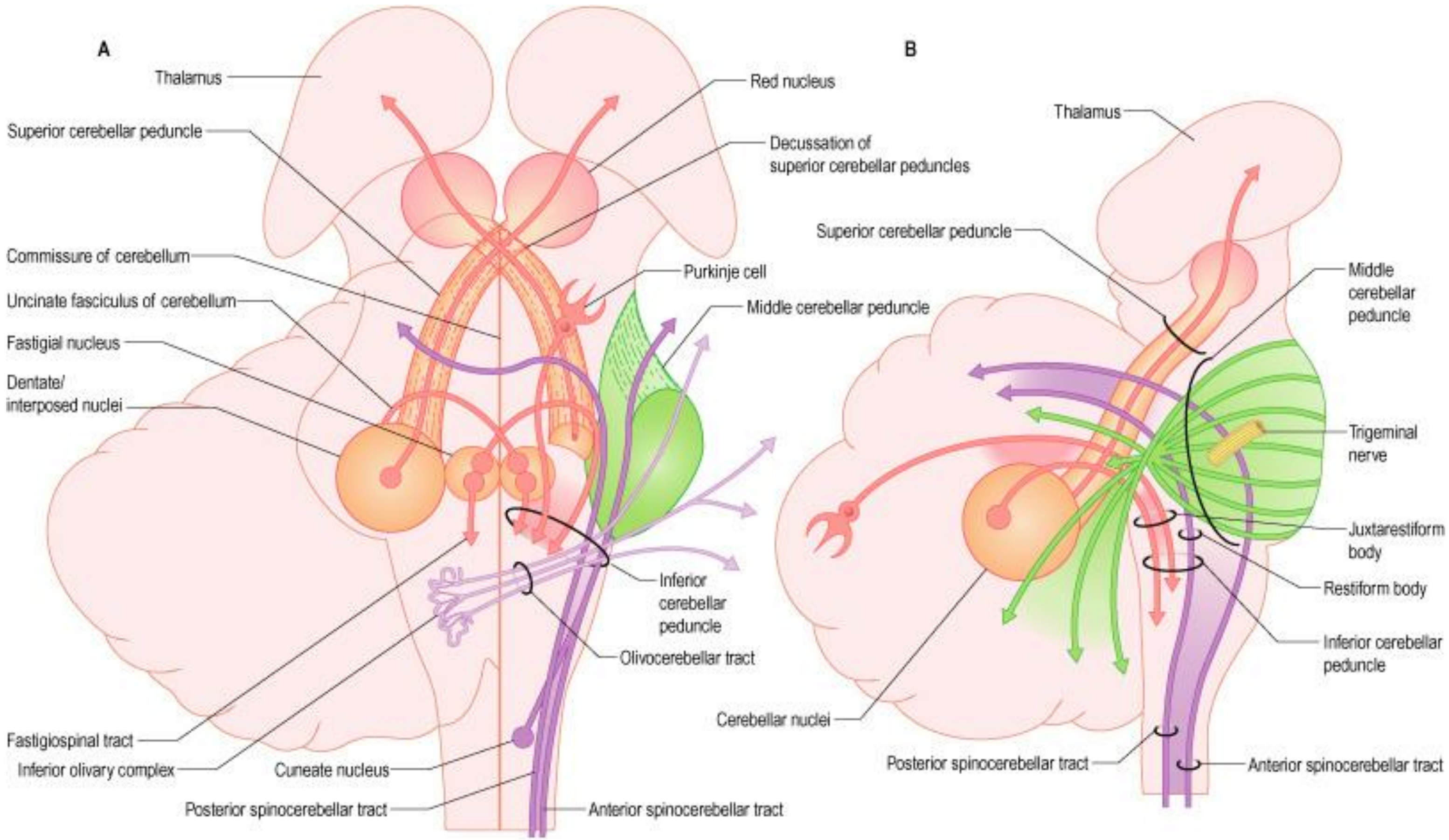
- Cerebello-fastigio-vestibular
- Cerebello-dento-rubro

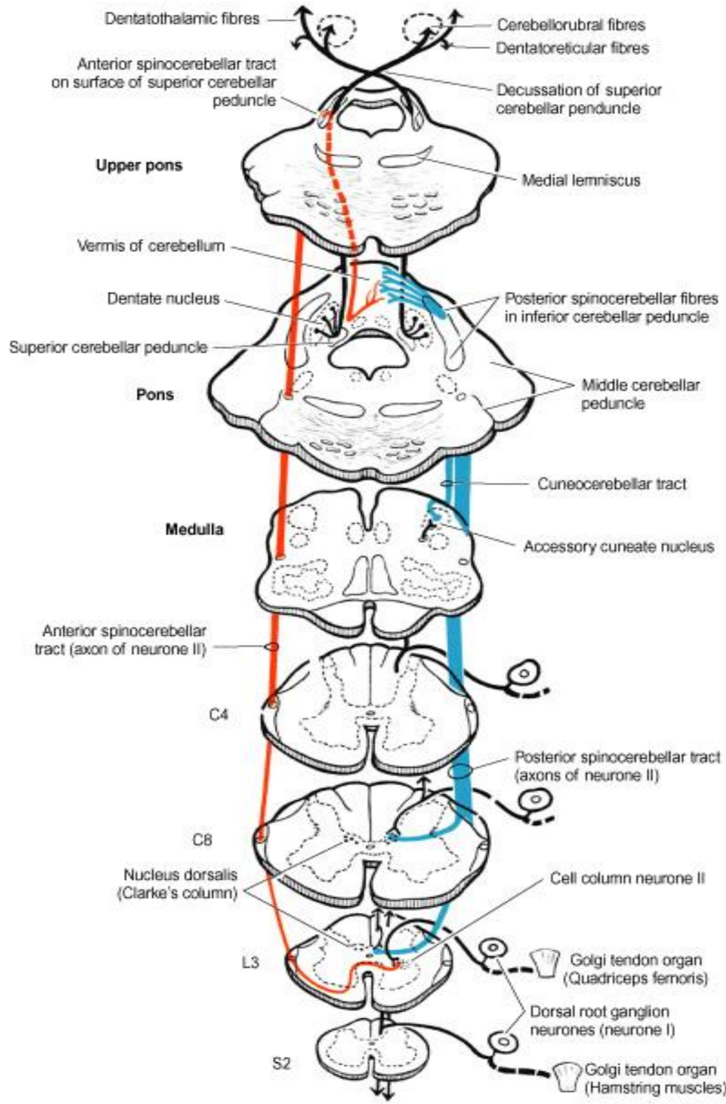

A
Hemisphere
Vermis
Primary fissure
Anterior lobe
Simple
Folium
Tuber
Pyramis
Uvula
Nodule
Biventral
lobule
Tonsil
Flocculus
Vestibular nerve
Vestibular ganglion


B
C
Primary fissure
Simple
Folium
Culmen
Tuber
Central lobule
Pyramis
Lingula
Uvula
Nodule
Superior
Lateral
Vestibular nuclei
Medial
Inferior



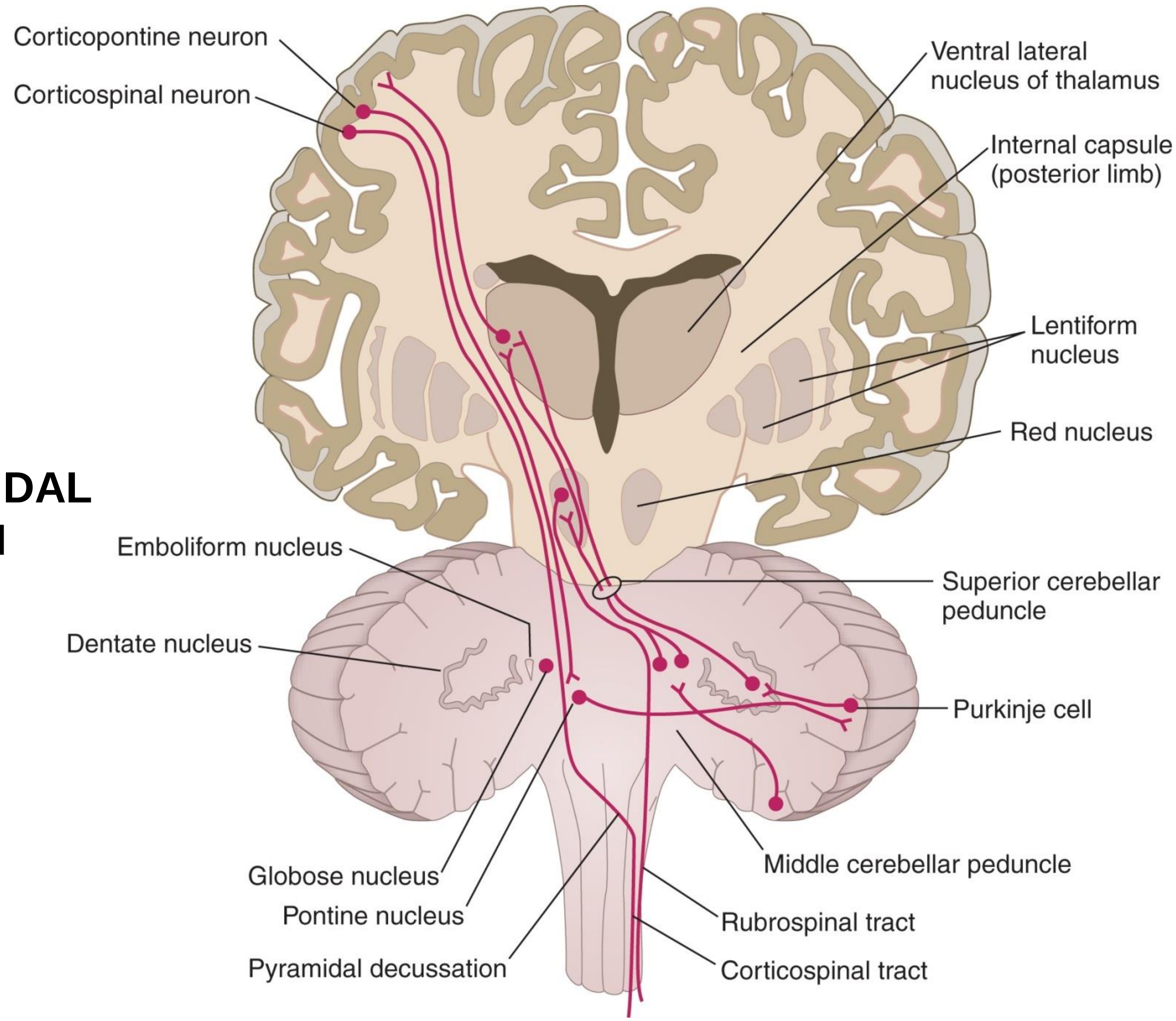
vie vestibolo-cerebellari (parte destra dell'illustrazione)
vie cerebello-vestibolari (parte sinistra dell'illustrazione)
terminazioni eccitatorie
terminazioni inibitorie
verme
nucleo del tetto
nucleo globoso
nucleo emboliforme
nucleo dentato
fascicolo uncinato del Russel
nuclei vestibolari
superiore
laterale
mediale
inferiore
flocculo
fibre muscoidi
cellula granulare
cellula del Purkinje
fibre dalle creste
ganglio vestibolare
fibre dalle macule
n. vestibolare
nodulo
F. Netter M.D.
© CIBA

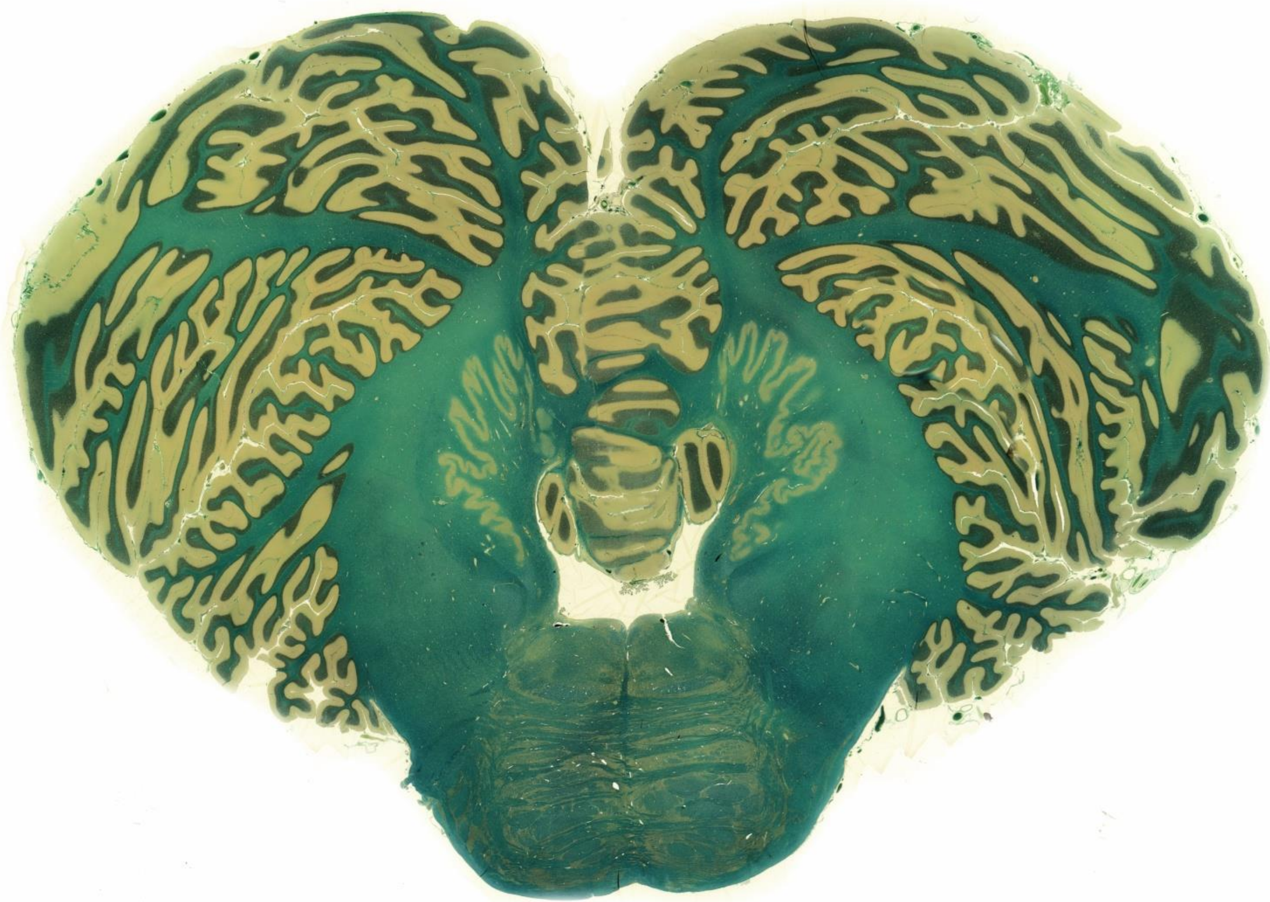

A
Thalamus
Superior cerebellar peduncle
Commissure of cerebellum
Uncinate fasciculus of cerebellum
Fastigial nucleus
Dentate/
interposed nuclei
Red nucleus
Decussation of
superior cerebellar peduncles
Purkinje cell
Middle cerebellar peduncle
Inferior
cerebellar
peduncle
Olivocerebellar tract
Fastigiospinal tract
Inferior olivary complex
Cuneate nucleus
Posterior spinocerebellar tract
Anterior spinocerebellar tract
B
Thalamus
Superior cerebellar peduncle
Middle
cerebellar
peduncle
Trigeminal
nerve
Juxtarestiform
body
Restiform body
Inferior cerebellar
peduncle
Cerebellar nuclei
Posterior spinocerebellar tract
Anterior spinocerebellar tract

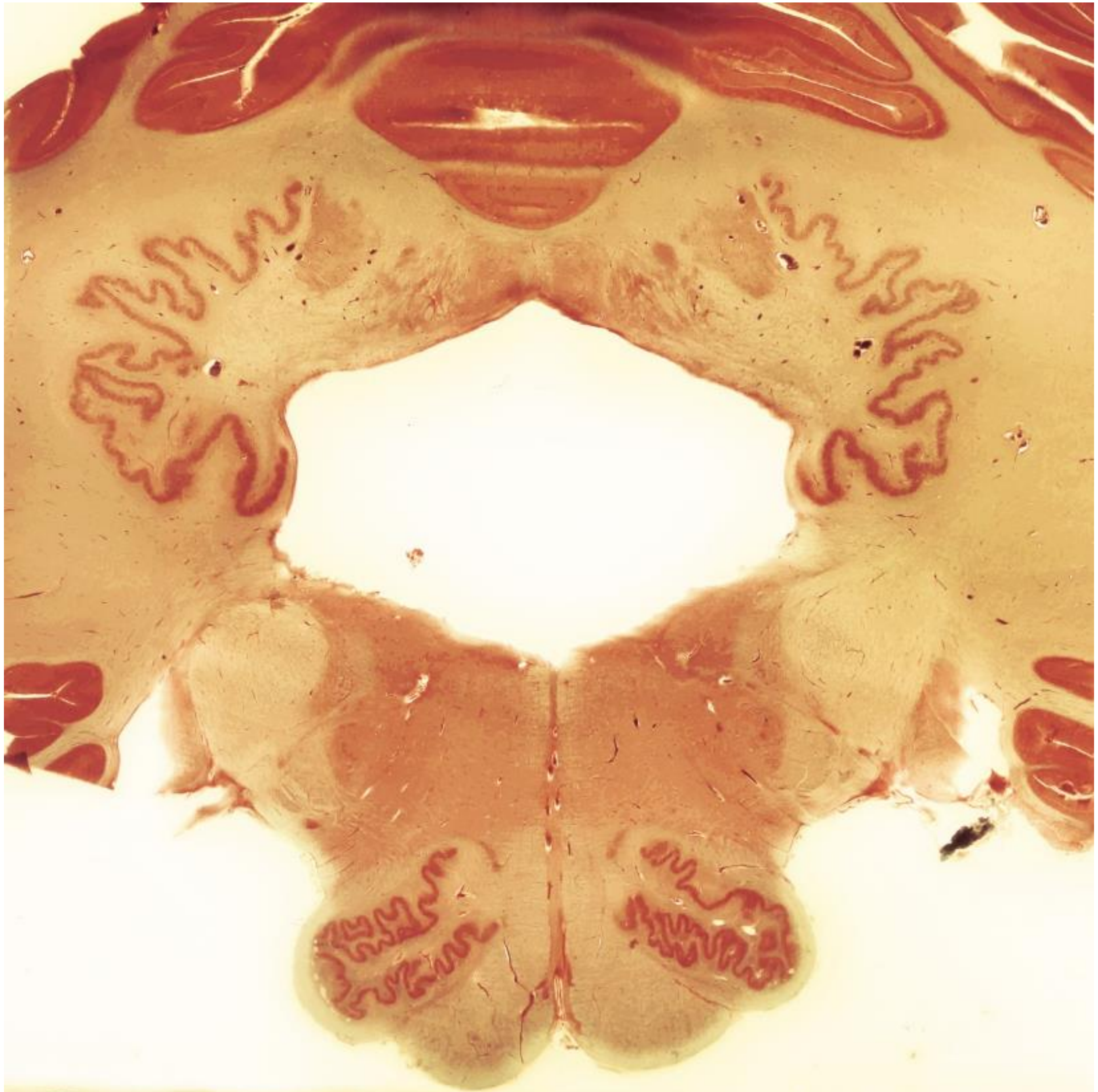


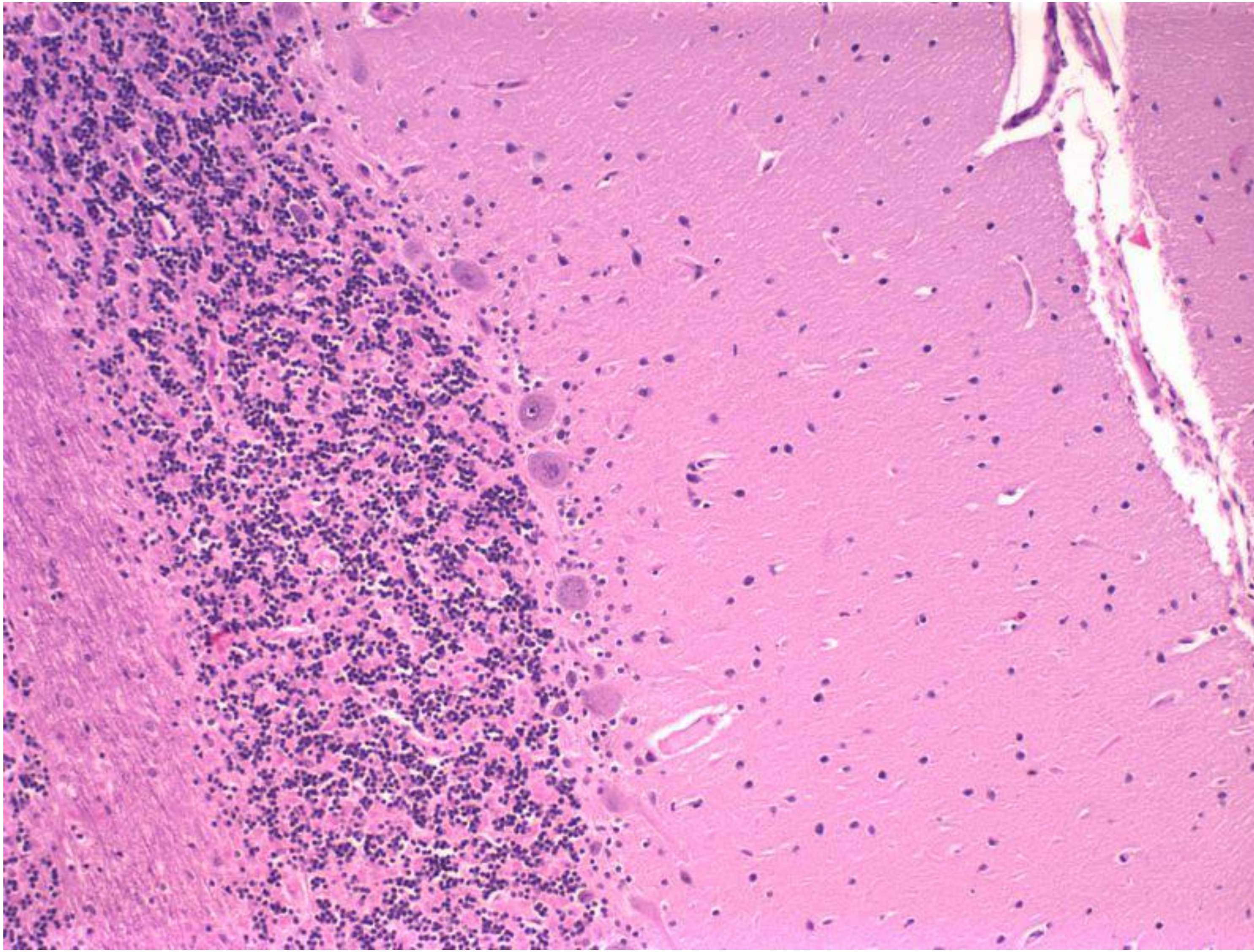
Dentatothalamic fibres
Cerebellorubral fibres
Dentatoreticular fibres
Anterior spinocerebellar tract on surface of superior cerebellar peduncle
Decussation of superior cerebellar penduncle
Upper pons
Medial lemniscus
Vermis of cerebellum
Dentate nucleus
Posterior spinocerebellar fibres in inferior cerebellar peduncle
Superior cerebellar peduncle
Middle cerebellar peduncle
Pons
Cuneocerebellar tract
Medulla
Accessory cuneate nucleus
Anterior spinocerebellar tract (axon of neurone II)
C4
Posterior spinocerebellar tract (axons of neurone II)
C8
Cell column neurone II
Nucleus dorsalis (Clarke's column)
L3
Golgi tendon organ (Quadriceps femoris)
Dorsal root ganglion neurones (neurone I)
S2
Golgi tendon organ (Hamstring muscles)

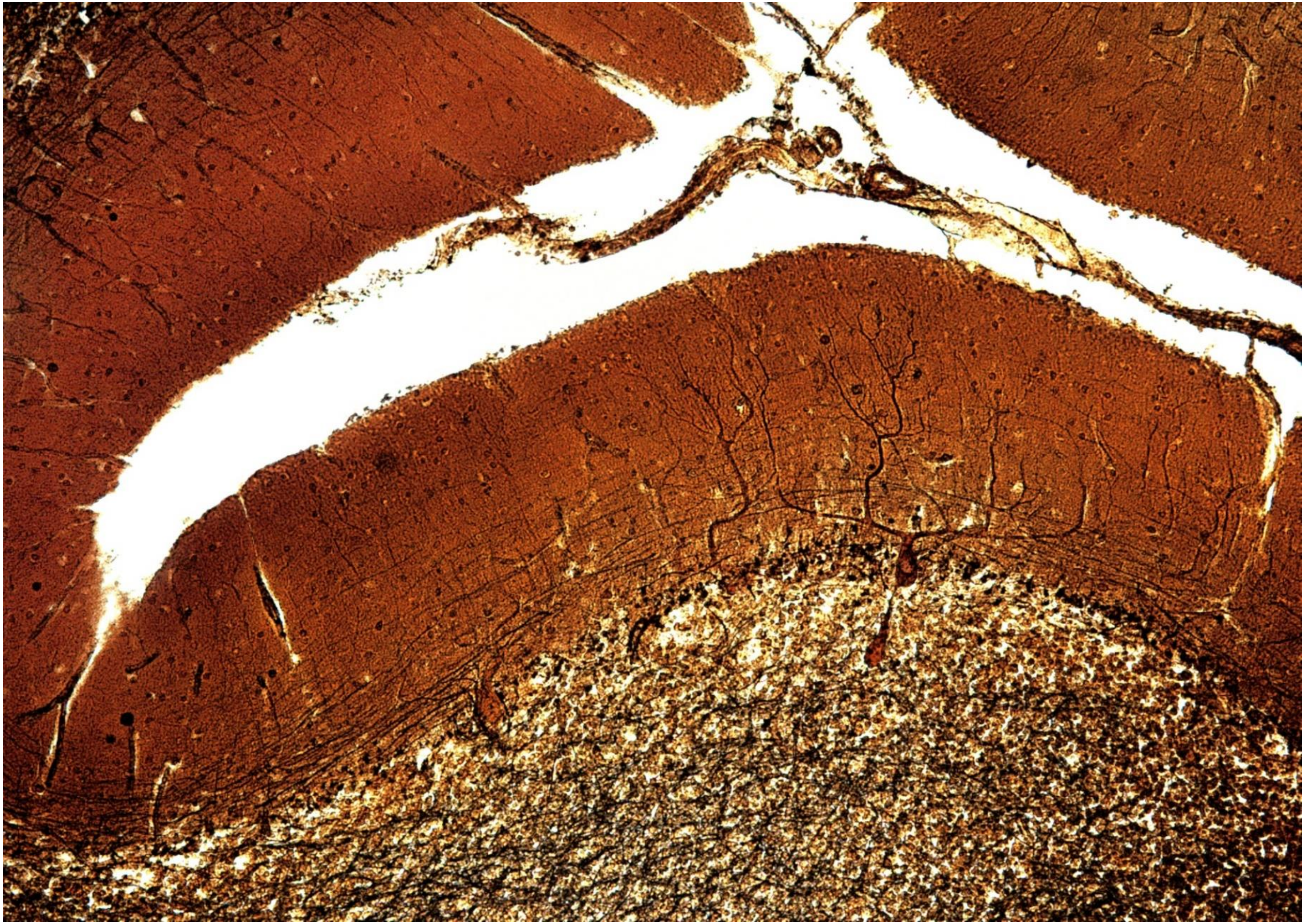
ESOPYRAMIDAL SYSTEM

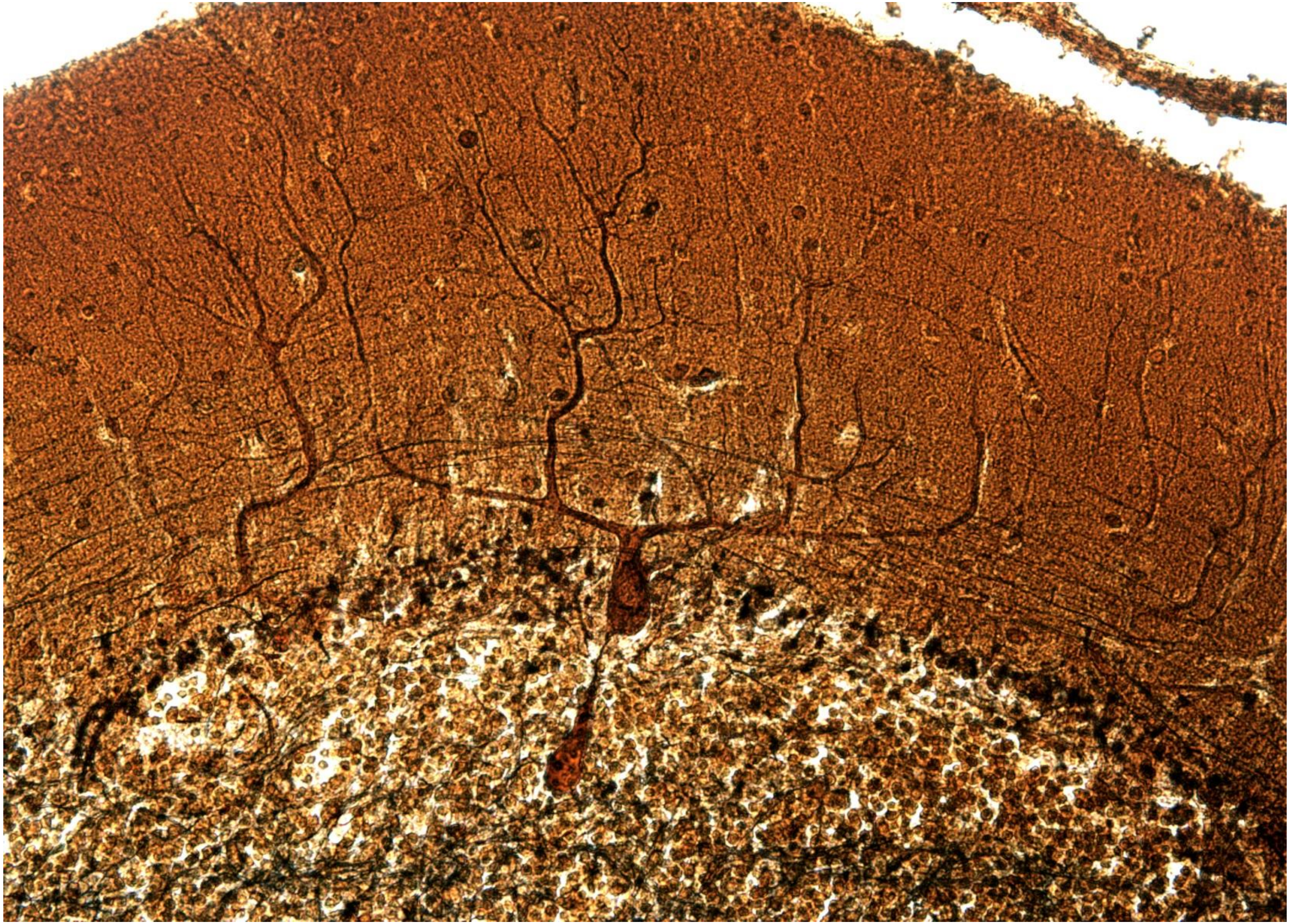


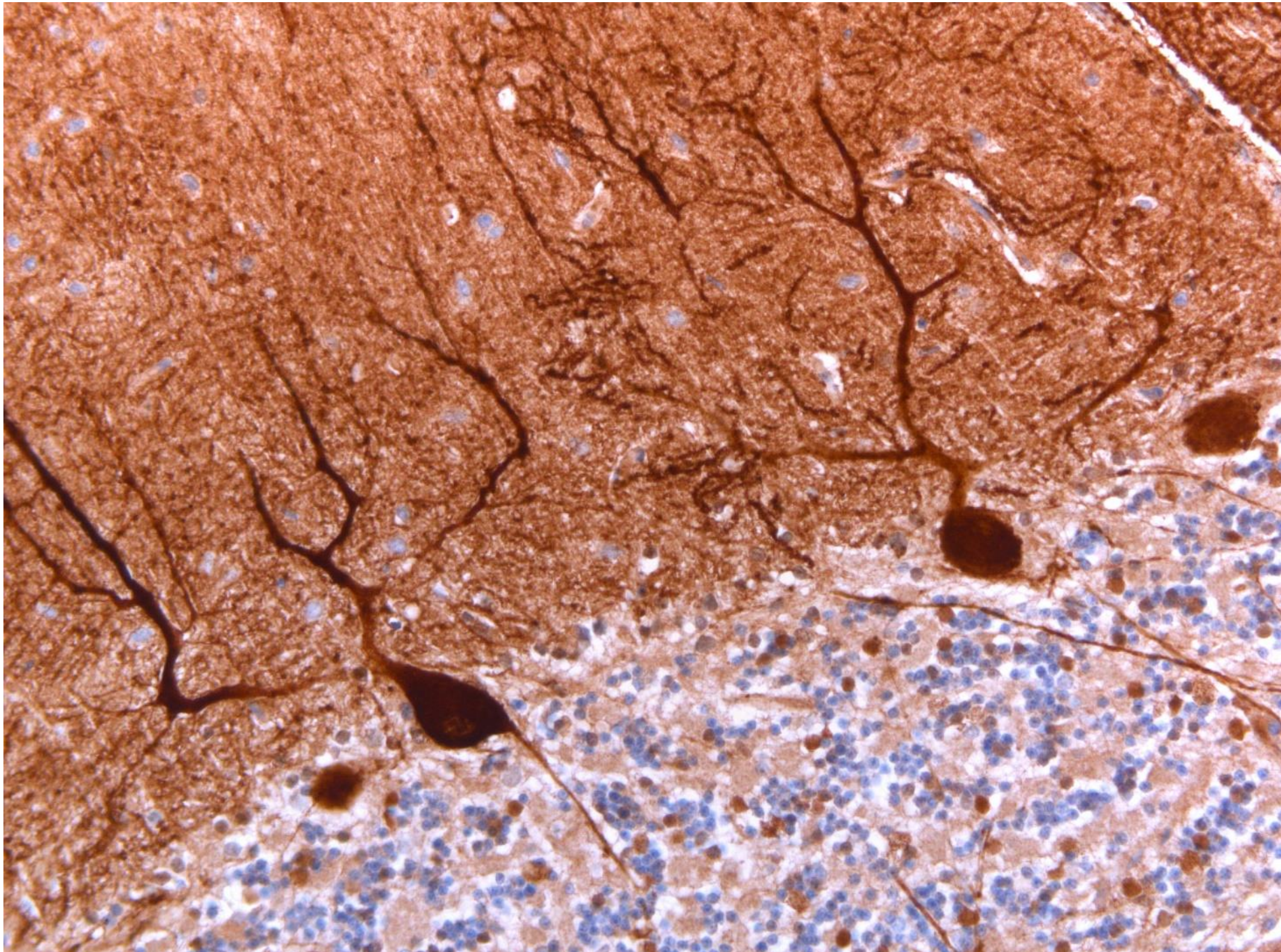


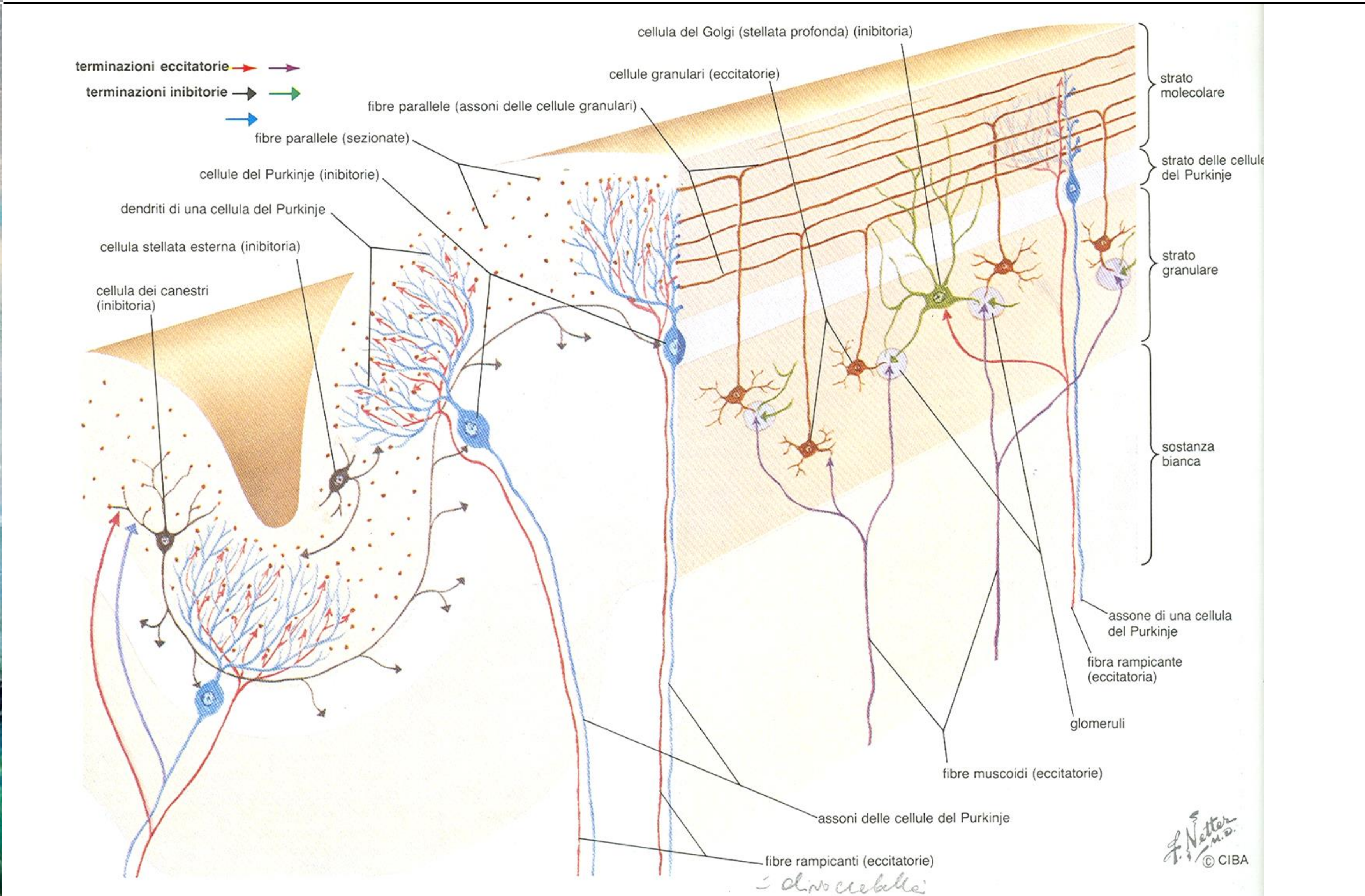












= olivo cerebellari

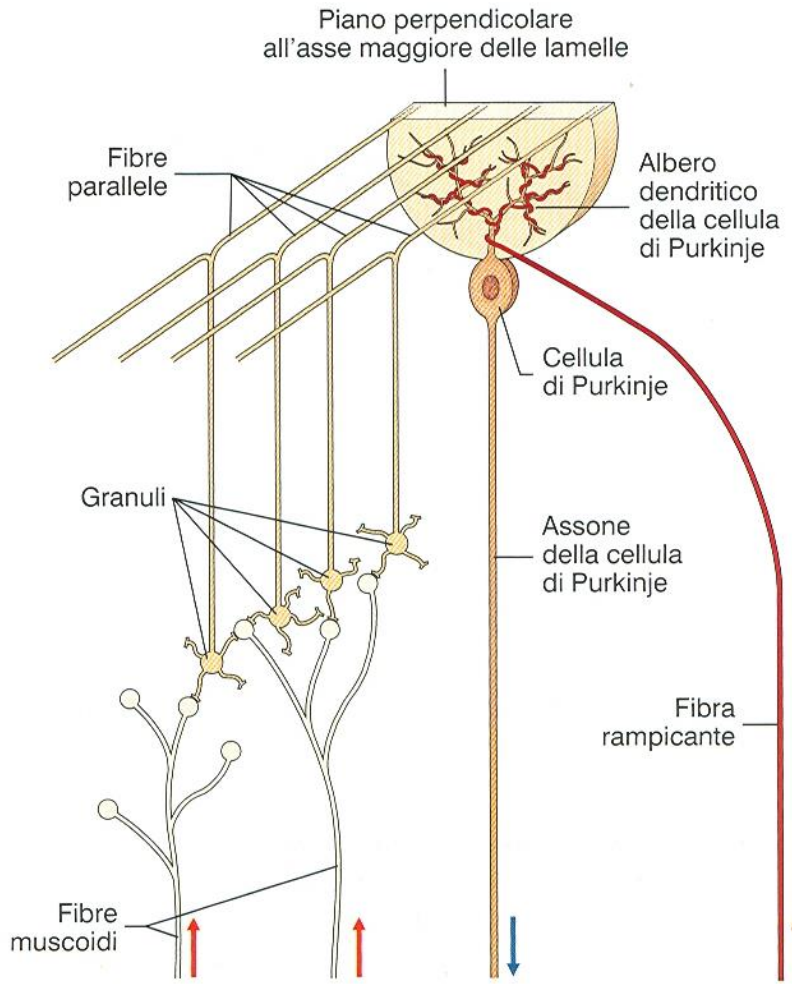


Figura R14.5-1 - Afferenze ed efferenze della corteccia cerebellare.

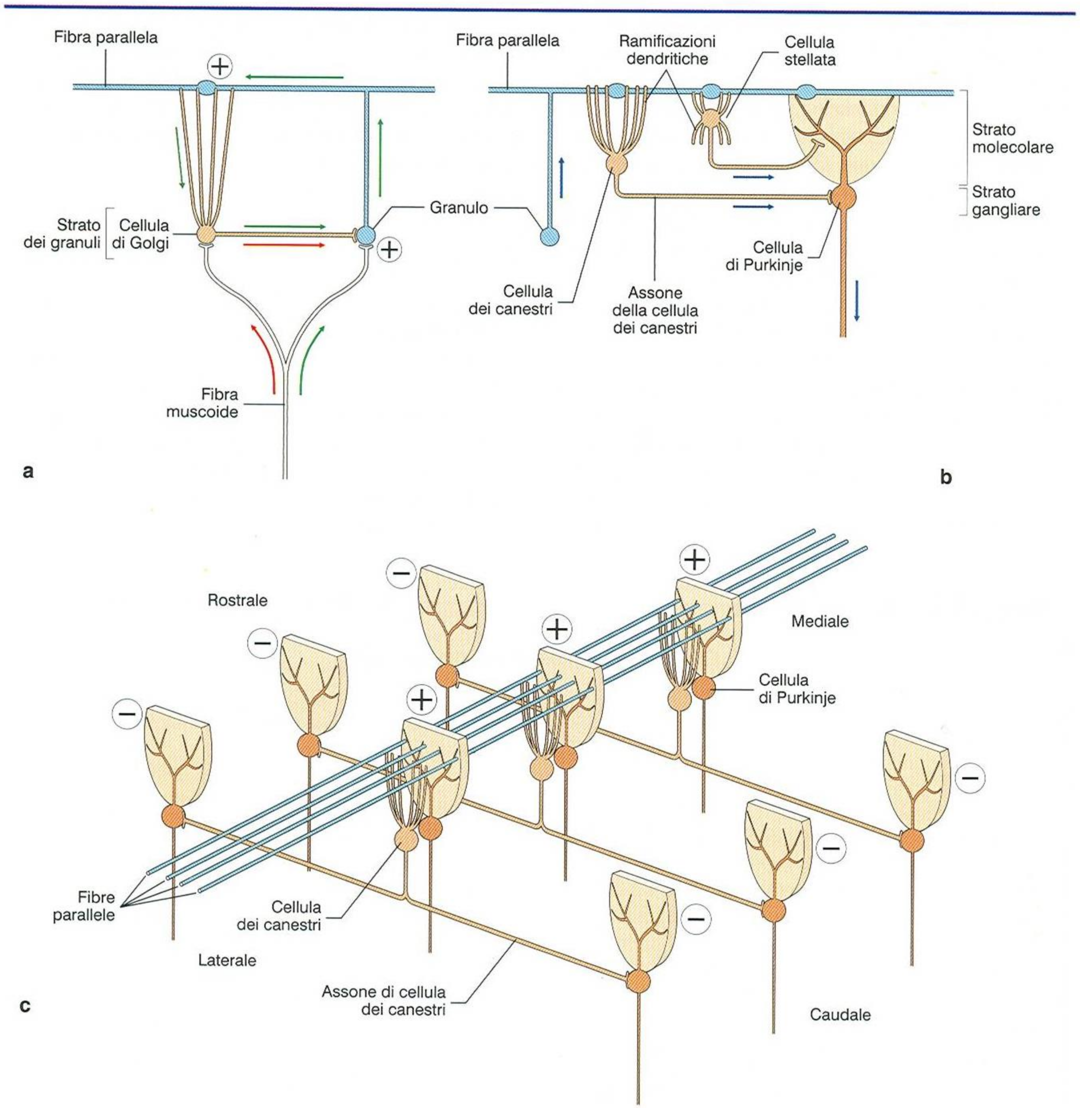


Figura R14.5-2 - Ruolo degli interneuroni inibitori nei circuiti corticali del cervelletto.

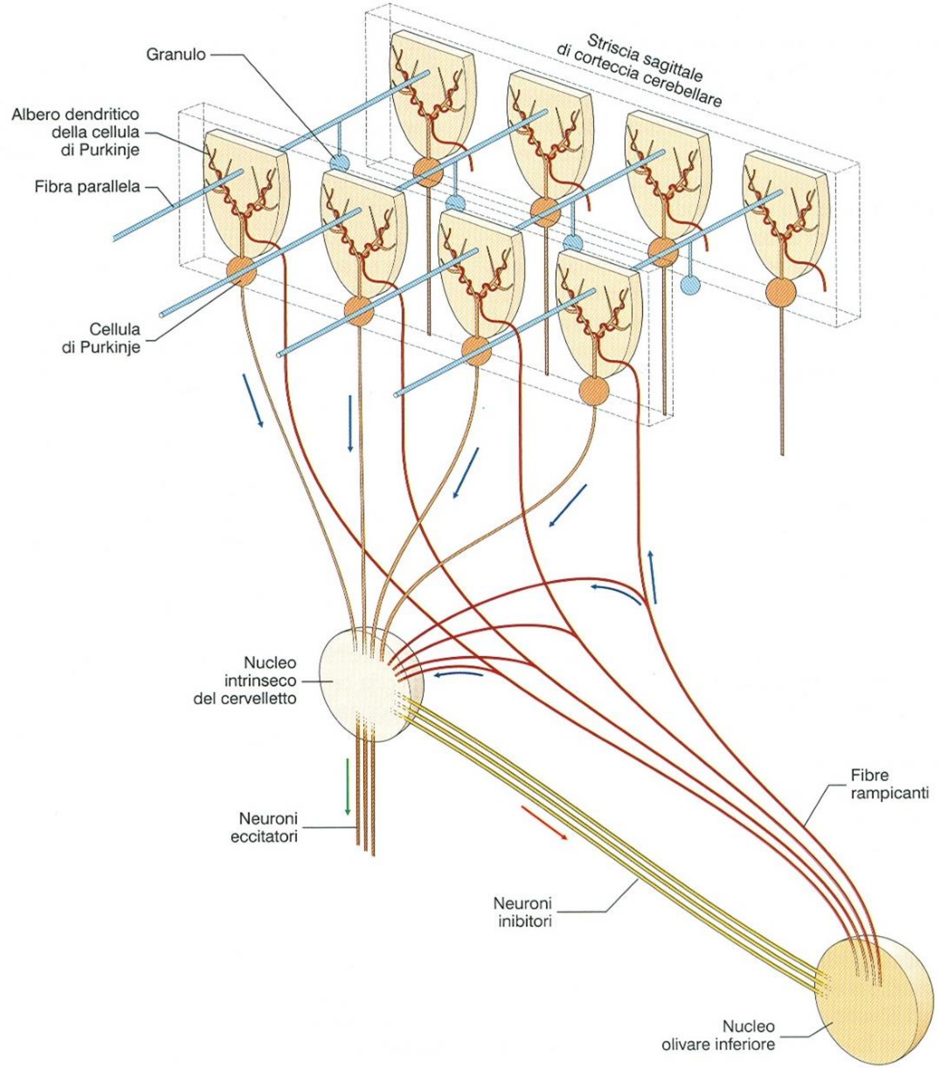
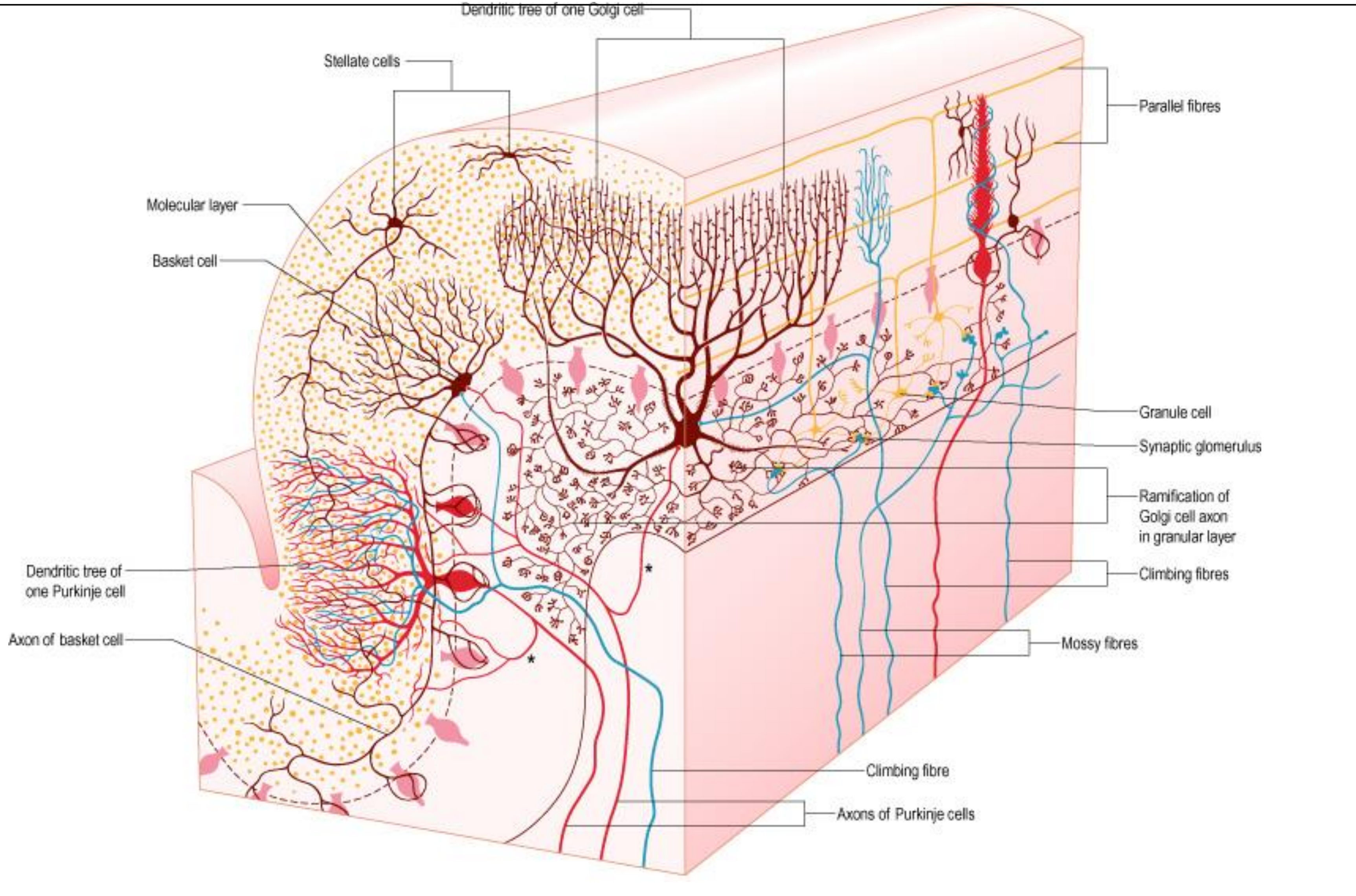
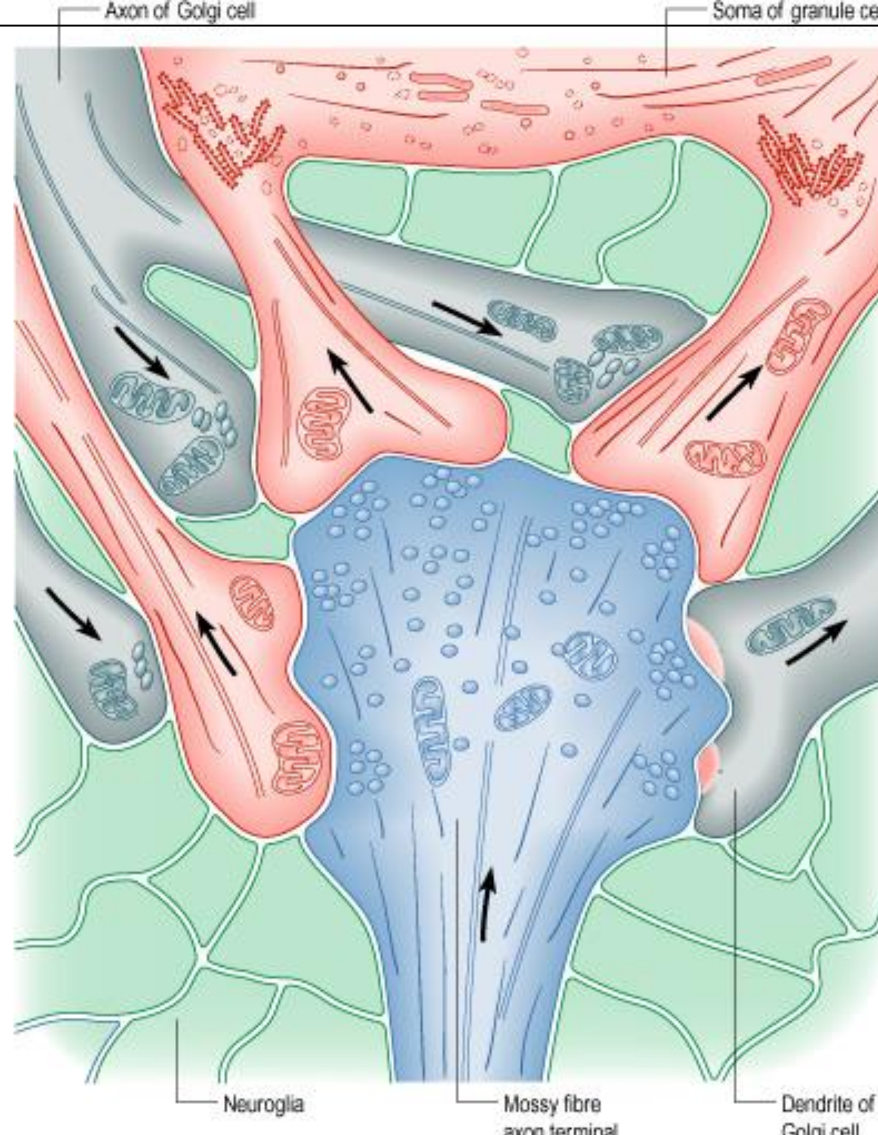
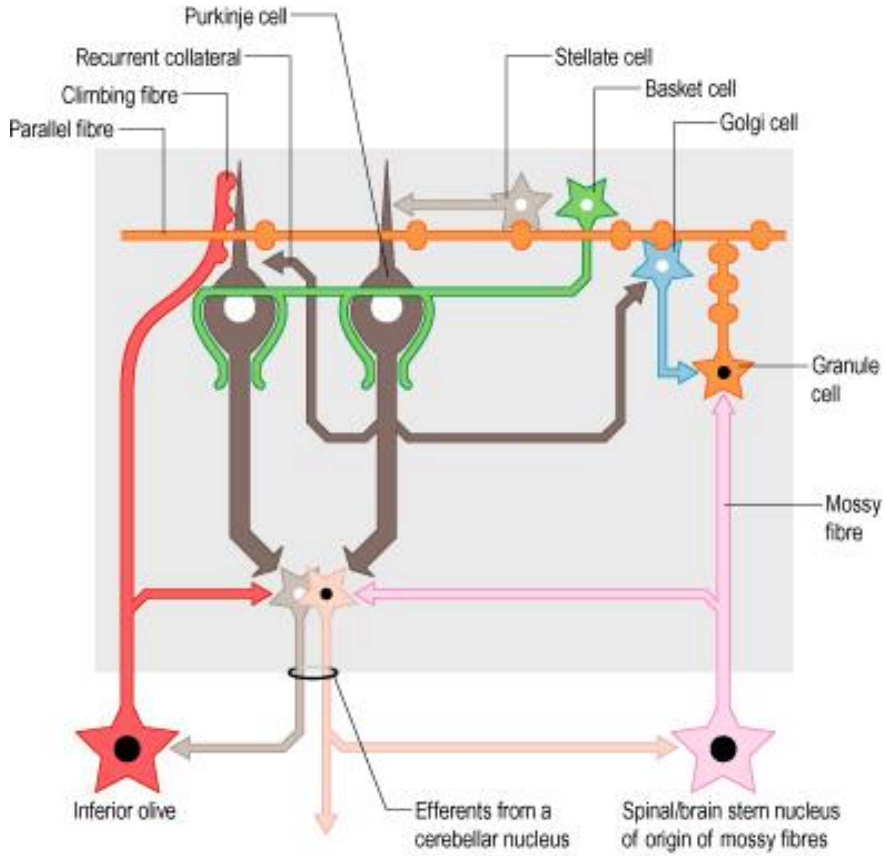


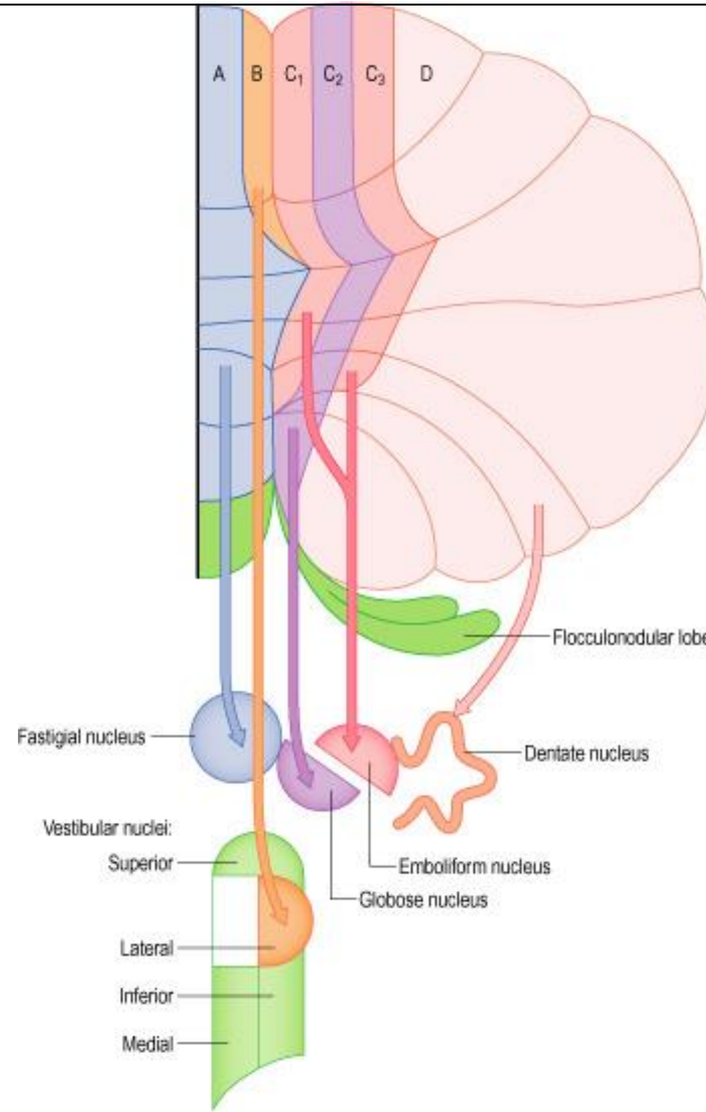
Figura R14.5-3 - Organizzazione di una microzona di cervelletto.

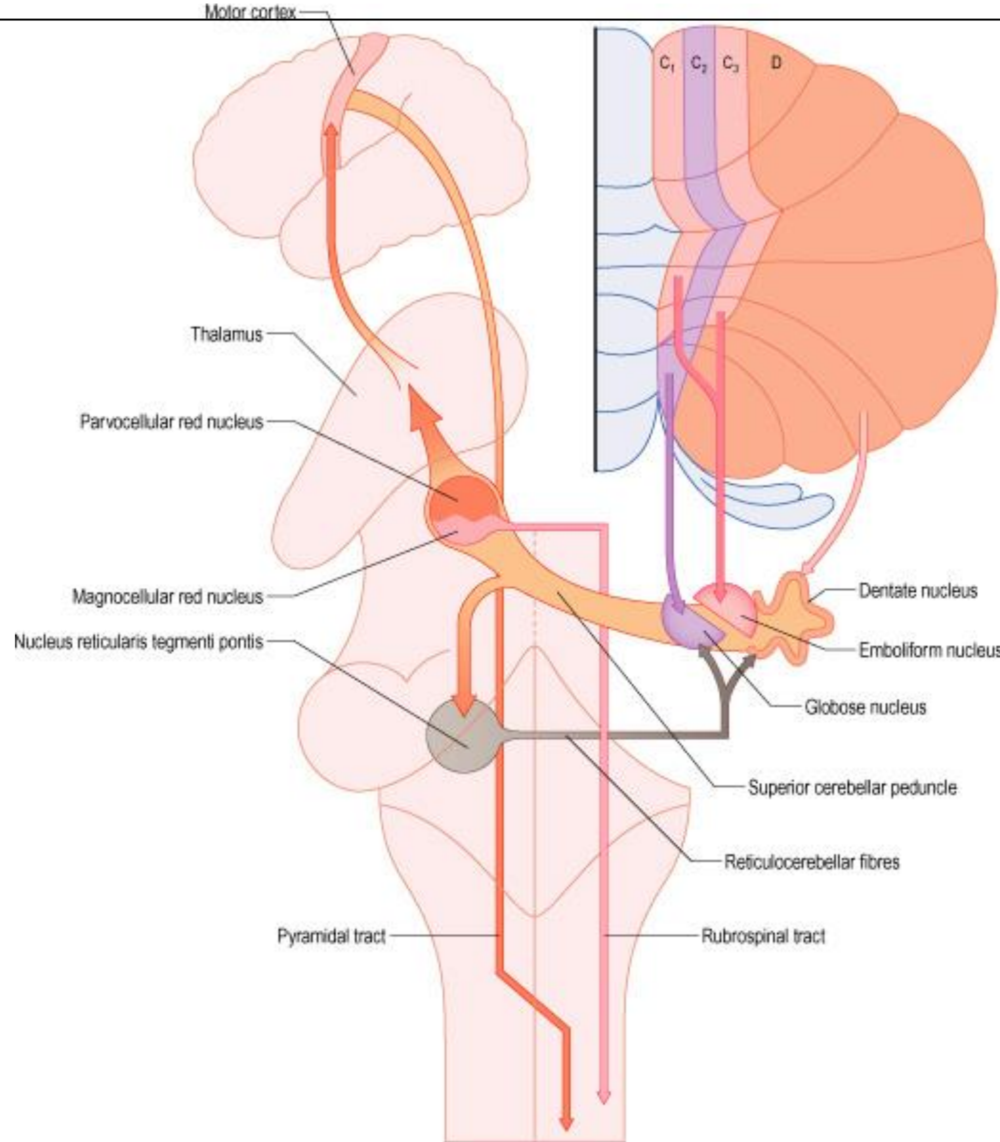


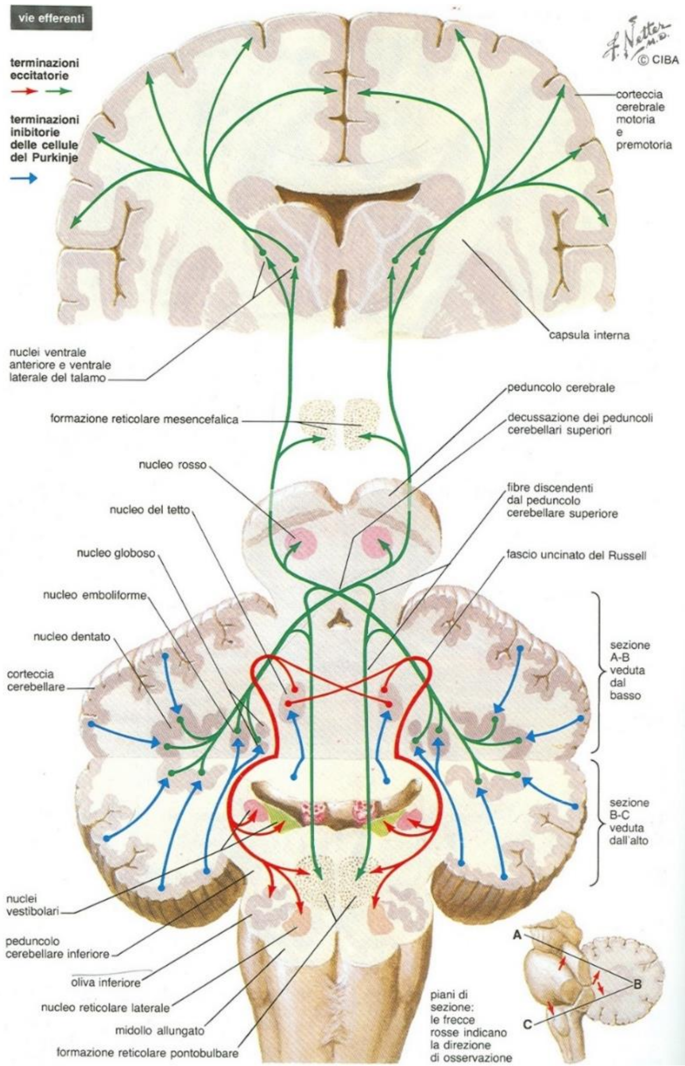
Dendritic tree of one Golgi cell
Stellate cells
Molecular layer
Basket cell
Dendritic tree of one Purkinje cell
Axon of basket cell
Parallel fibres
Granule cell
Synaptic glomerulus
Ramification of Golgi cell axon in granular layer
Climbing fibres
Mossy fibres
Climbing fibre
Axons of Purkinje cells


Axon of Golgi cell
Soma of granule cell
Neuroglia
Mossy fibre
axon terminal
Dendrite of
Golgi cell


Purkinje cell
Recurrent collateral
Climbing fibre
Parallel fibre
Stellate cell
Basket cell
Golgi cell
Granule cell
Mossy fibre
Inferior olive
Efferents from a cerebellar nucleus
Spinal/brain stem nucleus of origin of mossy fibres

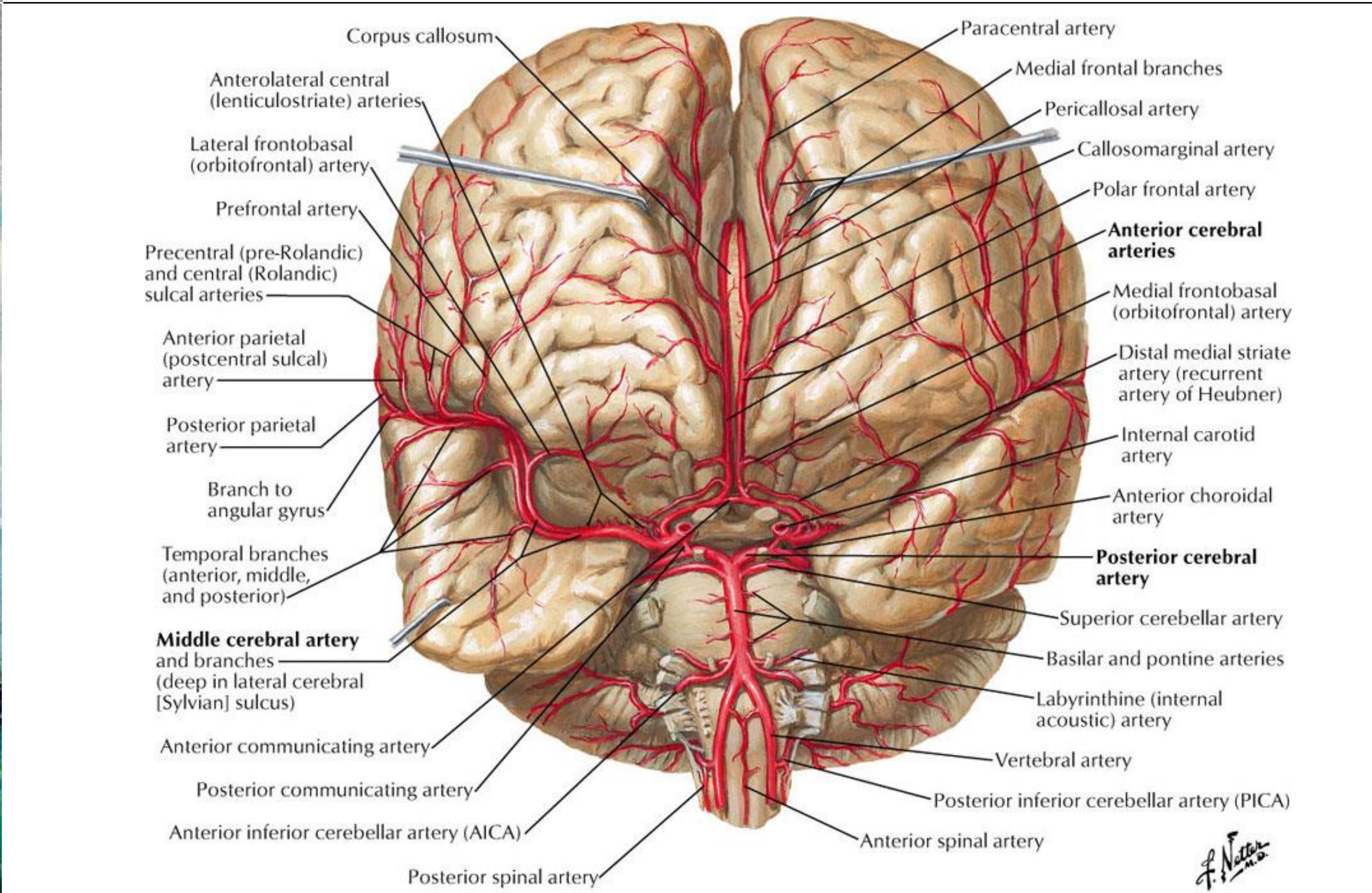

A
B
C_1
C_2
C_3
D
Flocculonodular lobe
Fastigial nucleus
Dentate nucleus
Vestibular nuclei:
Superior
Emboliform nucleus
Globose nucleus
Lateral
Inferior
Medial

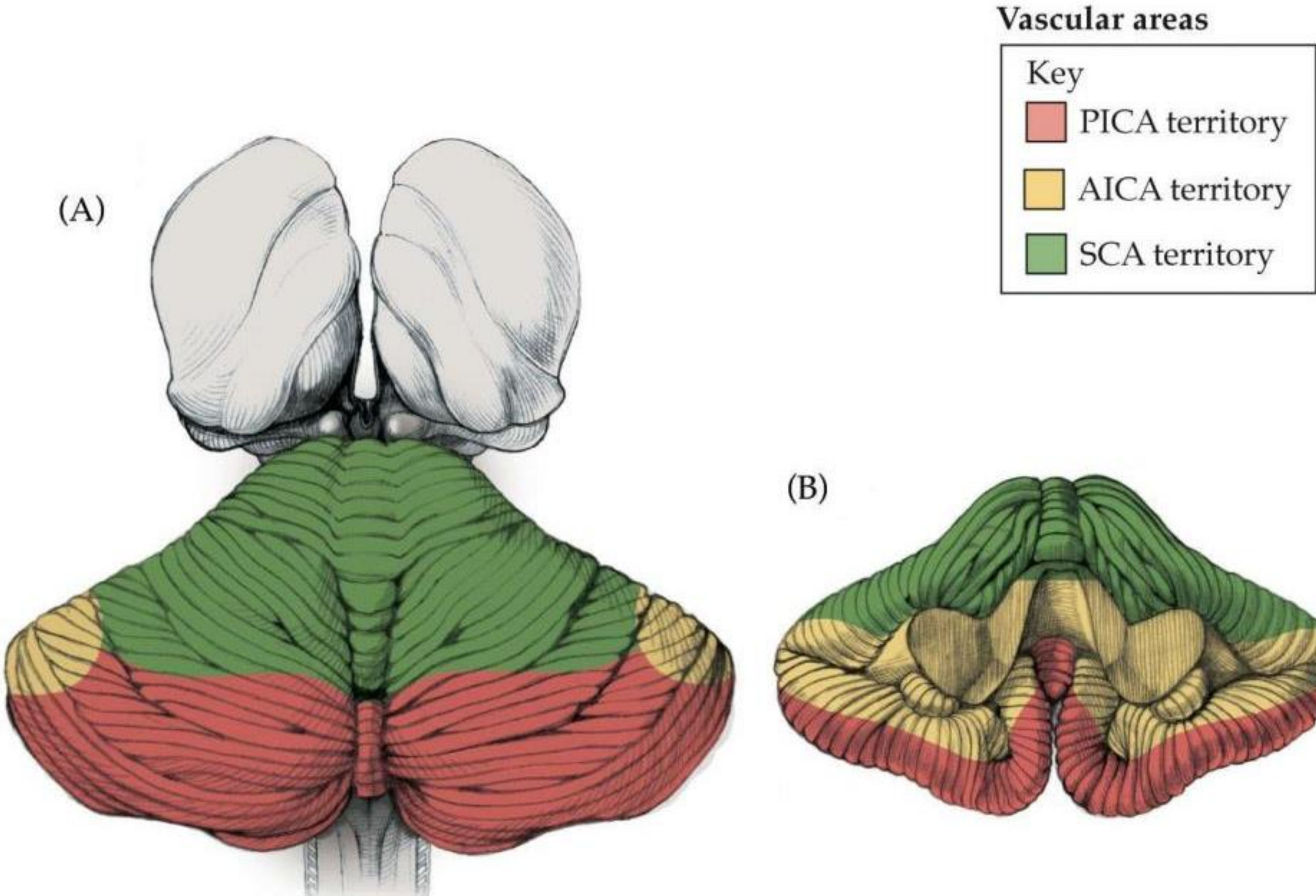

Motor cortex
C1
C2
C3
D
Thalamus
Parvocellular red nucleus
Magnocellular red nucleus
Nucleus reticularis tegmenti pontis
Dentate nucleus
Emboliform nucleus
Globose nucleus
Superior cerebellar peduncle
Reticulocerebellar fibres
Pyramidal tract
Rubrospinal tract


vie efferenti
terminazioni eccitatorie
terminazioni inibitorie delle cellule del Purkinje
© CIBA
corteccia cerebrale motoria e premotoria
capsula interna
nuclei ventrale anteriore e ventrale laterale del talamo
peduncolo cerebrale
formazione reticolare mesencefalica
decussazione dei peduncoli cerebellari superiori
nucleo rosso
nucleo del tetto
fibre discendenti dal peduncolo cerebellare superiore
nucleo globoso
fascio uncinato del Russell
nucleo emboliforme
nucleo dentato
corteccia cerebellare
sezione A-B veduta dal basso
sezione B-C veduta dall'alto
nuclei vestibolari
peduncolo cerebellare inferiore
oliva inferiore
nucleo reticolare laterale
midollo allungato
formazione reticolare pontobulbare
piani di sezione: le frecce rosse indicano la direzione di osservazione
A
B
C

CLINICAL NEUROANATOMY

CEREBELLUM


Corpus callosum
Anterolateral central (lenticulostriate) arteries
Lateral frontobasal (orbitofrontal) artery
Prefrontal artery
Precentral (pre-Rolandic) and central (Rolandic) sulcal arteries
Anterior parietal (postcentral sulcal) artery
Posterior parietal artery
Branch to angular gyrus
Temporal branches (anterior, middle, and posterior)
Middle cerebral artery and branches (deep in lateral cerebral [Sylvian] sulcus)
Anterior communicating artery
Posterior communicating artery
Anterior inferior cerebellar artery (AICA)
Posterior spinal artery
Paracentral artery
Medial frontal branches
Pericallosal artery
Callosomarginal artery
Polar frontal artery
Anterior cerebral arteries
Medial frontobasal (orbitofrontal) artery
Distal medial striate artery (recurrent artery of Heubner)
Internal carotid artery
Anterior choroidal artery
Posterior cerebral artery
Superior cerebellar artery
Basilar and pontine arteries
Labyrinthine (internal acoustic) artery
Vertebral artery
Posterior inferior cerebellar artery (PICA)
Anterior spinal artery
F. Netter M.D.


Vascular areas
Key
PICA territory
AICA territory
SCA territory
(A)
(B)

Clinical Aspects - Cerebellar Lesions

- Ataxia -> lack of coordination, dysrhytmia and dysmetria
- Unsteady Gait
- Dysdiadochokinesia
- Vertigo
- Nausea
- Horizontal Nystagmus
- Headache

ATAXIA IS ALWAYS HOMOLATERAL!

Truncal Ataxia

- **Lesions of the Cerebellar Vermis**

Unsteady gait (Drunk-Like walking pattern)

Appendicular (Limb) Ataxia

- **Lesions of the Cerebellar Hemispheres (intermediate and lateral)**

Ataxic movements of the limbs, depending on the localization of the lesion.

Evaluating **Coordination and Gait**

APPENDICULAR COORDINATION

- Finger-nose-finger test (check also for overshoot!)
- Heel-shin test

ROMBERG TEST (Stability)

GAIT EXAMINATION

- Check stance, posture, stability, trajectory, circumduction
- Tandem gait , Forced gait


ATAXIA


ATAXIA

CLINICAL CASE 1

70Y M JANITOR w Hypertension

The patient went to work at 7.00AM and had sudden onset of nausea, vomiting and unsteadiness. In the ER, neurological examination revealed mild slurred speech, slowed tongue movements, dysmetria on finger to nose test on the left, dysmetria on heel to shin test on the left, left dysdiadochokinesia. Romberg test evidences side falls to the left w eyes open; unable to stand. No other signs.

Where is the site of the lesion?

What's the likely diagnosis?

CLINICAL CASE 2

76Y M w History of cigarette smoking habit

Patient developed progressive walking difficulty over the course of 1 month. Reports feeling “woozy” when standing up with a “drunk-like” gait. Frequent loss of balance, with staggering and unsteadiness. Frequent mild headaches with progressive worsening. Neurological exam reveals wide-based unsteady gait with tendency to fall to the left, especially in tandem walking. No ataxia in finger-to-nose or heel-to-shin test. Rapidly alternating movements were normal. No history of alcohol intake.

Where is the site of the lesion?

What’s the likely diagnosis?

CLINICAL CASE 3

13Y M w no prior medical history

Patient is referred to the pediatrician for 2 month progressive left occipital headaches, nausea, slurred speech and unsteadiness. Reported symptoms began with headaches in the left occipital region, sometimes accompanied with nausea and vomiting. Difficulties concentrating and learning. Increasing gait instability and mildly slurred speech.

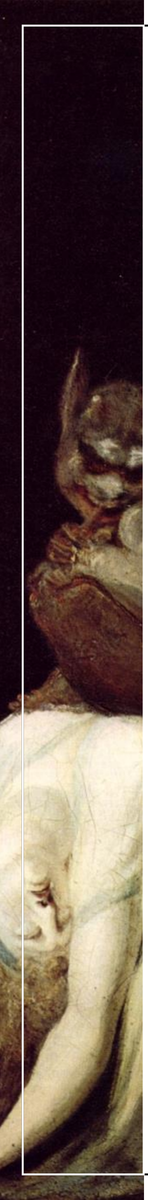
Neurological examination reveals mild bilateral papilledema, horizontal and vertical nystagmus, worse upwards. Speech slurred with an irregular rate. Marked dysmetria on finger-to-nose testing, dysdiadochokinesia worse on the left, heel-to-shin movements are ataxic on the left. Wide-based gait, unsteady, staggering to the left. Unable to perform tandem test. Romberg does not worsen already present instability.

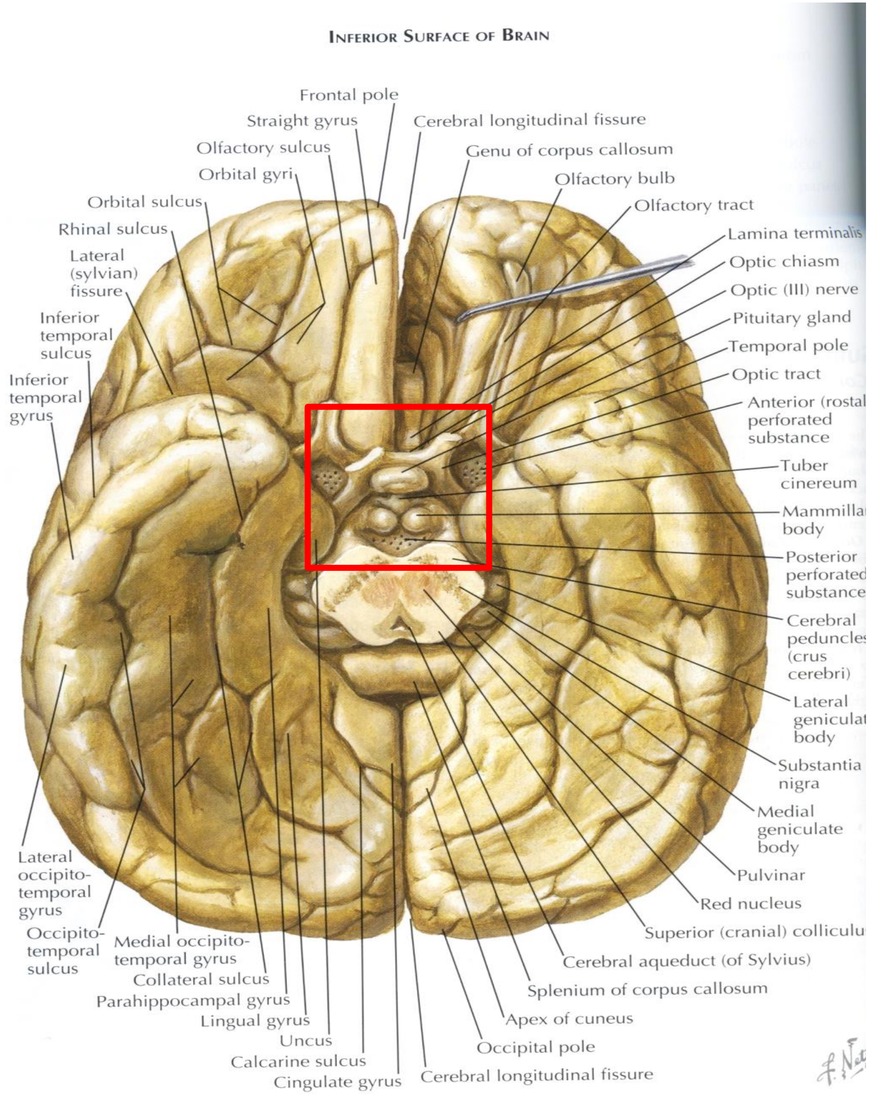
Where is the site of the lesion?

What’s the likely diagnosis?

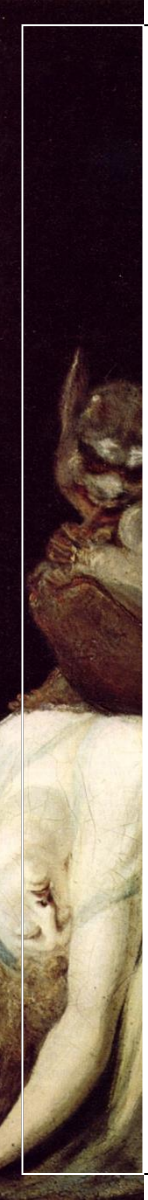
The Diencephalon

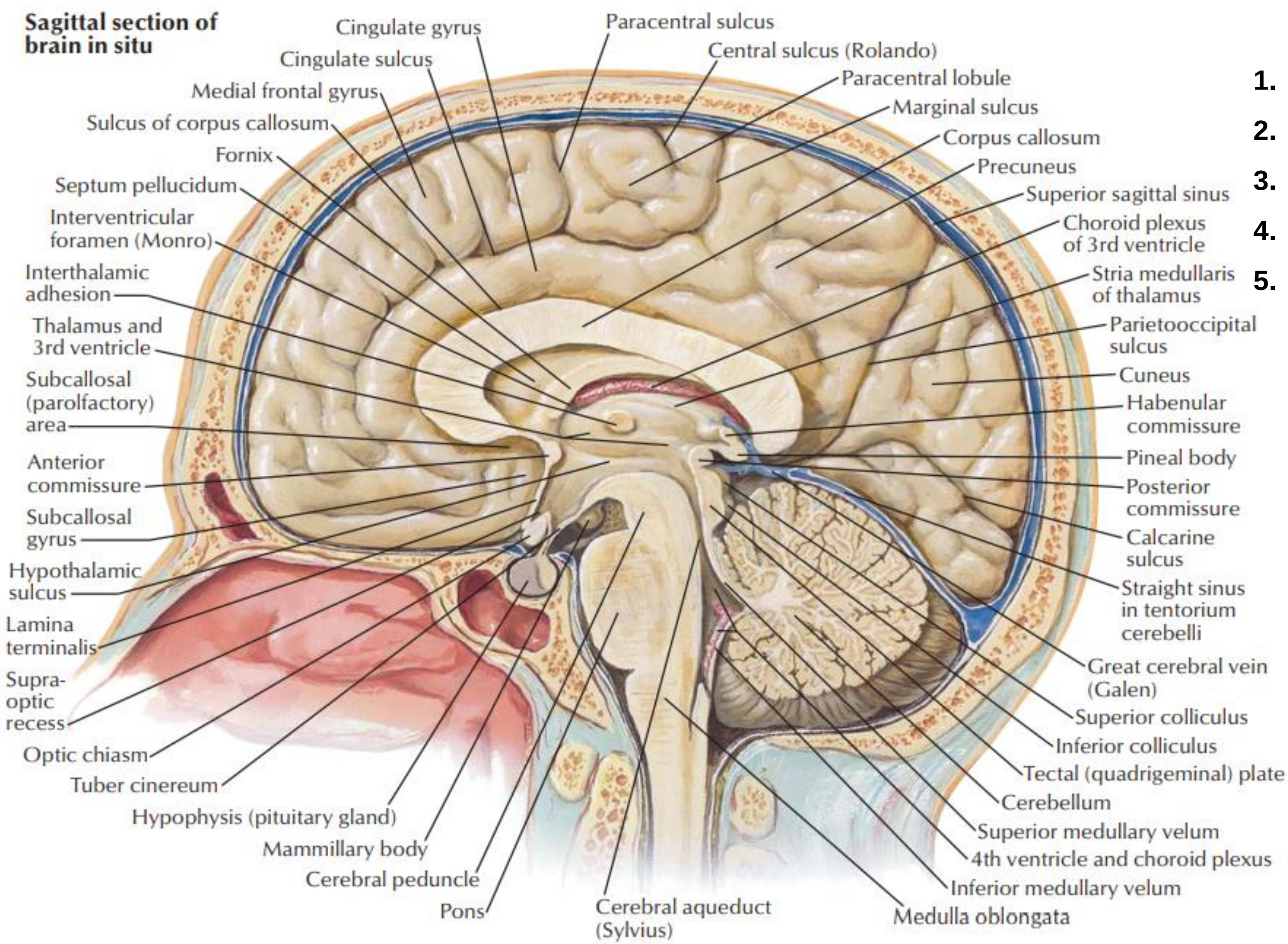
H. Fuseli – The Nightmare





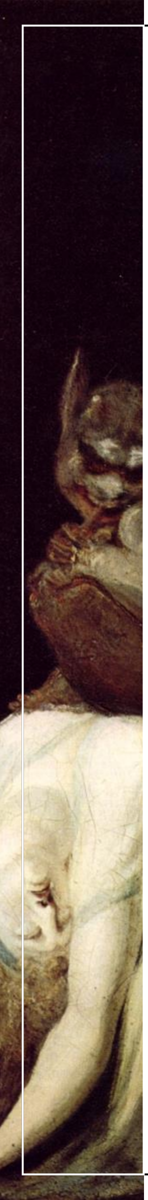
Diencephalon – External Surface

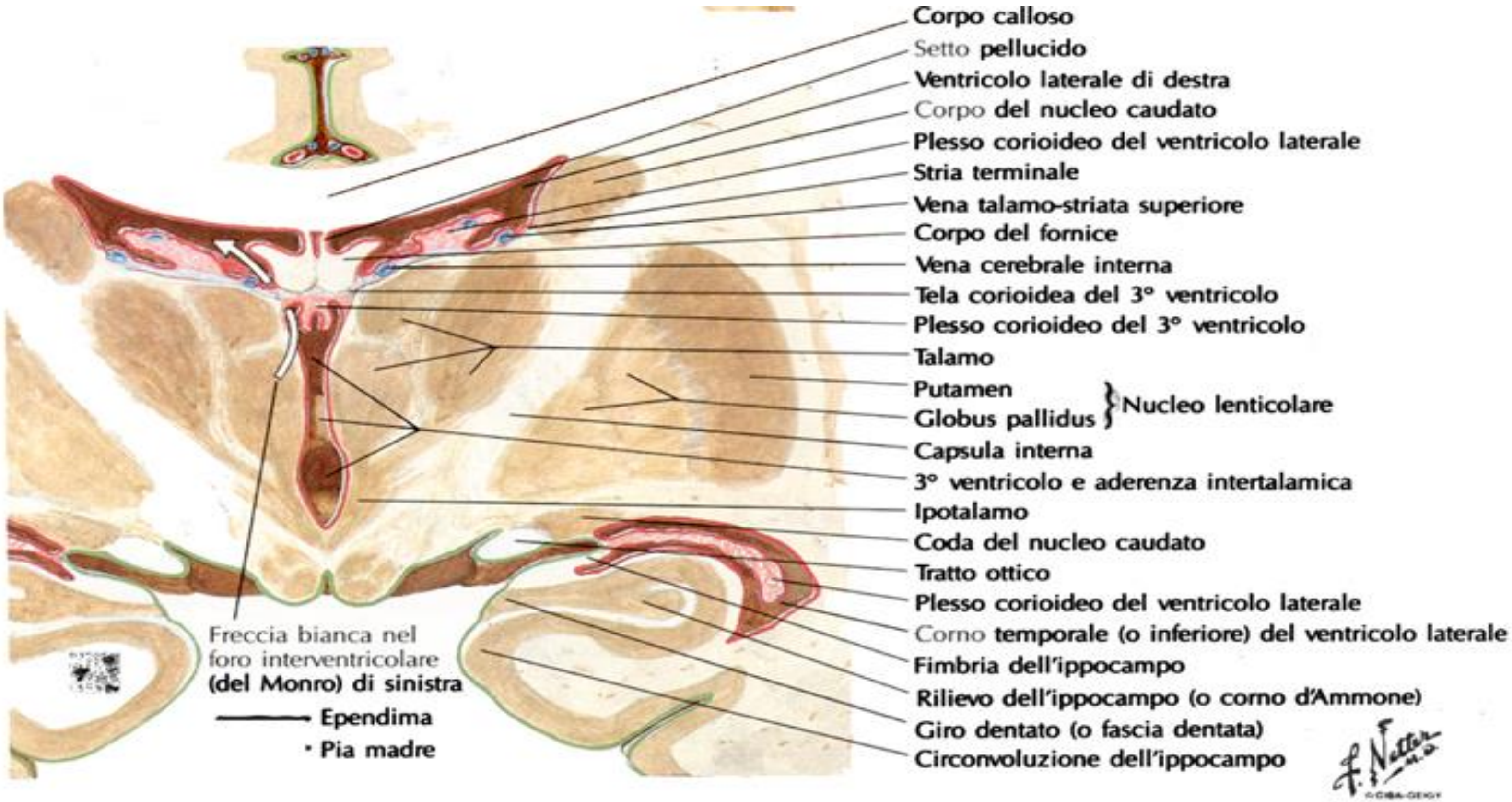




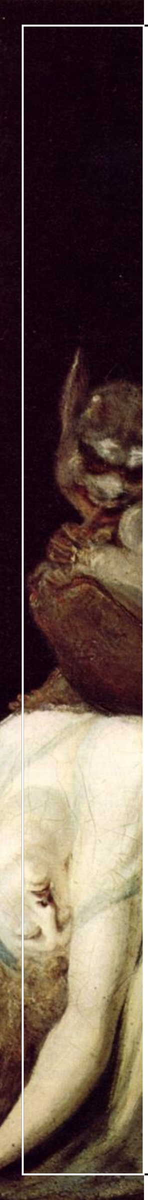
Diencephalon:

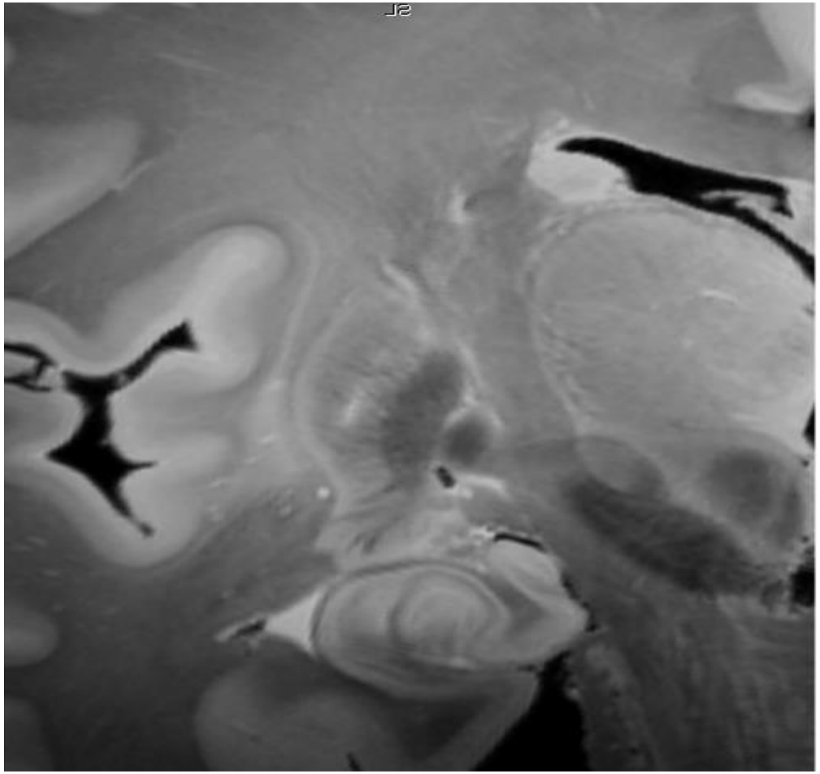
1. **Thalamus**
2. **Subthalamus**
3. **Hypothalamus**
4. **Epithalamus**
5. **Metathalamus**

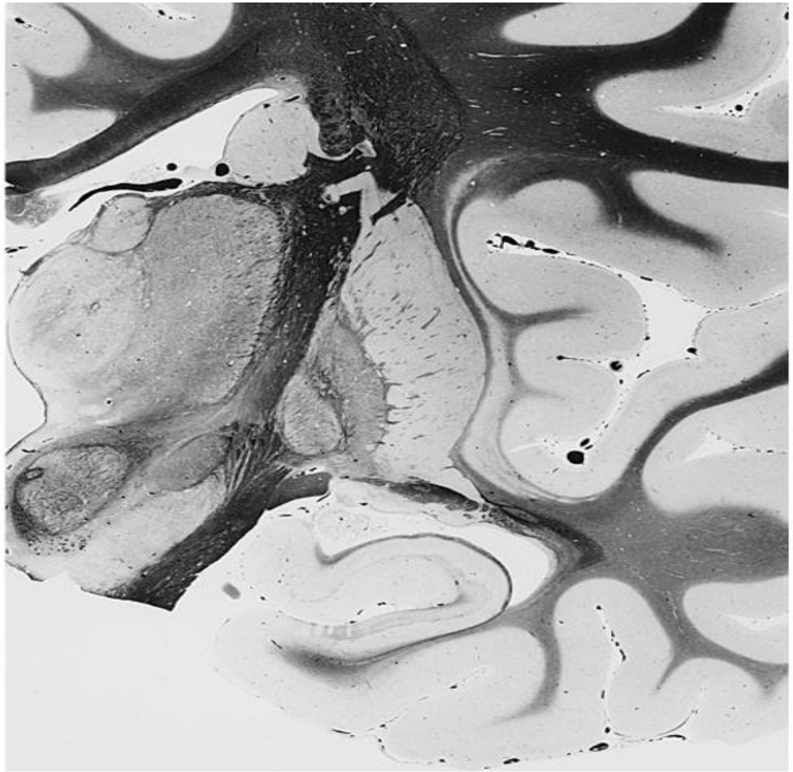


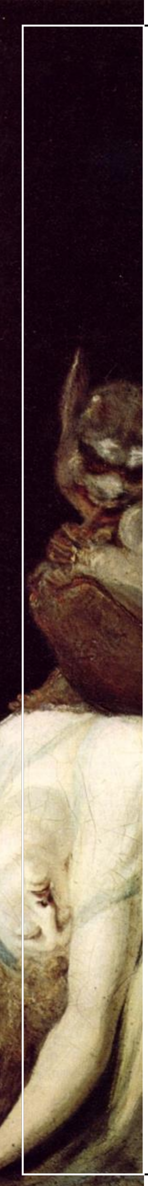


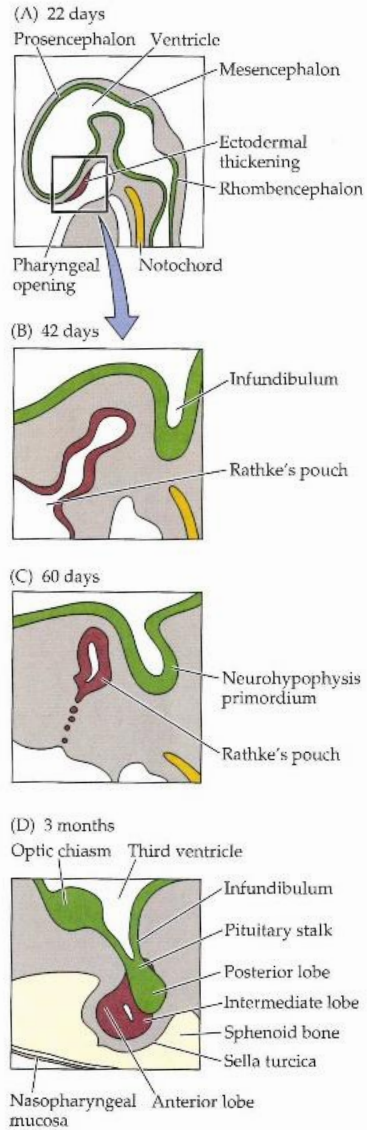
Sezione frontale del cervello (veduta posteriore)

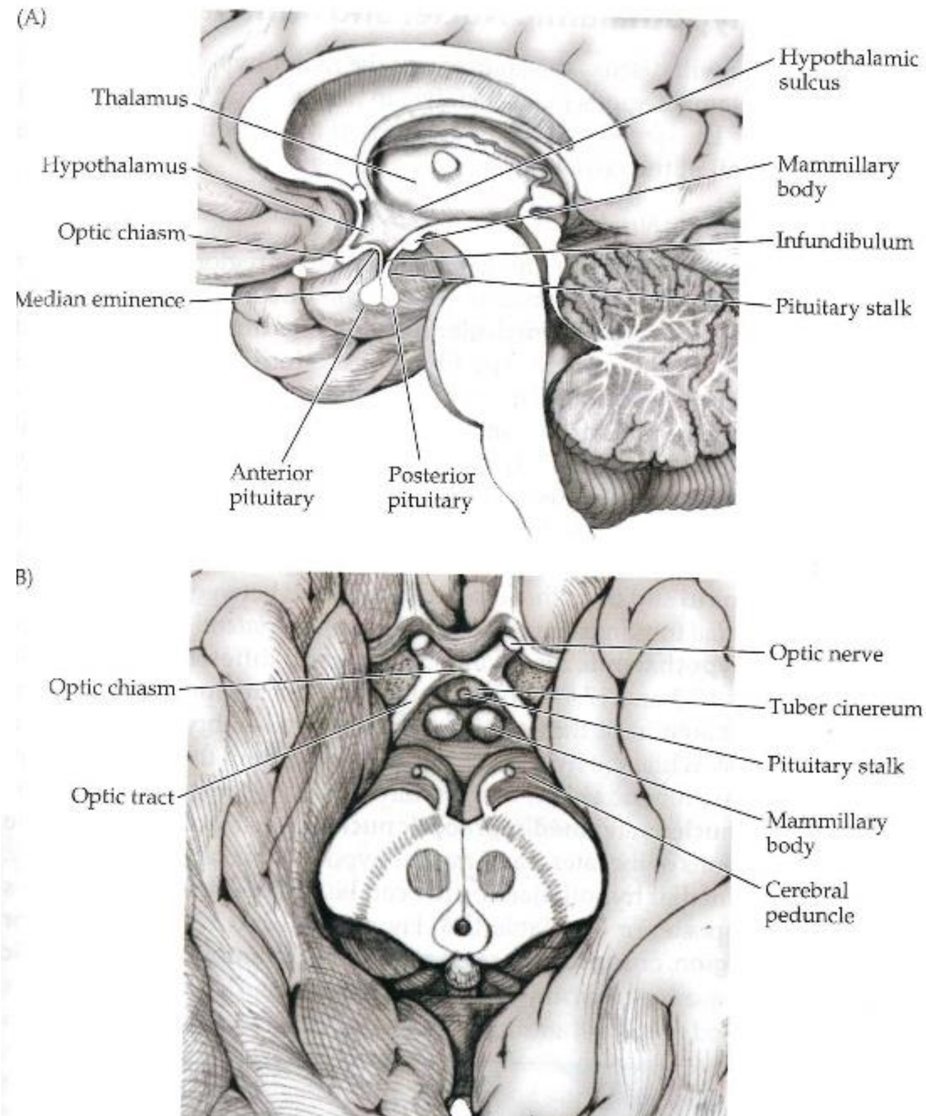


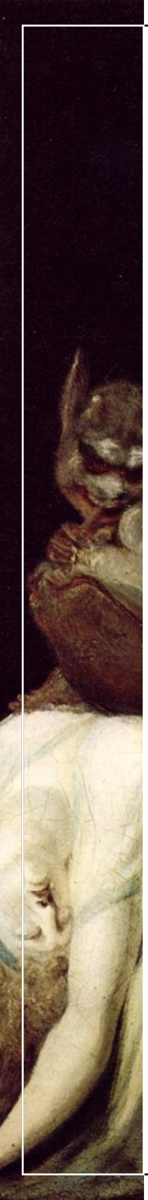


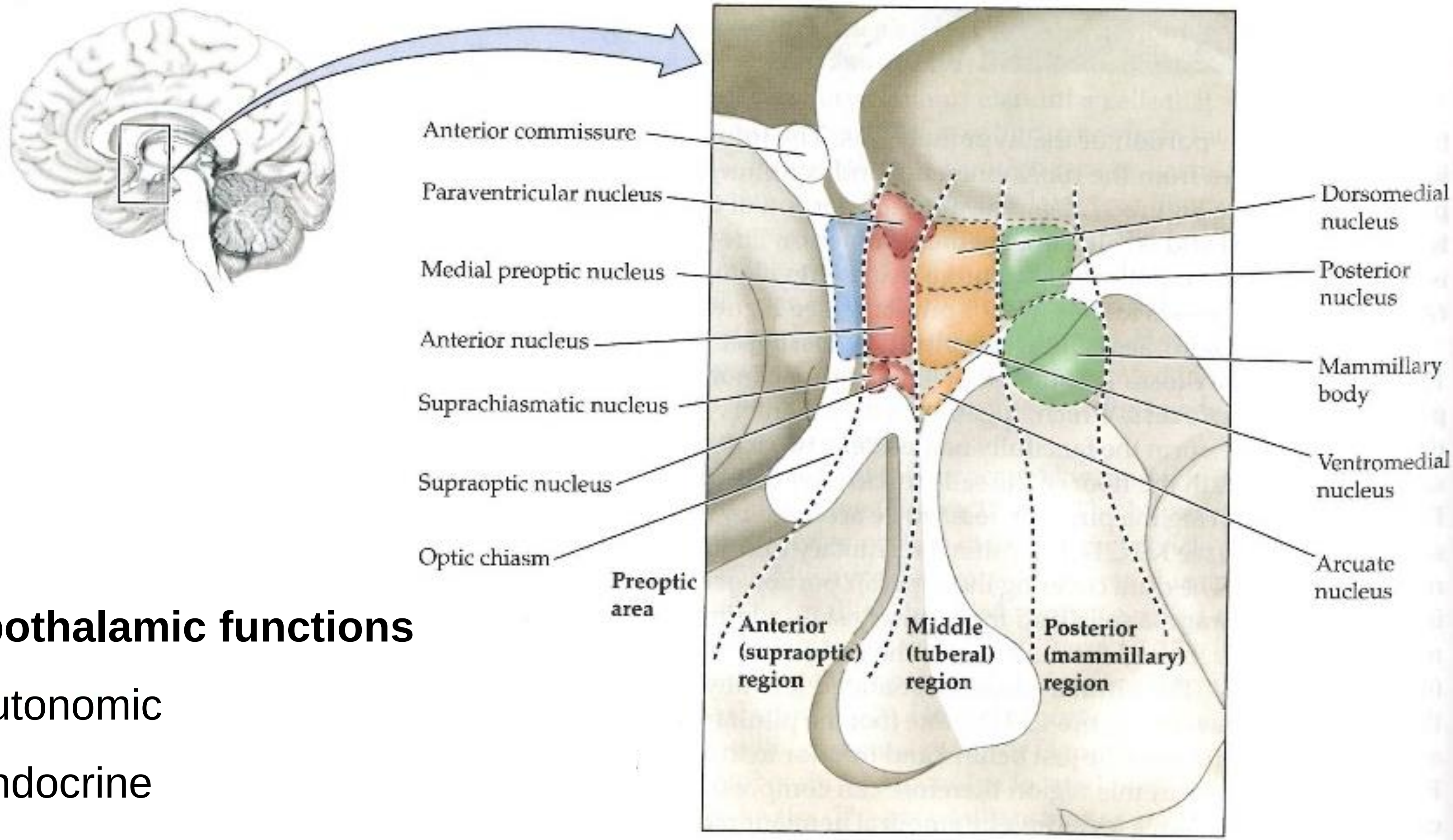





(A) 22 days
Prosencephalon
Ventricle
Mesencephalon
Ectodermal thickening
Rhombencephalon
Pharyngeal opening
Notochord
(B) 42 days
Infundibulum
Rathke's pouch
(C) 60 days
Neurohypophysis primordium
Rathke's pouch
(D) 3 months
Optic chiasm
Third ventricle
Infundibulum
Pituitary stalk
Posterior lobe
Intermediate lobe
Sphenoid bone
Sella turcica
Nasopharyngeal mucosa
Anterior lobe

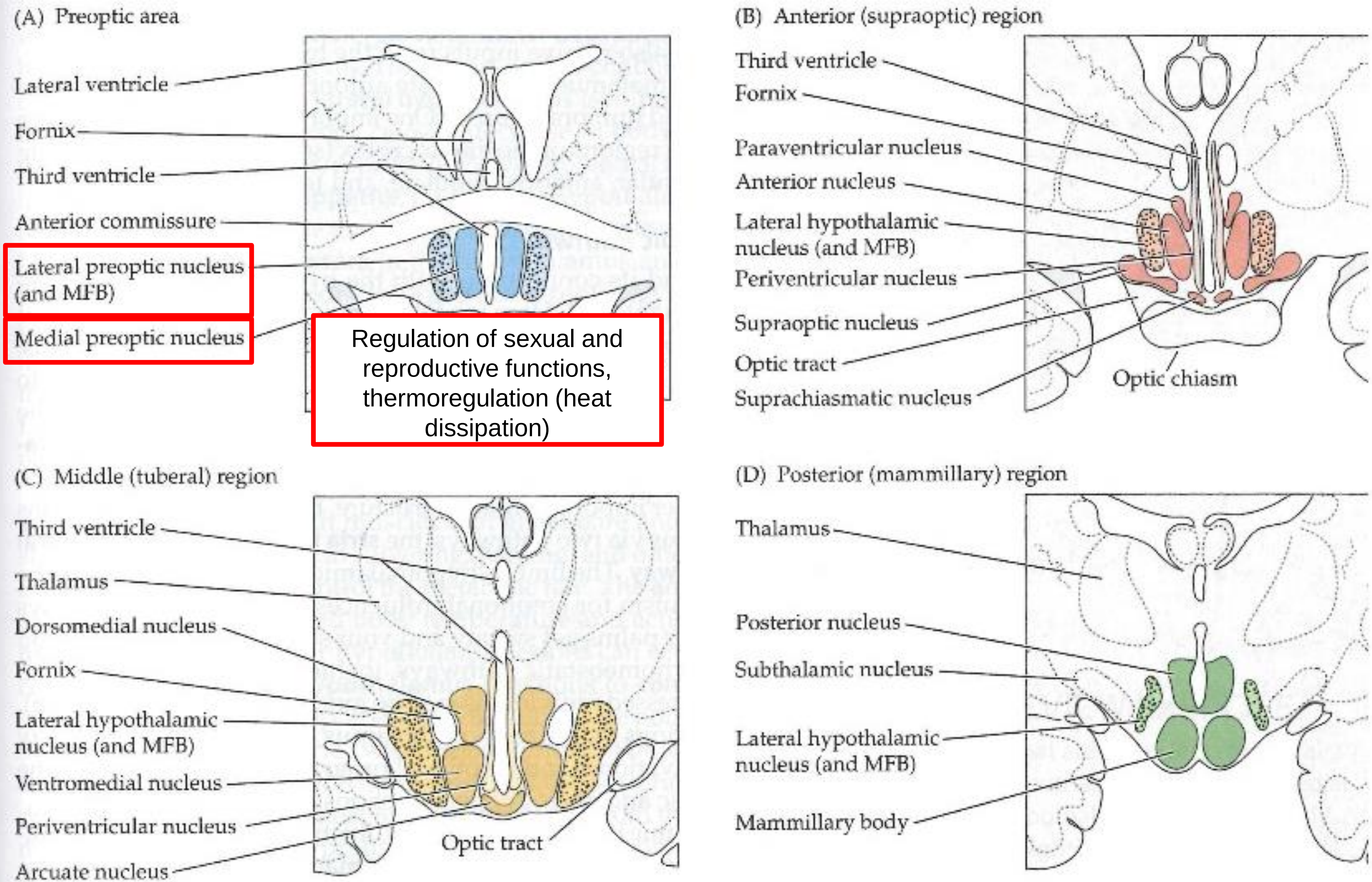

(A)
Thalamus
Hypothalamus
Optic chiasm
Median eminence
Anterior pituitary
Posterior pituitary
Hypothalamic sulcus
Mammillary body
Infundibulum
Pituitary stalk
B)
Optic chiasm
Optic tract
Optic nerve
Tuber cinereum
Pituitary stalk
Mammillary body
Cerebral peduncle

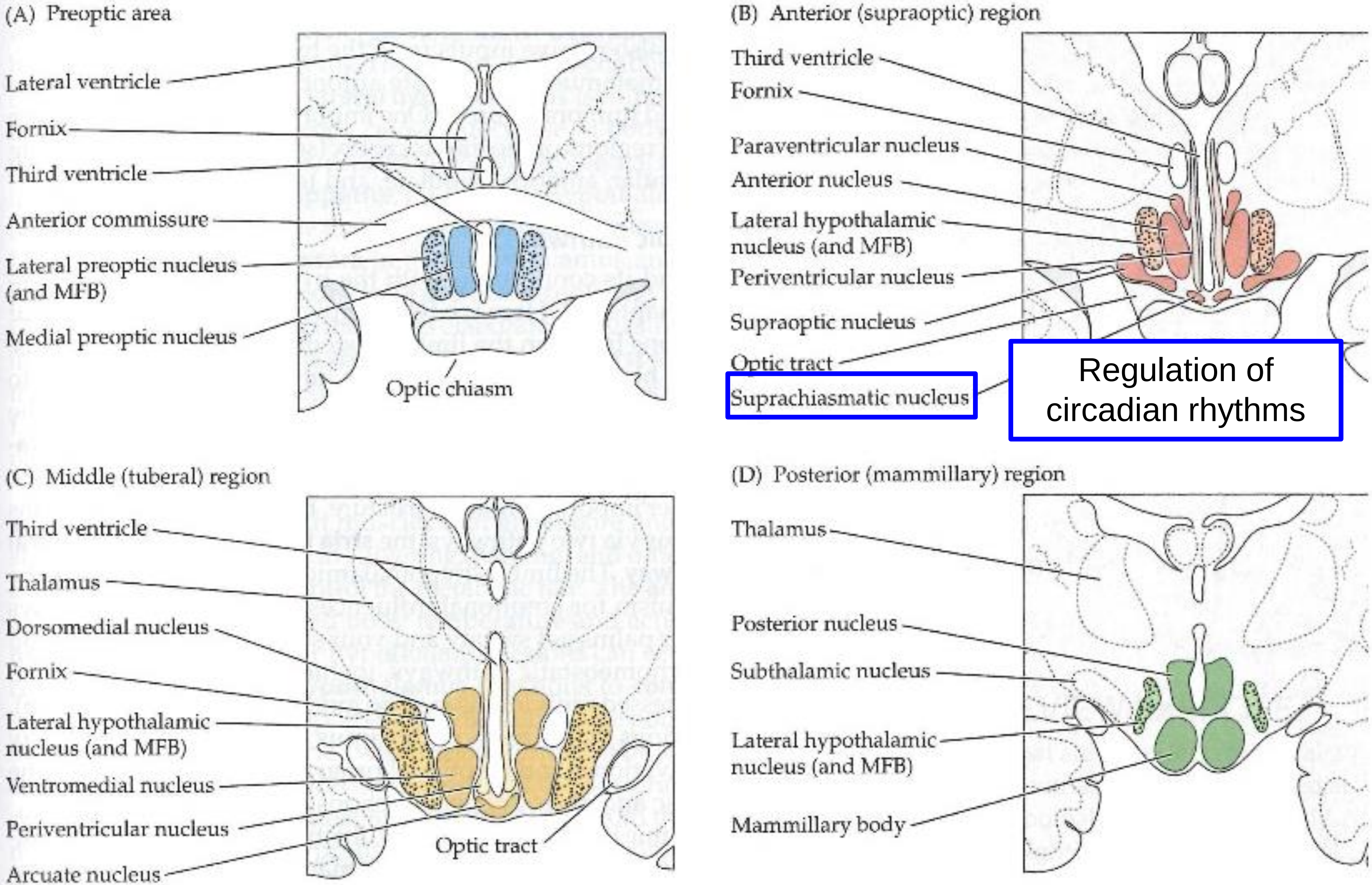


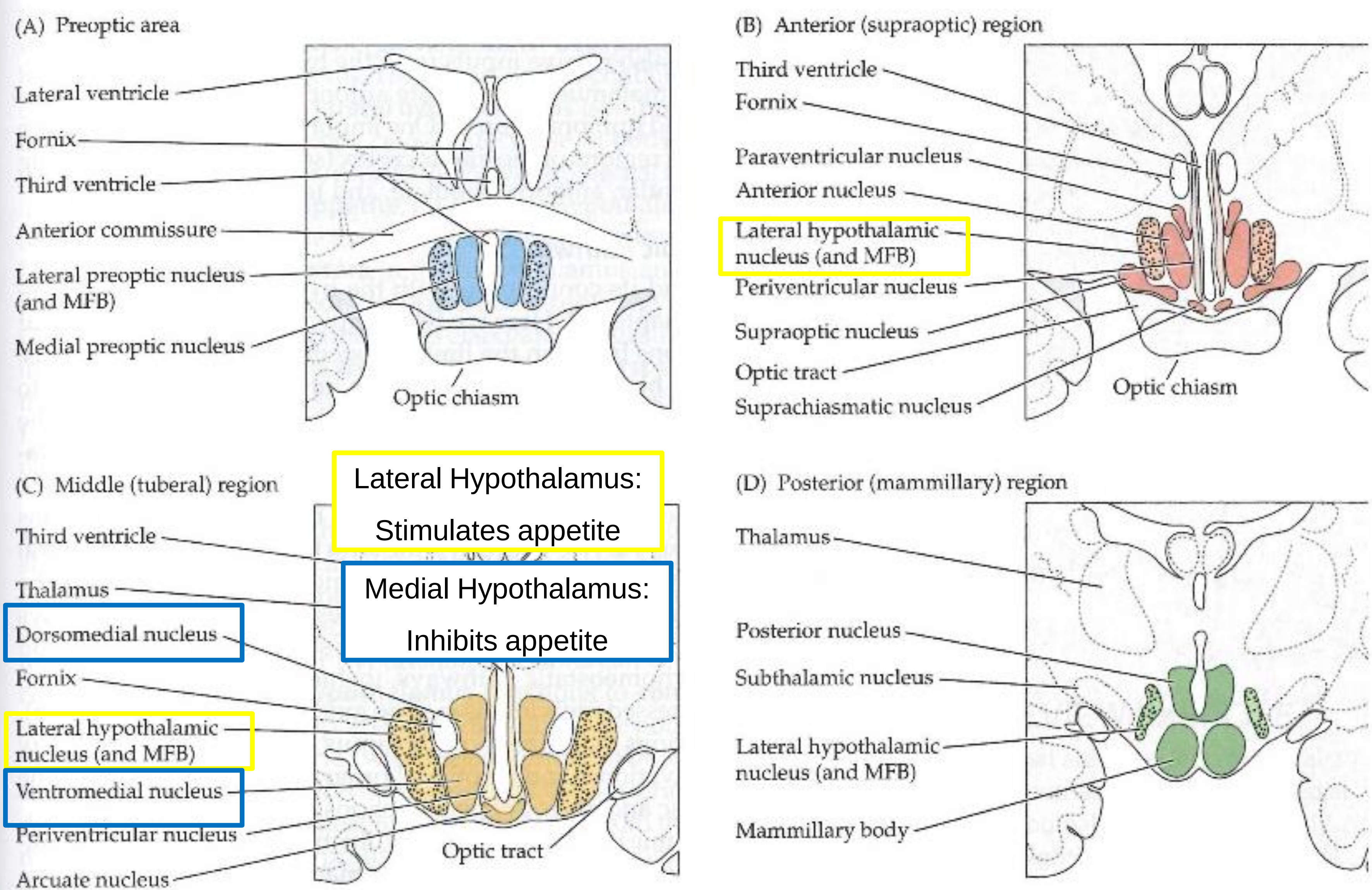


Hypothalamic functions

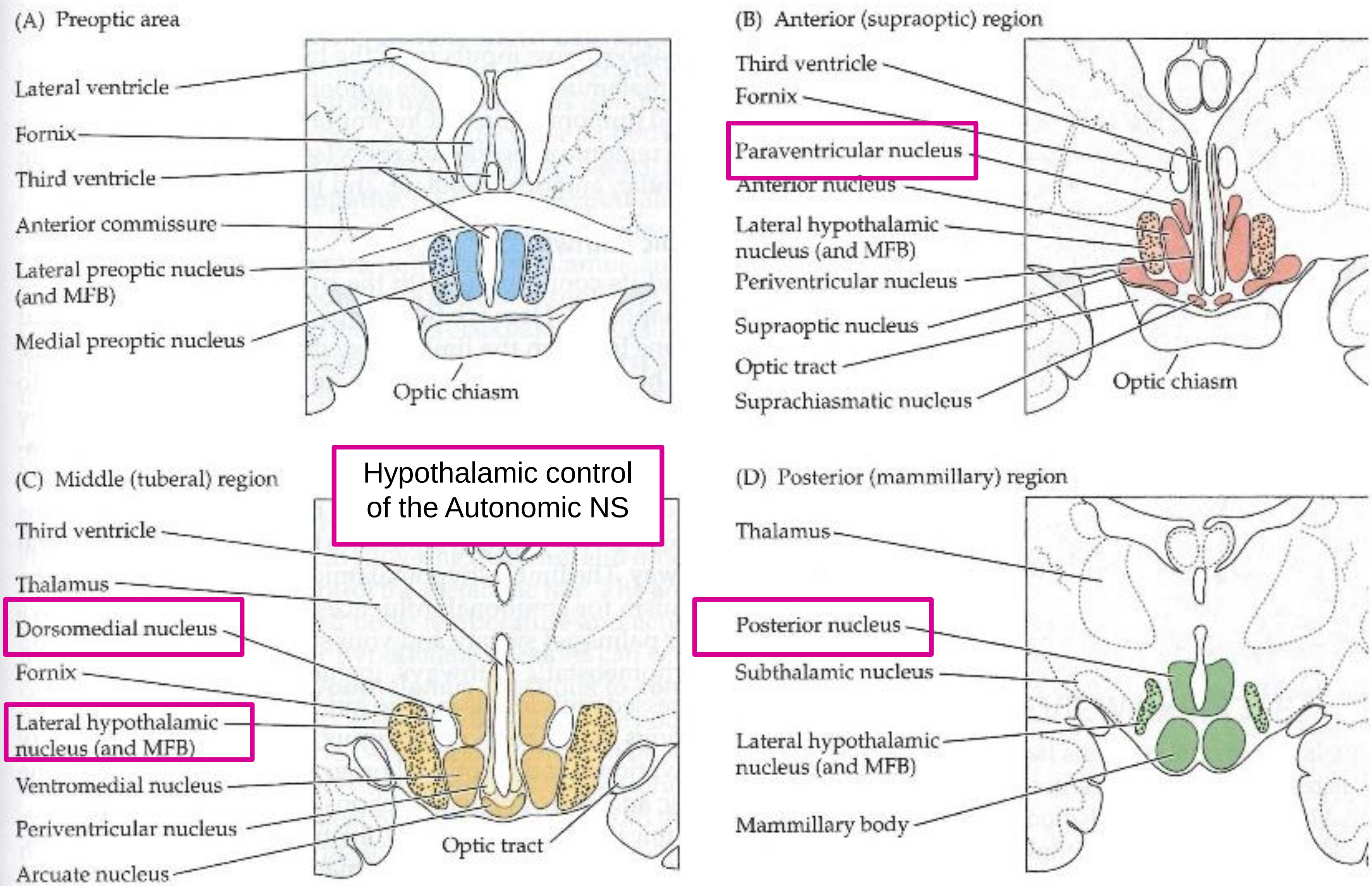
- Autonomic
- Endocrine
- Homeostatic
- Limbic

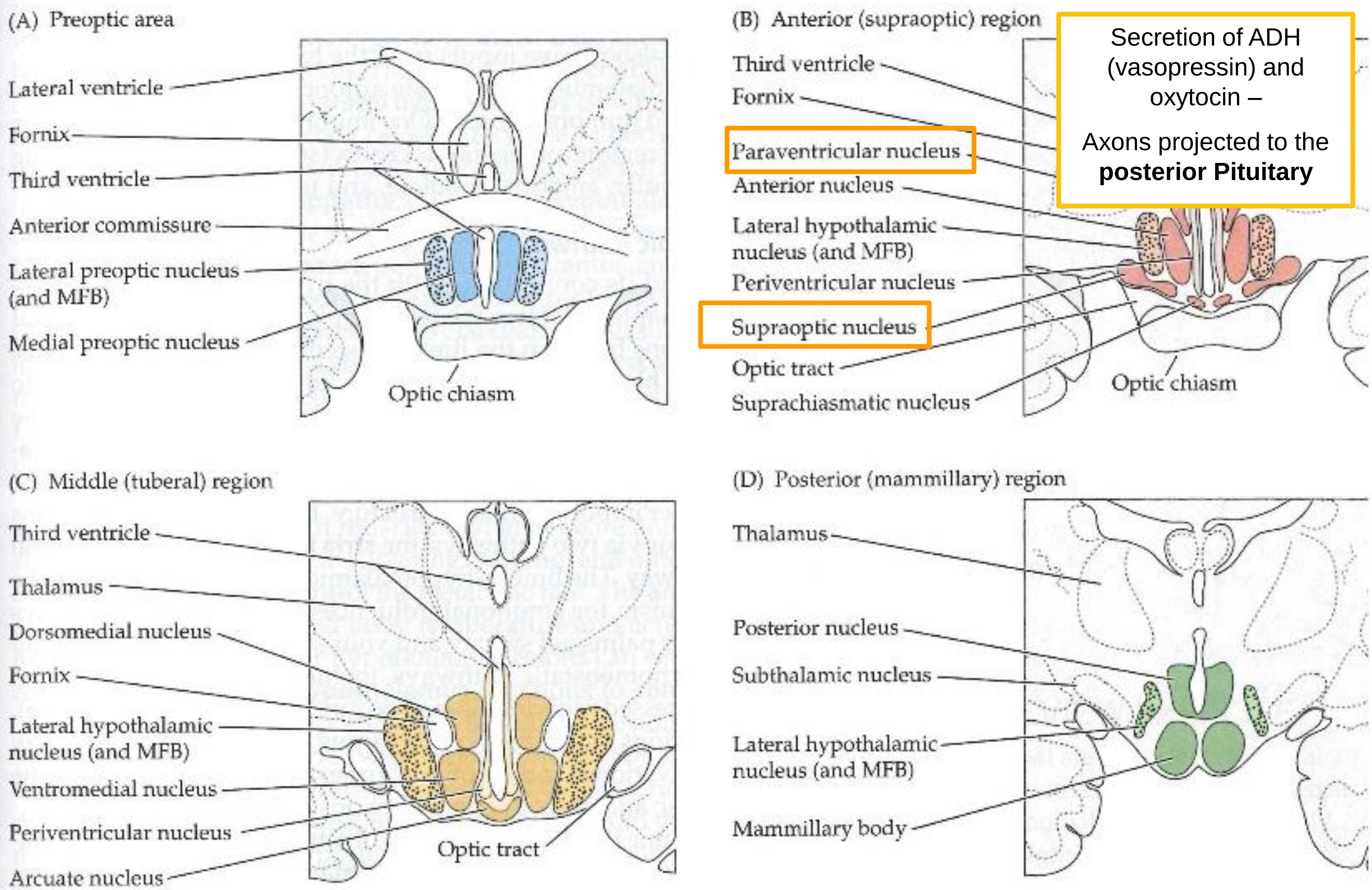

(A) Preoptic area
Lateral ventricle
Fornix
Third ventricle
Anterior commissure
Lateral preoptic nucleus (and MFB)
Medial preoptic nucleus
Regulation of sexual and reproductive functions, thermoregulation (heat dissipation)
(B) Anterior (supraoptic) region
Third ventricle
Fornix
Paraventricular nucleus
Anterior nucleus
Lateral hypothalamic nucleus (and MFB)
Periventricular nucleus
Supraoptic nucleus
Optic tract
Suprachiasmatic nucleus
Optic chiasm
(C) Middle (tuberal) region
Third ventricle
Thalamus
Dorsomedial nucleus
Fornix
Lateral hypothalamic nucleus (and MFB)
Ventromedial nucleus
Periventricular nucleus
Arcuate nucleus
Optic tract
(D) Posterior (mammillary) region
Thalamus
Posterior nucleus
Subthalamic nucleus
Lateral hypothalamic nucleus (and MFB)
Mammillary body

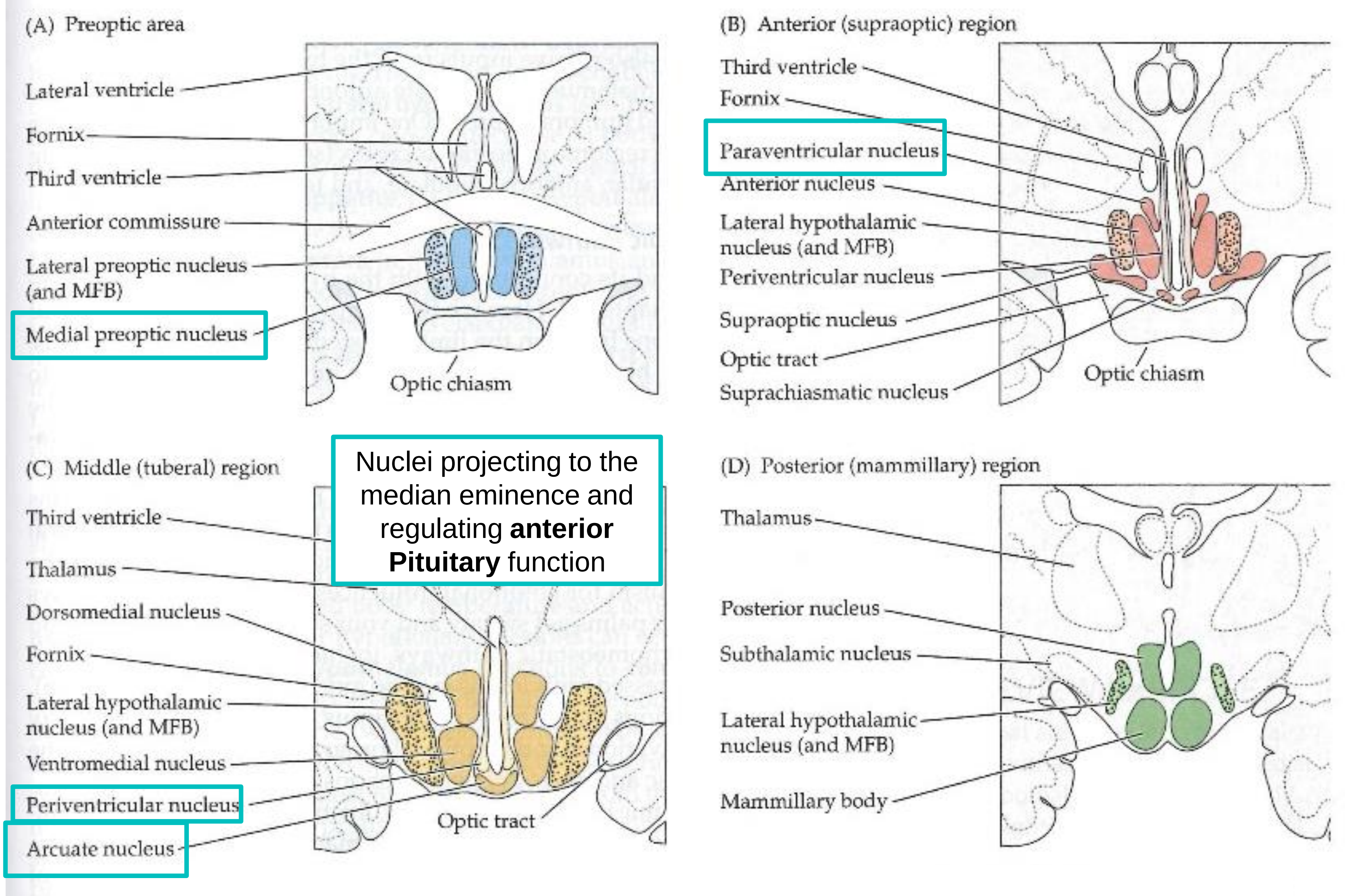

(A) Preoptic area
Lateral ventricle
Fornix
Third ventricle
Anterior commissure
Lateral preoptic nucleus (and MFB)
Medial preoptic nucleus
Optic chiasm
(B) Anterior (supraoptic) region
Third ventricle
Fornix
Paraventricular nucleus
Anterior nucleus
Lateral hypothalamic nucleus (and MFB)
Periventricular nucleus
Supraoptic nucleus
Optic tract
Suprachiasmatic nucleus
Regulation of circadian rhythms
(C) Middle (tuberal) region
Third ventricle
Thalamus
Dorsomedial nucleus
Fornix
Lateral hypothalamic nucleus (and MFB)
Ventromedial nucleus
Periventricular nucleus
Arcuate nucleus
Optic tract
(D) Posterior (mammillary) region
Thalamus
Posterior nucleus
Subthalamic nucleus
Lateral hypothalamic nucleus (and MFB)
Mammillary body

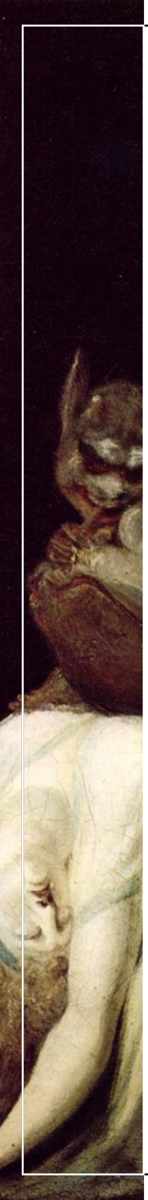

(A) Preoptic area
Lateral ventricle
Fornix
Third ventricle
Anterior commissure
Lateral preoptic nucleus (and MFB)
Medial preoptic nucleus
Optic chiasm
(B) Anterior (supraoptic) region
Third ventricle
Fornix
Paraventricular nucleus
Anterior nucleus
Lateral hypothalamic nucleus (and MFB)
Periventricular nucleus
Supraoptic nucleus
Optic tract
Suprachiasmatic nucleus
Optic chiasm
(C) Middle (tuberal) region
Lateral Hypothalamus:
Stimulates appetite
Medial Hypothalamus:
Inhibits appetite
Third ventricle
Thalamus
Dorsomedial nucleus
Fornix
Lateral hypothalamic nucleus (and MFB)
Ventromedial nucleus
Periventricular nucleus
Arcuate nucleus
Optic tract
(D) Posterior (mammillary) region
Thalamus
Posterior nucleus
Subthalamic nucleus
Lateral hypothalamic nucleus (and MFB)
Mammillary body

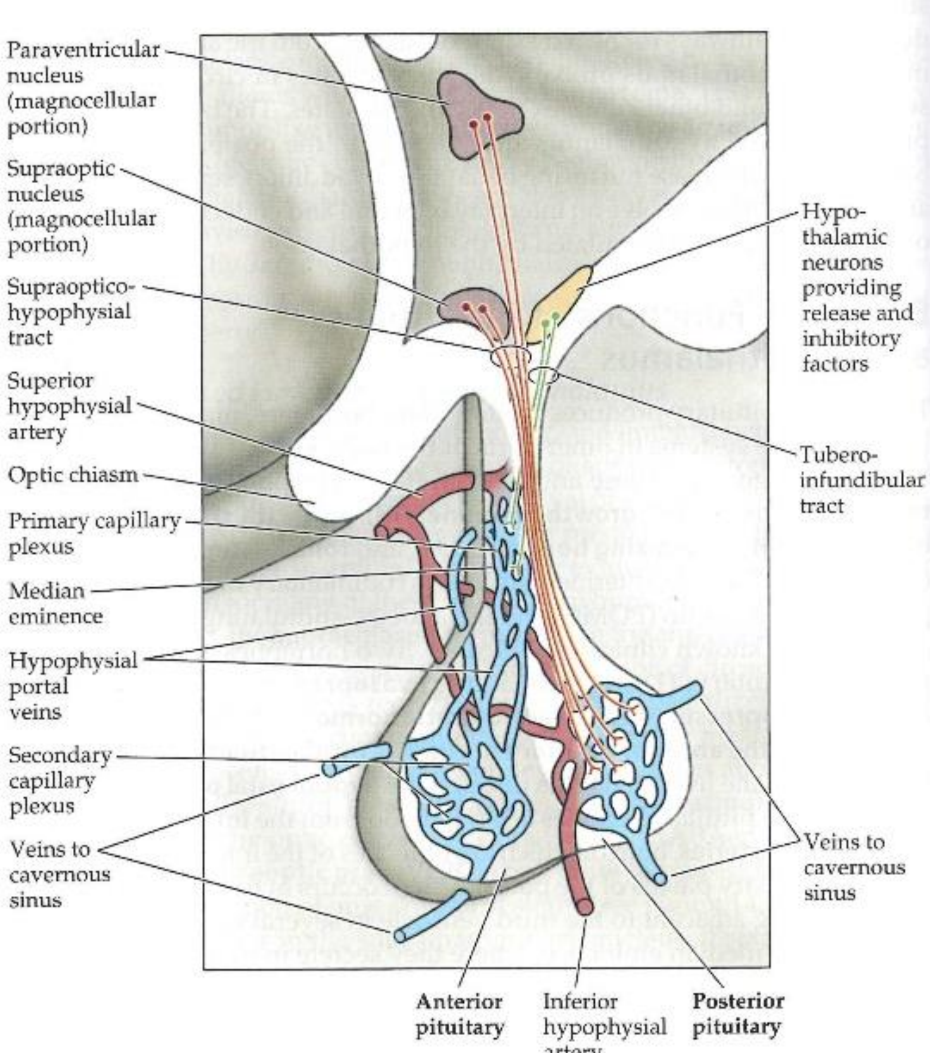
Hypothalamic control of the Autonomic NS




(A) Preoptic area
Lateral ventricle
Fornix
Third ventricle
Anterior commissure
Lateral preoptic nucleus (and MFB)
Medial preoptic nucleus
Optic chiasm
(B) Anterior (supraoptic) region
Third ventricle
Fornix
Paraventricular nucleus
Anterior nucleus
Lateral hypothalamic nucleus (and MFB)
Periventricular nucleus
Supraoptic nucleus
Optic tract
Suprachiasmatic nucleus
Optic chiasm
Secretion of ADH (vasopressin) and oxytocin –
Axons projected to the **posterior Pituitary**
(C) Middle (tuberal) region
Third ventricle
Thalamus
Dorsomedial nucleus
Fornix
Lateral hypothalamic nucleus (and MFB)
Ventromedial nucleus
Periventricular nucleus
Arcuate nucleus
Optic tract
(D) Posterior (mammillary) region
Thalamus
Posterior nucleus
Subthalamic nucleus
Lateral hypothalamic nucleus (and MFB)
Mammillary body


(A) Preoptic area
Lateral ventricle
Fornix
Third ventricle
Anterior commissure
Lateral preoptic nucleus (and MFB)
Medial preoptic nucleus
Optic chiasm
(B) Anterior (supraoptic) region
Third ventricle
Fornix
Paraventricular nucleus
Anterior nucleus
Lateral hypothalamic nucleus (and MFB)
Periventricular nucleus
Supraoptic nucleus
Optic tract
Suprachiasmatic nucleus
Optic chiasm
(C) Middle (tuberal) region
Nuclei projecting to the median eminence and regulating **anterior Pituitary** function
Third ventricle
Thalamus
Dorsomedial nucleus
Fornix
Lateral hypothalamic nucleus (and MFB)
Ventromedial nucleus
Periventricular nucleus
Arcuate nucleus
Optic tract
(D) Posterior (mammillary) region
Thalamus
Posterior nucleus
Subthalamic nucleus
Lateral hypothalamic nucleus (and MFB)
Mammillary body





Paraventricular nucleus (magnocellular portion)
Supraoptic nucleus (magnocellular portion)
Supraoptico-hypophysial tract
Superior hypophysial artery
Optic chiasm
Primary capillary plexus
Median eminence
Hypophysial portal veins
Secondary capillary plexus
Veins to cavernous sinus
Hypo-thalamic neurons providing release and inhibitory factors
Tubero-infundibular tract
Veins to cavernous sinus
Anterior pituitary
Inferior hypophysial artery
Posterior pituitary

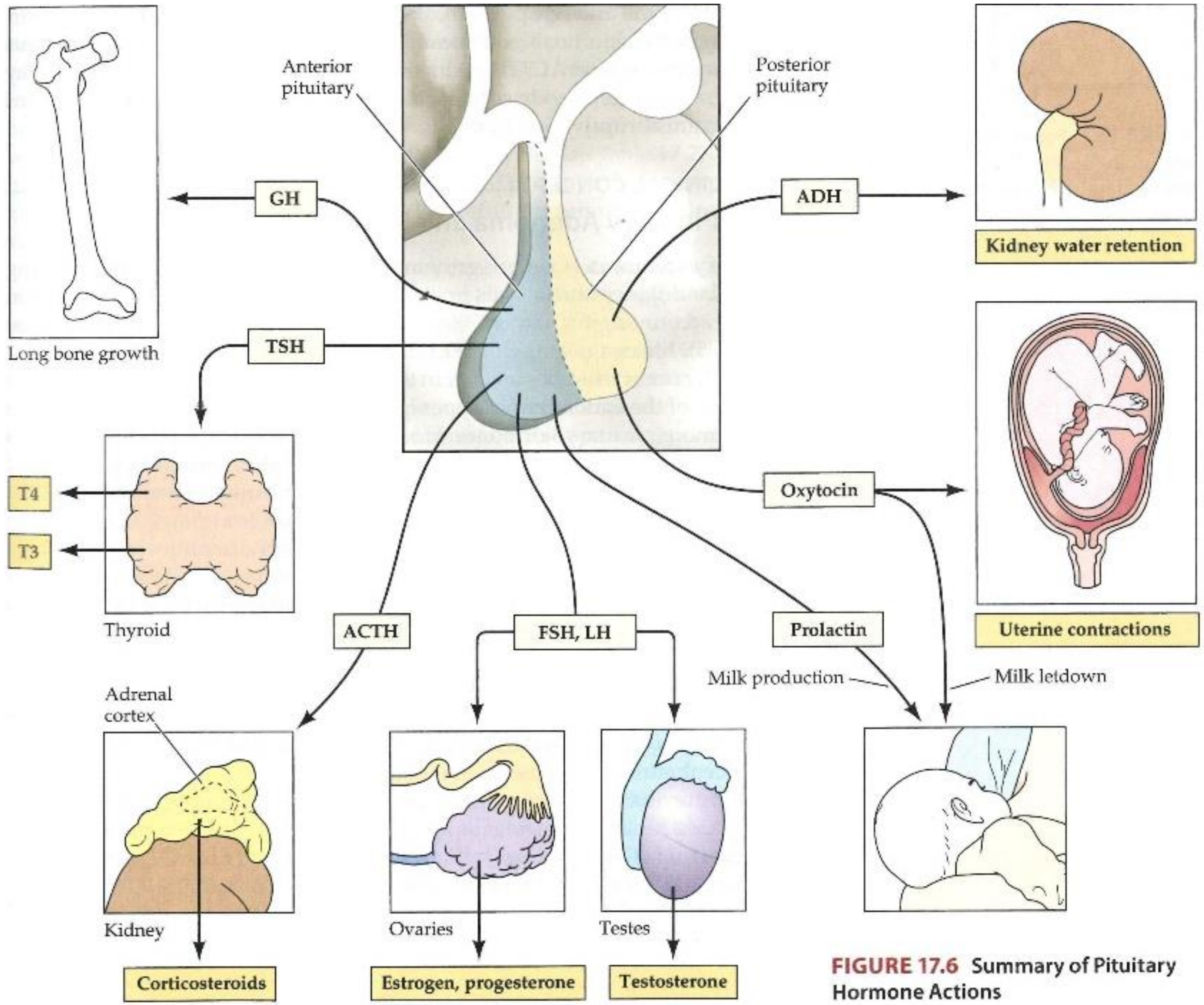
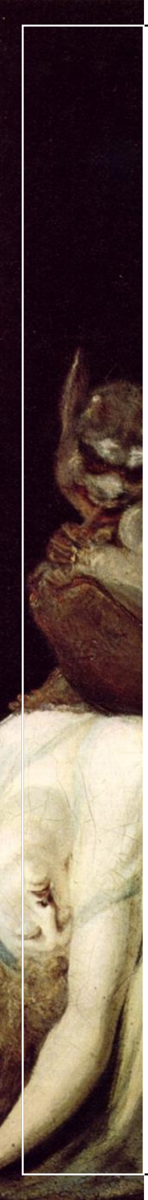
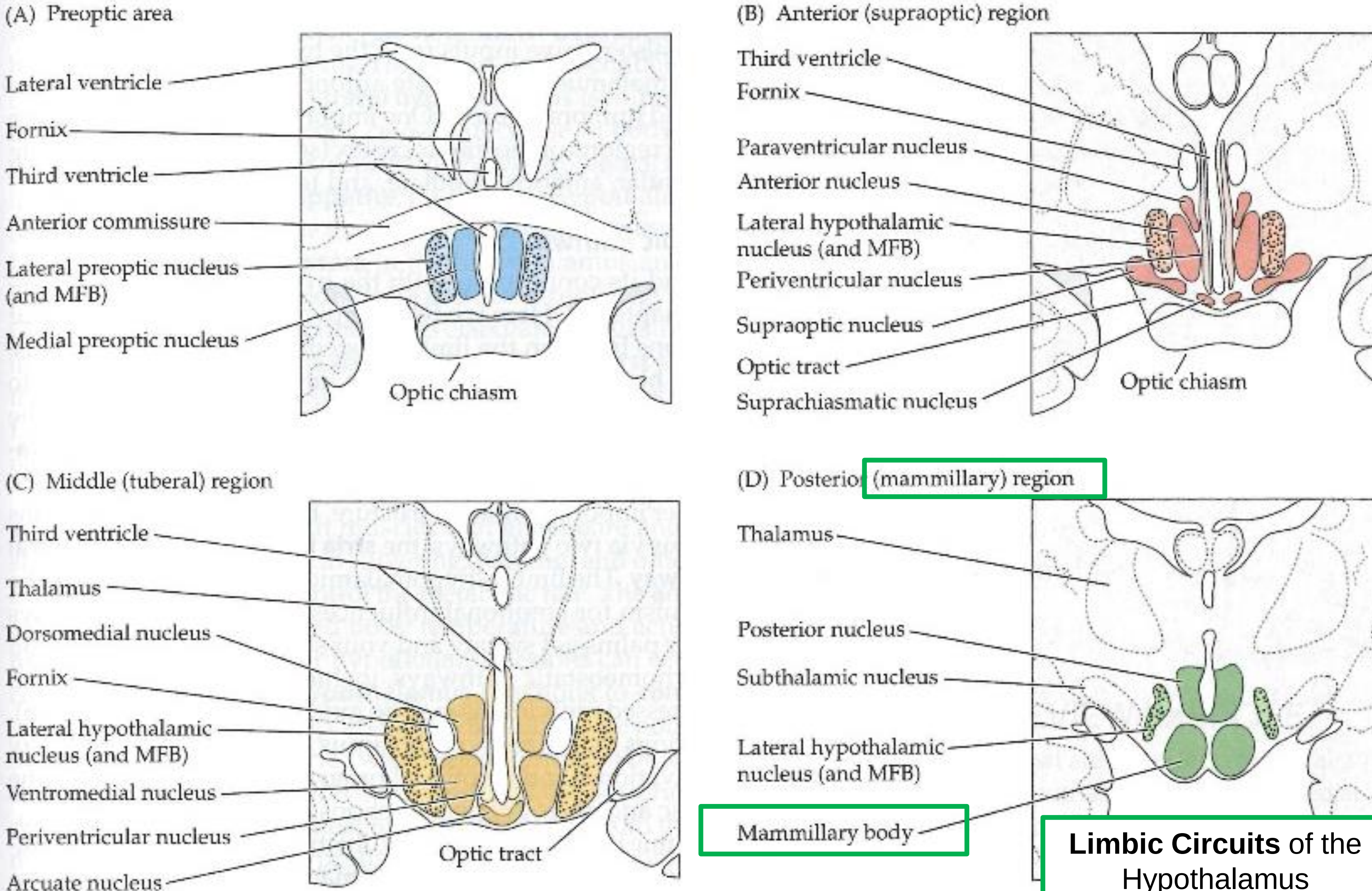


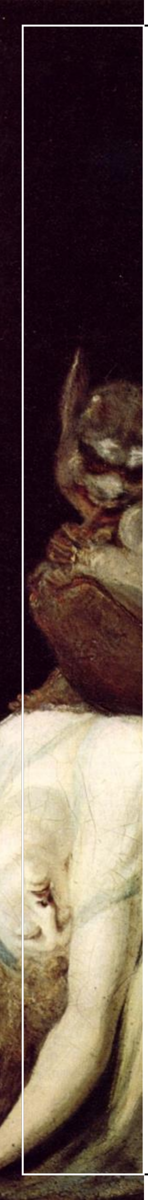
FIGURE 17.6 Summary of Pituitary Hormone Actions

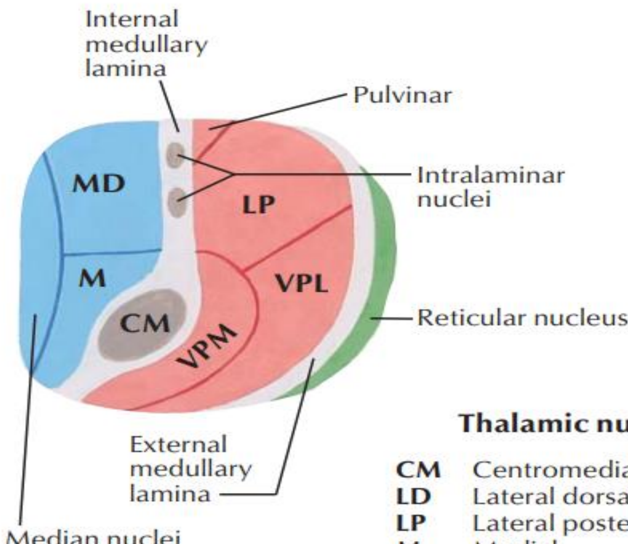


PITUITARY HORMONE	HYPOTHALAMIC RELEASING FACTORS	HYPOTHALAMIC INHIBITORY FACTORS
Adrenocorticotropic hormone (ACTH)	Corticotropin-releasing hormone (CRH), vasopressin, and other peptides	—
Thyroid-stimulating hormone (TSH)	Thyrotropin-releasing hormone (TRH)	Growth hormone–inhibiting hormone (GIH, somatostatin)
Growth hormone (GH)	Growth hormone–releasing hormone (GHRH)	Growth hormone–inhibiting hormone (GIH, somatostatin)
Prolactin	Prolactin-releasing factor (PRF) and thyrotropin-releasing hormone (TRH)	Prolactin release–inhibiting factor (PIF, dopamine)
Luteinizing hormone (LH)	Gonadotropin-releasing hormone (GnRH)	—
Follicle-stimulating hormone (FSH)	Gonadotropin-releasing hormone (GnRH)	—



Limbic Circuits of the Hypothalamus

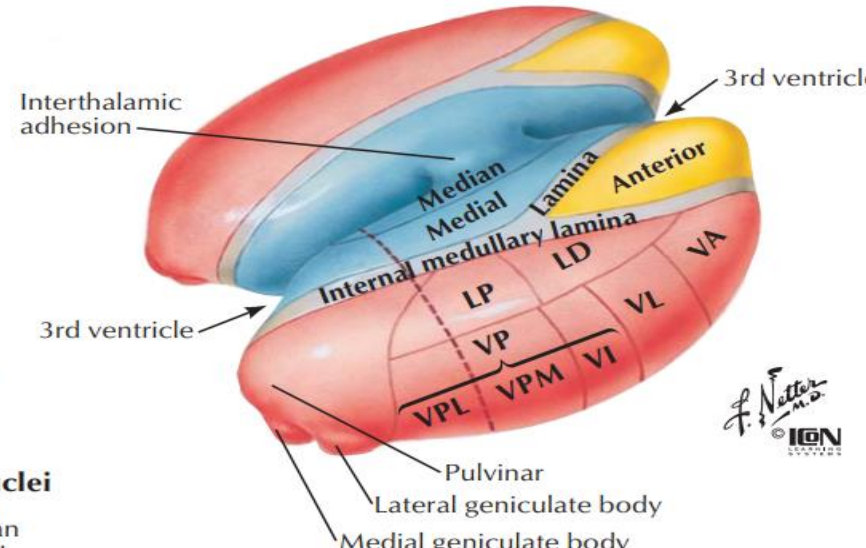




Schematic section through thalamus
(at level of broken line shown in figure at right)

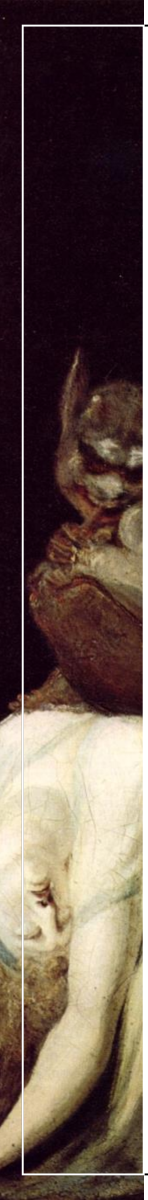
Thalamic nuclei

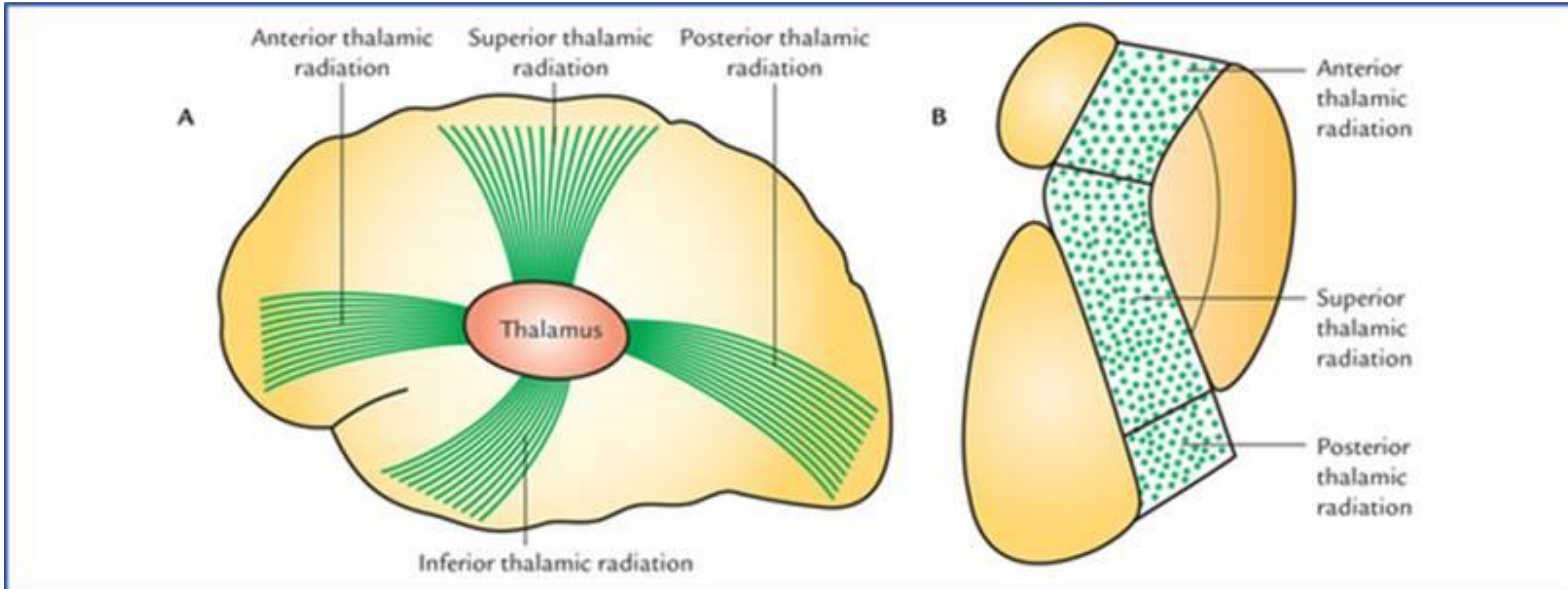
CM	Centromedian
LD	Lateral dorsal
LP	Lateral posterior
M	Medial
MD	Medial dorsal
VA	Ventral anterior
VI	Ventral intermedial
VL	Ventral lateral
VP	Ventral posterior
VPL	Ventral posterolateral
VPM	Ventral posteromedial

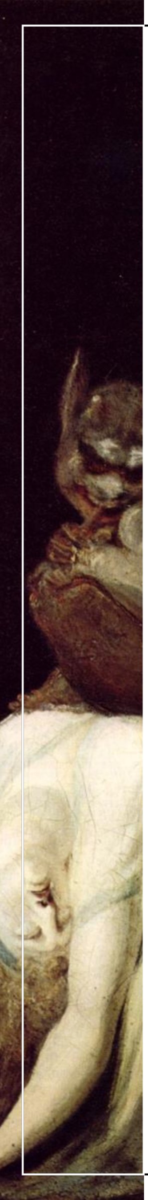


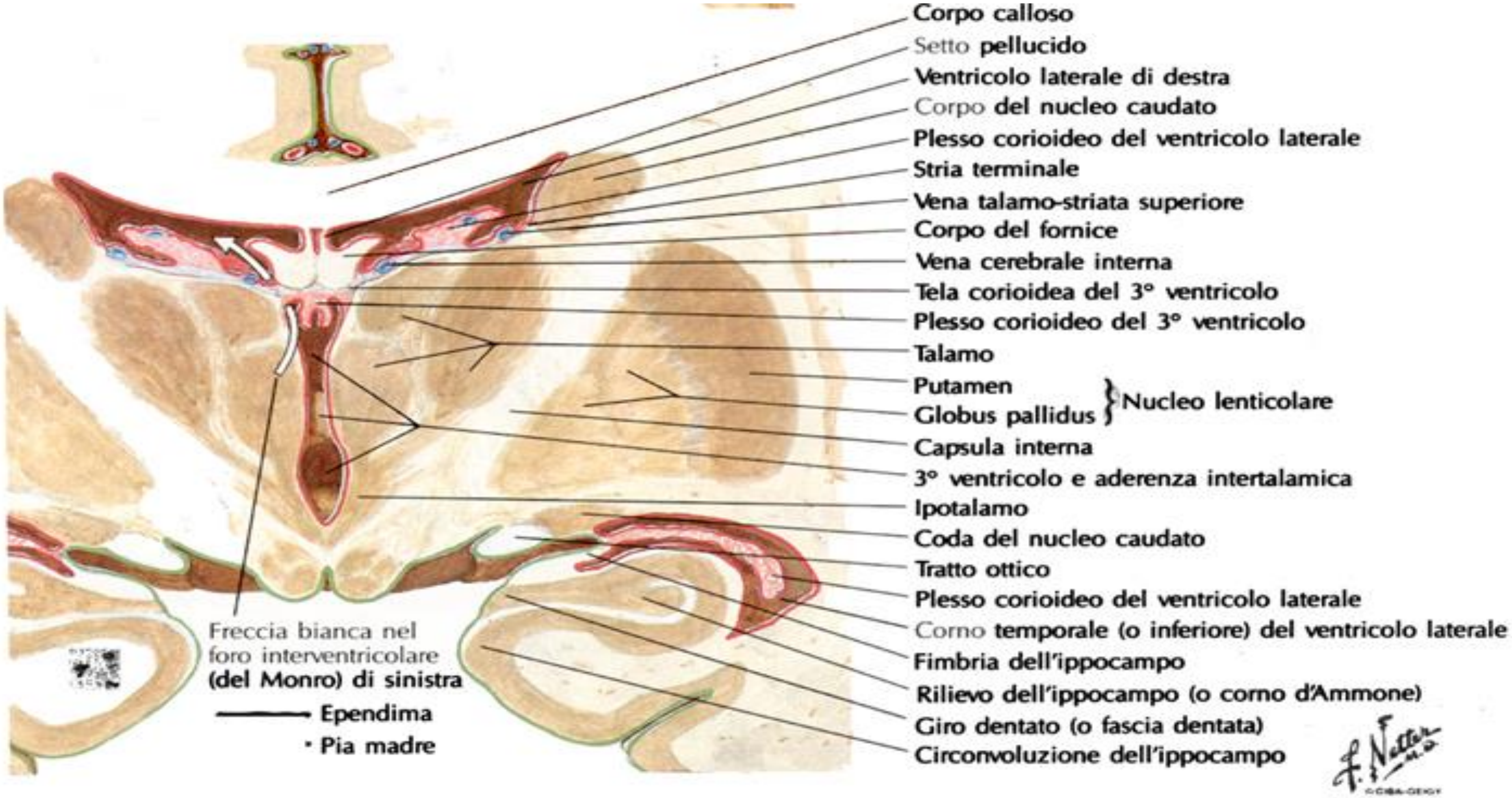
Schematic representation of thalamus
(external medullary lamina and reticular nuclei removed)

Lateral nuclei
Medial nuclei
Anterior nuclei

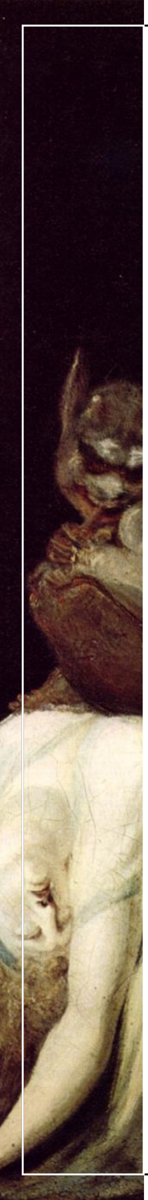



A
Anterior thalamic radiation
Superior thalamic radiation
Posterior thalamic radiation
Thalamus
Inferior thalamic radiation
B
Anterior thalamic radiation
Superior thalamic radiation
Posterior thalamic radiation





Sezione frontale del cervello (veduta posteriore)



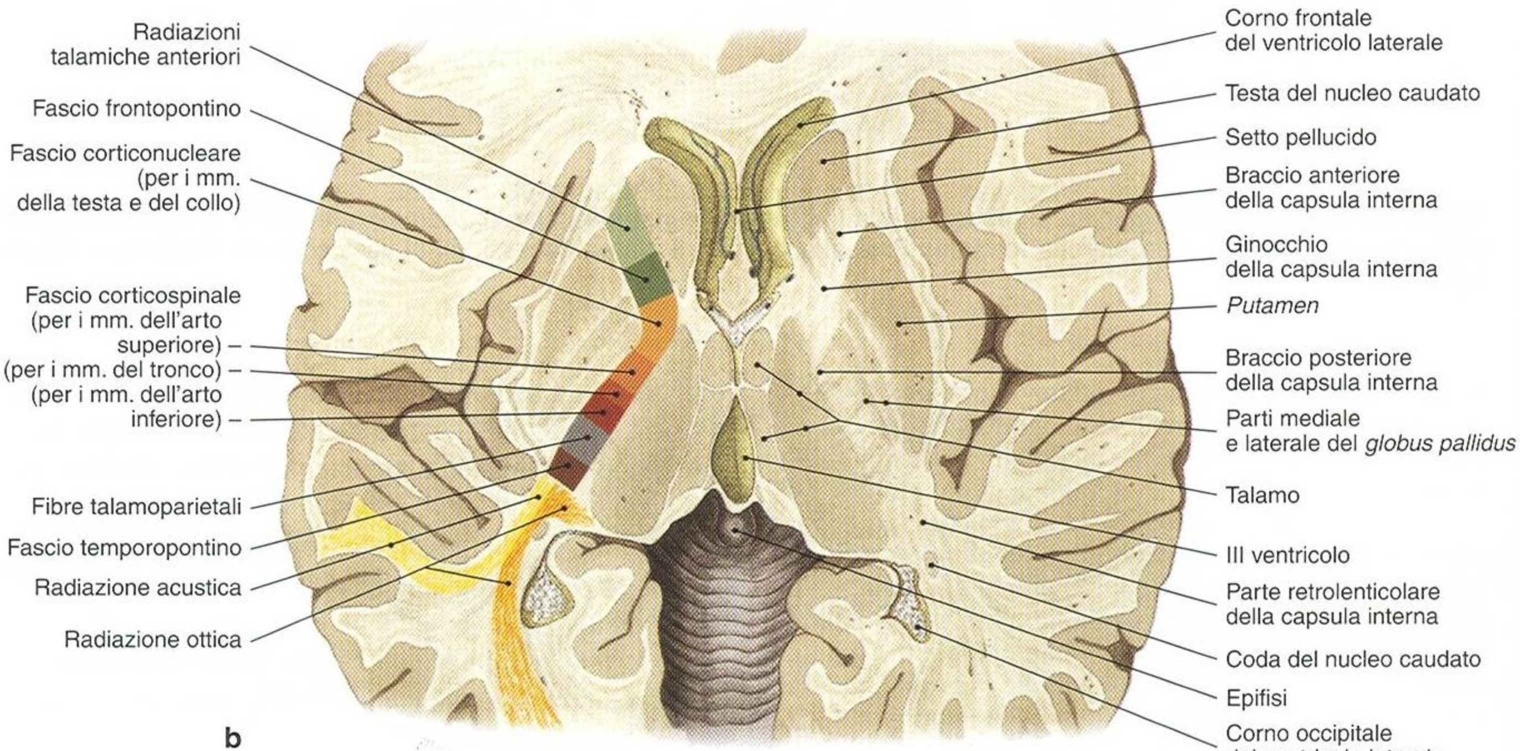
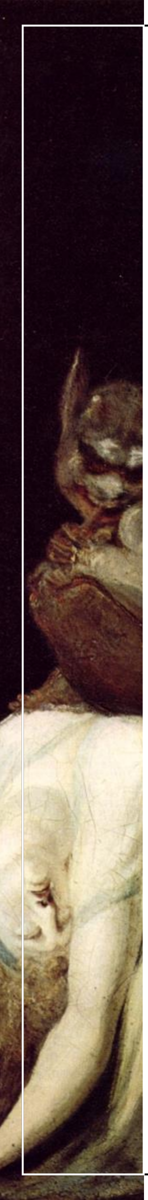
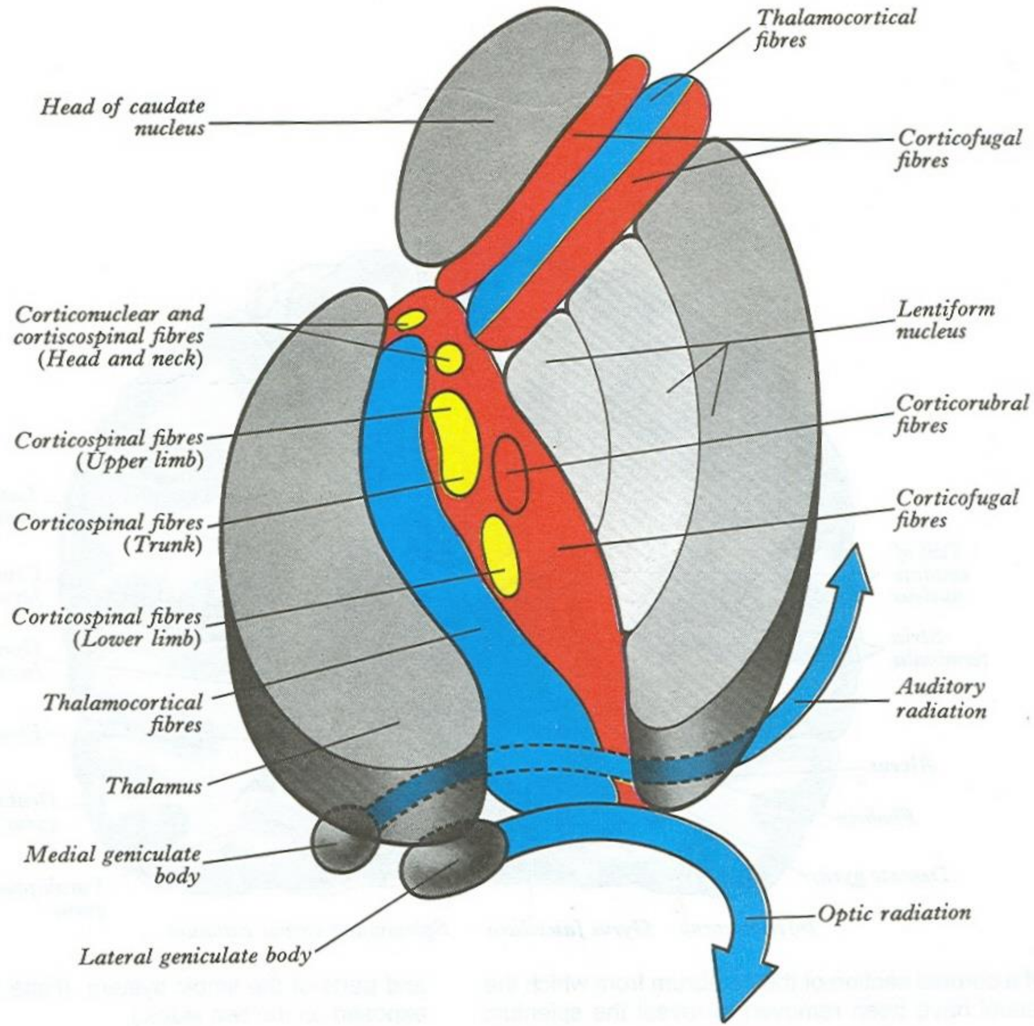
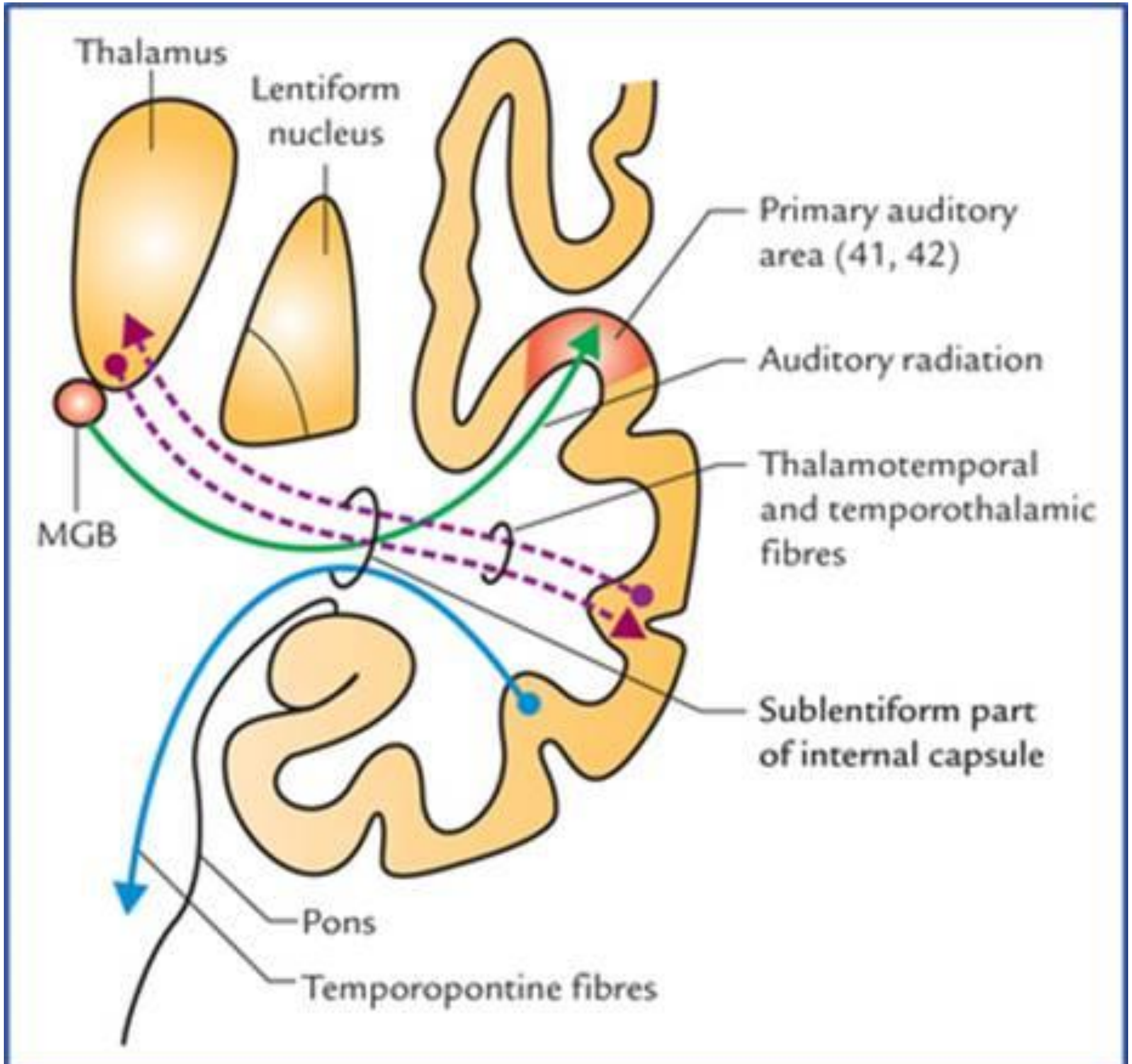


Figura 14.79 - Nuclei del proencefalo e capsula interna. **a**, Talamo, corpo striato (nuclei caudato e *putamen*) e nucleo lenticolare (*putamen* e *globus pallidus*) con capsula interna, proiezione occipitolaterale destra. **b**, Sezione orizzontale della capsula interna e dei nuclei adiacenti. A sinistra le parti principali della capsula interna sono state messe in evidenza con colori differenti. Proiezione parietale (da Köpf-Maier P, ed.: Wolf-Heidegger's Atlas of Human Anatomy, 5th, completely revised and supplemented edition, Basel, Karger, 2000, with permission from S. Karger AG, Basel).

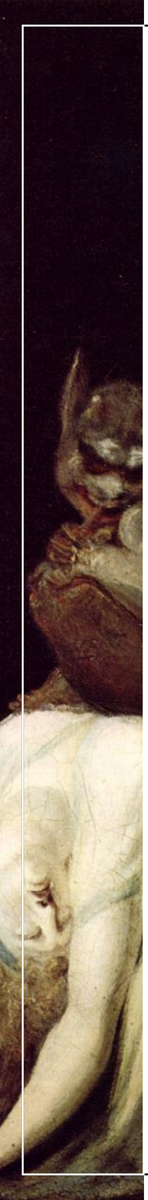


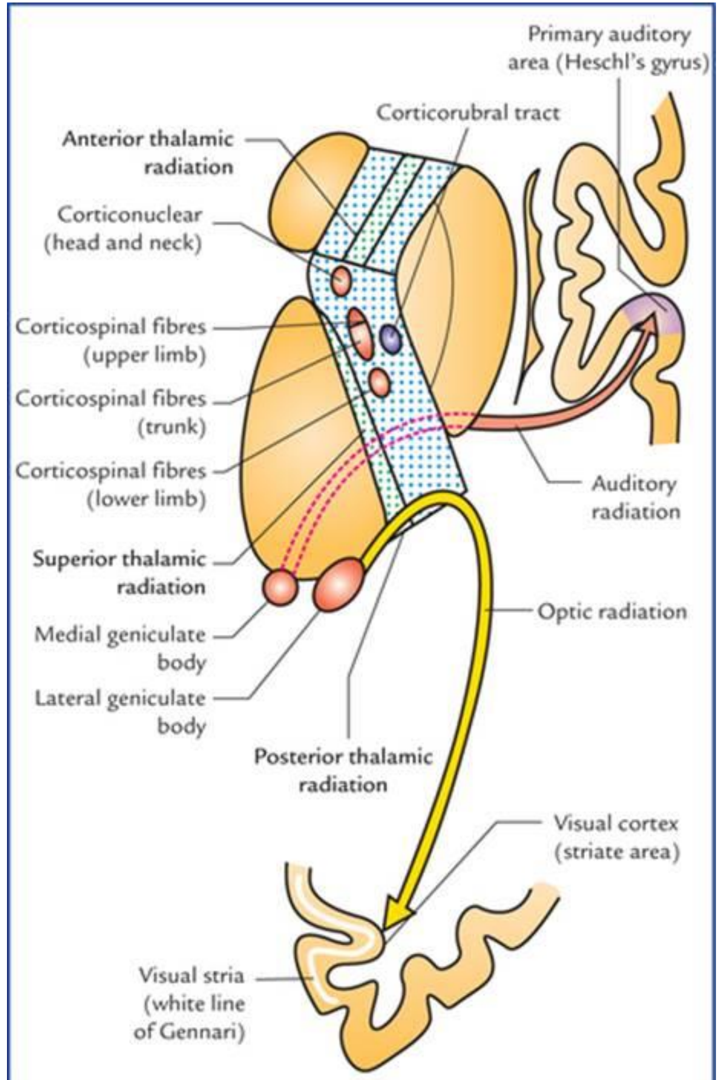


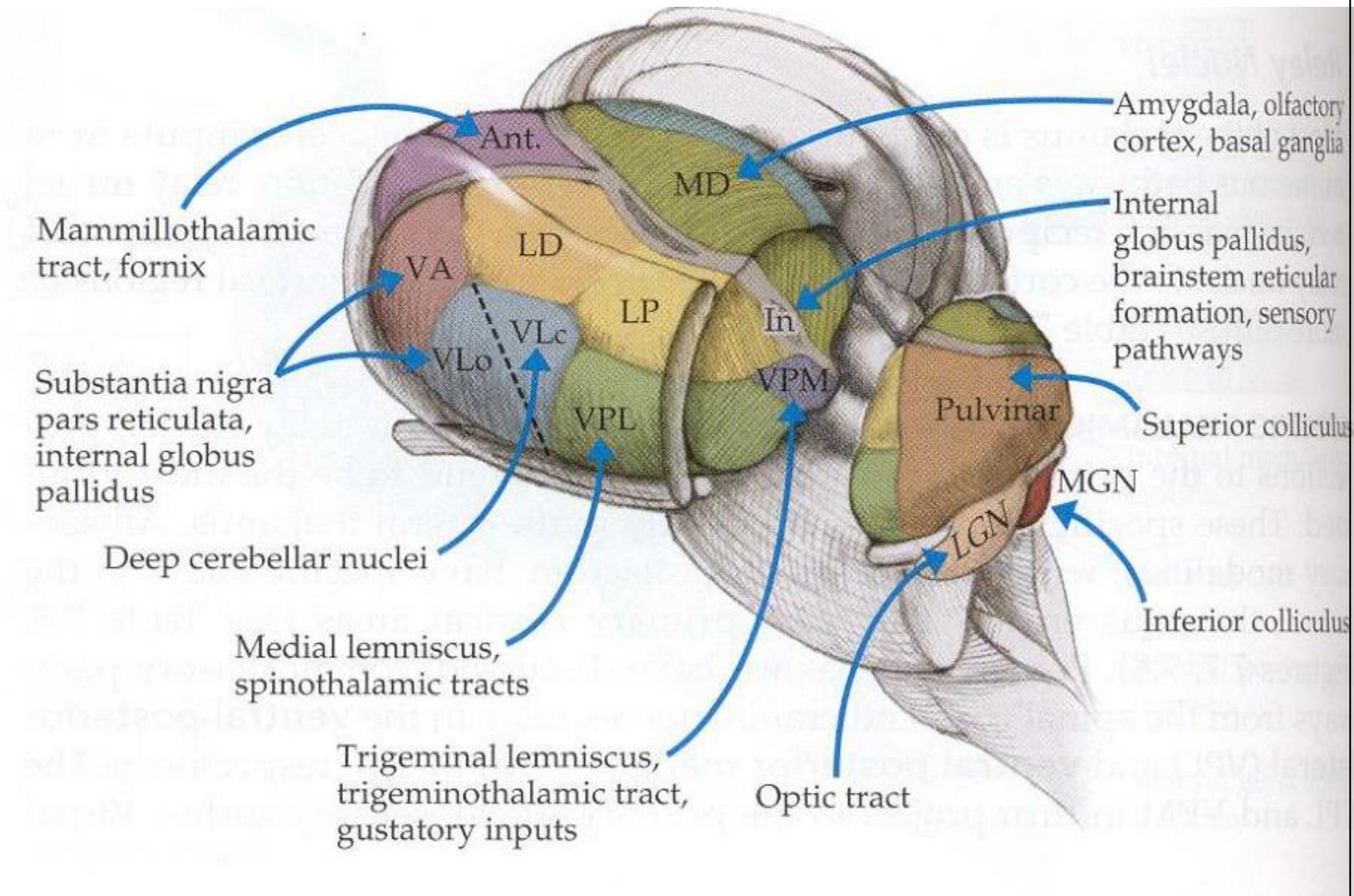
Thalamocortical fibres
Head of caudate nucleus
Corticofugal fibres
Corticonuclear and cortiscospinal fibres (Head and neck)
Lentiform nucleus
Corticorubral fibres
Corticospinal fibres (Upper limb)
Corticospinal fibres (Trunk)
Corticofugal fibres
Corticospinal fibres (Lower limb)
Thalamocortical fibres
Auditory radiation
Thalamus
Medial geniculate body
Optic radiation
Lateral geniculate body



Thalamus
Lentiform nucleus
Primary auditory area (41, 42)
Auditory radiation
MGB
Thalamotemporal and temporothalamic fibres
Sublentiform part of internal capsule
Pons
Temporopontine fibres




Primary auditory area (Heschl's gyrus)
Corticorubral tract
Anterior thalamic radiation
Corticonuclear (head and neck)
Corticospinal fibres (upper limb)
Corticospinal fibres (trunk)
Corticospinal fibres (lower limb)
Superior thalamic radiation
Medial geniculate body
Lateral geniculate body
Posterior thalamic radiation
Auditory radiation
Optic radiation
Visual cortex (striate area)
Visual stria (white line of Gennari)


Ant.
MD
LD
VA
LP
VLc
VLo
In
VPM
VPL
Pulvinar
MGN
LGN
Mammillothalamic tract, fornix
Substantia nigra pars reticulata, internal globus pallidus
Deep cerebellar nuclei
Medial lemniscus, spinothalamic tracts
Trigeminal lemniscus, trigeminothalamic tract, gustatory inputs
Optic tract
Amygdala, olfactory cortex, basal ganglia
Internal globus pallidus, brainstem reticular formation, sensory pathways
Superior colliculus
Inferior colliculus

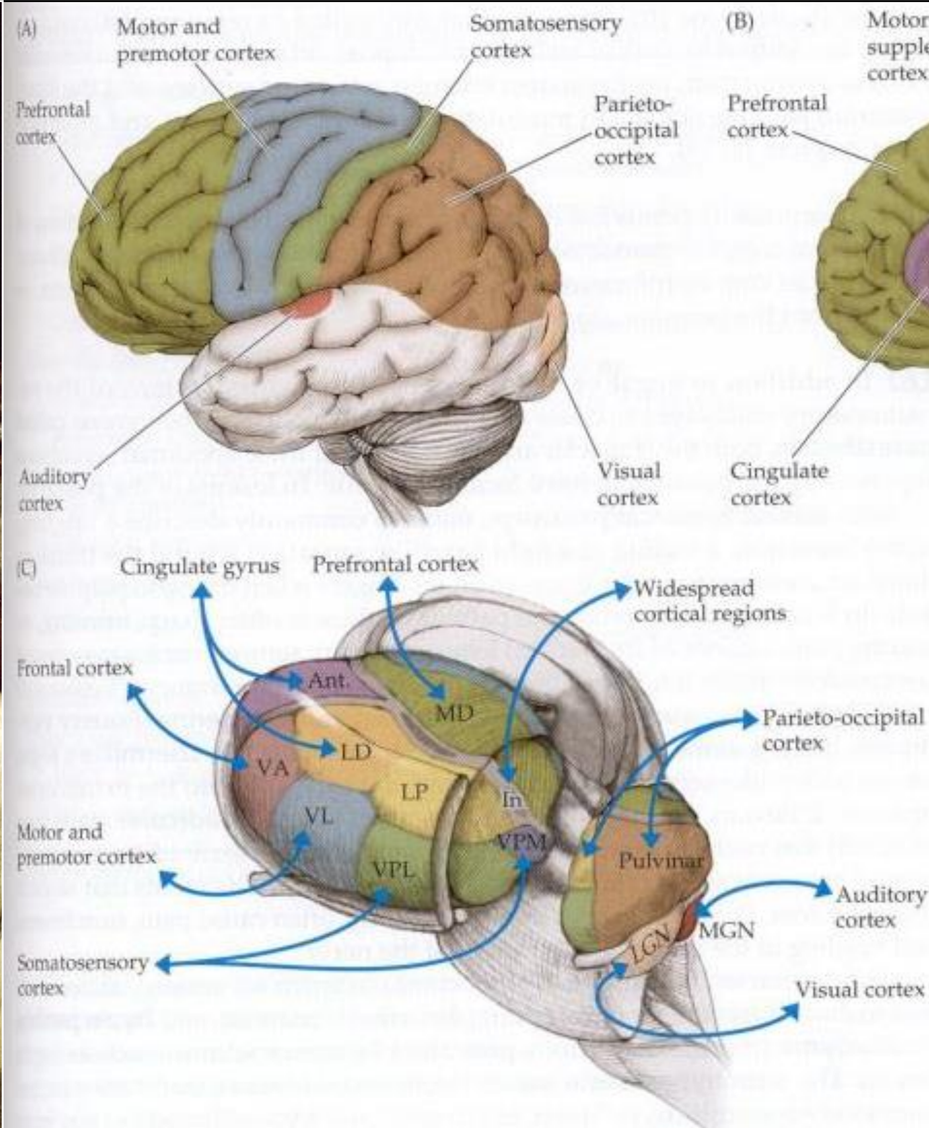
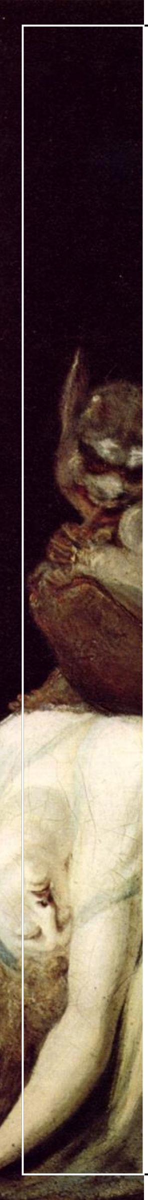
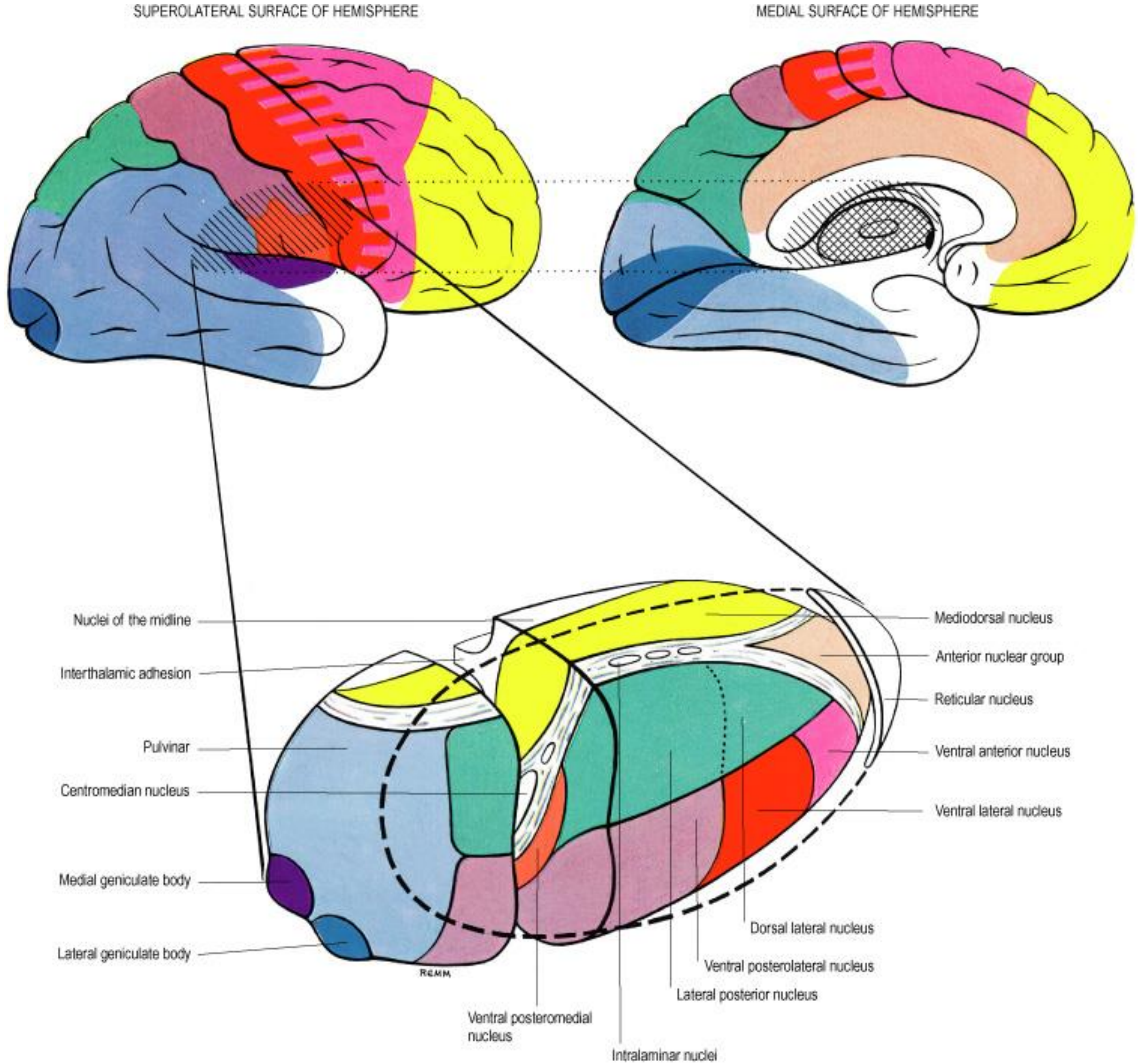


Figure 7.8 Reciprocal Connections between Thalamus and Cortex Major connections between thalamic nuclei and cortical areas are shown using corresponding colors. (A) Cortex, lateral view. (B) Cortex, medial view. (C) Thalamus. See Table 7.3 for additional details. Abbreviations are the same as in Figure 7.7.




SUPEROLATERAL SURFACE OF HEMISPHERE
MEDIAL SURFACE OF HEMISPHERE
Nuclei of the midline
Interthalamic adhesion
Pulvinar
Centromedian nucleus
Medial geniculate body
Lateral geniculate body
Mediodorsal nucleus
Anterior nuclear group
Reticular nucleus
Ventral anterior nucleus
Ventral lateral nucleus
Dorsal lateral nucleus
Ventral posterolateral nucleus
Lateral posterior nucleus
Ventral posteromedial nucleus
Intralaminar nuclei
REMM

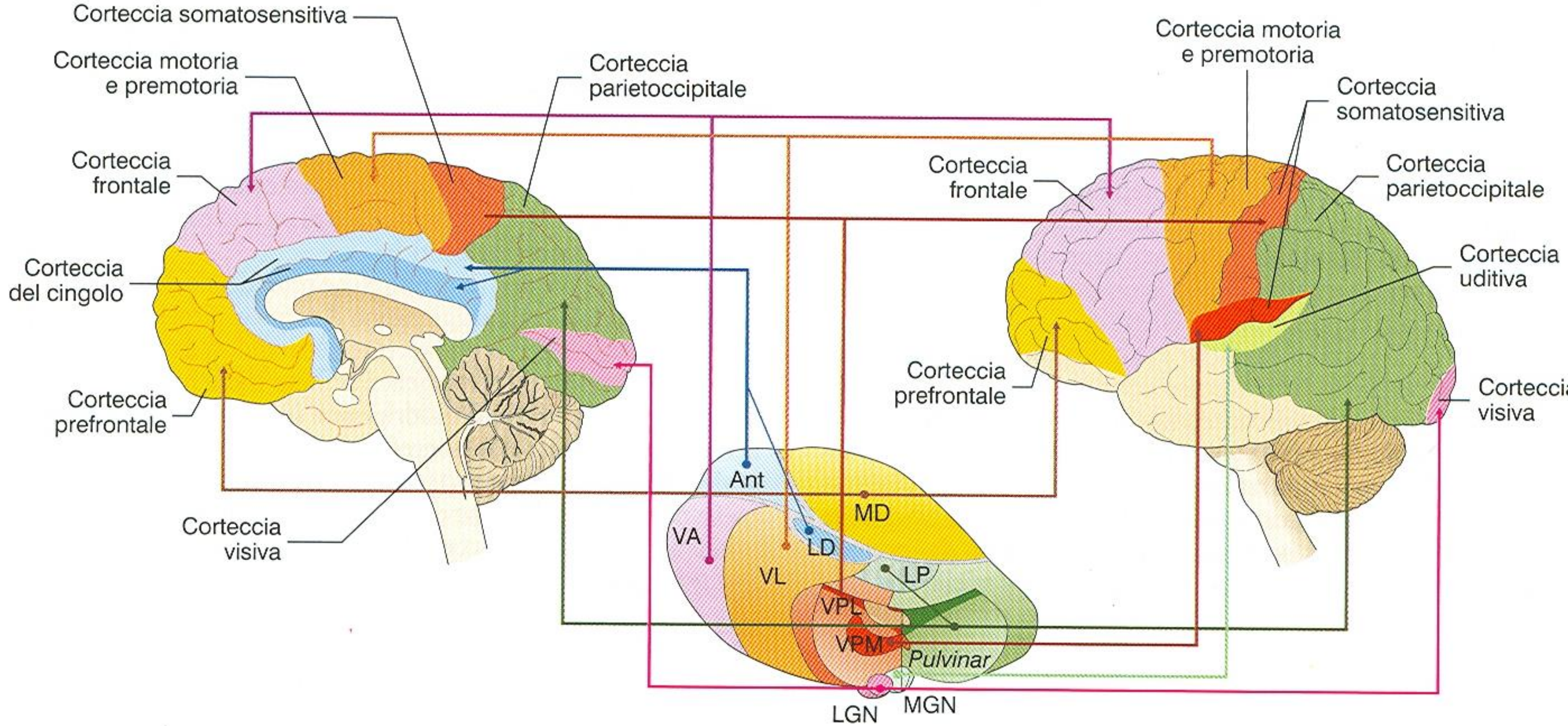
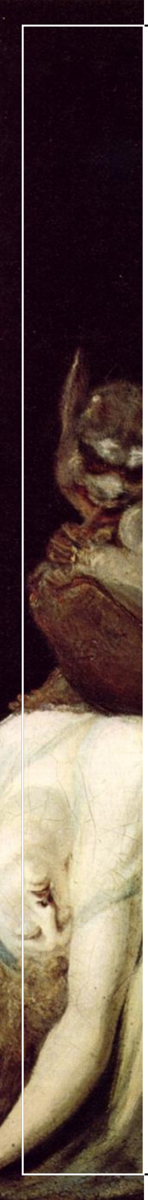


Figura 14.74 - Principali raggruppamenti nucleari del talamo e relative proiezioni corticali.



PRION DISEASES – FATAL FAMILIAL INSOMNIA

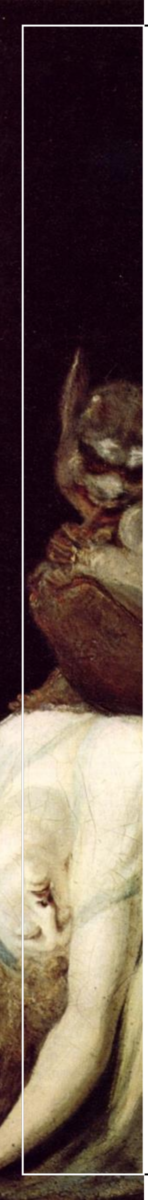
Prion diseases are fatal neurological disorders that are thought to be caused by the misfolding of a benign, widely expressed protein (PrP^{C}) into a distinct pathological conformation(s) (PrP^{Sc}) which is regarded as the disease agent.

Prion diseases affect a range of important food production species and include scrapie in sheep and goats, bovine spongiform encephalopathy (BSE) in cattle and chronic wasting disease (CWD) in deer.

Sporadic (sCJD, sFI)

Acquired (vCJD, Kuru)

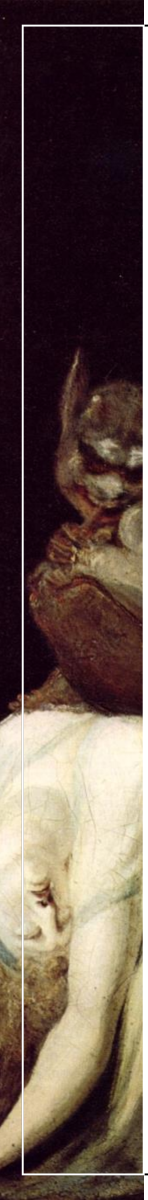
Genetic (gCJD, **FFI**, GSS)



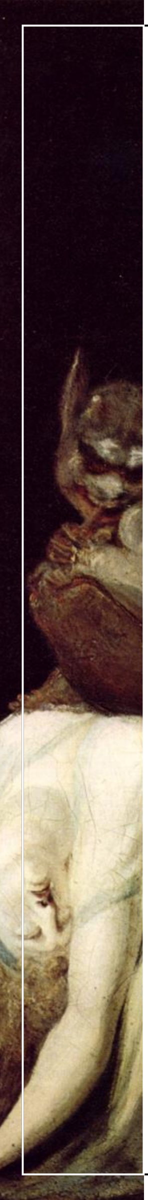
PRION DISEASES – FATAL FAMILIAL INSOMNIA

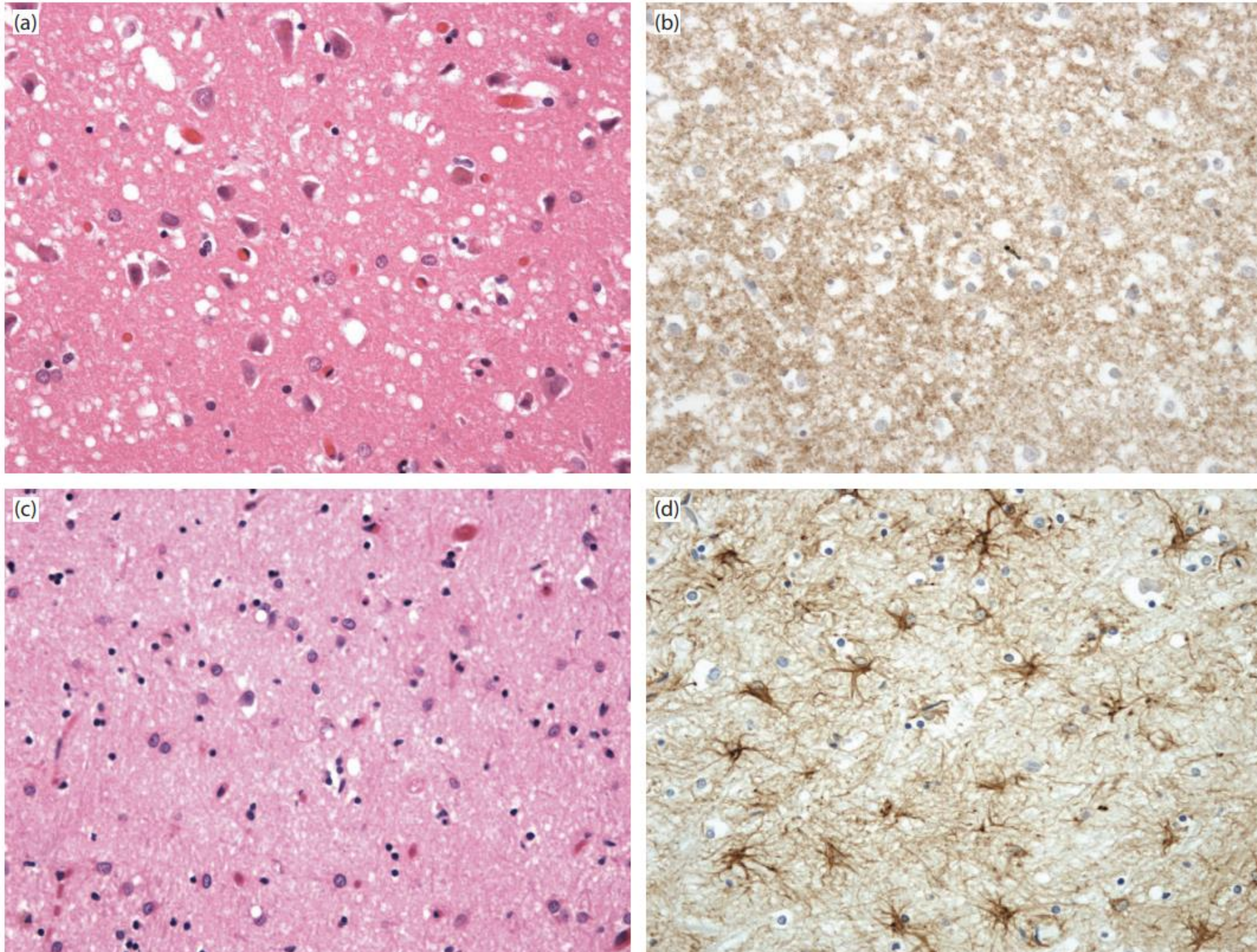
Fatal familial insomnia is a very rare and invariably fatal autosomal dominant neurodegenerative prion disease caused by a mutation of the prion protein (PRNP) gene. Hallmarks of the disease include aggressively progressive insomnia, subsequent autonomic disturbances, including tachycardia, hyperhidrosis, and hypertension, cognitive disturbances including deficits in short-term memory and attention, balance problems, and endocrine dysfunction.

To date at least 70 kindreds affected by FFI with 198 members and 18 unrelated carriers have been published.



The cardinal symptoms of FFI, i.e. apathetic behaviour, attention deficit, hypovigilance and loss of sleep, sympathetic hyperactivity, and progressive attenuation of autonomic and hormonal circadian oscillations, may be related to **selective involvement of the AV and MD thalamic nuclei**. In fact, the severe and consistent atrophy of these nuclei is the only common finding shared by all FFI cases




(a)
(b)
(c)
(d)

The Somatosensory Systems

Michelangelo Buonarroti – The Creation of Adam

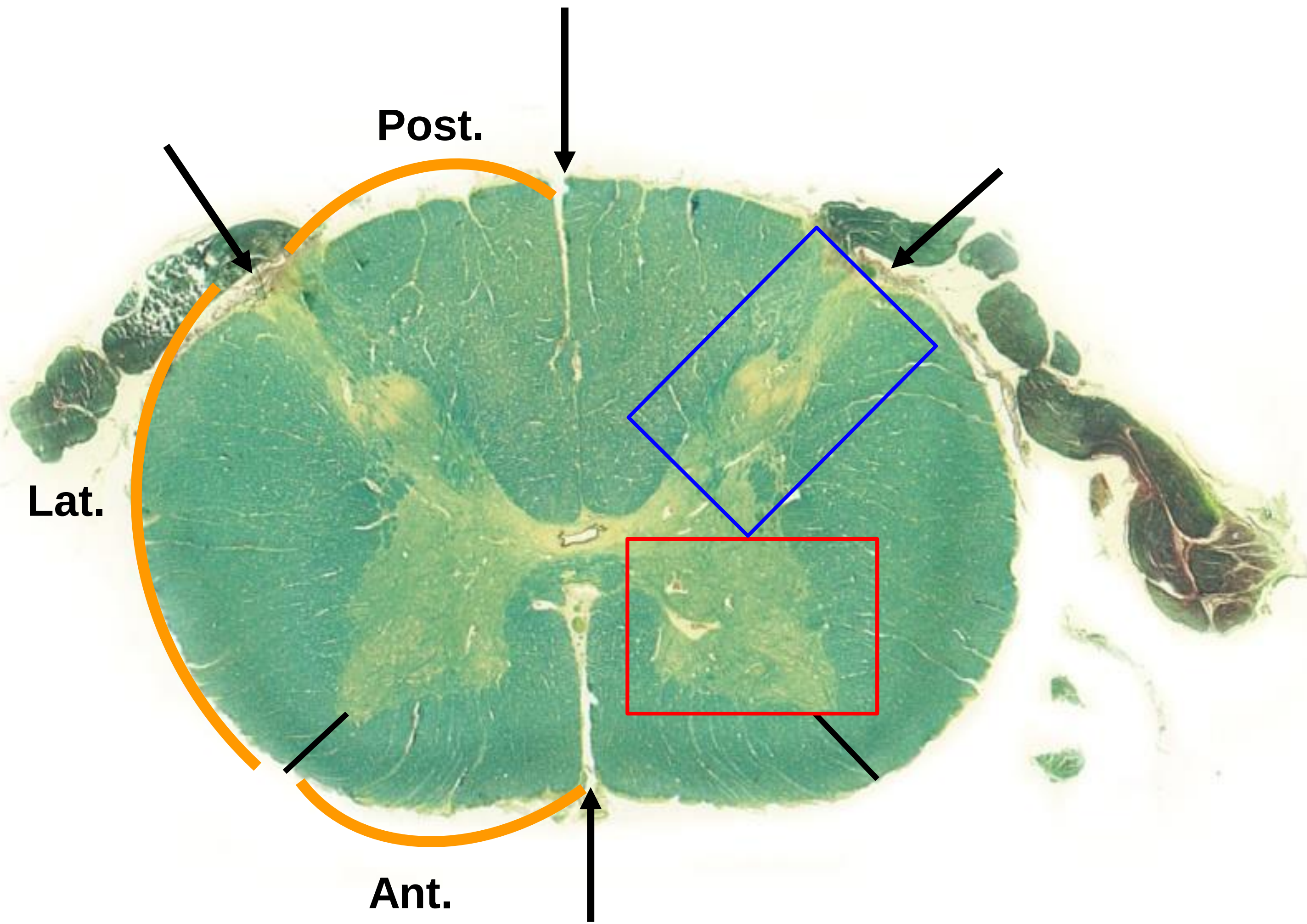
Myself wanting to finish examining slides from a case and go home

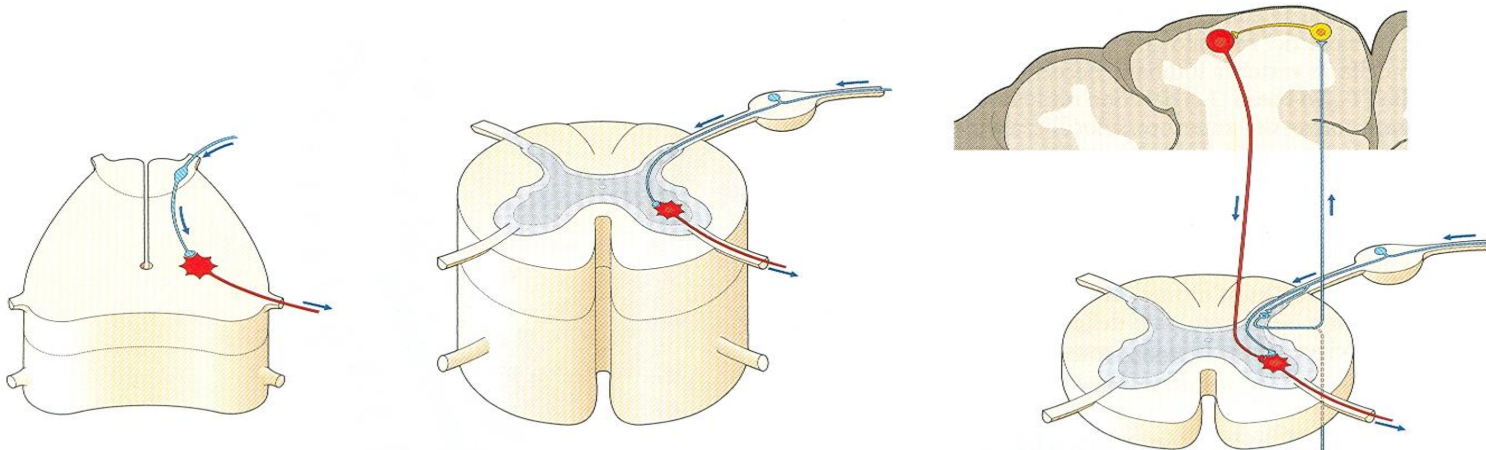
De Caro at 8PM asking to see more memes from the students

My favorite (so far)

anatomy professors trying to organize the human body course:

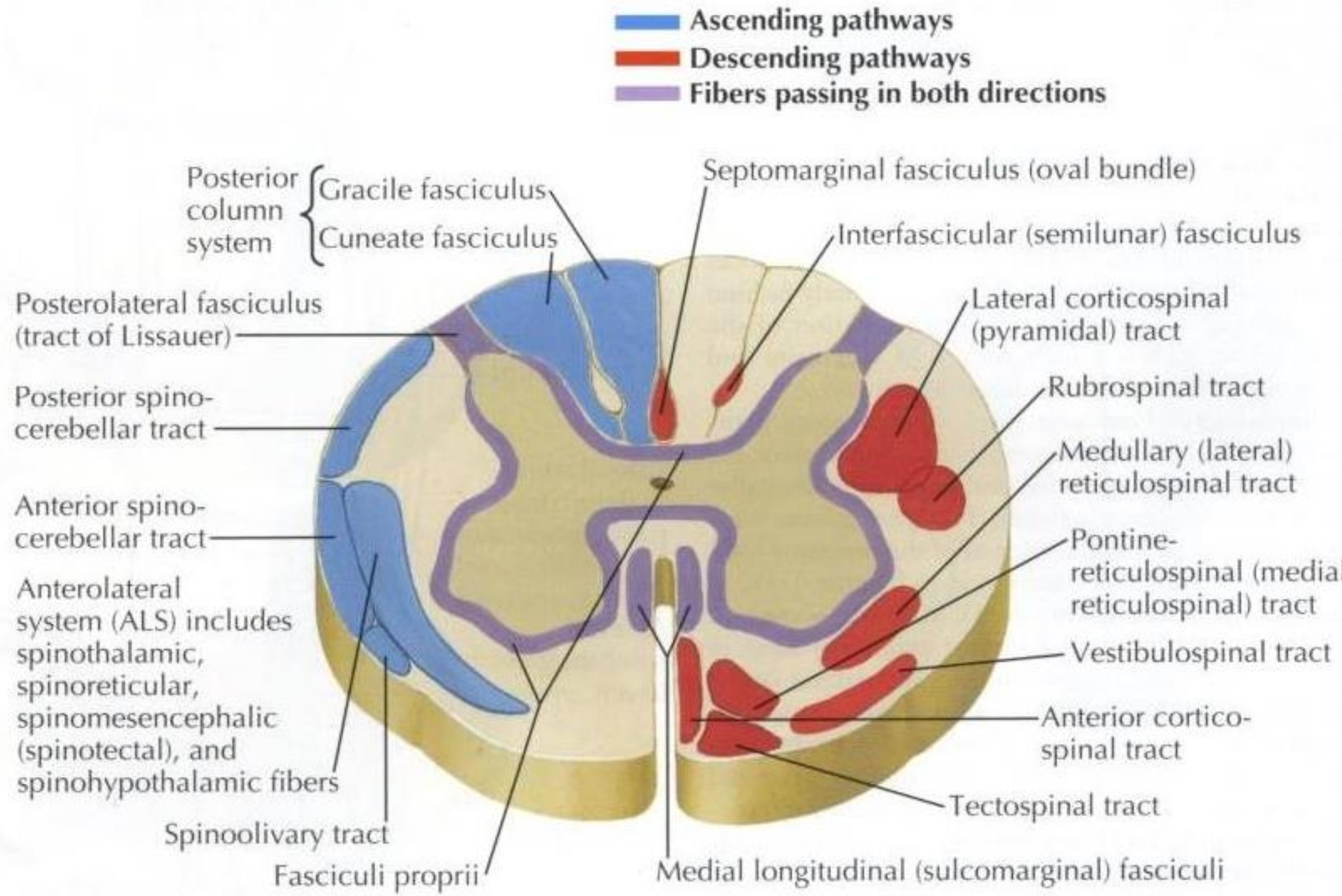
De Caro’s favorite (so far)

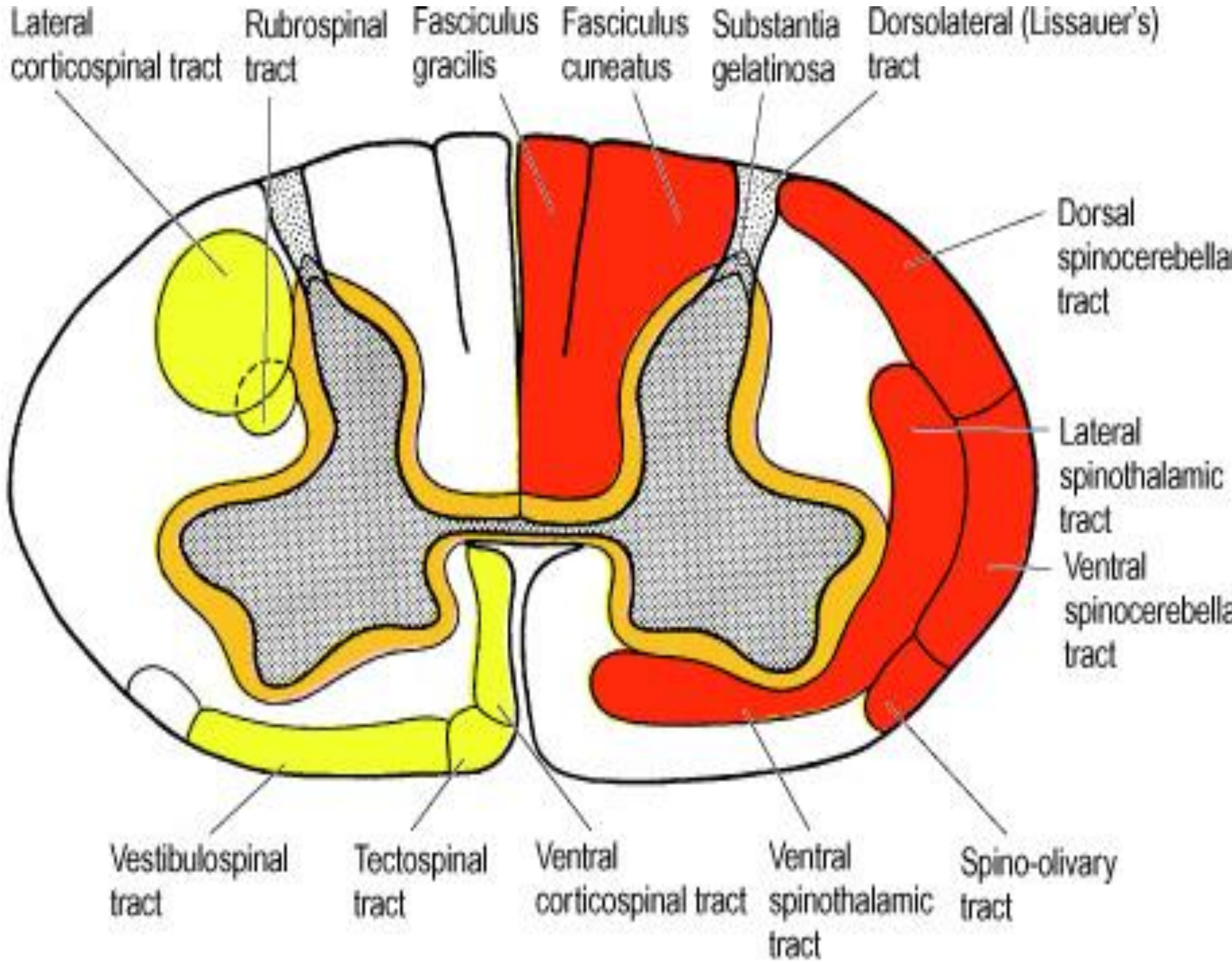

Post.
Lat.
Ant.



a b c

Figura 14.30 - Rappresentazione schematica dei rapporti che si stabiliscono tra neuroni sensitivi (**blu**) e neuroni di moto (**rosso**) in organizzazioni nervose centralizzate. **a**, Nei Cefalocordati, gli elementi sensitivi e quelli effettori sono localizzati nell'asse nervoso; **b**, nei Vertebrati, il protoneurone sensitivo ha sede al di fuori del nevrasse, in formazioni chiamate gangli; **c**, archi riflessi orizzontali a disposizione segmentaria e archi verticali in cui si riconoscono linee di collegamento ascendenti e discendenti.


Ascending pathways
Descending pathways
Fibers passing in both directions
Posterior column system
Gracile fasciculus
Cuneate fasciculus
Septomarginal fasciculus (oval bundle)
Interfascicular (semilunar) fasciculus
Posterolateral fasciculus (tract of Lissauer)
Lateral corticospinal (pyramidal) tract
Rubrospinal tract
Posterior spino-cerebellar tract
Medullary (lateral) reticulospinal tract
Anterior spino-cerebellar tract
Pontine-reticulospinal (medial reticulospinal) tract
Anterolateral system (ALS) includes spinothalamic, spinoreticular, spinomesencephalic (spinotectal), and spinohypothalamic fibers
Vestibulospinal tract
Anterior cortico-spinal tract
Tectospinal tract
Spinoolivary tract
Fasciculi proprii
Medial longitudinal (sulcomarginal) fasciculi



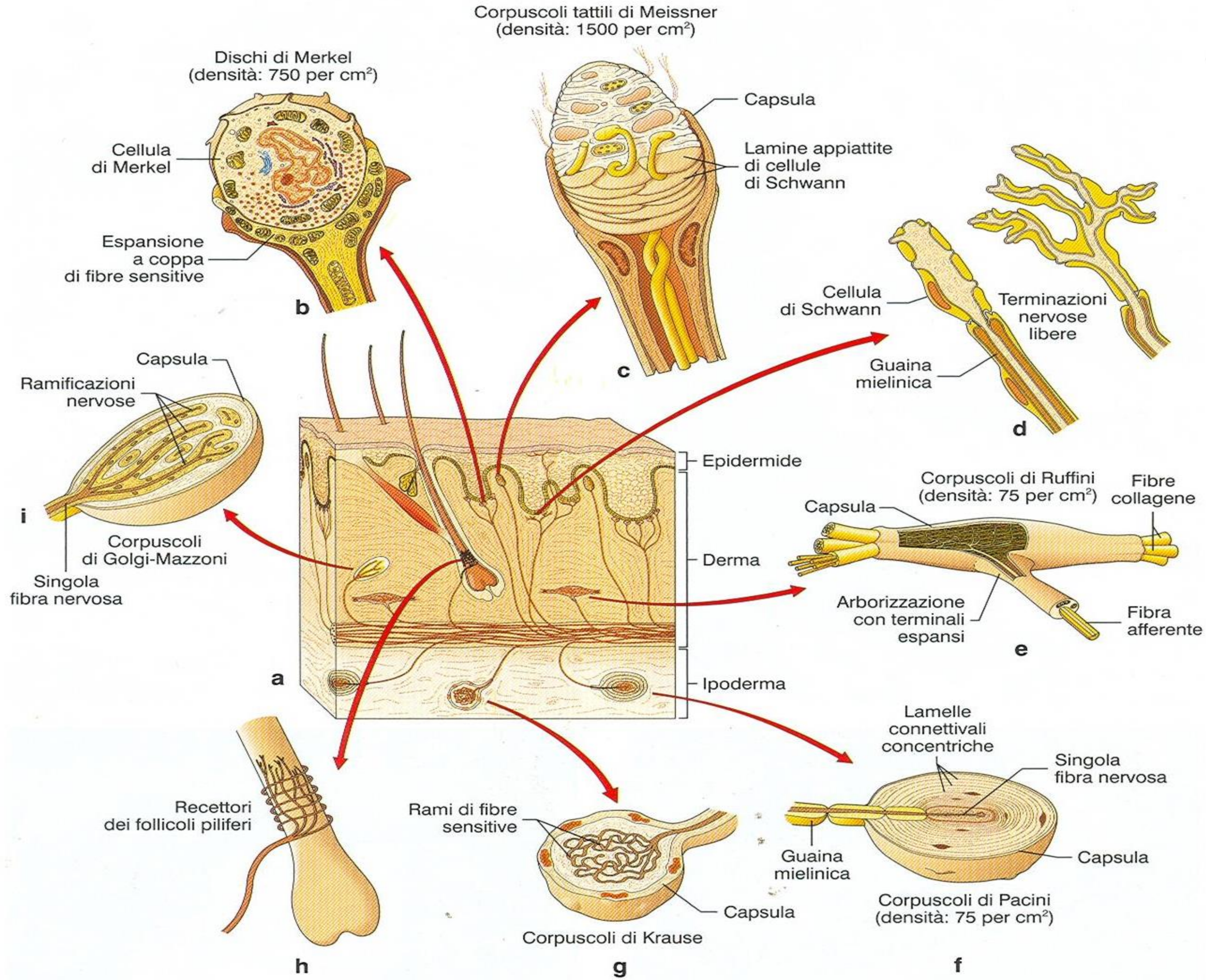
Lateral corticospinal tract
Rubrospinal tract
Fasciculus gracilis
Fasciculus cuneatus
Substantia gelatinosa
Dorsolateral (Lissauer's) tract
Dorsal spinocerebellar tract
Lateral spinothalamic tract
Ventral spinocerebellar tract
Vestibulospinal tract
Tectospinal tract
Ventral corticospinal tract
Ventral spinothalamic tract
Spino-olivary tract

Types of Sensitivity

- *Tactile (Touch):* - Protopartic

  - Epicritic

- *Proprioceptive* (Conscious vs Non-Conscious)
- *Enteroceptive*
- *Nociceptive* (Pain and Temperature)



Corpuscoli tattili di Meissner
(densità: 1500 per cm²)
Dischi di Merkel
(densità: 750 per cm²)
Capsula
Cellula
di Merkel
Lamine appiattite
di cellule
di Schwann
Espansione
a coppa
di fibre sensitive
b
c
Cellula
di Schwann
Terminazioni
nervose
libere
Guaina
mielinica
d
Capsula
Ramificazioni
nervose
i
Corpuscoli
di Golgi-Mazzoni
Singola
fibra nervosa
Epidermide
Derma
Ipoderma
a
Corpuscoli di Ruffini
(densità: 75 per cm²)
Fibre
collagene
Capsula
Arborizzazione
con terminali
espansi
Fibra
afferente
e
Lamelle
connettivali
concentriche
Singola
fibra nervosa
Guaina
mielinica
Capsula
Corpuscoli di Pacini
(densità: 75 per cm²)
f
Recettori
dei follicoli piliferi
h
Rami di fibre
sensitive
Capsula
Corpuscoli di Krause
g

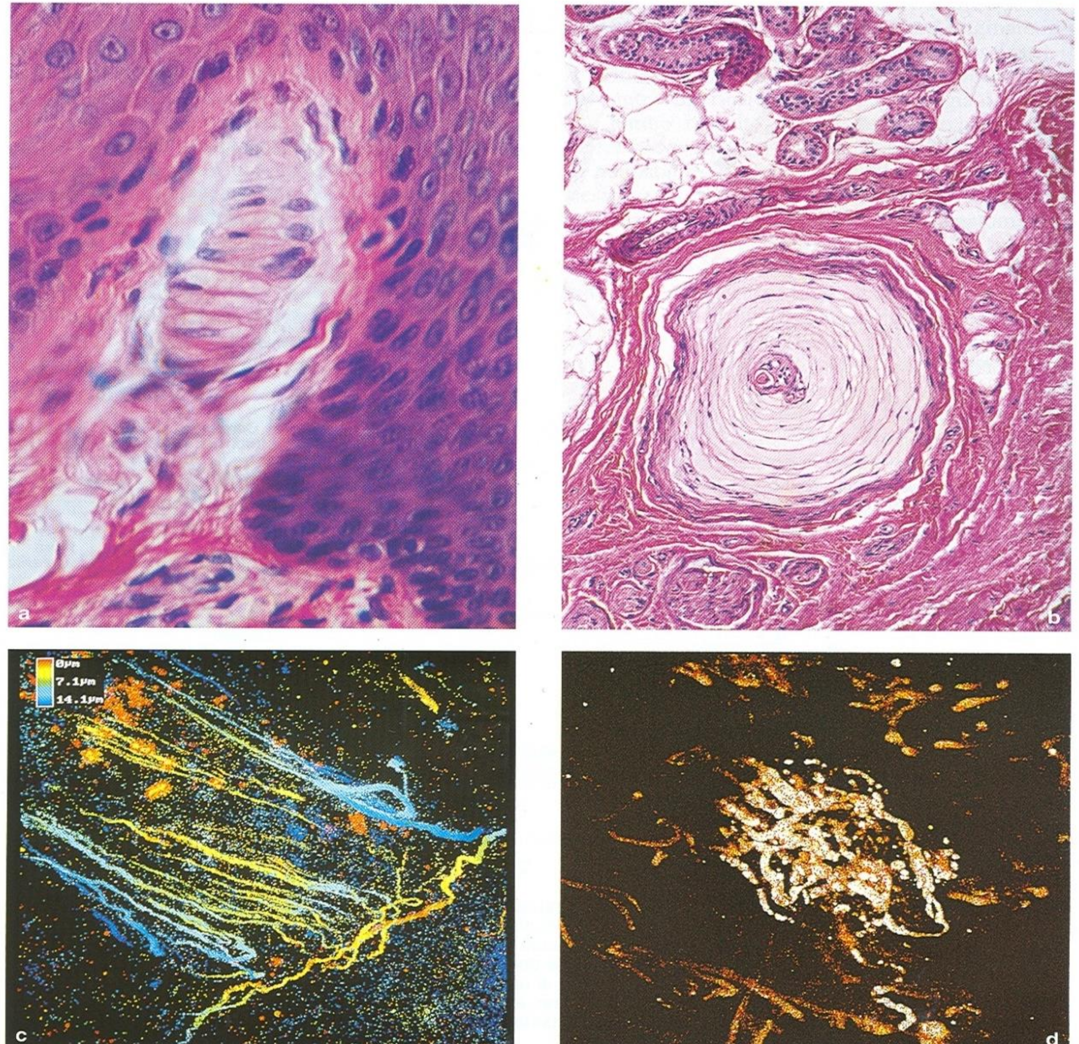


Figura R14.1-2 - Alcune terminazioni corpuscolate della pelle umana. **a**, Corpuscolo di Meissner entro una papilla dermica; **b**, corpuscolo di Pacini, in sezione trasversale, nel derma profondo; **c**, reticolo perifollicolare; **d**, clava di Krause (del freddo) nel derma intermedio (**b**, **c**: microscopio confocale a scansione laser).

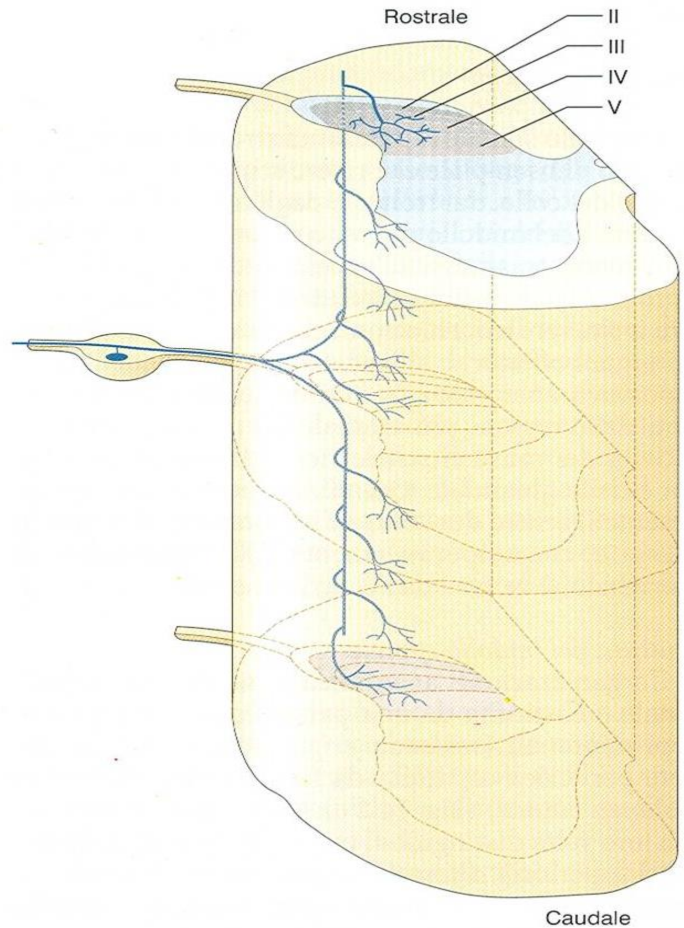
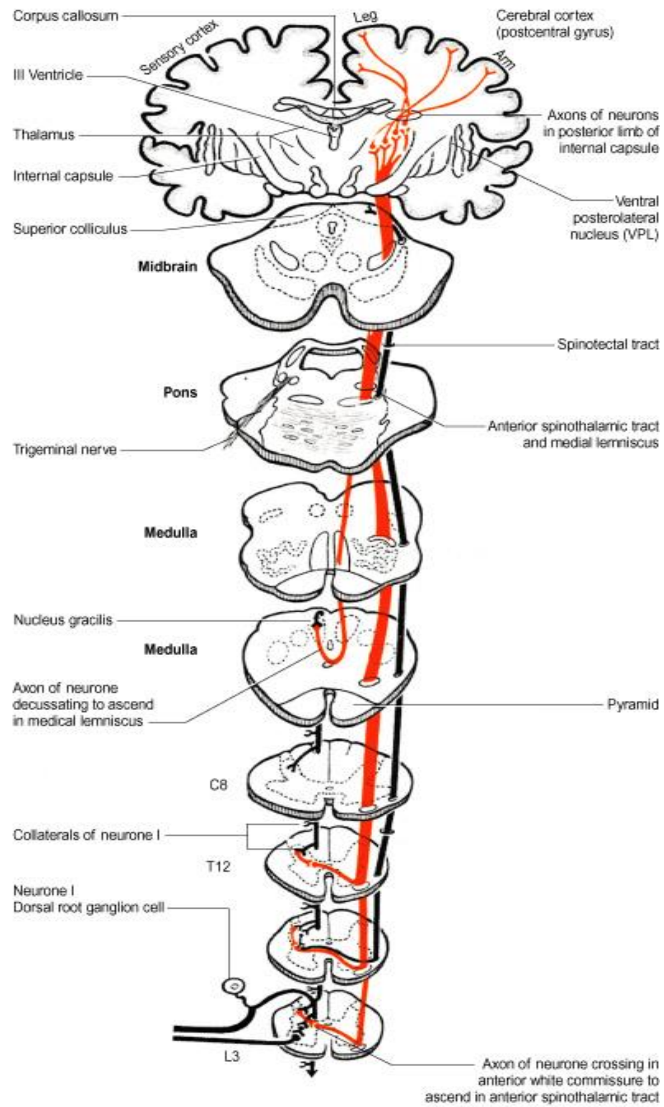
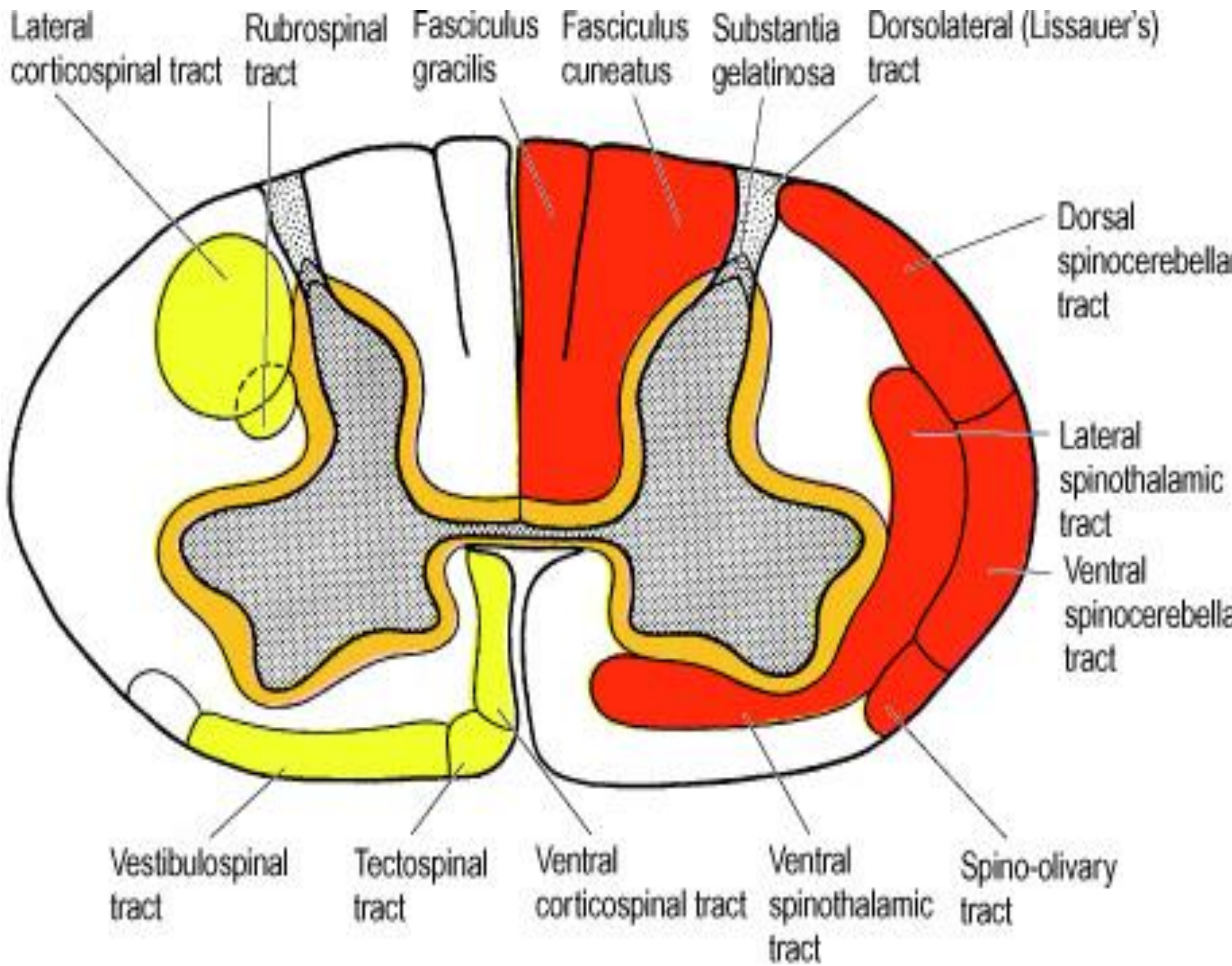
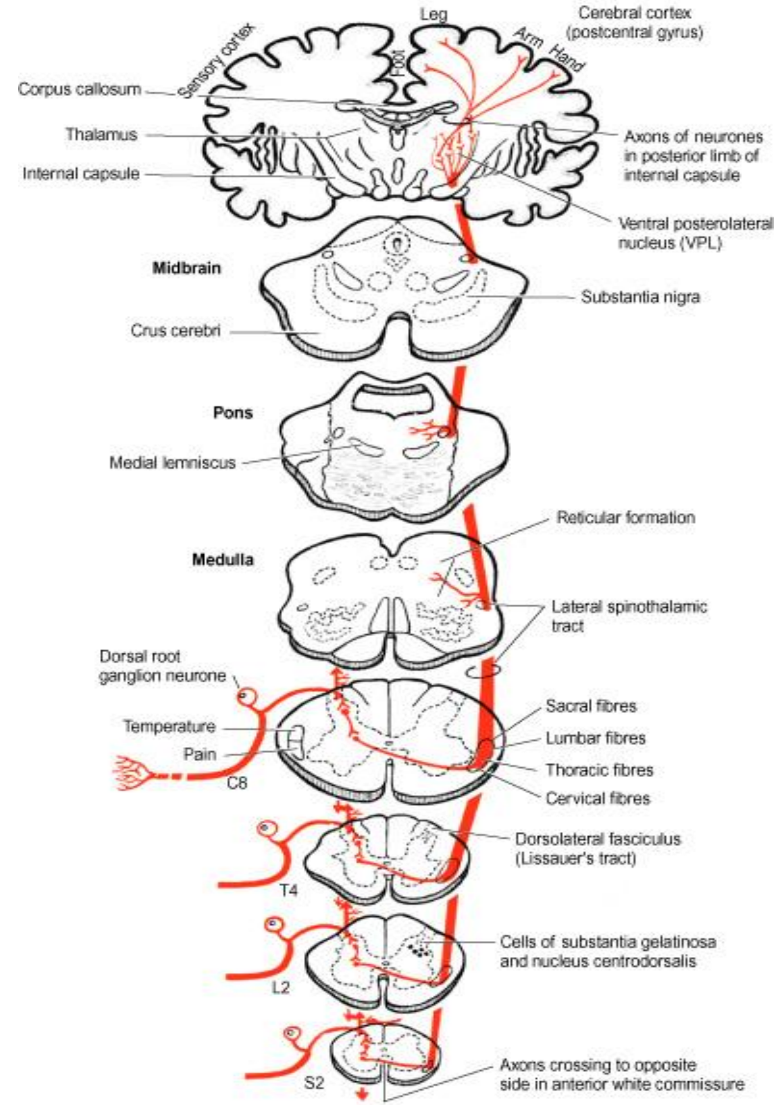


Figura R14.1-4 - Ricostruzione tridimensionale del corno posteriore del midollo spinale. Sono rappresentate la biforcazione a T del ramo centripeto del neurone gangliare e la distribuzione delle sue collaterali all'interno della sostanza grigia del corno posteriore.

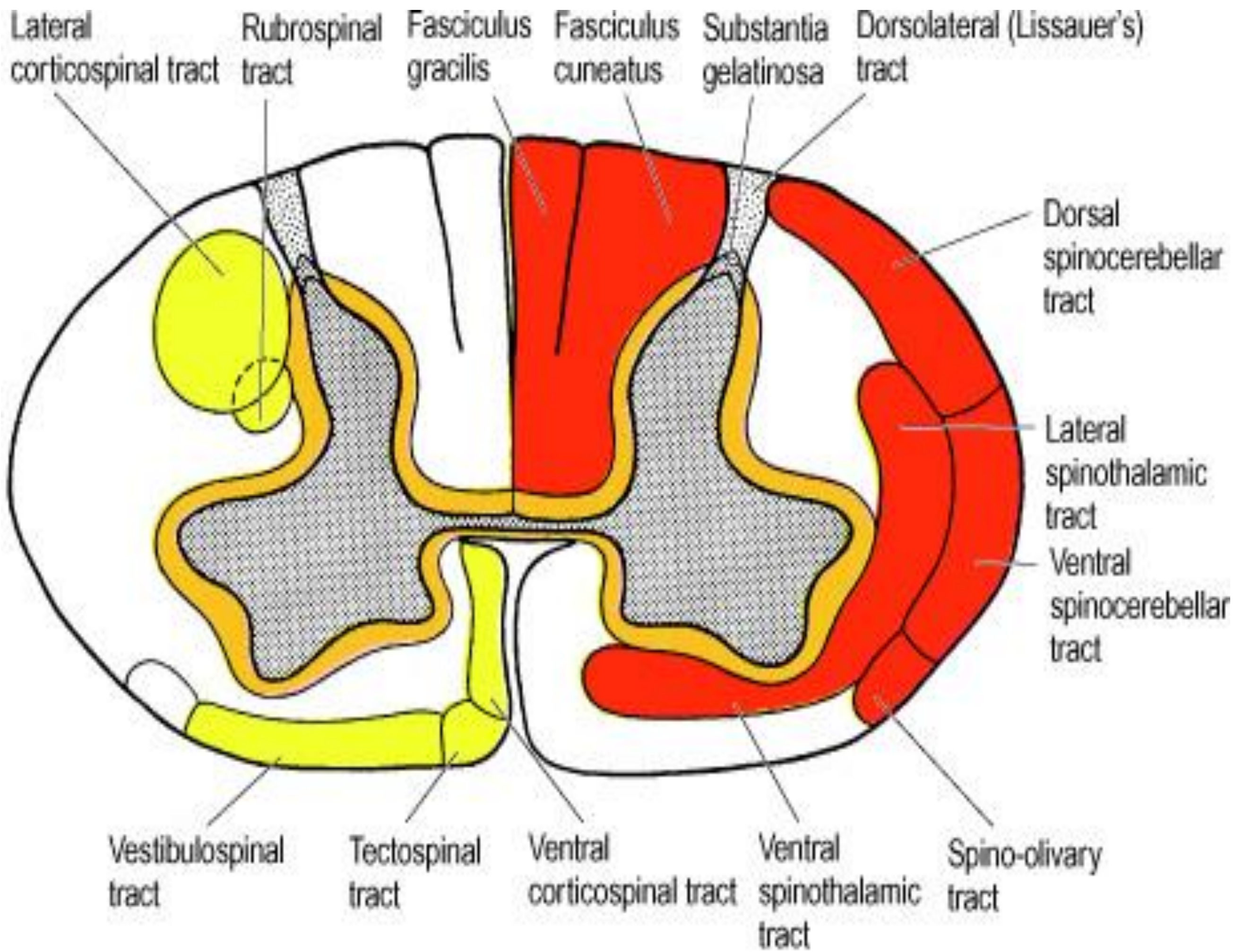

Corpus callosum
Sensory cortex
Leg
Cerebral cortex
(postcentral gyrus)
Arm
III Ventricle
Thalamus
Internal capsule
Axons of neurons
in posterior limb of
internal capsule
Ventral
posterolateral
nucleus (VPL)
Superior colliculus
Midbrain
Spinotectal tract
Pons
Anterior spinothalamic tract
and medial lemniscus
Trigeminal nerve
Medulla
Nucleus gracilis
Medulla
Axon of neurone
decussating to ascend
in medical lemniscus
Pyramid
C8
Collaterals of neurone I
T12
Neurone I
Dorsal root ganglion cell
L3
Axon of neurone crossing in
anterior white commissure to
ascend in anterior spinothalamic tract

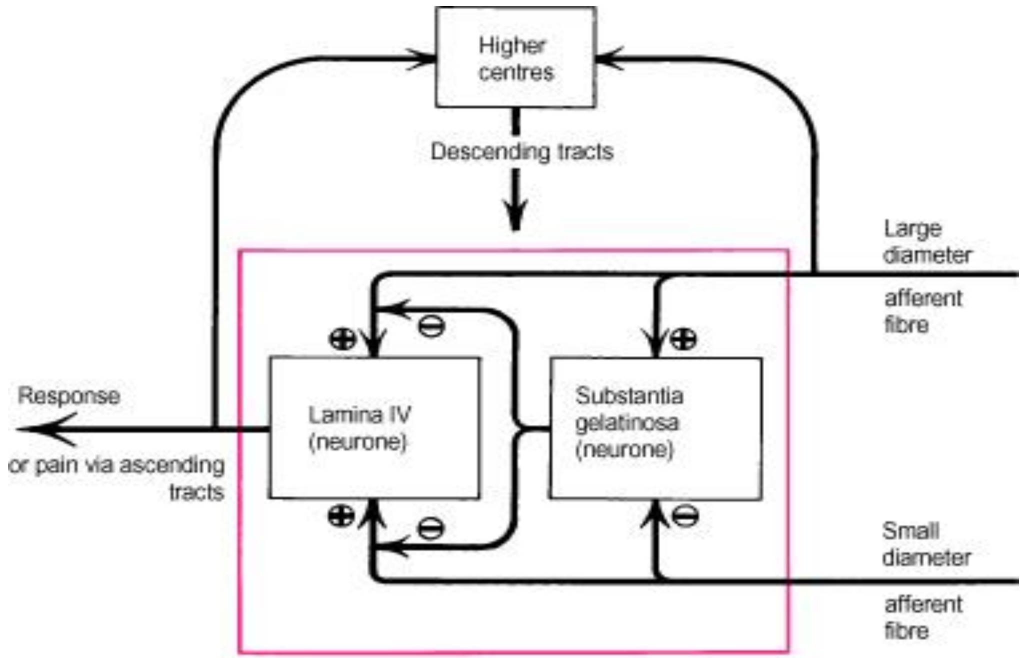


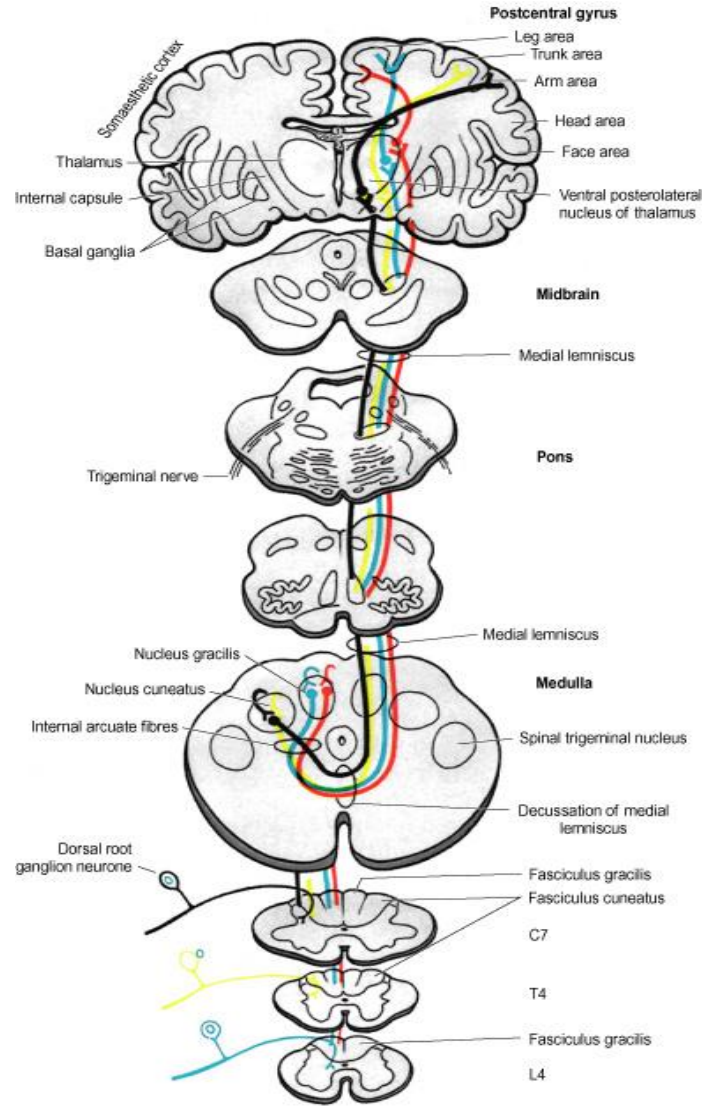
Lateral corticospinal tract
Rubrospinal tract
Fasciculus gracilis
Fasciculus cuneatus
Substantia gelatinosa
Dorsolateral (Lissauer's) tract
Dorsal spinocerebellar tract
Lateral spinothalamic tract
Ventral spinocerebellar tract
Vestibulospinal tract
Tectospinal tract
Ventral corticospinal tract
Ventral spinothalamic tract
Spino-olivary tract

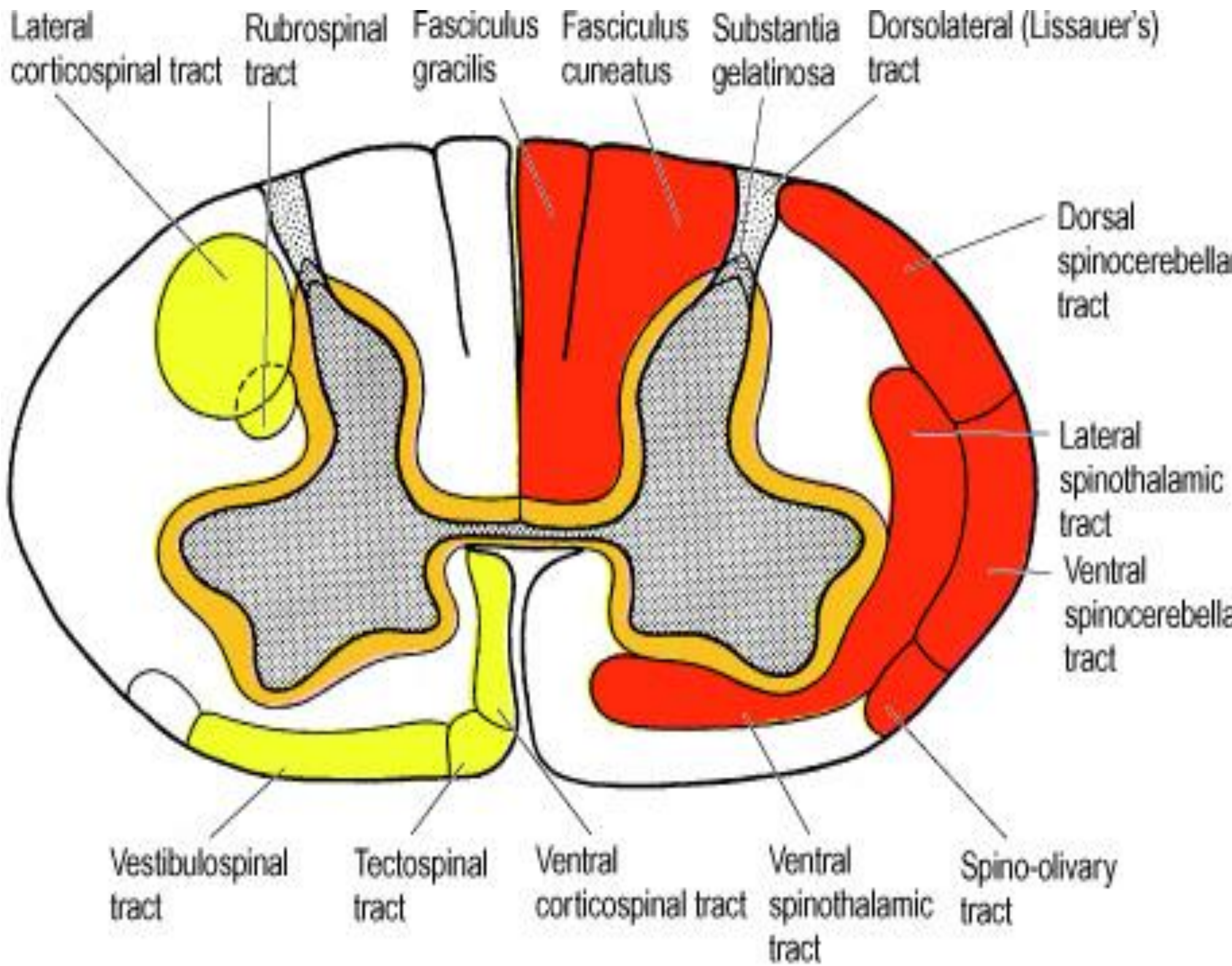


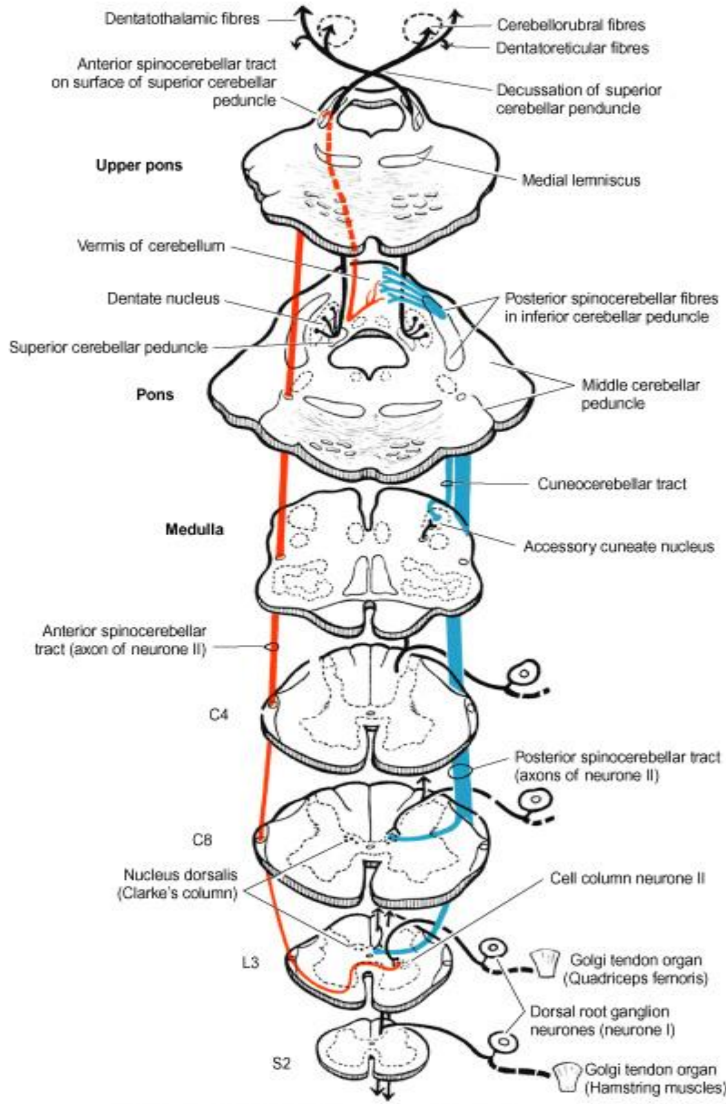
Leg
Cerebral cortex
(postcentral gyrus)
Sensory cortex
Foot
Arm
Hand
Corpus callosum
Thalamus
Internal capsule
Axons of neurones
in posterior limb of
internal capsule
Ventral posterolateral
nucleus (VPL)
Midbrain
Substantia nigra
Crus cerebri
Pons
Medial lemniscus
Reticular formation
Medulla
Lateral spinothalamic
tract
Dorsal root
ganglion neurone
Temperature
Pain
C8
Sacral fibres
Lumbar fibres
Thoracic fibres
Cervical fibres
Dorsolateral fasciculus
(Lissauer's tract)
T4
Cells of substantia gelatinosa
and nucleus centrodorsalis
L2
S2
Axons crossing to opposite
side in anterior white commissure


Lateral corticospinal tract
Rubrospinal tract
Fasciculus gracilis
Fasciculus cuneatus
Substantia gelatinosa
Dorsolateral (Lissauer's) tract
Dorsal spinocerebellar tract
Lateral spinothalamic tract
Ventral spinocerebellar tract
Vestibulospinal tract
Tectospinal tract
Ventral corticospinal tract
Ventral spinothalamic tract
Spino-olivary tract

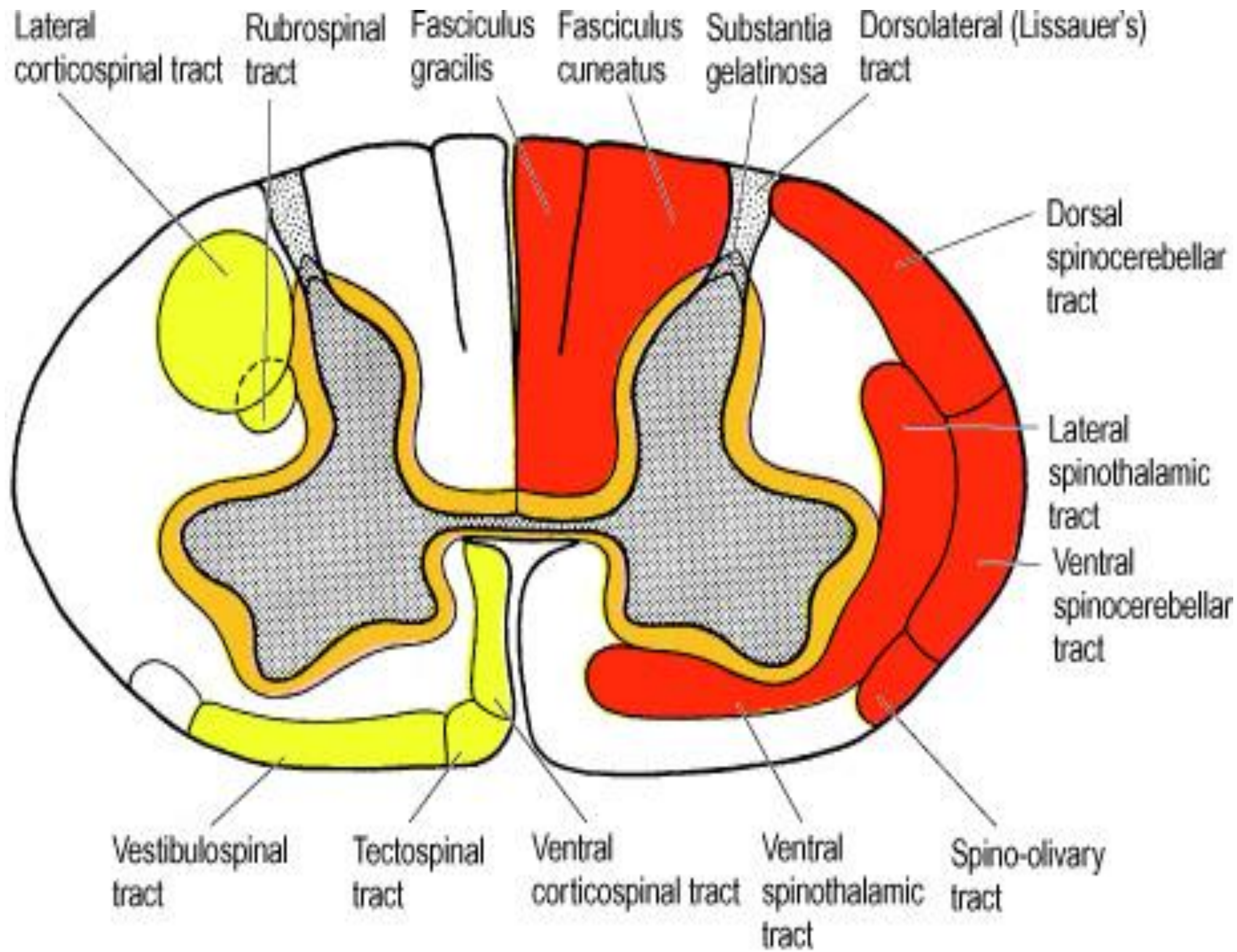

Higher
centres
Descending tracts
Large
diameter
afferent
fibre
Response
or pain via ascending
tracts
Lamina IV
(neurone)
Substantia
gelatinosa
(neurone)
Small
diameter
afferent
fibre


Postcentral gyrus
Leg area
Trunk area
Arm area
Head area
Face area
Somaesthetic cortex
Thalamus
Internal capsule
Basal ganglia
Ventral posterolateral nucleus of thalamus
Midbrain
Medial lemniscus
Pons
Trigeminal nerve
Medial lemniscus
Nucleus gracilis
Nucleus cuneatus
Internal arcuate fibres
Medulla
Spinal trigeminal nucleus
Decussation of medial lemniscus
Dorsal root ganglion neurone
Fasciculus gracilis
Fasciculus cuneatus
C7
T4
Fasciculus gracilis
L4

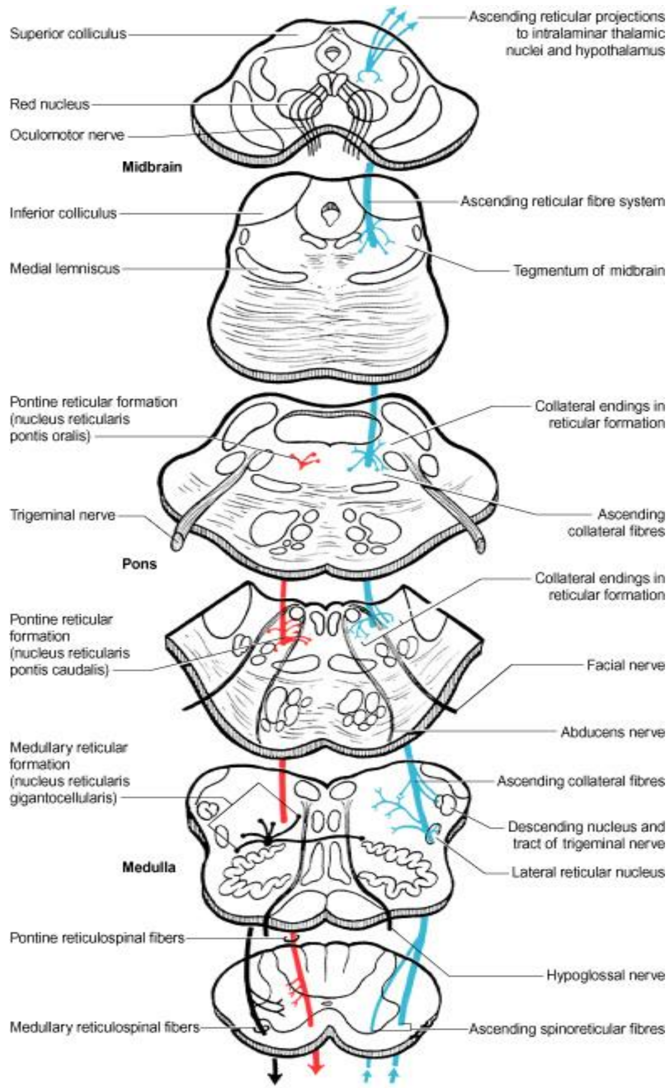

Lateral corticospinal tract
Rubrospinal tract
Fasciculus gracilis
Fasciculus cuneatus
Substantia gelatinosa
Dorsolateral (Lissauer's) tract
Dorsal spinocerebellar tract
Lateral spinothalamic tract
Ventral spinocerebellar tract
Vestibulospinal tract
Tectospinal tract
Ventral corticospinal tract
Ventral spinothalamic tract
Spino-olivary tract



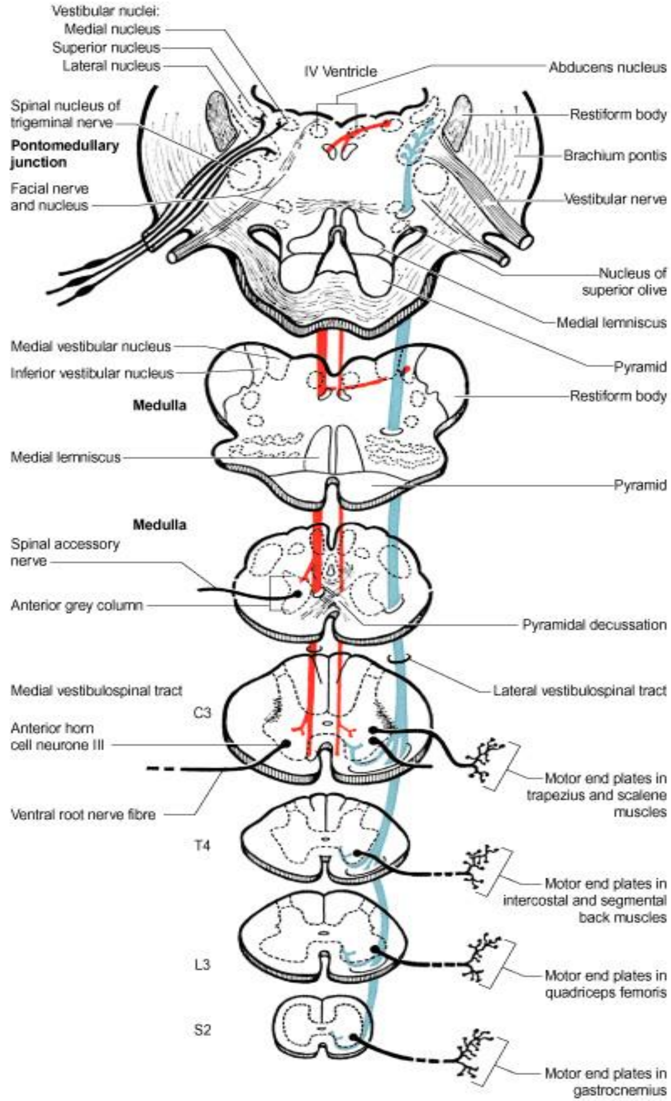
Dentatothalamic fibres
Cerebellorubral fibres
Dentatoreticular fibres
Anterior spinocerebellar tract on surface of superior cerebellar peduncle
Decussation of superior cerebellar peduncle
Upper pons
Medial lemniscus
Vermis of cerebellum
Dentate nucleus
Posterior spinocerebellar fibres in inferior cerebellar peduncle
Superior cerebellar peduncle
Pons
Middle cerebellar peduncle
Cuneocerebellar tract
Medulla
Accessory cuneate nucleus
Anterior spinocerebellar tract (axon of neurone II)
C4
Posterior spinocerebellar tract (axons of neurone II)
C8
Nucleus dorsalis (Clarke's column)
Cell column neurone II
L3
Golgi tendon organ (Quadriceps femoris)
Dorsal root ganglion neurones (neurone I)
S2
Golgi tendon organ (Hamstring muscles)



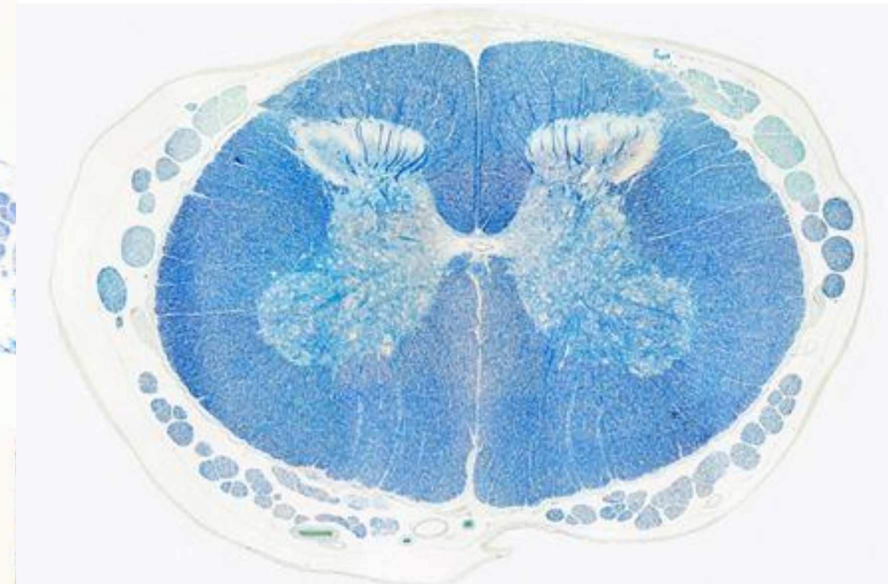
Lateral corticospinal tract
Rubrospinal tract
Fasciculus gracilis
Fasciculus cuneatus
Substantia gelatinosa
Dorsolateral (Lissauer's) tract
Dorsal spinocerebellar tract
Lateral spinothalamic tract
Ventral spinocerebellar tract
Vestibulospinal tract
Tectospinal tract
Ventral corticospinal tract
Ventral spinothalamic tract
Spino-olivary tract



Superior colliculus
Red nucleus
Oculomotor nerve
Midbrain
Ascending reticular projections to intralaminar thalamic nuclei and hypothalamus
Inferior colliculus
Medial lemniscus
Ascending reticular fibre system
Tegmentum of midbrain
Pontine reticular formation (nucleus reticularis pontis oralis)
Trigeminal nerve
Pons
Collateral endings in reticular formation
Ascending collateral fibres
Pontine reticular formation (nucleus reticularis pontis caudalis)
Collateral endings in reticular formation
Facial nerve
Abducens nerve
Medullary reticular formation (nucleus reticularis gigantocellularis)
Medulla
Ascending collateral fibres
Descending nucleus and tract of trigeminal nerve
Lateral reticular nucleus
Pontine reticulospinal fibers
Medullary reticulospinal fibers
Hypoglossal nerve
Ascending spinoreticular fibres

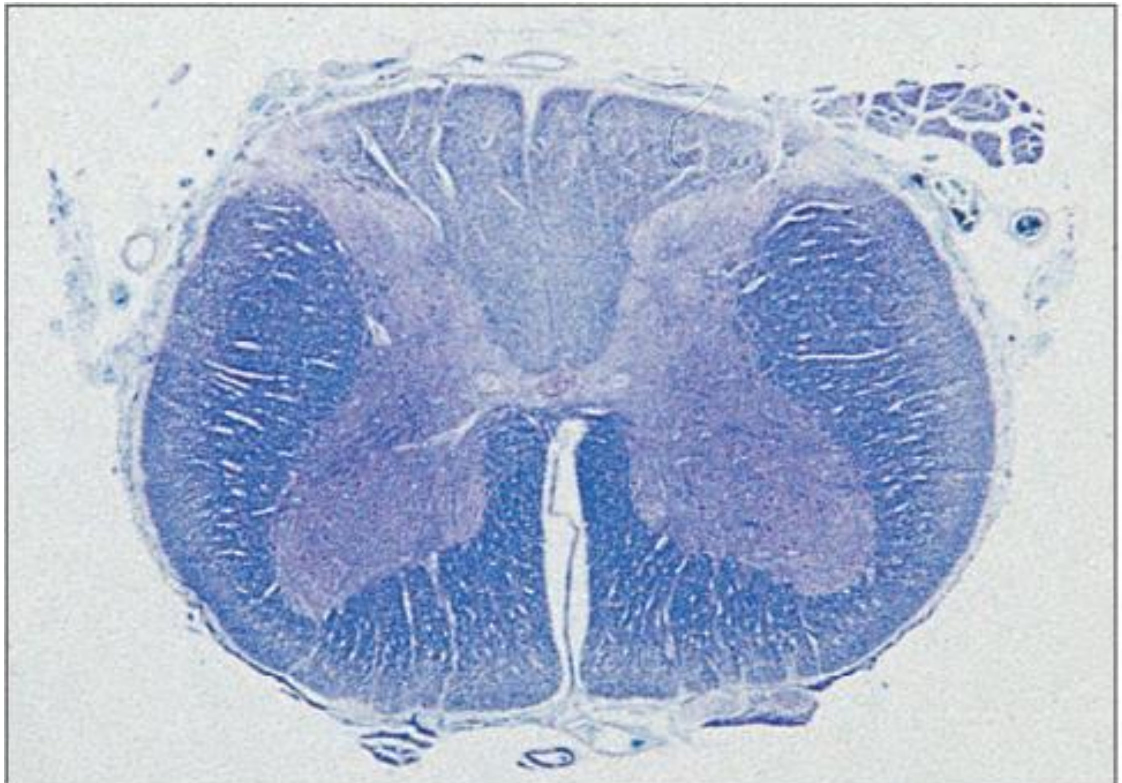


Vestibular nuclei:
Medial nucleus
Superior nucleus
Lateral nucleus
IV Ventricle
Abducens nucleus
Spinal nucleus of trigeminal nerve
Restiform body
Pontomedullary junction
Brachium pontis
Facial nerve and nucleus
Vestibular nerve
Nucleus of superior olive
Medial lemniscus
Medial vestibular nucleus
Pyramid
Inferior vestibular nucleus
Restiform body
Medulla
Medial lemniscus
Pyramid
Medulla
Spinal accessory nerve
Anterior grey column
Pyramidal decussation
Medial vestibulospinal tract
Lateral vestibulospinal tract
C3
Anterior horn cell neurone III
Motor end plates in trapezius and scalene muscles
Ventral root nerve fibre
T4
Motor end plates in intercostal and segmental back muscles
L3
Motor end plates in quadriceps femoris
S2
Motor end plates in gastrocnemius

FRIEDREICH'S ATAXIA

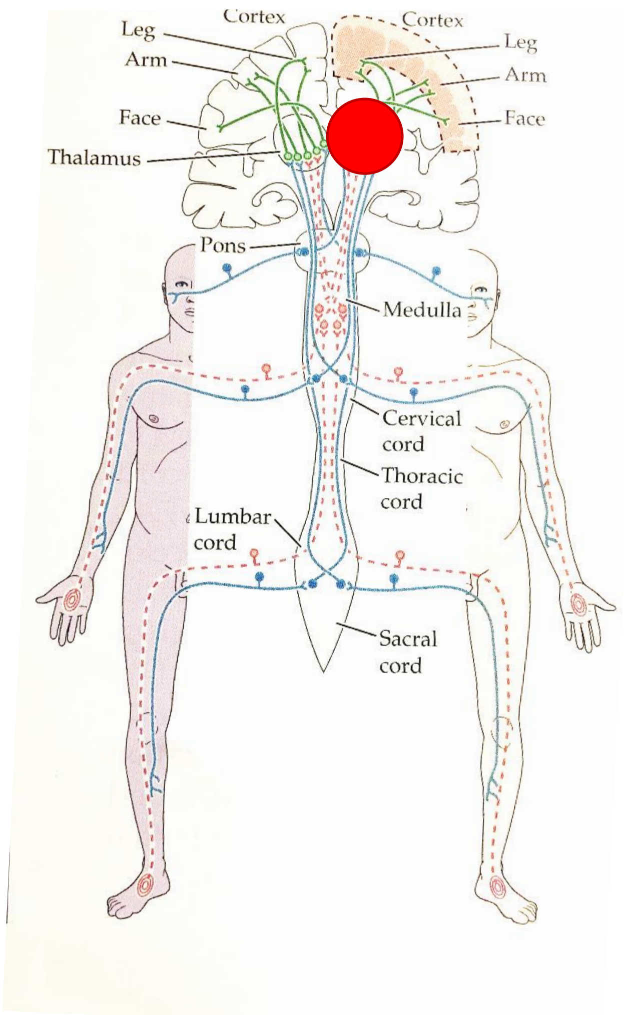
Caused by expansion of GAA triplets (normal 6-34, pathological 1000+), chromosome 9q in FRDA, encoding frataxin.
- Low levels of frataxin lead to iron accumulation in mitochondria -> oxidative stress and neurodegeneration

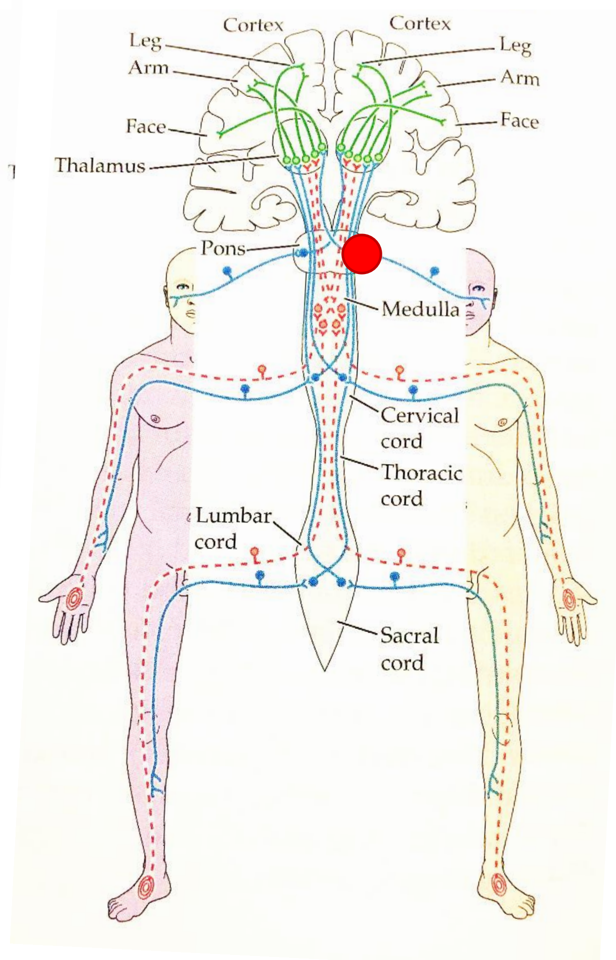


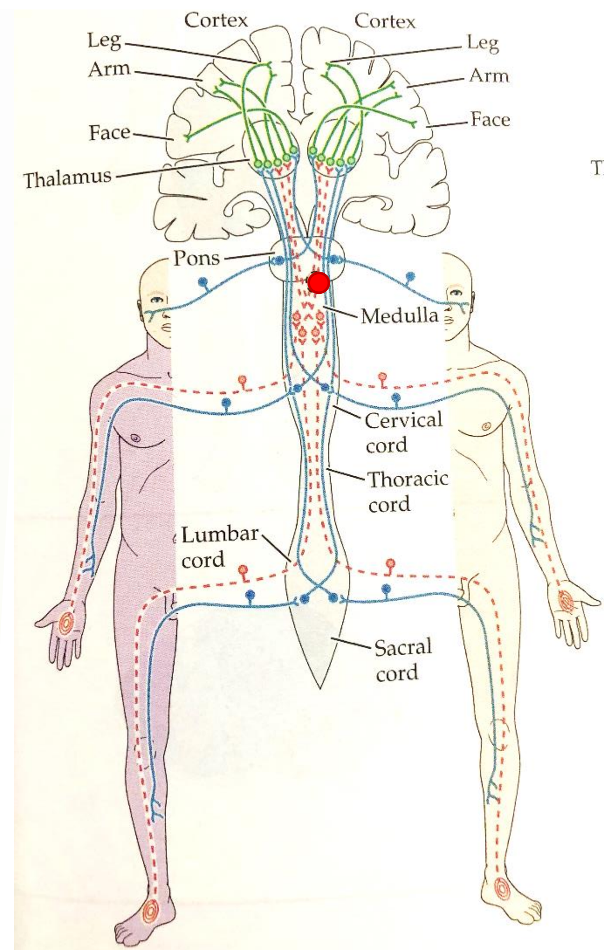
Tabes Dorsalis

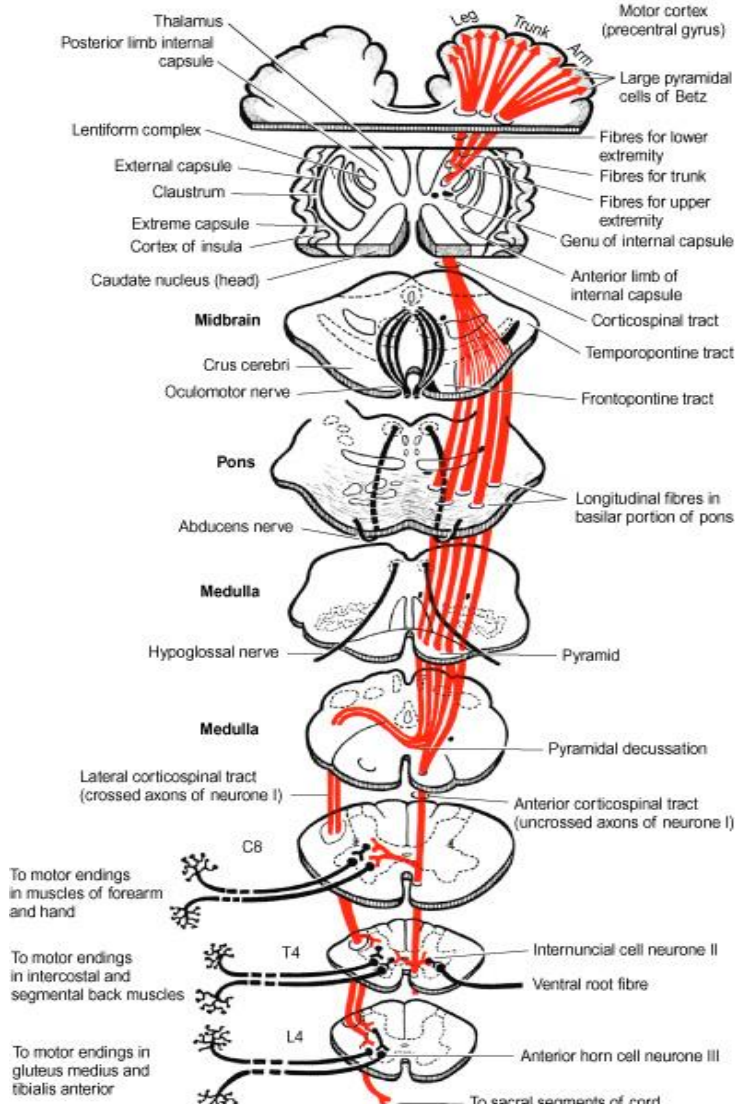
- Following syphilitic infection (15-20 years following first infection)
- Due to chronic inflammatory disease of the dorsal roots and ganglia with associated degeneration of the posterior columns of the spinal cord.
- With progression, loss of pain and proprioceptive sensation may lead to recurrent joint trauma and degeneration (Charcot's joints), and ulceration of the feet.
- characteristic shuffling broad-based gait due to the proprioceptive deficit.

Thalamic or Cortical lesion **Lateral pontine or medullary lesion** **Medial medullary lesion**

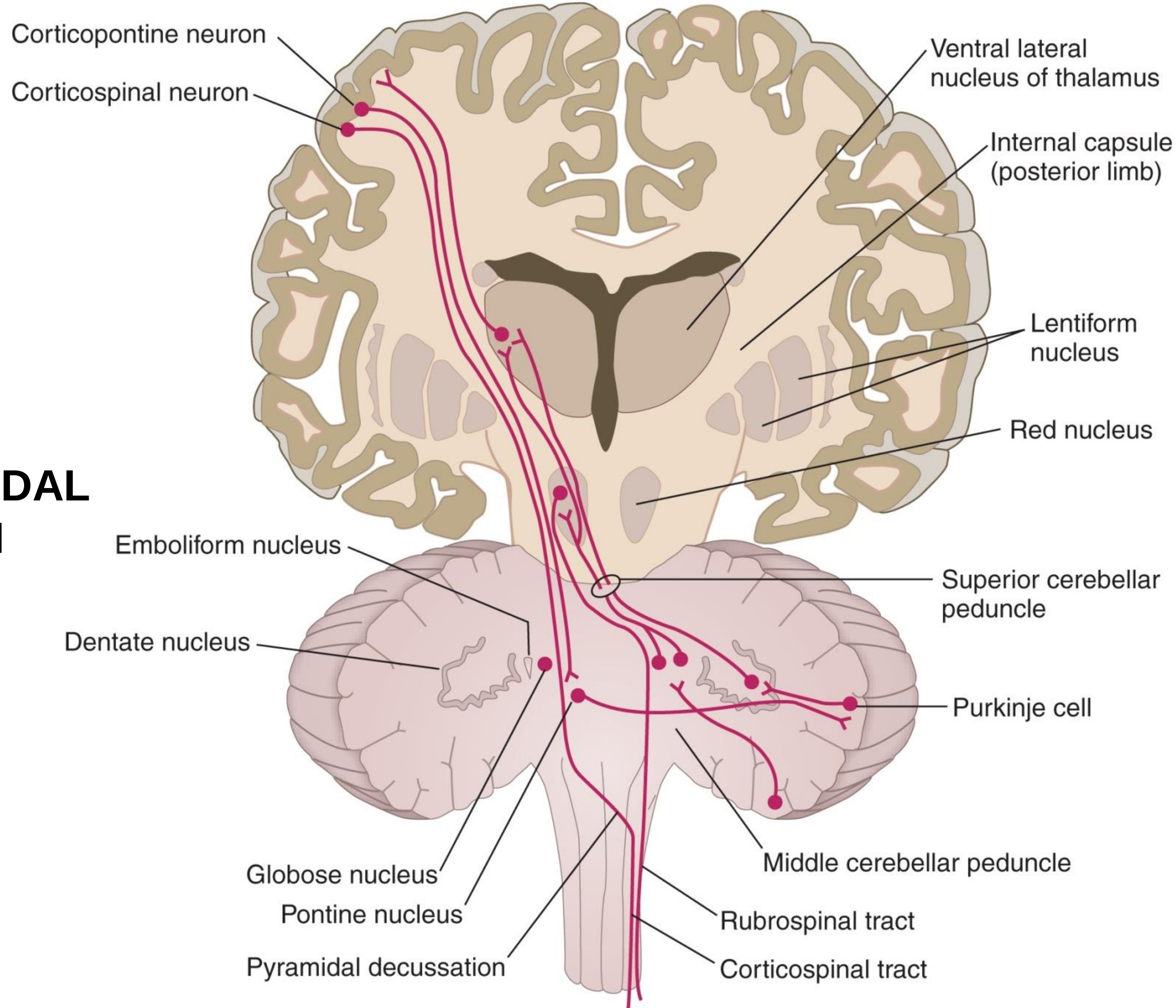






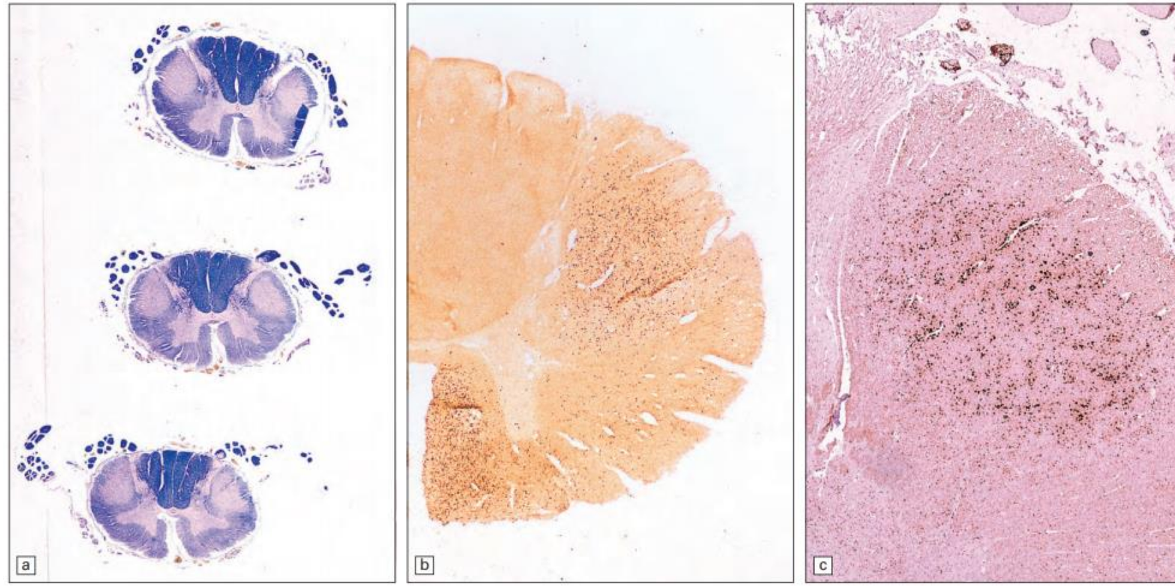

Thalamus
Posterior limb internal capsule
Leg
Trunk
Arm
Motor cortex (precentral gyrus)
Large pyramidal cells of Betz
Lentiform complex
External capsule
Claustrum
Extreme capsule
Cortex of insula
Caudate nucleus (head)
Fibres for lower extremity
Fibres for trunk
Fibres for upper extremity
Genu of internal capsule
Anterior limb of internal capsule
Corticospinal tract
Temporopontine tract
Frontopontine tract
Midbrain
Crus cerebri
Oculomotor nerve
Pons
Longitudinal fibres in basilar portion of pons
Abducens nerve
Medulla
Hypoglossal nerve
Pyramid
Medulla
Pyramidal decussation
Lateral corticospinal tract (crossed axons of neurone I)
Anterior corticospinal tract (uncrossed axons of neurone I)
C8
To motor endings in muscles of forearm and hand
T4
Internuncial cell neurone II
To motor endings in intercostal and segmental back muscles
Ventral root fibre
L4
To motor endings in gluteus medius and tibialis anterior
Anterior horn cell neurone III
To sacral segments of cord

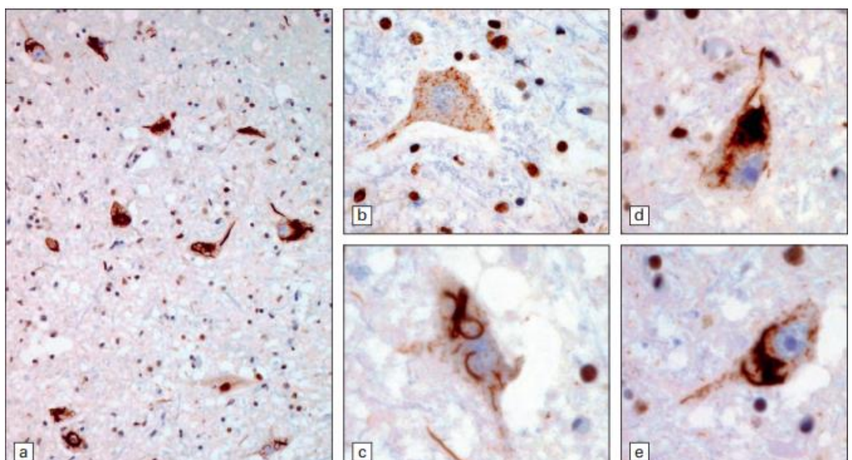
ESOPYRAMIDAL SYSTEM

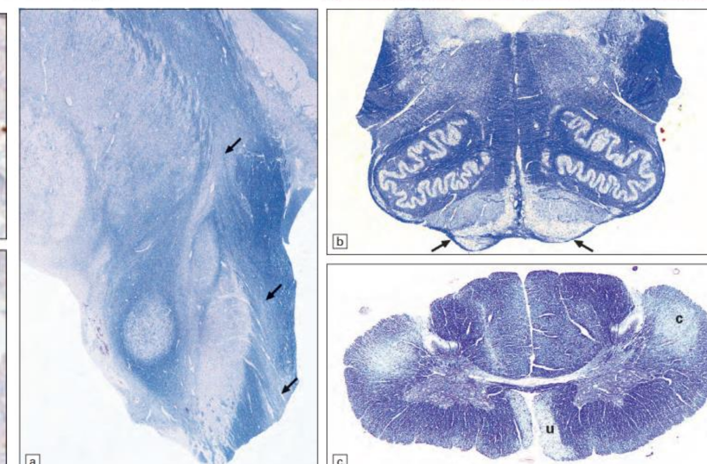


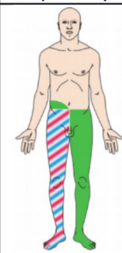
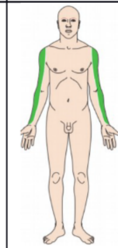
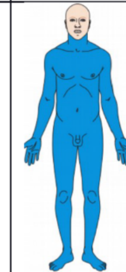
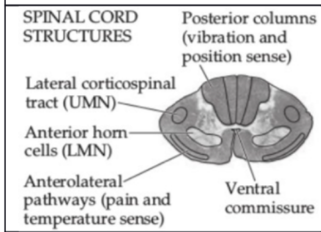
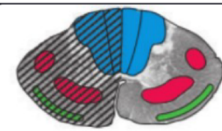
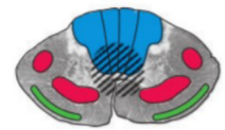
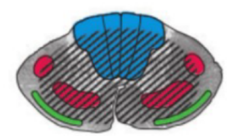
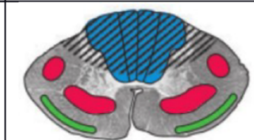
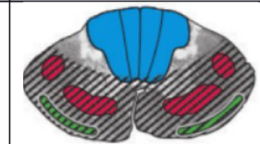
Aymotrophic Lateral Sclerosis

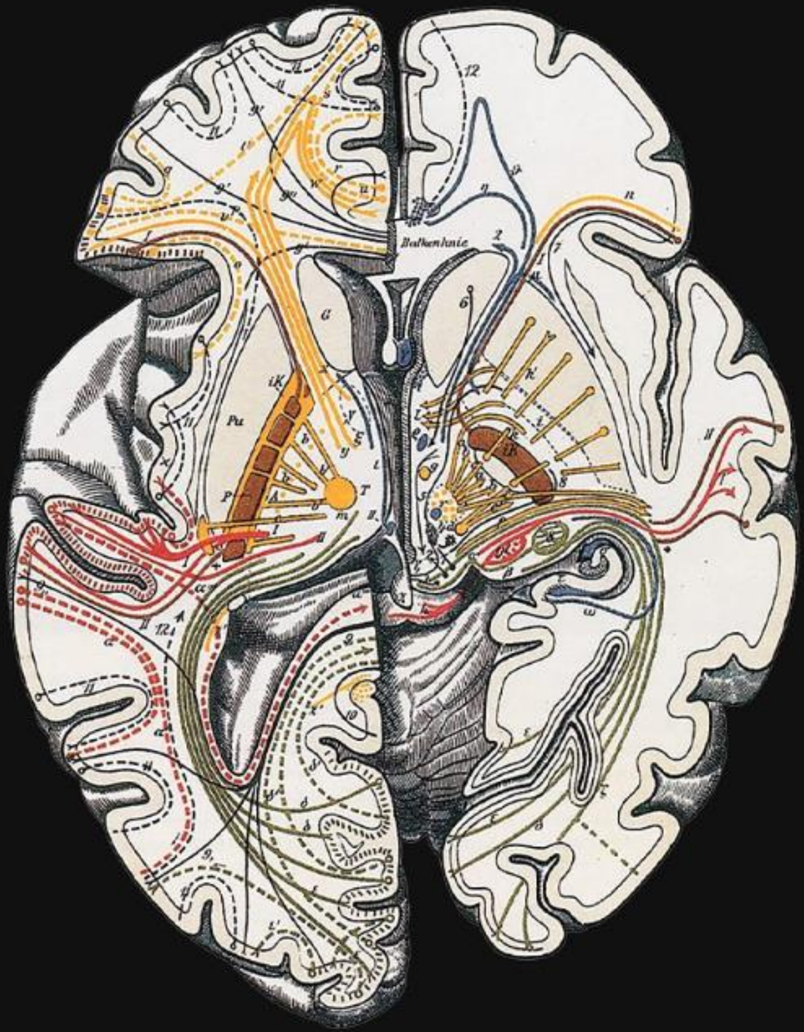
- TDP-43 linked neurodegeneration
- Same protein involved in FTLD (TDP-43 type, non tau FTLD)
- Upper and Lower motor neuron involvement
- Degeneration of cortico-spinal tract







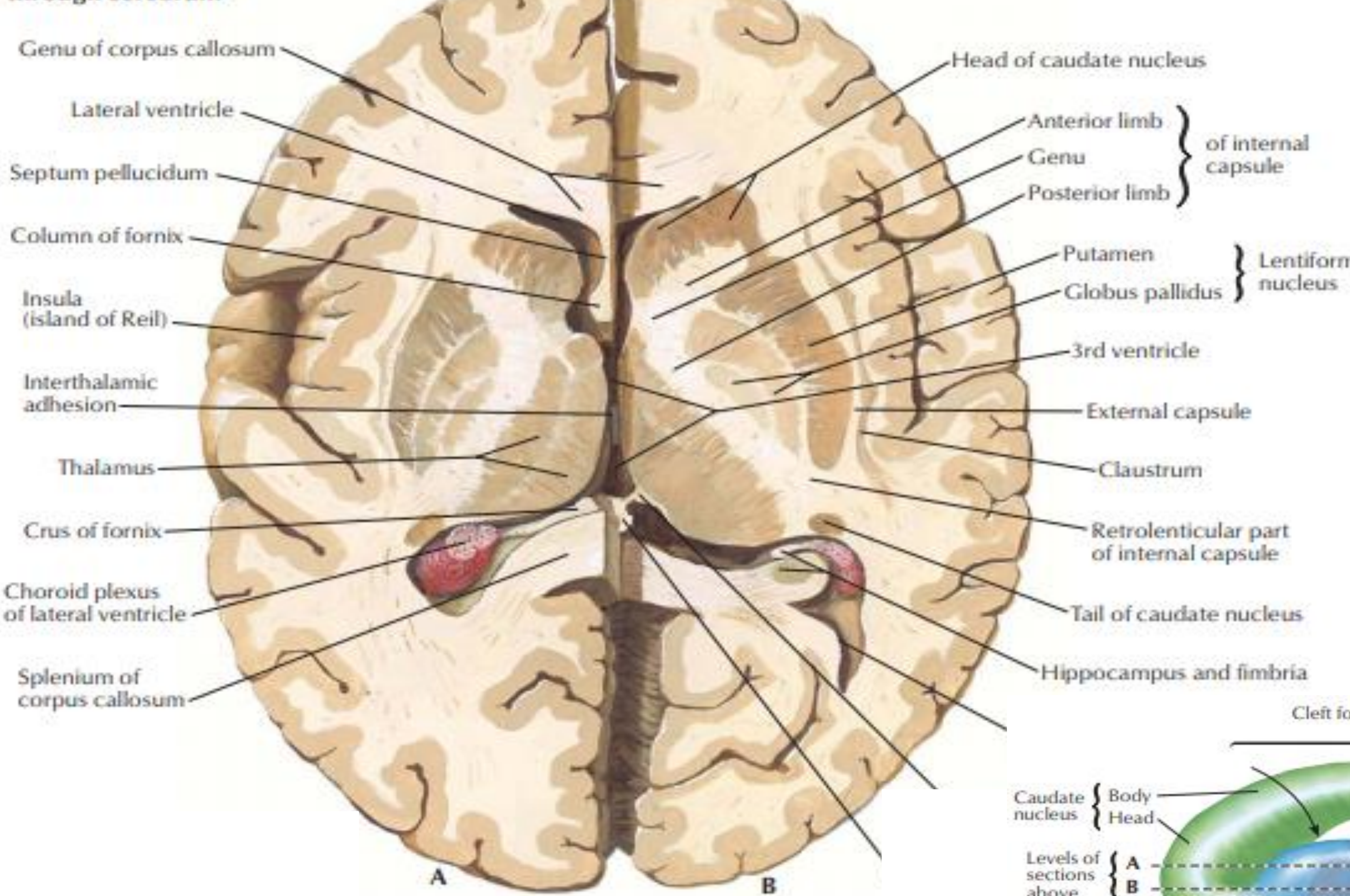
	Transverse cord lesion	Hemicordlesion: Brown-Séquard Syndrome	Central cord syndrome (small lesions)	Central cord syndrome (large lesion)	Posterior cord syndrome	Anterior cord sydrome
KEY Lesion SENSORY/MOTOR LOSS: Vibration and position sense loss Pain and temperature sense loss Motor loss						
						
Lesion	All sensory motor pathways are either partially or completely interrupted.	1. Lateral corticospinal tract 2. Posterior columns 3. Anterolateral system	1. Spinothalamic fibers crossing in the ventral commissure 2. Cervical cord	1. Anterior horn cells are damaged (a); Corticospinal tracts are affected (b); Posterior columns may be involved as well 2. Anterolateral pathways compressed from medial surface	1. Posterior columns 2. With larger lesions there may also be encroachment on the lateral cortico-spinal tracts	1. Anterolateral pathways 2. With lager lesions the lateral corticospinal tracts may also be involved SPHINCTER FUNTCION controlling descending pathways (ventrally located)
Deficit	**Sensory level**: Diminished sensation in all dermatomes below the level of the lesion	1. *Ipsilateral* upper motor neuron-type weakness 2. *Ipsilateral* sensory loss of vibration and joint sense 3. *Contralateral* sensory loss of pain and temperature (begins slightly below the lesion because the anterolateral fibers ascend two or more segments as they cross into the ventral commissure); *Ipsilateral sensory* loss of pain and temperature in strip of one of two segments (damage to posterior horn cells before their axons have crossed over)	1. Bilateral suspended sensory loss to pain and temperature. 2. Classic cape distribution (suspended dermatomes of pain and temperature sensory loss)	1. Lower motor neuron deficits at the level of the lesion (a); Upper motor neuron signs (b). 2. Near complete loss of pain in and temperature sensation below the lesion except for in a region of **sacral sparing** (review somatotopic distribution of anterolateral systems).	1. Loss of vibration and position sense below the level of the lesion 2. Upper motor neuron-type weakness	1. Loss of pain and temperature sensation below the level of the lesion. 2. Upper motor neuron signs INCONTINENCE
Reason	Trauma, tumor, multiple sclerosis, and transverse myelitis	Penetrating injuries, multiple sclerosis, and lateral compression from tumors.		Contusion, nontraumatic or posttraumatic syringomyelia, and intrinsic spinal cord tumors such as hemangioblastoma, ependymoma, or astrocytoma.	Trauma, extrinsic compression from posteriorly located tumors, and multiple sclerosis. Vitamin B12 deficiency and tabes dorsalis (tertiary syphilis) affect the posterior cord.	Trauma, multiple sclerosis, and anterior spinal artery infarct.



The Telencephalon

P. Flechsig - Gehirn und Seele

Horizontal sections through cerebrum



Organization of basal nuclei (ganglia)

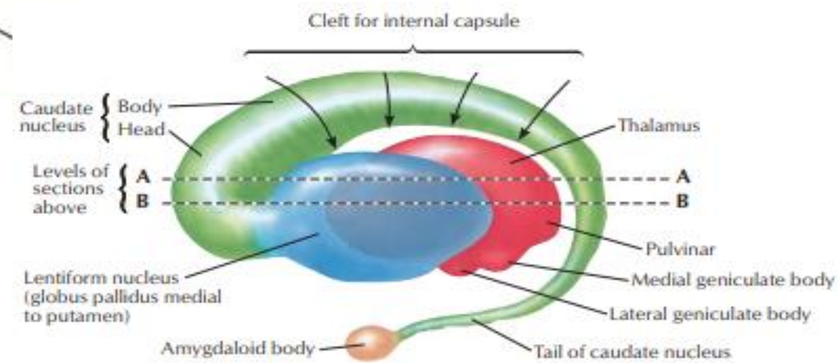
Caudate nucleus — Putamen — Globus pallidus

Caudate nucleus + Putamen = Striatum

Putamen + Globus pallidus = Lentiform nucleus

Striatum + Lentiform nucleus = Corpus striatum

Corpus striatum = Basal nuclei (ganglia)



Interrelationship of thalamus, lentiform nucleus, caudate nucleus and amygdaloid body (schema): left lateral view

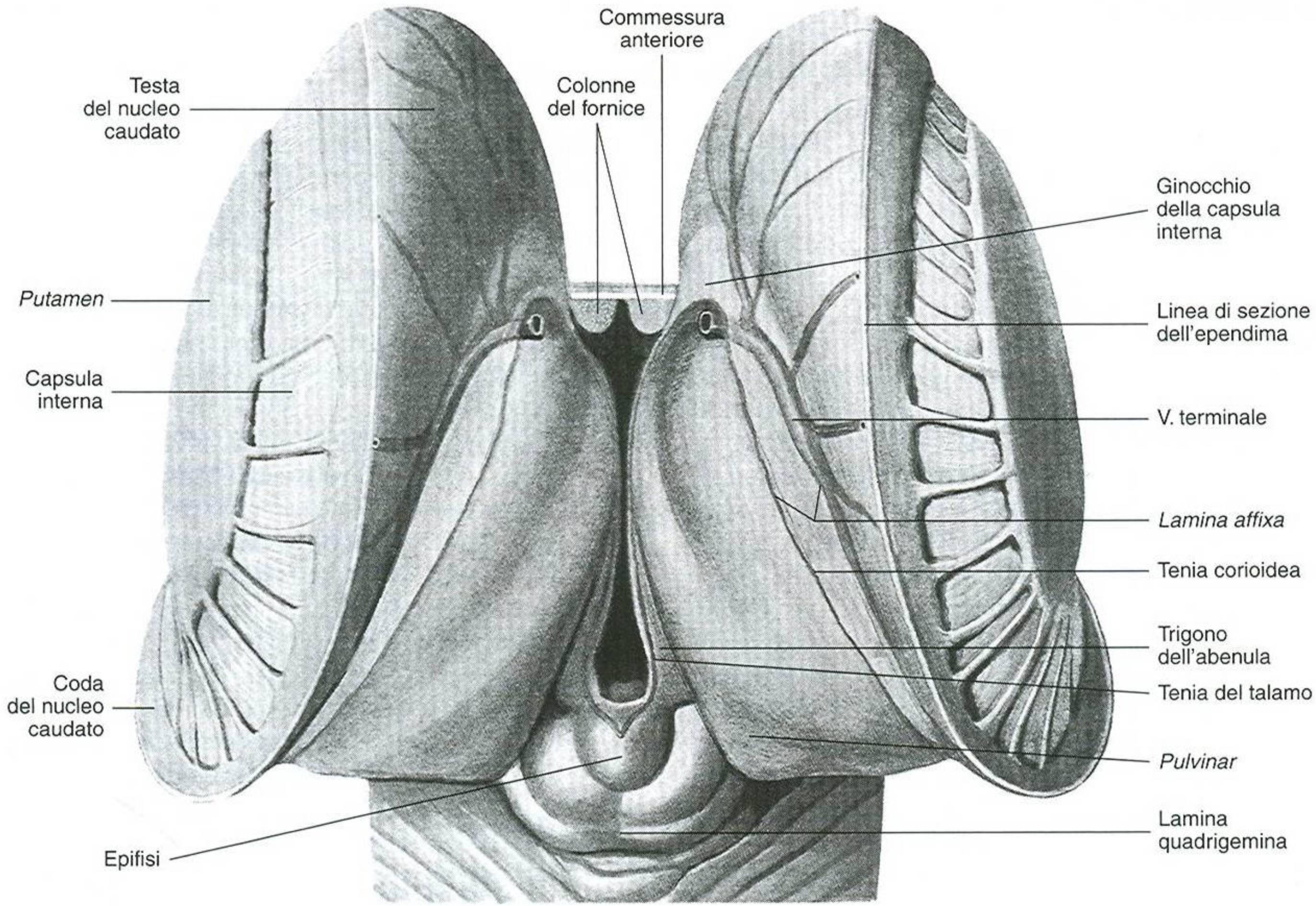
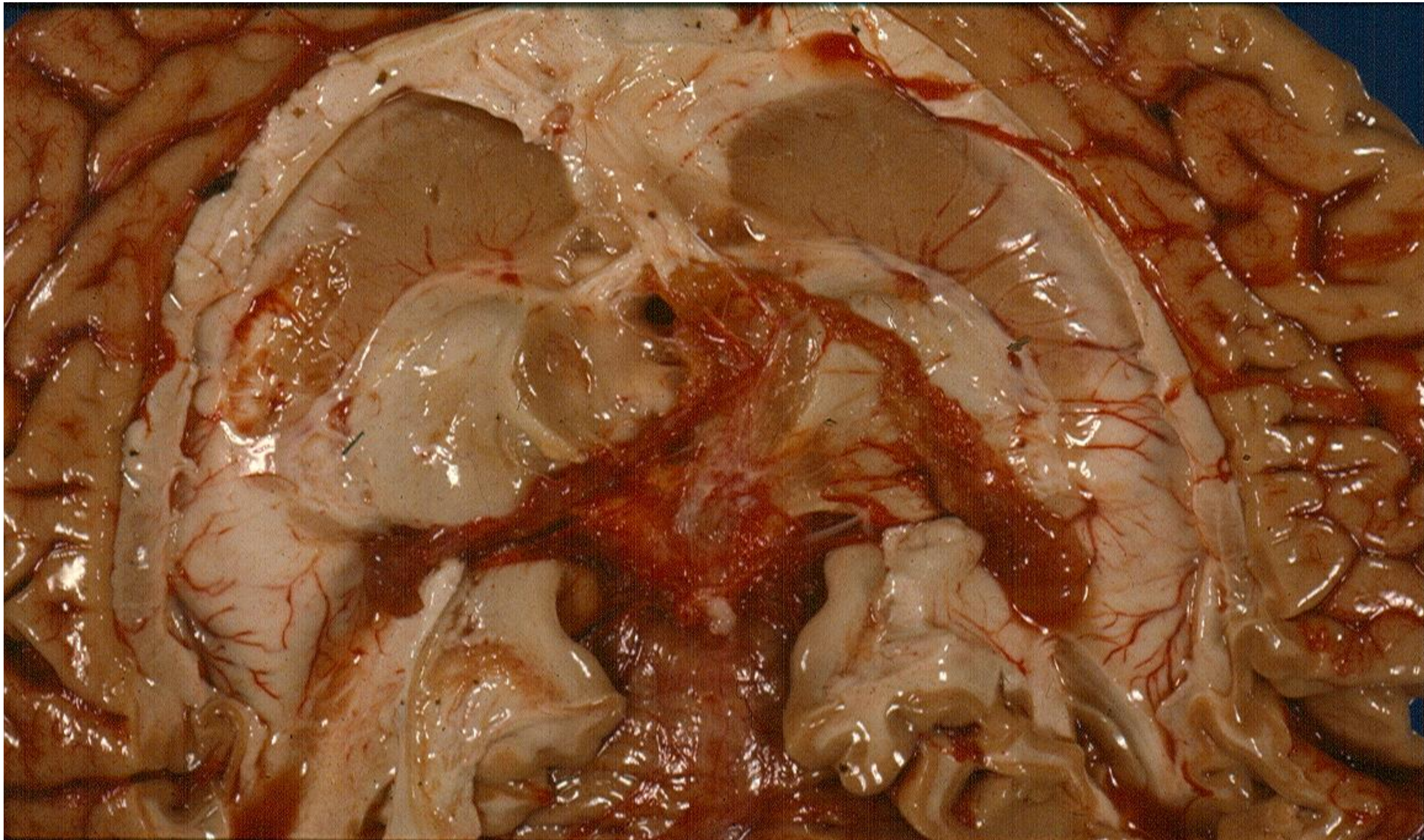
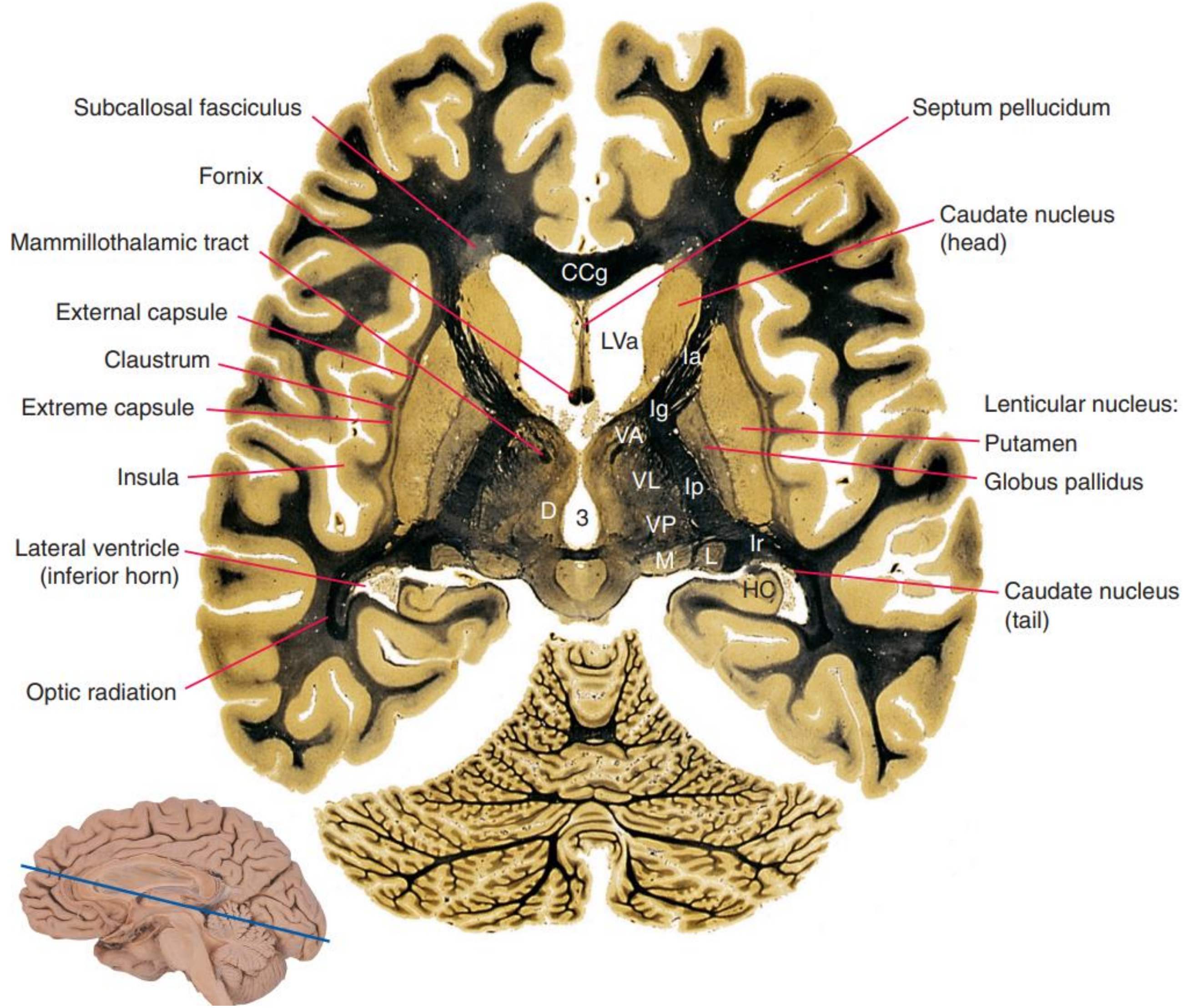
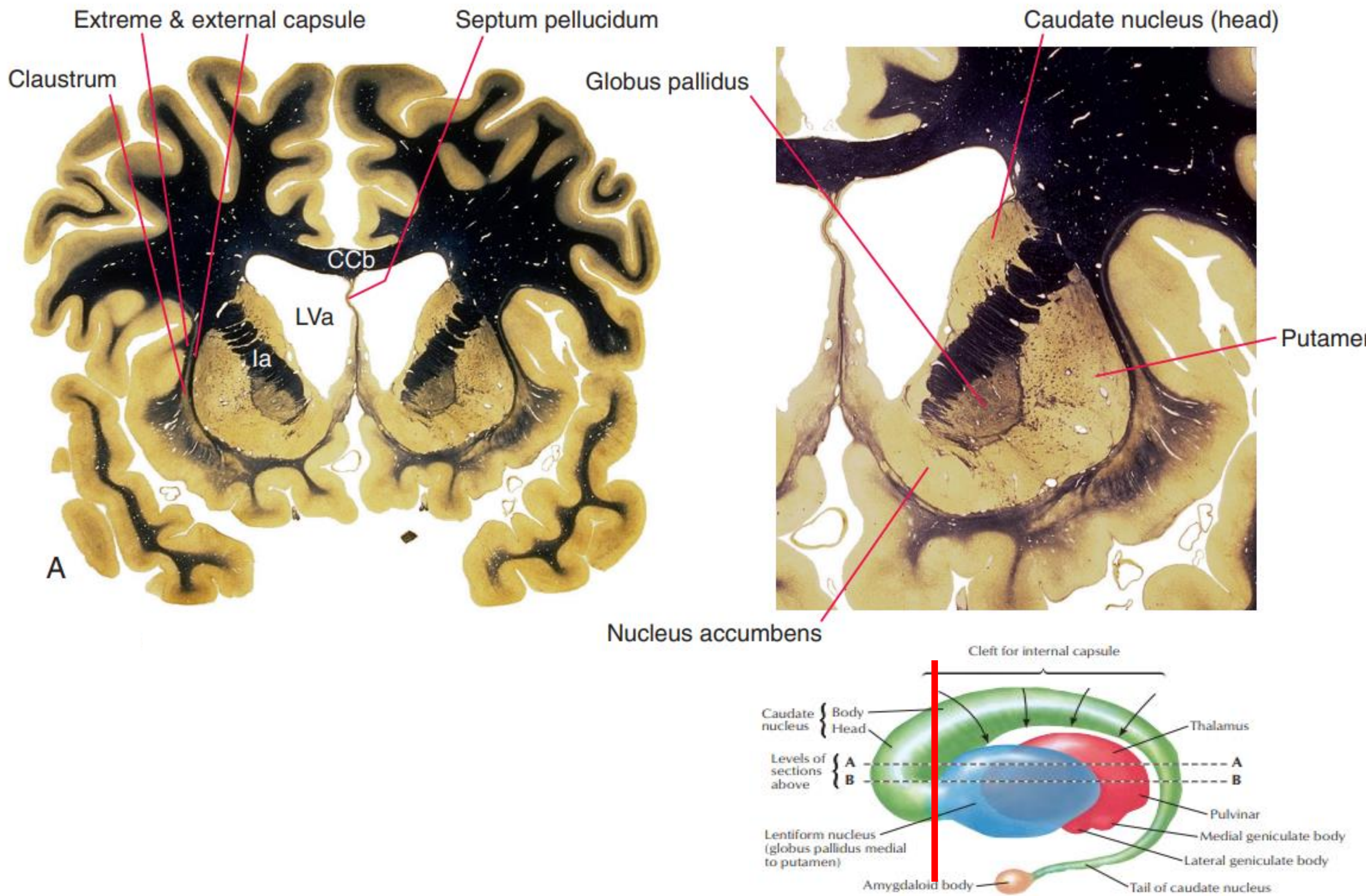
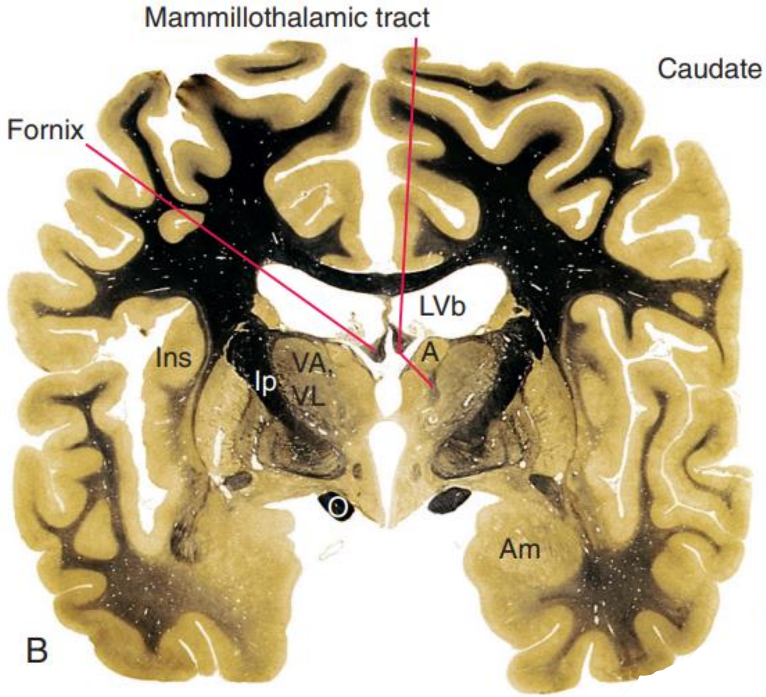


Figura 14.76 - Il talamo e il corpo striato con le formazioni bianche interposte sono visti dal lato dorsale, dopo demolizione degli emisferi telencefalici. Posteriormente e medialmente rispetto ai talami e rostralmente alla lamina quadrigemina si trovano le varie formazioni dell'epitalamo.

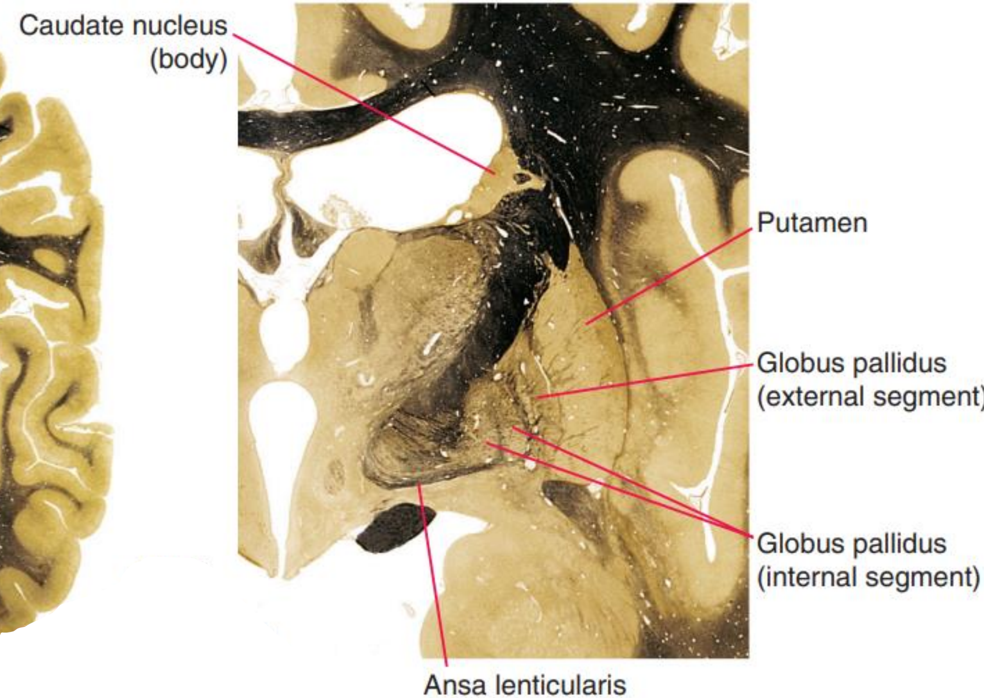



Subcallosal fasciculus
Fornix
Mammillothalamic tract
External capsule
Claustrum
Extreme capsule
Insula
Lateral ventricle
(inferior horn)
Optic radiation
Septum pellucidum
Caudate nucleus
(head)
Lenticular nucleus:
Putamen
Globus pallidus
Caudate nucleus
(tail)
CCg
LVa
Ia
Ig
VA
VL
Ip
D
3
VP
M
L
Ir
HC

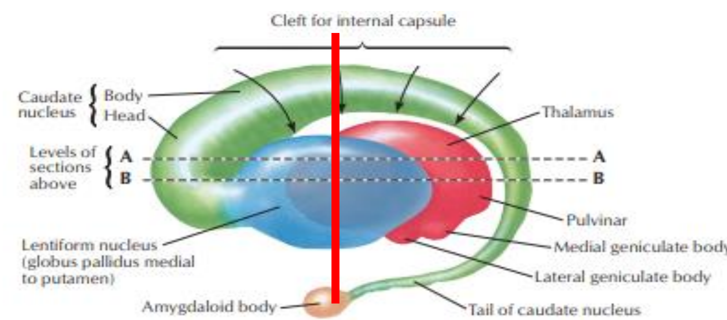

Extreme & external capsule
Septum pellucidum
Caudate nucleus (head)
Claustrum
Globus pallidus
CCb
LVa
Ia
Putamen
A
Nucleus accumbens
Cleft for internal capsule
Caudate nucleus
Body
Head
Thalamus
Levels of sections above
A
B
A
B
Pulvinar
Medial geniculate body
Lentiform nucleus (globus pallidus medial to putamen)
Lateral geniculate body
Amygdaloid body
Tail of caudate nucleus



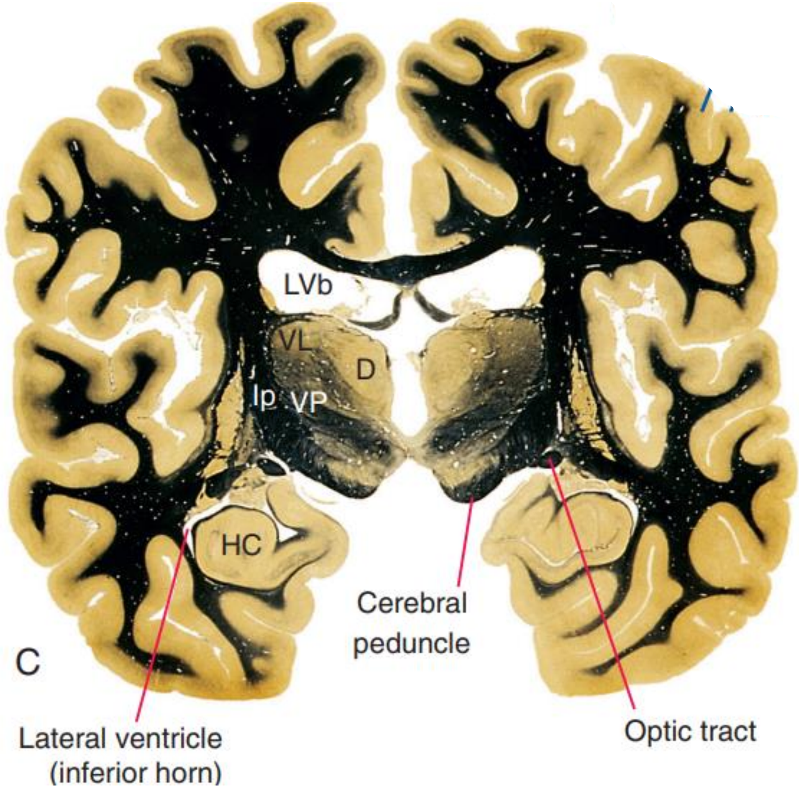
Mammillothalamic tract
Fornix
LVb
Ins
Ip
VA,
VL
A
O
Am
B

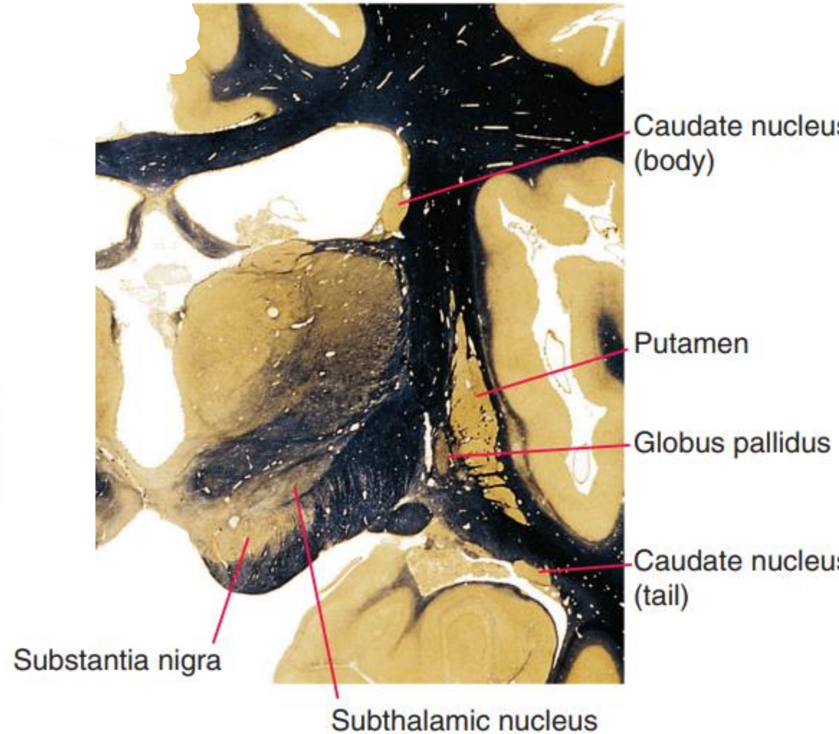


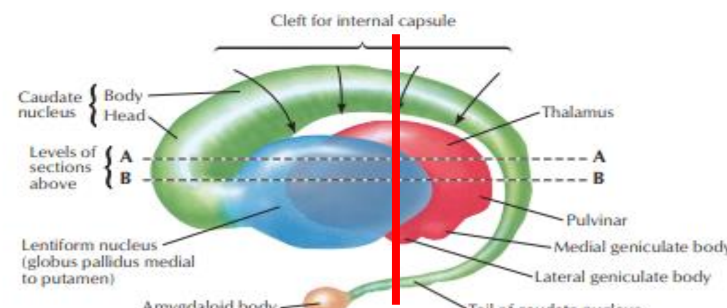
Caudate nucleus (body)
Putamen
Globus pallidus (external segment)
Globus pallidus (internal segment)
Ansa lenticularis

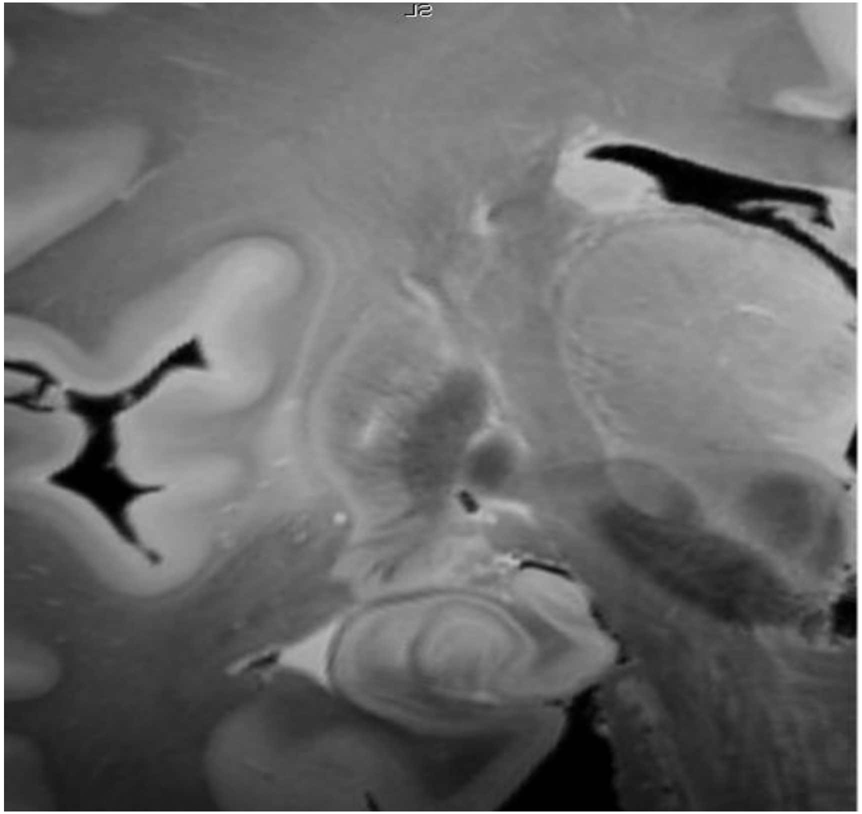


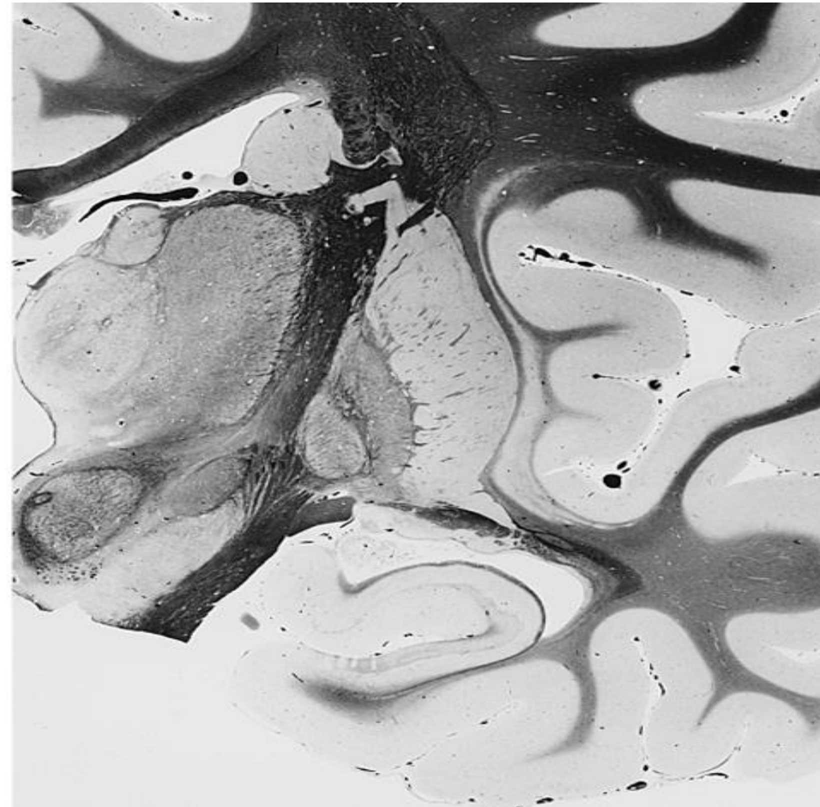
Cleft for internal capsule
Caudate nucleus
Body
Head
Levels of sections above
A
B
Thalamus
Pulvinar
Medial geniculate body
Lateral geniculate body
Tail of caudate nucleus
Lentiform nucleus (globus pallidus medial to putamen)
Amygdaloid body


LVb
VL
D
Ip
VP
HC
C
Cerebral peduncle
Lateral ventricle (inferior horn)
Optic tract


Caudate nucleus (body)
Putamen
Globus pallidus
Caudate nucleus (tail)
Substantia nigra
Subthalamic nucleus


Cleft for internal capsule
Caudate nucleus
Body
Head
Levels of sections above
A
B
Lentiform nucleus (globus pallidus medial to putamen)
Amygdaloid body
Thalamus
A
B
Pulvinar
Medial geniculate body
Lateral geniculate body
Tail of caudate nucleus



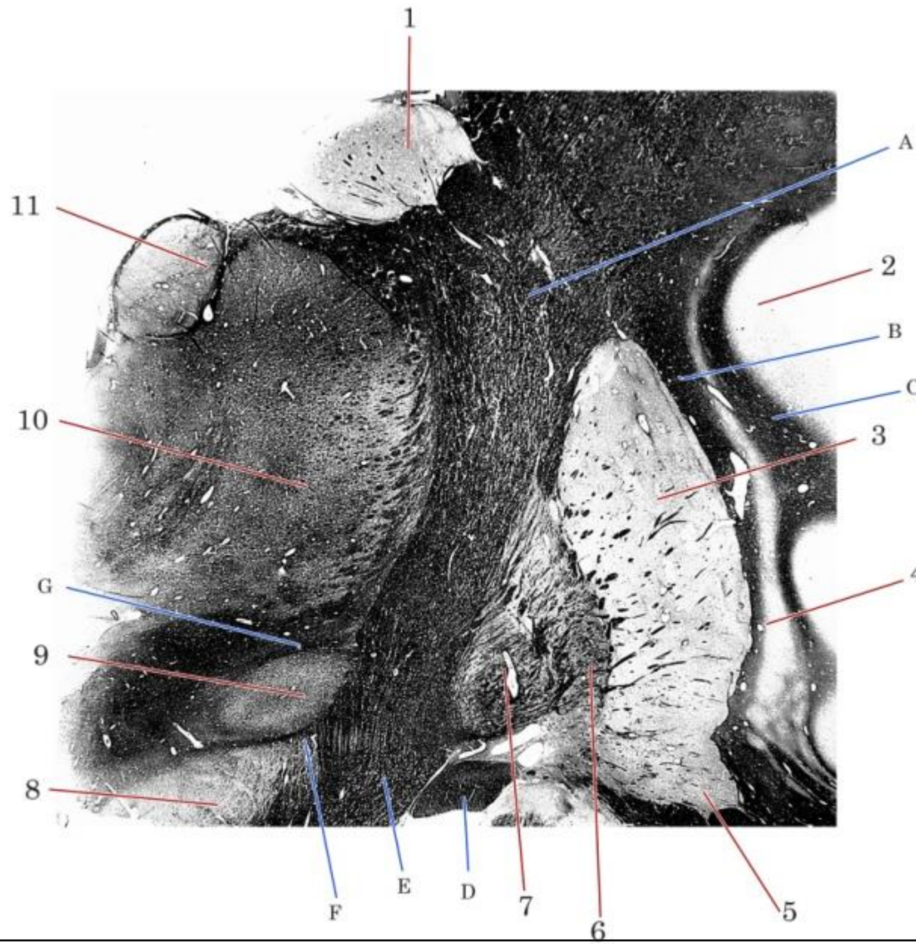


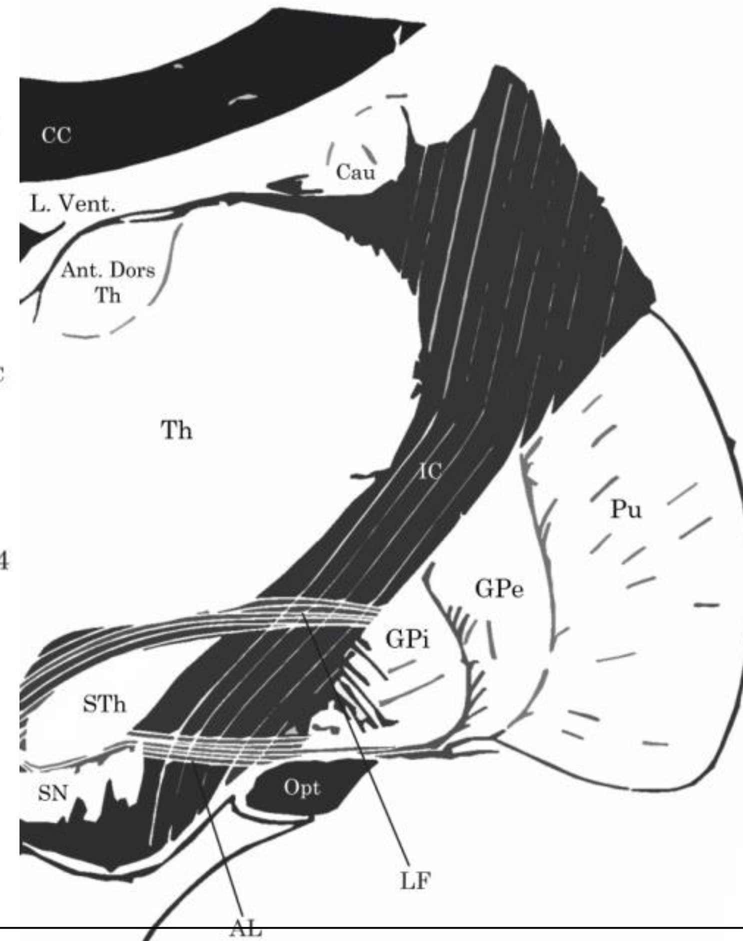
Anatomy and Connectivity of the Subthalamic Nucleus in Humans and Non-human Primates

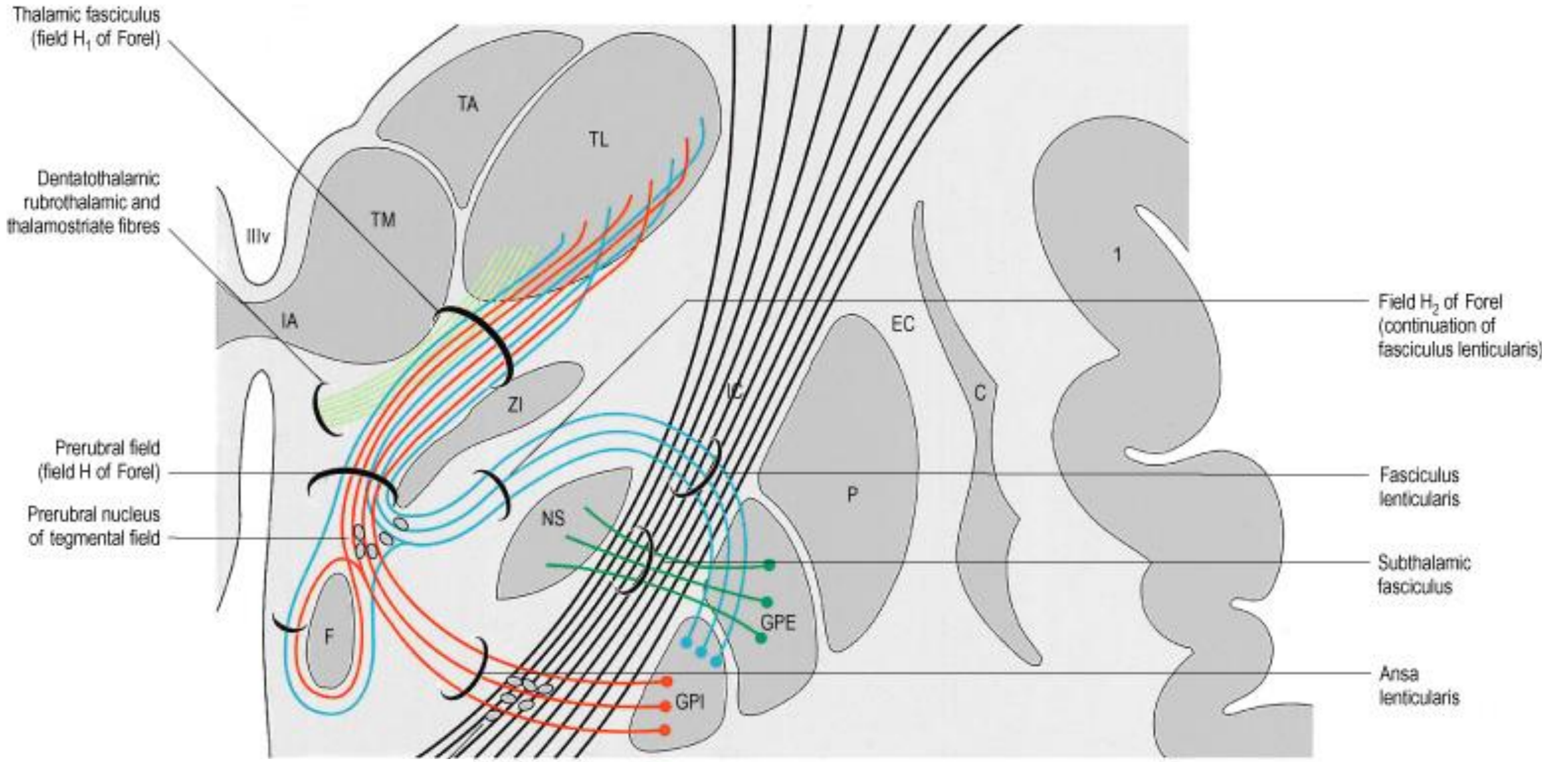
frontiers in Neuroanatomy

Aron Emmi[1], Angelo Antonini[2], Veronica Macchi[1], Andrea Porzionato[1*] and Raffaele De Caro[1]

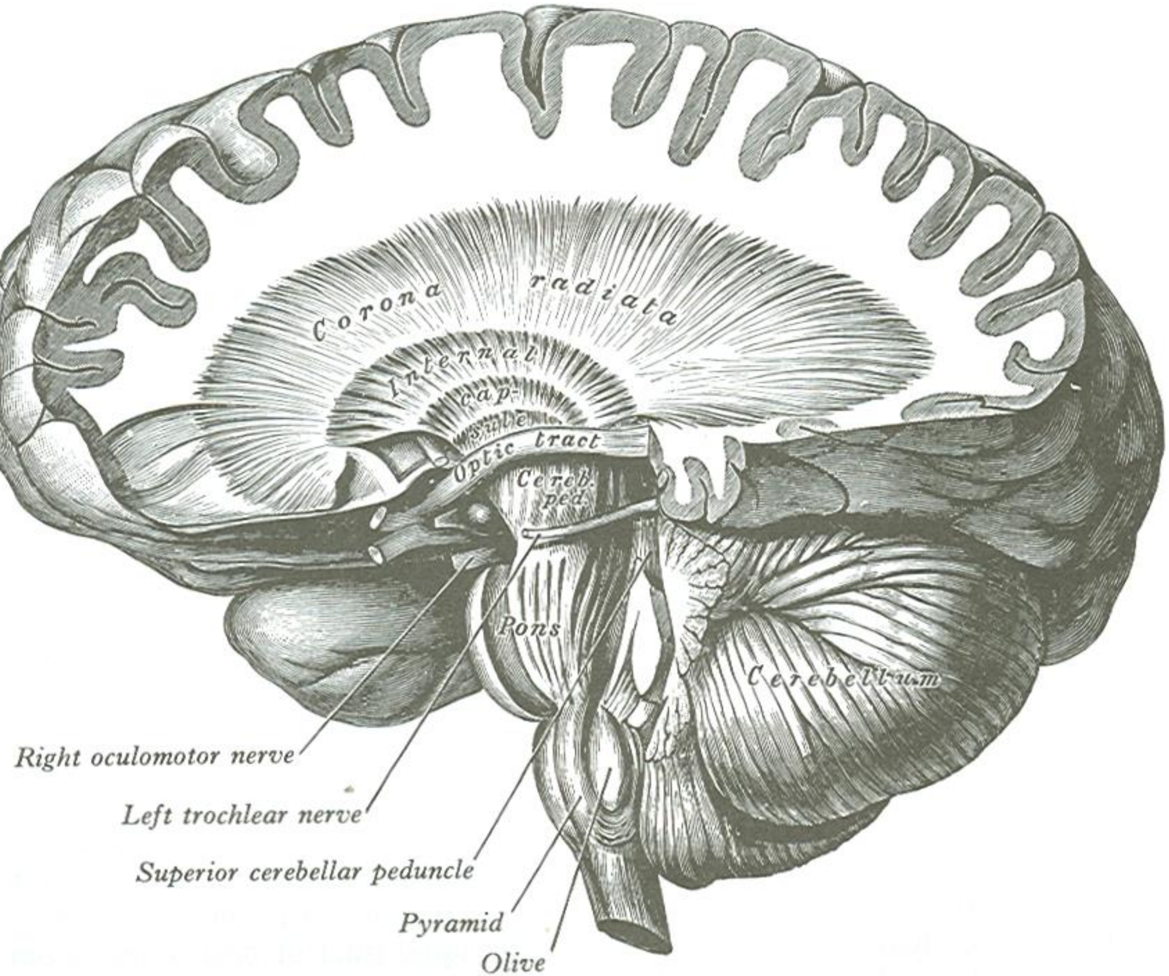
Front. Neuroanat., 22 April 2020 | https://doi.org/10.3389/fnana.2020.00013

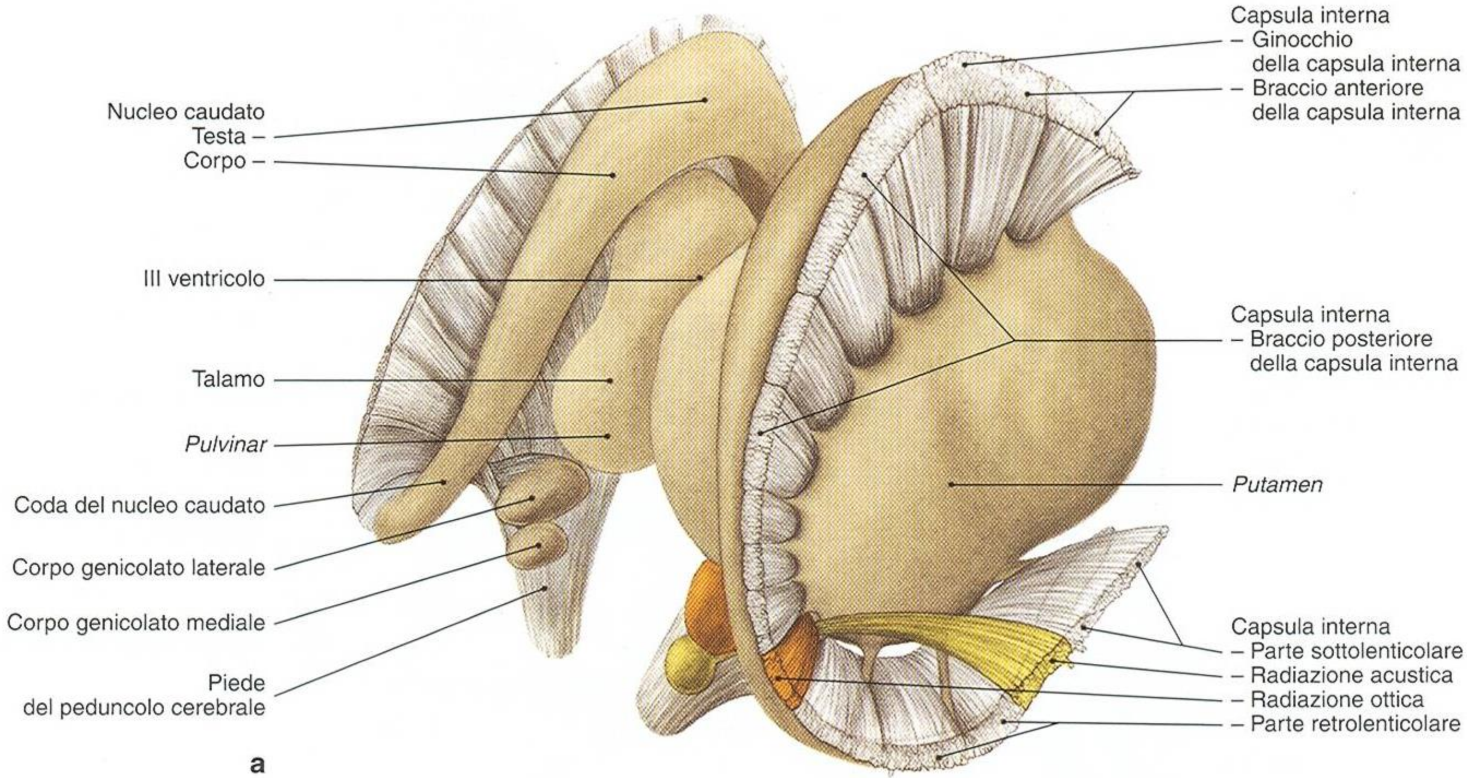






Thalamic fasciculus
(field H_1 of Forel)
Dentatothalamic
rubrothalamic and
thalamostriate fibres
Prerubral field
(field H of Forel)
Prerubral nucleus
of tegmental field
TA
TL
TM
IIIv
IA
ZI
NS
F
IC
EC
C
1
P
GPE
GPI
Field H_2 of Forel
(continuation of
fasciculus lenticularis)
Fasciculus
lenticularis
Subthalamic
fasciculus
Ansa
lenticularis


Corona radiata
Internal capsule
Optic tract
Cereb. ped.
Pons
Cerebellum
Right oculomotor nerve
Left trochlear nerve
Superior cerebellar peduncle
Pyramid
Olive


Nucleo caudato
Testa –
Corpo –
III ventricolo
Talamo
Pulvinar
Coda del nucleo caudato
Corpo genicolato laterale
Corpo genicolato mediale
Piede
del peduncolo cerebrale
a
Capsula interna
– Ginocchio
della capsula interna
– Braccio anteriore
della capsula interna
Capsula interna
– Braccio posteriore
della capsula interna
Putamen
Capsula interna
– Parte sottolenticolare
– Radiazione acustica
– Radiazione ottica
– Parte retrolenticolare

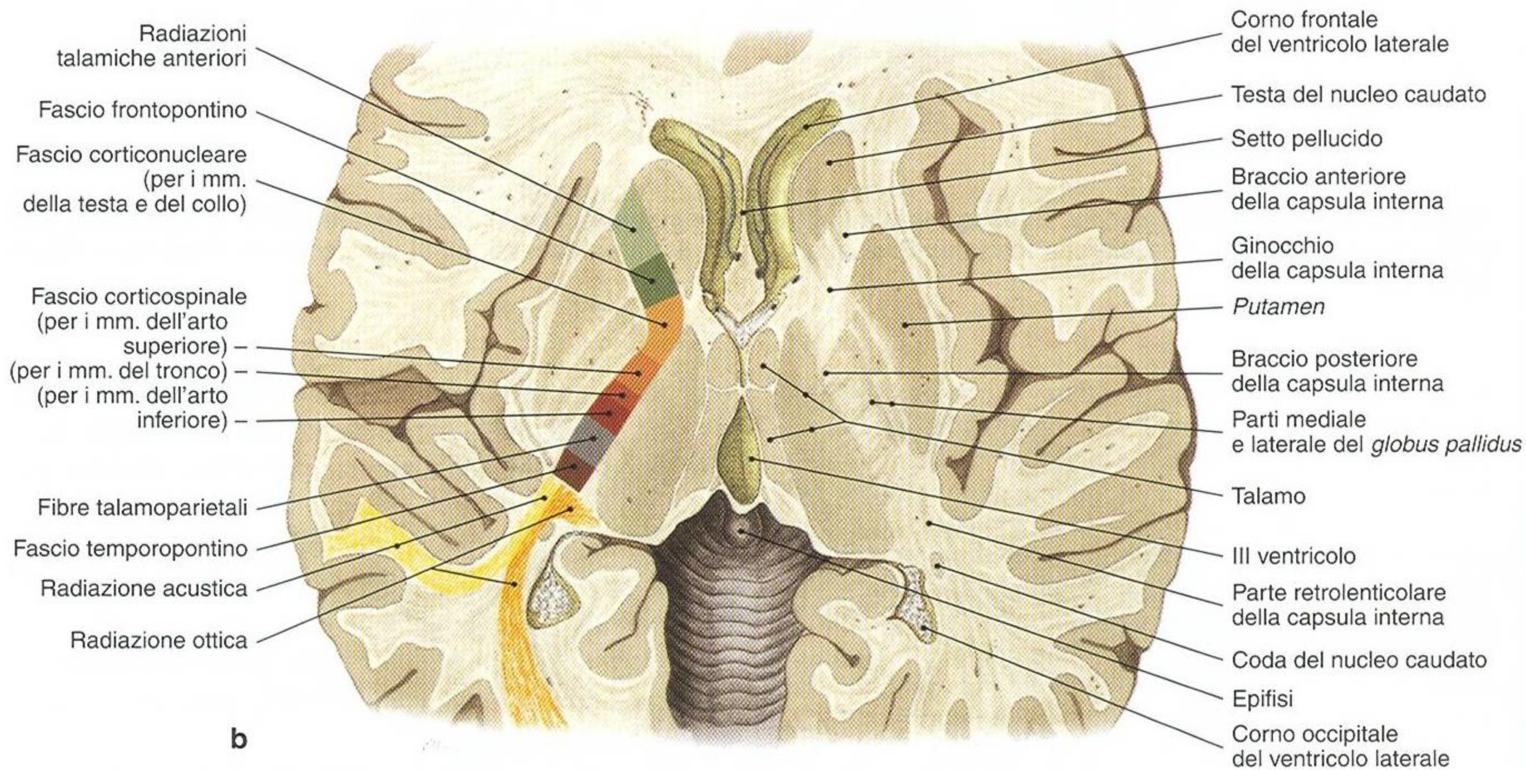
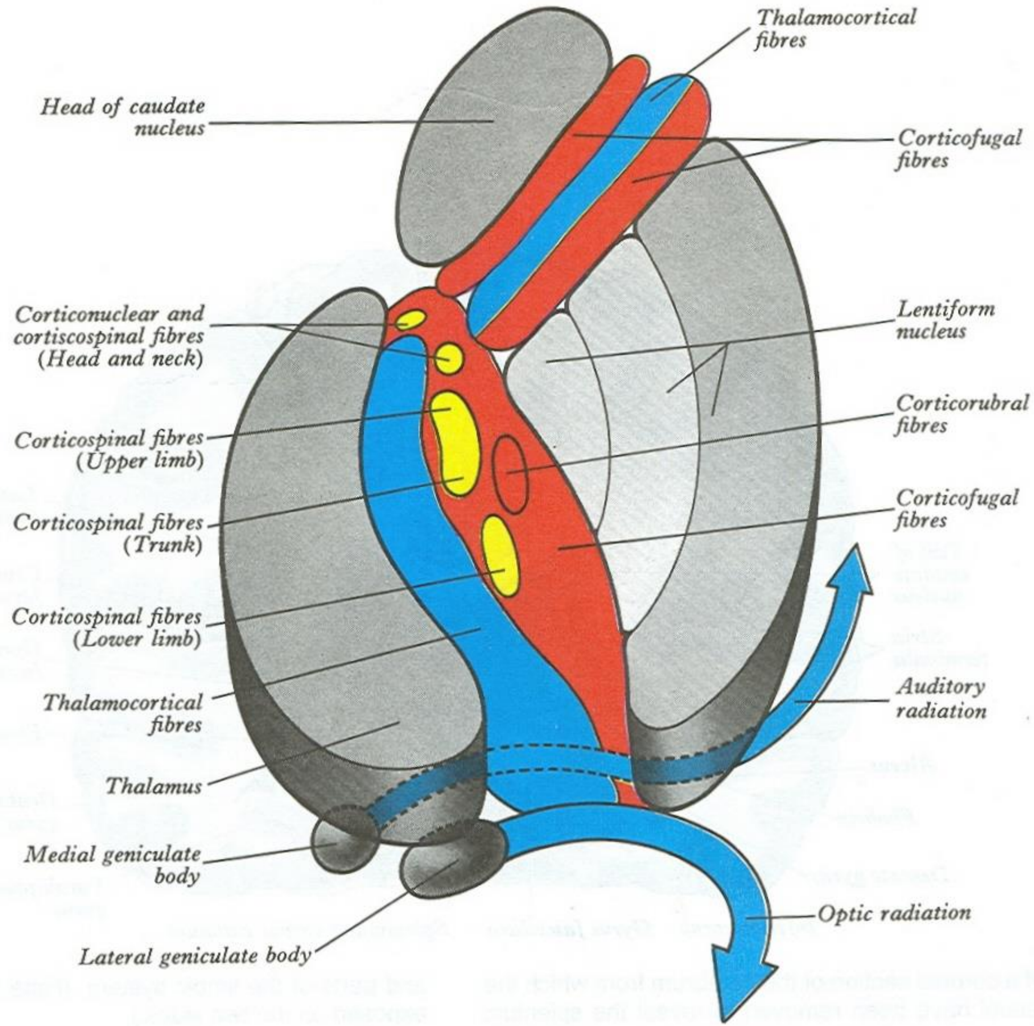
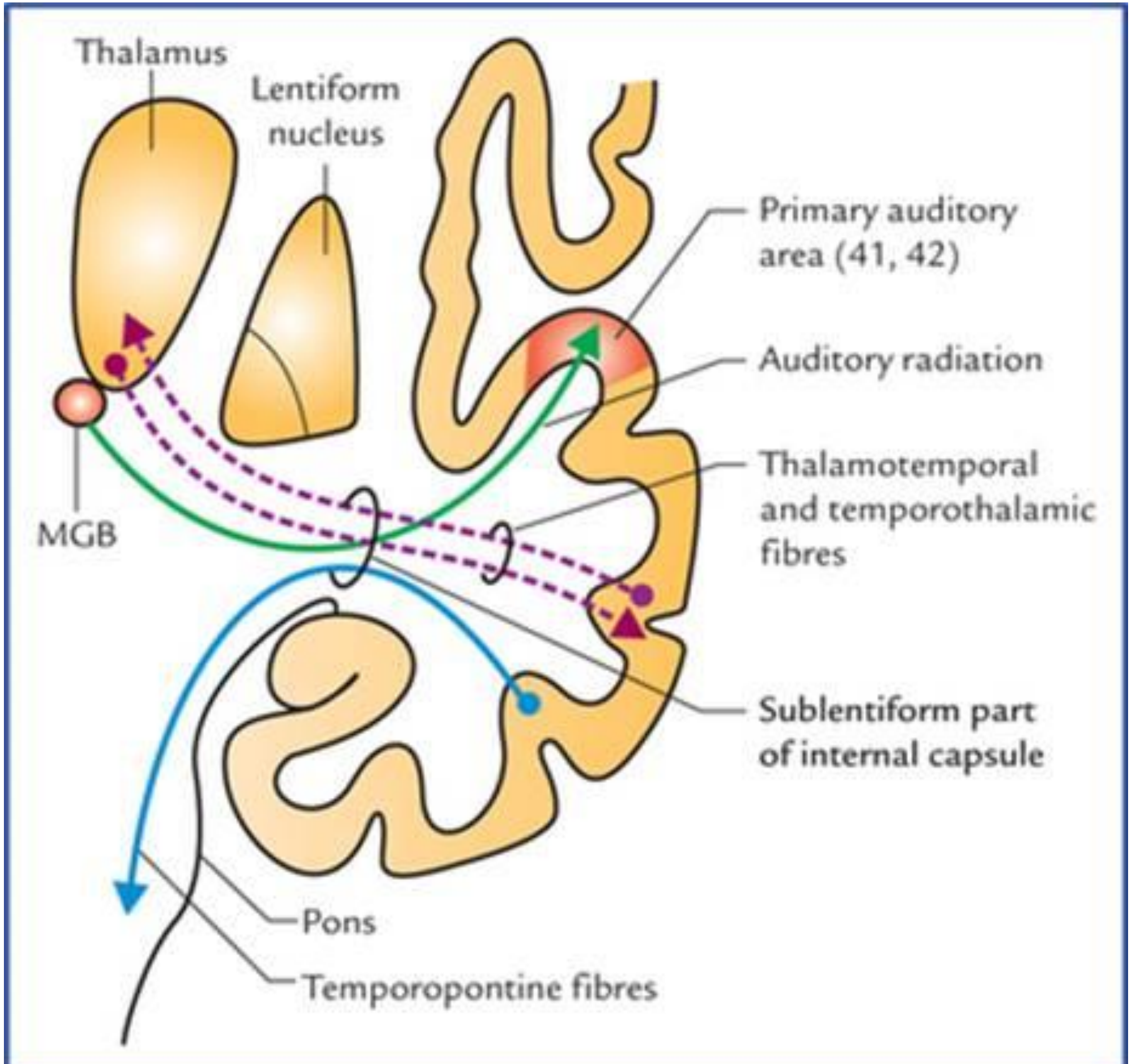
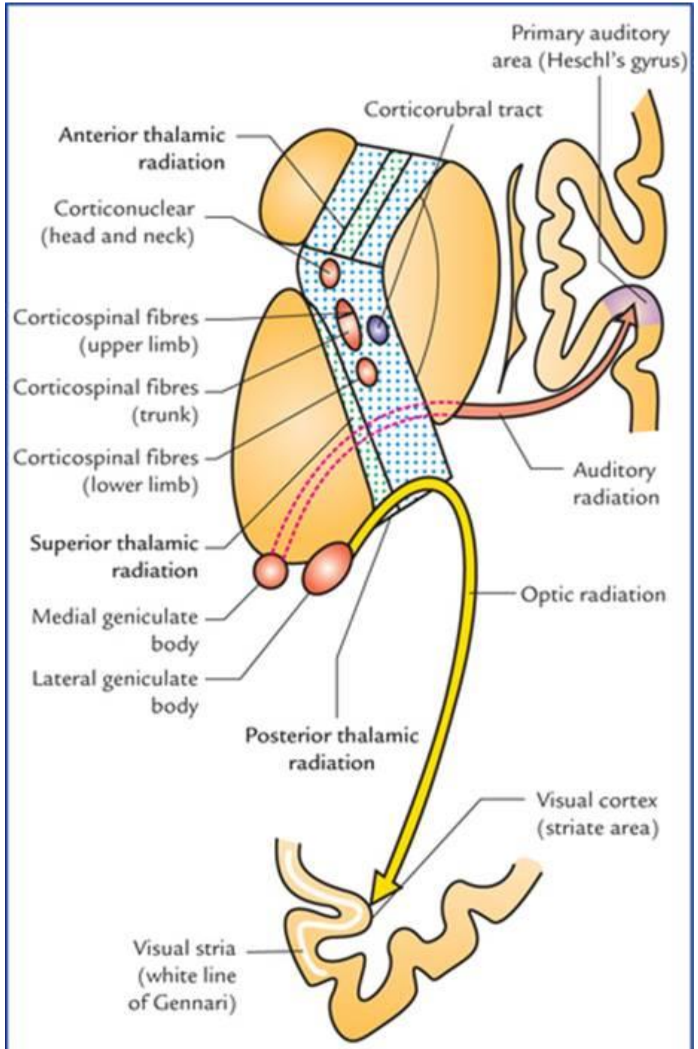


Figura 14.79 - Nuclei del proencefalo e capsula interna. **a**, Talamo, corpo striato (nuclei caudato e *putamen*) e nucleo lenticolare (*putamen* e *globus pallidus*) con capsula interna, proiezione occipitolaterale destra. **b**, Sezione orizzontale della capsula interna e dei nuclei adiacenti. A sinistra le parti principali della capsula interna sono state messe in evidenza con colori differenti. Proiezione parietale (da Köpf-Maier P, ed.: Wolf-Heidegger's Atlas of Human Anatomy, 5th, completely revised and supplemented edition, Basel, Karger, 2000, with permission from S. Karger AG, Basel).



Thalamocortical fibres
Head of caudate nucleus
Corticofugal fibres
Corticonuclear and cortiscospinal fibres (Head and neck)
Lentiform nucleus
Corticorubral fibres
Corticospinal fibres (Upper limb)
Corticospinal fibres (Trunk)
Corticofugal fibres
Corticospinal fibres (Lower limb)
Auditory radiation
Thalamocortical fibres
Thalamus
Medial geniculate body
Optic radiation
Lateral geniculate body


Thalamus
Lentiform nucleus
Primary auditory area (41, 42)
Auditory radiation
Thalamotemporal and temporothalamic fibres
MGB
Sublentiform part of internal capsule
Pons
Temporopontine fibres



Primary auditory area (Heschl's gyrus)
Corticorubral tract
Anterior thalamic radiation
Corticonuclear (head and neck)
Corticospinal fibres (upper limb)
Corticospinal fibres (trunk)
Corticospinal fibres (lower limb)
Auditory radiation
Superior thalamic radiation
Optic radiation
Medial geniculate body
Lateral geniculate body
Posterior thalamic radiation
Visual cortex (striate area)
Visual stria (white line of Gennari)

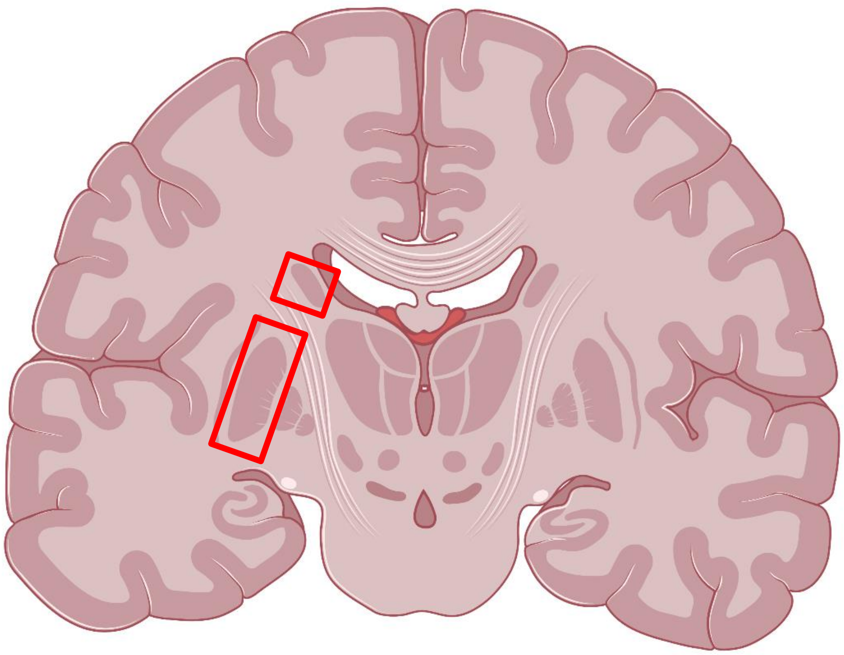
THE BASAL GANGLIA – Functional Anatomy

Input nuclei:
- Caudate nucleus
- Putamen

Relais nuclei:
- External globus pallidus (GPe)
- Subthalamic Nucleus (STh)

Output nuclei:
- Internal globus pallidus (GPi)
- Non-dopaminergic substantia nigra (SNND)

Modulating structures:
- Dopaminergic substantia nigra (SND)



Hardman et al. 2002

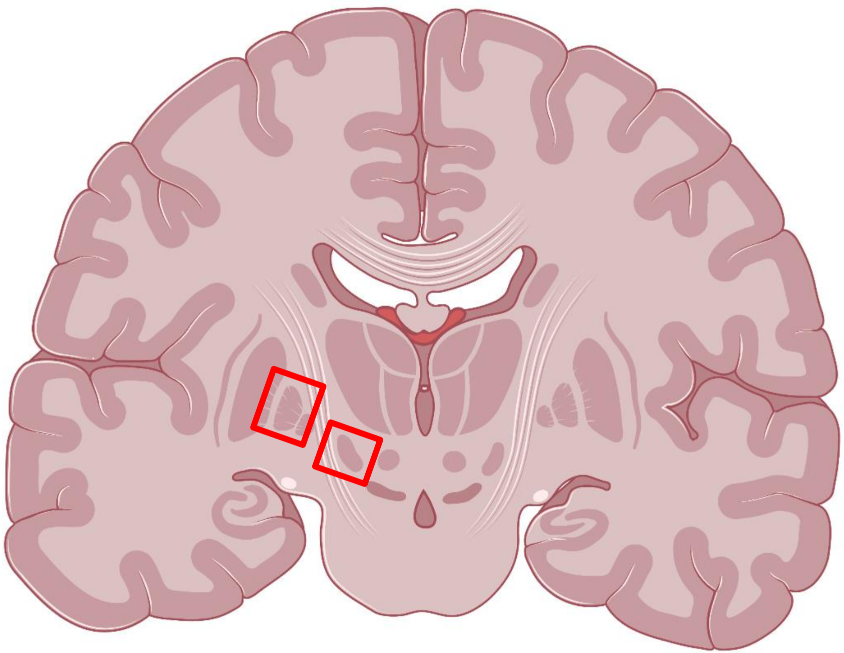
THE BASAL GANGLIA – Functional Anatomy

Input nuclei:
- Caudate nucleus
- Putamen

Relais nuclei:
- External globus pallidus (GPe)
- Subthalamic Nucleus (STh)

Output nuclei:
- Internal globus pallidus (GPi)
- Non-dopaminergic substantia nigra (SNND)

Modulating structures:
- Dopaminergic substantia nigra (SND)



Hardman et al. 2002

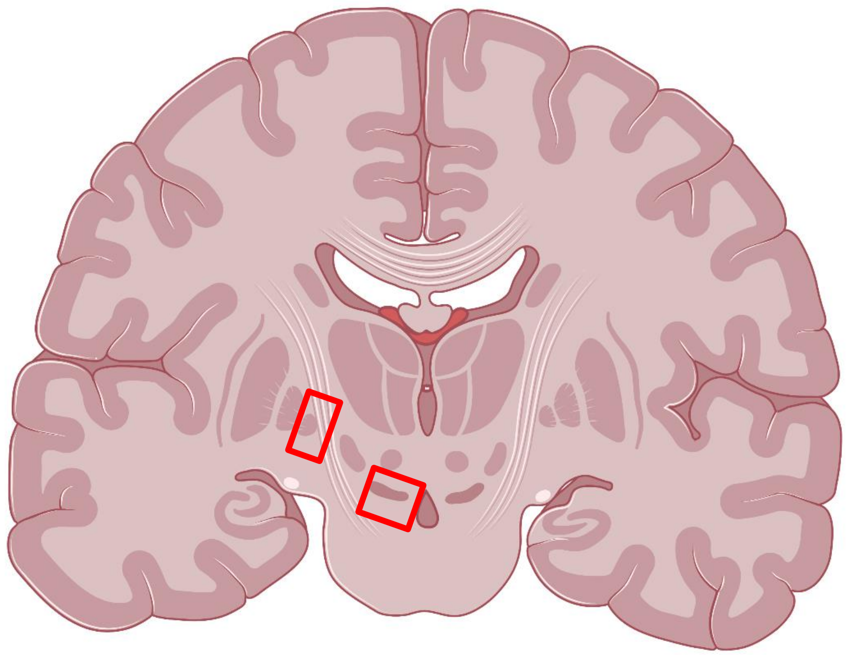
THE BASAL GANGLIA – Functional Anatomy

Input nuclei:
- Caudate nucleus
- Putamen

Relais nuclei:
- External globus pallidus (GPe)
- Subthalamic Nucleus (STh)

Output nuclei:
- Internal globus pallidus (GPi)
- Non-dopaminergic substantia nigra (SNND)

Modulating structures:
- Dopaminergic substantia nigra (SND)



Hardman et al. 2002

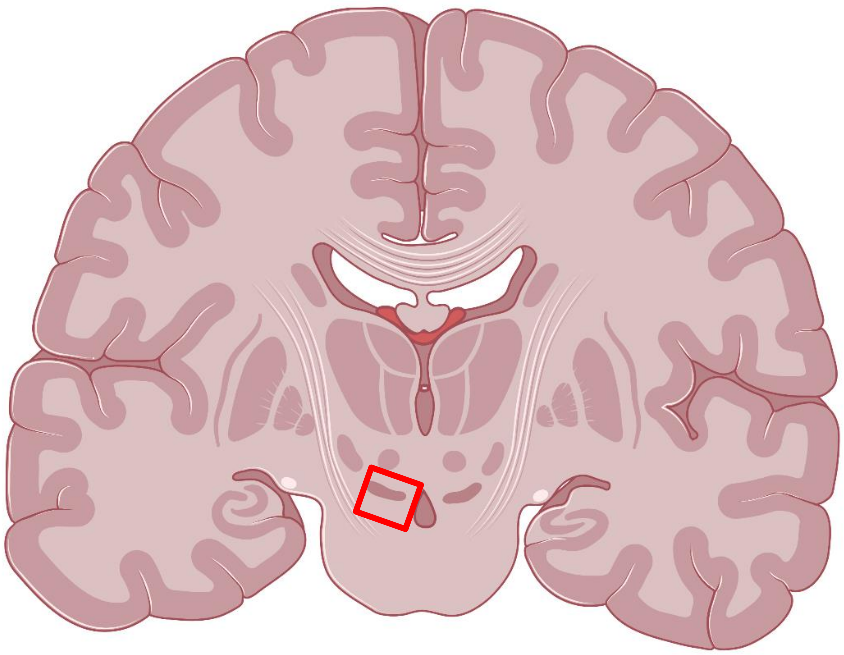
THE BASAL GANGLIA – Functional Anatomy

Input nuclei:
- Caudate nucleus
- Putamen

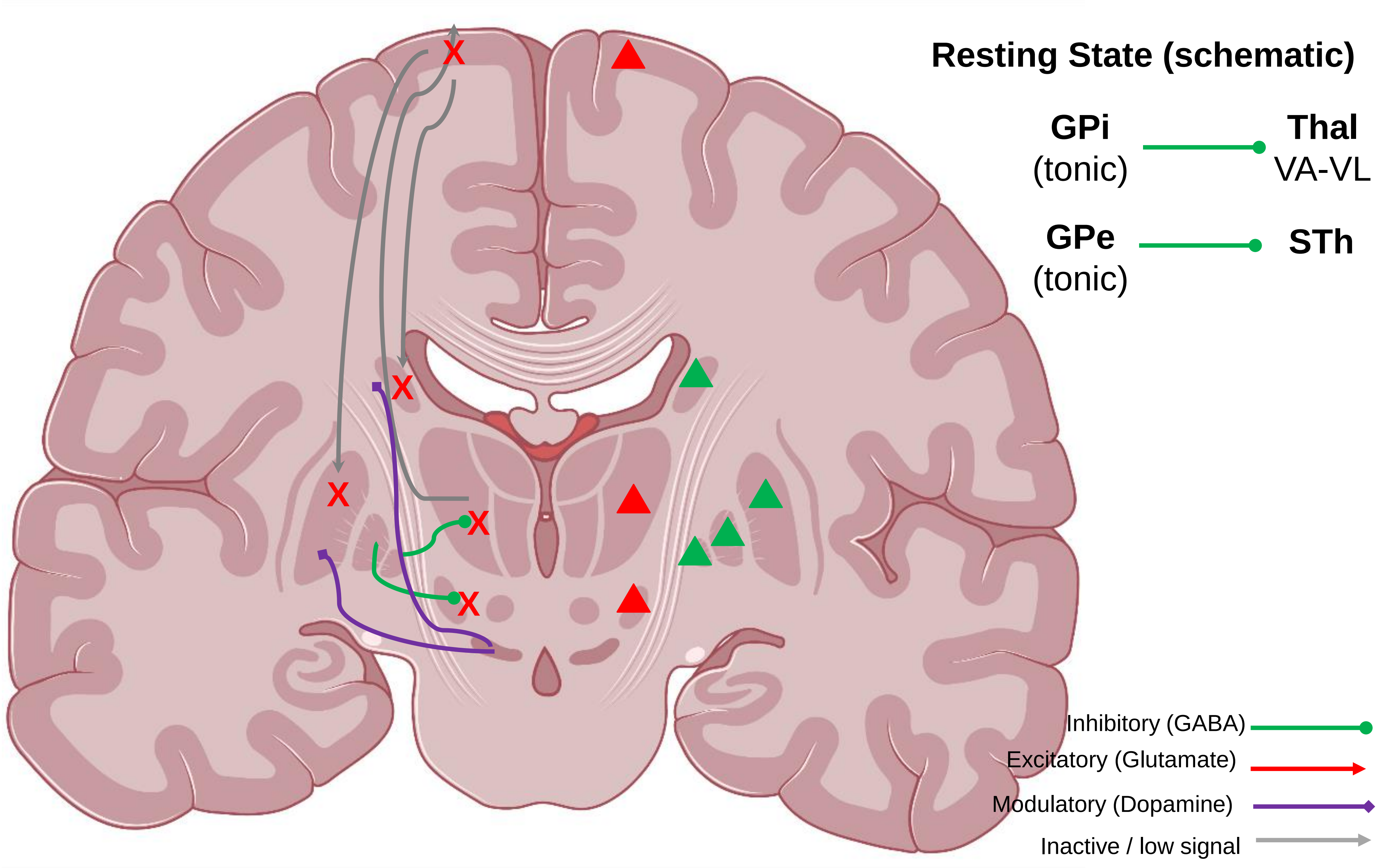
Relais nuclei:
- External globus pallidus (GPe)
- Subthalamic Nucleus (STh)

Output nuclei:
- Internal globus pallidus (GPi)
- Non-dopaminergic substantia nigra (SNND)

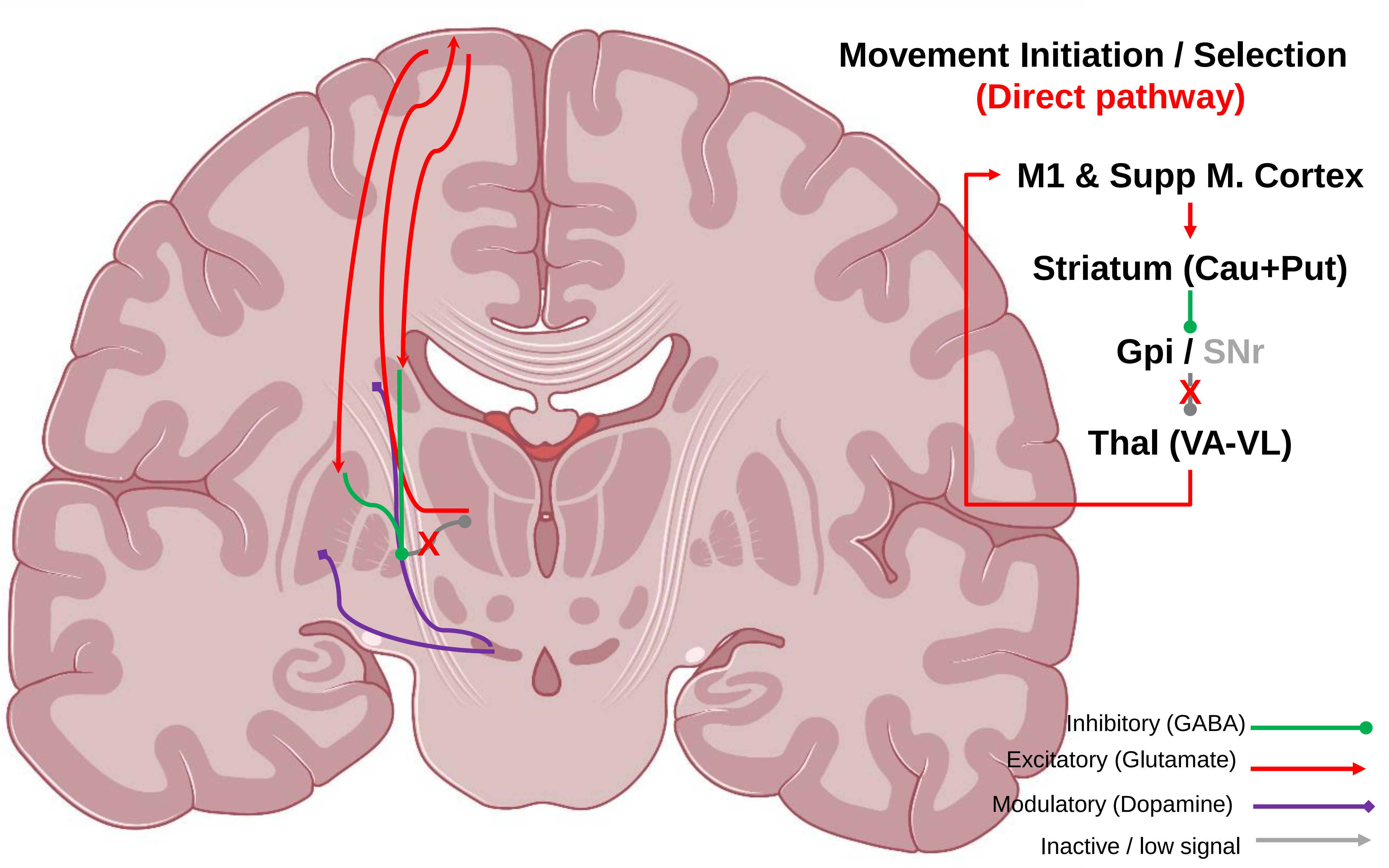
Modulating structures:
- Dopaminergic substantia nigra (SND)



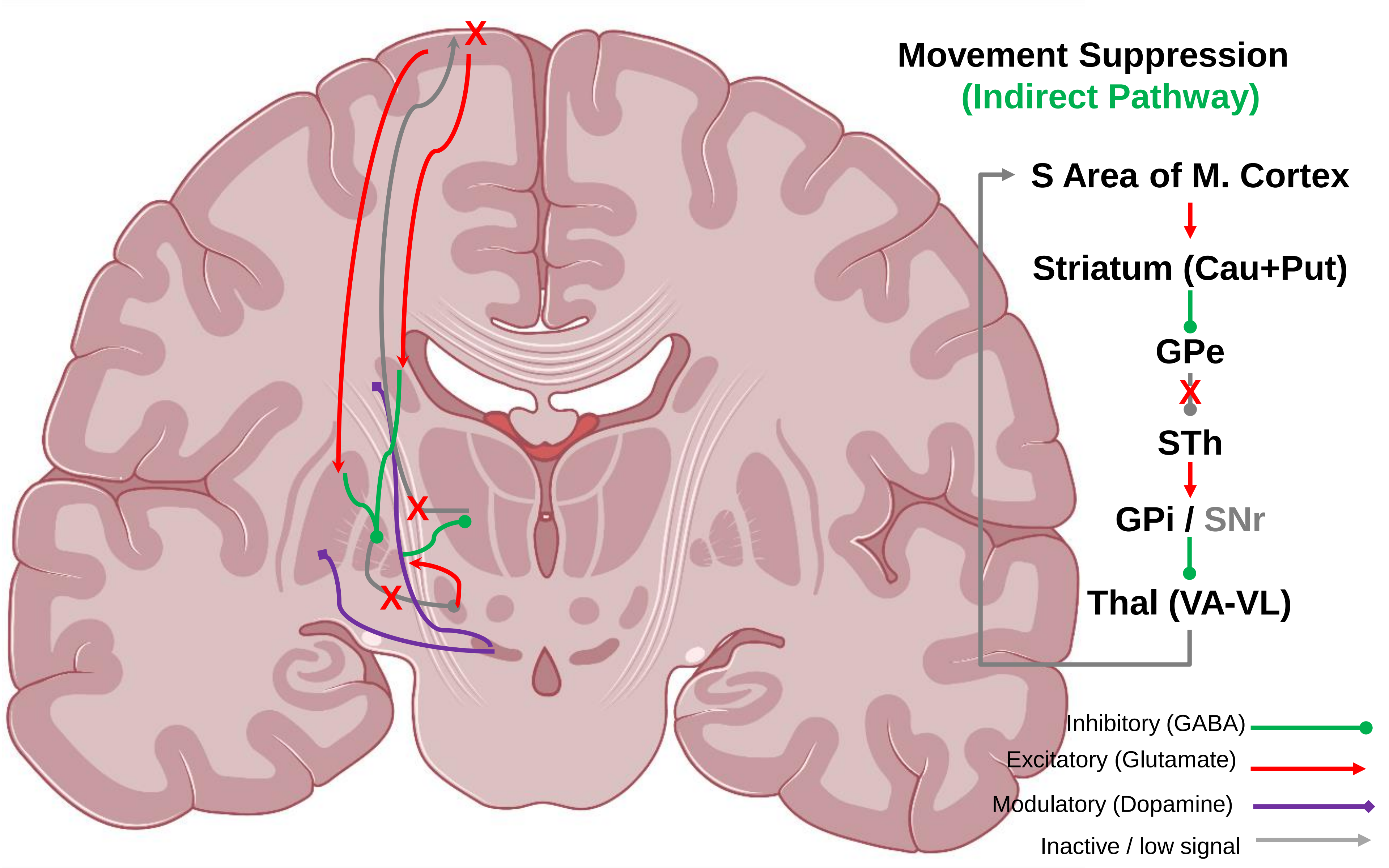
Hardman et al. 2002

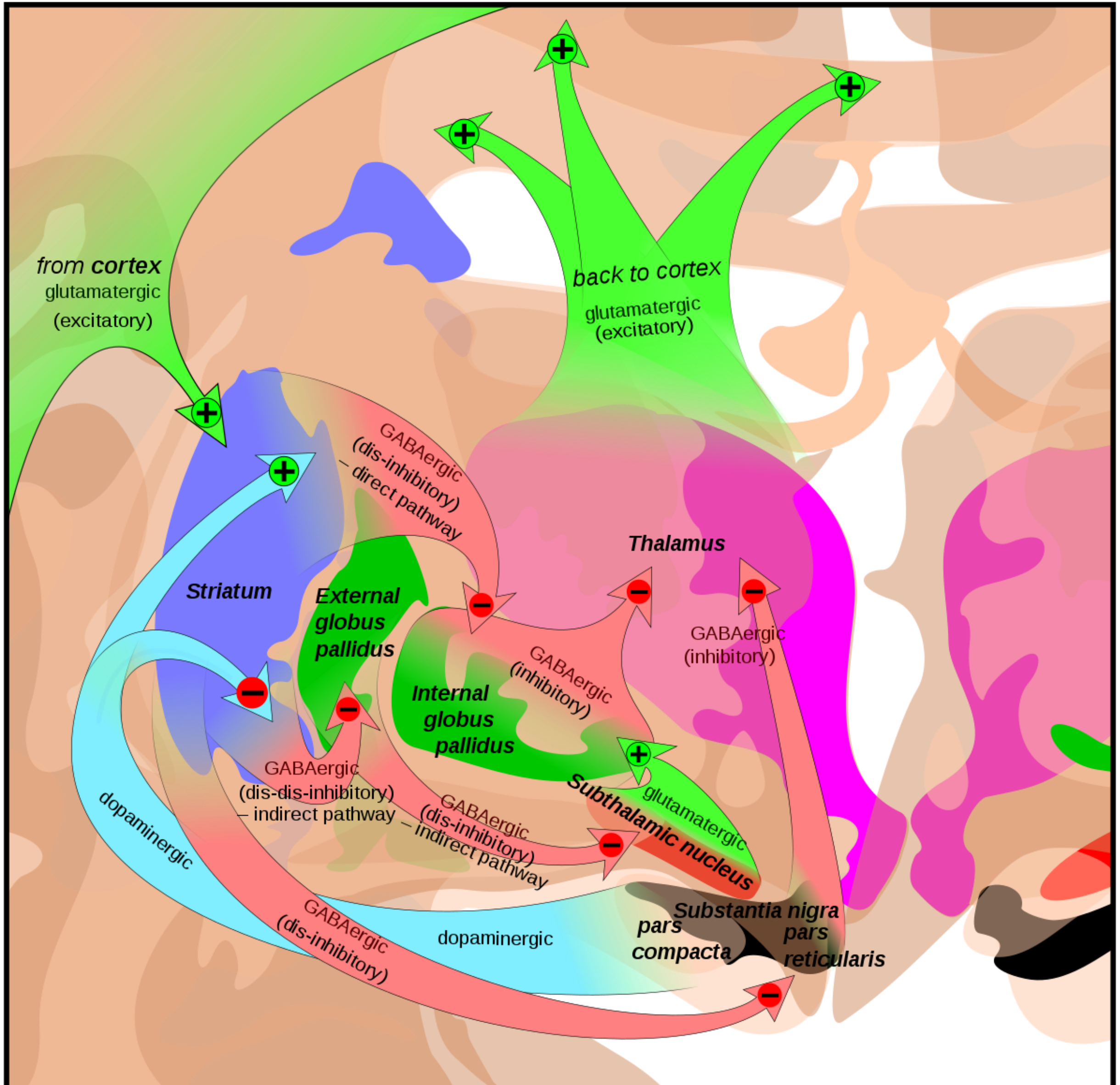


Resting State (schematic)
GPi
(tonic)
Thal
VA-VL
GPe
(tonic)
STh
Inhibitory (GABA)
Excitatory (Glutamate)
Modulatory (Dopamine)
Inactive / low signal



Movement Initiation / Selection
(Direct pathway)
M1 & Supp M. Cortex
Striatum (Cau+Put)
Gpi / SNr
X
Thal (VA-VL)
X
Inhibitory (GABA)
Excitatory (Glutamate)
Modulatory (Dopamine)
Inactive / low signal

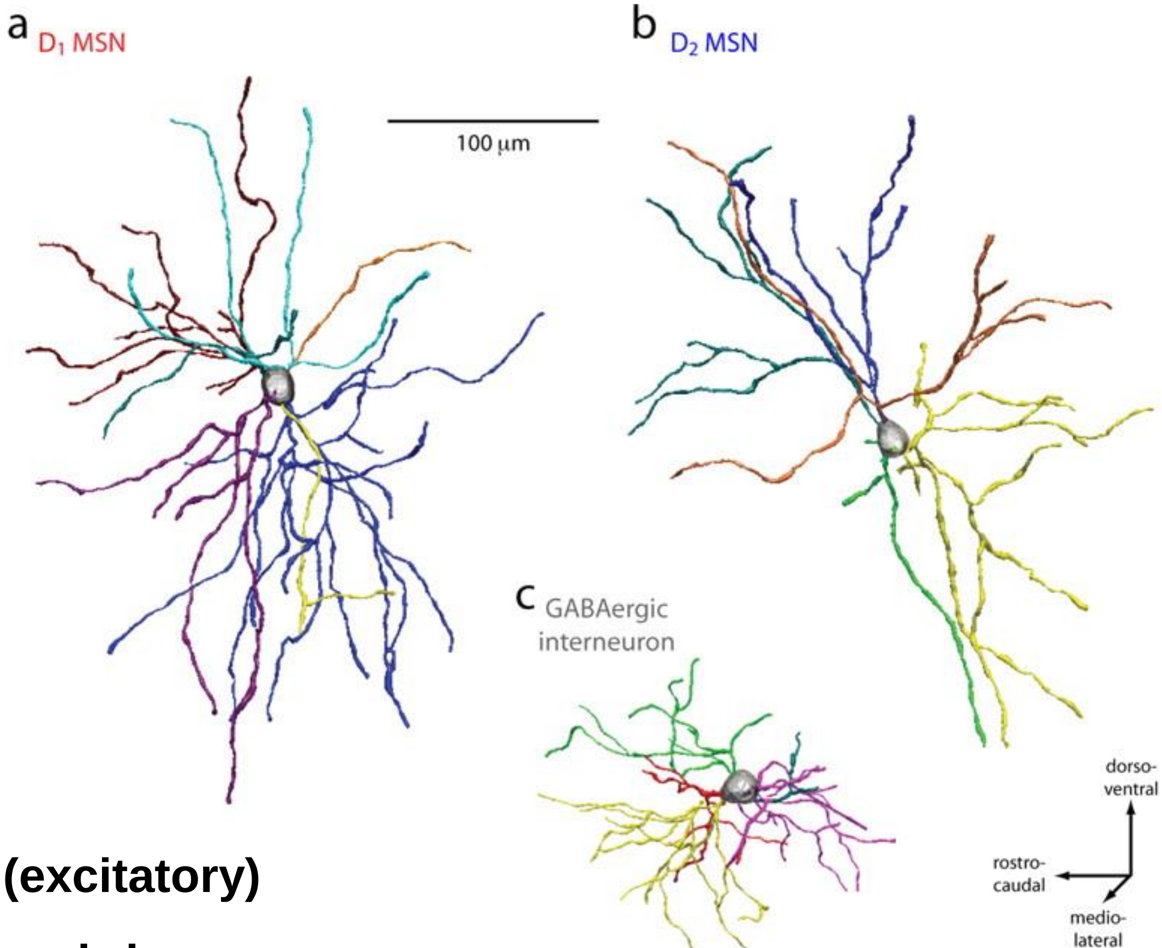

Movement Suppression
(Indirect Pathway)
S Area of M. Cortex
Striatum (Cau+Put)
GPe
STh
GPi / SNr
Thal (VA-VL)
Inhibitory (GABA)
Excitatory (Glutamate)
Modulatory (Dopamine)
Inactive / low signal



from cortex
glutamatergic
(excitatory)
back to cortex
glutamatergic
(excitatory)
GABAergic
(dis-inhibitory)
– direct pathway
Thalamus
Striatum
External
globus
pallidus
GABAergic
(inhibitory)
GABAergic
(inhibitory)
Internal
globus
pallidus
GABAergic
(dis-dis-inhibitory)
– indirect pathway
GABAergic
(dis-inhibitory)
– indirect pathway
glutamatergic
Subthalamic nucleus
dopaminergic
Substantia nigra
pars
compacta
pars
reticularis
GABAergic
(dis-inhibitory)
dopaminergic

D2 (inhibitory)

Enkephalin



D1 (excitatory)

Dynophrin

Substance P

Matrix

70-80%

D2 MSN

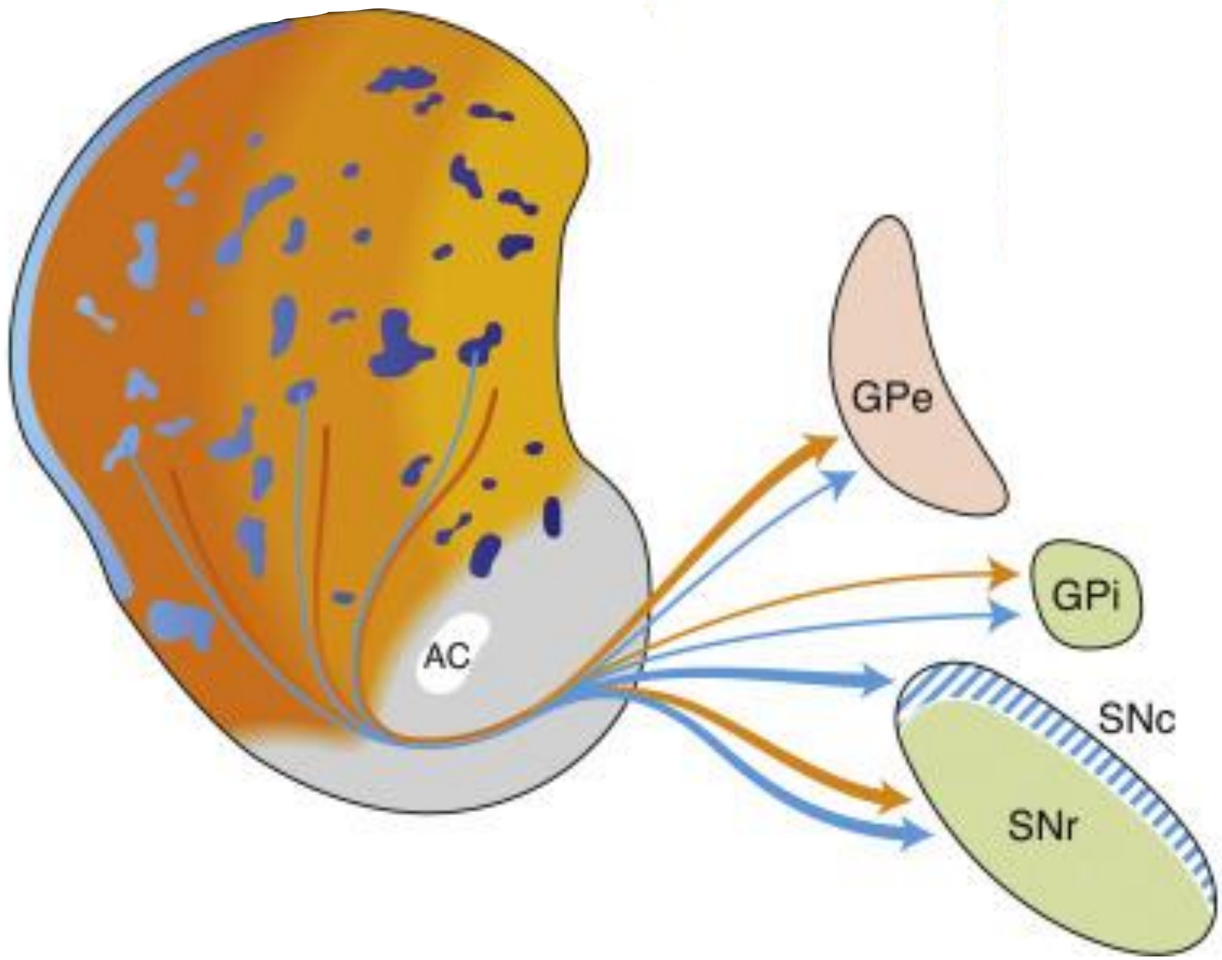
Indirect Pathway

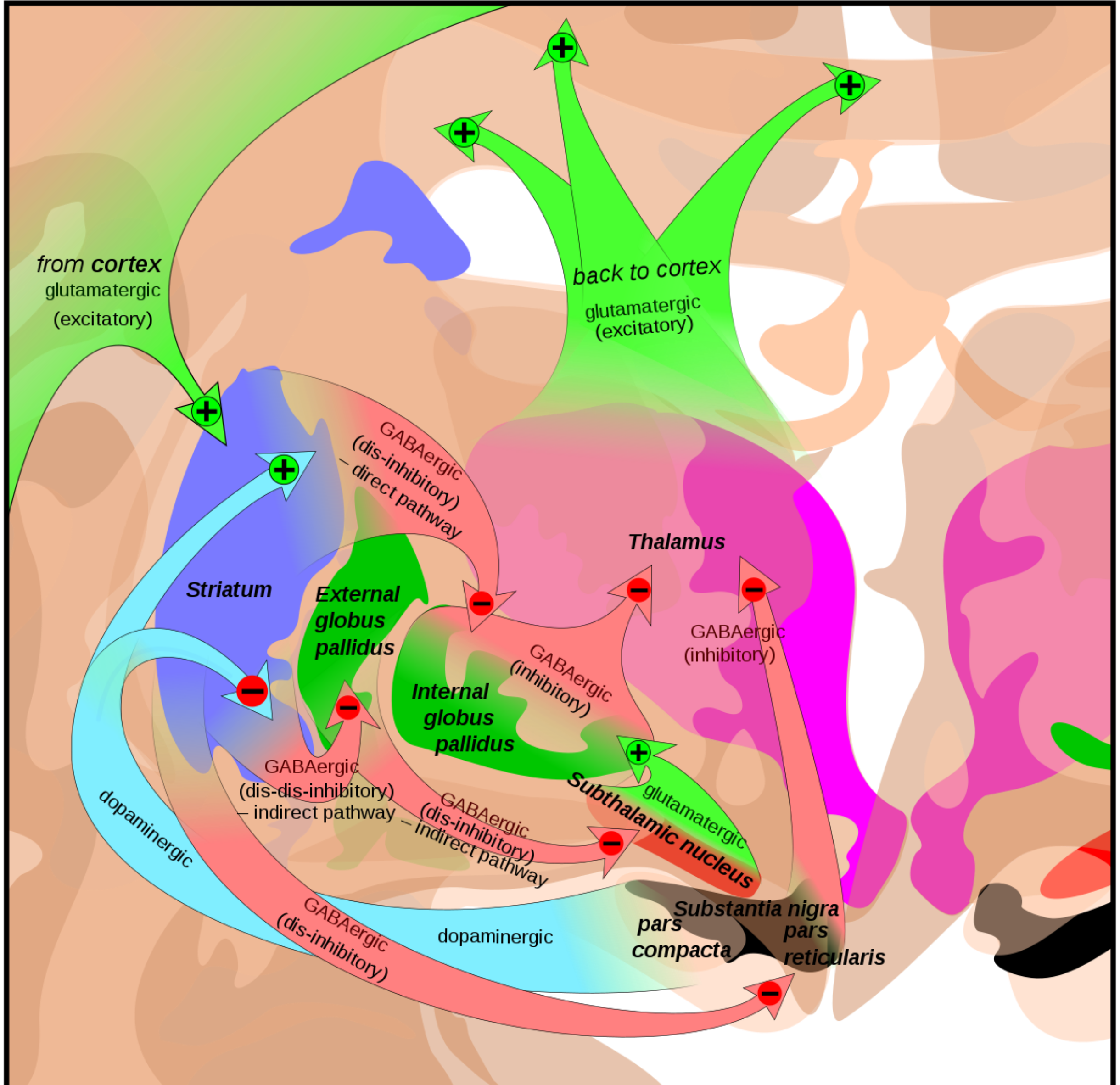
Striosomes

20-30%

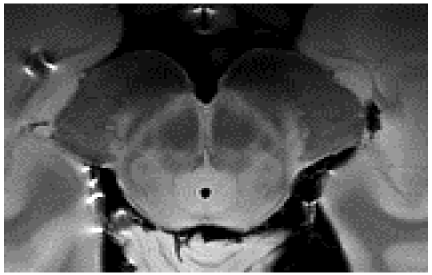
D1 MSN

Direct Pathway

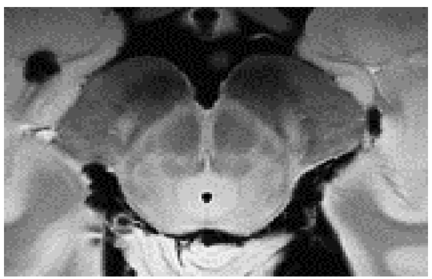



from cortex
glutamatergic
(excitatory)
back to cortex
glutamatergic
(excitatory)
GABAergic
(dis-inhibitory)
– direct pathway
Thalamus
Striatum
External
globus
pallidus
Internal
globus
pallidus
GABAergic
(inhibitory)
GABAergic
(inhibitory)
GABAergic
(dis-dis-inhibitory)
– indirect pathway
GABAergic
(dis-inhibitory)
– indirect pathway
glutamatergic
Subthalamic nucleus
dopaminergic
dopaminergic
GABAergic
(dis-inhibitory)
Substantia nigra
pars
compacta
pars
reticularis

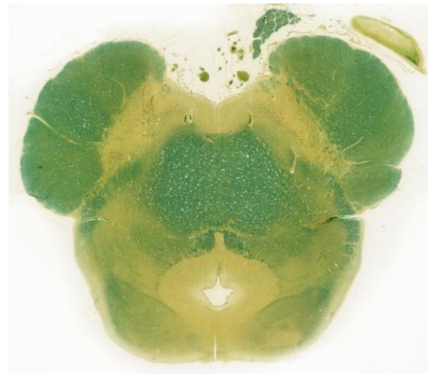
2D SE DP

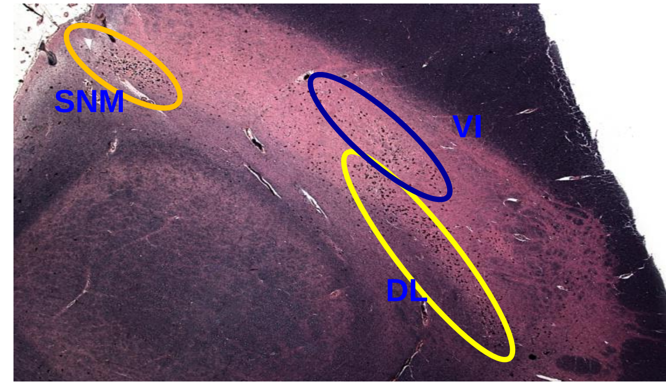


2D GRE T2*

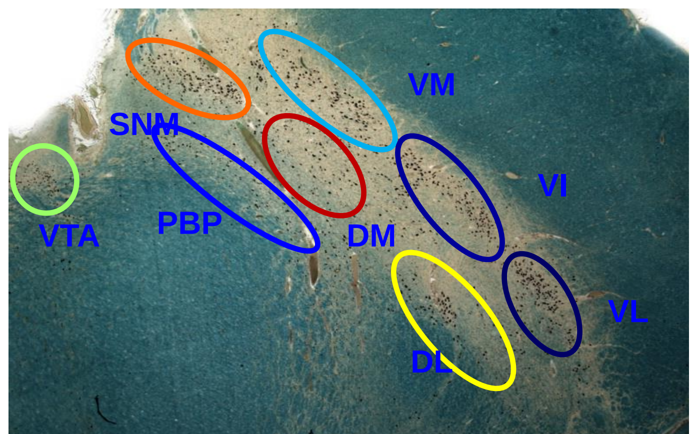


2D SE T2

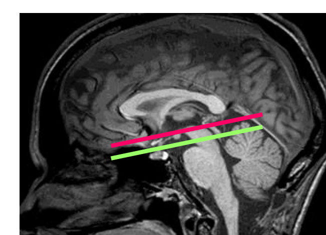




Sezione trasversa rostrale (RN)



Sezione trasversa caudale (PCS)



CLINICAL CASE 2

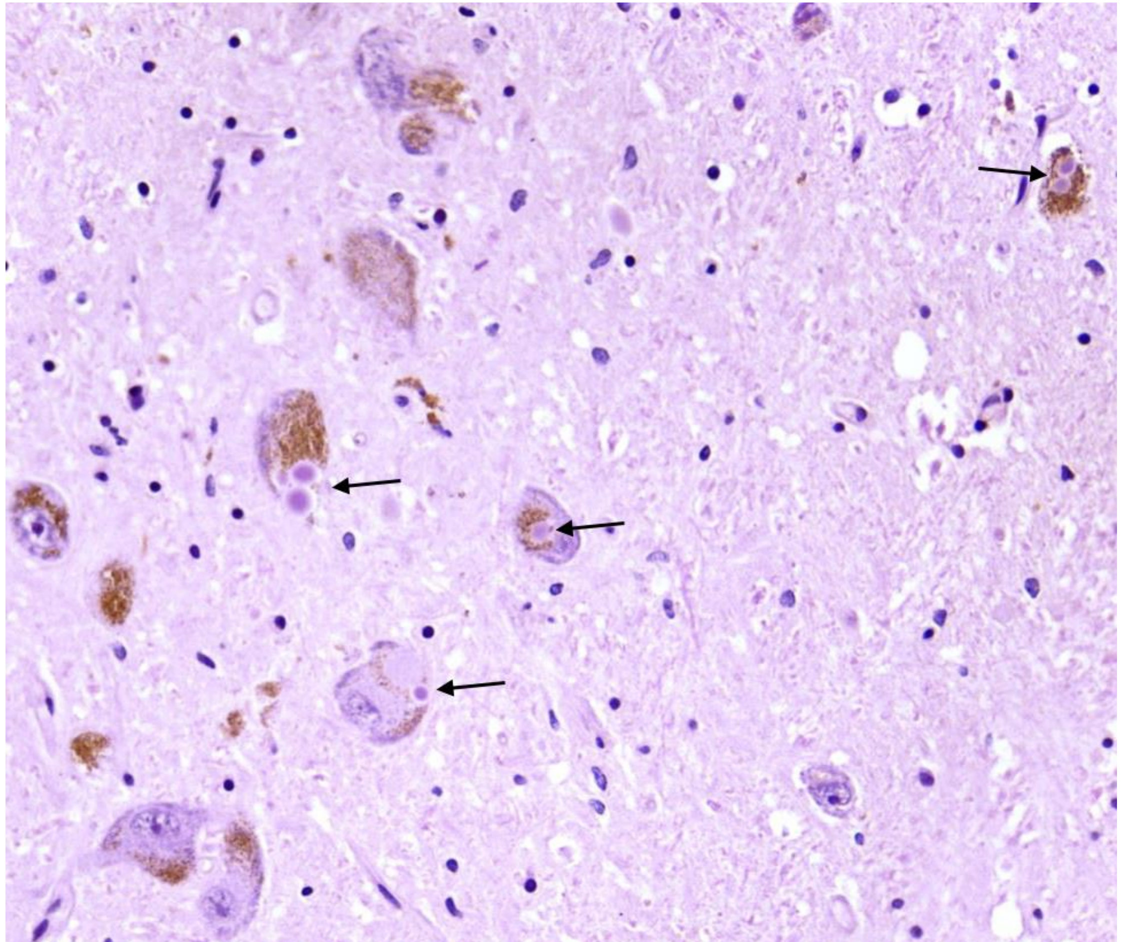
62-year-old Male

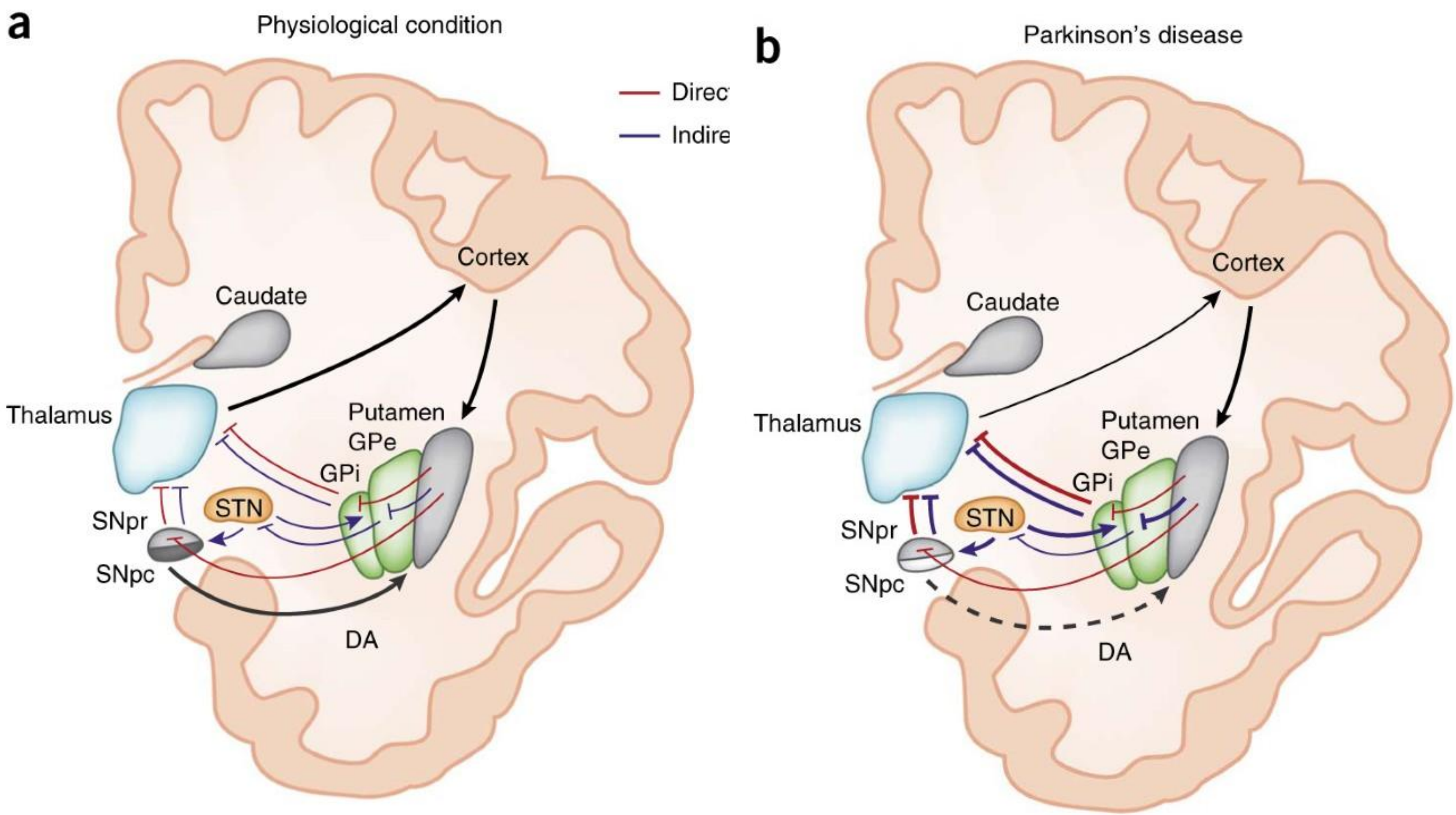
The patient reports onset of mild right upper limb stiffness (10 years prior). Symptoms progressed to difficulty with fine motor control and micrographia. Five years after the onset of the first symptoms, he developed right hand tremor. The tremor spread to involve head and jaw, and had difficulties in initiating movements. CT and MRI scans were normal. Neuropsychological testing revealed mild frontal executive dysfunction.

Neurological examination:
Alert and oriented, speech fluent. Micrographia.
Reduced blink rate, mask-like facial expression.
Motor examination: cogwheel rigidity, bradykinesia (especially of the right upper limb).
Gait: slow, stiff gait with short steps and reduced arm swing.

Where is the site of the lesion?
What’s the likely diagnosis?

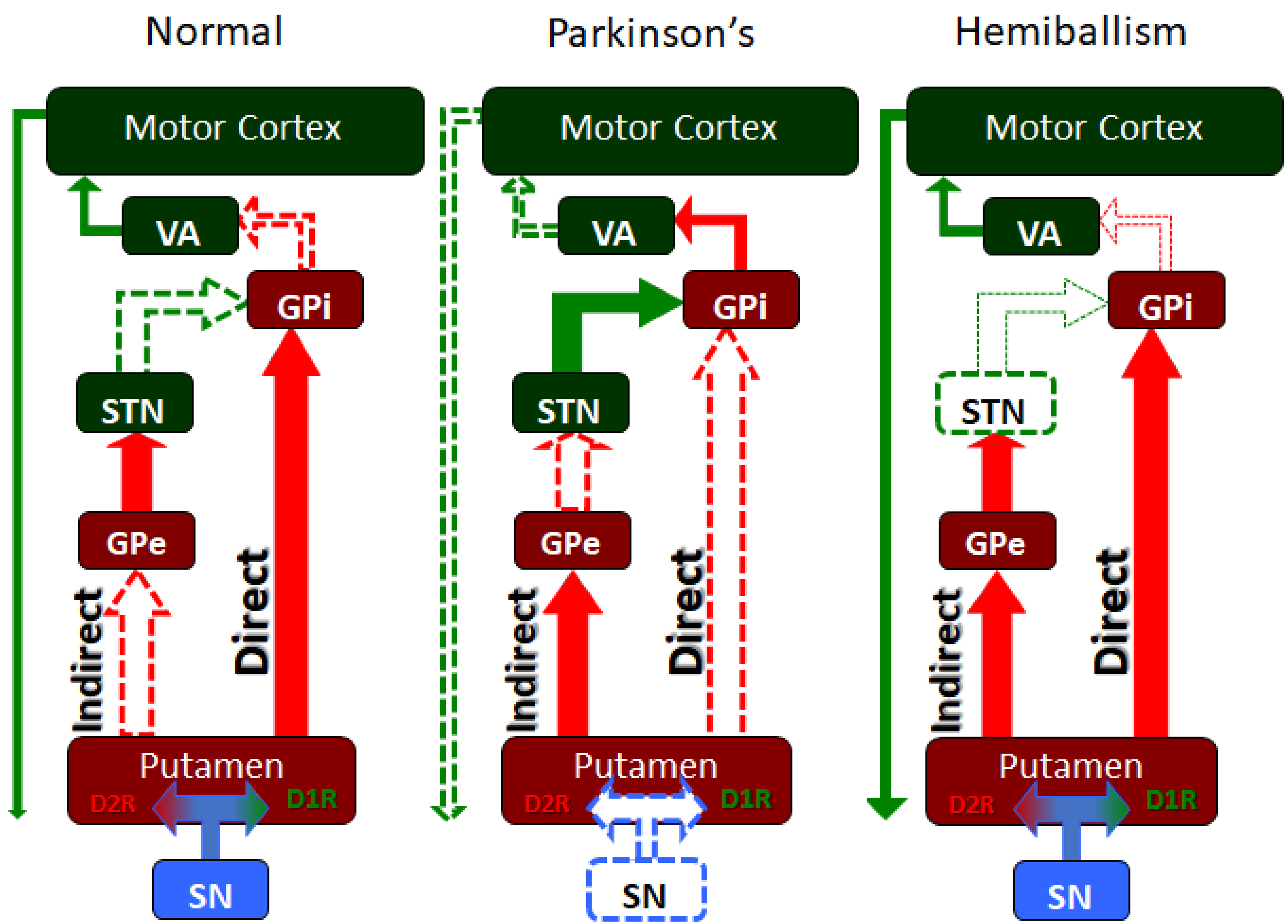
Histopathology





PD → Nigral Degeneration (VL) → Striatal dopaminergic denervation →

- **Matrix is less inhibited**
- **Striosomes are less excitable**


Normal
Parkinson's
Hemiballism
Motor Cortex
VA
GPi
STN
GPe
Indirect
Direct
Putamen
D2R
D1R
SN
Motor Cortex
VA
GPi
STN
GPe
Indirect
Direct
Putamen
D2R
D1R
SN
Motor Cortex
VA
GPi
STN
GPe
Indirect
Direct
Putamen
D2R
D1R
SN

CLINICAL CASE 1

40-year-old Male

The patient’s girlfriend reports irregular jerking movements, initially of the upper limbs, and progressively of the trunk, neck and lower limbs. The patient denies having any involuntary movements. Also, behaviour is disinhibited with flat affect.

Neurological examination:
Alert and oriented, fluent speech. Mild blunted affect.
Saccadic eye movements appear slowed.
Motor examination: sporadic, brief and irregular movements of the face, neck, trunk and upper estremities. Tandem gait unsteady.

Where is the site of the lesion?
What’s the likely diagnosis?

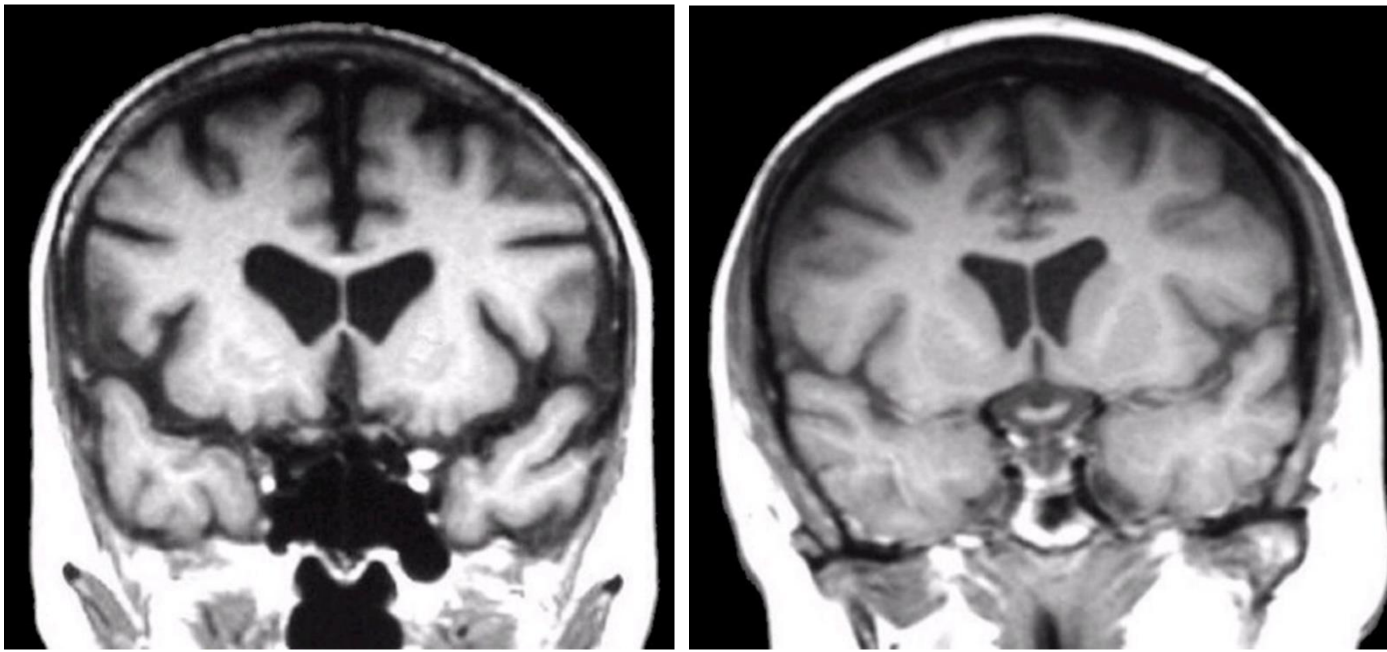
CLINICAL CASE 1

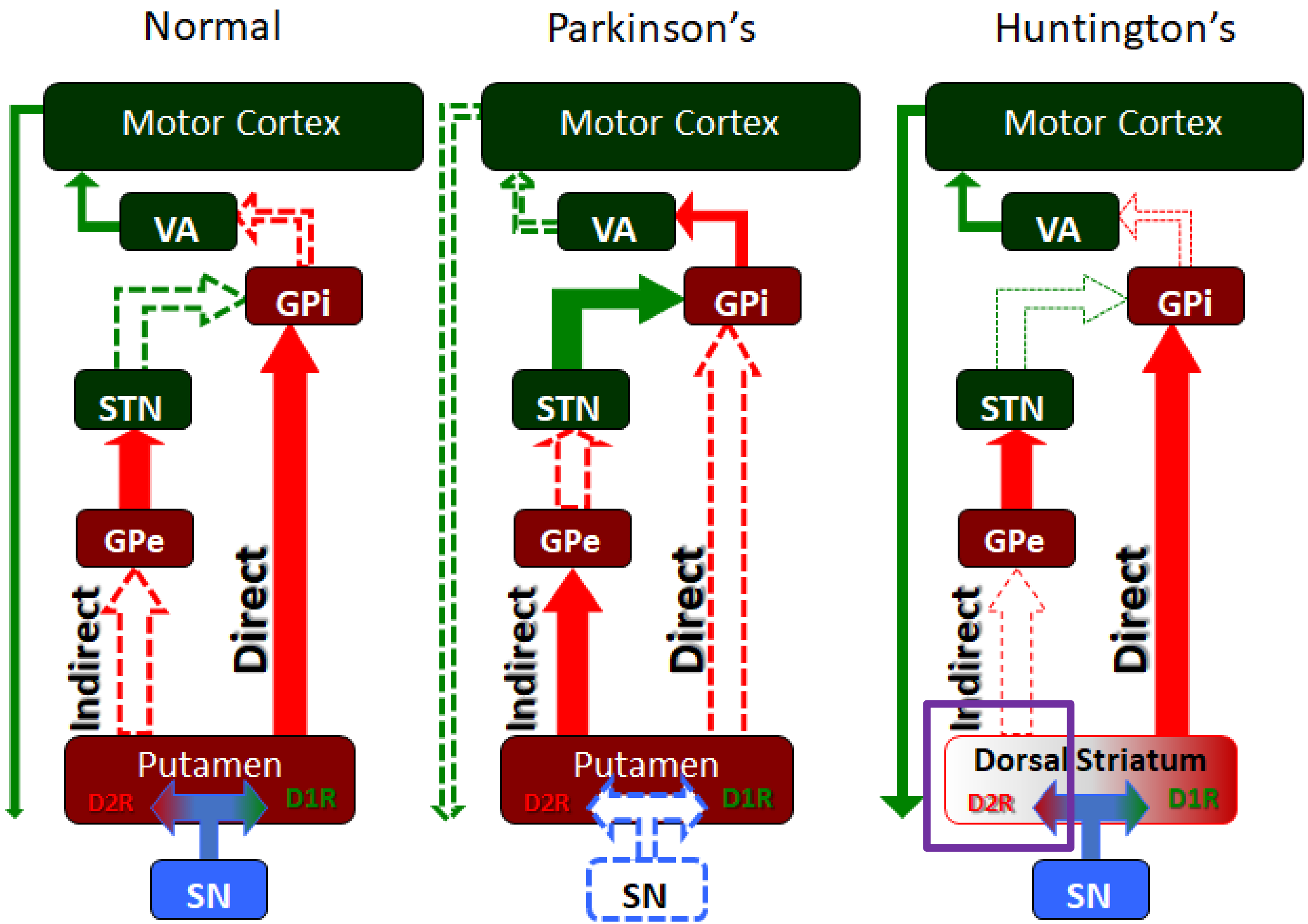
40-year-old Male

Family history: No siblings. Father was affected by the same symptoms and died 5 years following initial onset at age 49. Mother's family was unaffected.

Patient MRI

Healthy MRI

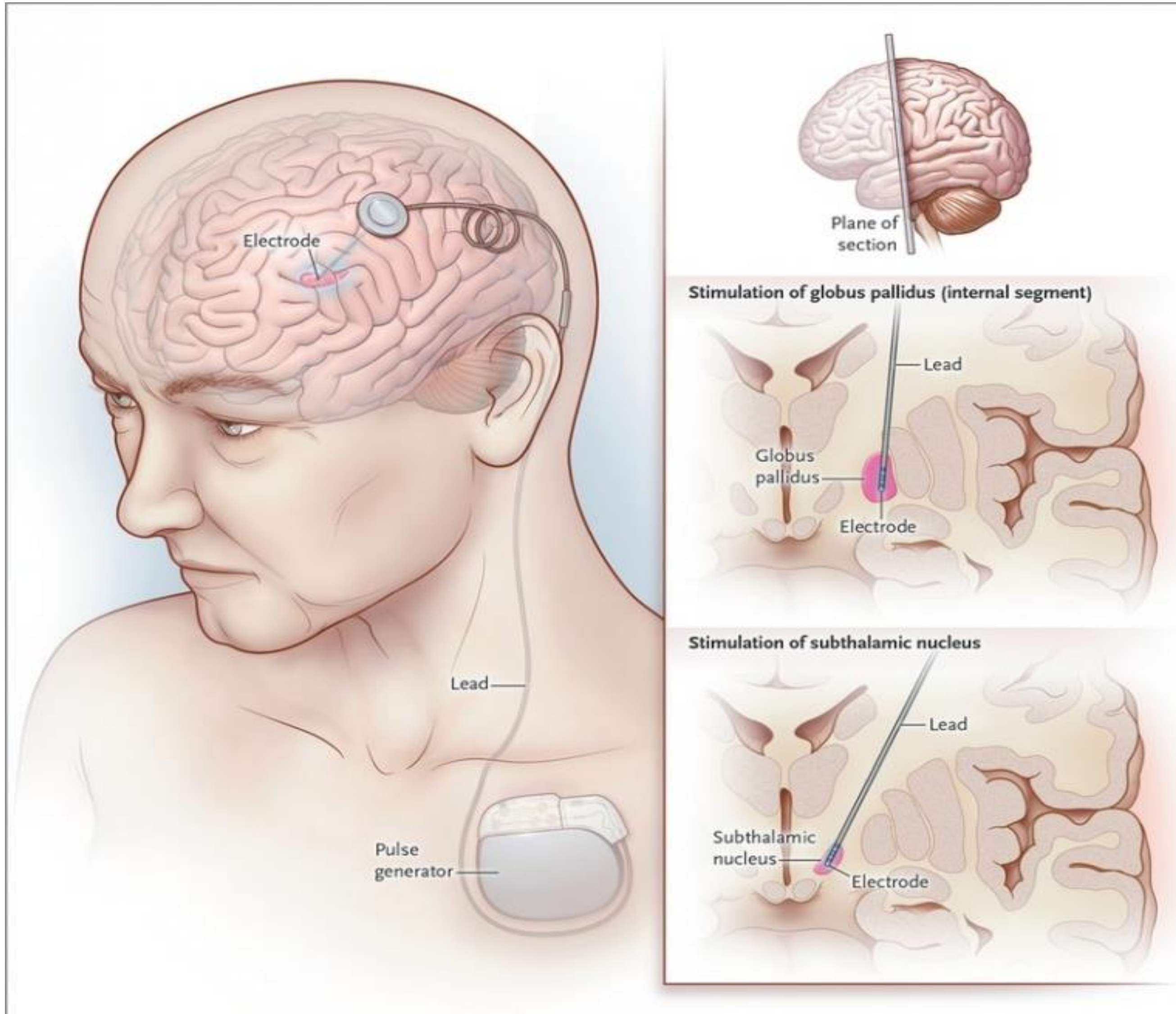


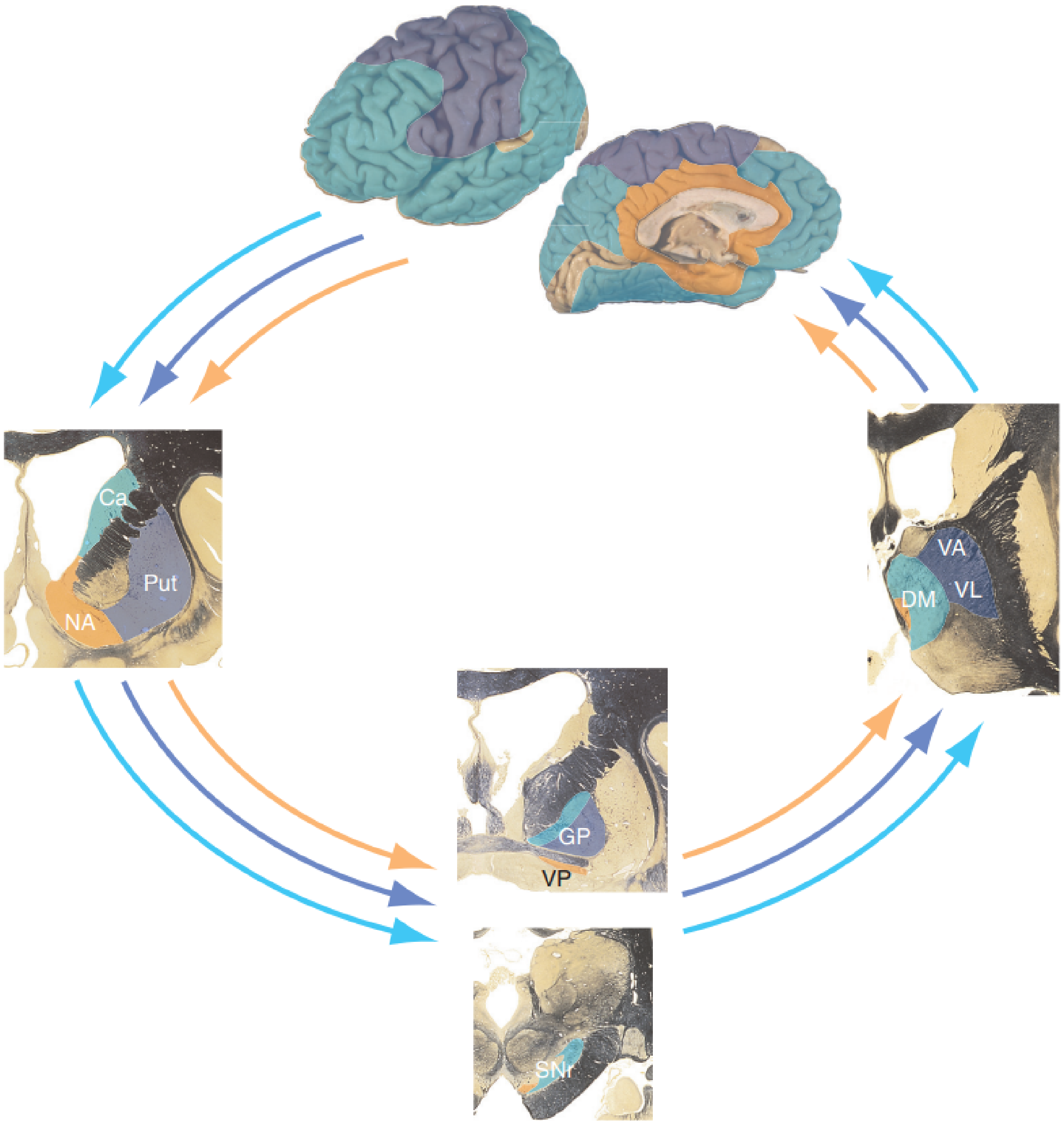
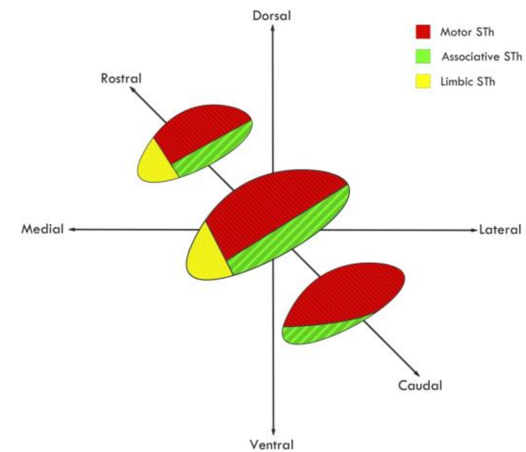


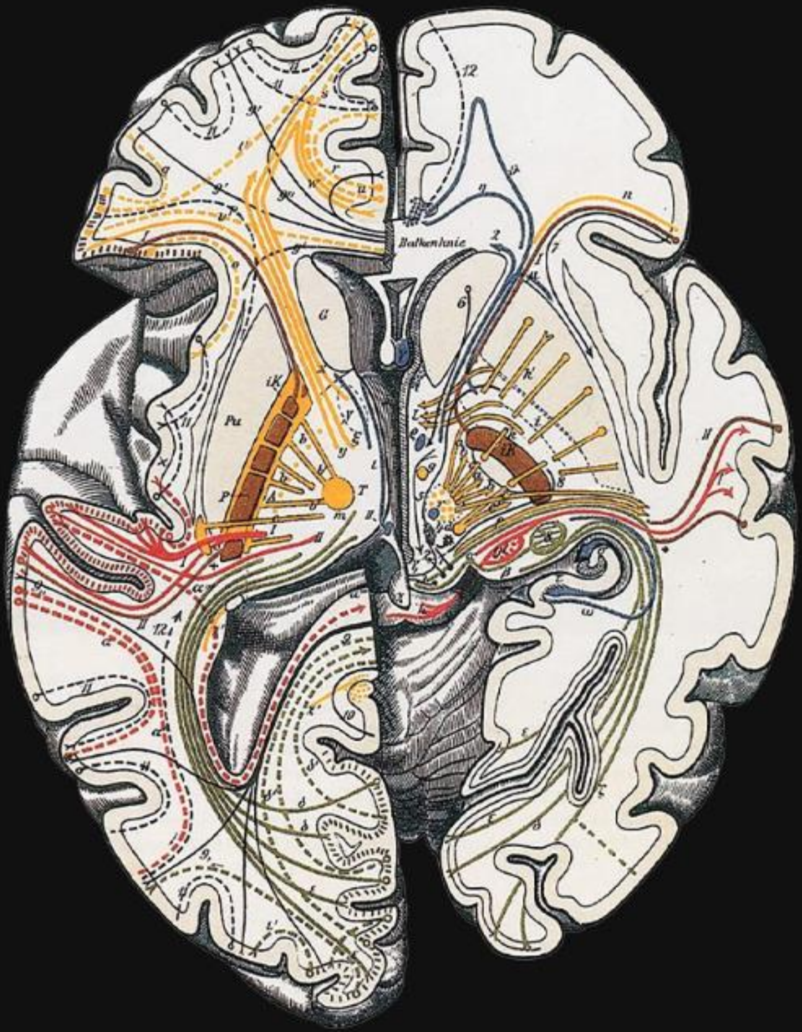
Autosomal dominant –

degeneration of matrix MSN

Deep brain stimulation for movement disorders




Ca
Put
NA
GP
VP
SNr
VA
VL
DM

Dorsal
Motor STh
Associative STh
Limbic STh
Rostral
Medial
Lateral
Caudal
Ventral

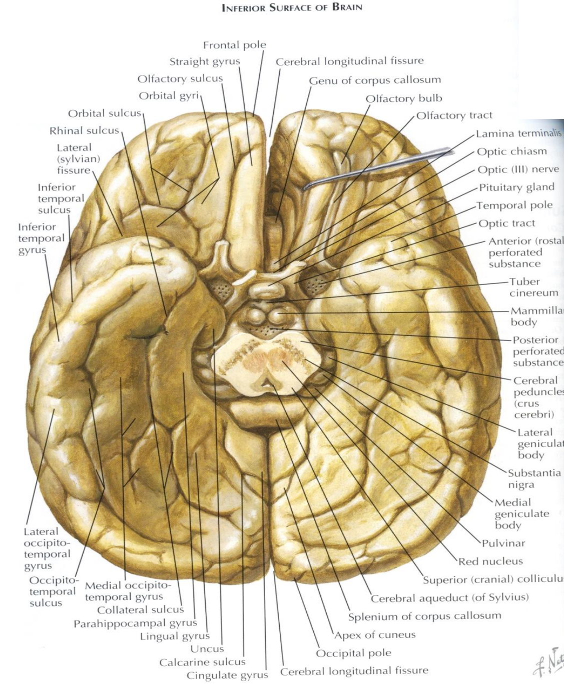


The Telencephalon

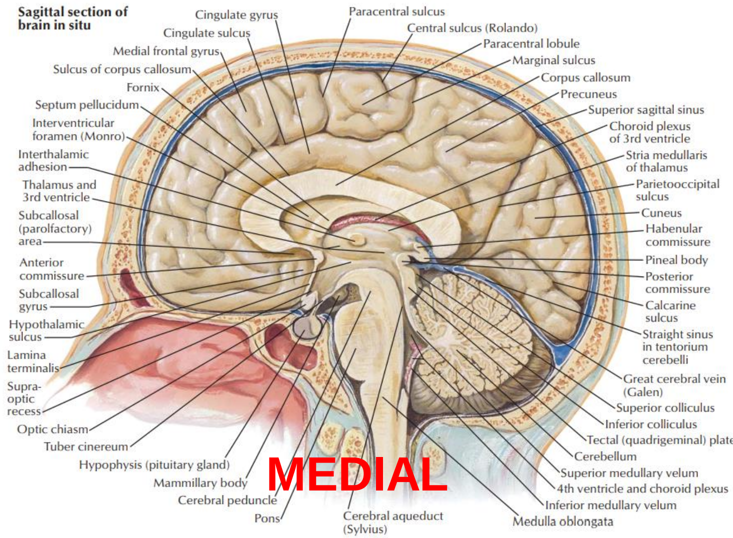
P. Flechsig - Gehirn und Seele

SURFACES OF THE CEREBRAL HEMISPHERES

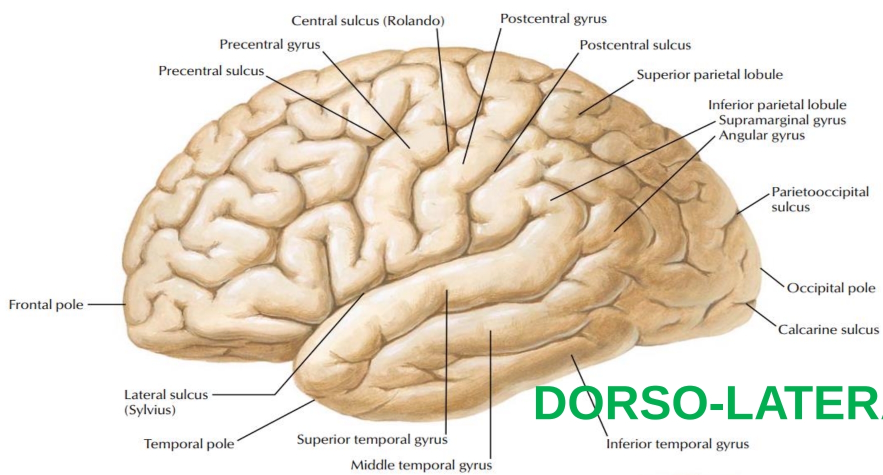
INFERIOR / VENTRAL

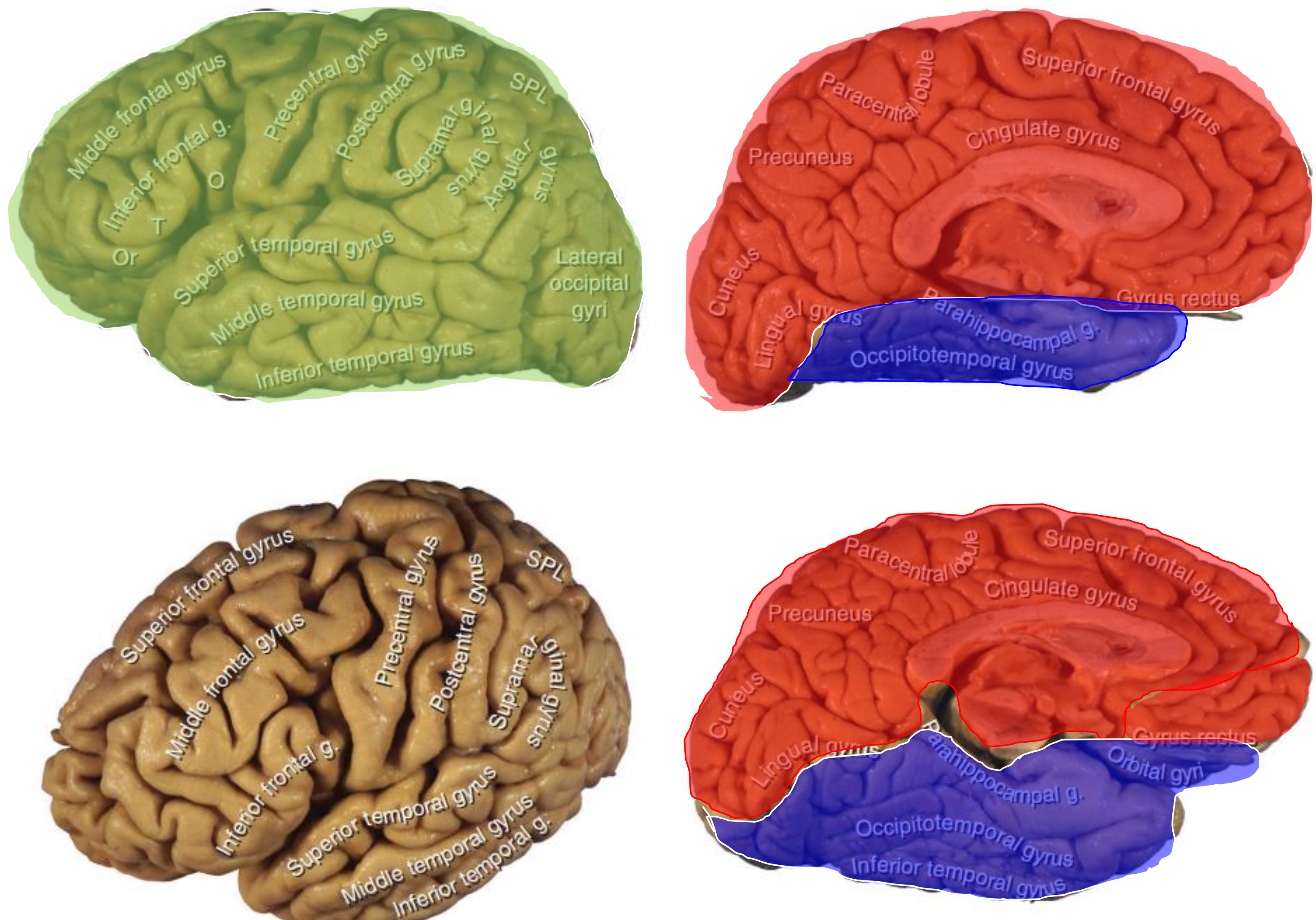


MEDIAL



DORSO-LATERAL



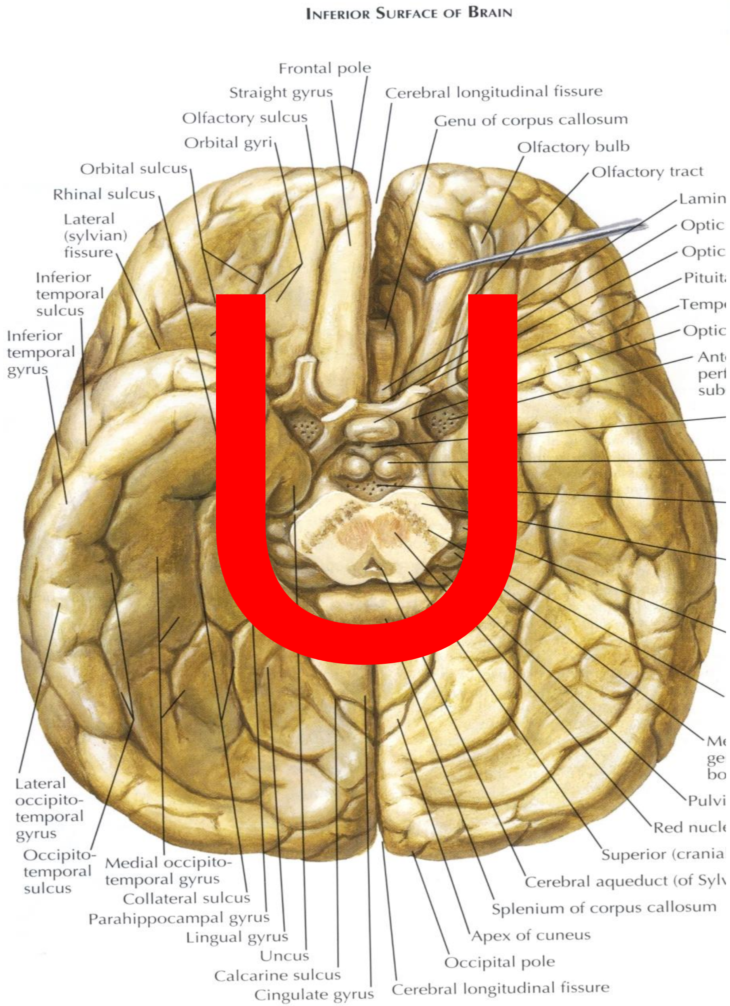

Middle frontal gyrus
Precentral gyrus
Postcentral gyrus
SPL
Inferior frontal g.
O
T
Or
Supramarginal gyrus
Angular gyrus
Superior temporal gyrus
Lateral occipital gyri
Middle temporal gyrus
Inferior temporal gyrus
Paracentral lobule
Superior frontal gyrus
Cingulate gyrus
Precuneus
Cuneus
Lingual gyrus
Parahippocampal g.
Gyrus rectus
Occipitotemporal gyrus
Superior frontal gyrus
Middle frontal gyrus
Precentral gyrus
Postcentral gyrus
SPL
Supramarginal gyrus
Inferior frontal g.
Superior temporal gyrus
Middle temporal gyrus
Inferior temporal g.
Paracentral lobule
Superior frontal gyrus
Cingulate gyrus
Precuneus
Cuneus
Lingual gyrus
Parahippocampal g.
Gyrus rectus
Orbital gyri
Occipitotemporal gyrus
Inferior temporal gyrus

Surface Landmarks

The cerebral hemispheres present a convoluted surface characterized by

- Cerebral convolutions or **gyri**
- Cerebral **furrows** (*sulci, scissures and fissures*).

- **Fissures**: deep clefts which separate large anatomical regions (no variation)
- **Scissures:** deep clefts that separate the hemispheres into distinct **lobes** (little variation)
- **Sulci:** separate gyri from eachother (high variability)



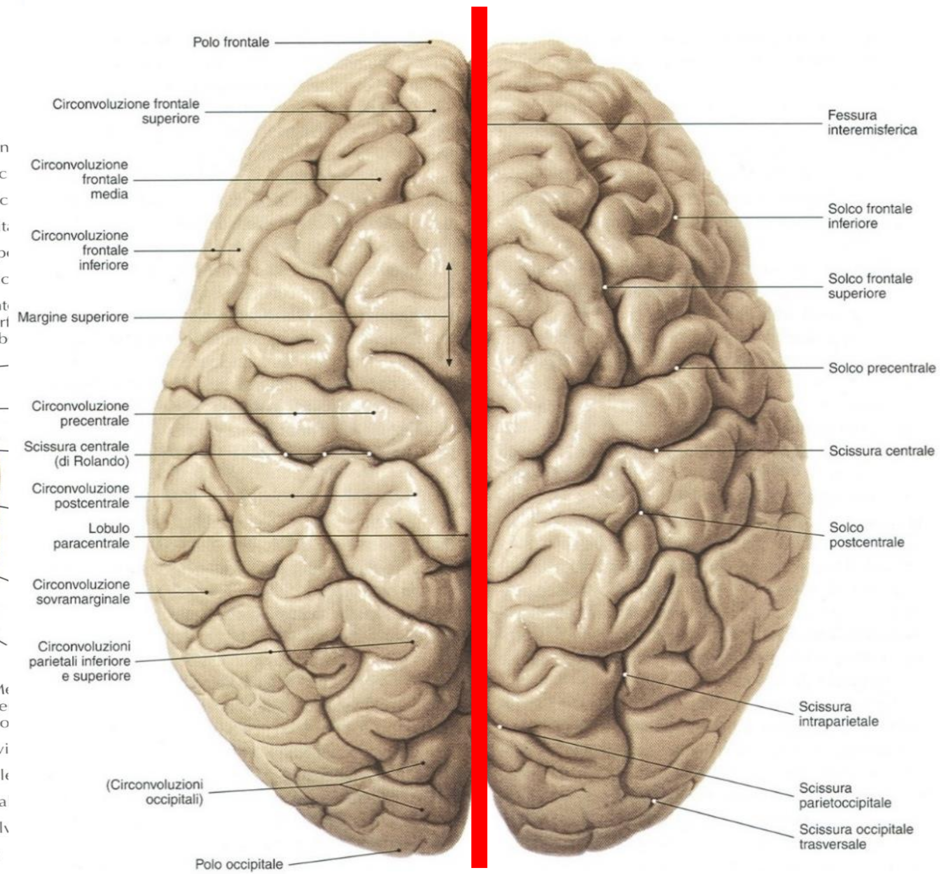


Figura 14.87 - Emisferi cerebrali, proiezione superiore (da Köpf-Maier P, ed.: Wolf-Heidegger's Atlas of Human Anatomy, 5th, completely revised and supplemented edition, Basel, Karger, 2000, with permission from S. Karger AG, Basel).

Transverse fissure of Bichat

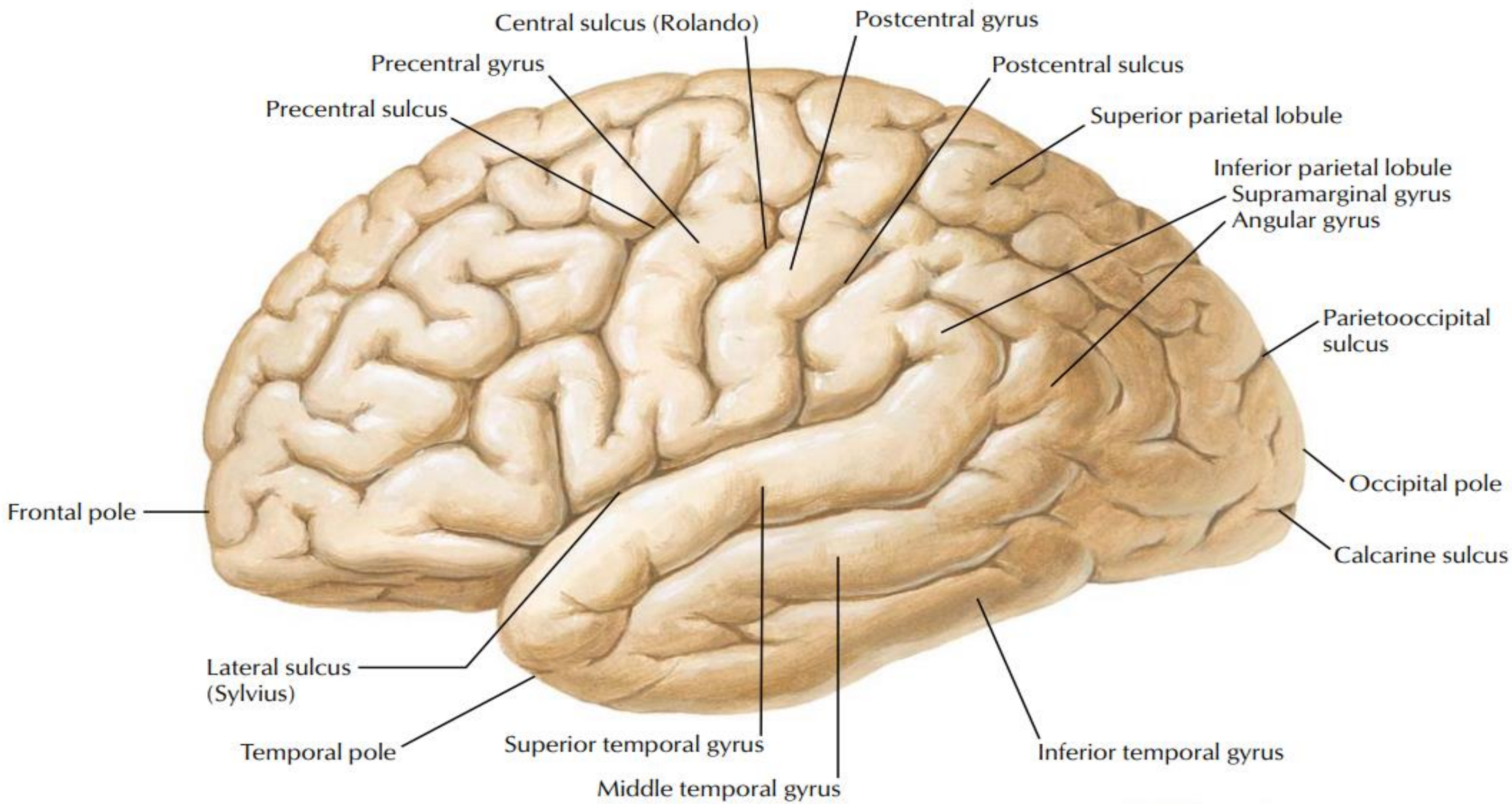
Interhemispheric fissure

LATERAL SURFACE

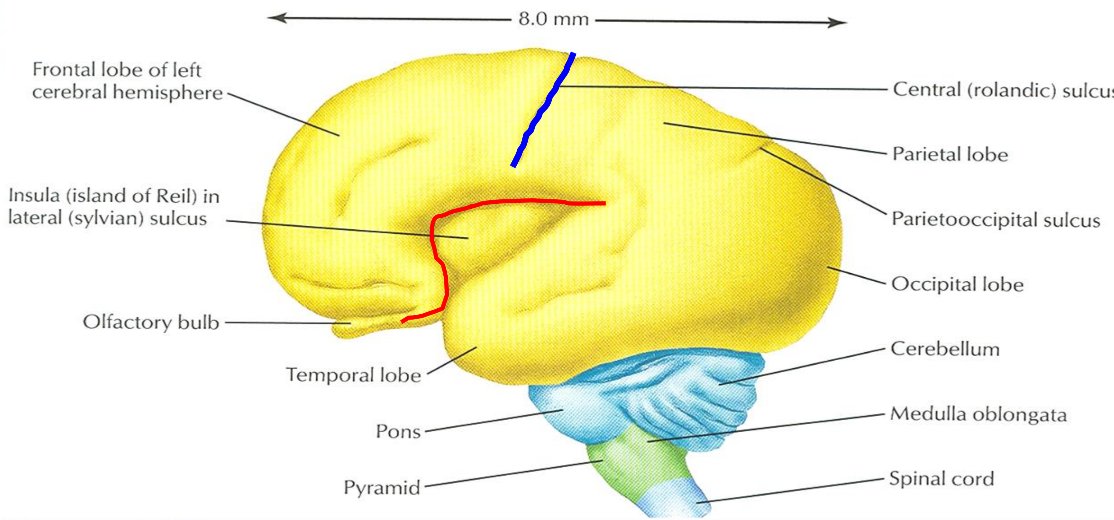
2 Scissures:

Lateral Scissure (Sylvius)

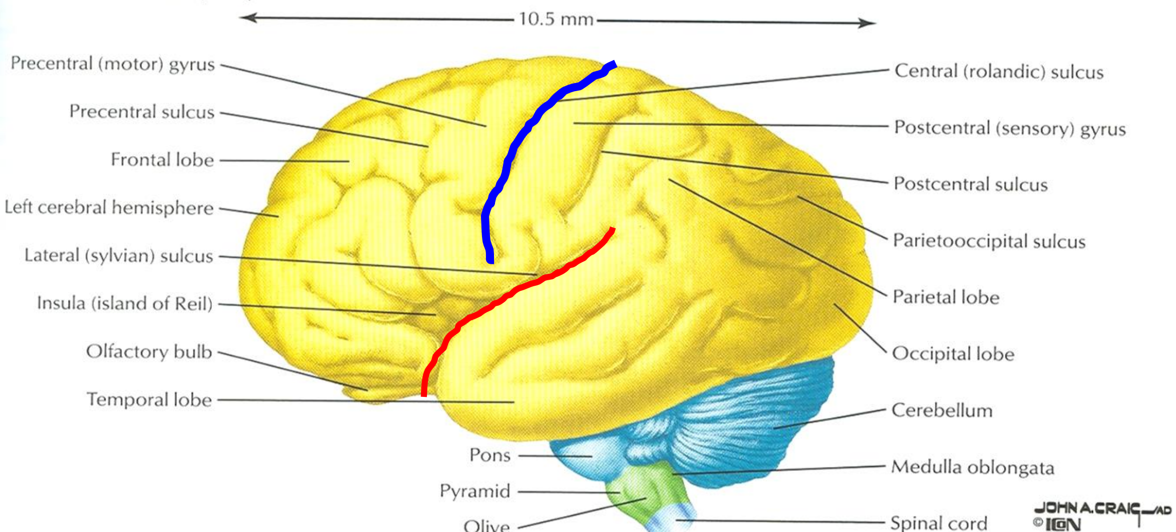
Central Scissure (Rolandus)



Brain at 6 months



Brain at 9 months (birth)



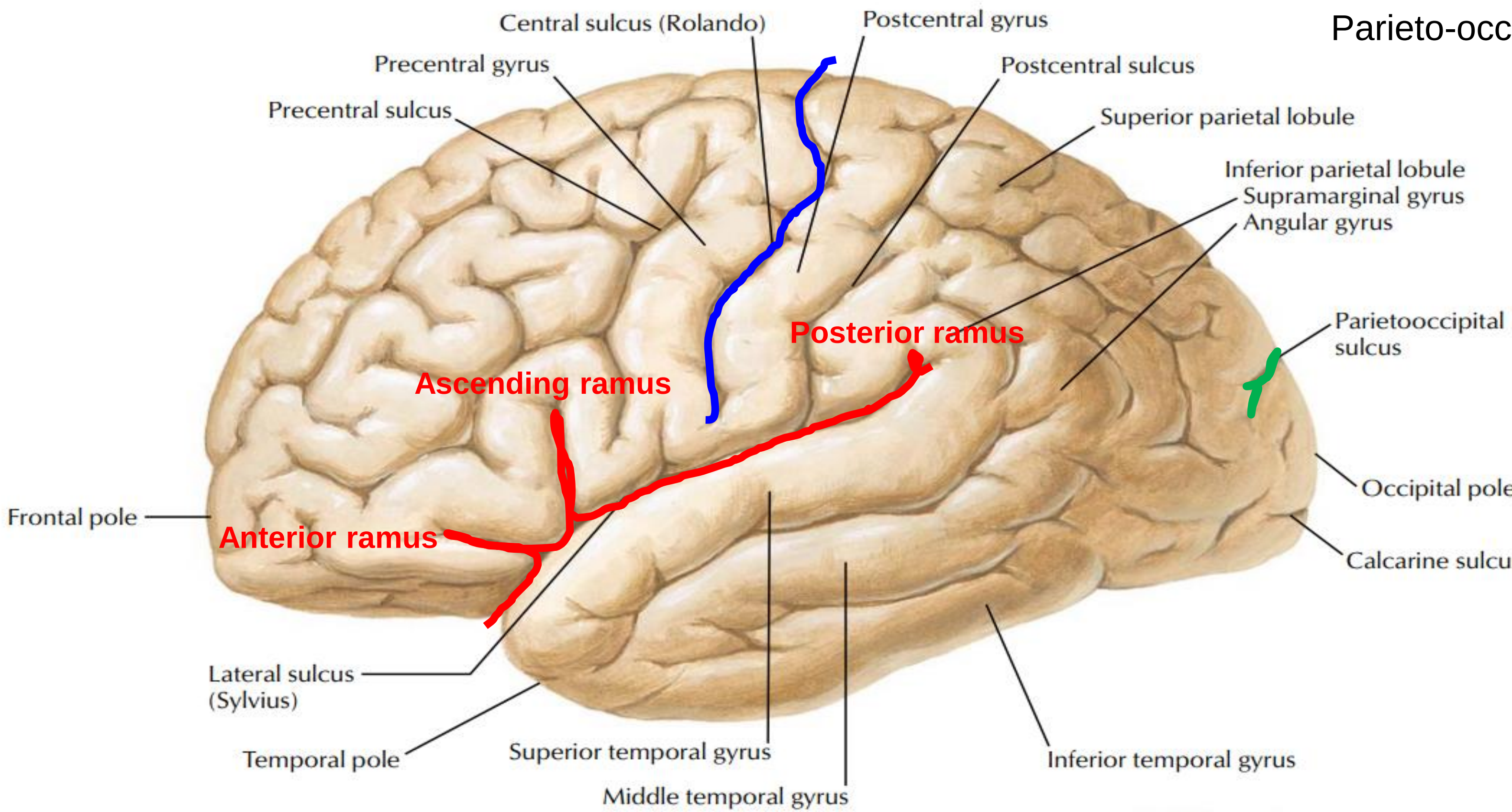
LATERAL SURFACE

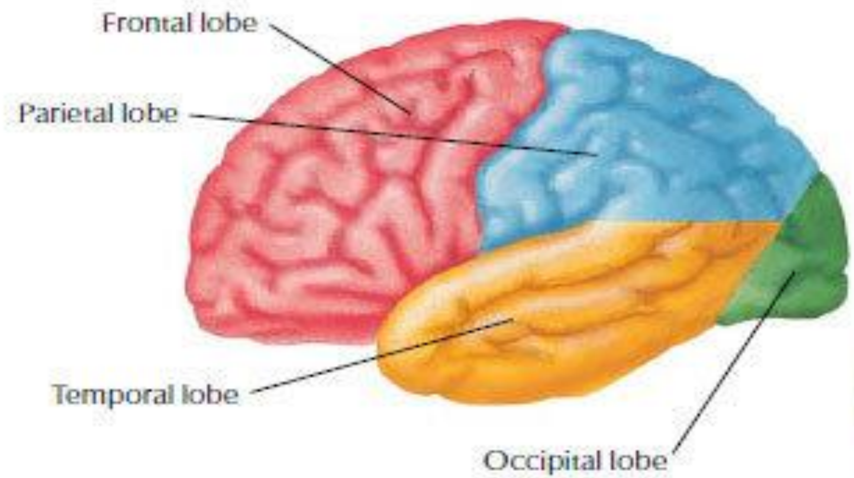
3 Scissures:

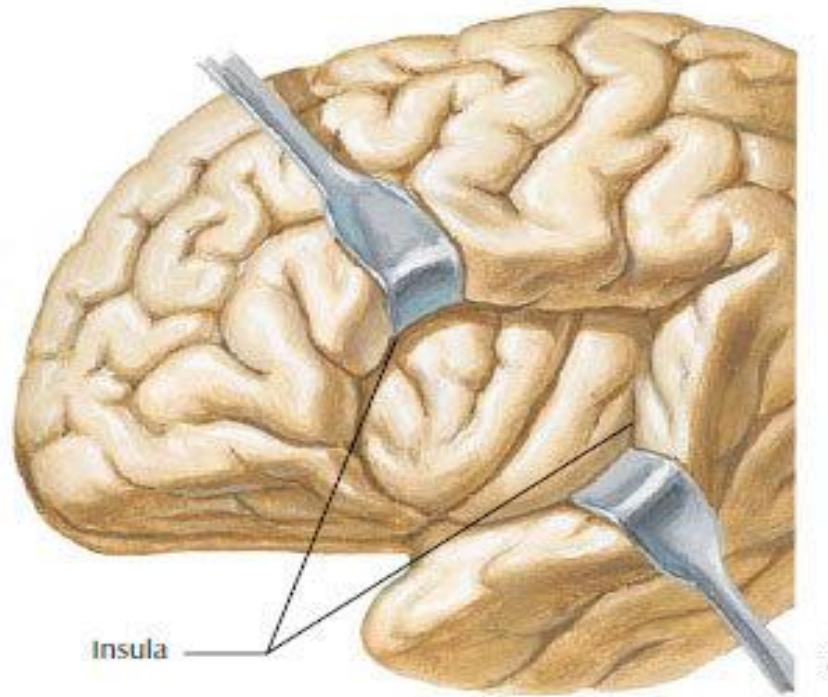
Lateral Scissure (Sylvius)

Central Scissure (Rolandus)

Parieto-occipital







6 Lobes

1. Frontal
2. Parietal
3. Temporal
4. Occipital

Visible (also) from the lateral surface

5. Insular — Visible by widening the Sylvian Scissure
6. Limbic — Visible <u>only</u> from the medial and inferior surface

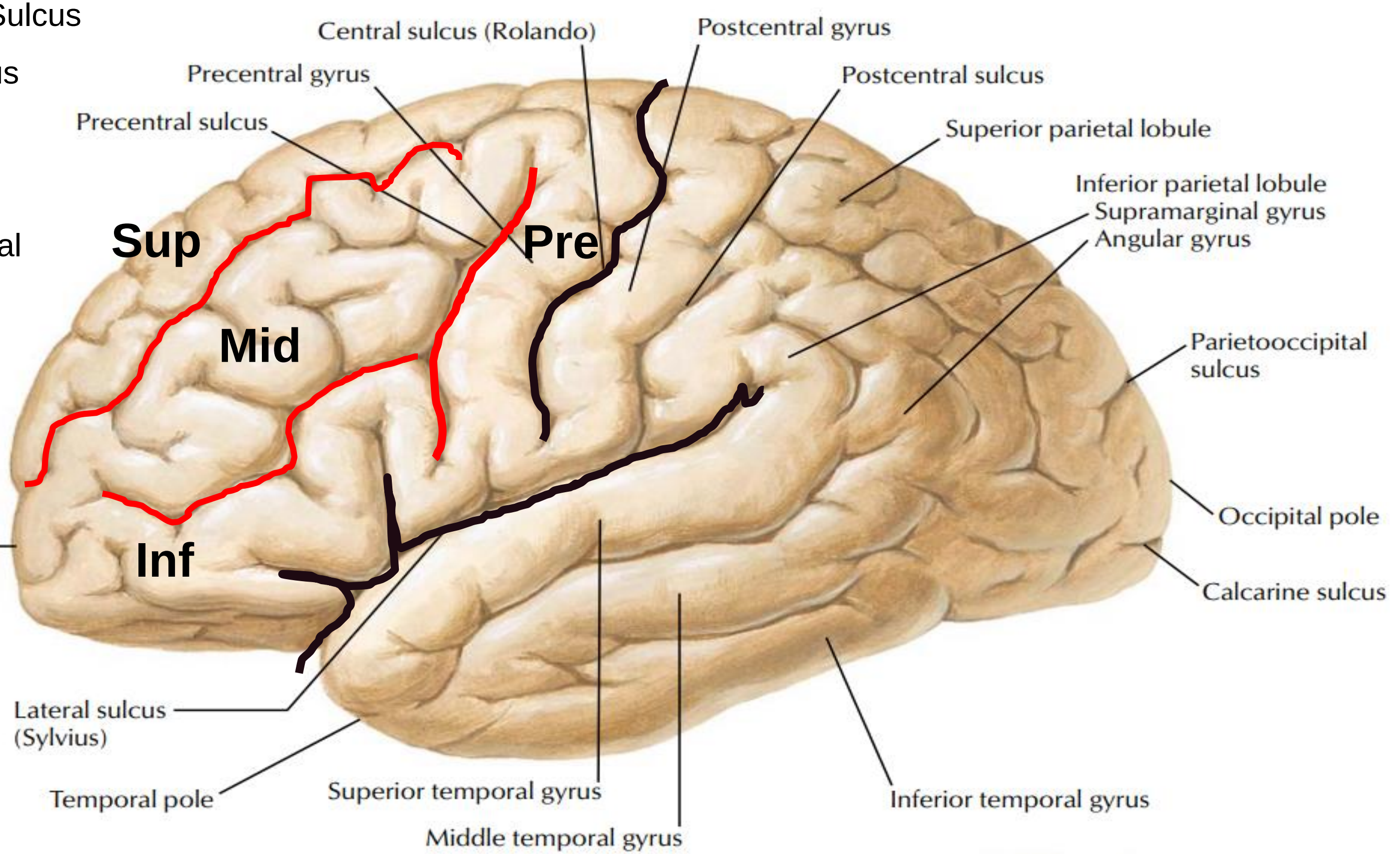
Frontal Lobe – Lateral Surface

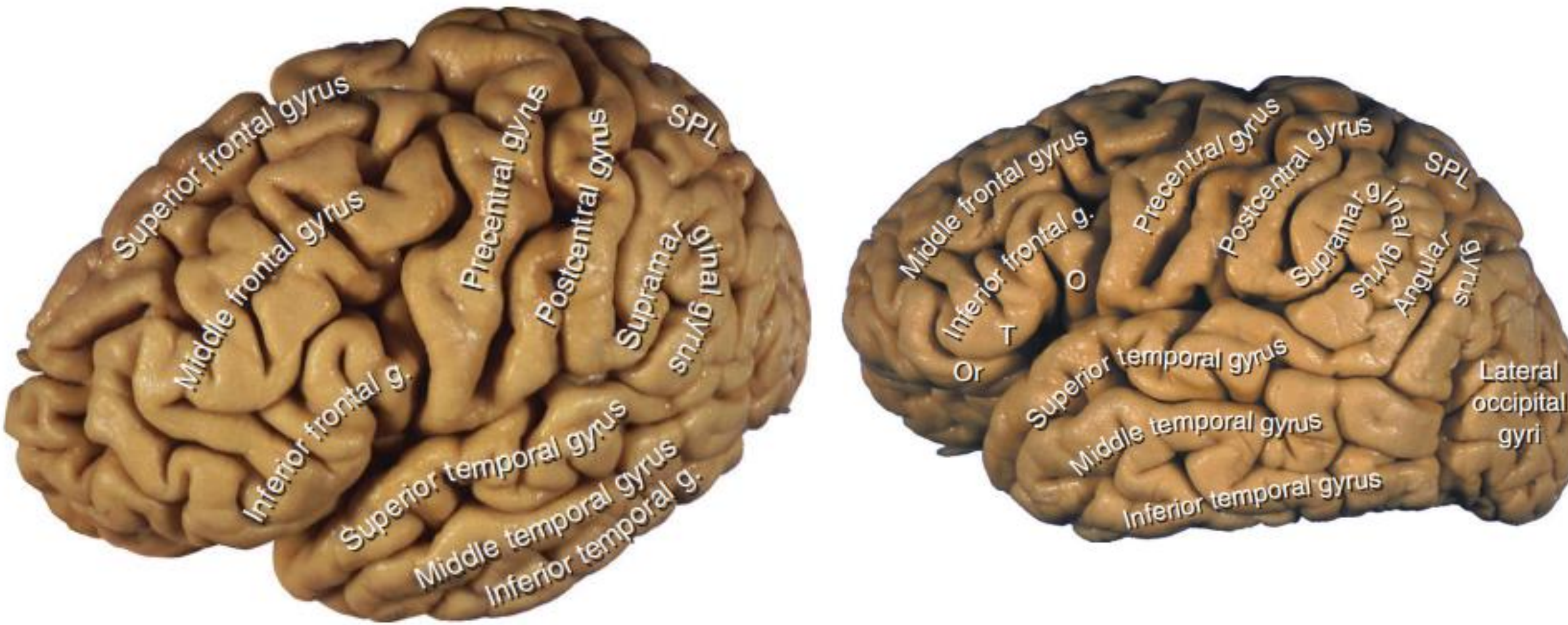
Three sulci

1. Superior Frontal Sulcus
2. Inferior Frontal Sulcus
3. Precentral Sulcus

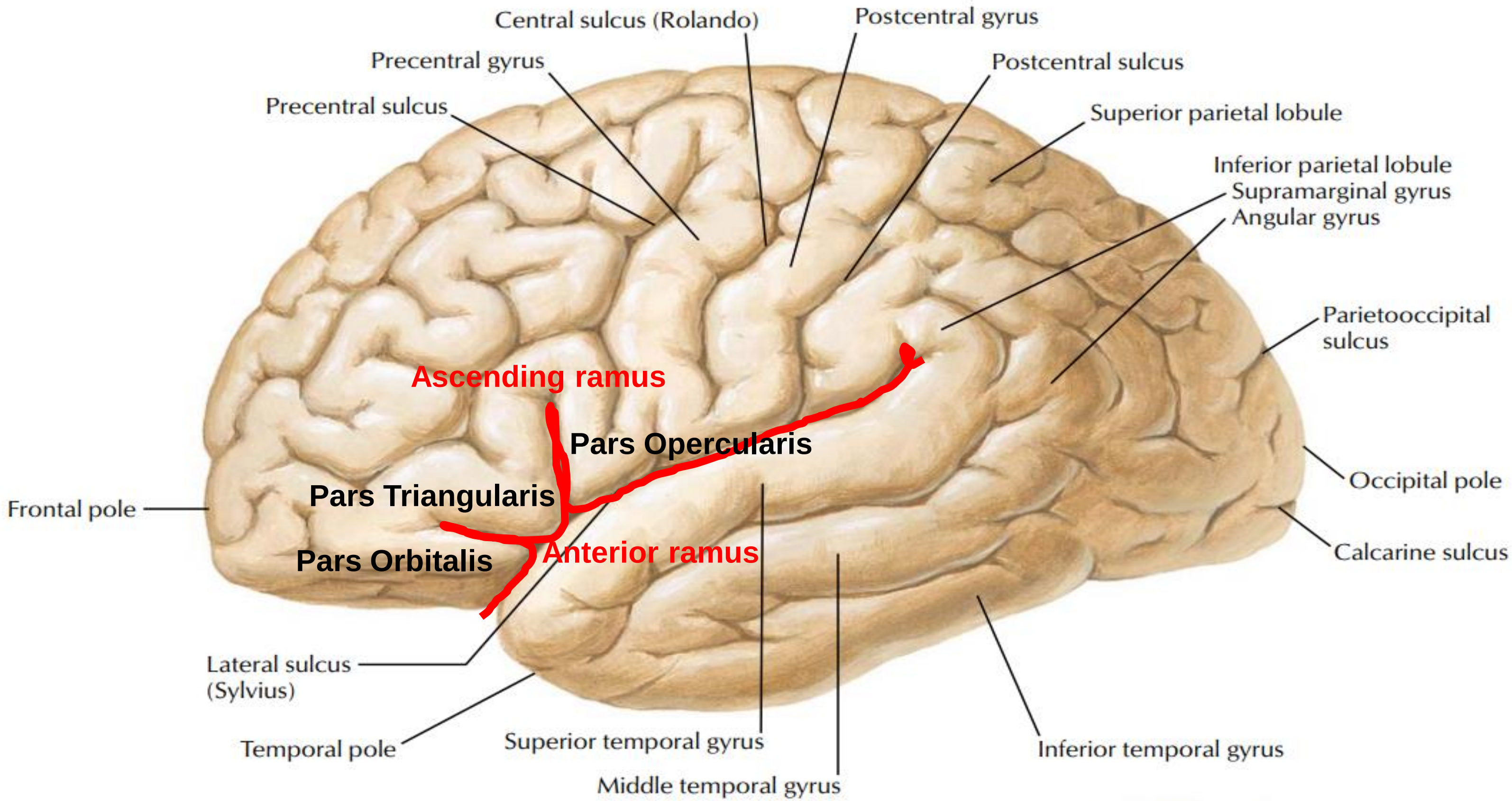
Four Gyri

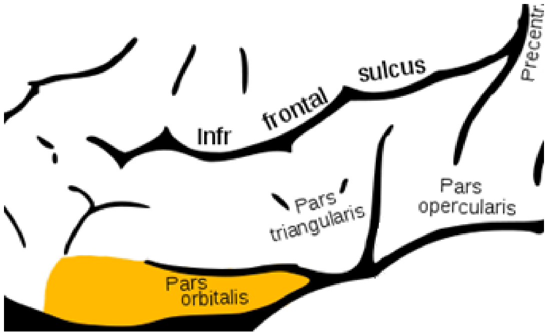
1. Superior Frontal
2. Middle Frontal
3. Inferior Frontal
4. Precentral



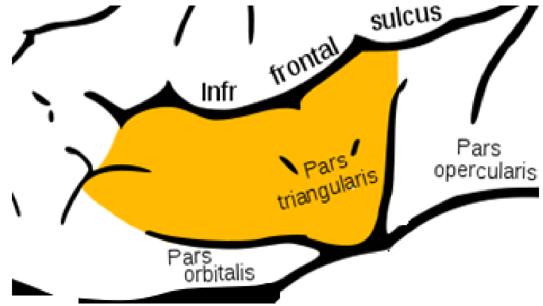

Superior frontal gyrus
Middle frontal gyrus
Precentral gyrus
Postcentral gyrus
SPL
Supramarginal gyrus
Inferior frontal g.
Superior temporal gyrus
Middle temporal gyrus
Inferior temporal g.
Middle frontal gyrus
Inferior frontal g.
Precentral gyrus
Postcentral gyrus
SPL
Supramarginal gyrus
Angular gyrus
O
T
Or
Superior temporal gyrus
Middle temporal gyrus
Inferior temporal gyrus
Lateral occipital gyri

Inferior Frontal Gyrus

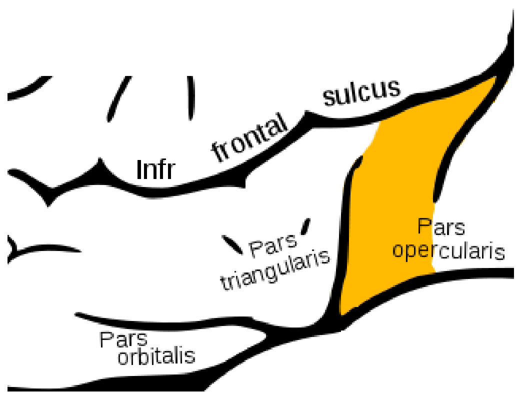




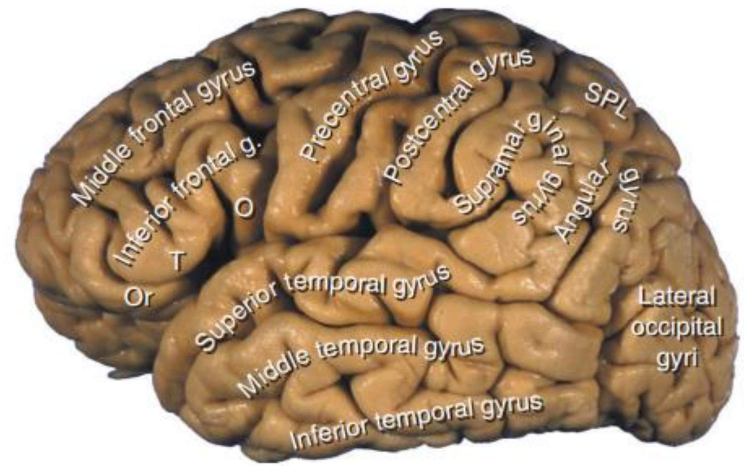
Infr frontal sulcus
Precentr.
Pars triangularis
Pars opercularis
Pars orbitalis



Infr frontal sulcus
Pars triangularis
Pars opercularis
Pars orbitalis



Infr frontal sulcus
Pars triangularis
Pars opercularis
Pars orbitalis



Middle frontal gyrus
Inferior frontal g.
Precentral gyrus
Postcentral gyrus
Supramarginal gyrus
Angular gyrus
SPL
O
T
Or
Superior temporal gyrus
Middle temporal gyrus
Inferior temporal gyrus
Lateral occipital gyri

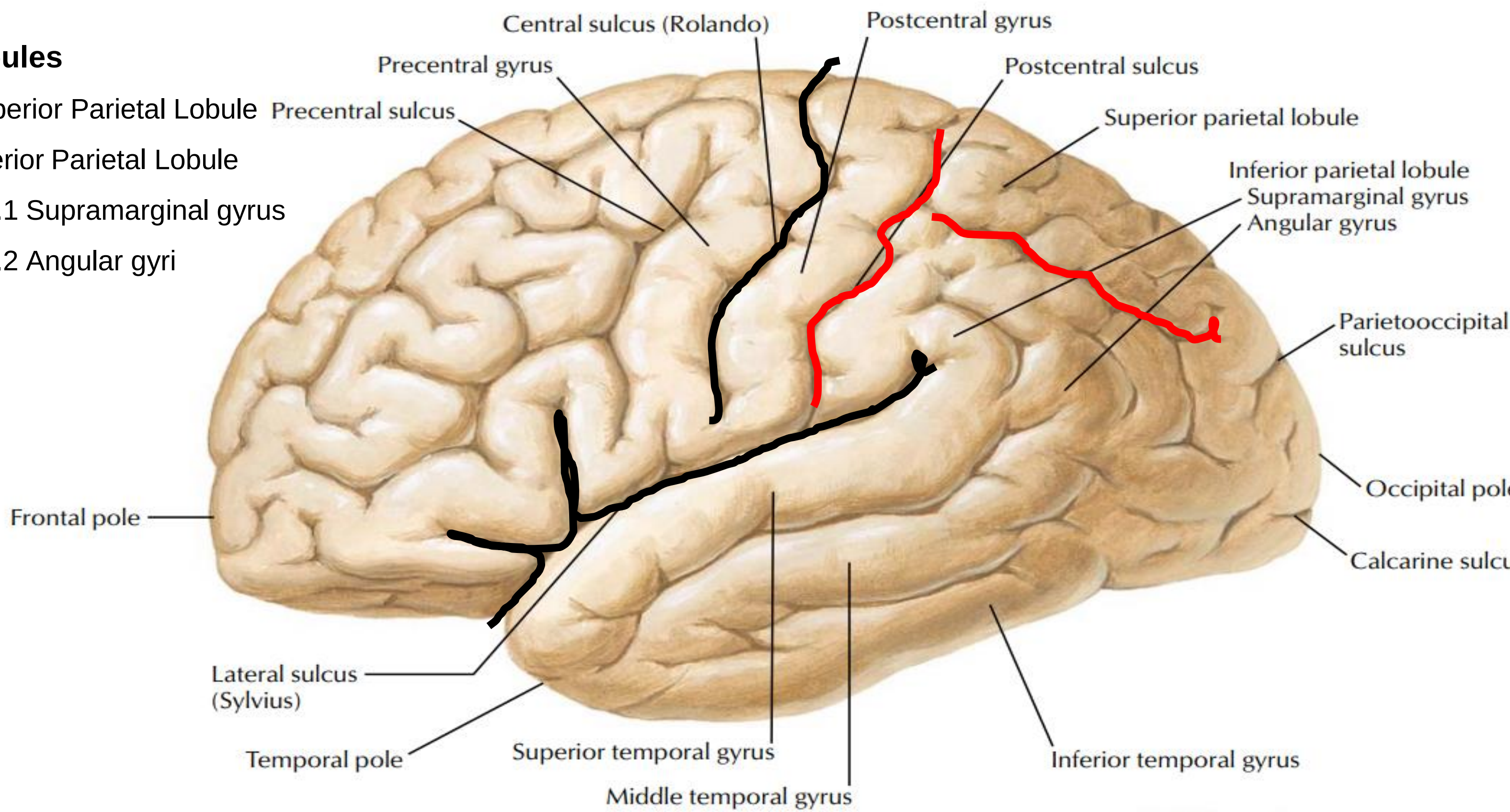
Parietal Lobe – Lateral Surface

Two Sulci

1. Postcentral sulcus
2. Intraparietal sulcus

Two lobules

1. Superior Parietal Lobule
2. Inferior Parietal Lobule
   - 2.1 Supramarginal gyrus
   - 2.2 Angular gyri



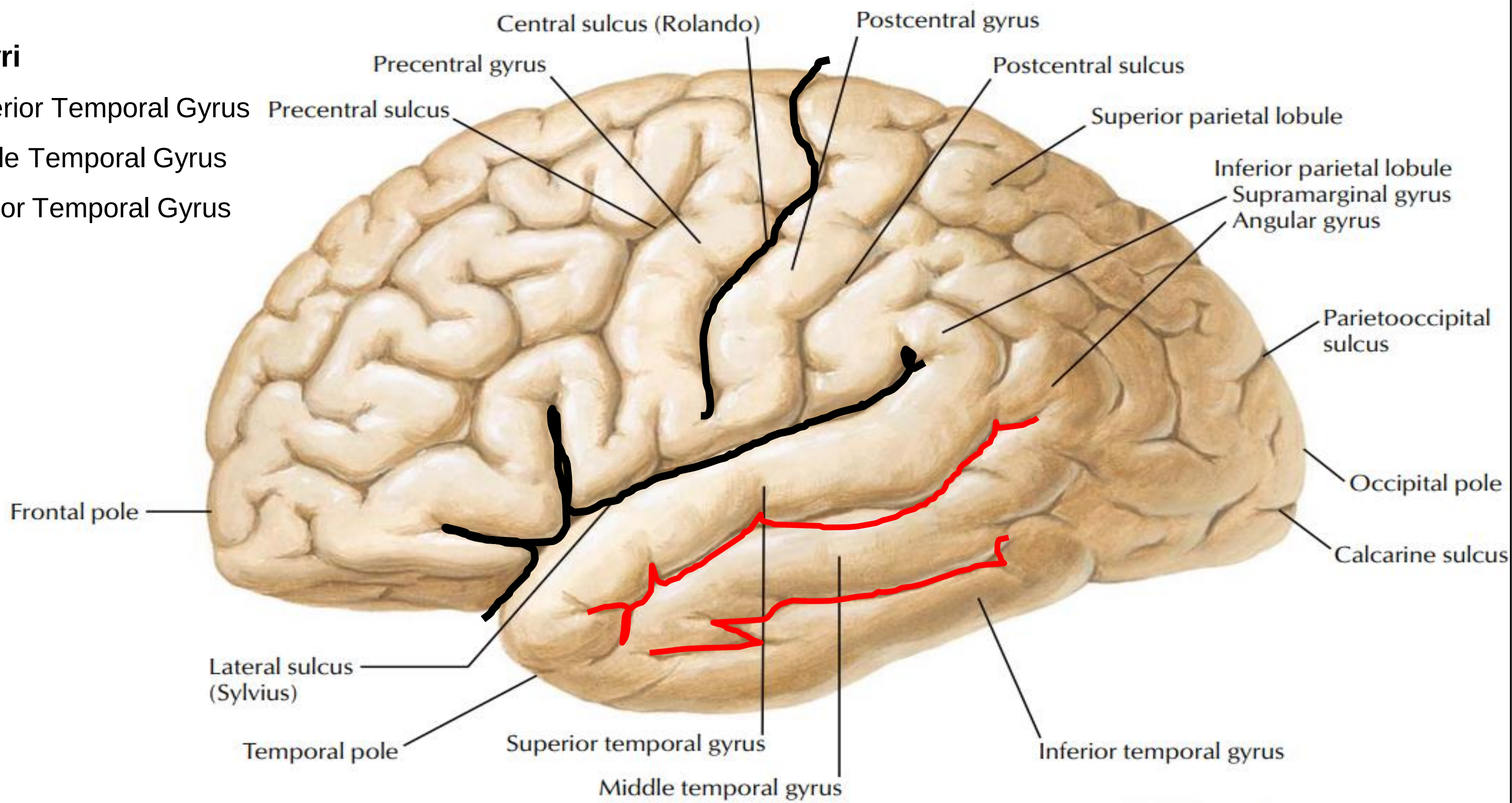
Temporal Lobe – Lateral Surface

Two Sulci

1. Superior Temporal Sulcus
2. Inferior Temporal Sulcus

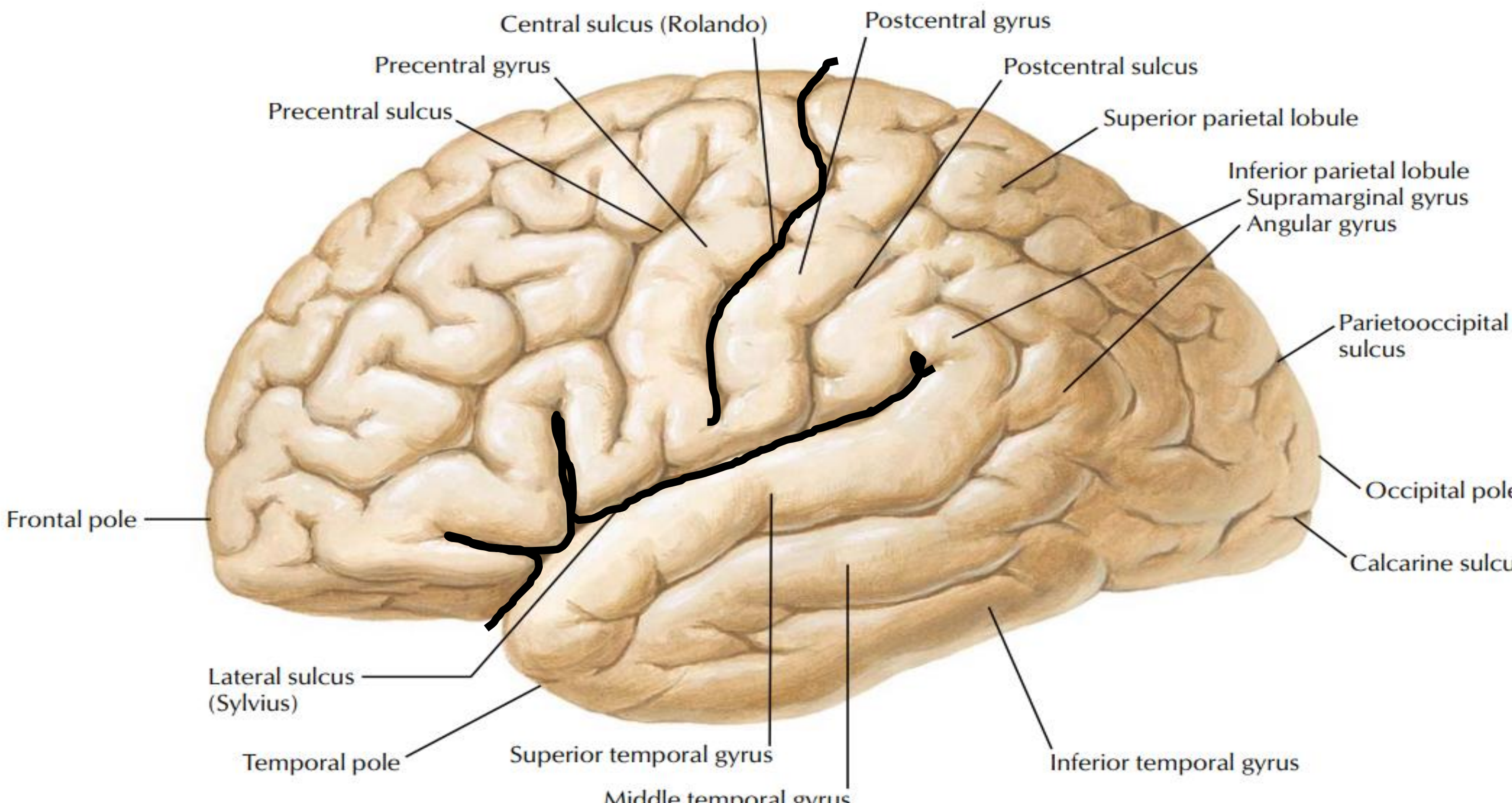
Three Gyri

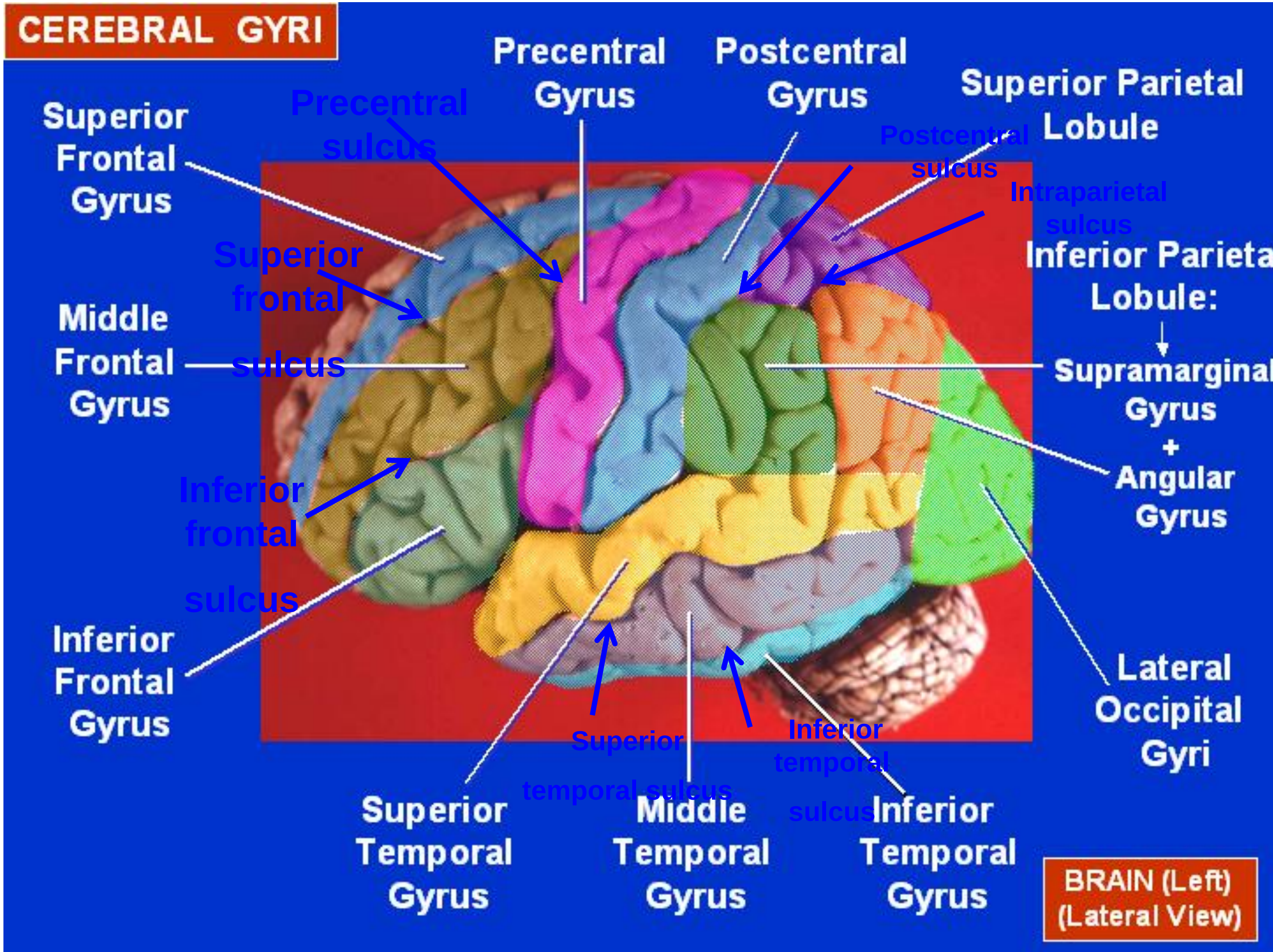
1. Superior Temporal Gyrus
2. Middle Temporal Gyrus
3. Inferior Temporal Gyrus

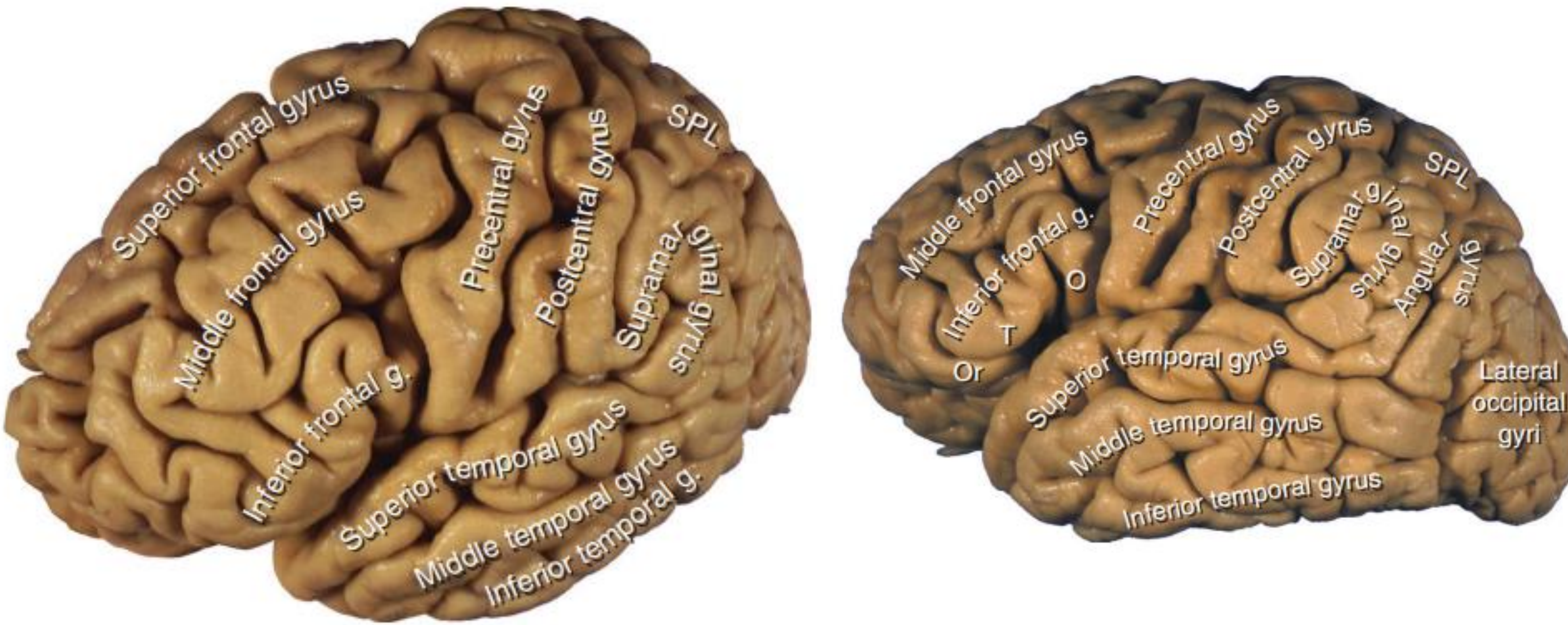


Occipital Lobe – Lateral Surface

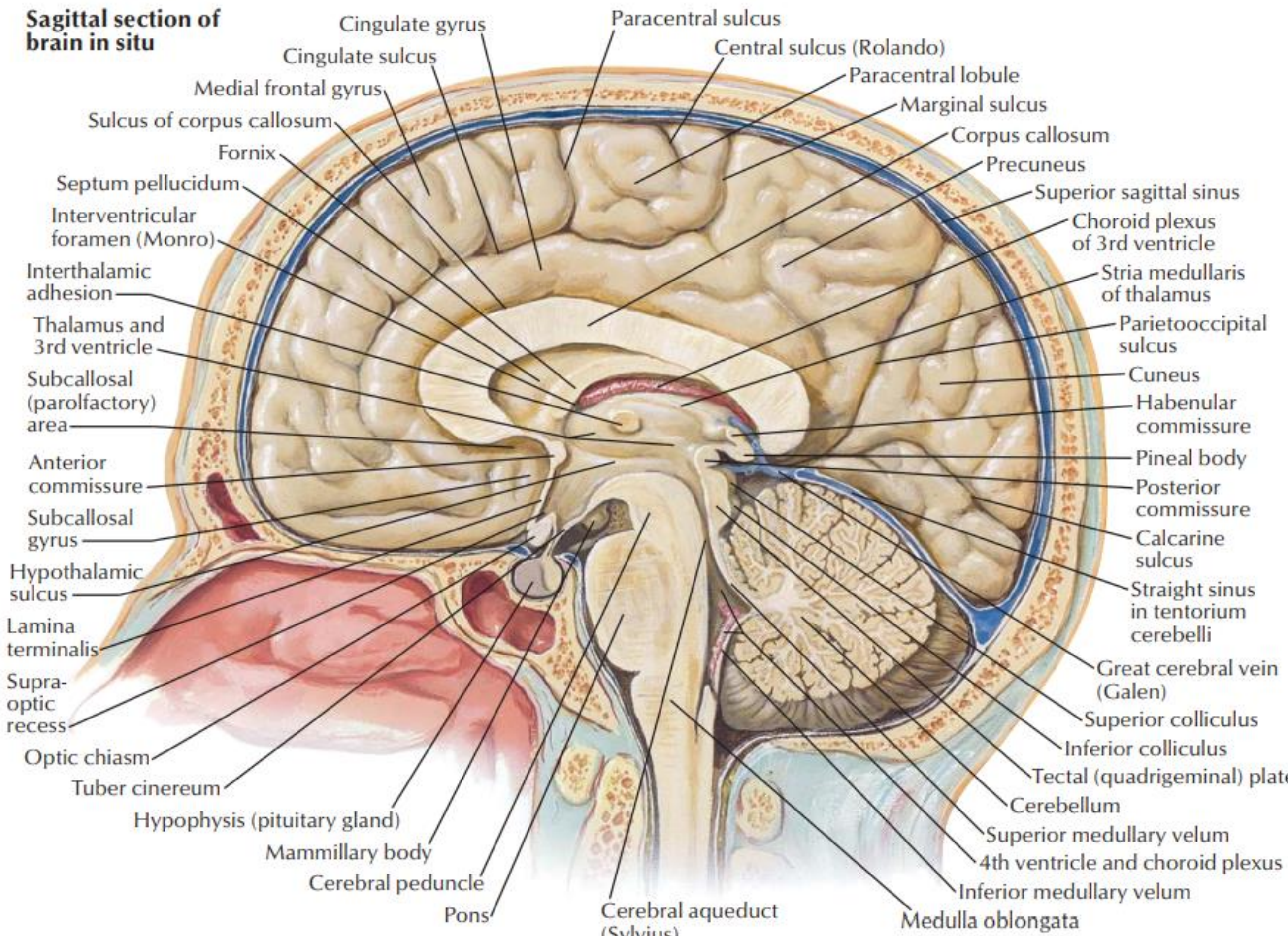
- No distinct gyri
- No distinct boundaries from the other lobes
- (only partially marked by parieto-occipital scissure)

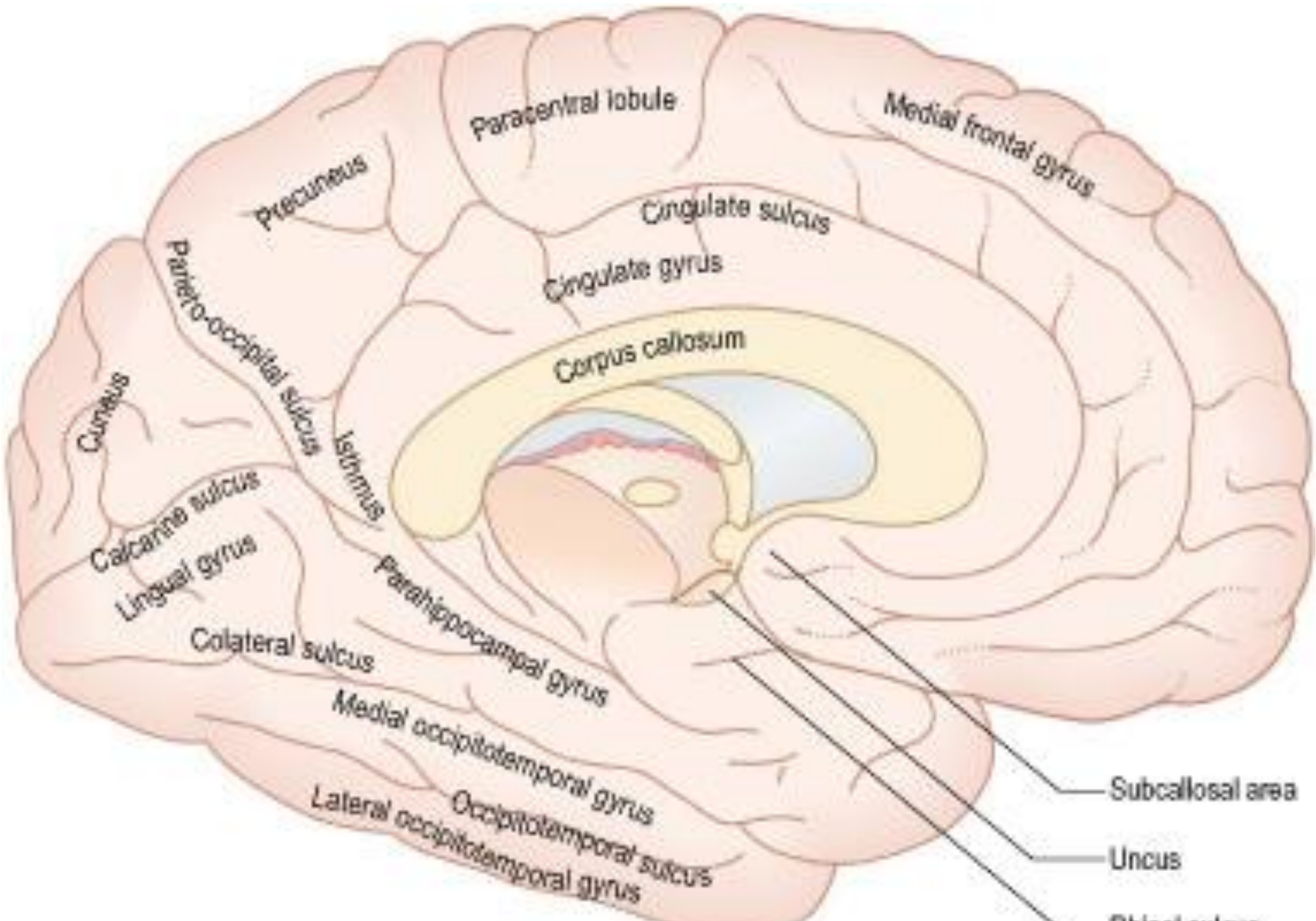



CEREBRAL GYRI
Precentral Gyrus
Postcentral Gyrus
Superior Parietal Lobule
Precentral sulcus
Postcentral sulcus
Intraparietal sulcus
Superior Frontal Gyrus
Superior frontal sulcus
Middle Frontal Gyrus
Inferior Parietal Lobule:
Supramarginal Gyrus
+
Angular Gyrus
Inferior frontal sulcus
Inferior Frontal Gyrus
Lateral Occipital Gyri
Superior temporal sulcus
Inferior temporal sulcus
Superior Temporal Gyrus
Middle Temporal Gyrus
Inferior Temporal Gyrus
BRAIN (Left) (Lateral View)

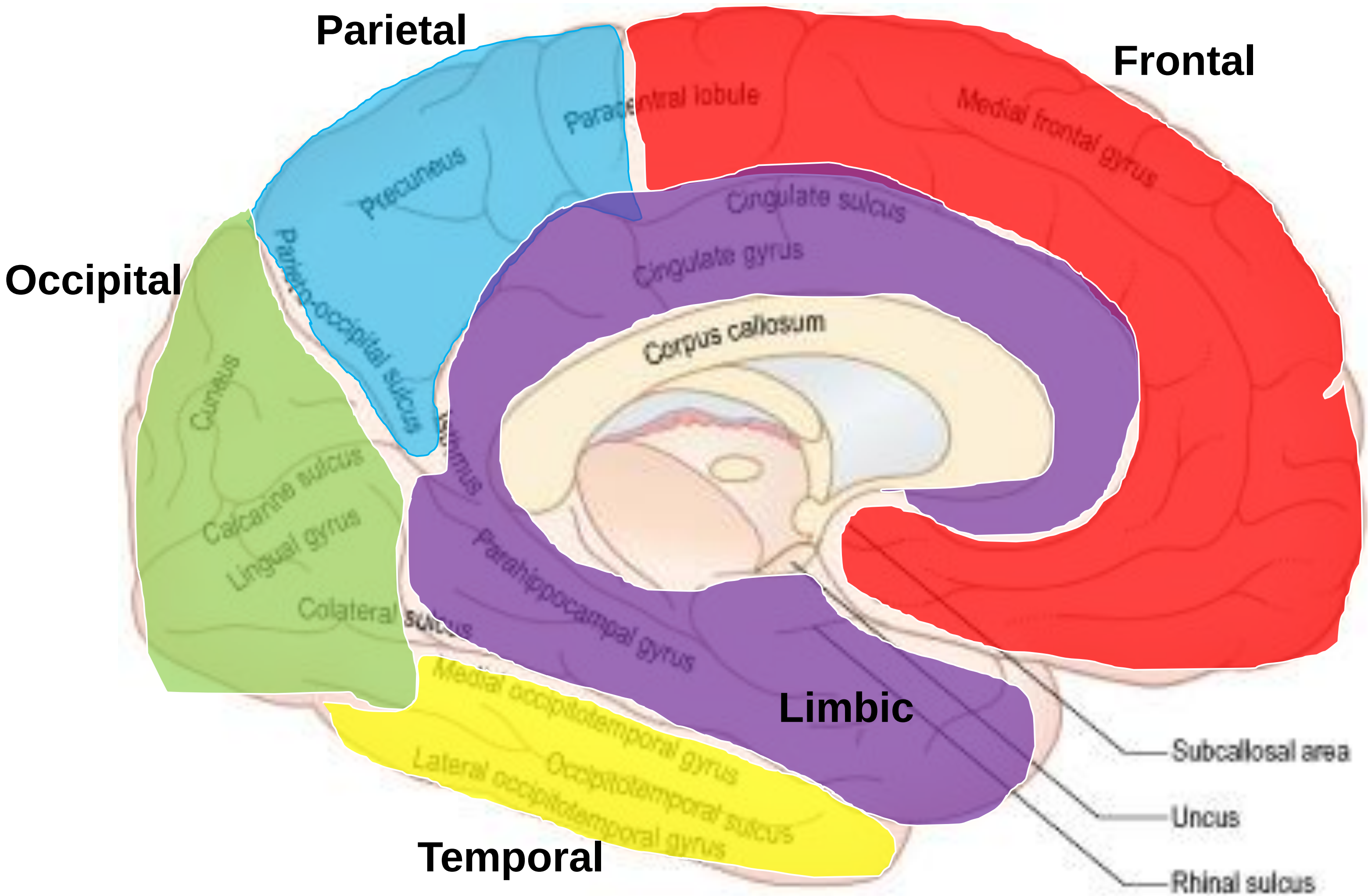

Superior frontal gyrus
Middle frontal gyrus
Inferior frontal g.
Precentral gyrus
Postcentral gyrus
SPL
Supramarginal gyrus
Superior temporal gyrus
Middle temporal gyrus
Inferior temporal g.
Middle frontal gyrus
Inferior frontal g.
O
T
Or
Precentral gyrus
Postcentral gyrus
SPL
Supramarginal gyrus
Angular gyrus
Superior temporal gyrus
Middle temporal gyrus
Inferior temporal gyrus
Lateral occipital gyri

MEDIAL SURFACE OF THE BRAIN



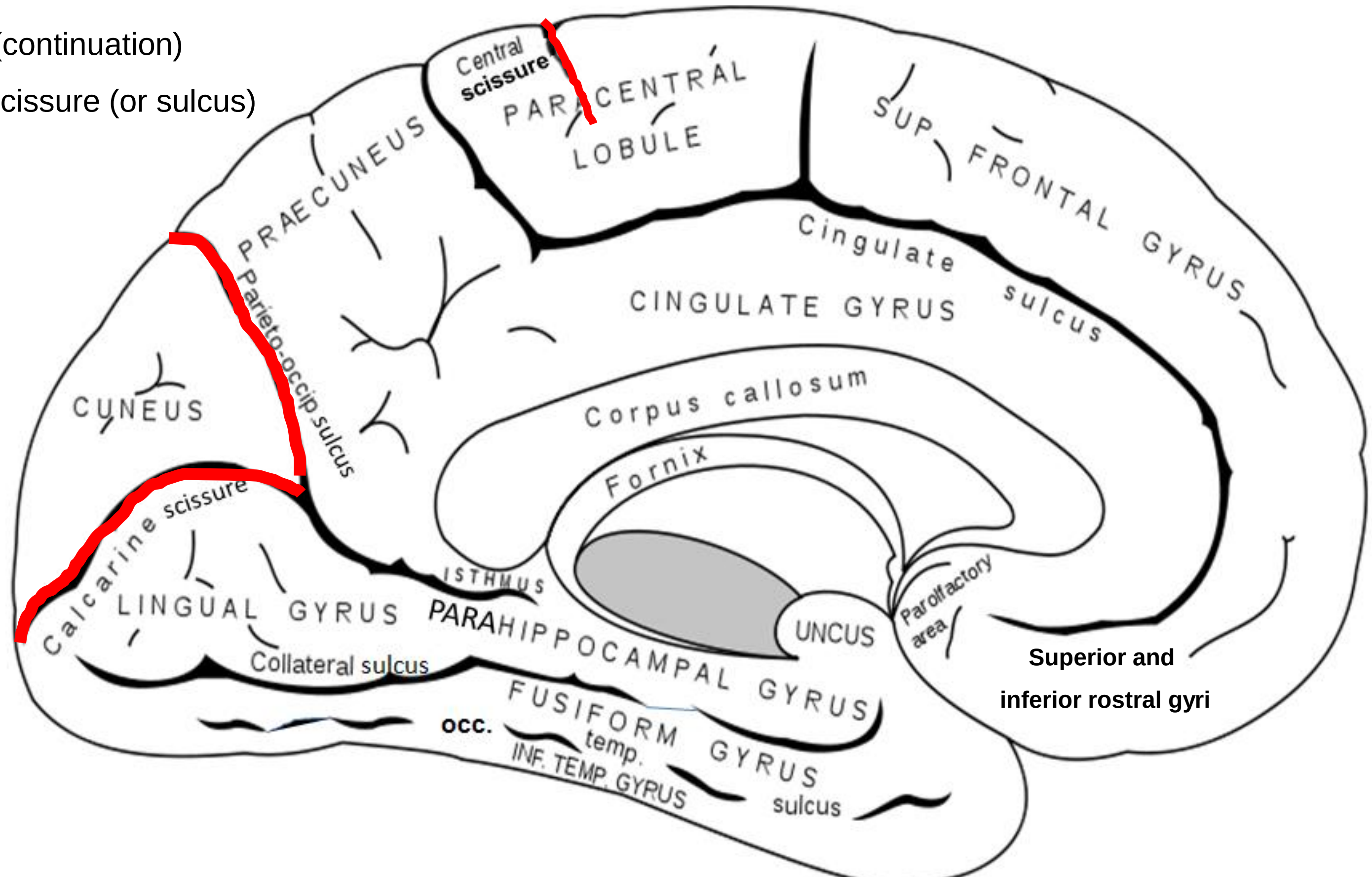


Paracentral lobule
Medial frontal gyrus
Precuneus
Cingulate sulcus
Cingulate gyrus
Parieto-occipital sulcus
Corpus callosum
Cuneus
Isthmus
Calcarine sulcus
Lingual gyrus
Parahippocampal gyrus
Colateral sulcus
Medial occipitotemporal gyrus
Occipitotemporal sulcus
Lateral occipitotemporal gyrus
Subcallosal area
Uncus
Rhinal sulcus


Parietal
Frontal
Occipital
Limbic
Temporal
Paracentral lobule
Medial frontal gyrus
Precuneus
Cingulate sulcus
Cingulate gyrus
Parieto-occipital sulcus
Corpus callosum
Cuneus
Calcarine sulcus
Lingual gyrus
Collateral sulcus
Isthmus
Parahippocampal gyrus
Medial occipitotemporal gyrus
Occipitotemporal sulcus
Lateral occipitotemporal gyrus
Subcallosal area
Uncus
Rhinal sulcus

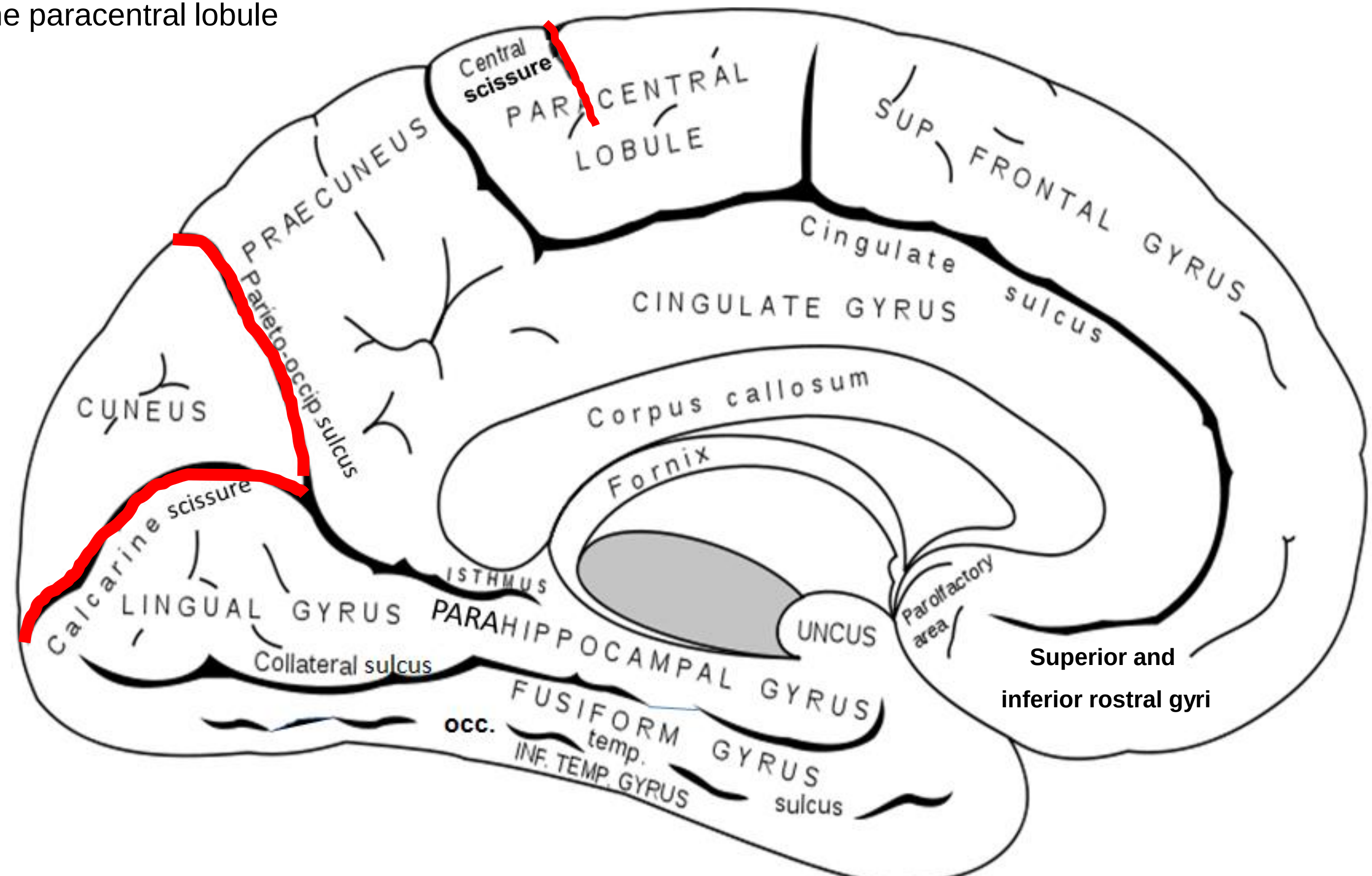
Main Scissures of the medial surface

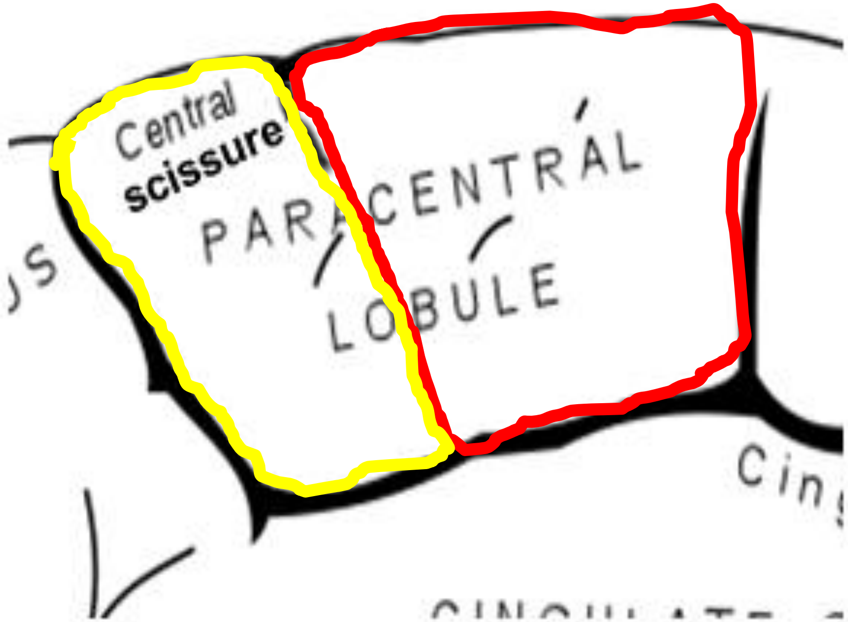
- Calcarine Scissure
- Central Scissure (continuation)
- Parieto-occipital scissure (or sulcus)



Frontal Lobe – Medial Surface

- Superior frontal gyrus (sometimes called medial frontal gyrus)
- Inferior and superior rostral gyri
- Anterior part of the paracentral lobule




Central
scissure
PARACENTRAL
LOBULE

Limbic Lobe

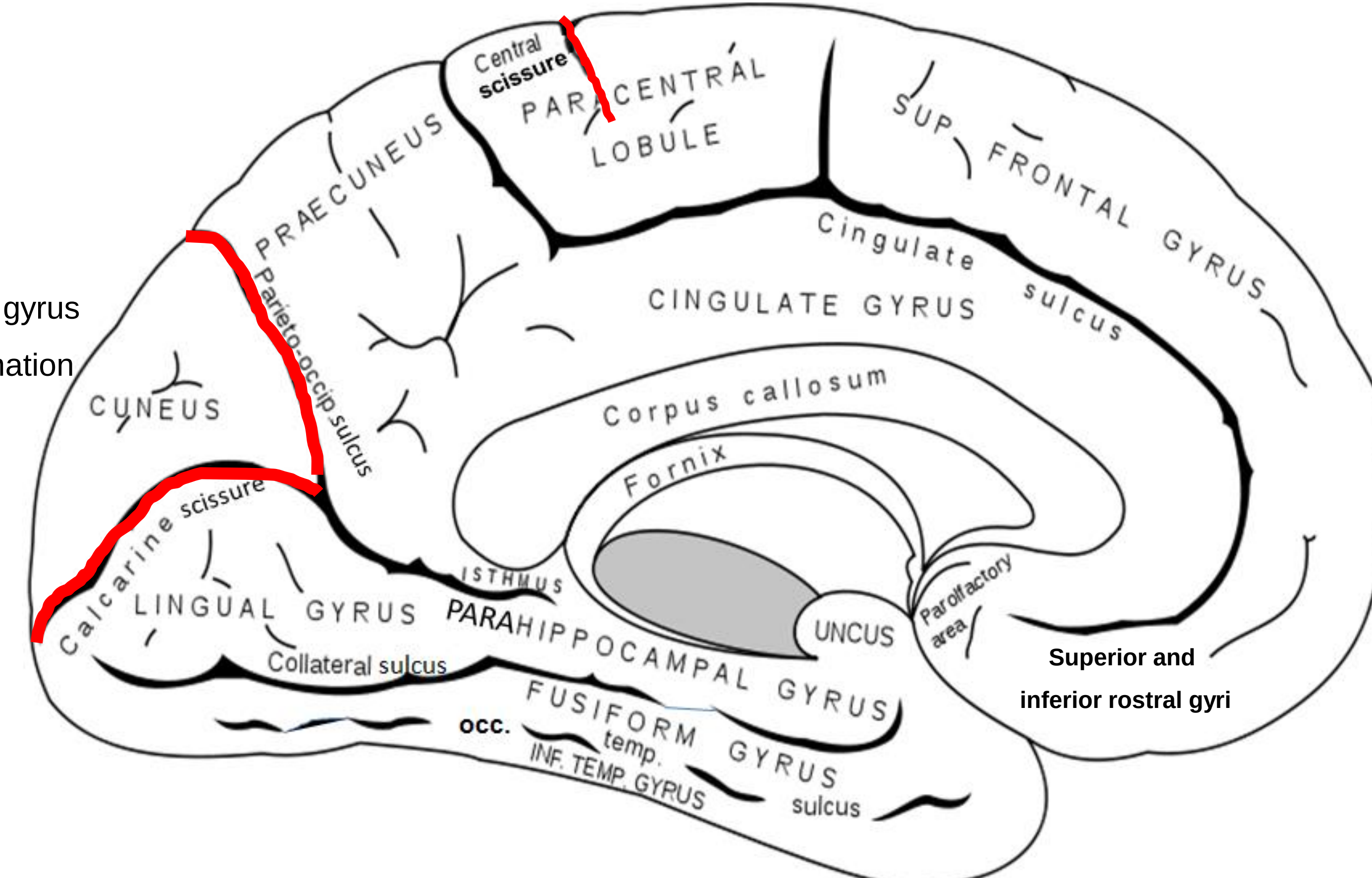
Limited by:

- Limbic Scissure (or callosal scissure)
- Cingulate Gyrus

Constituted by:

- Cingulate Gyrus
- Isthmus
- Parahippocampal gyrus
- Hippocampal formation

(hidden, not visible)



Parietal Lobe

- Posterior part of the paracentral lobule
- Praecuneus

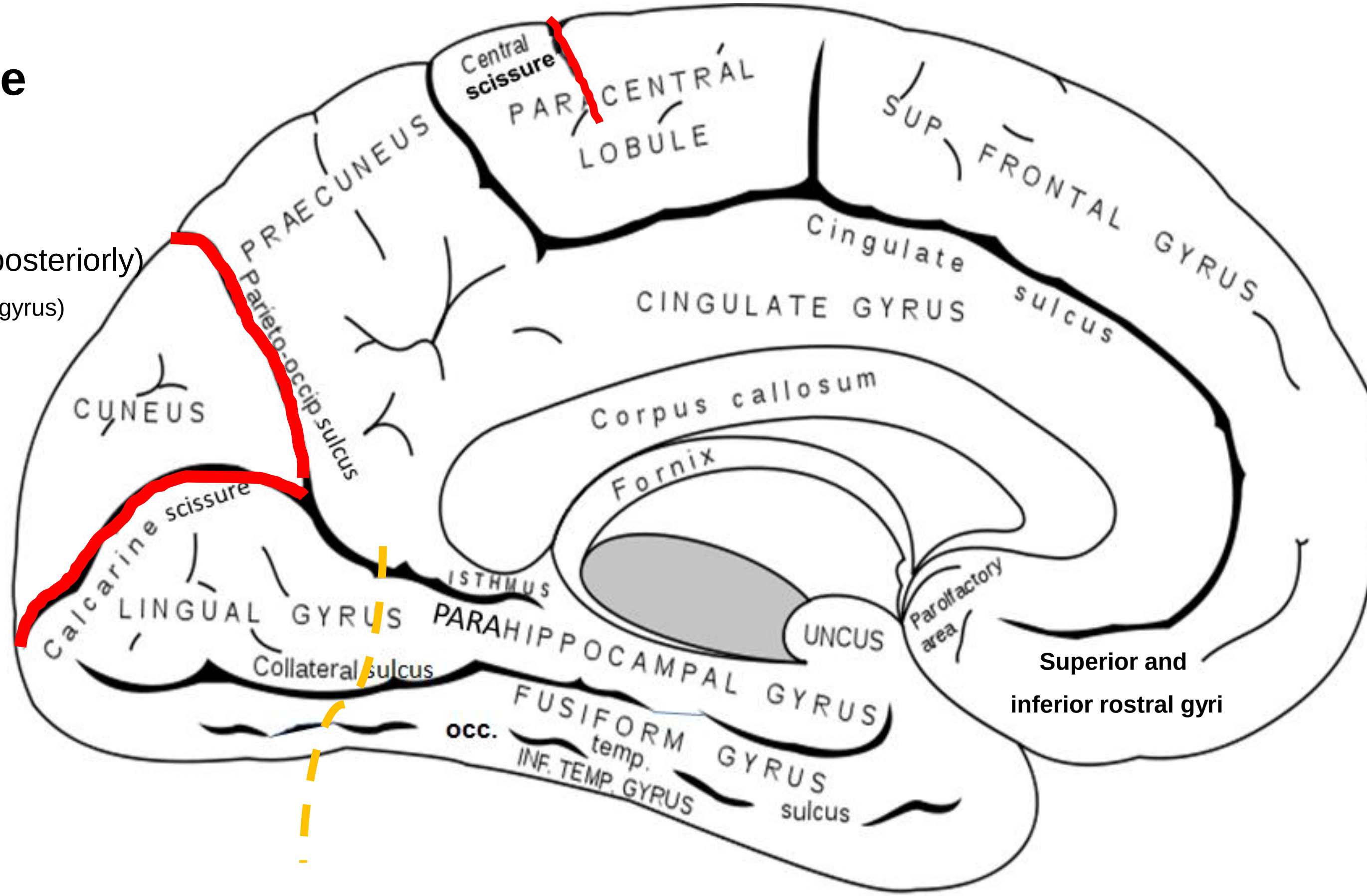
Occipital Lobe

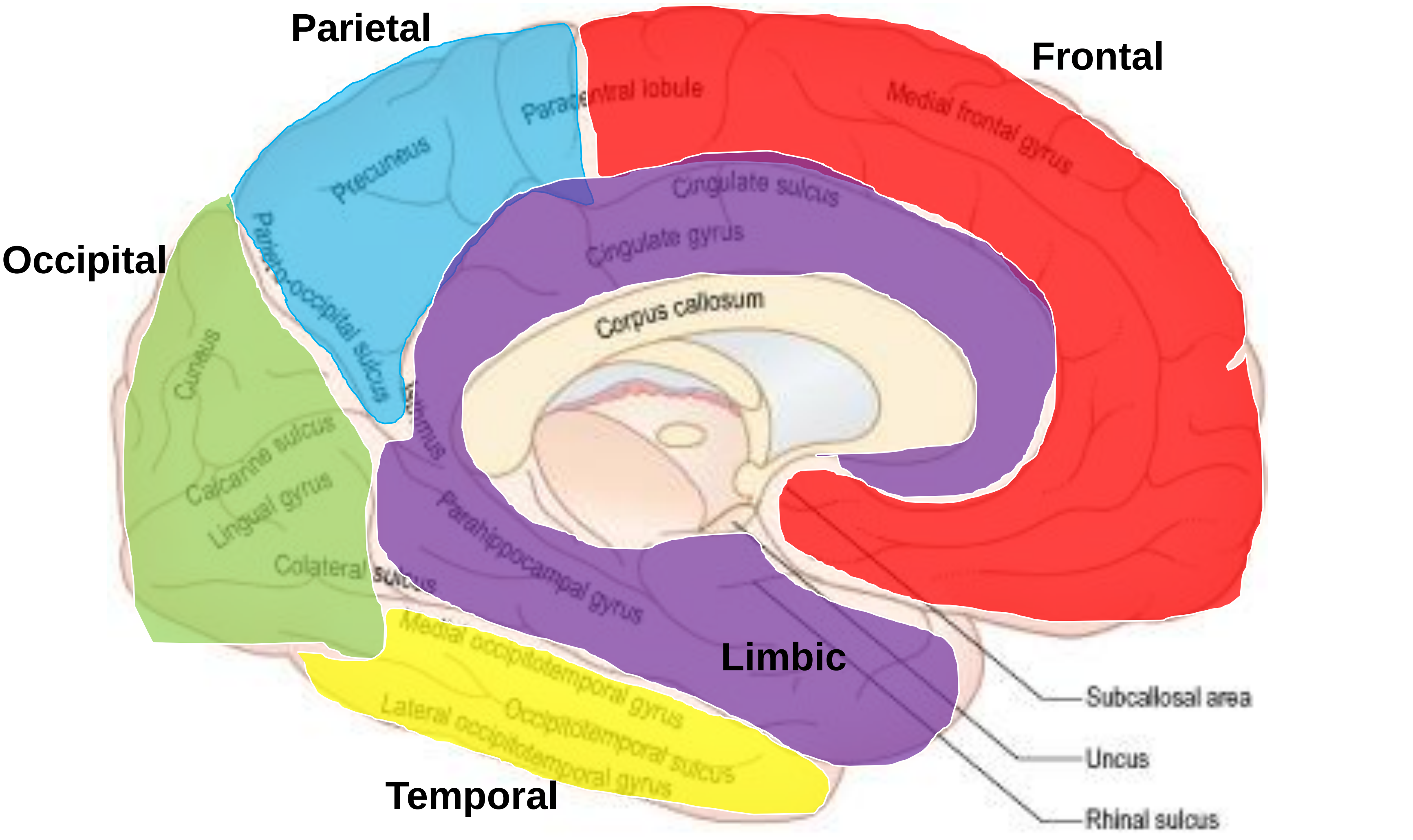
- Cuneus
- Lingual Gyrus
- Fusiform gyrus (posteriorly)

(or medial occipito-temporal gyrus)

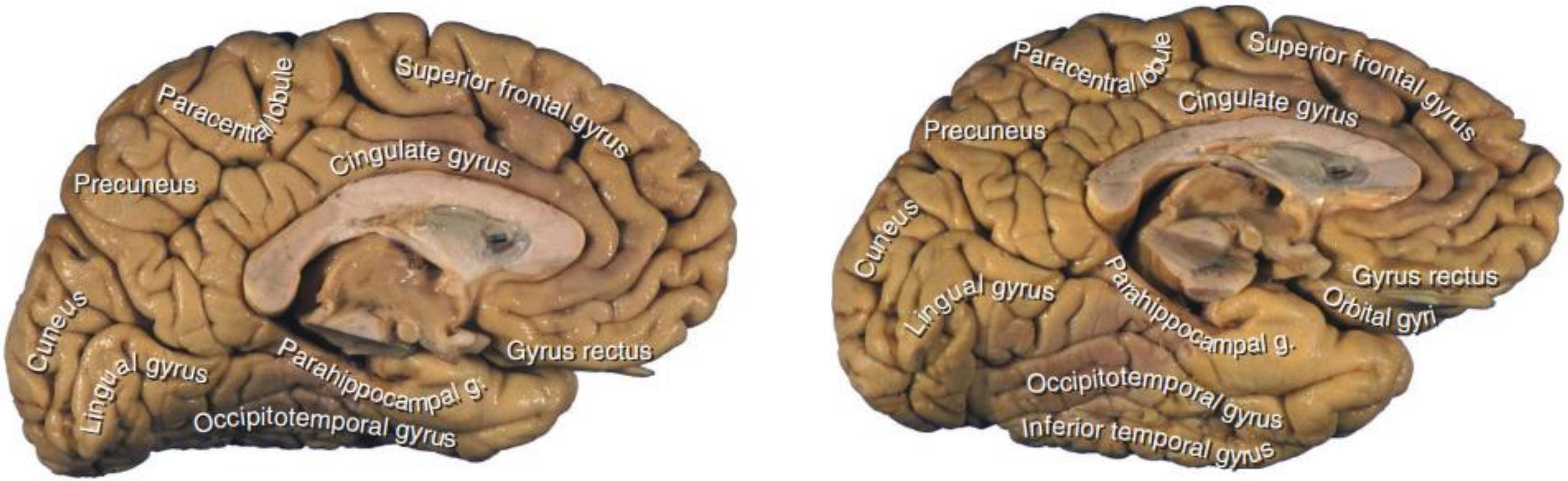
Temporal Lobe

- Fusiform Gyrus (anteriorly) (or medial occipito-temporal)
- Inferior temporal (or lateral occipito-temporal)



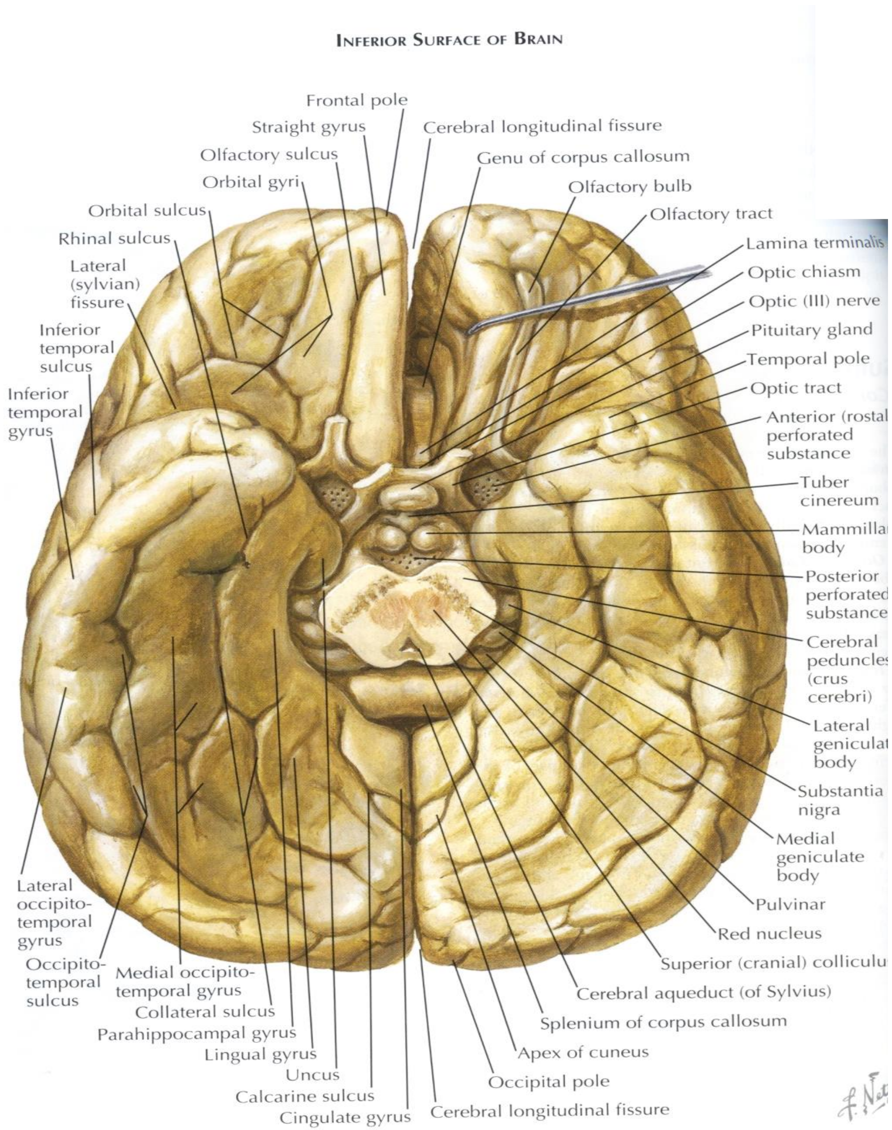


Parietal
Frontal
Occipital
Limbic
Temporal
Paracentral lobule
Medial frontal gyrus
Precuneus
Cingulate sulcus
Cingulate gyrus
Parieto-occipital sulcus
Corpus callosum
Cuneus
Isthmus
Calcarine sulcus
Lingual gyrus
Collateral sulcus
Parahippocampal gyrus
Medial occipitotemporal gyrus
Occipitotemporal sulcus
Lateral occipitotemporal gyrus
Subcallosal area
Uncus
Rhinal sulcus


Paracentral lobule
Superior frontal gyrus
Cingulate gyrus
Precuneus
Cuneus
Lingual gyrus
Parahippocampal g.
Gyrus rectus
Occipitotemporal gyrus
Paracentral lobule
Superior frontal gyrus
Cingulate gyrus
Precuneus
Cuneus
Lingual gyrus
Parahippocampal g.
Gyrus rectus
Orbital gyri
Occipitotemporal gyrus
Inferior temporal gyrus


MEDIAL
OCCIPITO-TEMPORAL
OCCIPITO-TEMPORAL
FUSIFORM
imgflip.com


Occipito-temporal
Medial Occipito-temporal
Fusiform
Fusiform v2



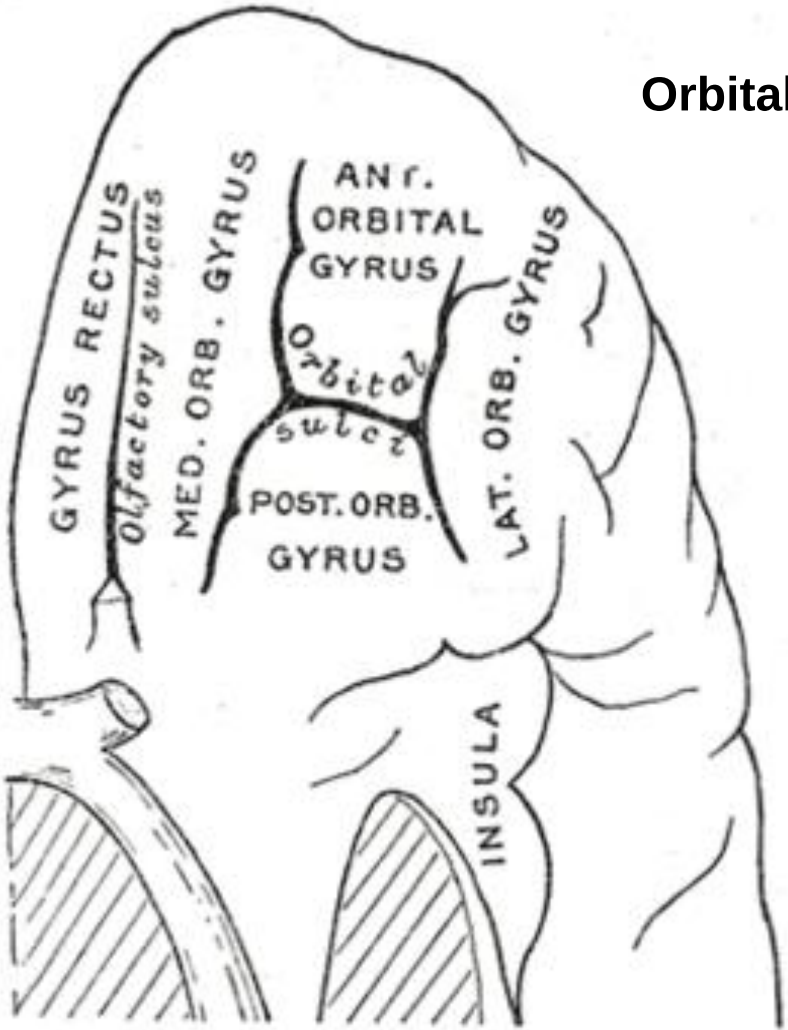
Inferior surface of the brain

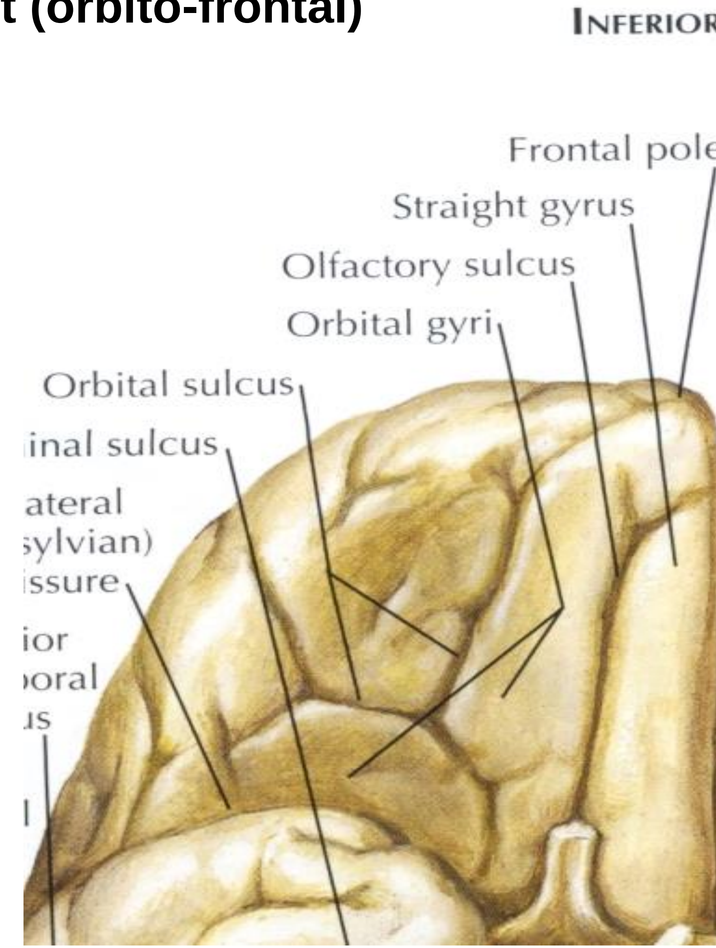
Two regions:

- Frontal
- Tentorial

Frontal lobe

Orbital part (orbito-frontal)





CEREBRAL GYRI

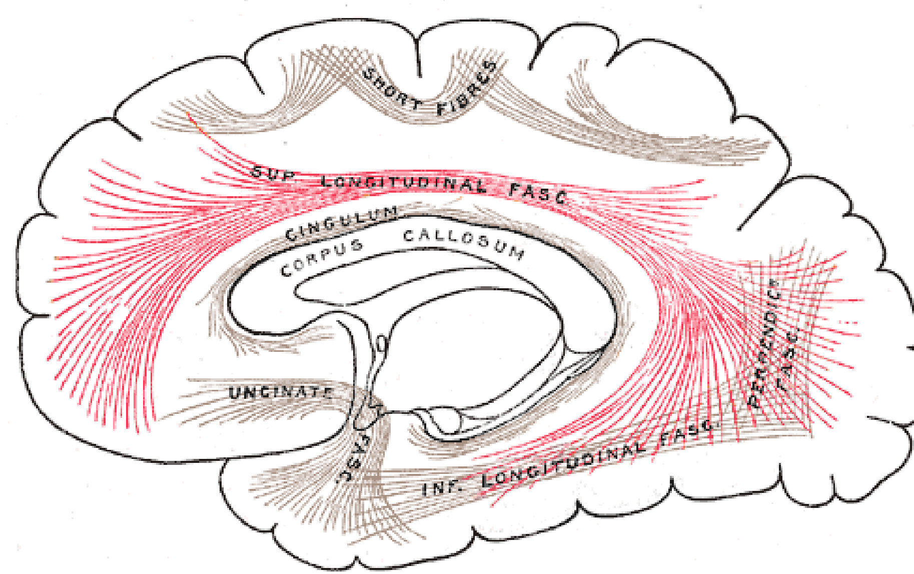
Tentorial part

- Temporal lobe
- Limbic Lobe
- Occipital Lobe


Middle frontal gyrus
Precentral gyrus
Postcentral gyrus
SPL
Supramarginal gyrus
Inferior frontal g.
O
Angular gyrus
T
Or
Superior temporal gyrus
Lateral occipital gyri
Middle temporal gyrus
Inferior temporal gyrus
Paracentral lobule
Superior frontal gyrus
Cingulate gyrus
Precuneus
Cuneus
Lingual gyrus
Parahippocampal g.
Gyrus rectus
Occipitotemporal gyrus
Superior frontal gyrus
SPL
Precentral gyrus
Postcentral gyrus
Middle frontal gyrus
Supramarginal gyrus
Inferior frontal g.
Superior temporal gyrus
Middle temporal gyrus
Inferior temporal g.
Paracentral lobule
Superior frontal gyrus
Cingulate gyrus
Precuneus
Cuneus
Lingual gyrus
Parahippocampal g.
Gyrus rectus
Orbital gyri
Occipitotemporal gyrus
Inferior temporal gyrus

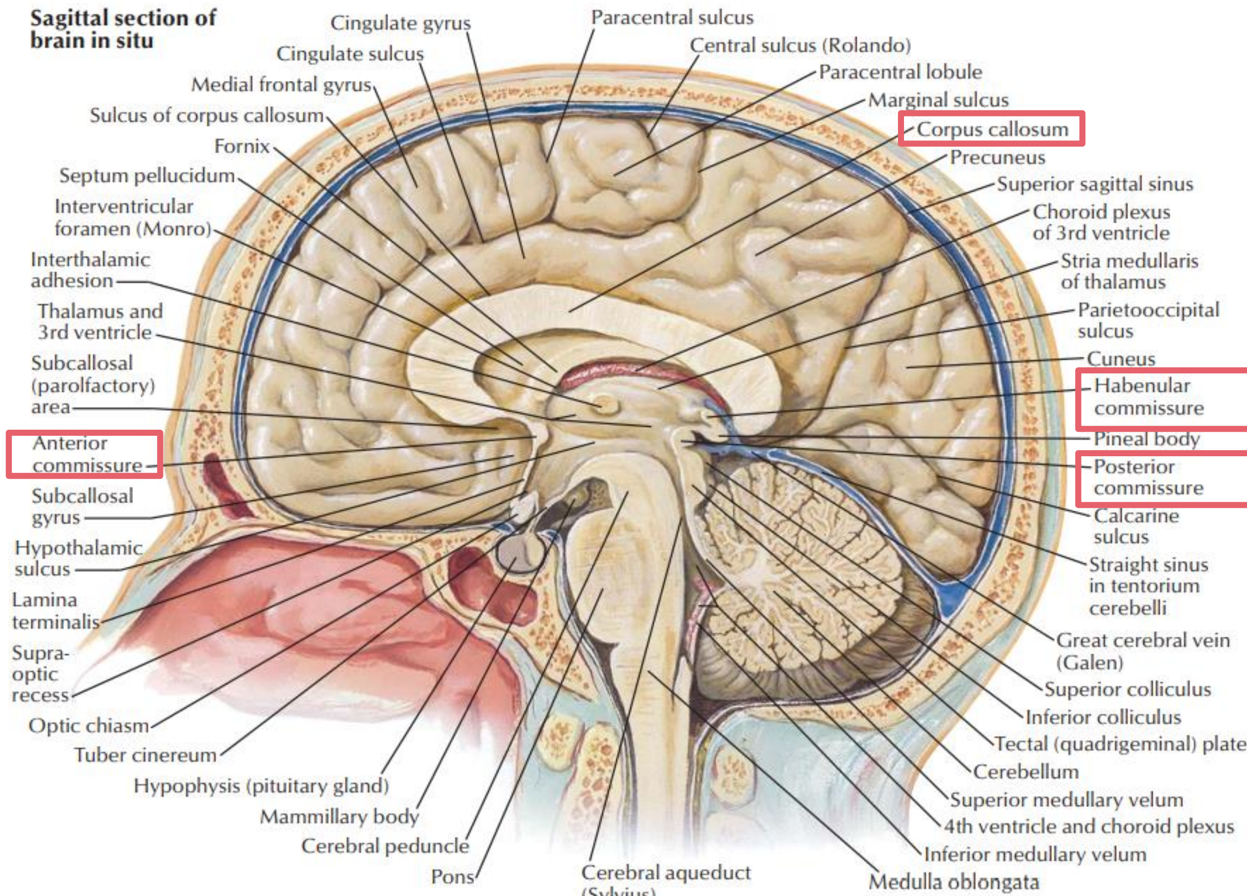
White Matter Anatomy

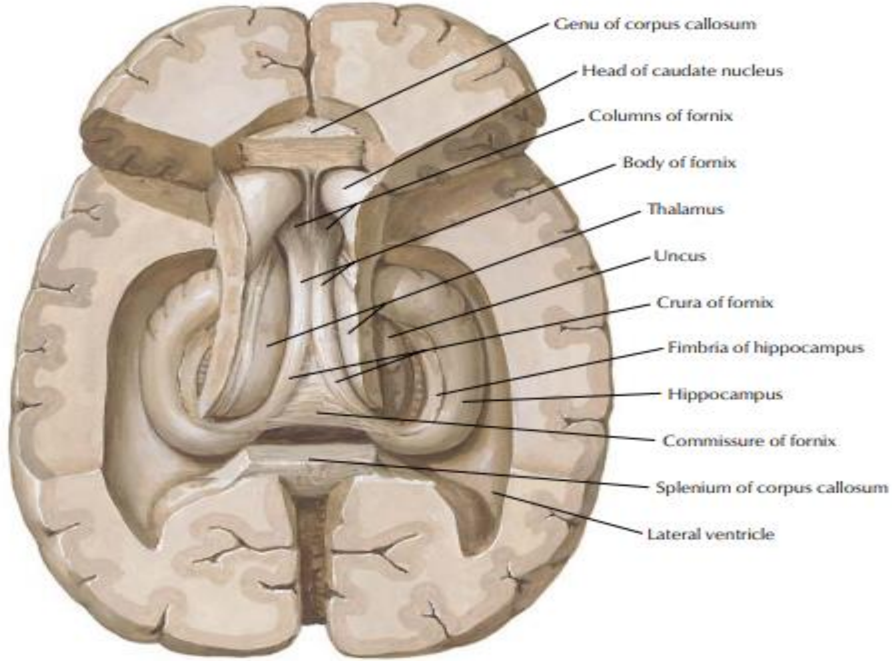
- Commissural fibers (telencephalon impar) (to the opposite hemisphere)
- Associative fibers (within the same hemisphere)
- Projection fibers (to lower targets, e.g. brainstem and spinal cord)



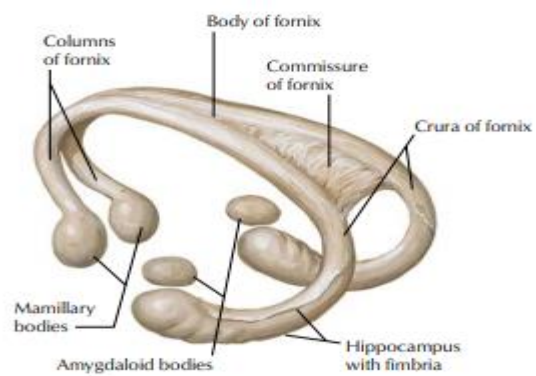
Commissural systems

- Corpus Callosum
- Anteior Commissure
- Posterior Commissure
- Habenular Commissure
- Commissure of the fornix





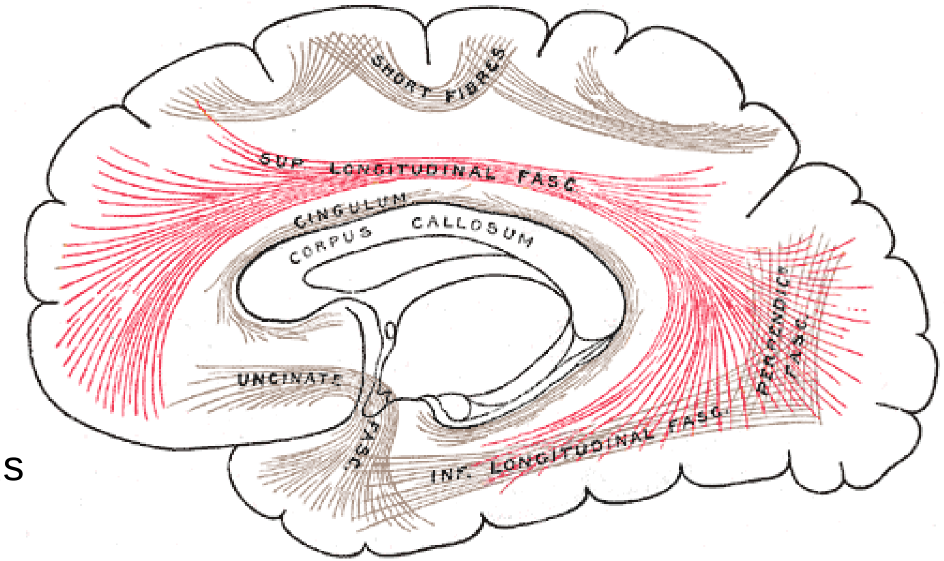
Genu of corpus callosum
Head of caudate nucleus
Columns of fornix
Body of fornix
Thalamus
Uncus
Crura of fornix
Fimbria of hippocampus
Hippocampus
Commissure of fornix
Splenium of corpus callosum
Lateral ventricle



Body of fornix
Columns of fornix
Commissure of fornix
Crura of fornix
Mamillary bodies
Amygdaloid bodies
Hippocampus with fimbria

Association systems

- Short fibers (within adjacent gyri)
- Long fibers:
    1. Cingulum (limbic lobe)
    2. Superior longitudinal fasciculus
    3. Inferior longitudinal fasciculus
    4. Superior and inferior occipito-frontal fasciculus
    5. Uncinate fasciculus
    6. Arcuate fasciculus



Projection fibers

Descending systems (cortico-…)

- Cortico-striatal (basal ganglia) — *Extayramidal*
- Cortico-ponto-cerebellar — *Esoyramidal*
- Cortico-nuclear
- Cortico-spinal

Pyramidal

THE ANATOMICAL BASES

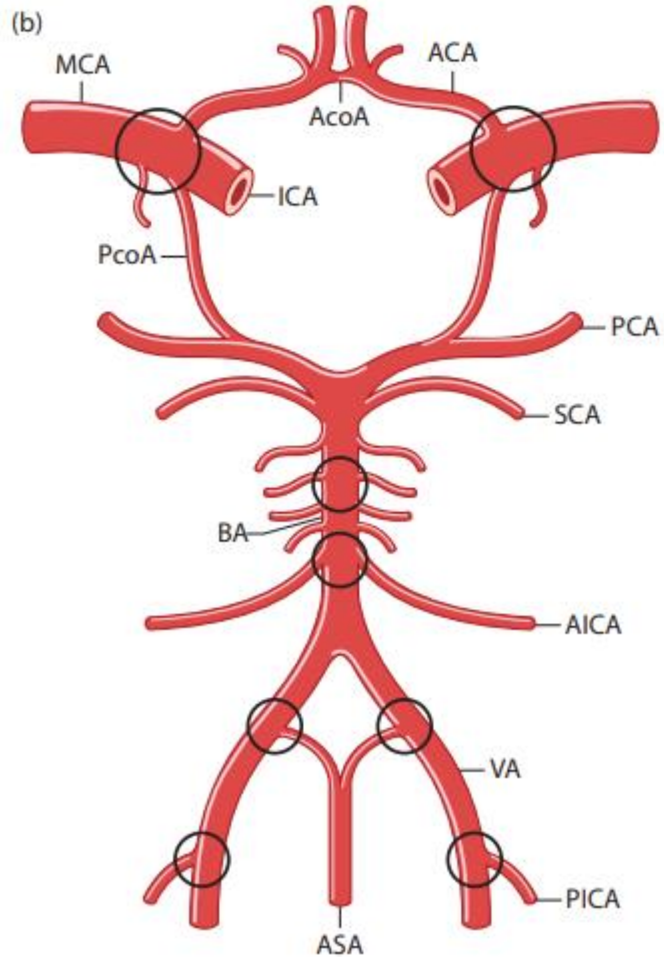
OF

CEREBRAL VASCULAR PATHOLOGY

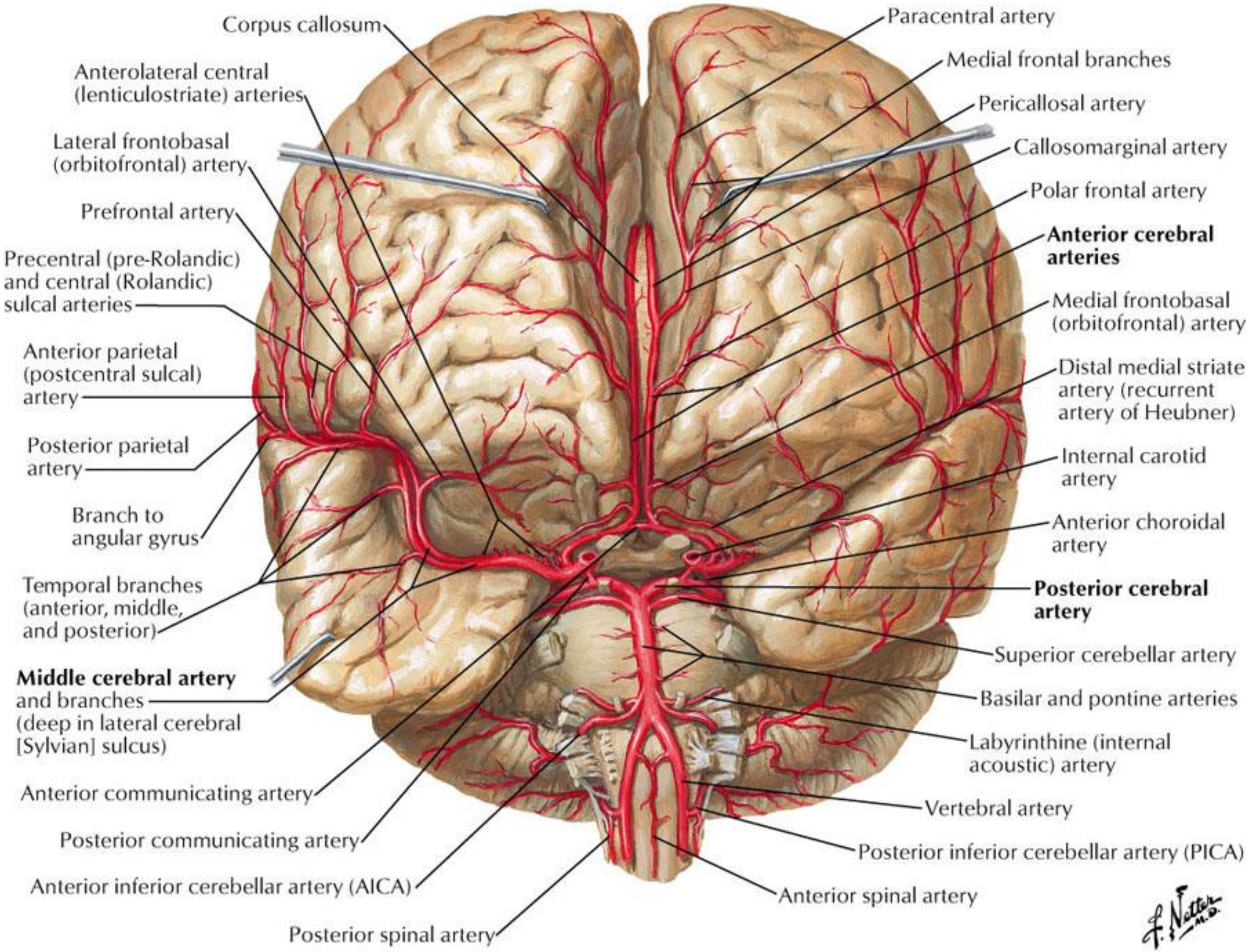
TABLE 2.1 Terminology: definitions of key terms and concepts

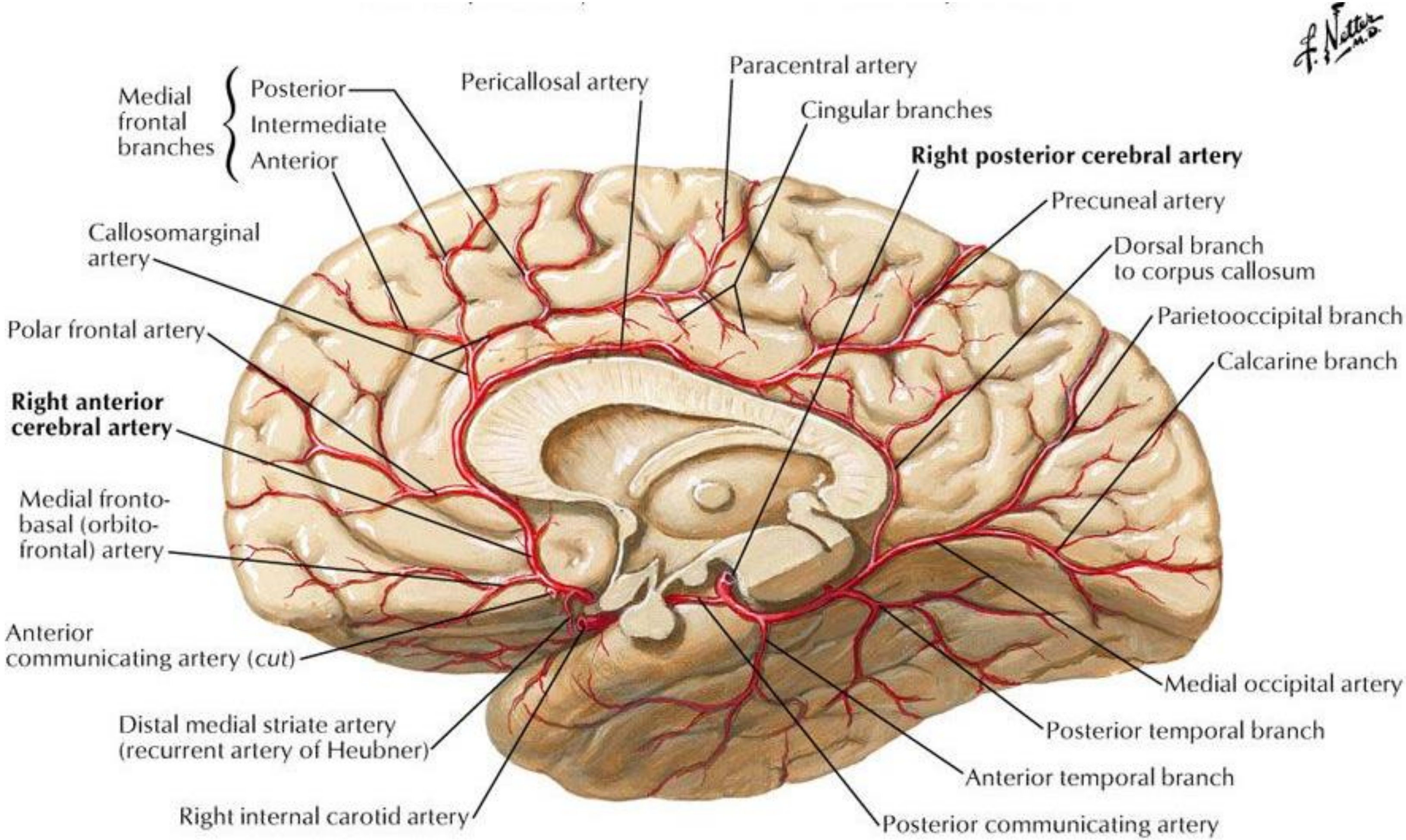
Term	Description	Type of damage in brain tissue	Comment
Anoxia	No oxygen	Not a specific or useful term by itself	Carries no specific meaning in the intact organism
Anoxaemia	No oxygen in blood	Impossible to assess in intact animal	An impossibility without cardiac bypass and removal of all blood O_2
Anaemic hypoxia	Low blood haemoglobin	No brain-damaging potential	Actually protective for stroke because of favourable rheology
Asphyxia	Inability to breathe	Can cause brain necrosis if ischaemia results	Includes suffocation, strangulation and some chemicals (cyanide, sulphide, azide) which paralyze breathing centres in medulla oblongata
Carbon monoxide (CO) toxicity	CO in blood, displacing O_2 from haemoglobin sites	Necrosis in pallido-reticularis, plus typical ischaemic distribution	Complex triad effected: anaemia (haemoglobin occupation by CO), histotoxic hypoxia (by binding to iron-rich globus pallidus), and global ischaemia due to heart failure
Haematoma	Localized bleeding (e.g. intracerebral, sub-arachnoid or sub-dural) from ruptured vessels or aneurysms	Haemorrhagic strokes result in tissue injury by causing compression of tissue from expanding bleeds	Not to be confused with hemiangioma

Hypoxia	Low oxygen, not further specified (tissue, blood, atmosphere)	See specific entities	Not a useful term without further qualification
Hypoxia/ischaemia	Combination of hypoxia and ischaemia	Hypoxia and ischaemia cause even greater necrosis	Occurs in strangulation and hanging; widely used incorrectly to describe pure ischaemia; cardiac arrest encephalopathy and global ischaemia are better terms, if that is what is meant
Hypoxaemia	Low oxygen in blood	Reversible synaptic alterations without neuronal necrosis	Seen in respiratory tract disease (larynx, trachea, bronchi, bronchioles), not in pure cardiovascular disease; tends to occur in younger patients; causes tissue hypoxia that is not necrotizing
Hypobaric hypoxia	Hypoxaemia accompanying decrease in ambient pO_2	Reversible synaptic alterations (at very high altitudes), but without neuronal necrosis	Temporary synaptic alterations produce 'high-altitude stupid' (HAS) syndrome; capillary leakage produces high altitude cerebral oedema (HACE), which is potentially lethal; both reverse on descent or on increasing inspired O_2
Histotoxic hypoxia	Tissue utilization of oxygen impaired	No brain-damaging potential without accompanying hypotension	Examples: poisoning by cyanide, sulphide and azide
Ischaemia	Cessation of blood flow to tissue; no perfusion	Variable cellular damage, neurons most vulnerable	Often also used (albeit imprecisely) to describe reduced blood flow — oligaemia
Oligaemia	Low blood flow, hypoperfusion	Selective vulnerability	Close to normal but still insufficient
Tissue hypoxia (global ischaemia)	Low tissue pO_2 due to global ischaemia	Necrosis (both pan-necrosis and selective neuronal necrosis) in brain regions of selective vulnerability	Decreased tissue pO_2 due to imbalance between delivery and utilization everywhere in brain
Tissue hypoxia (focal ischaemia)	Low tissue pO_2 due to focal ischaemia	Necrosis is usually pan-necrosis and does not spare glia	Decreased tissue pO_2 due to imbalance between delivery and utilization in focal arterial distribution
Watershed infarction	Localized to the border zones between territories of two major arteries (e.g. anterior cerebral artery [ACA] and middle cerebral artery [MCA] or MCA and posterior cerebral artery [PCA])	Ischaemic injury	Analogous to a lawn watered by multiple sprinklers: occlusion of the hose leads to a dry lawn in the territory centred on a sprinkler (or artery), but low pressure (hypotension) leads to a dry lawn between the sprinklers.

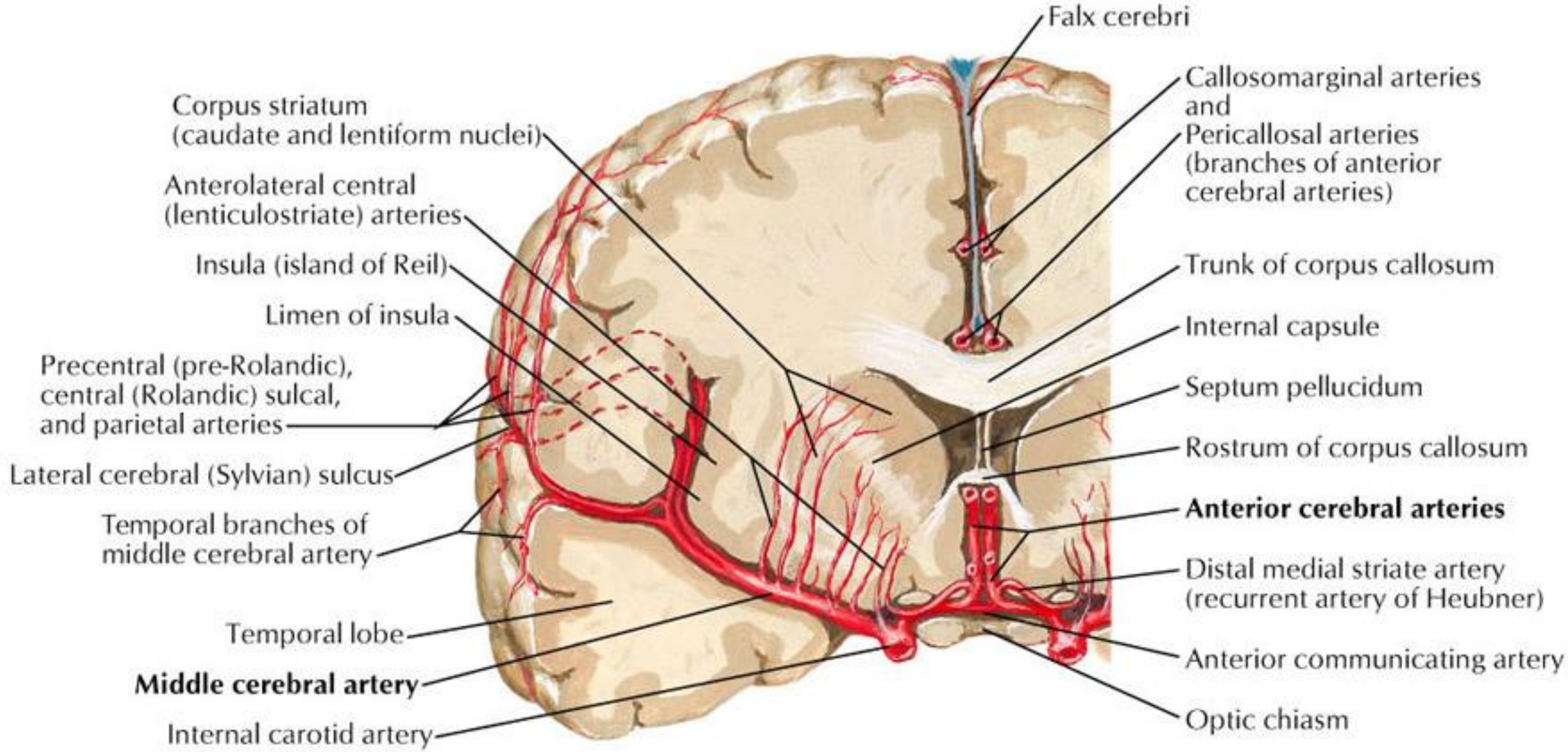

(b)
MCA
ACA
AcoA
ICA
PcoA
PCA
SCA
BA
AICA
VA
PICA
ASA

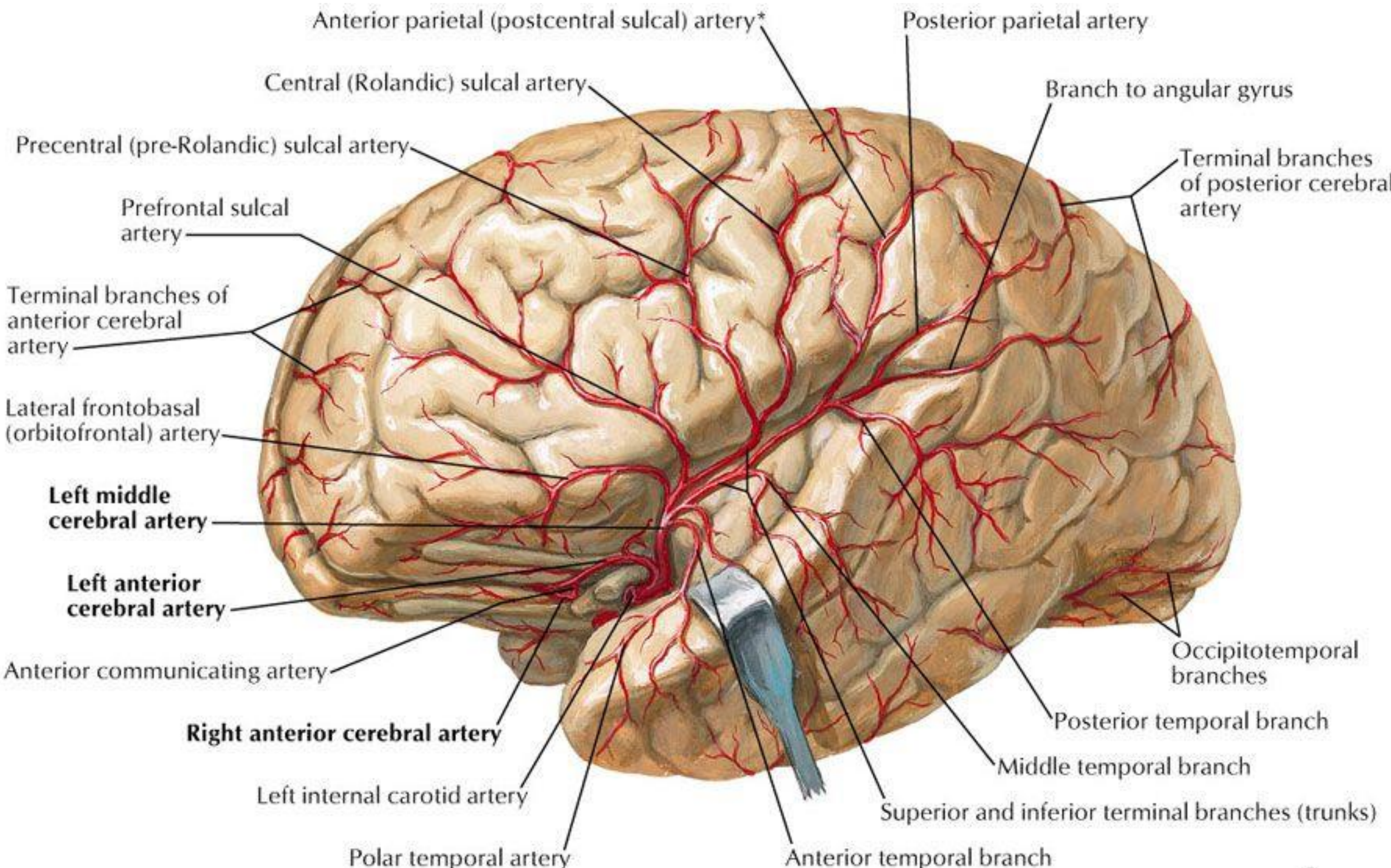

(a)

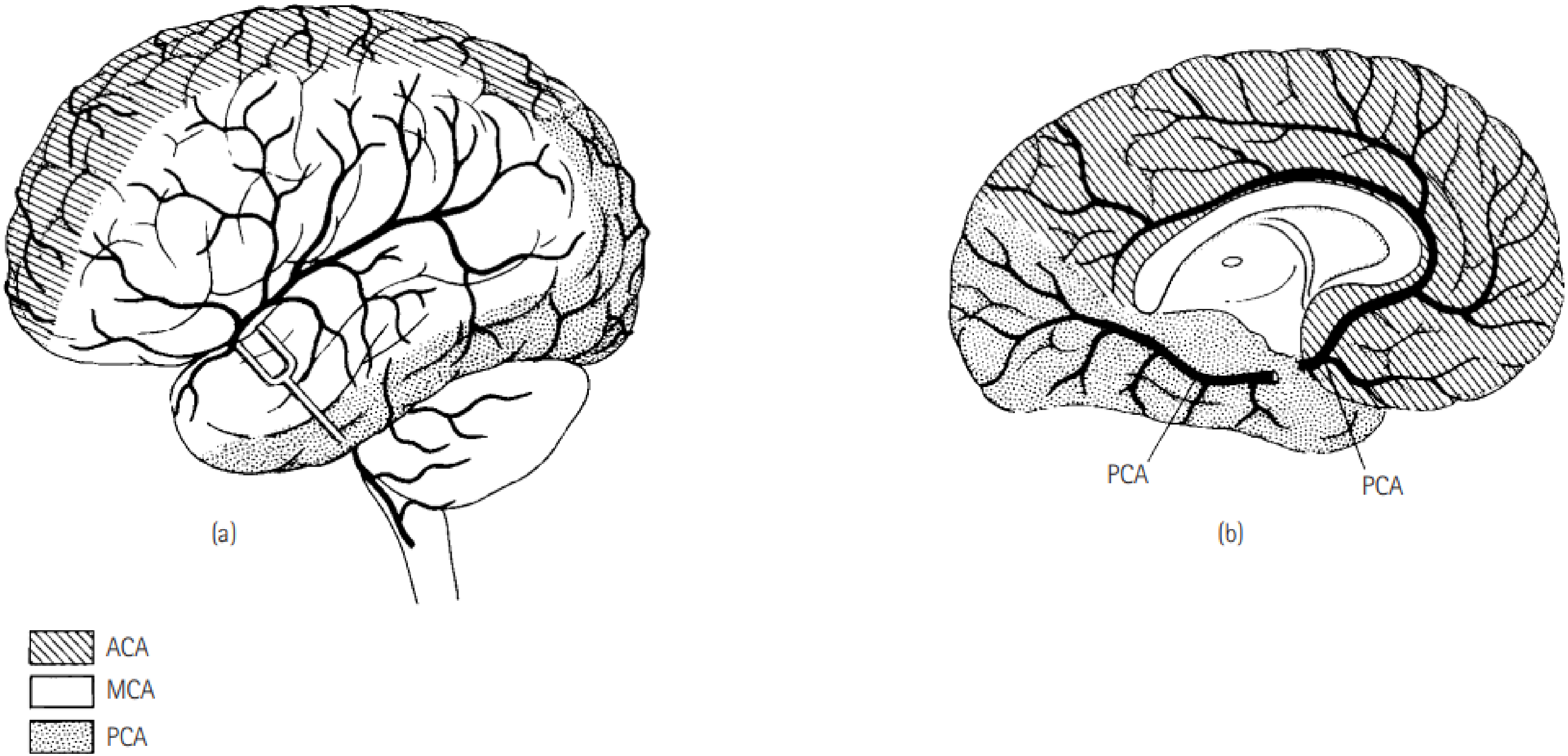

Corpus callosum
Anterolateral central (lenticulostriate) arteries
Lateral frontobasal (orbitofrontal) artery
Prefrontal artery
Precentral (pre-Rolandic) and central (Rolandic) sulcal arteries
Anterior parietal (postcentral sulcal) artery
Posterior parietal artery
Branch to angular gyrus
Temporal branches (anterior, middle, and posterior)
Middle cerebral artery and branches (deep in lateral cerebral [Sylvian] sulcus)
Anterior communicating artery
Posterior communicating artery
Anterior inferior cerebellar artery (AICA)
Posterior spinal artery
Paracentral artery
Medial frontal branches
Pericallosal artery
Callosomarginal artery
Polar frontal artery
Anterior cerebral arteries
Medial frontobasal (orbitofrontal) artery
Distal medial striate artery (recurrent artery of Heubner)
Internal carotid artery
Anterior choroidal artery
Posterior cerebral artery
Superior cerebellar artery
Basilar and pontine arteries
Labyrinthine (internal acoustic) artery
Vertebral artery
Posterior inferior cerebellar artery (PICA)
Anterior spinal artery
F. Netter M.D.

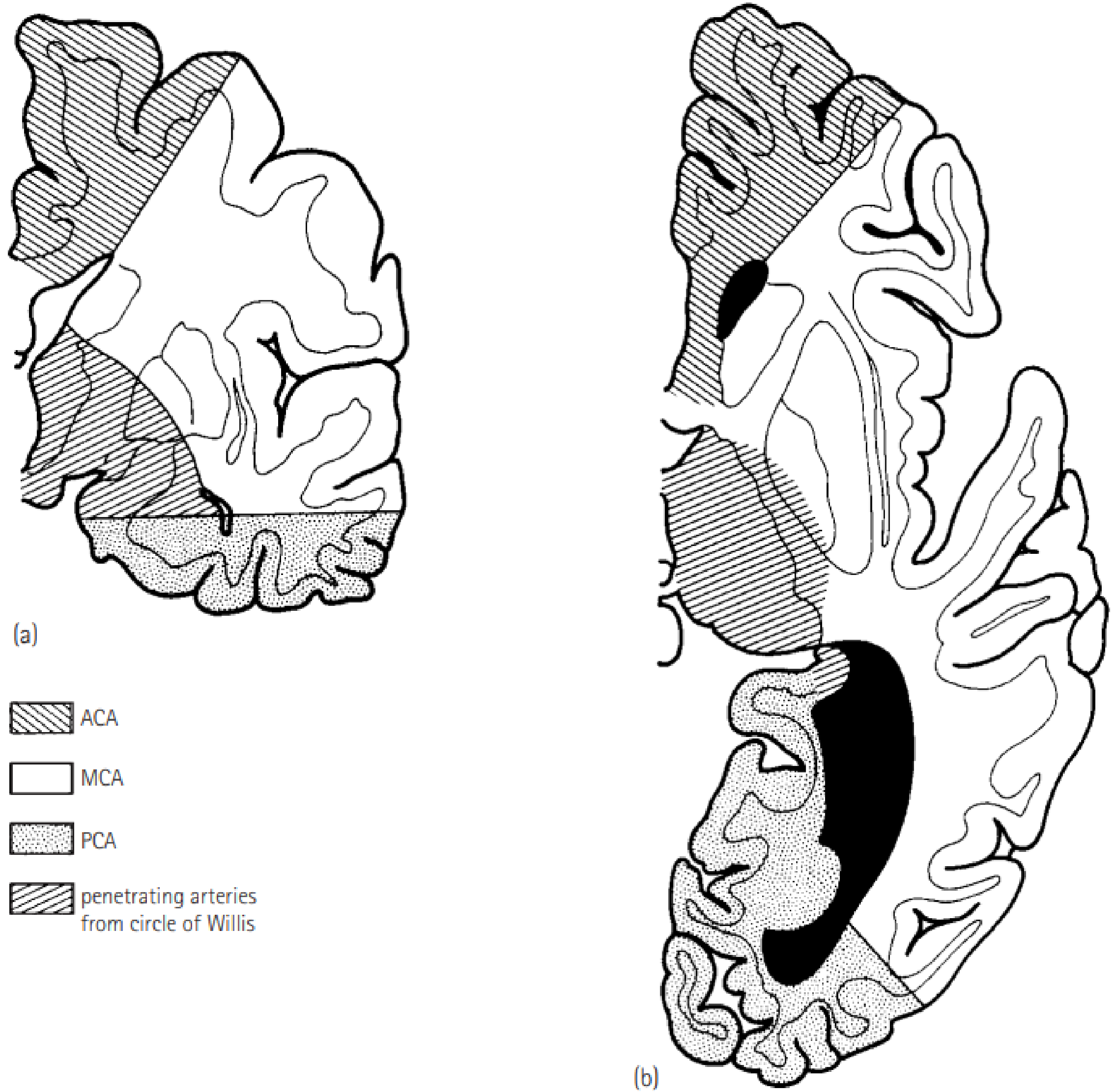


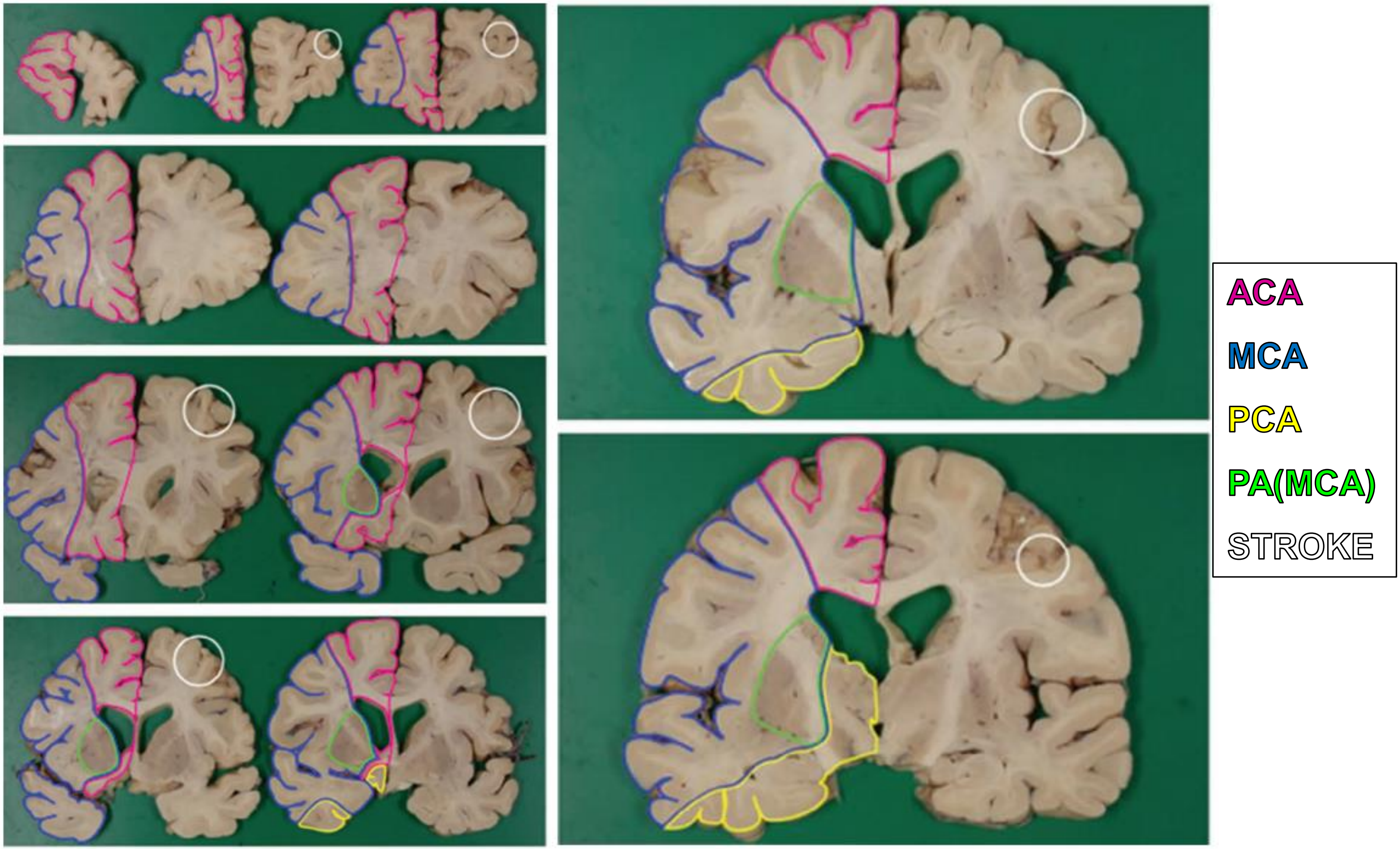
F. Netter M.D.
Medial frontal branches
Posterior
Intermediate
Anterior
Pericallosal artery
Paracentral artery
Cingular branches
Right posterior cerebral artery
Precuneal artery
Dorsal branch to corpus callosum
Parietooccipital branch
Calcarine branch
Callosomarginal artery
Polar frontal artery
Right anterior cerebral artery
Medial fronto-basal (orbito-frontal) artery
Anterior communicating artery (cut)
Distal medial striate artery (recurrent artery of Heubner)
Right internal carotid artery
Medial occipital artery
Posterior temporal branch
Anterior temporal branch
Posterior communicating artery

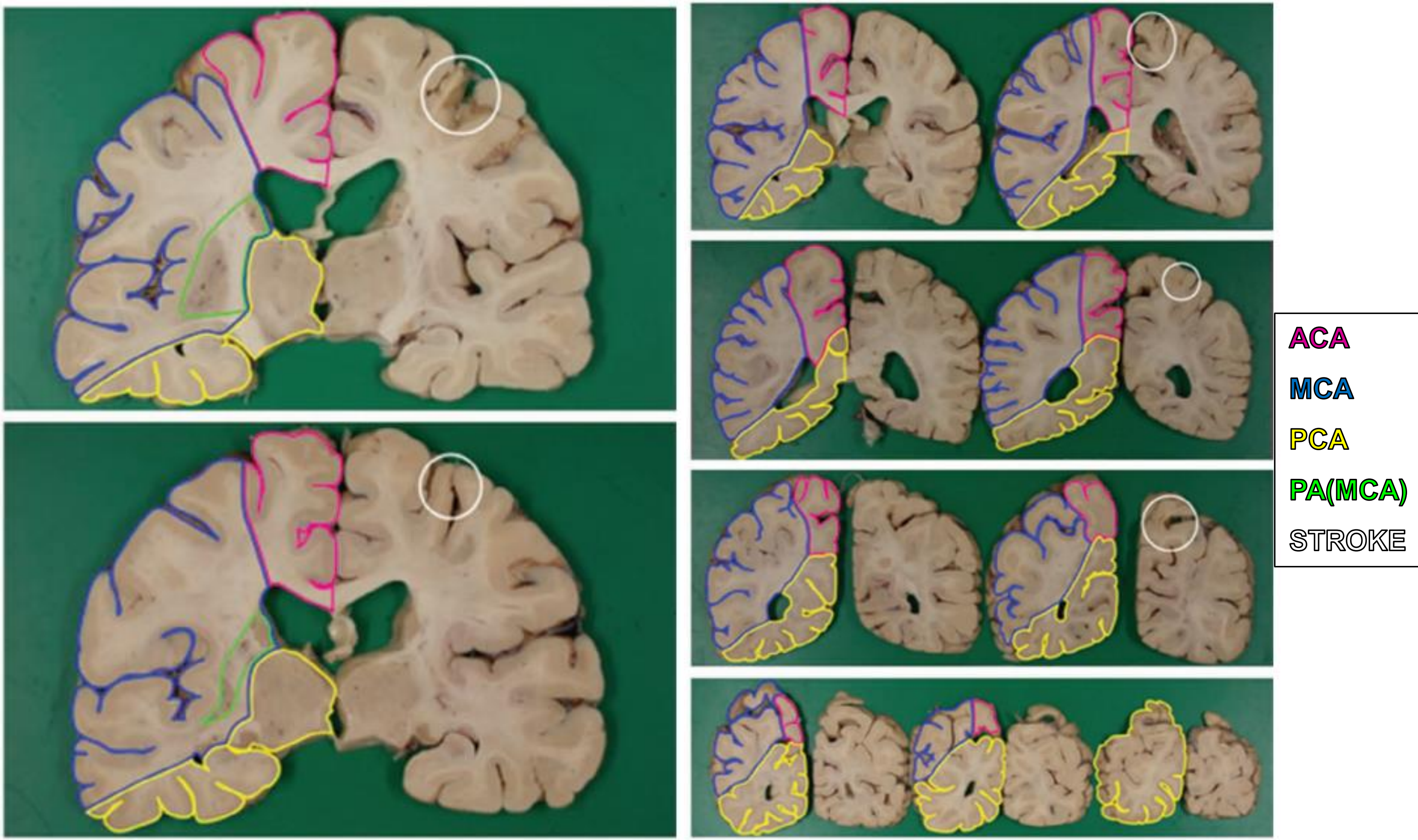

Falx cerebri
Callosomarginal arteries
and
Pericallosal arteries
(branches of anterior
cerebral arteries)
Corpus striatum
(caudate and lentiform nuclei)
Anterolateral central
(lenticulostriate) arteries
Insula (island of Reil)
Limen of insula
Precentral (pre-Rolandic),
central (Rolandic) sulcal,
and parietal arteries
Lateral cerebral (Sylvian) sulcus
Temporal branches of
middle cerebral artery
Temporal lobe
Middle cerebral artery
Internal carotid artery
Trunk of corpus callosum
Internal capsule
Septum pellucidum
Rostrum of corpus callosum
Anterior cerebral arteries
Distal medial striate artery
(recurrent artery of Heubner)
Anterior communicating artery
Optic chiasm

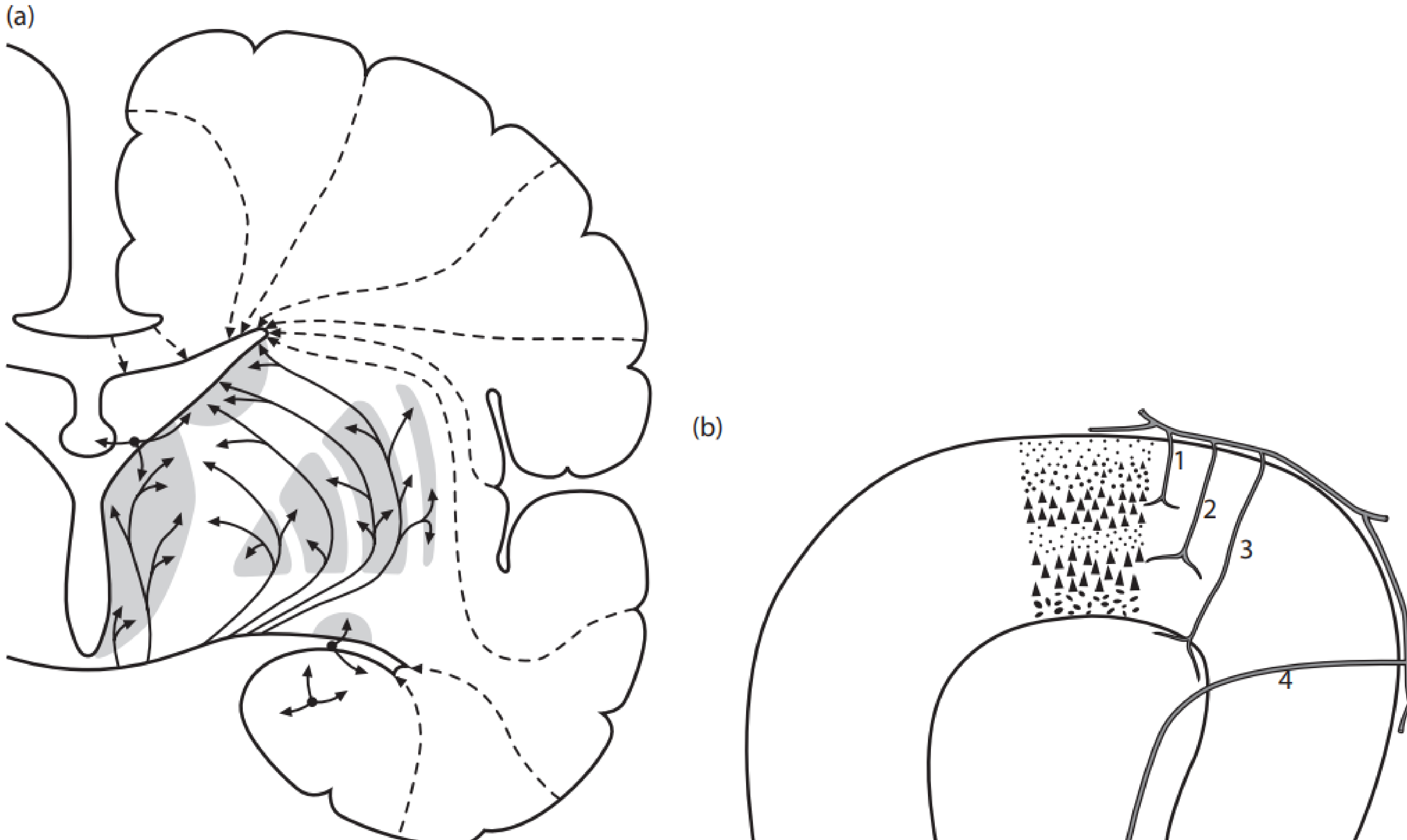

Anterior parietal (postcentral sulcal) artery*
Posterior parietal artery
Central (Rolandic) sulcal artery
Branch to angular gyrus
Precentral (pre-Rolandic) sulcal artery
Terminal branches of posterior cerebral artery
Prefrontal sulcal artery
Terminal branches of anterior cerebral artery
Lateral frontobasal (orbitofrontal) artery
Left middle cerebral artery
Left anterior cerebral artery
Anterior communicating artery
Occipitotemporal branches
Right anterior cerebral artery
Posterior temporal branch
Middle temporal branch
Left internal carotid artery
Superior and inferior terminal branches (trunks)
Polar temporal artery
Anterior temporal branch

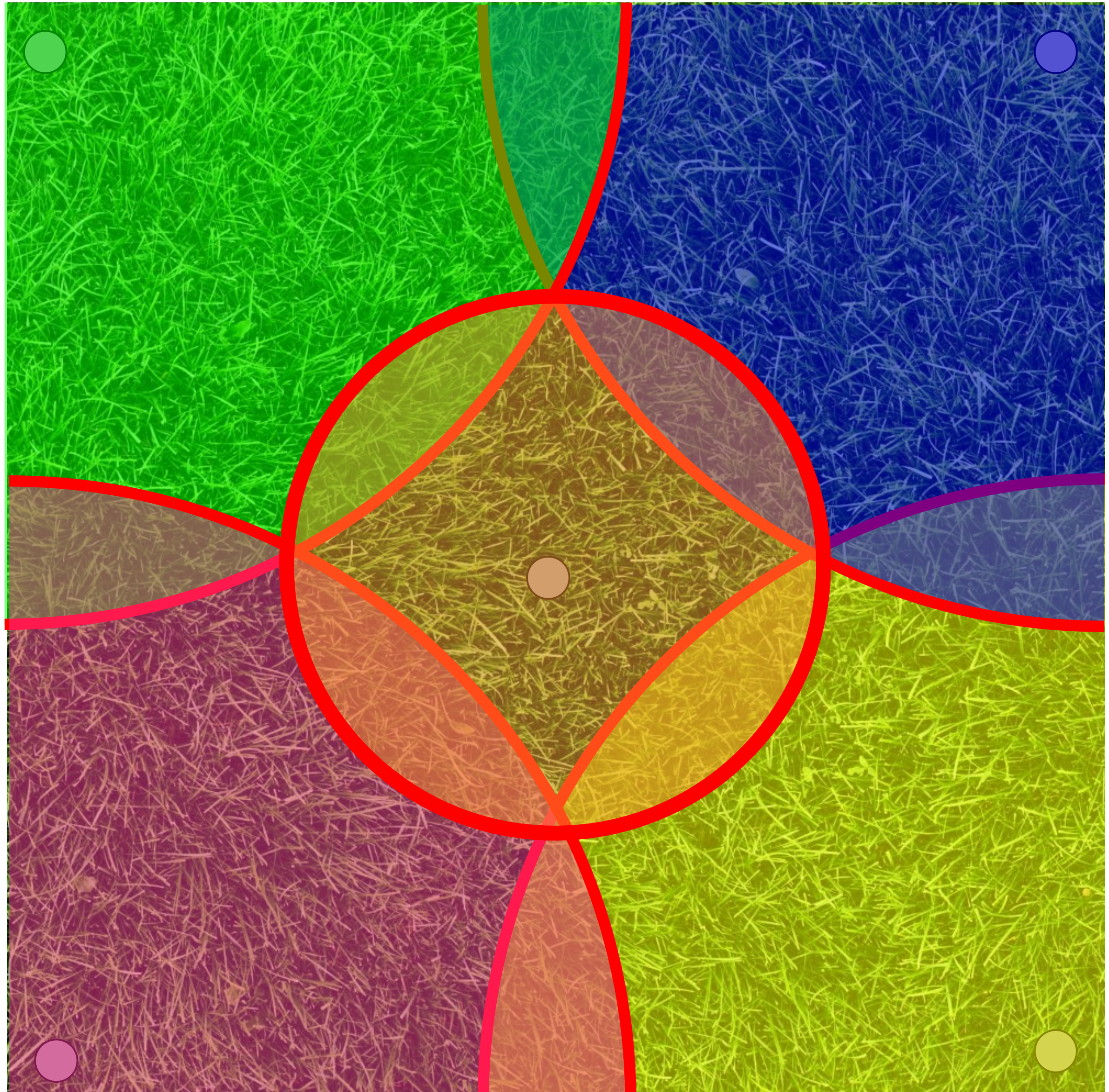

(a)
PCA
PCA
(b)
ACA
MCA
PCA


(a)
(b)
ACA
MCA
PCA
penetrating arteries
from circle of Willis


ACA
MCA
PCA
PA(MCA)
STROKE

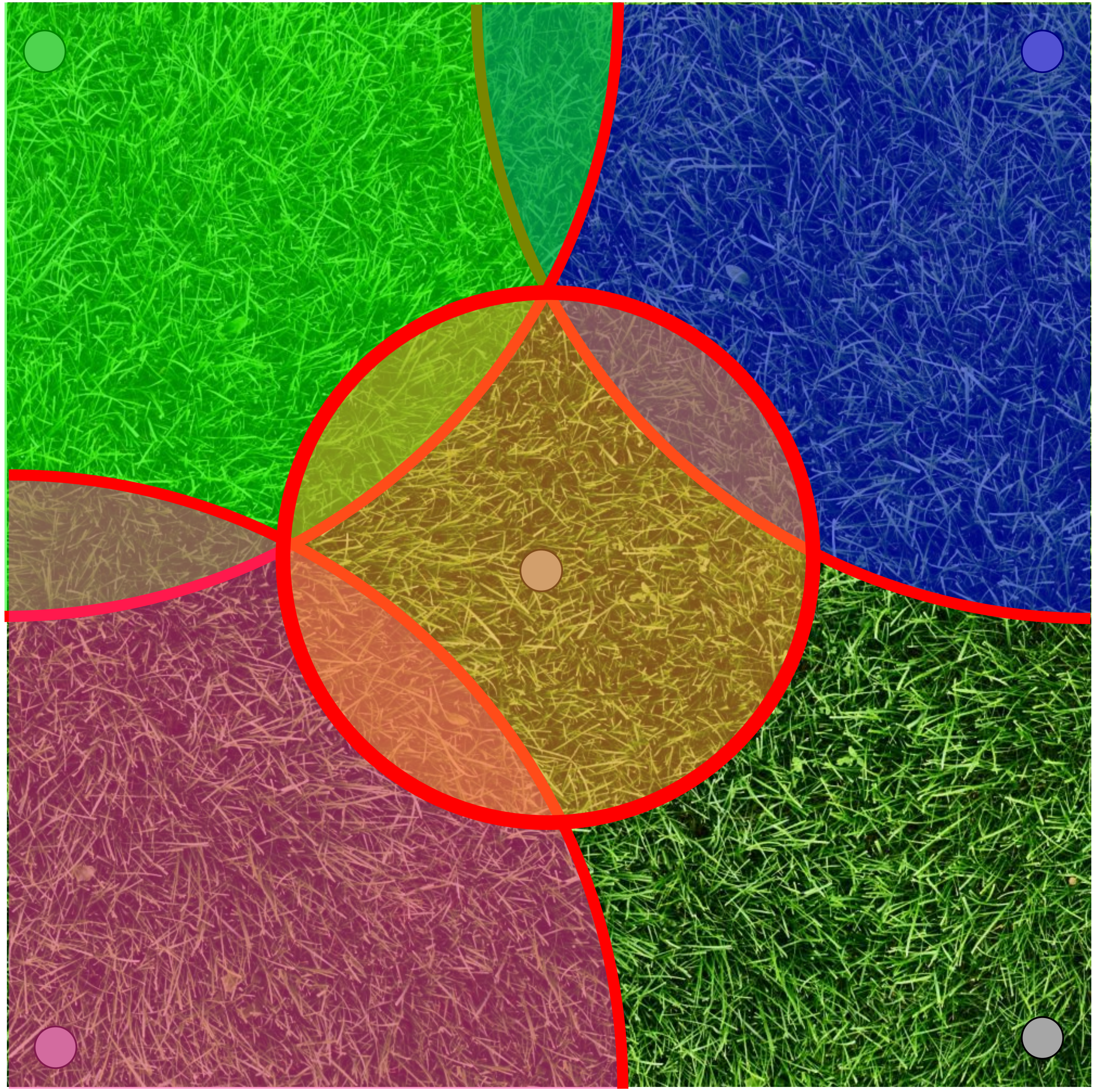

ACA
MCA
PCA
PA(MCA)
STROKE

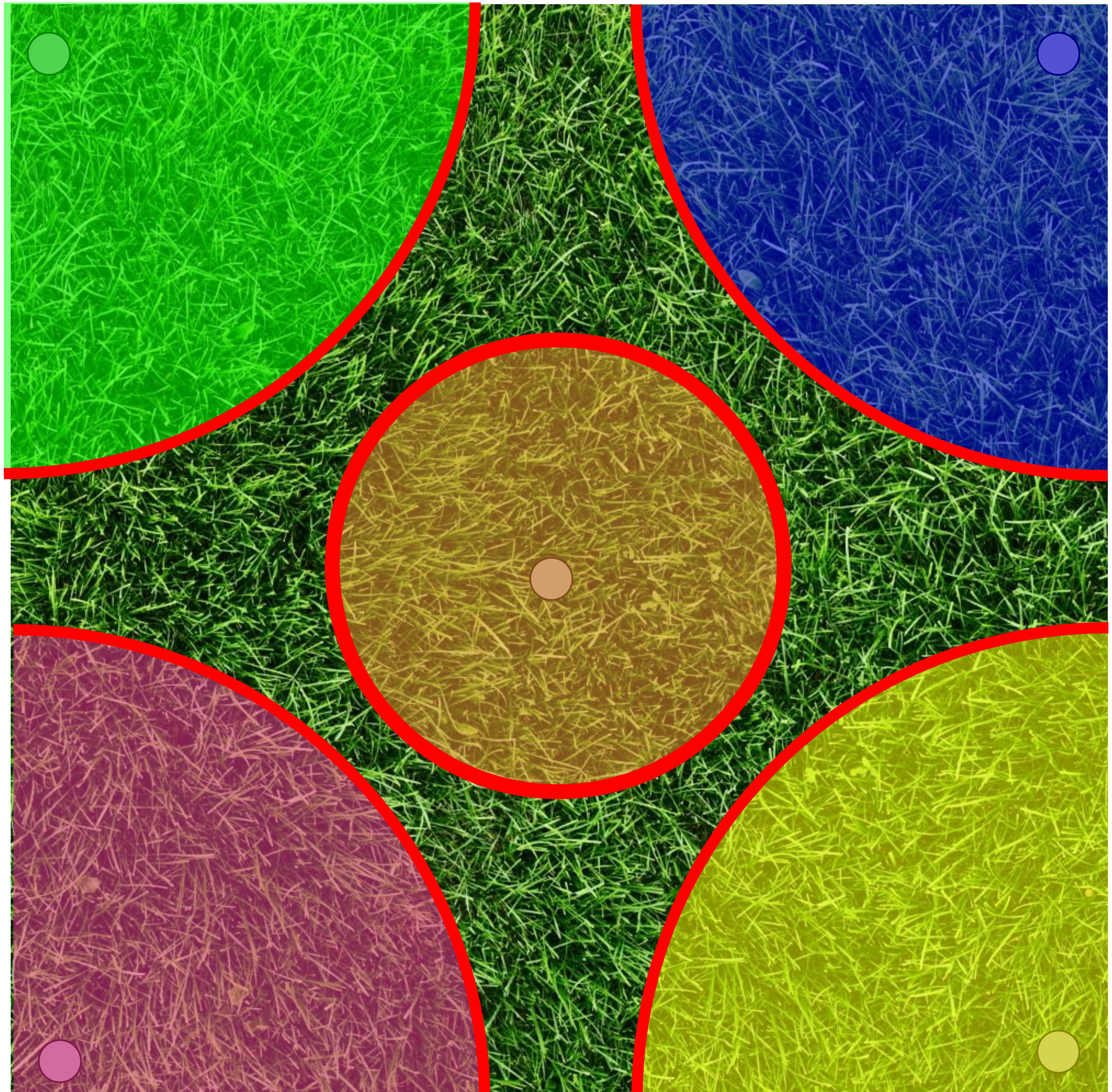

(a)
(b)
1
2
3
4



Artery Occlusion

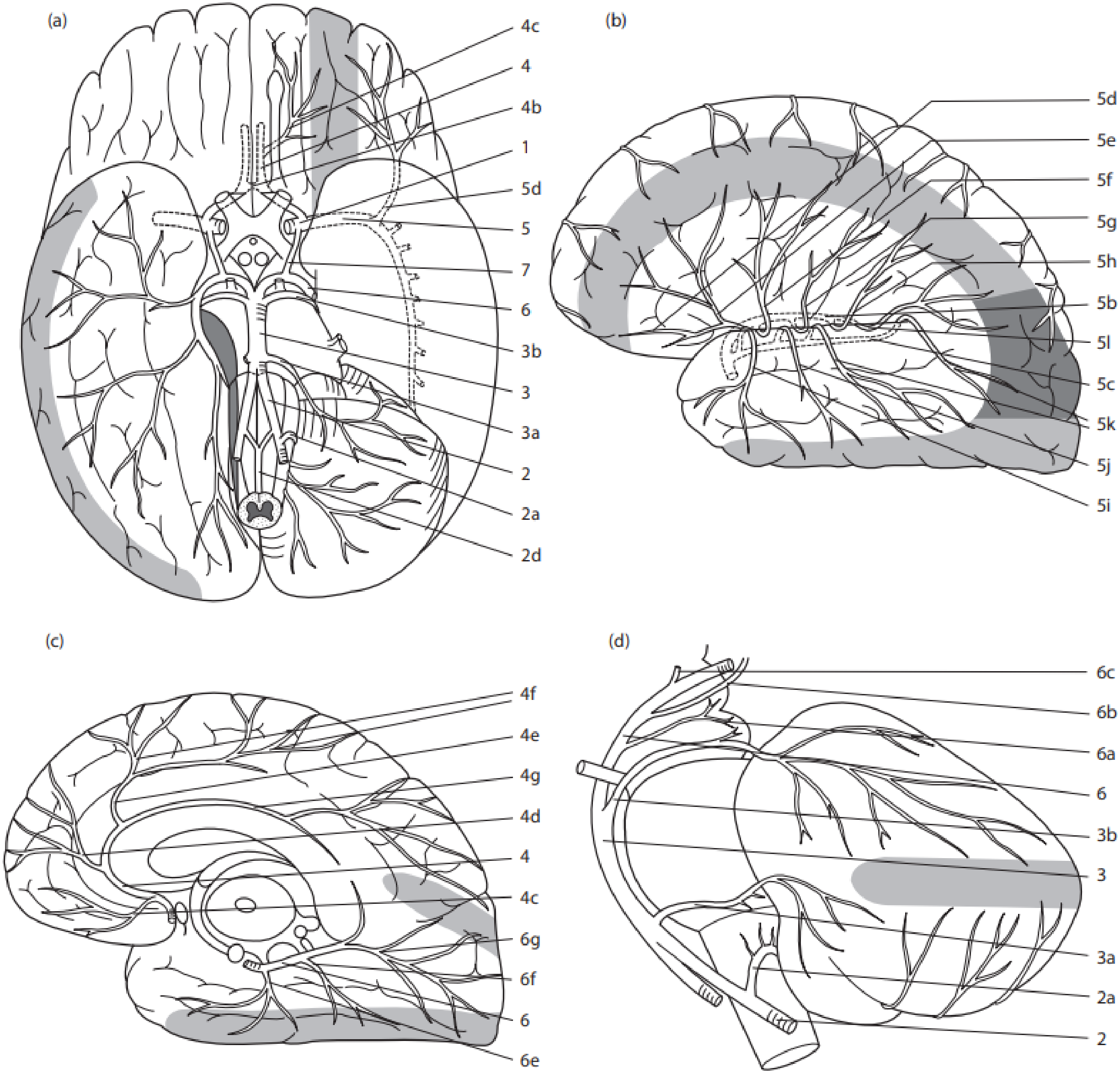
(territorial ischemia)



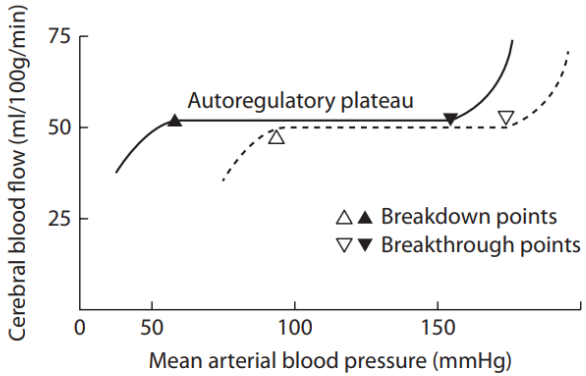


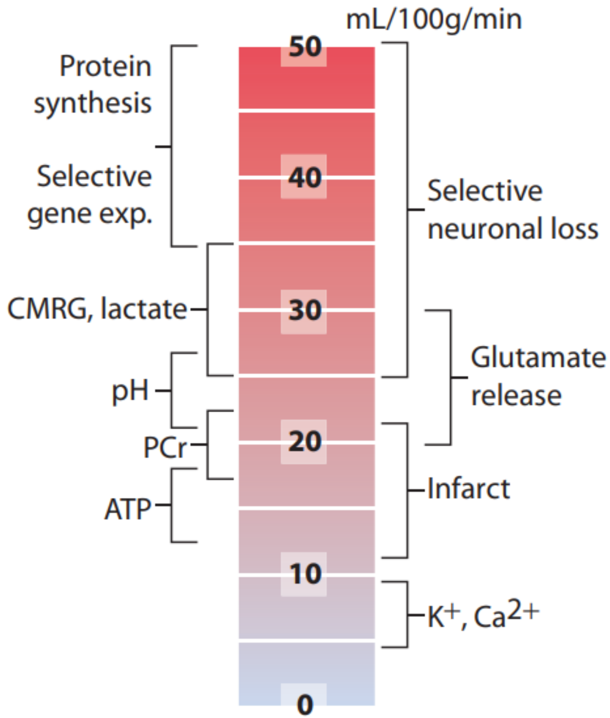
Hypotension

(Watershed ischemia)



(a)
4c
4
4b
1
5d
5
7
6
3b
3
3a
2
2a
2d
(b)
5d
5e
5f
5g
5h
5b
5l
5c
5k
5j
5i
(c)
4f
4e
4g
4d
4
4c
6g
6f
6
6e
(d)
6c
6b
6a
6
3b
3
3a
2a
2



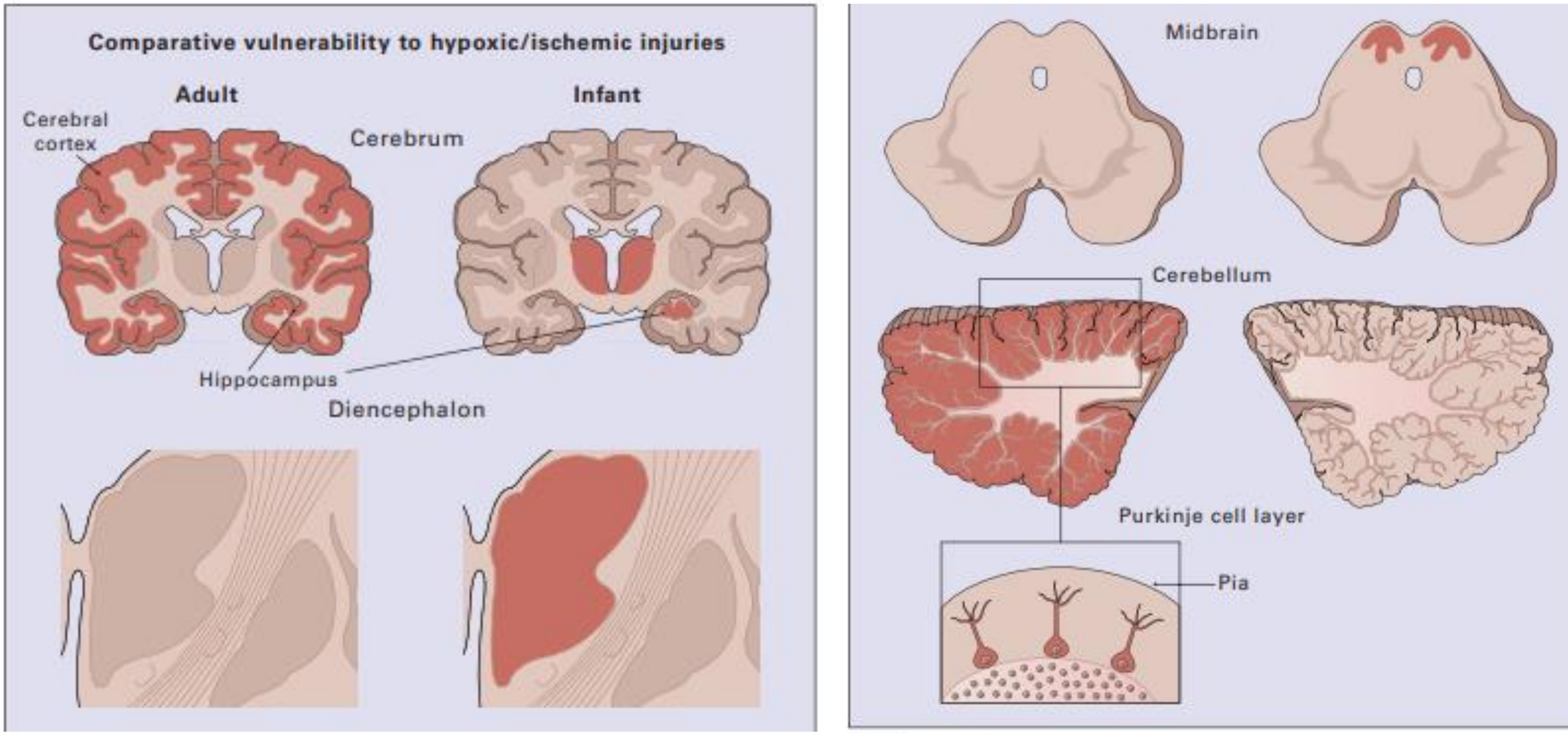


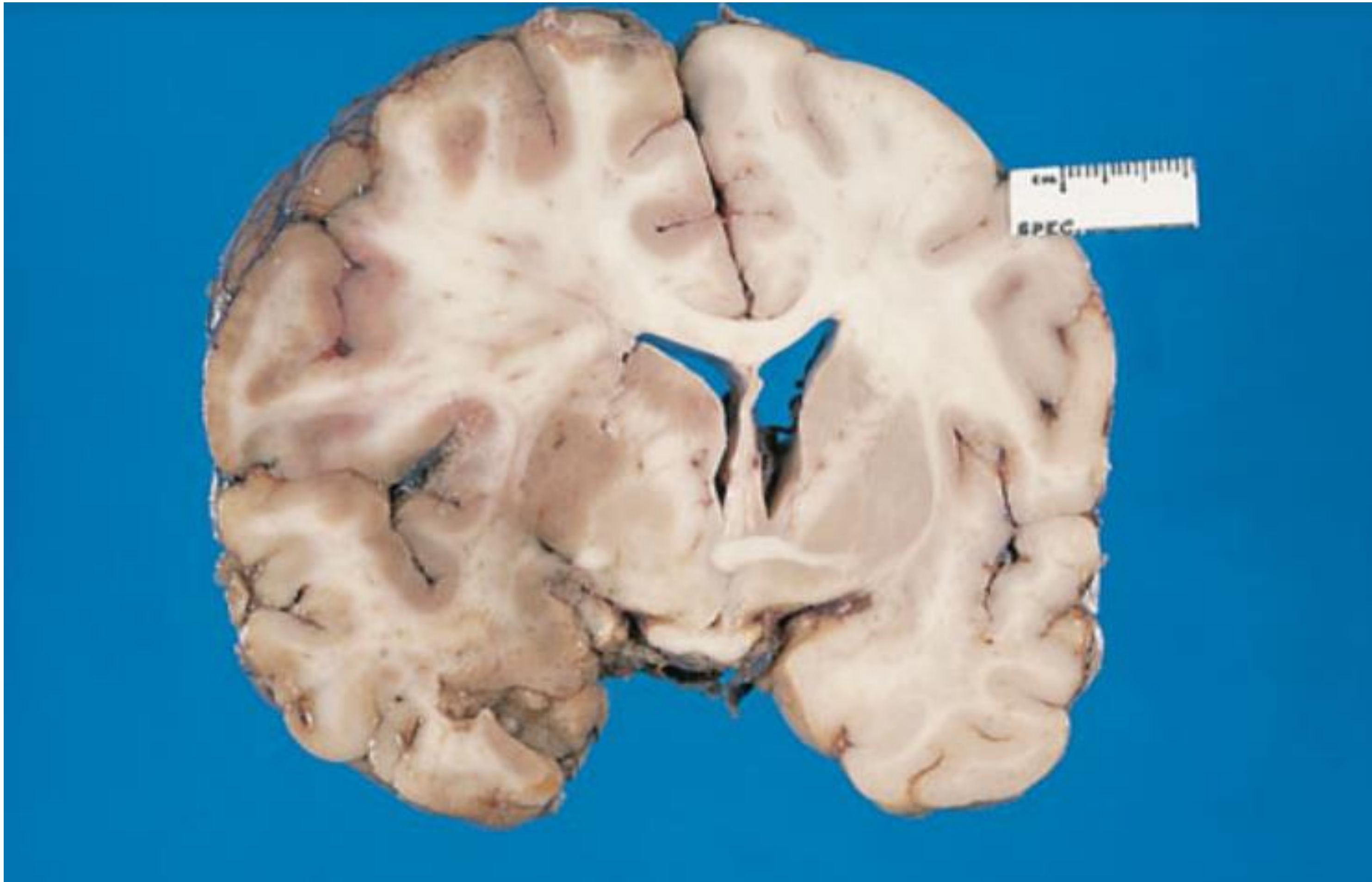
CEREBRAL BLOOD FLOW (CBF)

CBF = cerebral perfusion pressure (CPP)/cerebrovascular resistance (CVR)

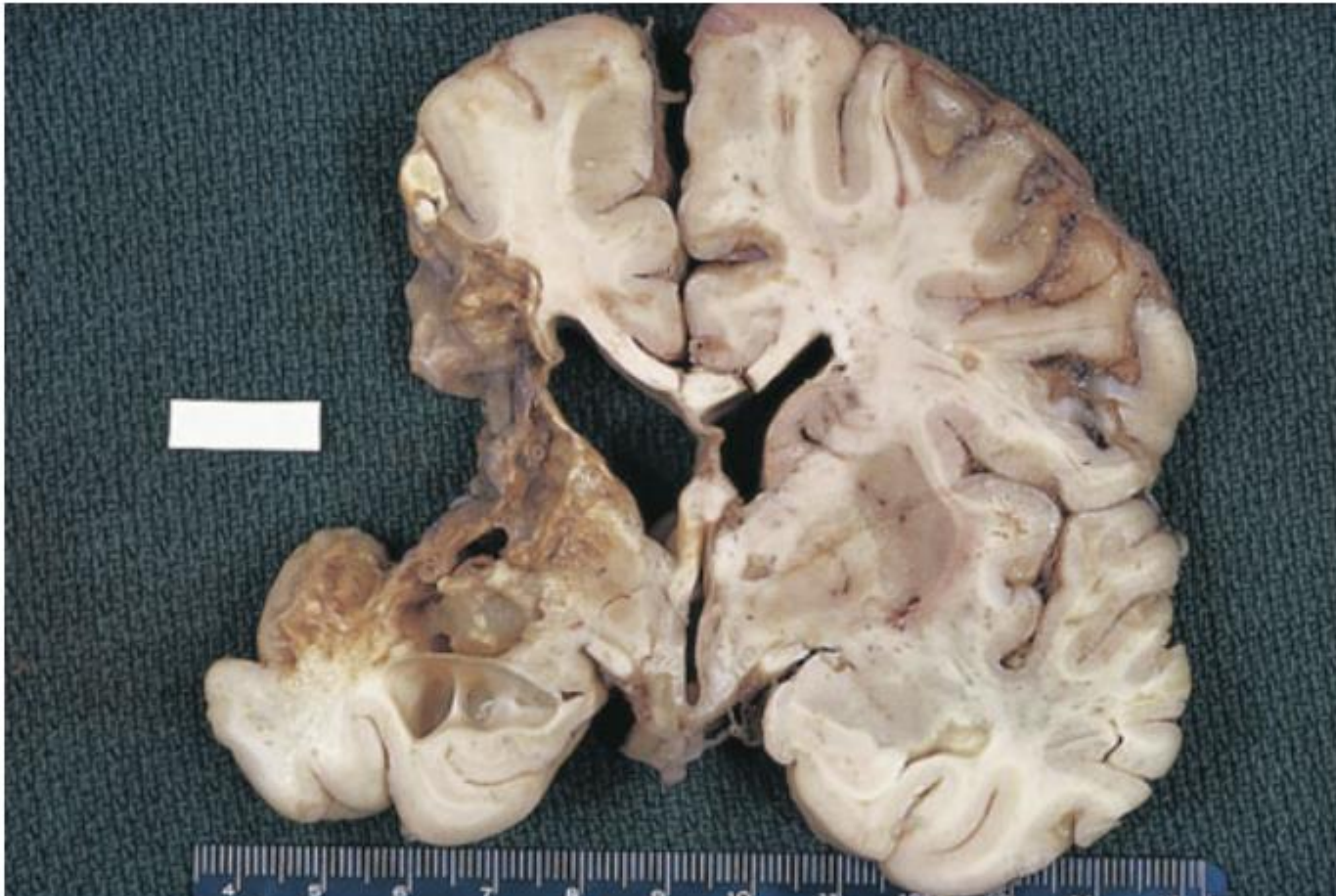
CPP = systemic arterial blood pressure – intracranial pressure (ICP)

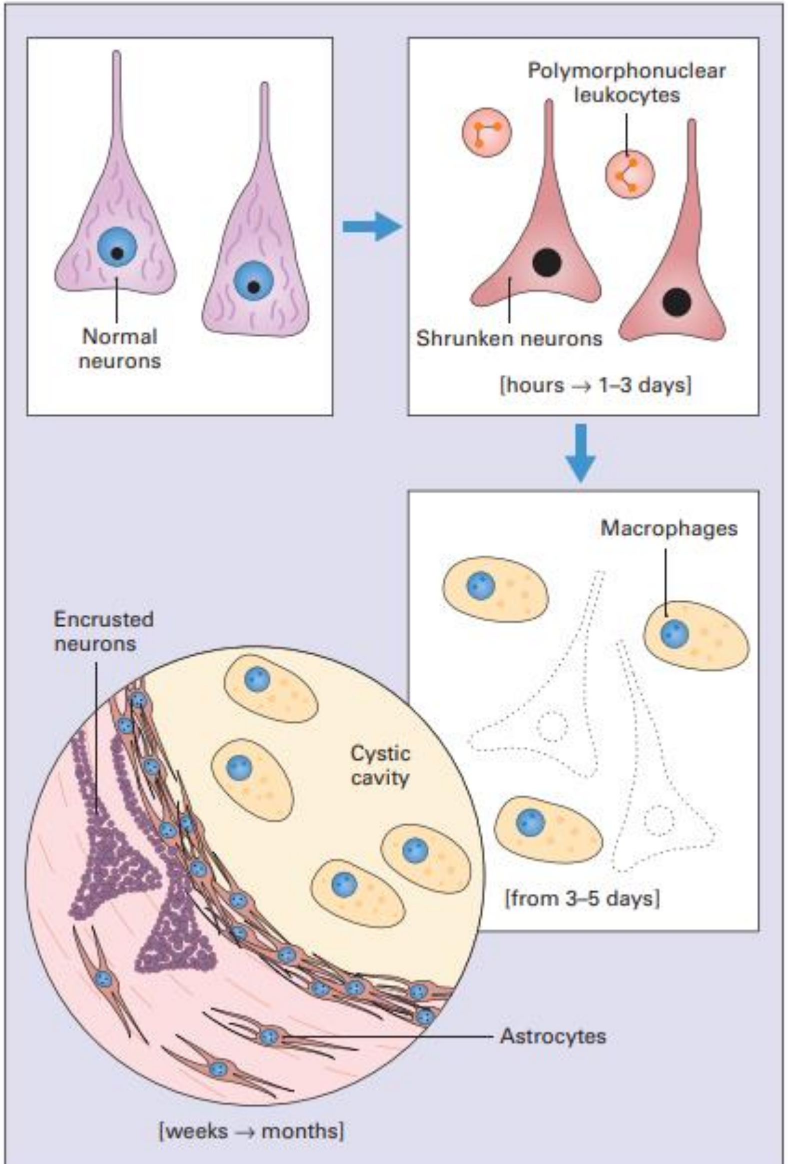
- CBF is approximately 750 mL/min, representing 15% of cardiac output.
- As long as mean CPP remains above approximately 5.3 kPa (~ 40 mmHg), the tone of vascular smooth muscle in intracranial arteries and arterioles (and hence CVR) adjusts in response to changes in CPP to maintain CBF in a constant range of 50–55 mL/100 g/min in adults (the value is higher in children). This is the phenomenon of autoregulation.
- Though overall CBF remains constant while CPP remains above the threshold for autoregulation, blood flow varies by anatomic region, according to demand for oxygen and glucose (largely dependent upon neuronal activity), a process described as functional hyperemia or neurovascular coupling. This variability of local blood flow is also used to advantage in functional MRI studies.
- The density of capillaries is greater in gray than white matter, reflecting the pronounced difference in their metabolic requirements and resulting in a corresponding difference in blood flow:
  - 80–100 mL/100 g/min in gray matter
  - 20–25 mL/100 g/min in white matter.
- If mean CPP falls below about 5.3 kPa, autoregulation becomes impaired or fails entirely, and CBF falls dramatically.
- Threshold CBF for infarction in primate brain is estimated to be 10–12 mL/100 g/min.


Comparative vulnerability to hypoxic/ischemic injuries
Adult
Infant
Cerebral cortex
Cerebrum
Hippocampus
Diencephalon
Midbrain
Cerebellum
Purkinje cell layer
Pia


cm
SPEC.

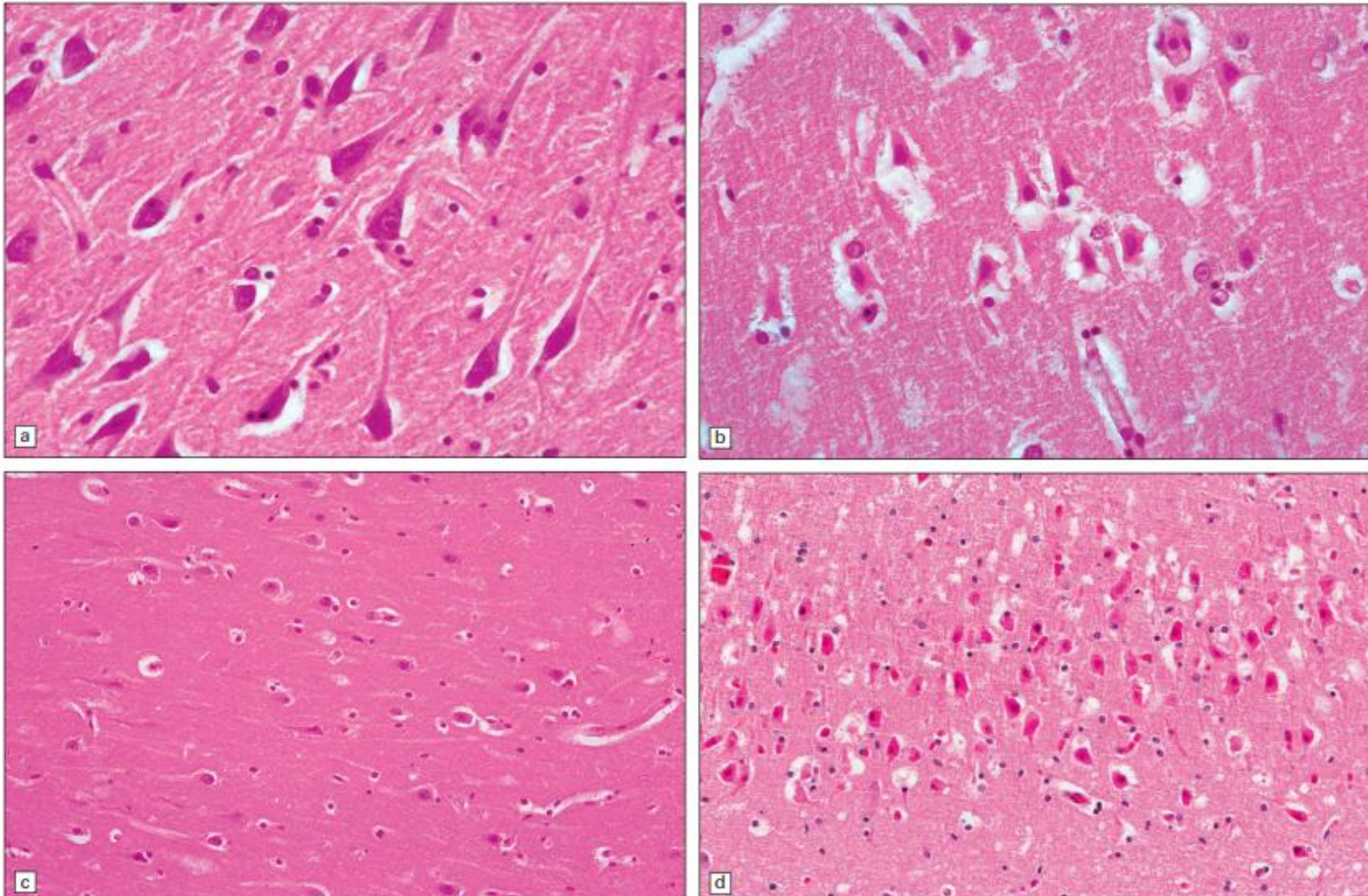

cm
1
2
SPECIMEN

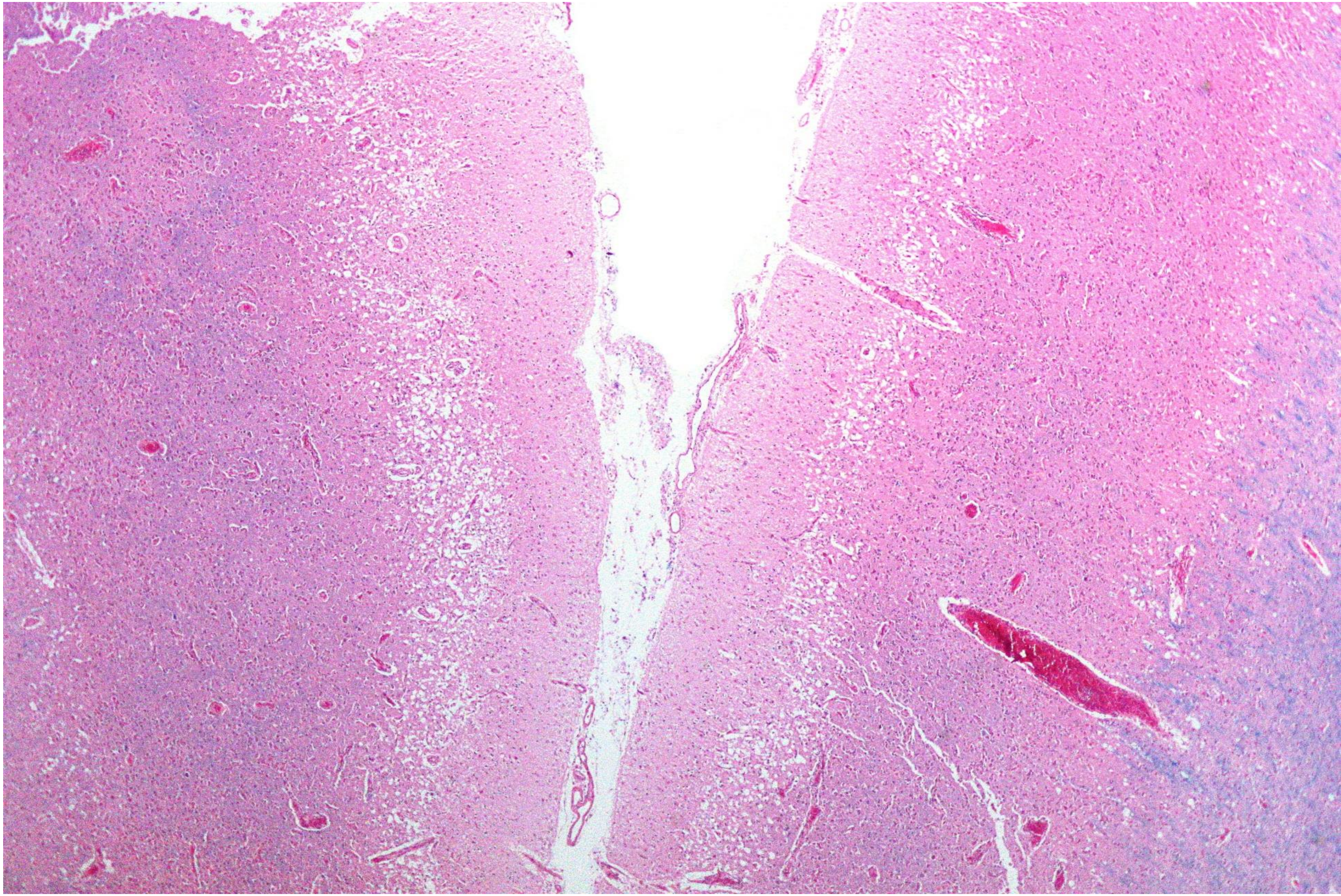

4 5 6 7 8 9 10 11 12 13 14 15



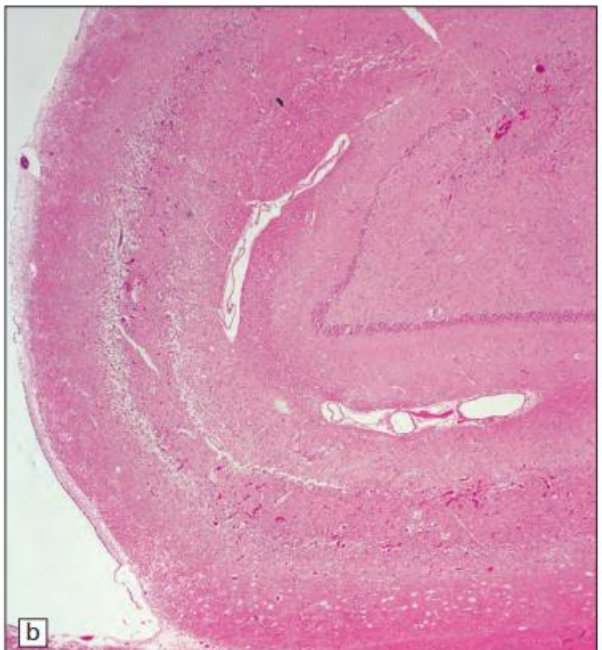
CELLULAR MECHANISMS OF ISCHEMIC CELL DEATH

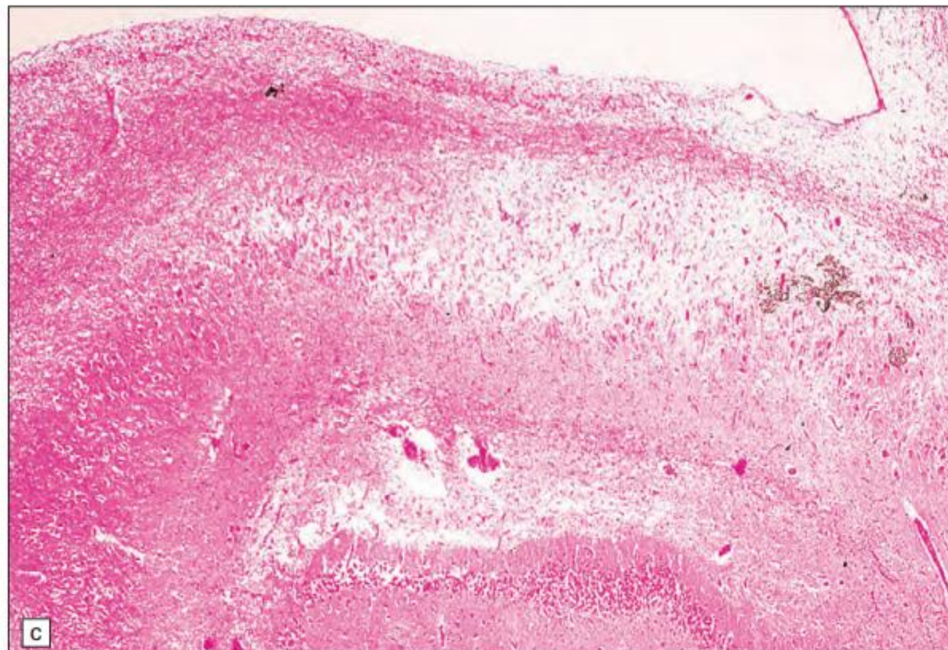
- Depolarization of neuronal/axonal membranes within 60–180 seconds of global anoxia leads to changes in extracellular and intracellular electrolyte composition and a decrease in ATP (secondary to impaired glycolysis and oxidative phosphorylation), with associated release of lactate and hydrogen ions and acidosis. ATP may decline to <25% of that in normally perfused tissue.
- Ionic fluxes include increased potassium ions (K^+) in the extracellular space and decreased extracellular calcium ions (Ca^{++}), with concomitant rise in intracellular Ca^{++} by up to 25%, a process mediated in part by NMDA receptors.
- Increased intracellular Ca^{++} activates calpain and other molecules, with deleterious effects on cytoskeletal and membrane structures.
- Mitochondrial injury secondary to Ca^{++} influx causes further decrease in ATP, an increase in free radicals, and a progressive inability to buffer Ca^{++} loads.
- Cytoskeletal damage can affect the machinery of protein synthesis, but this may eventually recover.
- Lipases, proteases and nucleases are activated, also with deleterious effects.
- Free radicals and NO/peroxynitrite, a mediator of NO toxicity, increase.
- Excitotoxic activation of glutamate receptors causes induction of heat shock proteins and rapid transcription of IE genes.


a
b
c
d



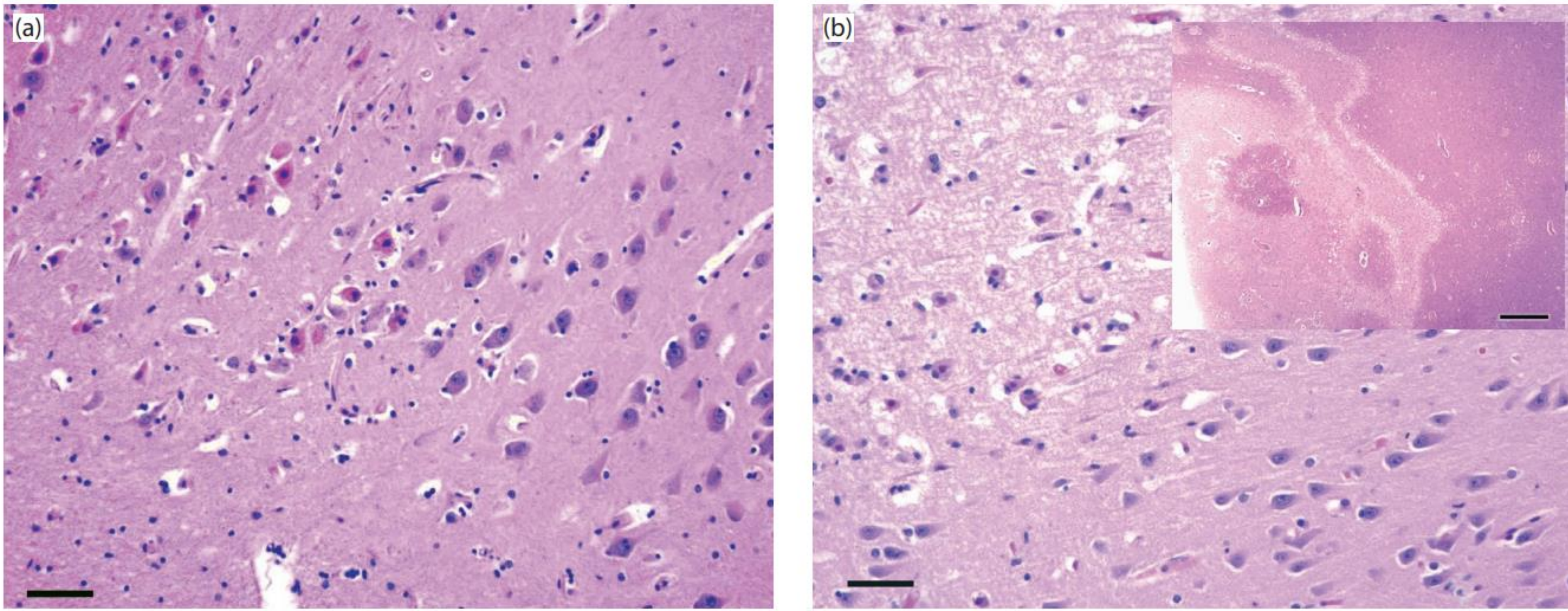
8.12 Selective vulnerability to hypoxic–ischemic change in the hippocampal pyramidal cell layer. **(a)** Normal hippocampus at low magnification. The figure includes part of the granule cell layer and part of the pyramidal cell layer as far as the prosubiculum/CA1 junction. **(b)** Segmental loss of neurons and prominent neuropil vacuolation within the CA1 sector of pyramidal cell layer. **(c)** There is an infarct involving virtually the entire CA1 field or sector and extending into the prosubiculum. Neuron loss and spongy change are seen in the affected neuropil. Note preservation of the granule cell layer (dentate fascia). **(d)** Normal CA1 zone of hippocampal pyramidal cell layer, contrasted with **(e)** a region with severe acute anoxic–ischemic change (neuronal eosinophilia, cytoplasmic and nuclear collapse, etc). **(f,g)** Severe hippocampal sclerosis in a patient with longstanding temporal lobe epilepsy. (f) Arrows indicate junction between sclerotic CA1 zone (at left) and intact prosubiculum (at right). (g) The junction between the two sectors is highlighted; gliotic tissue and neuron depletion in CA1, intact neurons in prosubiculum.





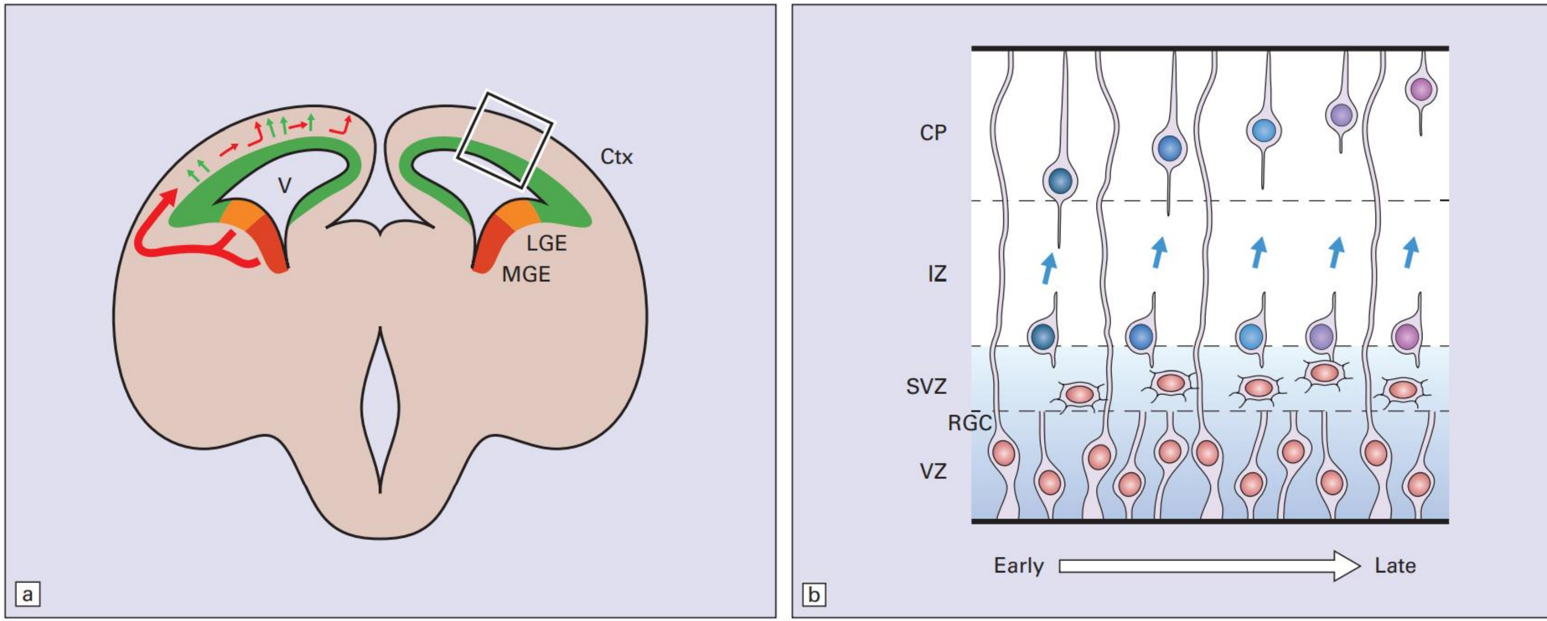
https://pathpresenter.net/#/public/display?token=84763618

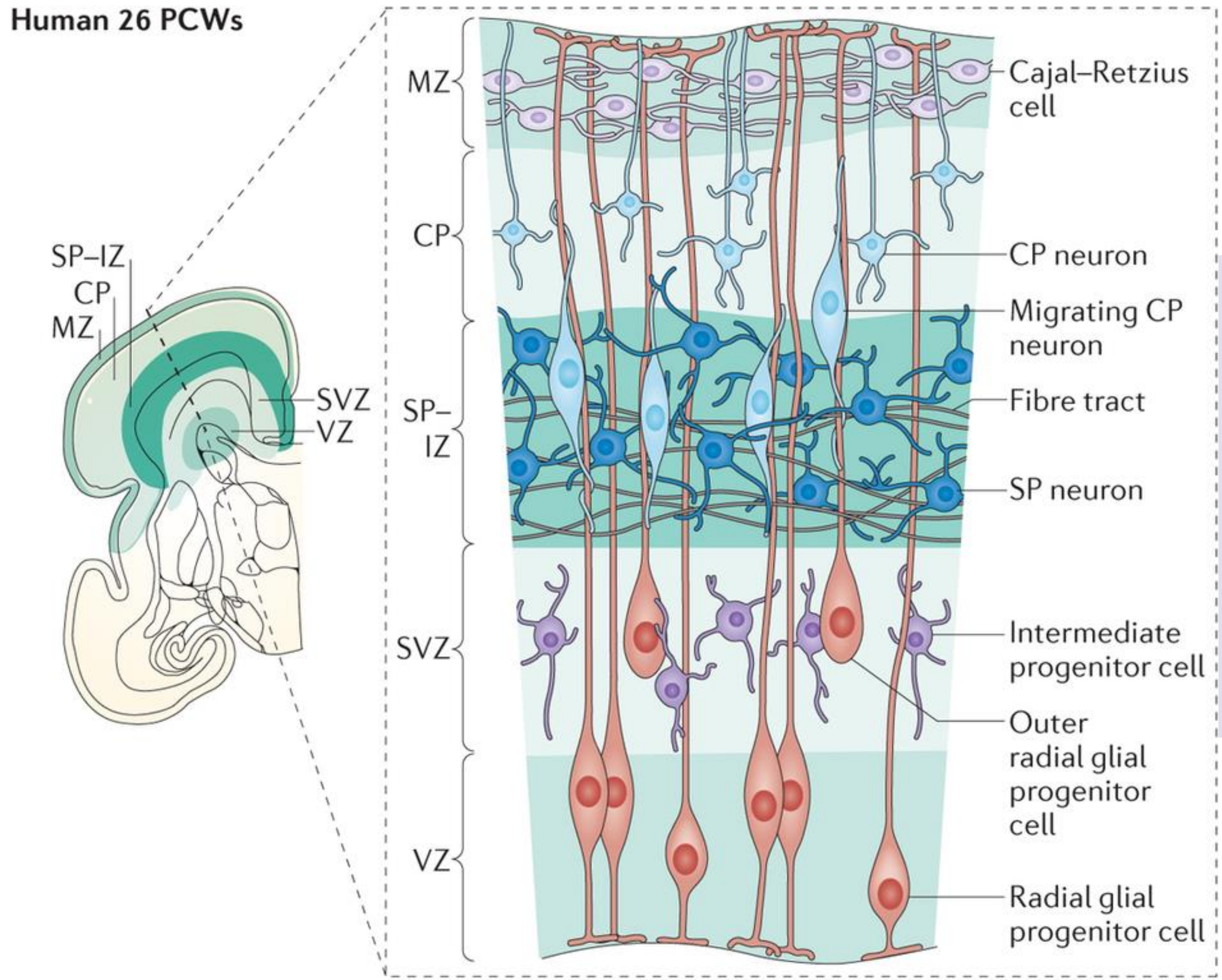
https://pathpresenter.net/#/public/displa
y?token=87833a59

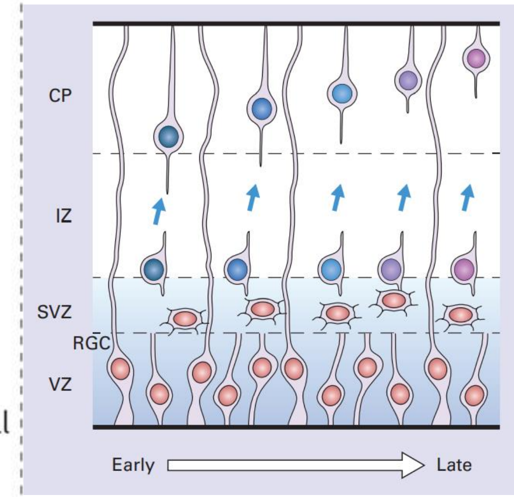


(a)
(b)

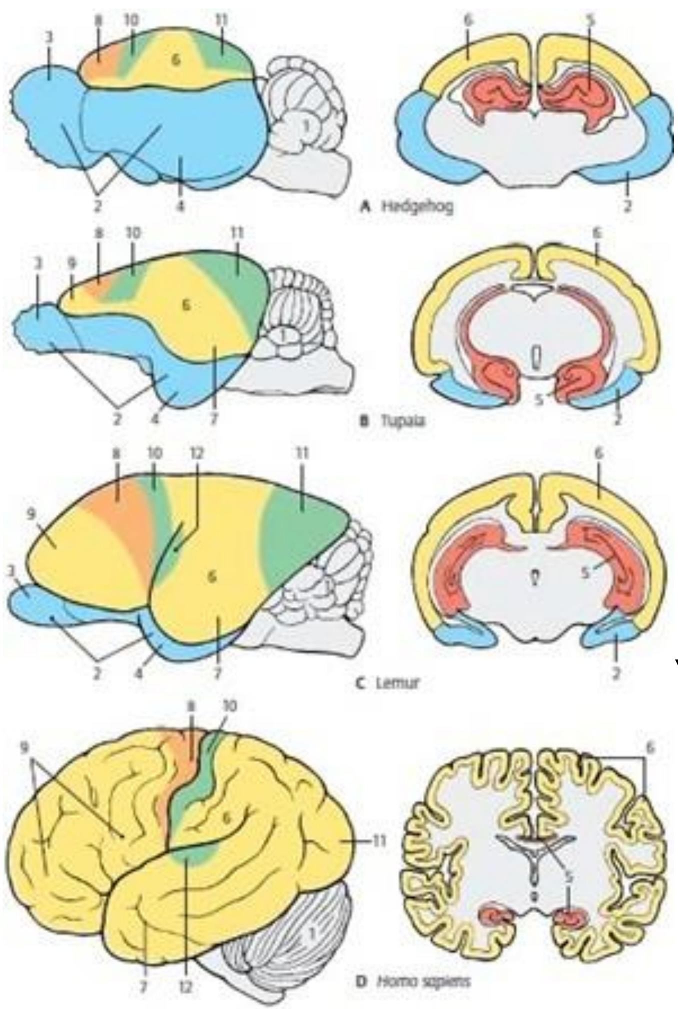
Functional Anatomy of the Telencephalon







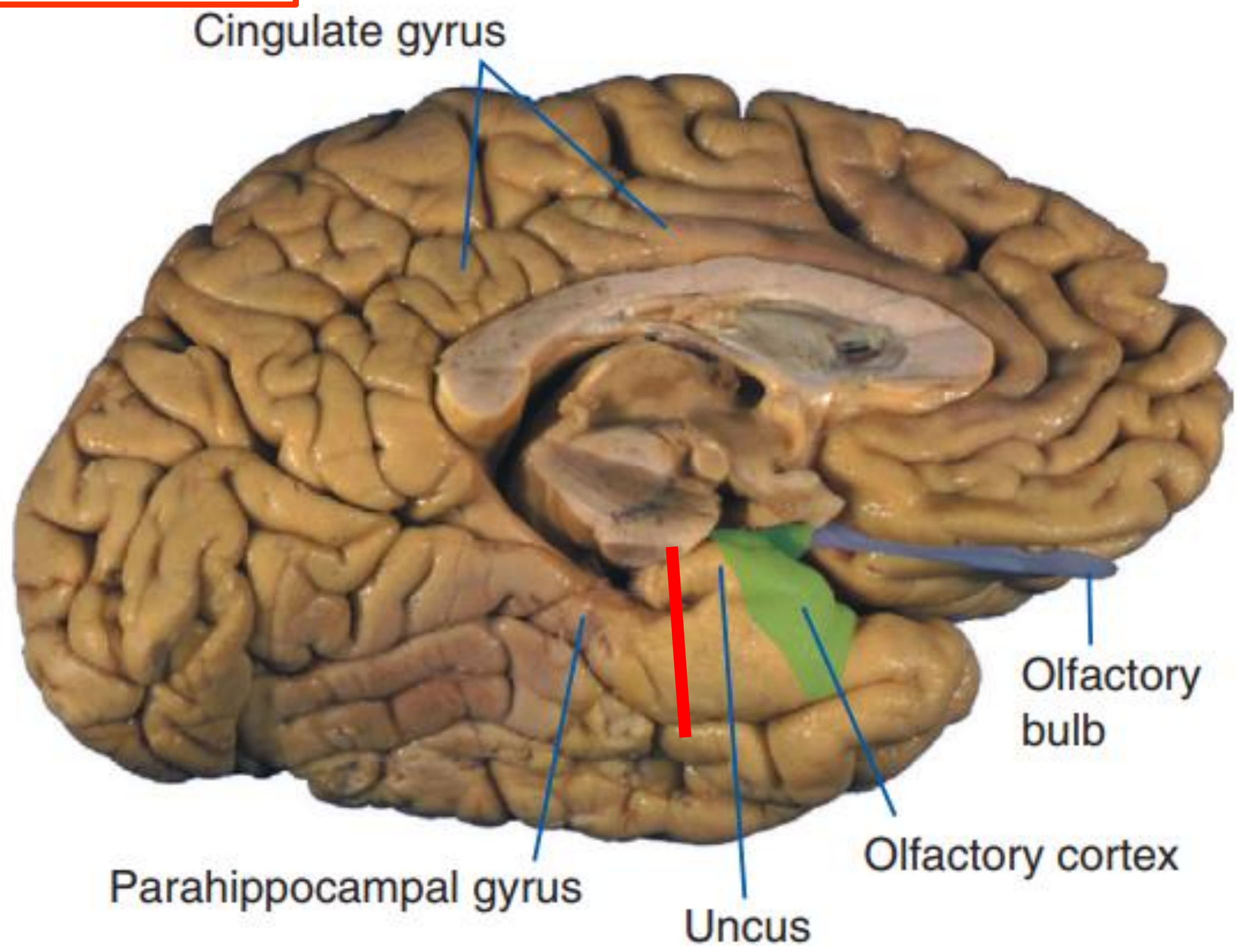
Nature Reviews | Neuroscience

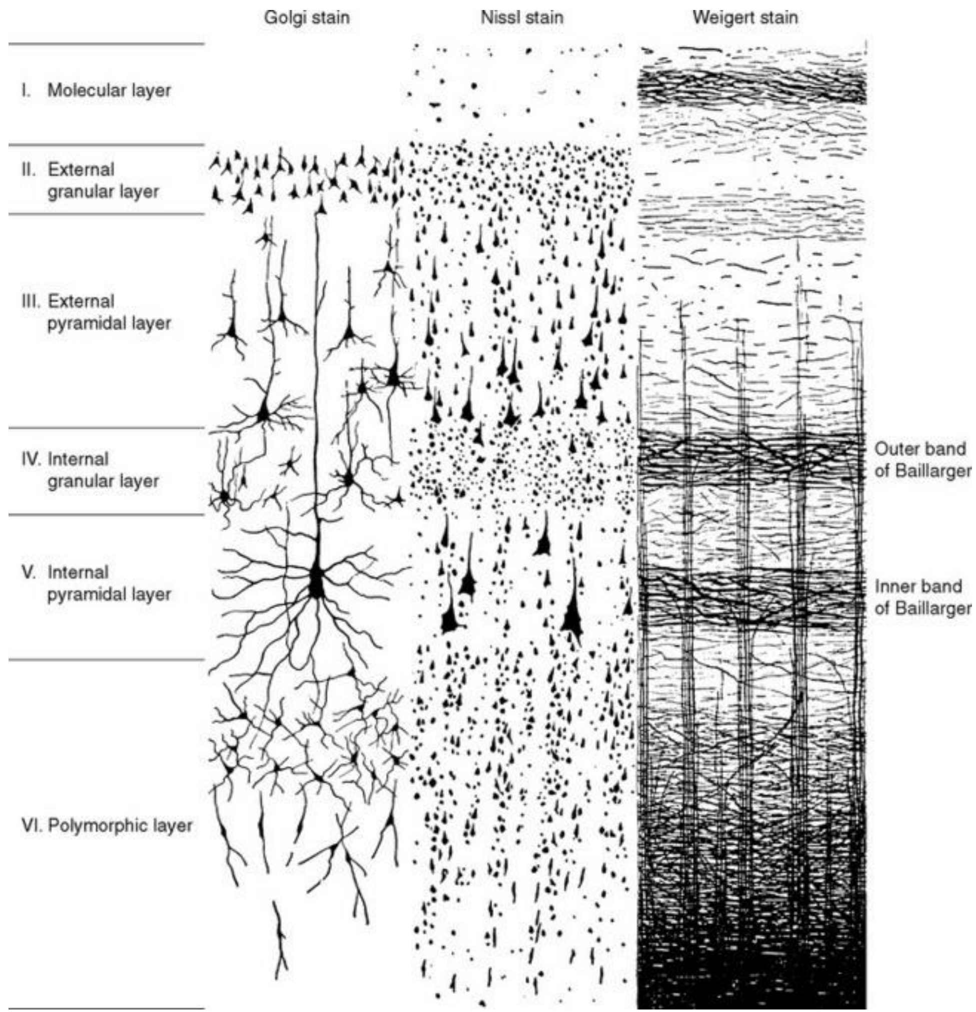


Phylogenesis of the Cerebral Cortex

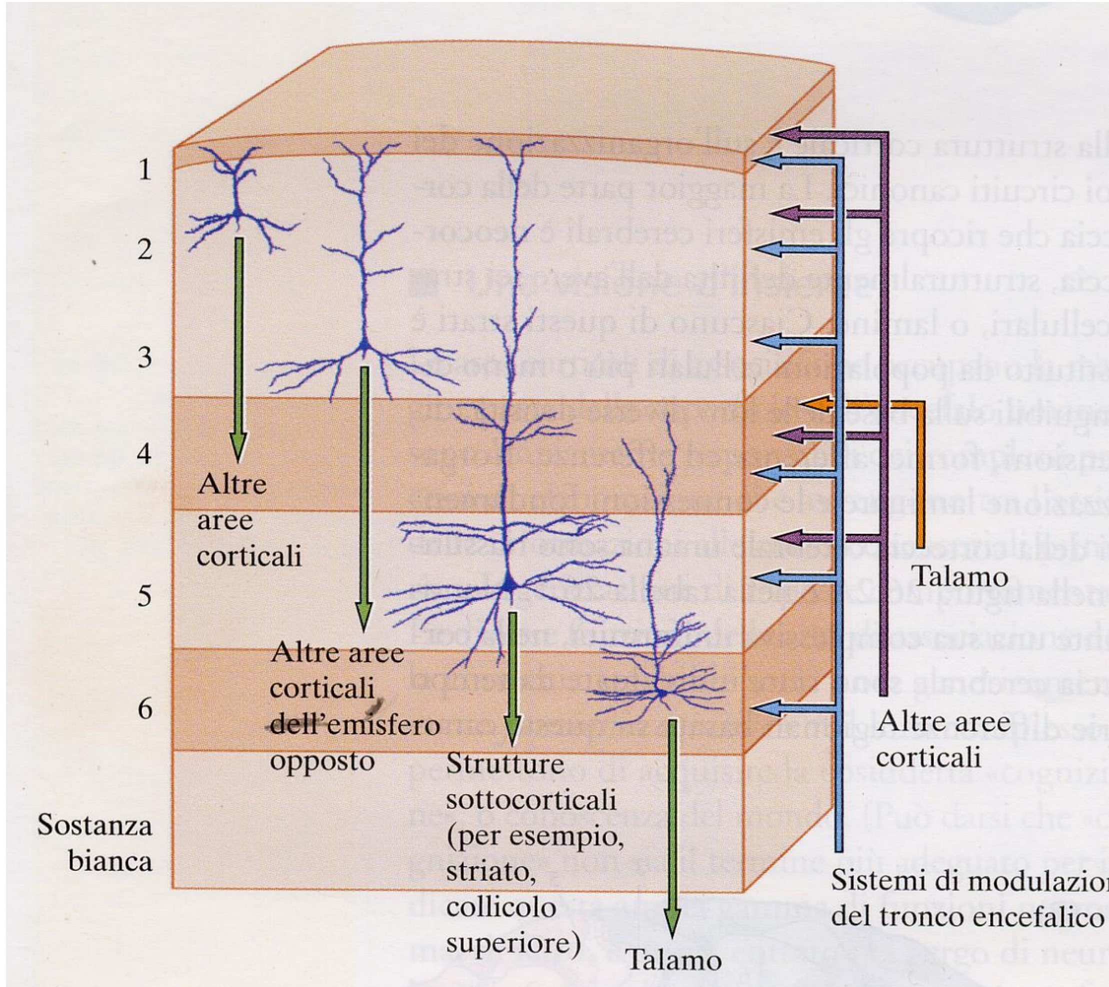
- **Allocortex:** also known as archicortex / archipallium. Most ancient part of the cortex. 3 Layers. Found in the hippocampal formation.
- **Mesocortex:** also known as paleocortex / paleopallium. 4-5 layers; represents an intermediate stage between the allocortex and the isocortex.
- **Isocortex:** also known as neocortex or neopallium. Most recent part of the cortex. 6 Layers. Makes up most of the cerebral cortex.

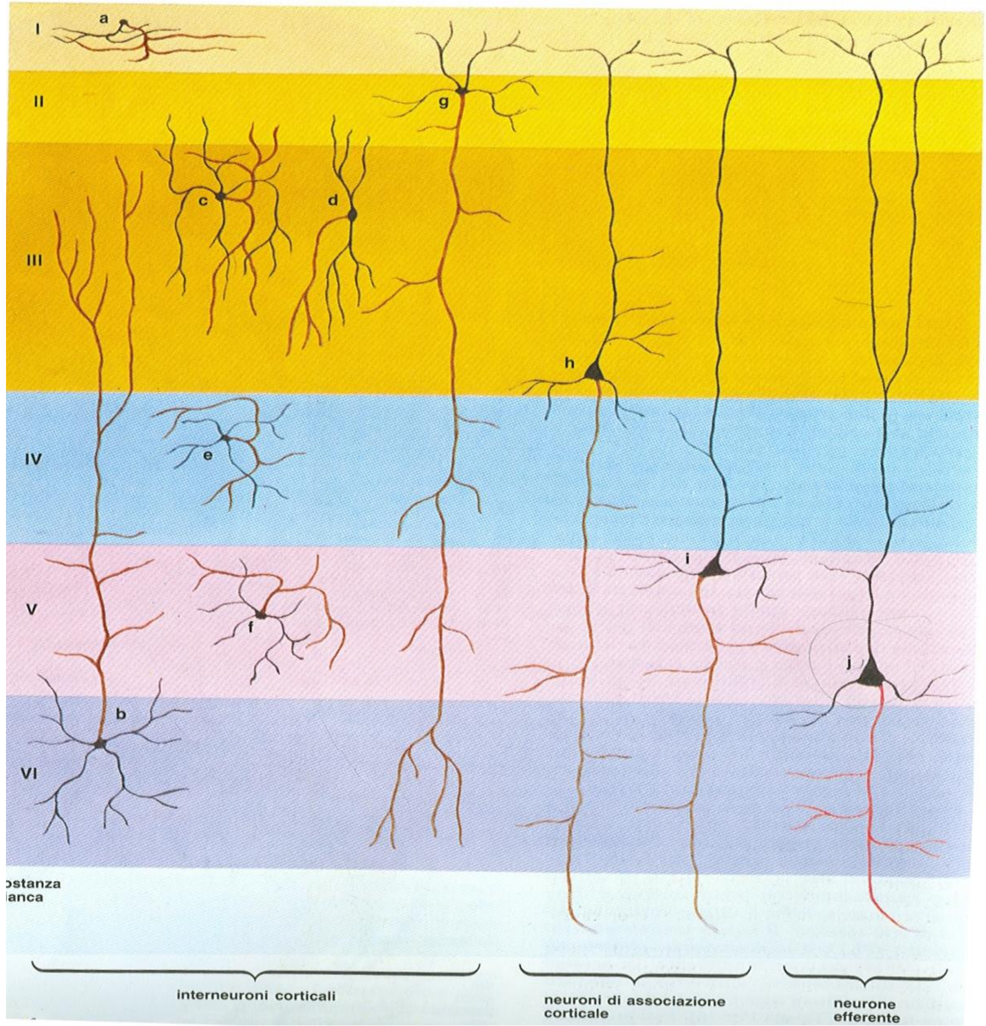
Non-neocortical areas



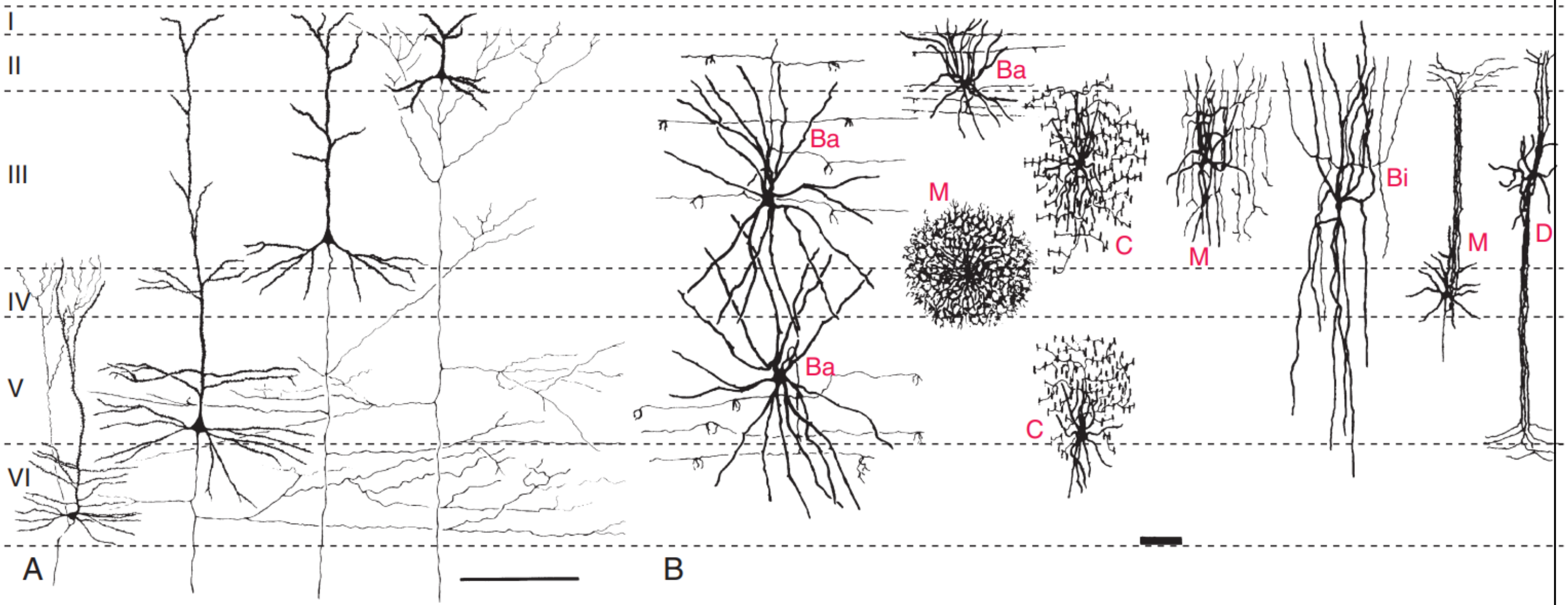


Golgi stain
Nissl stain
Weigert stain
I. Molecular layer
II. External granular layer
III. External pyramidal layer
IV. Internal granular layer
V. Internal pyramidal layer
VI. Polymorphic layer
Outer band of Baillarger
Inner band of Baillarger

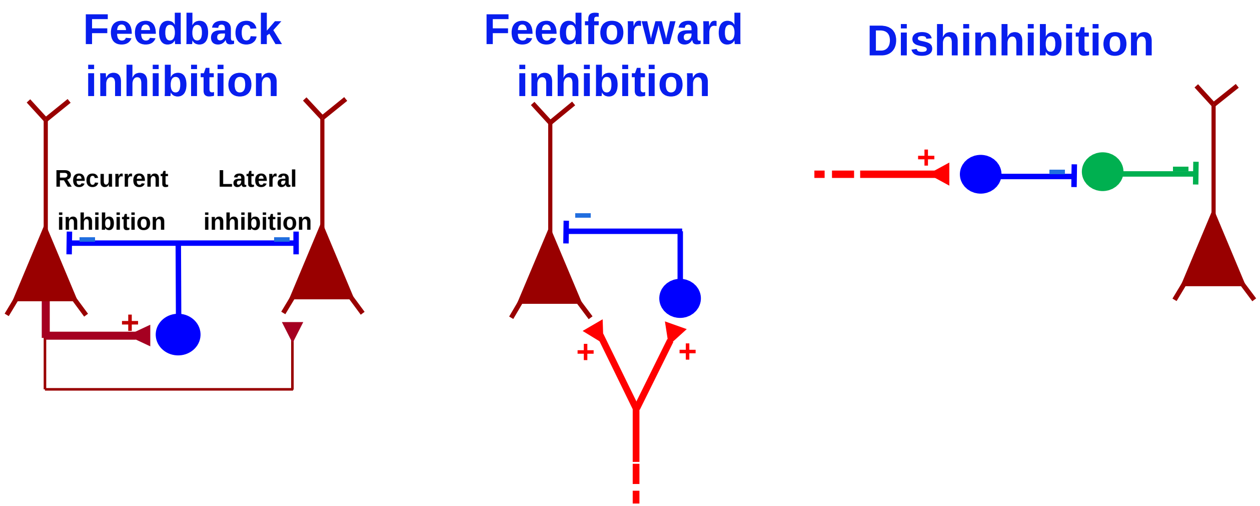

1
2
3
4
5
6
Sostanza bianca
Altre aree corticali
Altre aree corticali dell'emisfero opposto
Strutture sottocorticali (per esempio, striato, collicolo superiore)
Talamo
Talamo
Altre aree corticali
Sistemi di modulazion del tronco encefalico


I
II
III
IV
V
VI
a
b
c
d
e
f
g
h
i
j
ostanza
ianca
interneuroni corticali
neuroni di associazione
corticale
neurone
efferente


pia mater
I
II
III
IV
V
VI
white matter


I
II
III
IV
V
VI
A
B
Ba
Ba
Ba
M
C
M
Bi
M
D
C

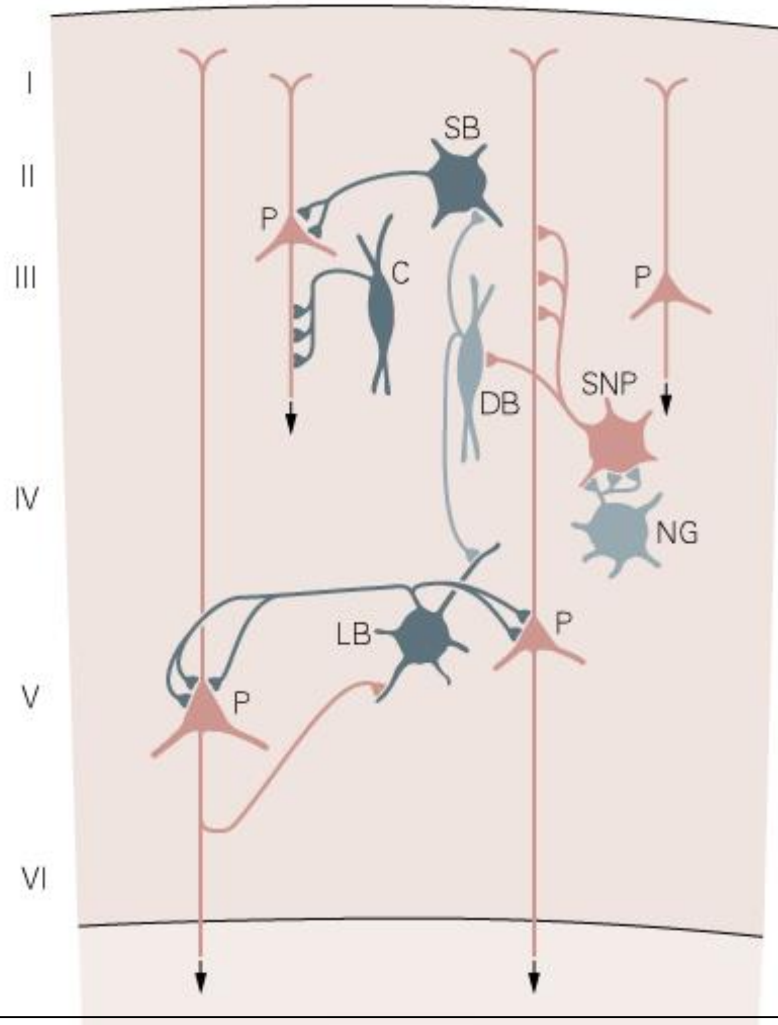
Three main cortical microcircuits core motifs involving inhibitory interneurons



--Essential for the correct processing of sensory information

(e.g. gain control and dynamic range modulation, sensory feature selectivity, surround suppression, synchronization, cell assemblies formation and competition)

--Essential to maintain a dynamic cellular excitatory-inhibitory (E/I) balance necessary for the transfer of information while preventing runaway excitation

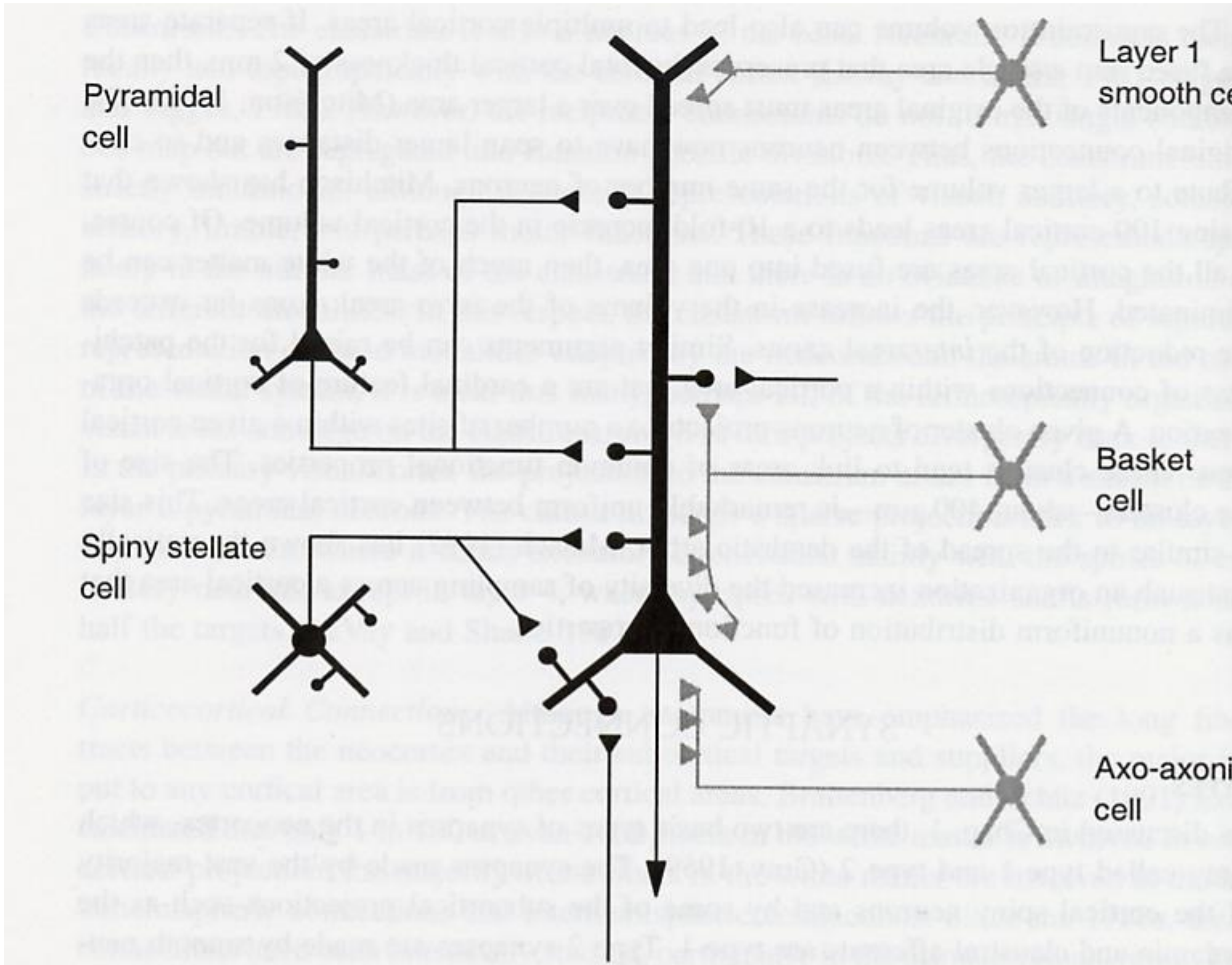


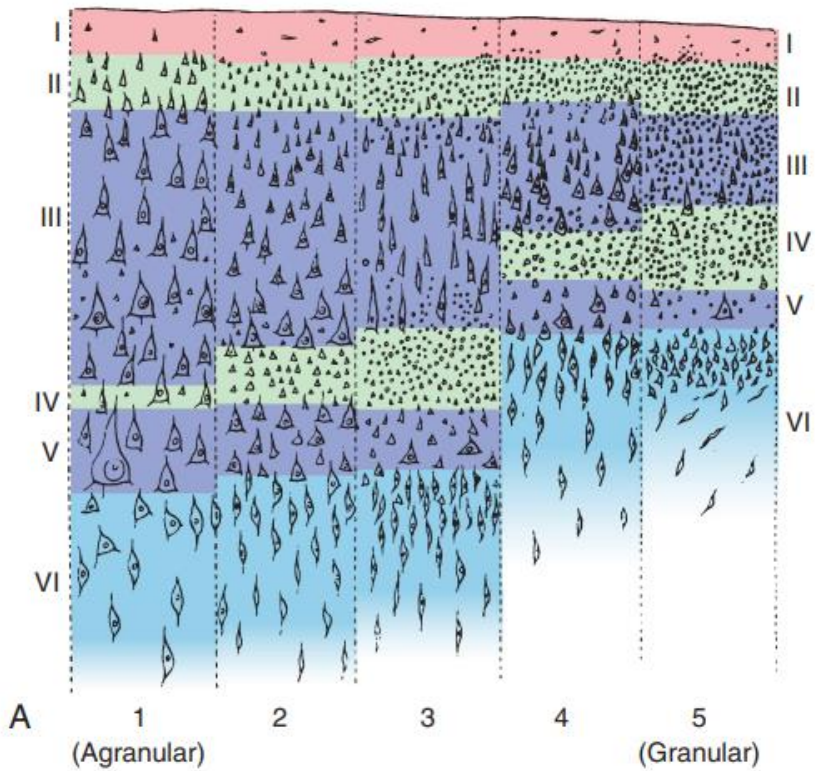
LB: large basket

SB: small basket

DB: double bouquet

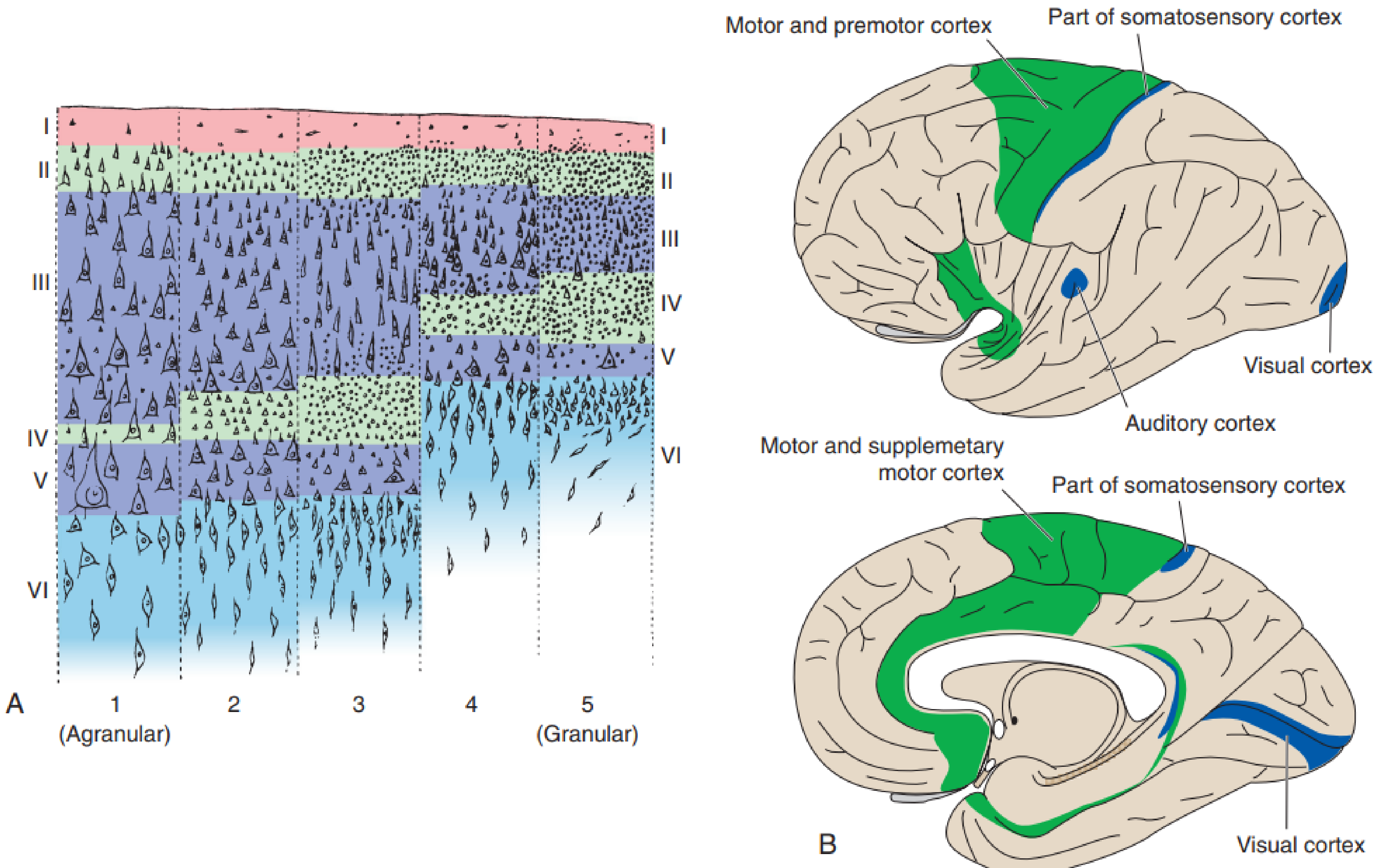
NG: neurogliaform


Pyramidal
cell
Spiny stellate
cell
Layer 1
smooth cel
Basket
cell
Axo-axonic
cell



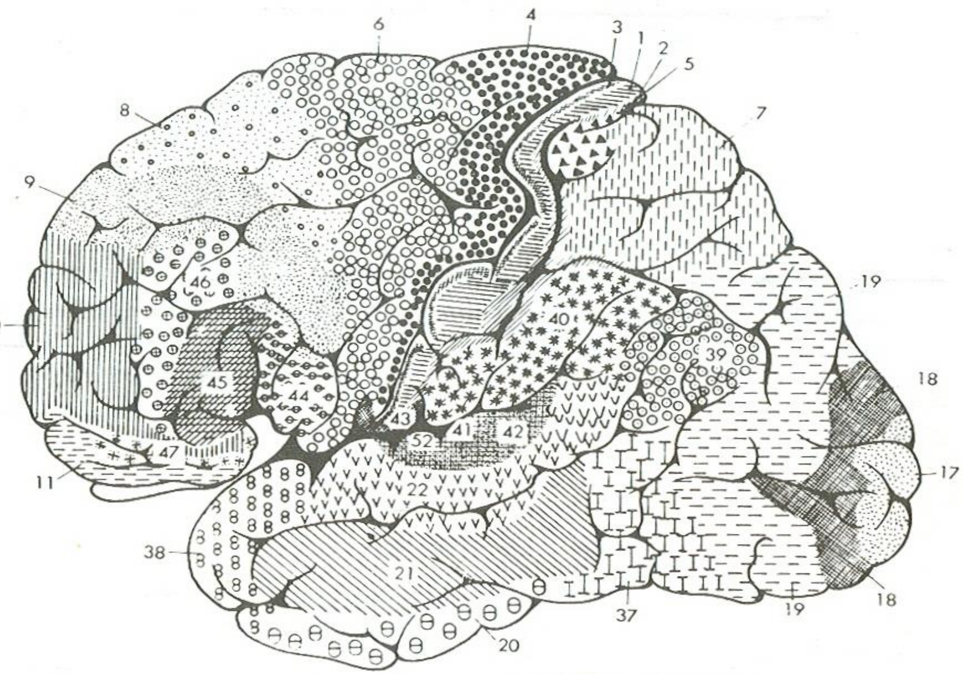
Zonal differences

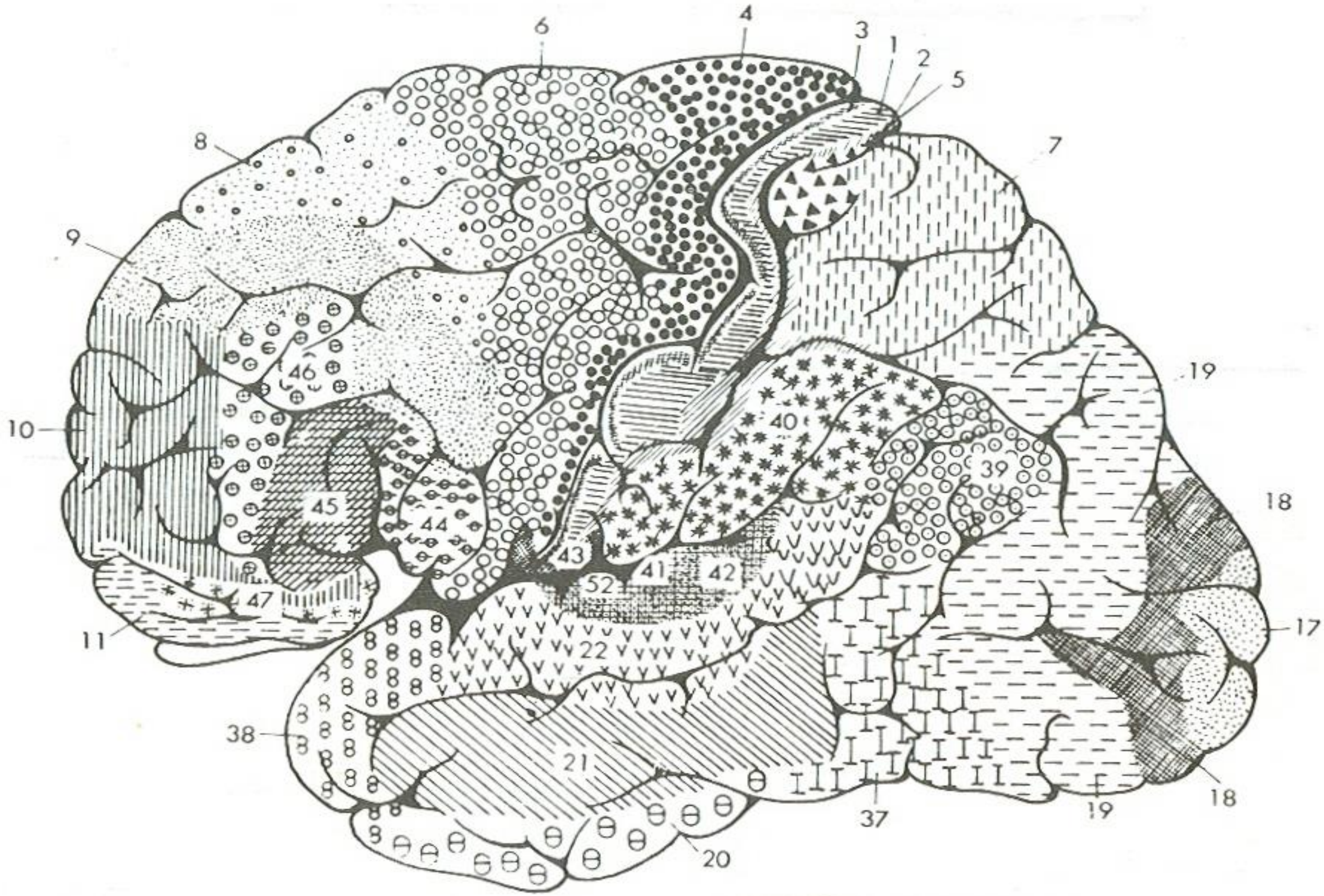
- **Agranular (1):** almost absent granular layers, very little incoming sensory fibers (astriate). Motor areas (M1).
- **Frontal (2):** little developed, yet present, granular layers. Mostly found in the frontal and parietal lobe (non primary motor/sensory areas).
- **Parietal (3)** Predominance of granule cell layers over pyramidal layers, but both are present and developed. Sensory cortices, balance between incoming (sensory) and outgoing (motor / association) fibers.
- **Polar (4):** thin layers of the frontal and occipital poles. Granular predominate over pyramidal. generally thinner than parietal cortices.
- **Granular (5):** almost absent pyramidal layers, layer V almost not distinguishable. Predominance of granule cells. Often also termed striate cortex due to prominent afferent fiber systems (eg. Stria of Gennari in the occipital lobe).

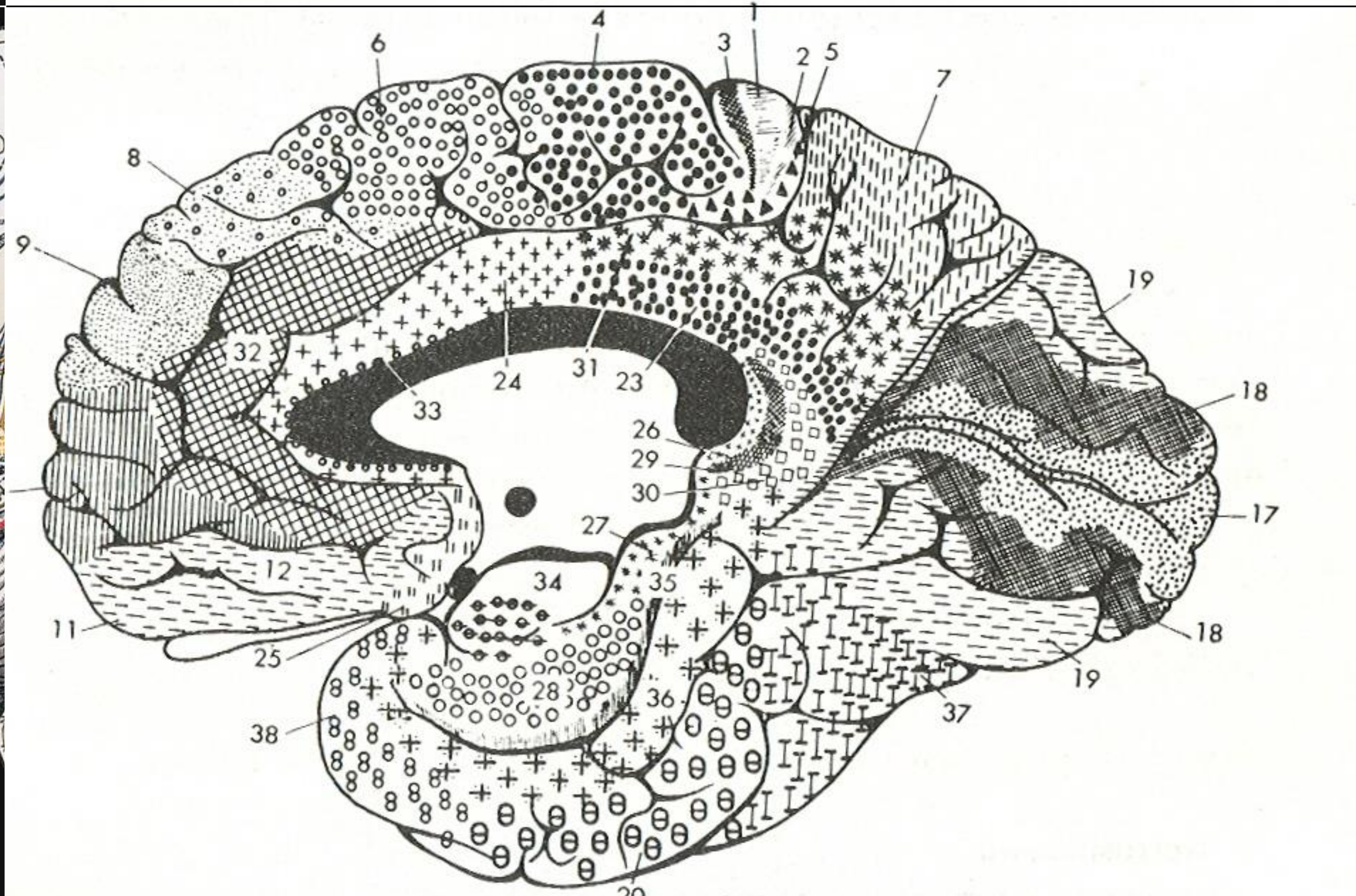

I
II
III
IV
V
VI
I
II
III
IV
V
VI
A
1
(Agranular)
2
3
4
5
(Granular)
Motor and premotor cortex
Part of somatosensory cortex
Visual cortex
Auditory cortex
Motor and supplemetary motor cortex
Part of somatosensory cortex
Visual cortex
B

Corbinus Brodmann (1909)

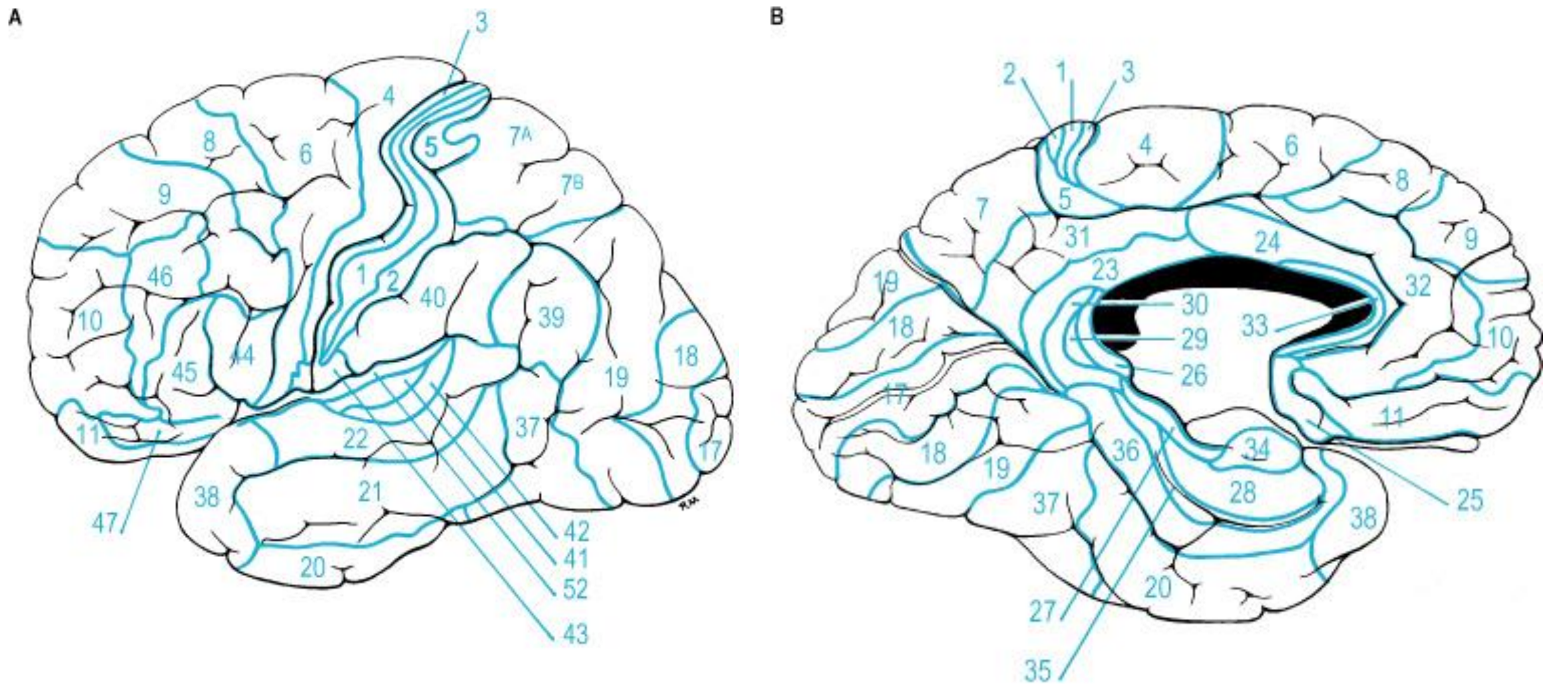
Map of cytoarchitectural areas of the cortex (1-52)




6
4
3
1
2
5
8
7
9
46
19
10
40
39
45
18
44
43
41
42
52
47
11
22
17
38
21
37
19
18
20



4
1
6
3
2
5
7
8
9
19
32
24
31
23
33
18
26
29
30
17
27
12
34
35
11
25
18
19
28
36
37
38
20



Lobe	Number	Location	Other Names
Frontal	4	Precentral gyrus, anterior paracentral lobule	Primary motor area; M1
	6	Superior and middle frontal gyri, precentral gyrus	Premotor area, supplementary motor area
	44, 45	Inferior frontal gyrus (opercular and triangular parts)	Broca's area (on the left)
Parietal	3, 1, 2	Postcentral gyrus, posterior paracentral lobule	Primary somatosensory area; S1
	5, 7	Superior parietal lobule	Somatosensory association area
	39	Inferior parietal lobule	Angular gyrus
	40	Inferior parietal lobule	Supramarginal gyrus
Occipital	17	Banks of calcarine sulcus	Primary visual area; V1
	18, 19	Surrounding 17	Visual association areas; V2, V3, V4, V5
Temporal	41	Transverse temporal gyri	Primary auditory area; A1
	42	Transverse temporal gyri	Auditory association area; A2
	22	Superior temporal gyrus	Auditory association area; posterior portion (on the left) = Wernicke's area

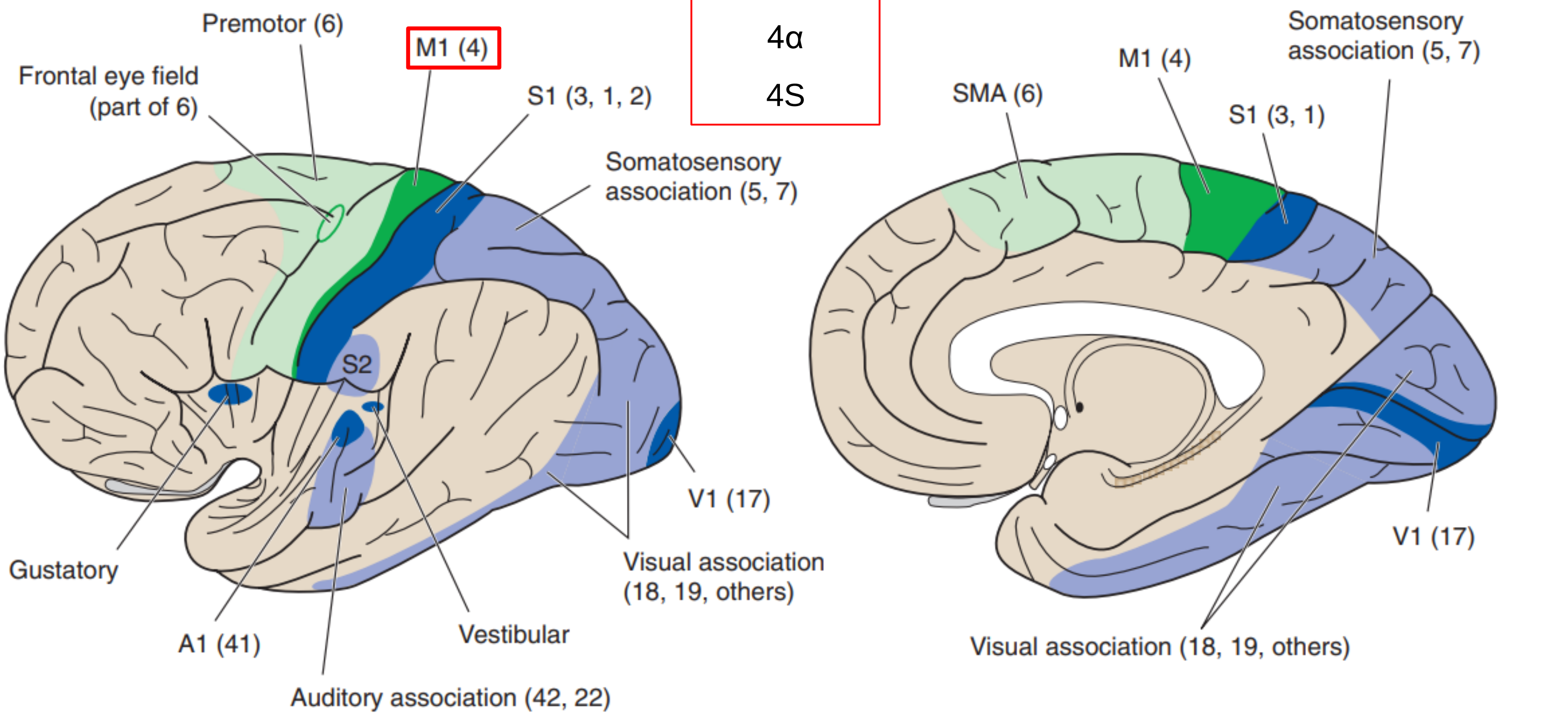
Primary Motor Area (M1)

Divides into:

4γ

4α

4S



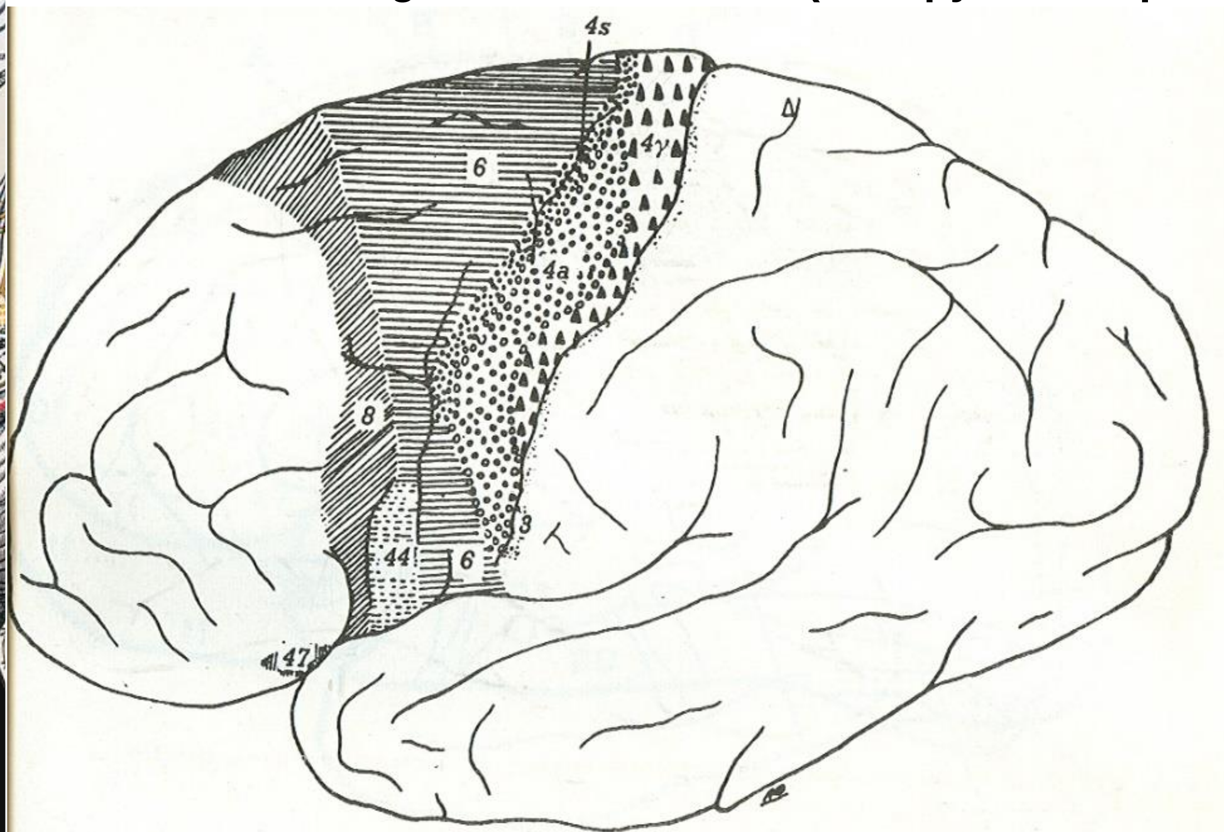
Form descending fibers (pyramidal pathway)

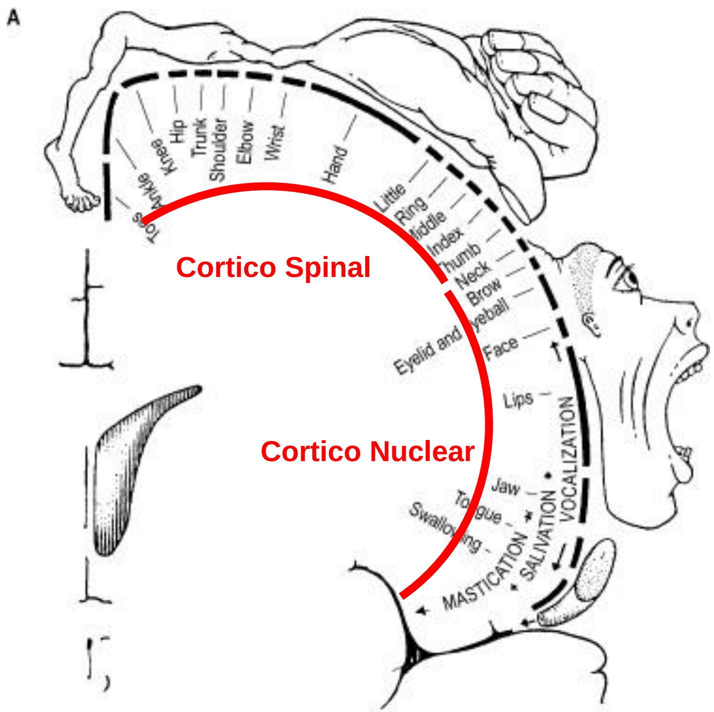
4γ

4α

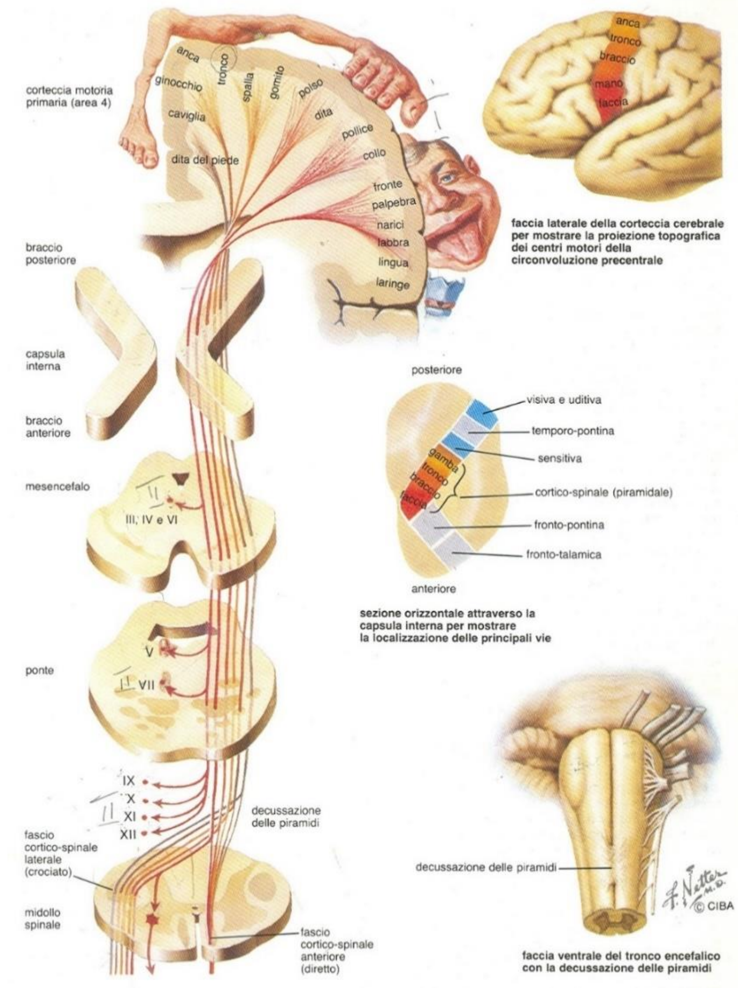
Form descending fibers to striatum (extrapyramidal pathway)

4S




A
Toes
Ankle
Knee
Hip
Trunk
Shoulder
Elbow
Wrist
Hand
Little
Ring
Middle
Index
Thumb
Neck
Brow
Eyelid and eyeball
Face
Lips
Jaw
Tongue
Swallowing
MASTICATION
SALIVATION
VOCALIZATION
Cortico Spinal
Cortico Nuclear

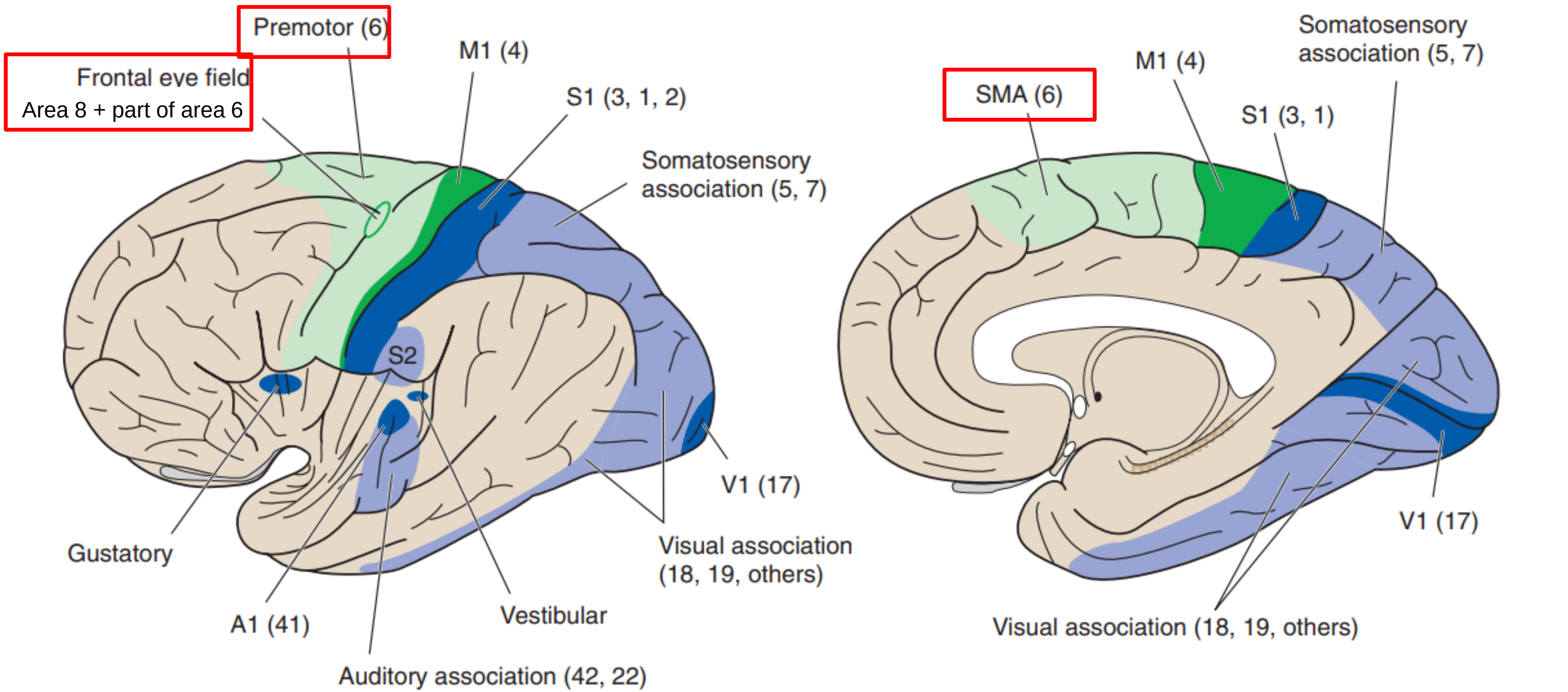

fineart
america



Lesion of M1

Contralateral paralysis

Premotor, Supplementary Motor & Frontal Eye Field (Area 6)



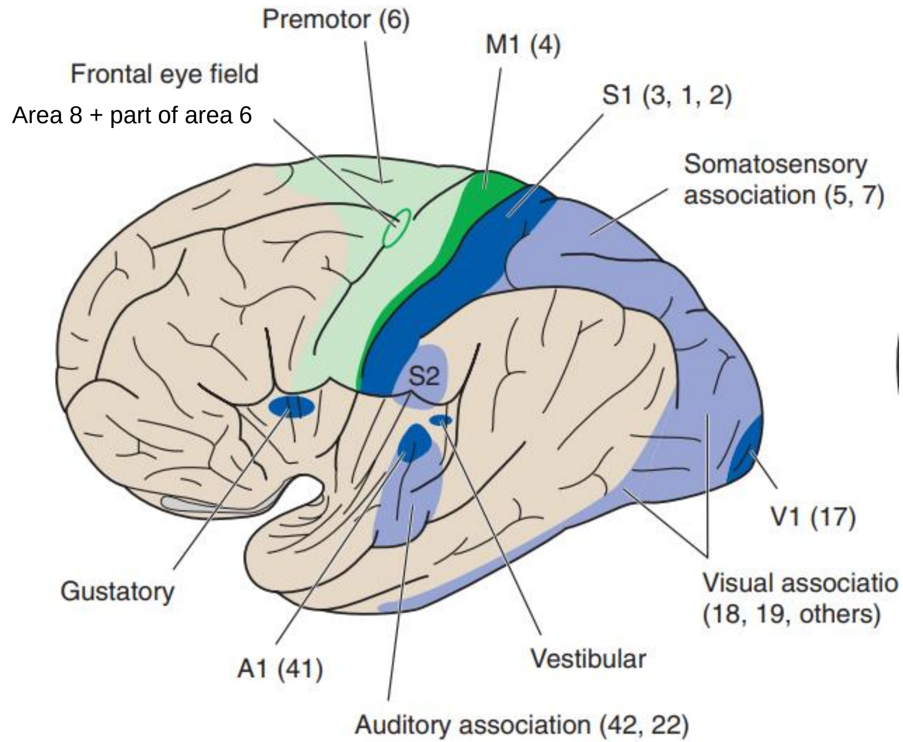
Premotor, Supplementary Motor & Frontal Eye Field (Area 6)

Premotor (lateral area 6):

Anterior to M1 (lateral area 6).

- Connected to the basal ganglia circuits
- Contributes to the pyramidal pathway

Function: motor preparation and movement



Frontal Eye Field (8+6):

- Connected to the oculomotor circuits
- Contributes to the cortico-nuclear pathway

Function: control of conjugated eye movements

<u>LESION: ipsilateral conjugate deviation of the eyes</u>

Premotor, Supplementary Motor & Frontal Eye Field (Area 6)

Supplementary Motor (Medial area 6):

Medial surface of the frontal lobe, anterior to the paracentral lobule.

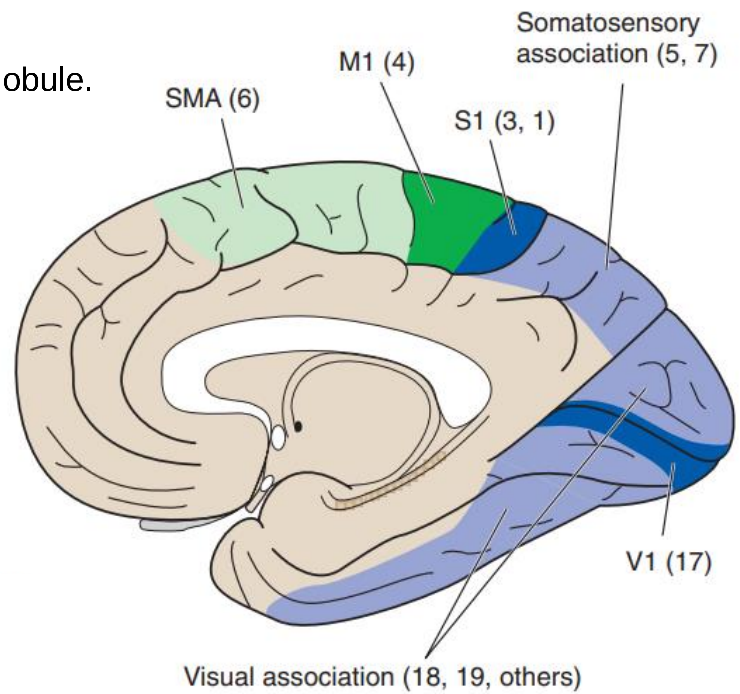
- Contributes to the pyramidal pathway
- Great quantity of connections with the frontal lobe

and motor areas

Function: Motor memory, complex movements

and sequential movements.

<u>LESION: similar to basal ganglia lesions and akinesia</u>

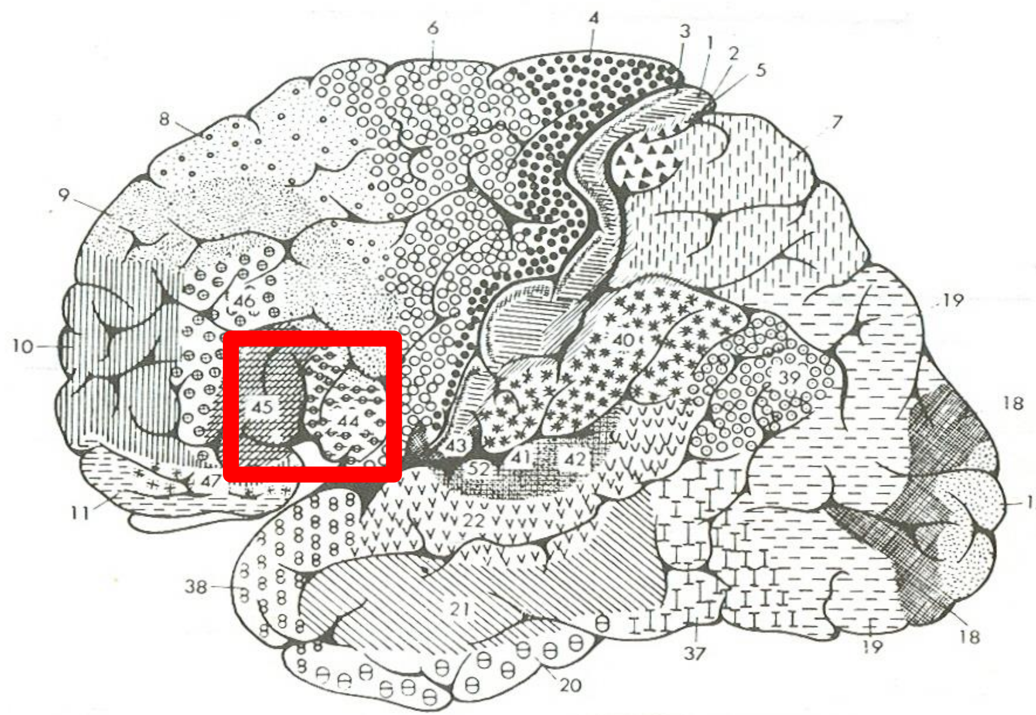


Prefrontal Cortex

Motor areas for speech (Broca’s Area): Area 44-45

- Opercular and triangular part of the inferior frontal gyrus
- In the dominating hemisphere: center for speech production

<u>LESION: non-fluent aphasia</u>



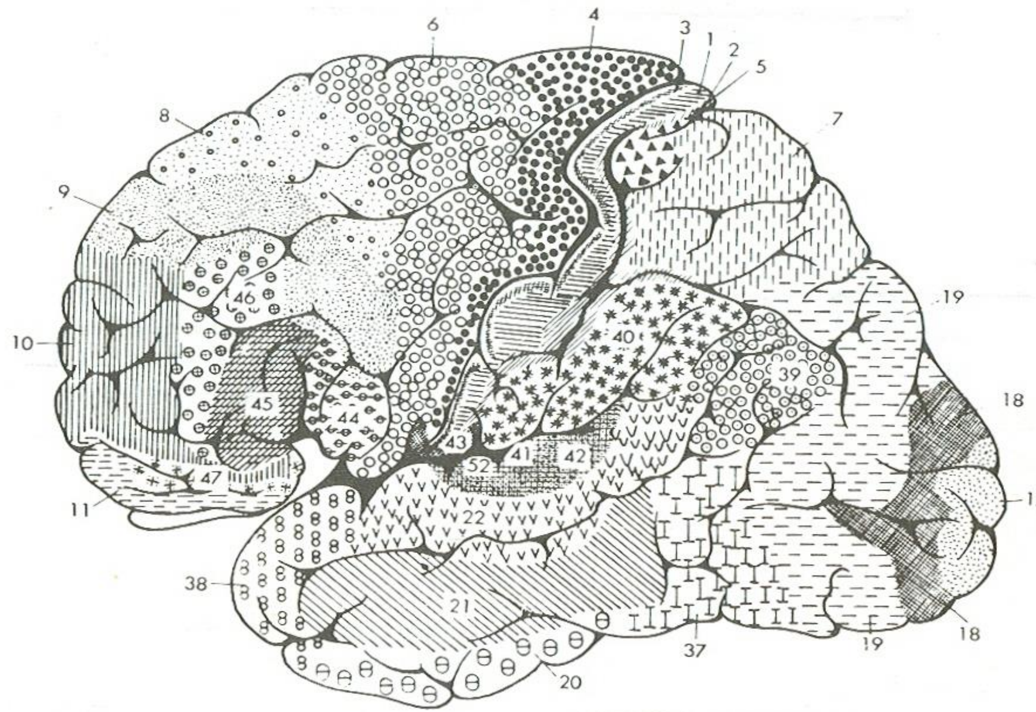
Non-fluent Aphasia (Broca’s Aphasia)

Prefrontal Cortex

Areas 9-10 (DL-PFC)

Areas 11 (orbitofrontal cortex)

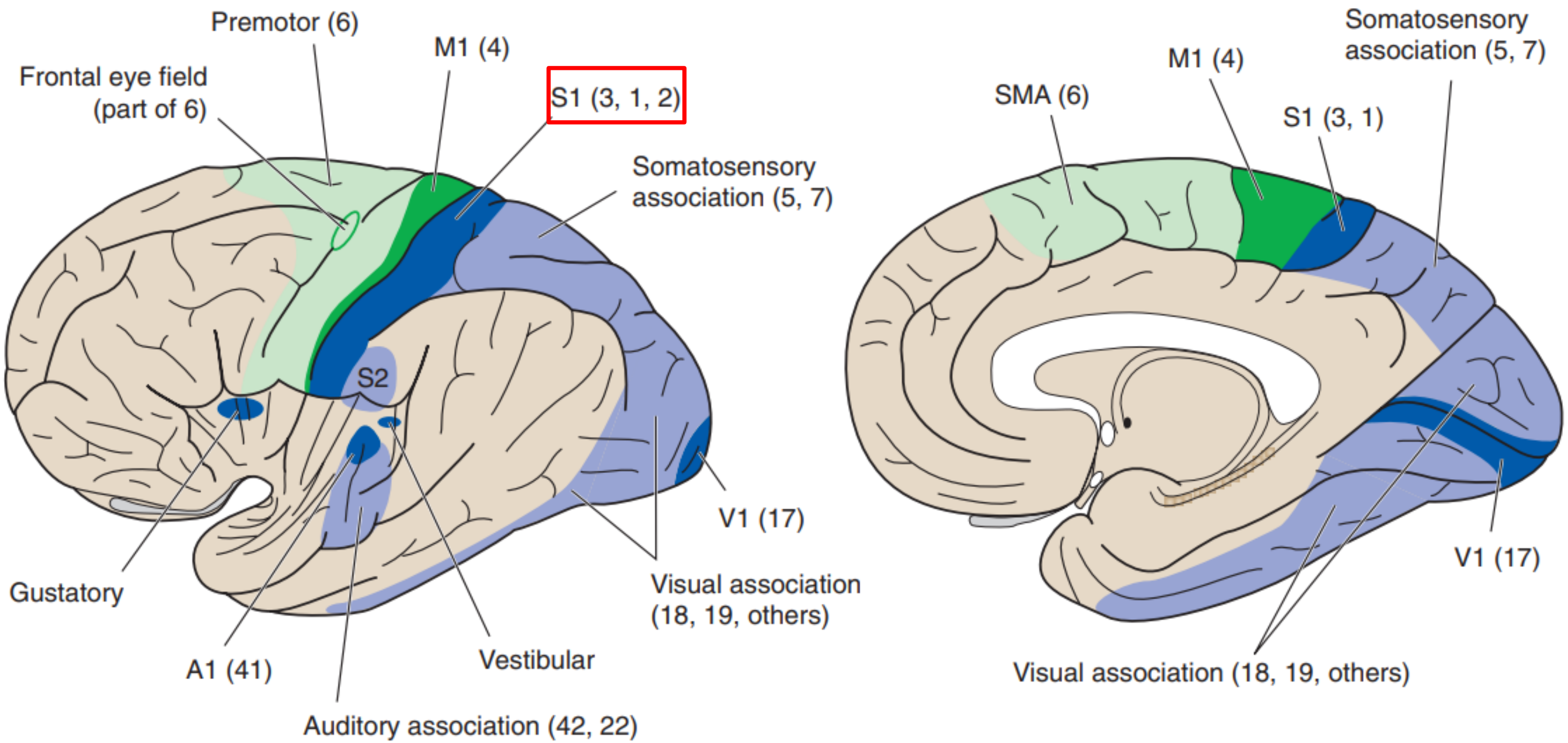
LESION: dysexecutive syndromes, lack of inhibition, complex cognitive disturbances



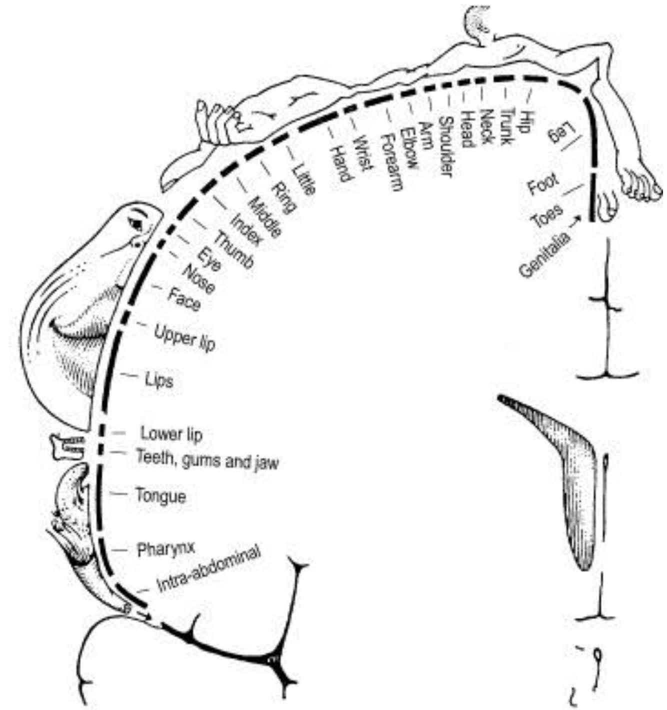
LESION: dysexecutive syndromes, lack of inhibition, complex cognitive disturbances

Case of Phineas Gage

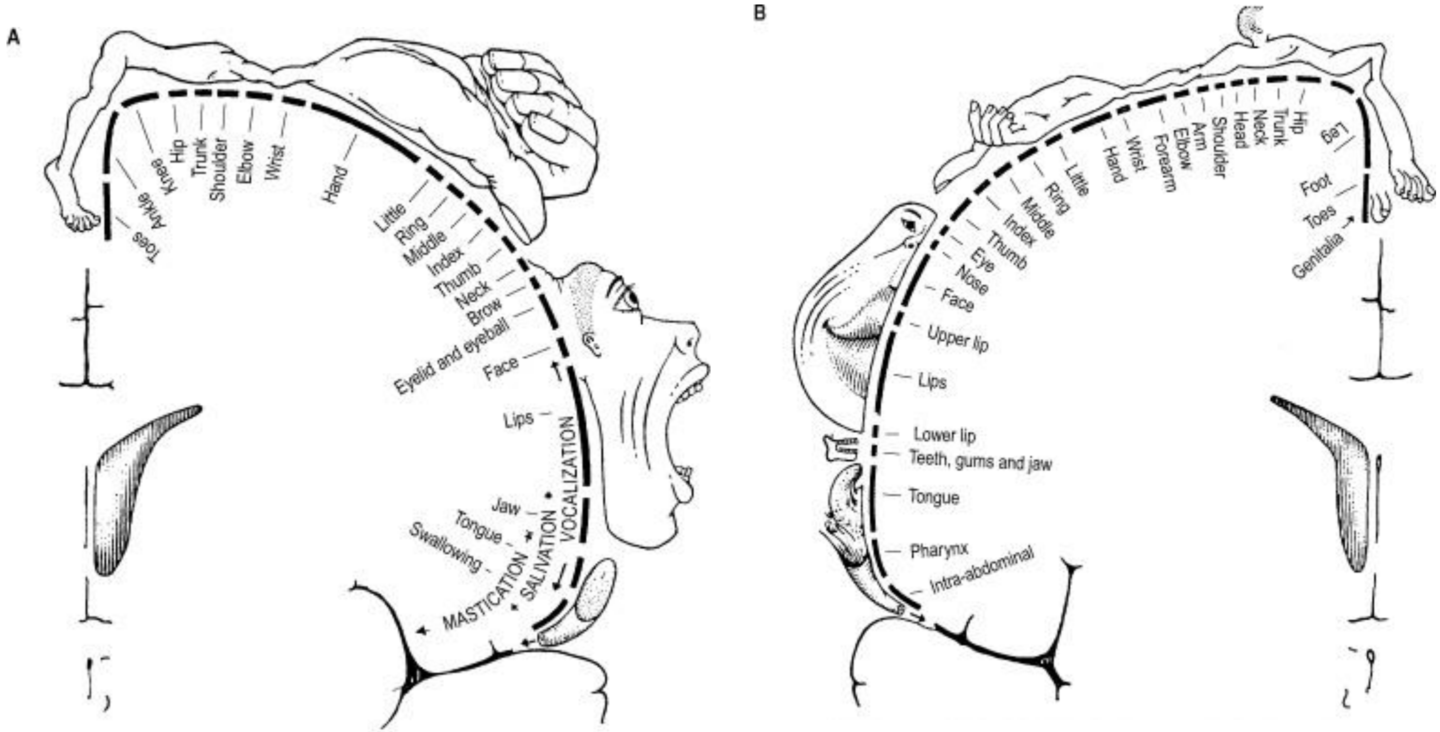
Somatosensory Area (S1)



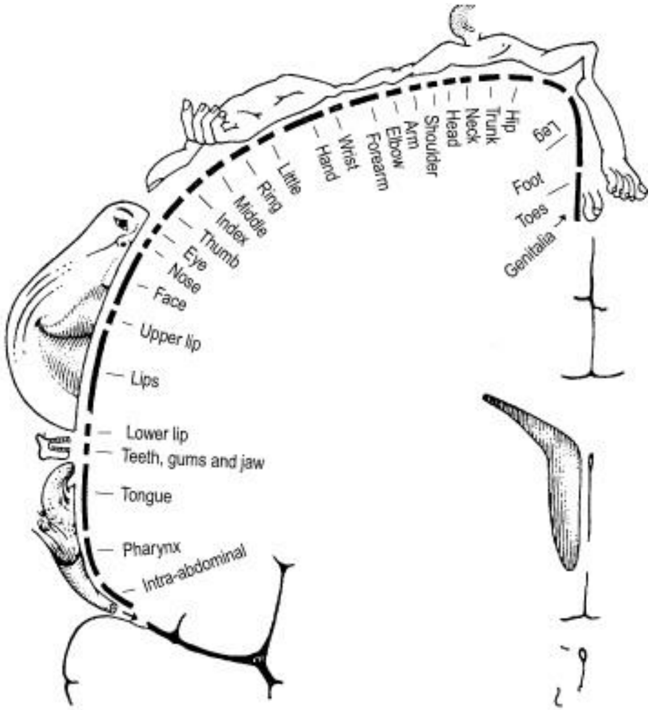
B

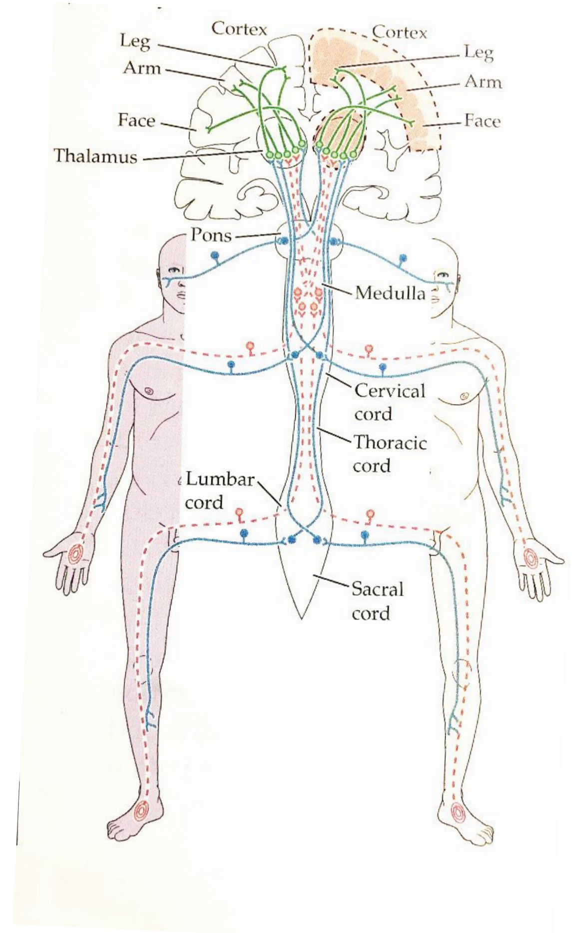


Hip
Trunk
Neck
Head
Shoulder
Arm
Elbow
Forearm
Wrist
Hand
Little
Ring
Middle
Index
Thumb
Eye
Nose
Face
Upper lip
Lips
Lower lip
Teeth, gums and jaw
Tongue
Pharynx
Intra-abdominal
Leg
Foot
Toes
Genitalia


A
Toes
Ankle
Knee
Hip
Trunk
Shoulder
Elbow
Wrist
Hand
Little
Ring
Middle
Index
Thumb
Neck
Brow
Eyelid and eyeball
Face
Lips
VOCALIZATION
Jaw
Tongue
Swallowing
SALIVATION
MASTICATION
B
Hip
Trunk
Neck
Head
Shoulder
Arm
Elbow
Forearm
Wrist
Hand
Little
Ring
Middle
Index
Thumb
Eye
Nose
Face
Upper lip
Lips
Lower lip
Teeth, gums and jaw
Tongue
Pharynx
Intra-abdominal
Leg
Foot
Toes
Genitalia

B

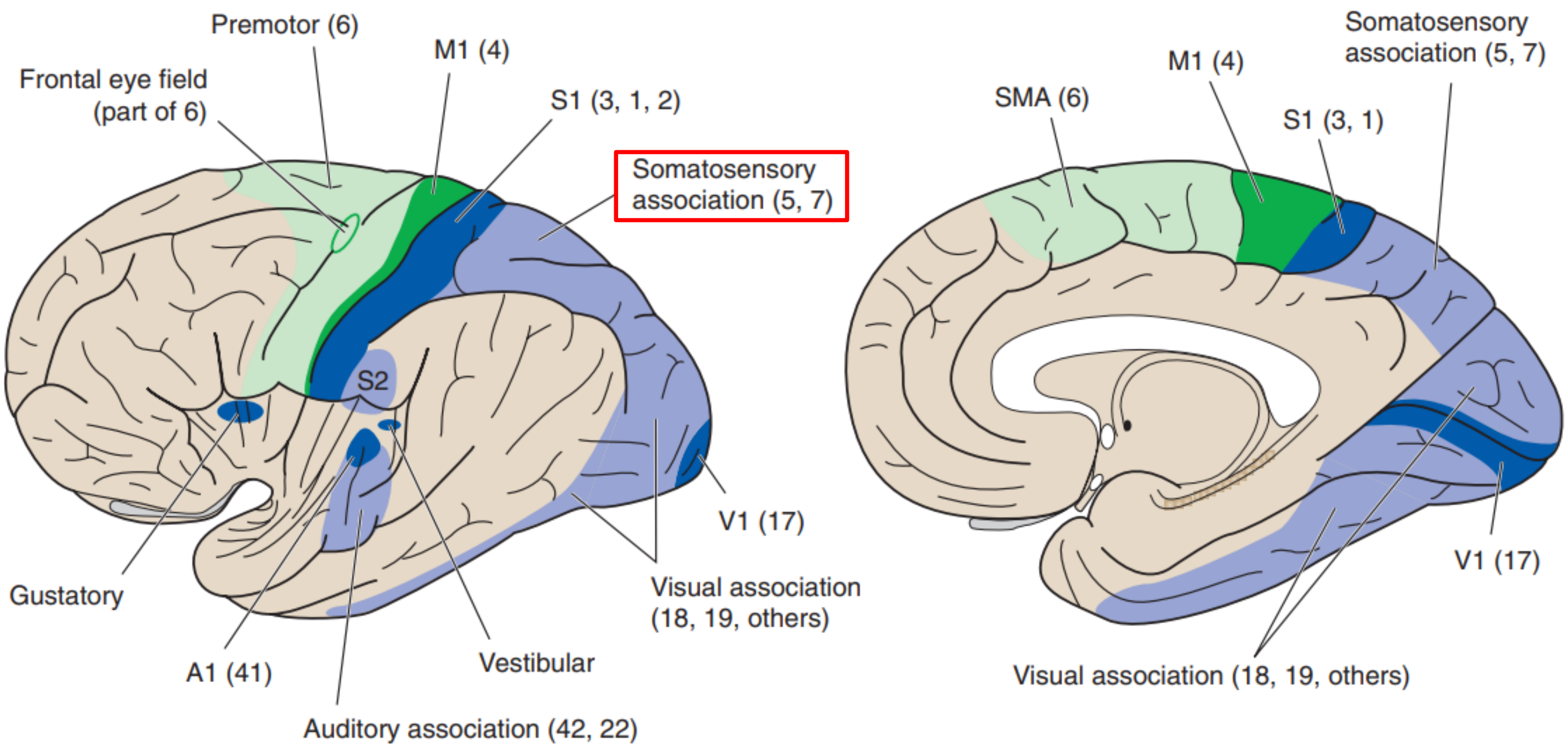

Leg
Hip
Trunk
Neck
Head
Shoulder
Arm
Elbow
Forearm
Wrist
Hand
Little
Ring
Middle
Index
Thumb
Eye
Nose
Face
Upper lip
Lips
Lower lip
Teeth, gums and jaw
Tongue
Pharynx
Intra-abdominal
Foot
Toes
Genitalia


Cortex
Cortex
Leg
Arm
Face
Leg
Arm
Face
Thalamus
Pons
Medulla
Cervical cord
Thoracic cord
Lumbar cord
Sacral cord

Associative somatosensory areas

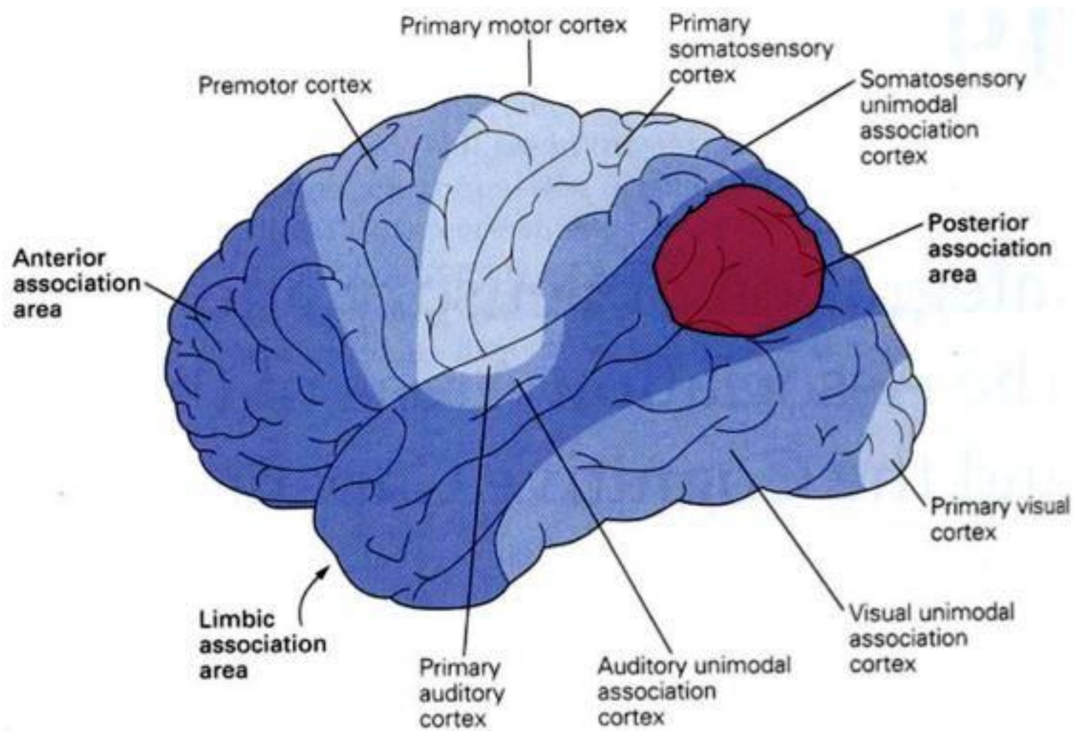
- Superior parietal lobule (cortex) – Areas 5-7
- Inferior parietal lobule (cortex) – Areas 49-40

Functionally related to **stereognosis**



Lesion of associative parietal areas (left hemisphere or dominant hemisphere)

- Inferior parietal lobule (cortex) – Areas 49-40



Gerstmann Syndrome

- Dysgraphia / Agraphia
- Dyscalculia / Acalculia
- Left-right disorientation
- Finger Anomia

Lesion of associative parietal areas (right hemisphere)

- Superior parietal lobule (cortex) – Areas 5-7

Neglect

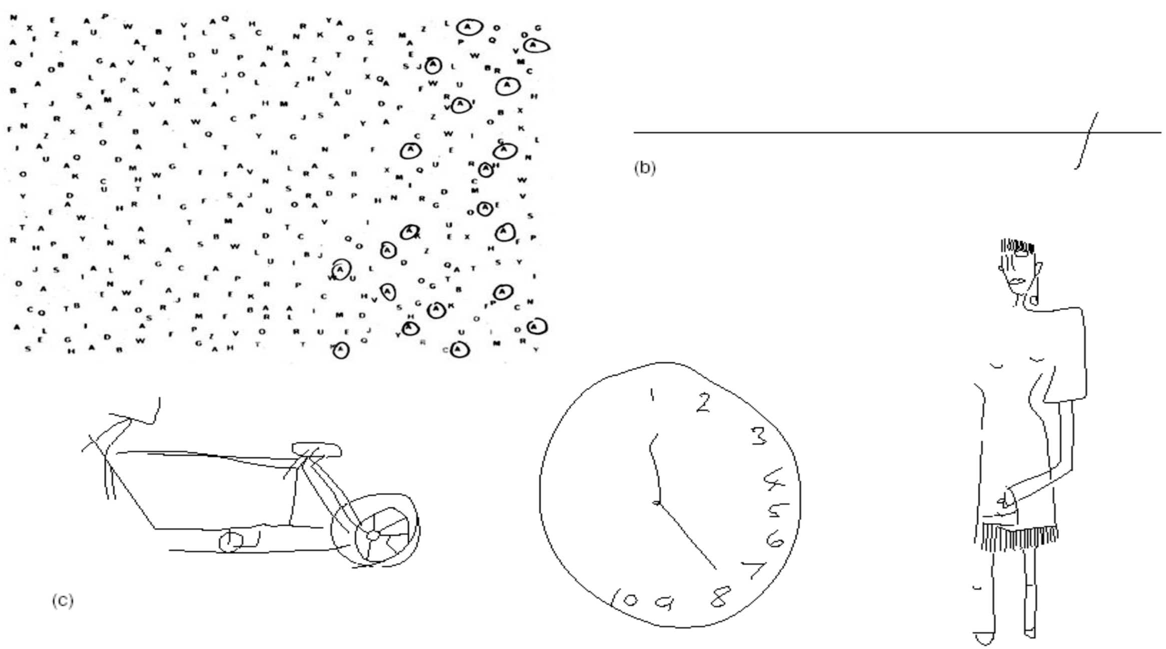
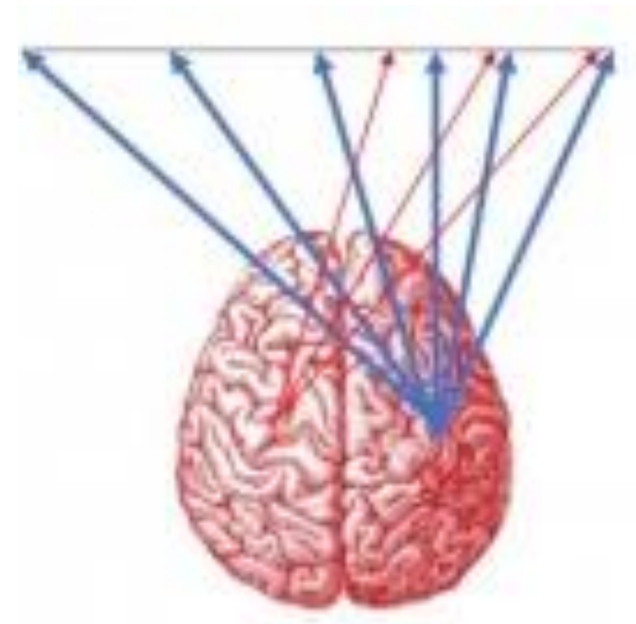


Figure 1. Examples of left-sided neglect after damage to the right hemisphere of the brain, in clinical paper-and-pencil tests. (a) Cancelation; (b) line bisection; (c) drawings of bicycle, clock and woman.



Neglect

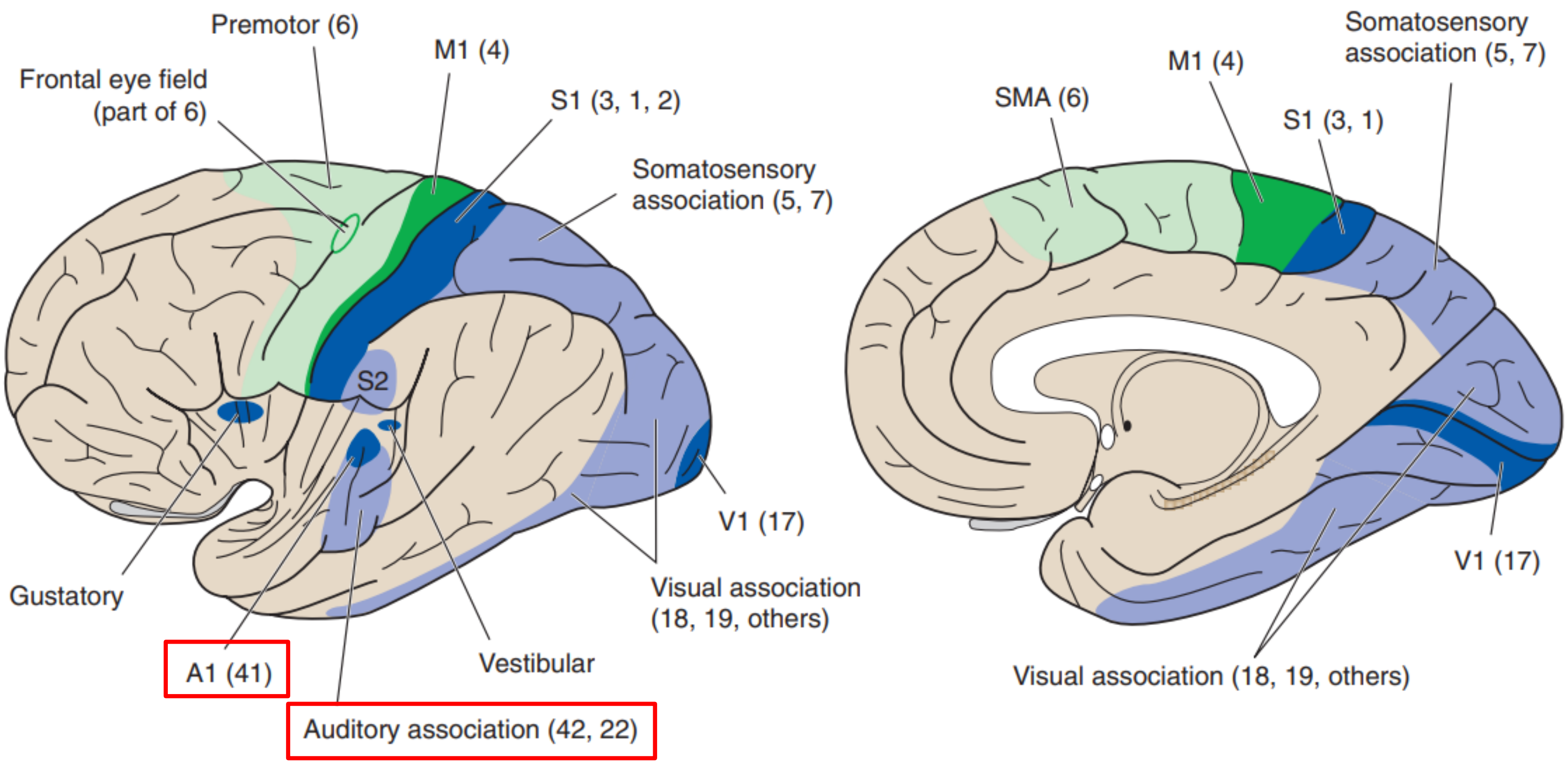
- Most often, limbic and emotional circuits are intact

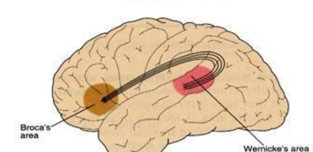
Primary and associative auditory areas

- Heschl's Gyri (cortex) – Area 41 (A1)
- Superior temporal and inferior parietal cortex – Areas 42-22

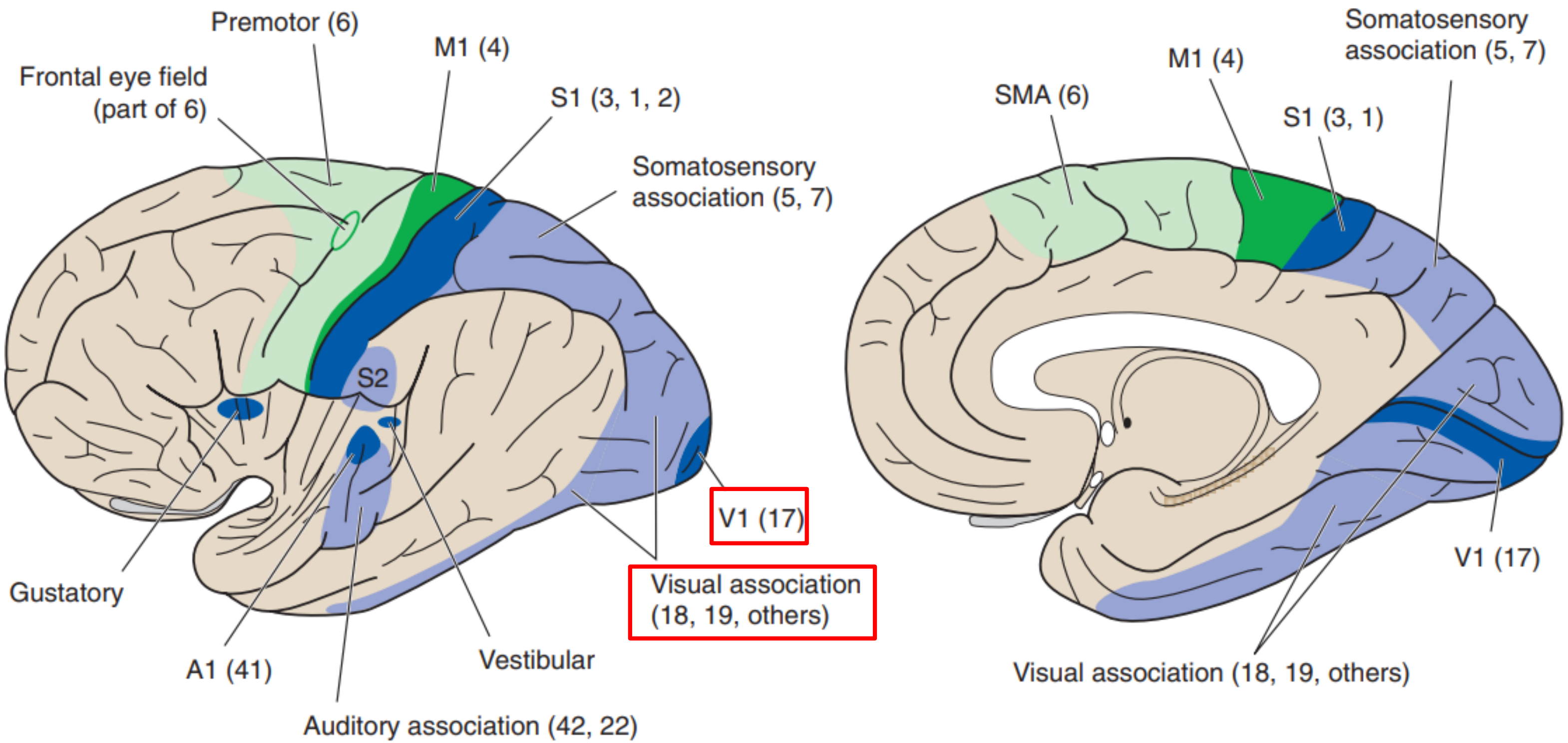
Lesion

- Cortical Deafness
- Fluent Aphasia
  Wernicke's aphasia



Aphasia Type	Fluency	Repetition	Comprehension	Typical Lesion Location*
Broca's	↓	↓	±	
Transcortical motor	↓	±	±	
Global	↓	↓	↓	
Wernicke's	±	↓	↓	
Transcortical sensory	±	±	↓	
Conduction	±	↓	±	

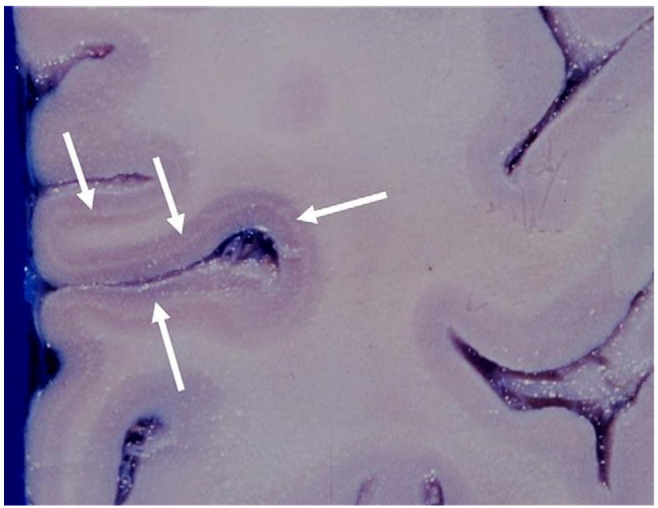
Primary (V1) and associative visual areas(V2-3)



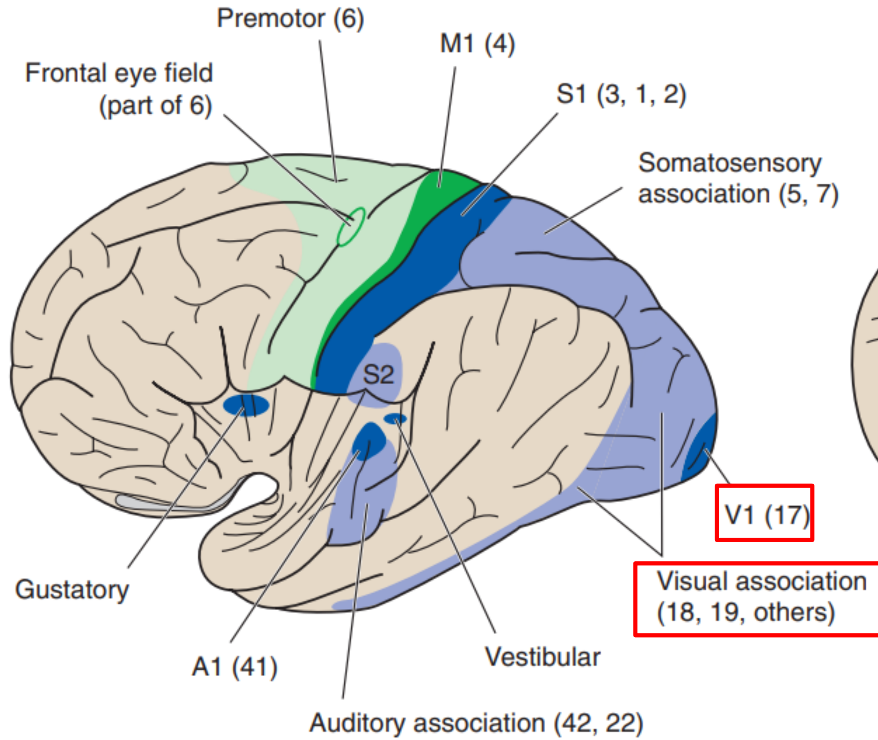
Primary (V1) and associative visual areas(V2-3)

V1 – Area 17

Primary visual cortex



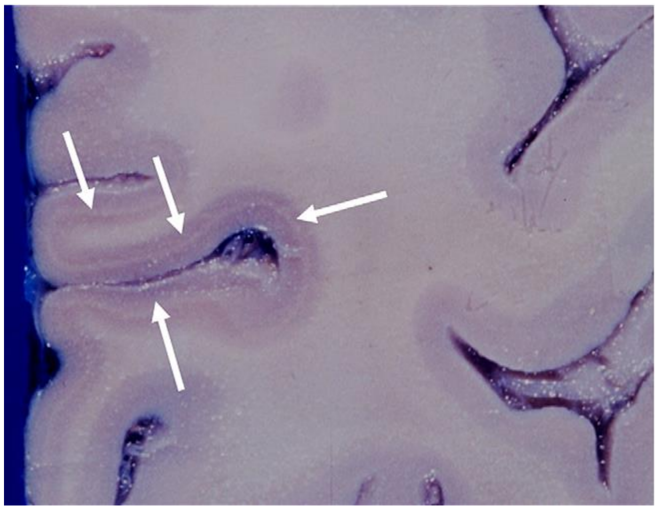
LESION: Anton's Syndrome (Cortical Blindness)

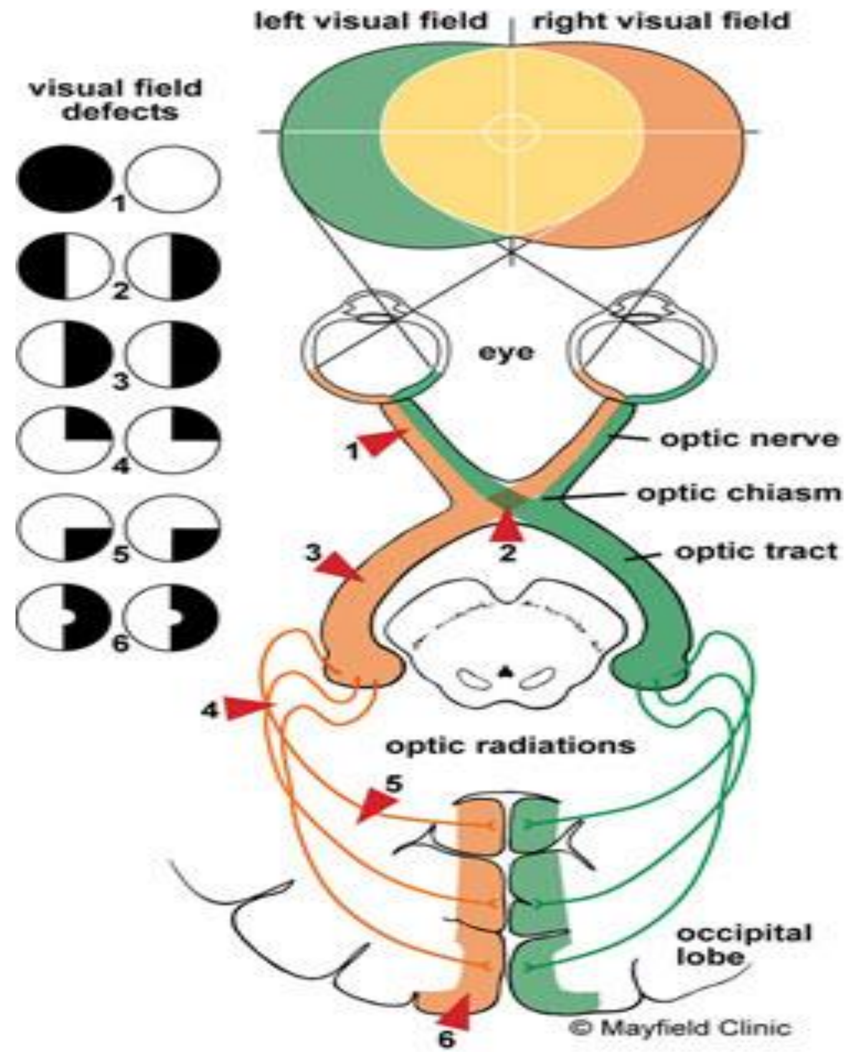


Primary visual areas (V1)

V1 – Area 17

Primary visual cortex





LESION: Anton's Syndrome (Cortical Blindness)

Primary (V1) and associative visual areas(V2-3)

V2-3 – Area 18-19

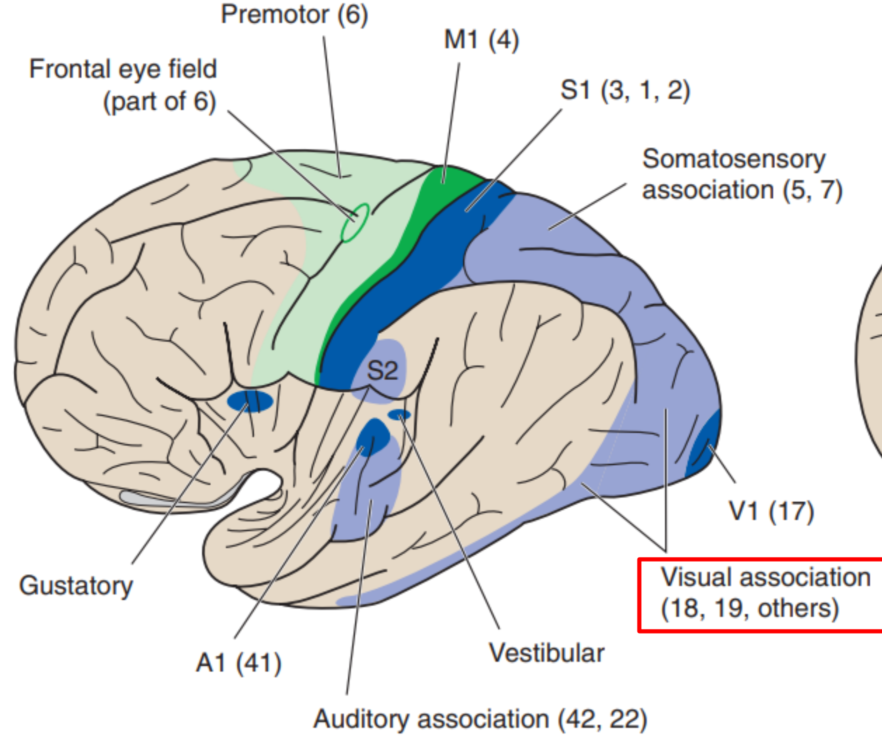
Associative visual cortices

- *Occipito-parietal circuit → Where?*

LESION: Optic Ataxia, Balint Holmes Syndrome

- *Occipito-temporal circuit → What?*

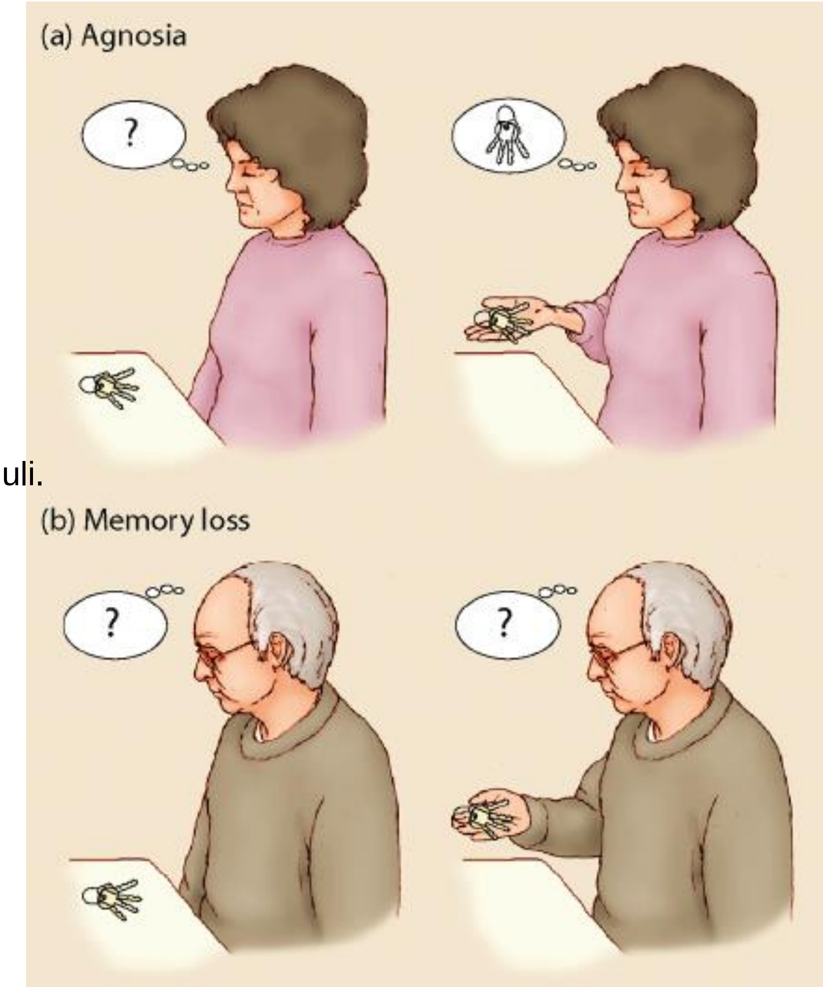
LESION: Agnosia, Prosopoagnosia

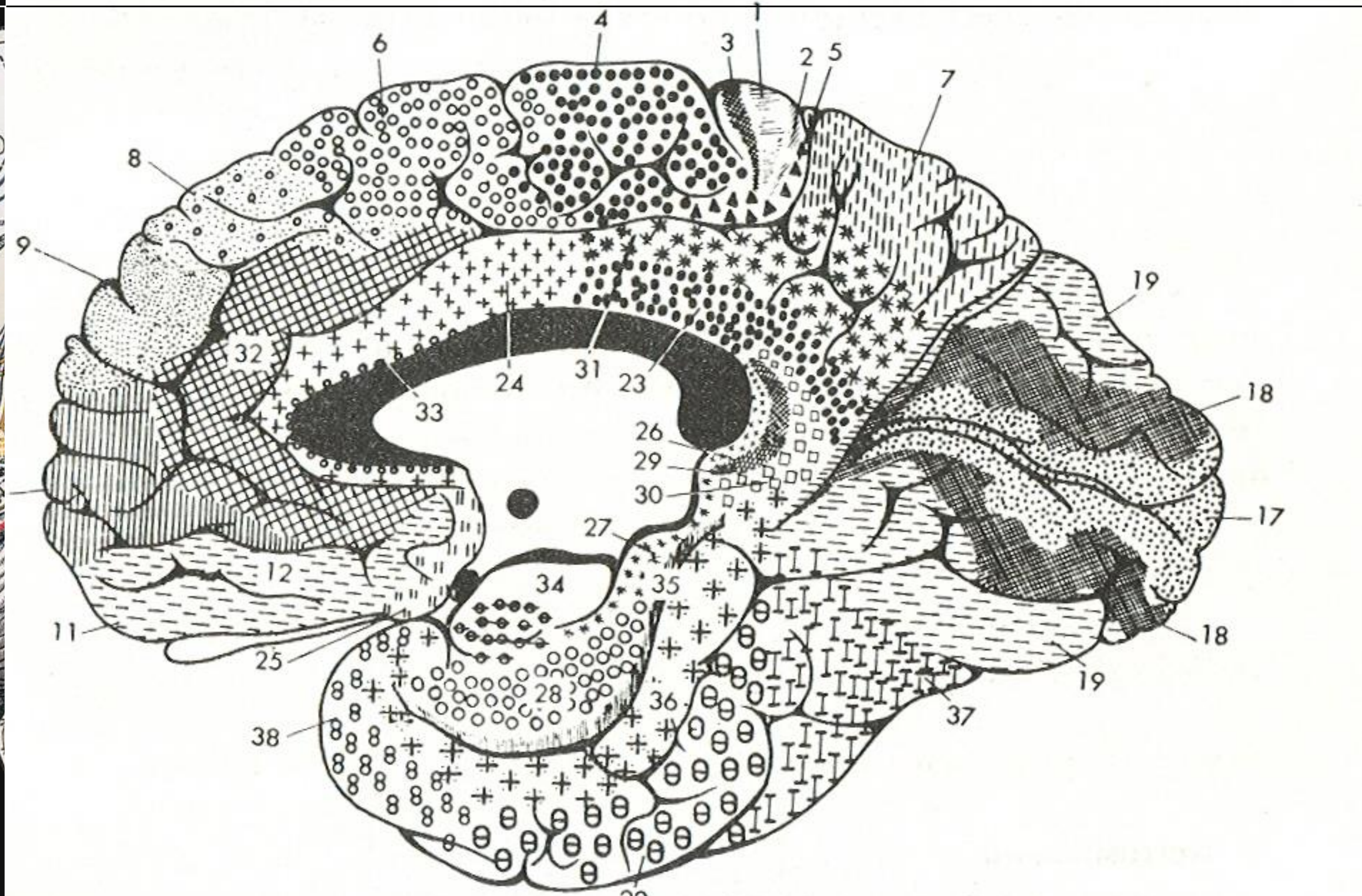


Agnosia

Deficit in the post-sensorial elaboration of stimuli.

(which are modality specific!)




4
1
6
3
2
5
7
8
9
19
32
24
31
23
33
18
26
29
30
17
27
12
34
35
11
25
18
19
28
36
37
38
20

Limbic System

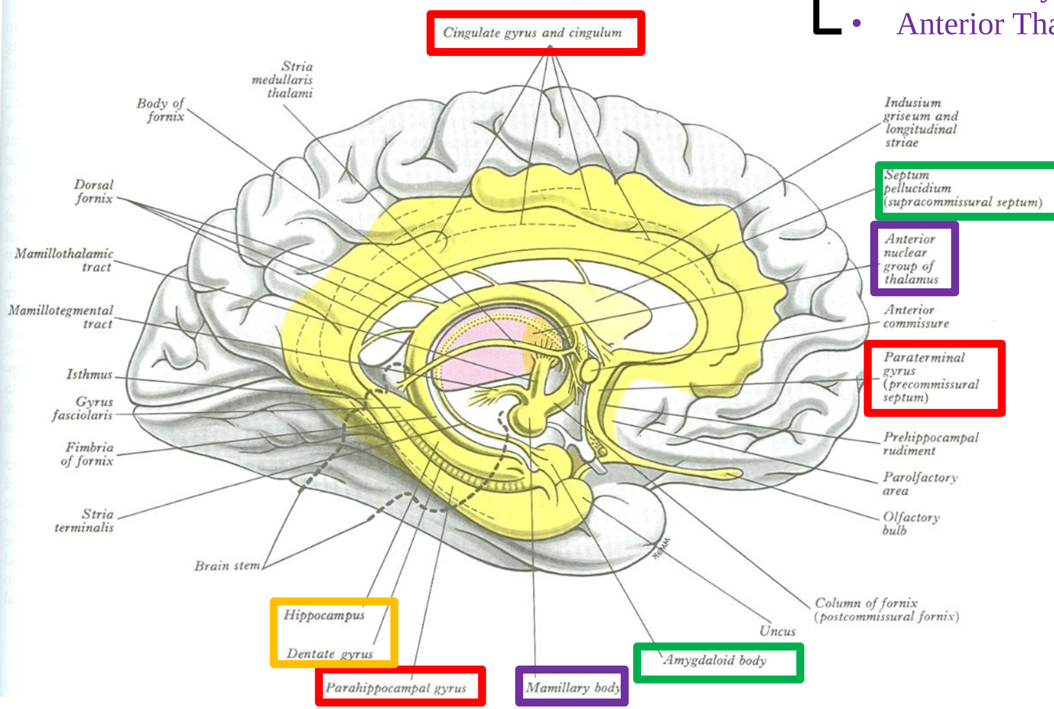
- Telencephalic structures: (Limbic Lobe)
  - Cingulate cortex
  - Subcallosal Cortex
  - Parahippocampal cortex
  - Hippocampal formation
  - Amygdala
  - Septal Nuclei
  - Nucleus Accumbens
- Diencephalic structures:
  - Mammillary Bodies
  - Anterior Thalamic nuclei

Neocortex

Archicortex

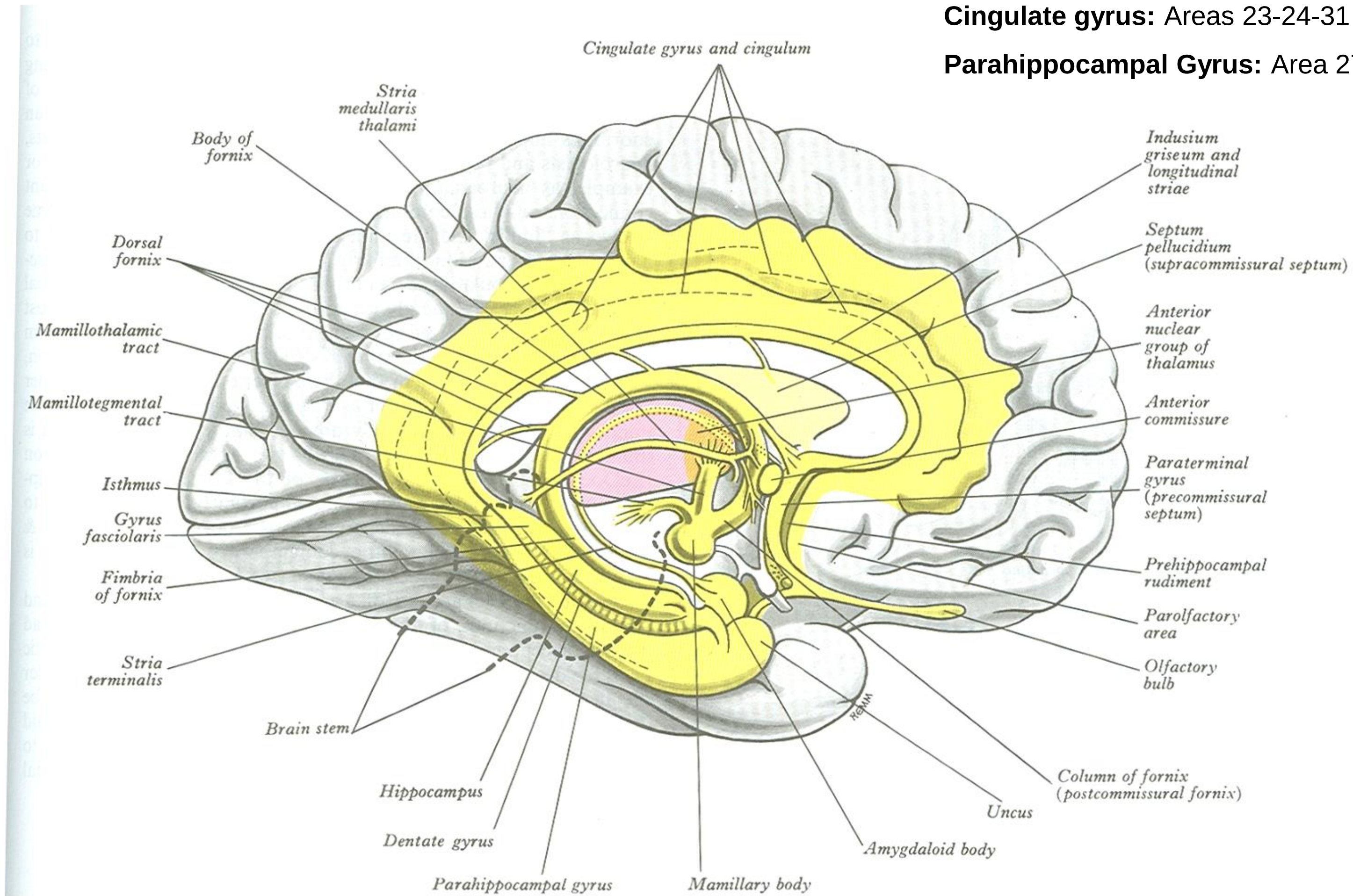
Deep nuclei (telencephalon)

Deep nuclei (diencephalon)

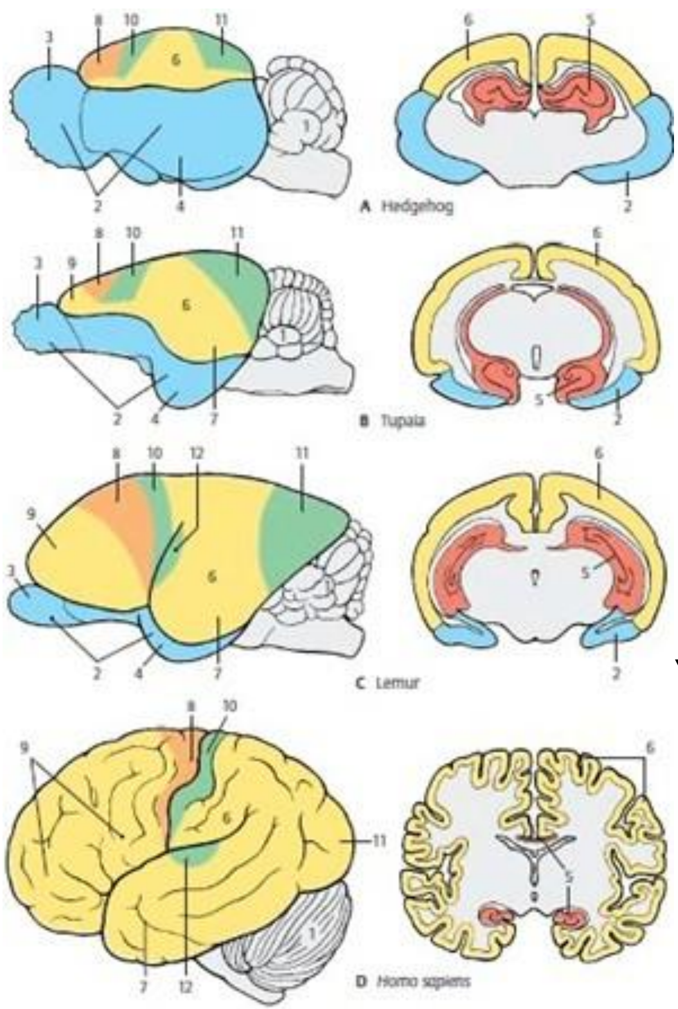


Cingulate gyrus: Areas 23-24-31

Parahippocampal Gyrus: Area 27-28-35

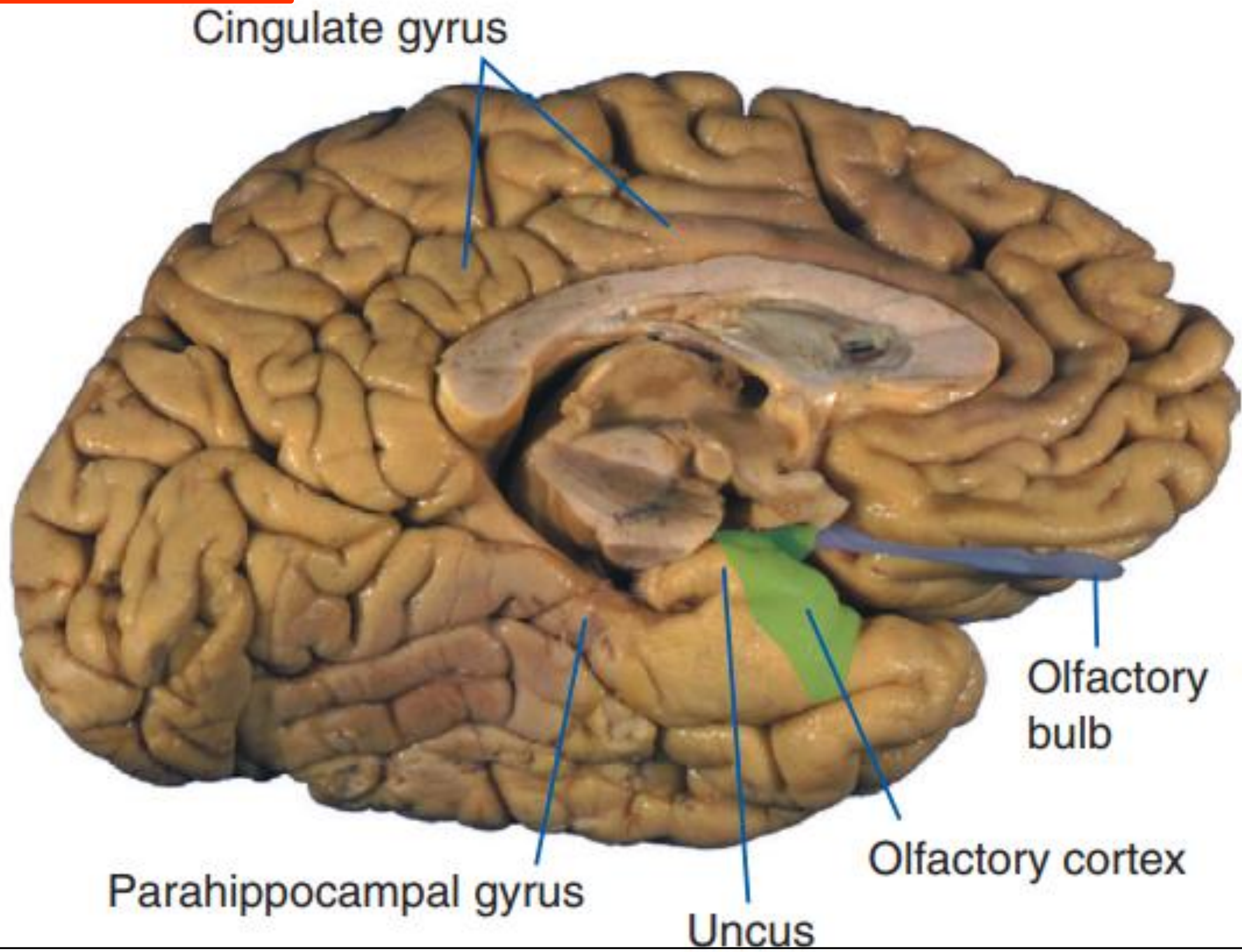


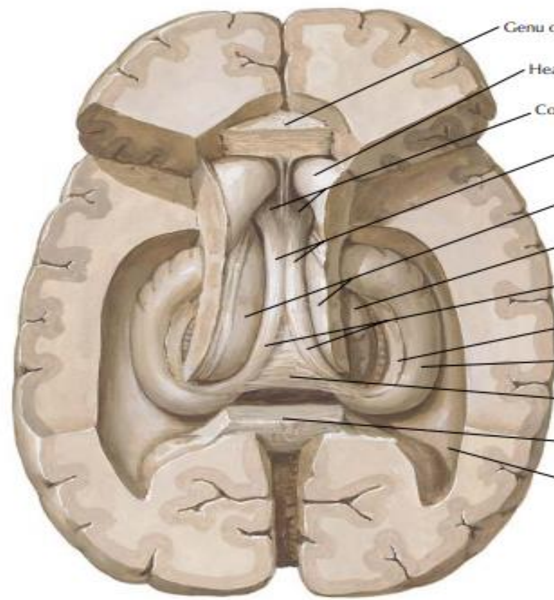
Phylogenesis of the Cerebral Cortex



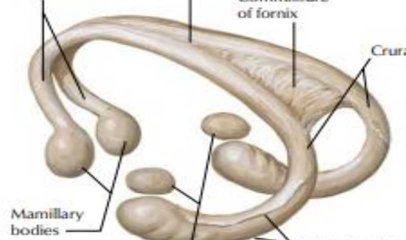
- **Allocortex:** also known as archicortex / archipallium. Most ancient part of the cortex. 3 Layers. Found in the hippocampal formation.
- **Mesocortex:** also known as paleocortex / paleopallium. 4-5 layers; represents an intermediate stage between the allocortex and the isocortex.
- **Isocortex:** also known as neocortex or neopallium. Most recent part of the cortex. 6 Layers. Makes up most of the cerebral cortex.

Non-neocortical areas

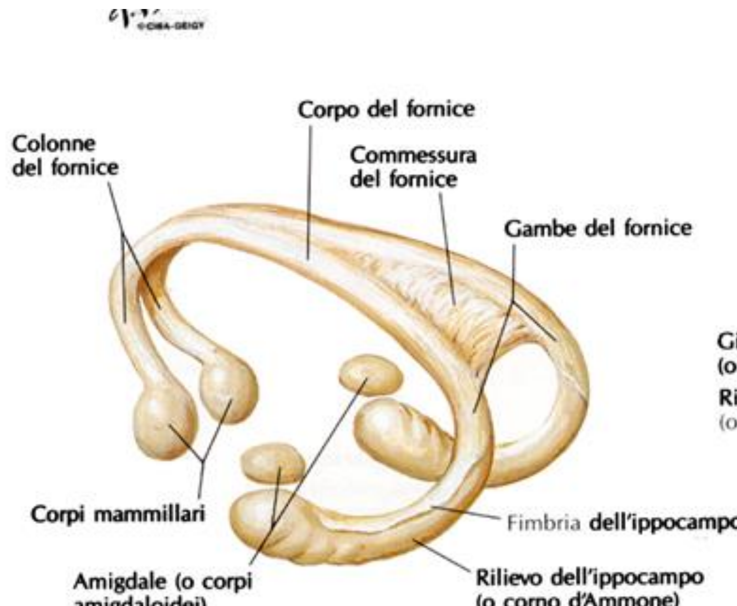




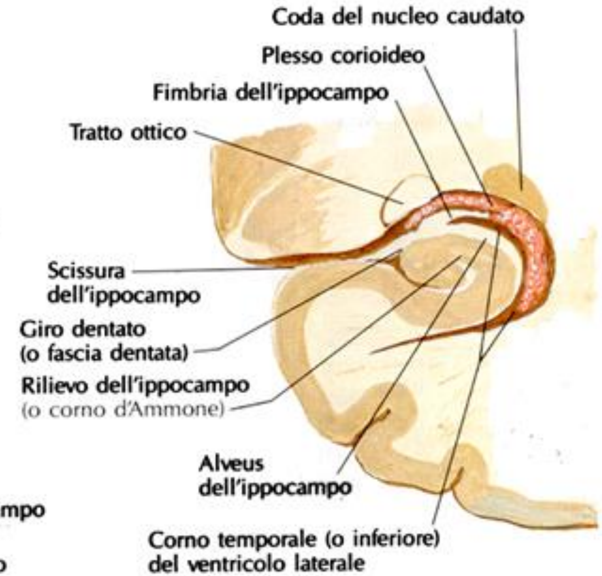
Genu of corpus callosum
Head of caudate nucleus
Columns of fornix
Body of fornix
Thalamus
Uncus
Crura of fornix
Fimbria of hippocampus
Hippocampus
Commissure of fornix
Splenium of corpus callosum
Lateral ventricle



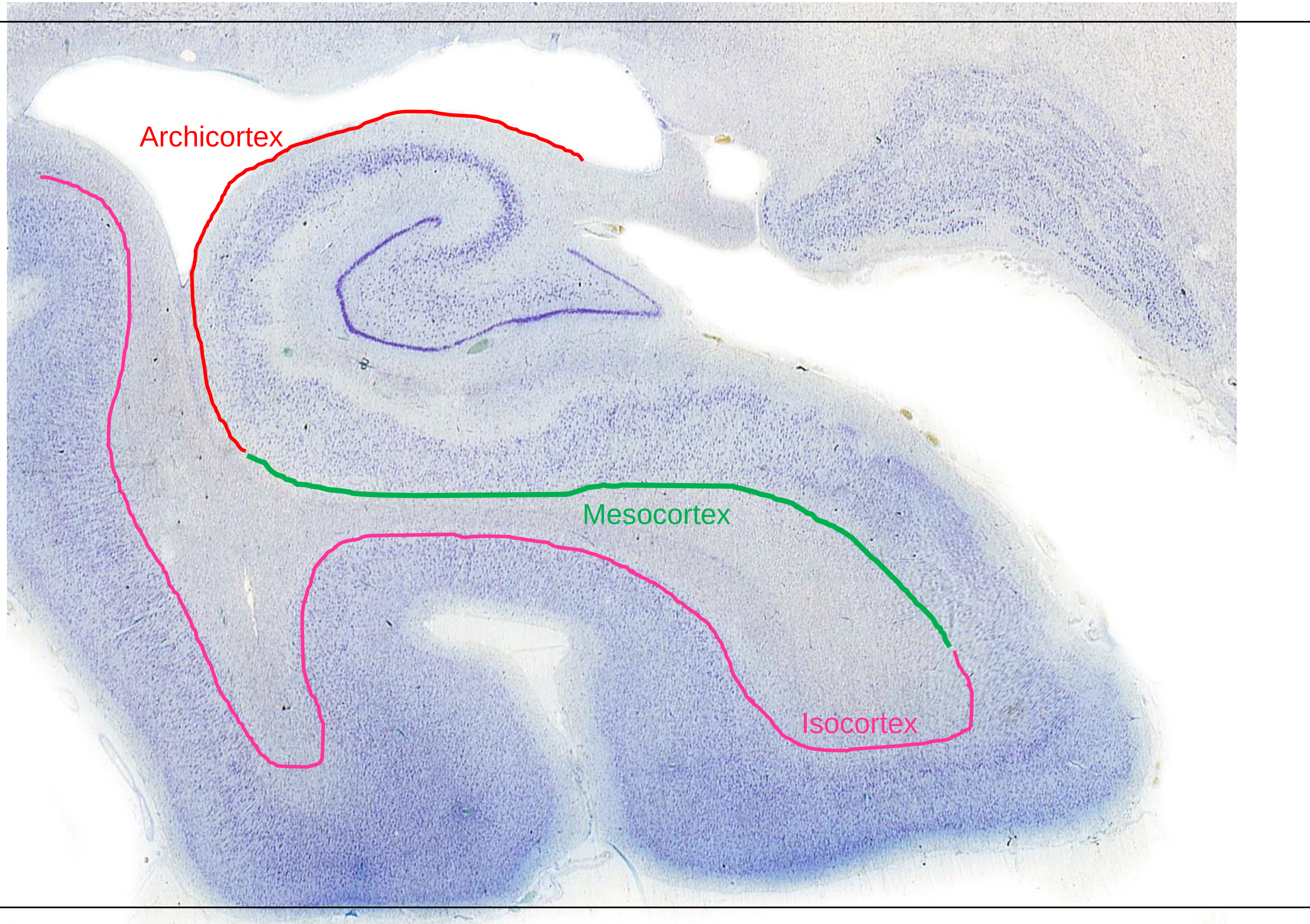
Body of fornix
Columns
of fornix
Commissure
of fornix
Crura of fornix
Mamillary
bodies
Amygdaloid bodies
Hippocampus
with fimbria

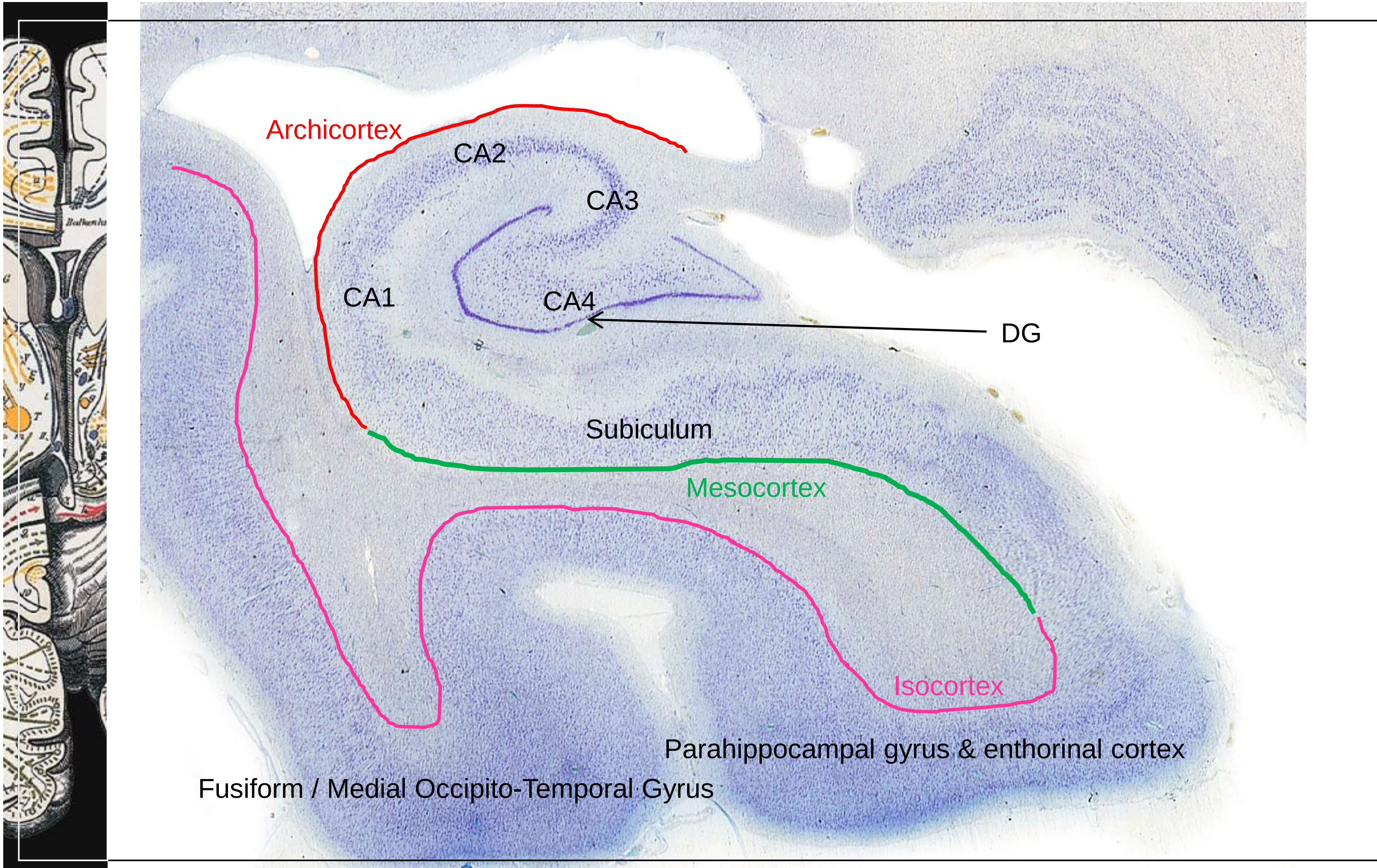


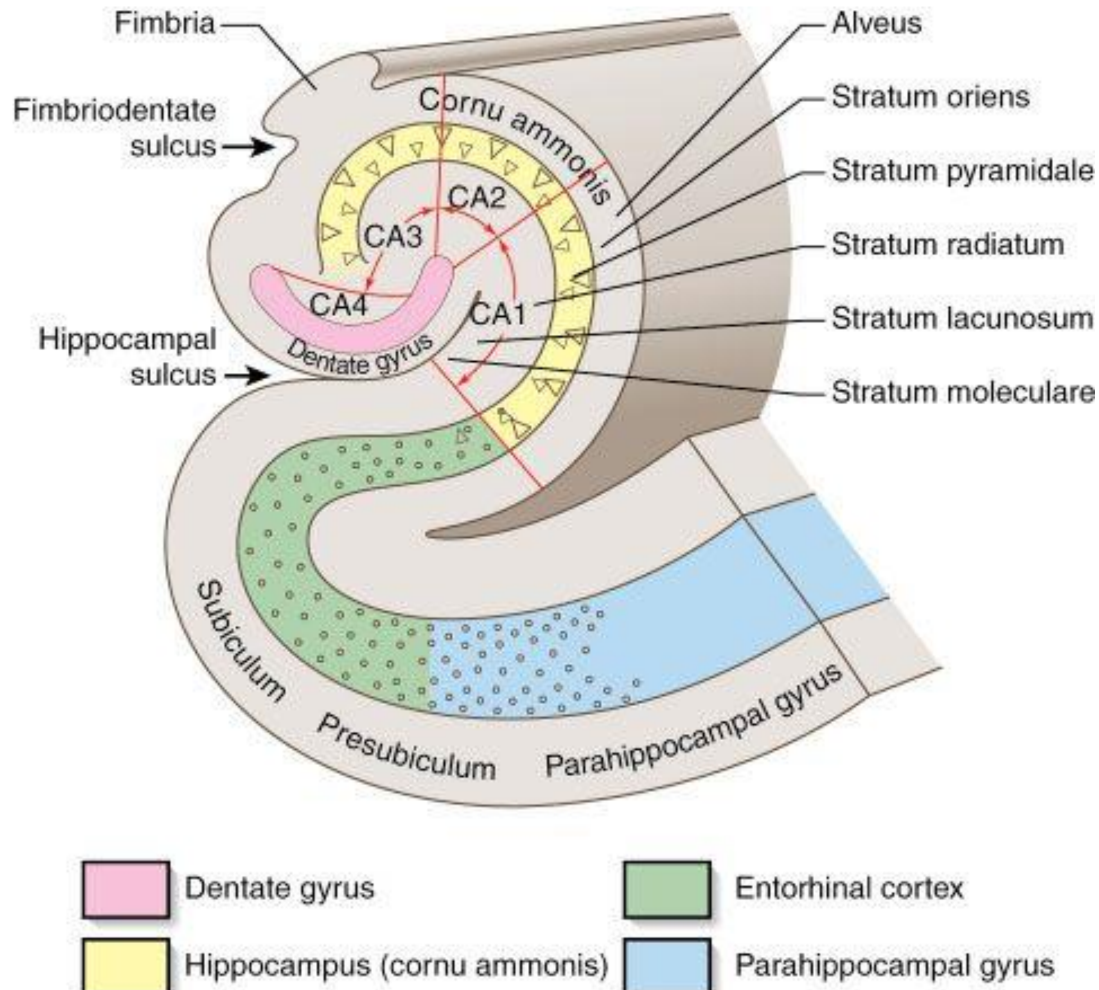
Fornice (schema)



Sezione frontale (veduta posteriore)

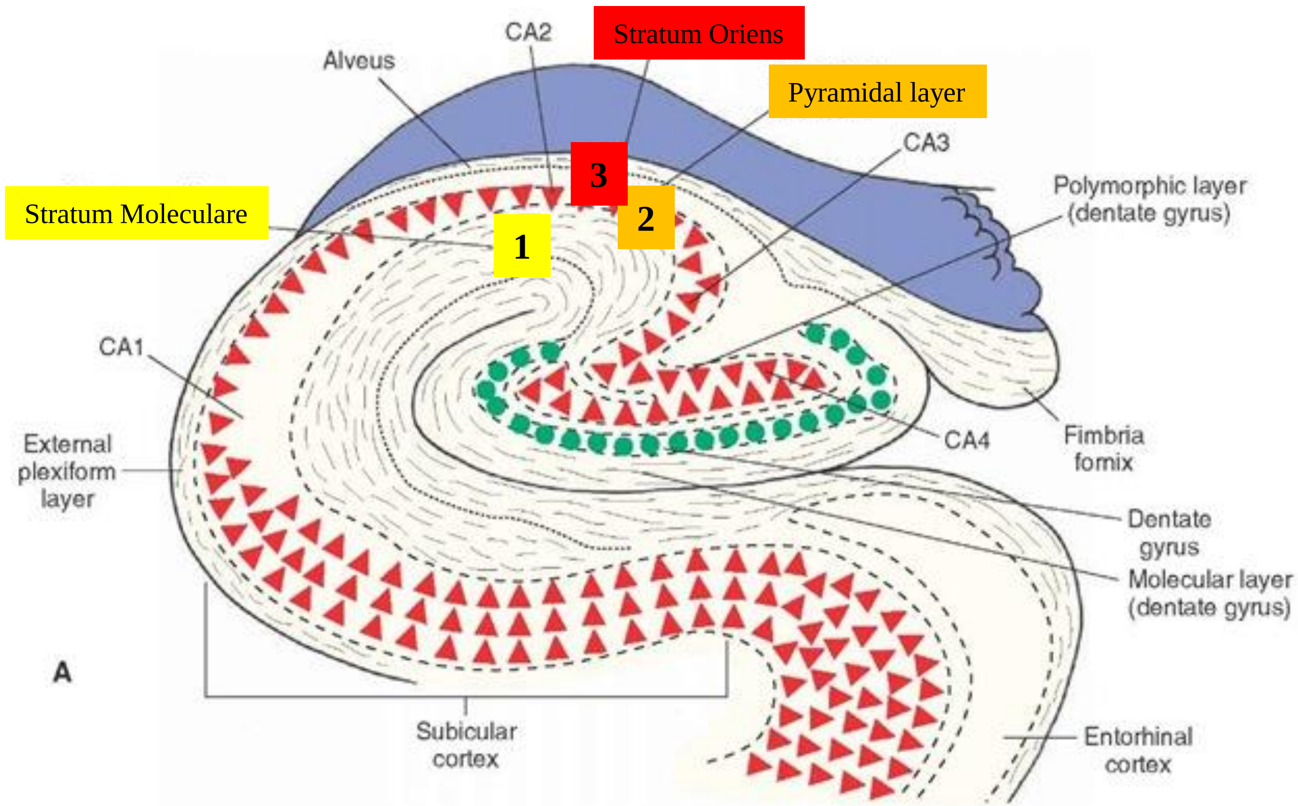

Archicortex
Mesocortex
Isocortex


Archicortex
CA2
CA3
CA1
CA4
DG
Subiculum
Mesocortex
Isocortex
Parahippocampal gyrus & enthorinal cortex
Fusiform / Medial Occipito-Temporal Gyrus

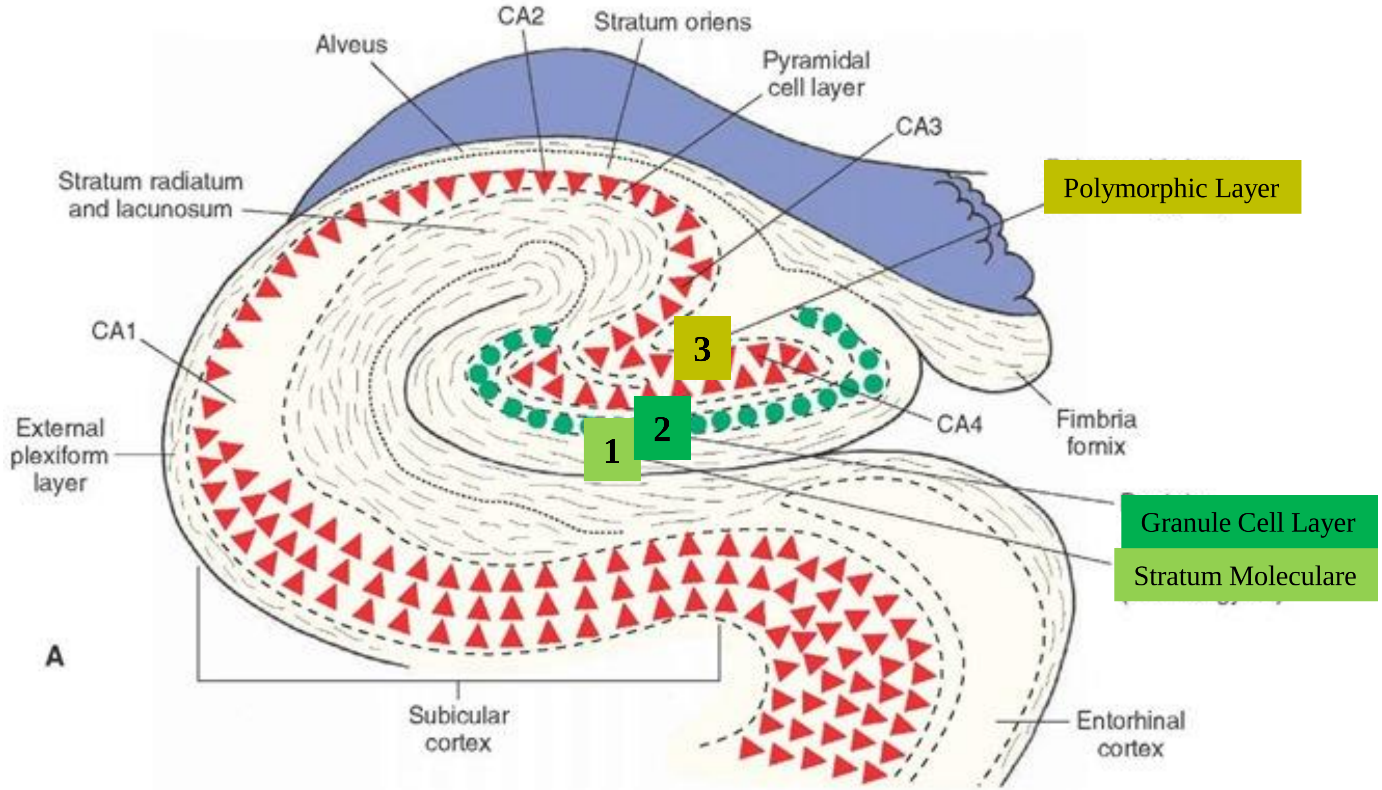

Fimbria
Fimbriodentate sulcus
Hippocampal sulcus
Cornu ammonis
CA2
CA3
CA4
CA1
Dentate gyrus
Alveus
Stratum oriens
Stratum pyramidale
Stratum radiatum
Stratum lacunosum
Stratum moleculare
Subiculum
Presubiculum
Parahippocampal gyrus
Dentate gyrus
Entorhinal cortex
Hippocampus (cornu ammonis)
Parahippocampal gyrus

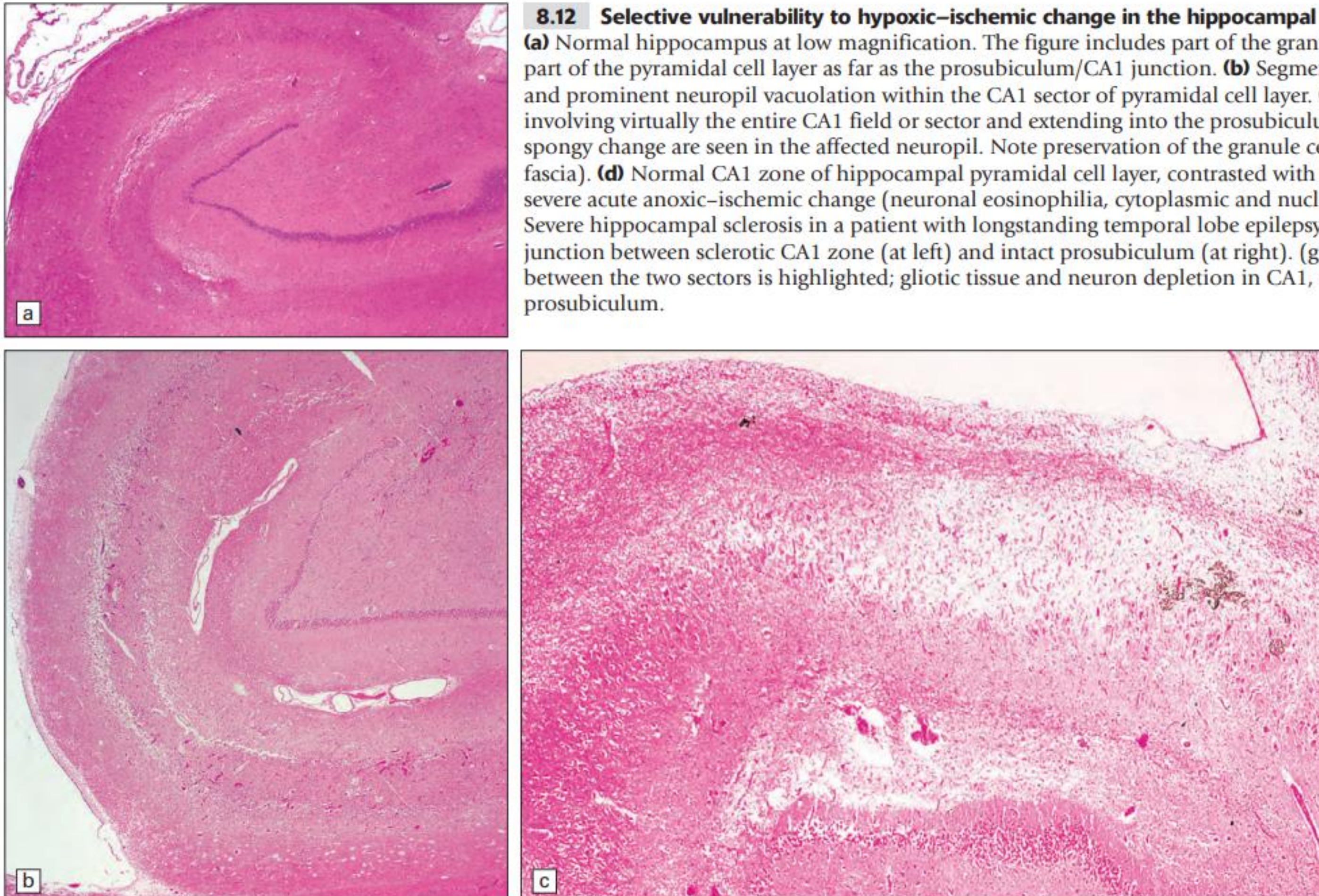
Ammon's Horn (CA):

1. Molecular Layer (Stratum Moleculare)
2. Pyramidal Layer
3. Polymorphic Layer (Stratum Oriens)



Dentate Gyrus:
1. Molecular Layer (Stratum Moleculare)
2. Granule Cell Layer
3. Polymorphic Layer (Stratum Oriens)





8.12 Selective vulnerability to hypoxic–ischemic change in the hippocampal pyramidal cell layer. **(a)** Normal hippocampus at low magnification. The figure includes part of the granule cell layer and part of the pyramidal cell layer as far as the prosubiculum/CA1 junction. **(b)** Segmental loss of neurons and prominent neuropil vacuolation within the CA1 sector of pyramidal cell layer. **(c)** There is an infarct involving virtually the entire CA1 field or sector and extending into the prosubiculum. Neuron loss and spongy change are seen in the affected neuropil. Note preservation of the granule cell layer (dentate fascia). **(d)** Normal CA1 zone of hippocampal pyramidal cell layer, contrasted with **(e)** a region with severe acute anoxic–ischemic change (neuronal eosinophilia, cytoplasmic and nuclear collapse, etc). **(f,g)** Severe hippocampal sclerosis in a patient with longstanding temporal lobe epilepsy. (f) Arrows indicate junction between sclerotic CA1 zone (at left) and intact prosubiculum (at right). (g) The junction between the two sectors is highlighted; gliotic tissue and neuron depletion in CA1, intact neurons in prosubiculum.

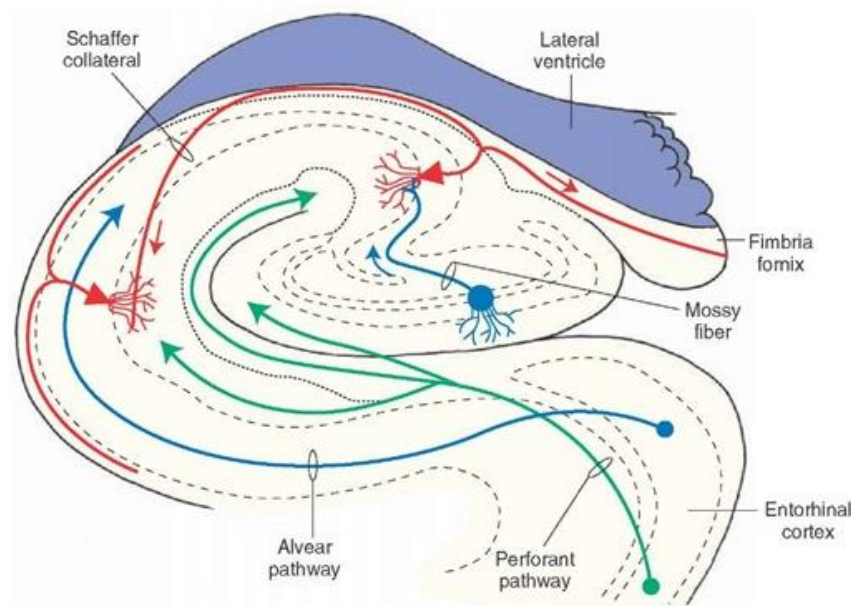
Afferences:

- Enthorinal Cortex
- Modulatory nuclei of the brainstem
- Septal nuclei

Two main intrinsic pathways in the Hippocampal Formation:

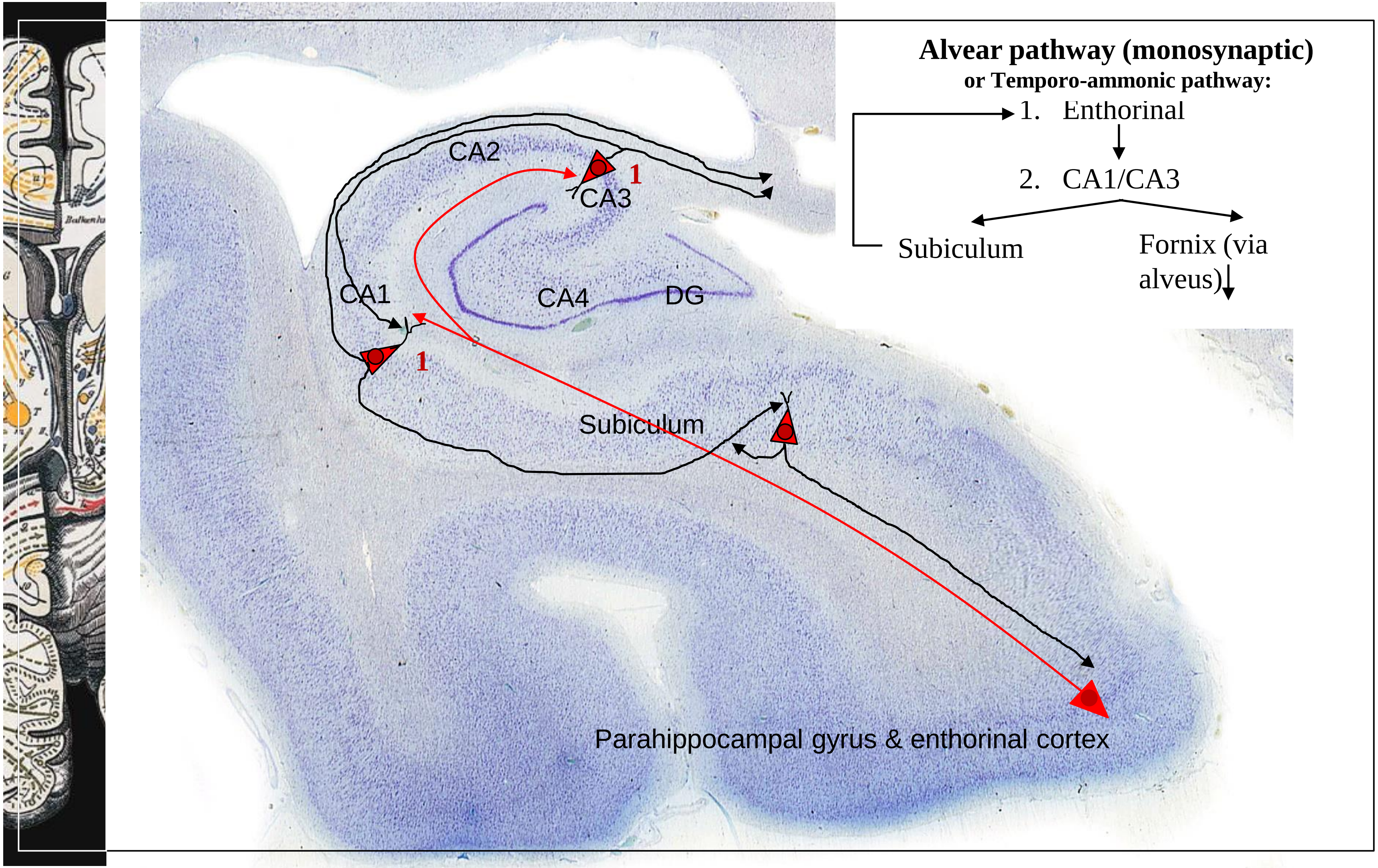
- **Alvear pathway**
- **Perforant Pathway**

B

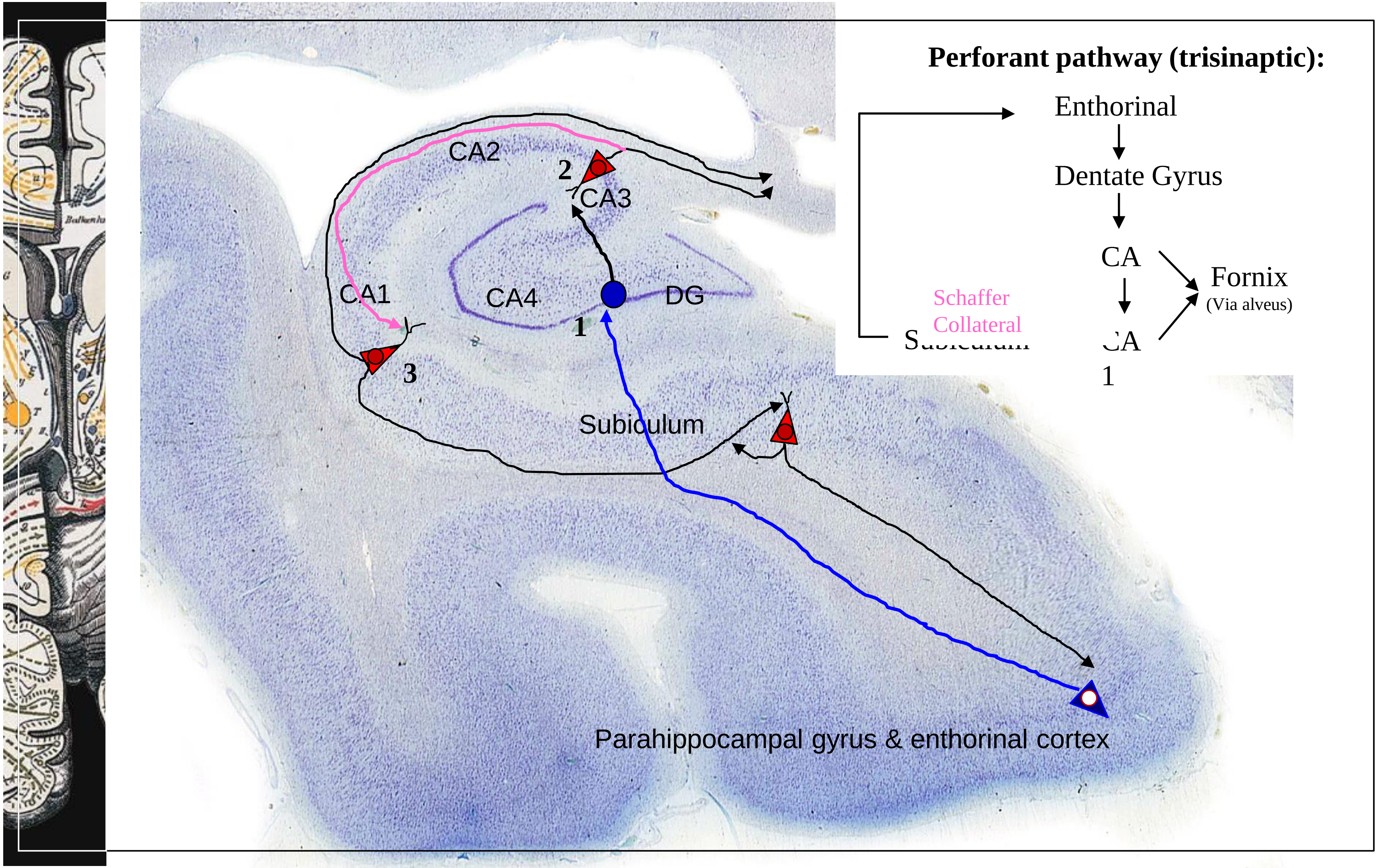


Efferences (via the Fornix):

- Septal nuclei (precommissural)
- Mammillary bodies (post commissural)
- Contralateral hippocampus (commissural)
- Enthorinal cortex and subiculum (loop)



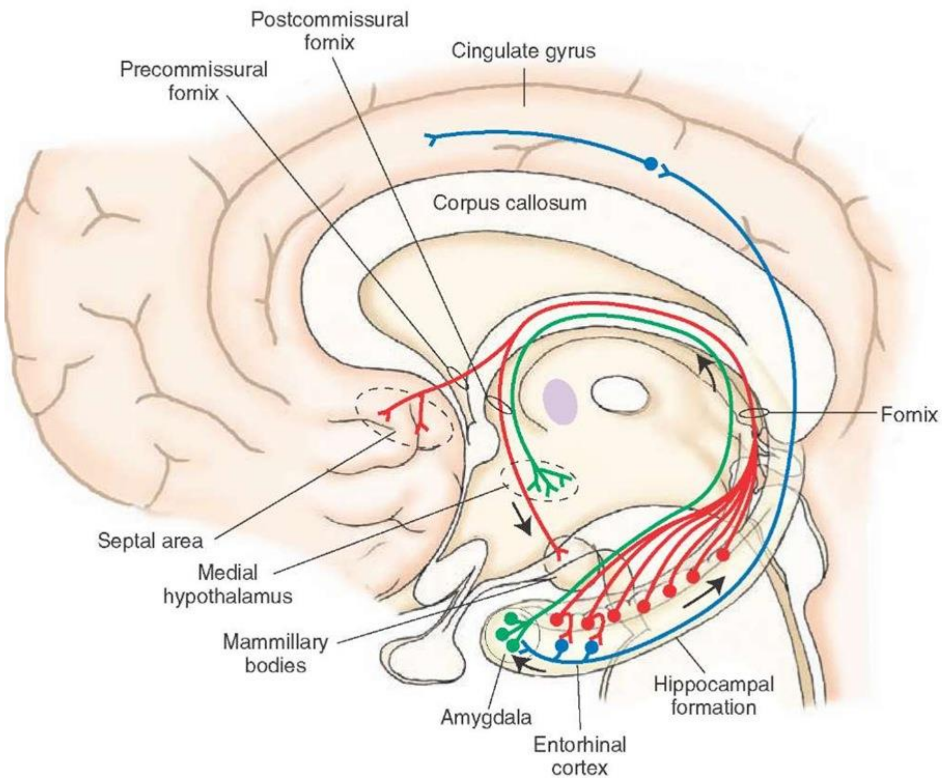
Alvear pathway (monosynaptic)
or Temporo-ammonic pathway:
1. Enthorinal
2. CA1/CA3
Subiculum
Fornix (via alveus)
CA2
CA3
1
CA1
CA4
DG
1
Subiculum
Parahippocampal gyrus & enthorinal cortex

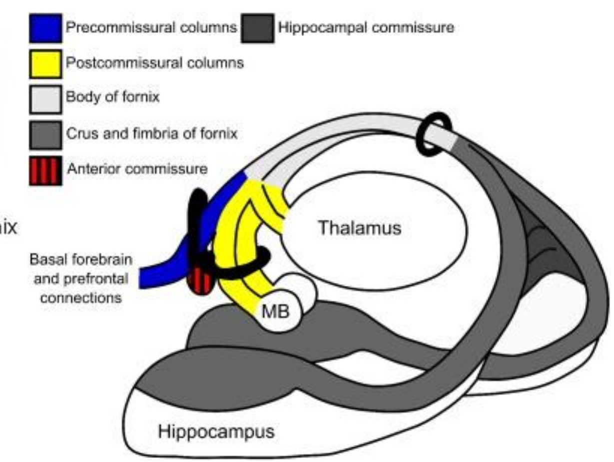


Perforant pathway (trisinaptic):
Enthorinal
Dentate Gyrus
CA
CA
1
Fornix
(Via alveus)
Schaffer
Collateral
CA2
CA3
CA1
CA4
DG
1
2
3
Subiculum
Parahippocampal gyrus & enthorinal cortex

Efferences (via the Fornix):

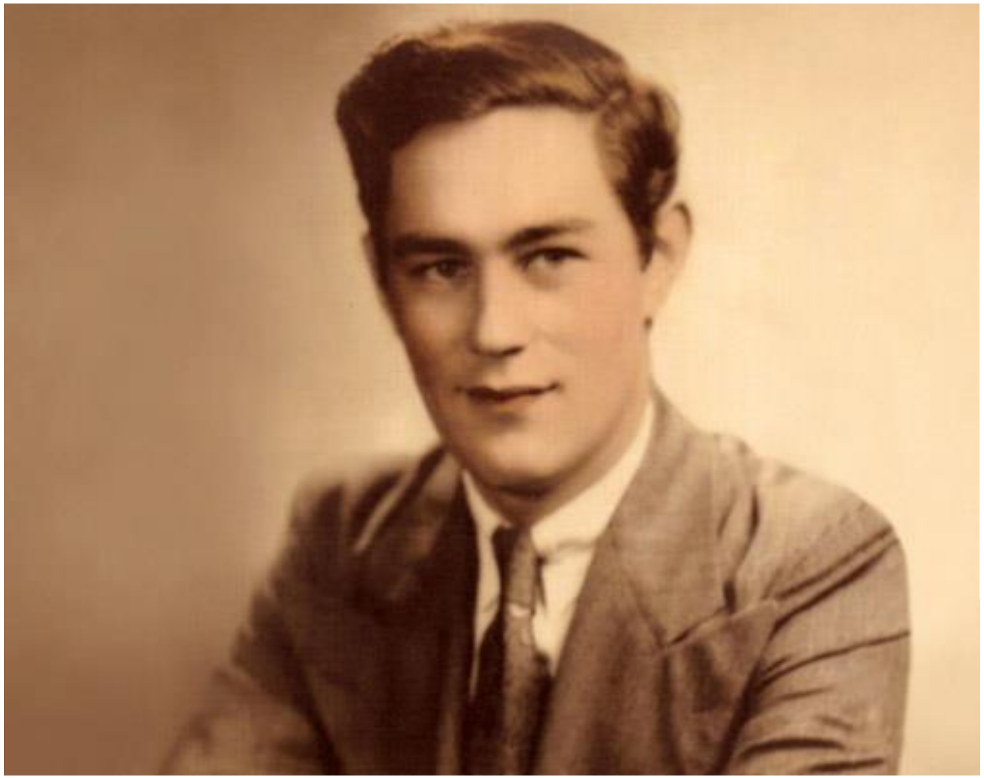
- Septal nuclei (precommissural)
- Mammillary bodies (post commissural)
- Contralateral hippocampus (commissural)
- Enthorinal cortex and subiculum (loop) → Associative cortices (long term memory storage)

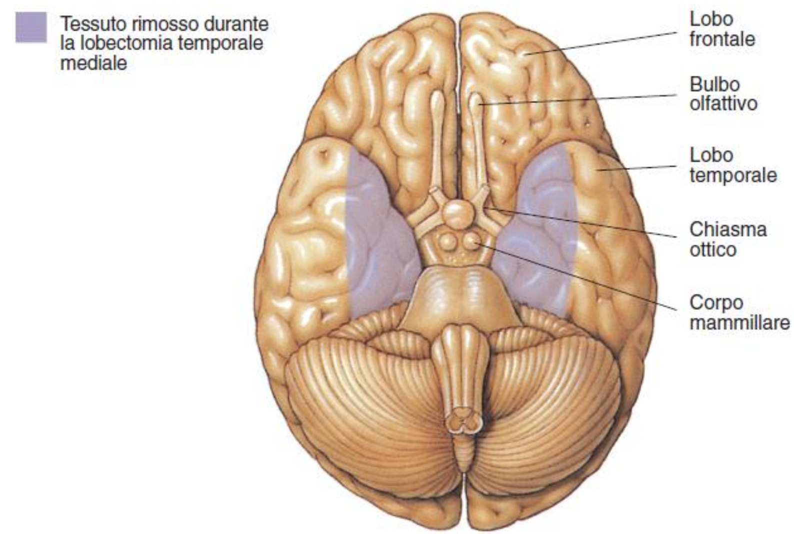




Patient H.M.

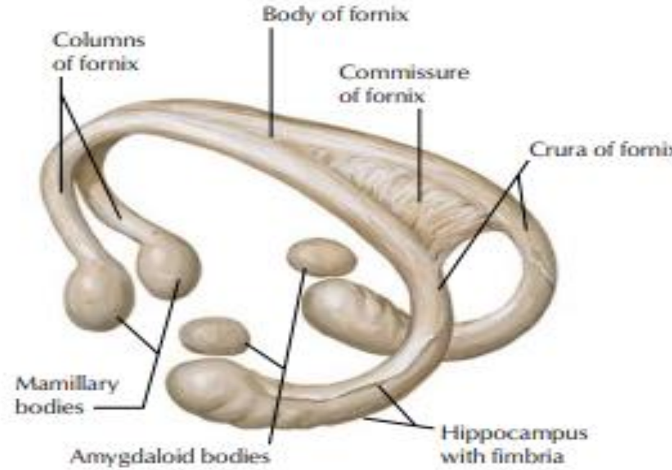
Total anterograde memory loss (unable to form new memories) following surgical resection of the medial temporal lobe (including hippocampus) due to intractable epilepsy.





The amygdala (amygdaloid body)

- Fear and salient stimuli, mediates survival-related quick responses

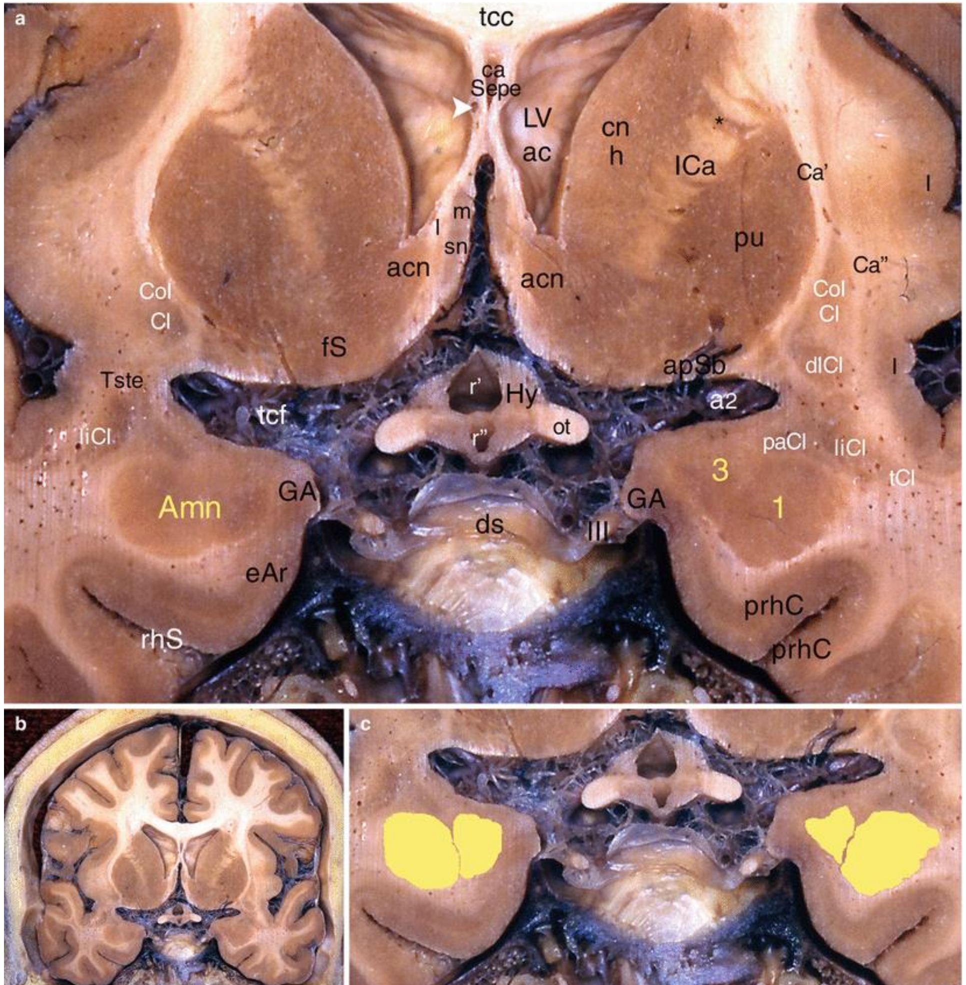


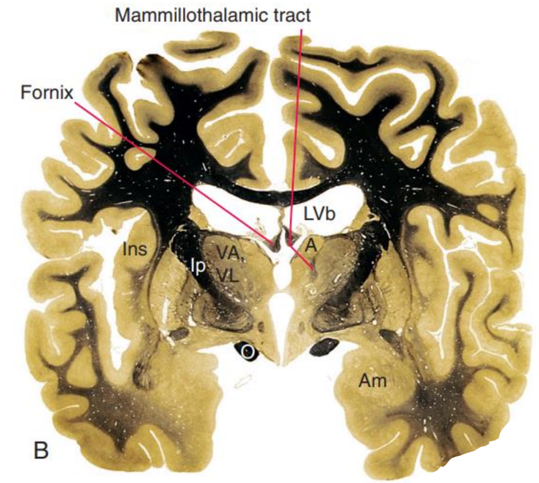
Afferences:

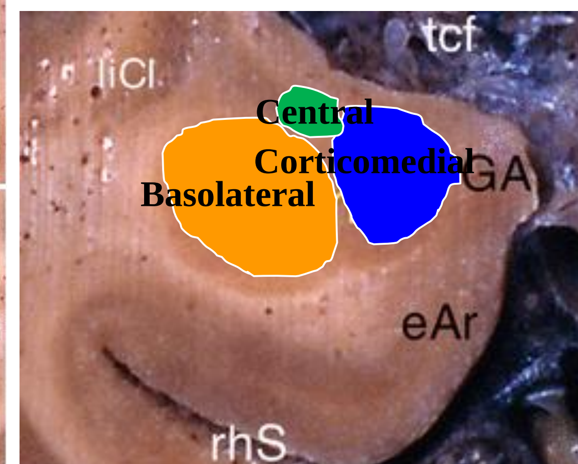
Sensory thalamus, Brainstem, Association Cortices

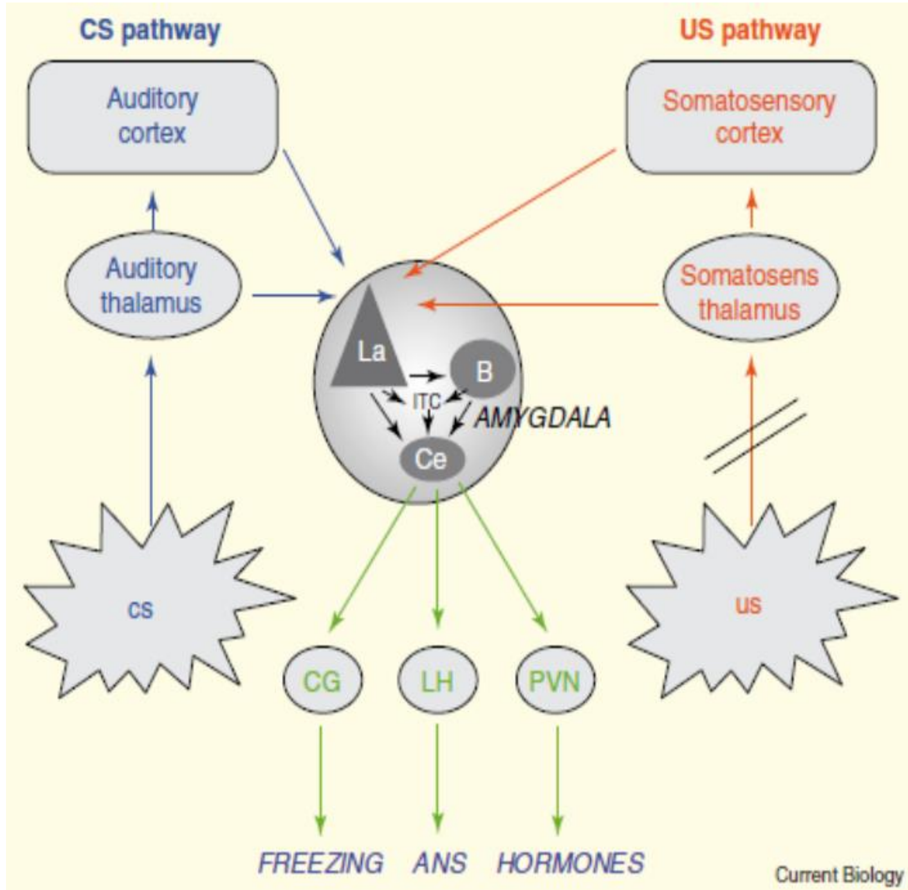
Efferences:

- Stria terminalis (to thalamus)
- Amygdalofugal pathways (to hypothalamus, brainstem, hippocampus)

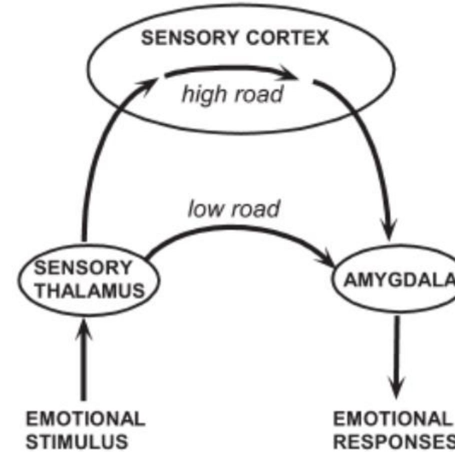

a
tcc
ca
Sepe
LV
ac
cn
h
ICa
Ca'
I
m
l
sn
acn
acn
pu
Ca"
Col
Cl
Col
Cl
fS
Tste
apSb
dlCl
I
r'
Hy
a2
tcf
ot
r"
liCl
paCl
liCl
3
tCl
GA
Amn
GA
1
ds
III
eAr
prhC
rhS
prhC
b
c


Mammillothalamic tract
Fornix
LVb
Ins
Ip
VA,
VL
A
Am
B

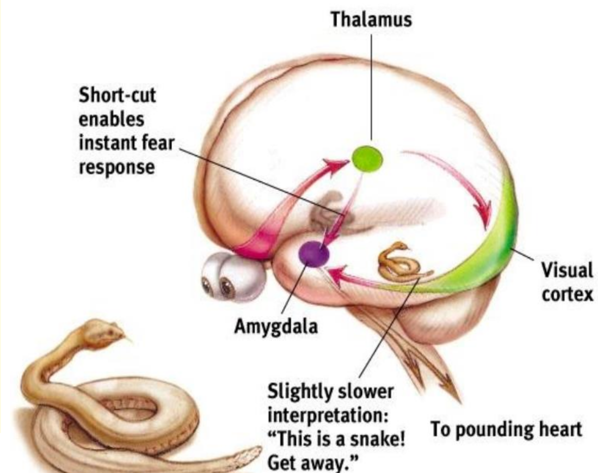

tcf
liCl
Central
Corticomedial
GA
Basolateral
eAr
rhS



CS pathway
US pathway
Auditory cortex
Somatosensory cortex
Auditory thalamus
Somatosens thalamus
La
B
ITC
Ce
AMYGDALA
CS
US
CG
LH
PVN
FREEZING
ANS
HORMONES
Current Biology



SENSORY CORTEX
high road
low road
SENSORY THALAMUS
AMYGDALA
EMOTIONAL STIMULUS
EMOTIONAL RESPONSES



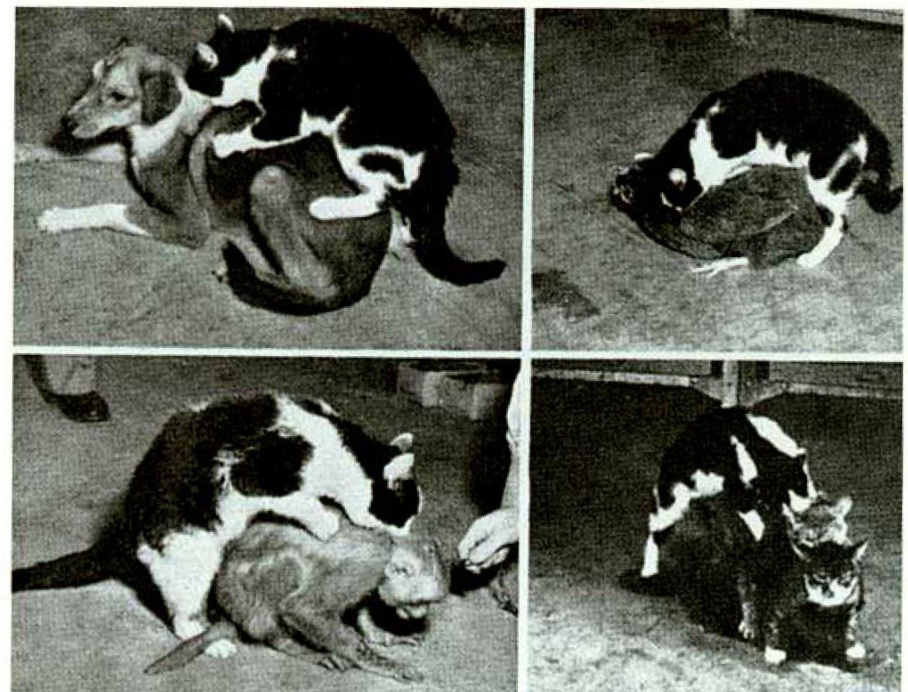
Thalamus
Short-cut enables instant fear response
Visual cortex
Amygdala
Slightly slower interpretation: "This is a snake! Get away."
To pounding heart

Amygdala

Klüver-Bucy syndrome

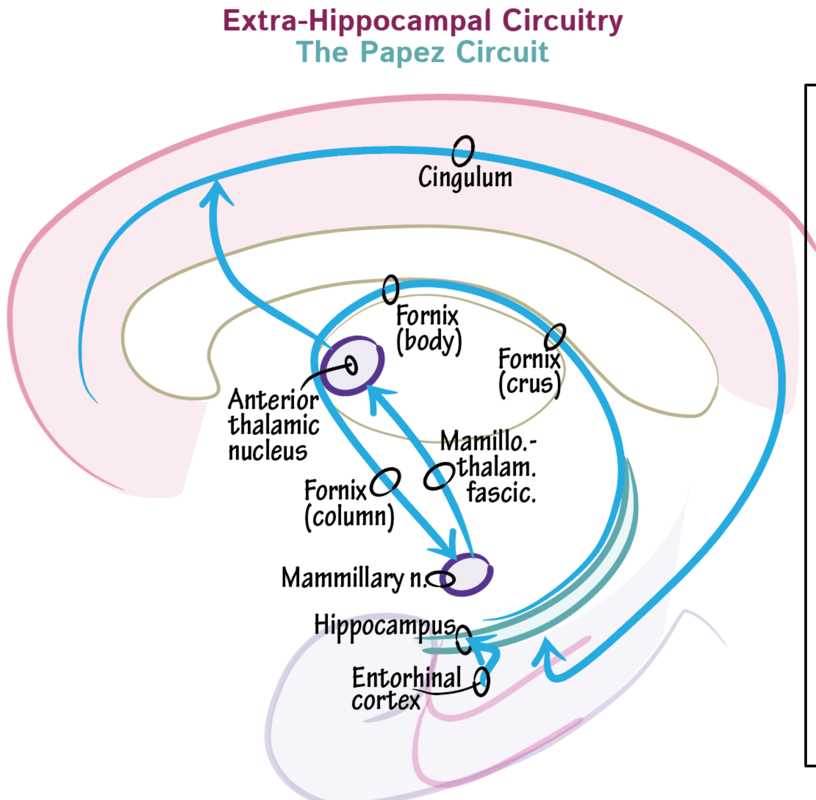
• bilateral lesions of amygdalae

• visual agnosia (auditory, tactile)
• hypermetamorphosis (compulsively explore the environment and overreact to visual stimuli)
• hyperorality
• hyperphagia
• hypersexuality
• extremely placid behavior; inability to experience fear



To summarize the Limbic System….

Papez's Circuit (1937)



Hippocampal formation
↓
Mammillary Nuclei
↓
Anterior Thalamus
↓
Cingulate Cortex
↓
Parahippocampal Cortex
↓
Enthorinal Cortex

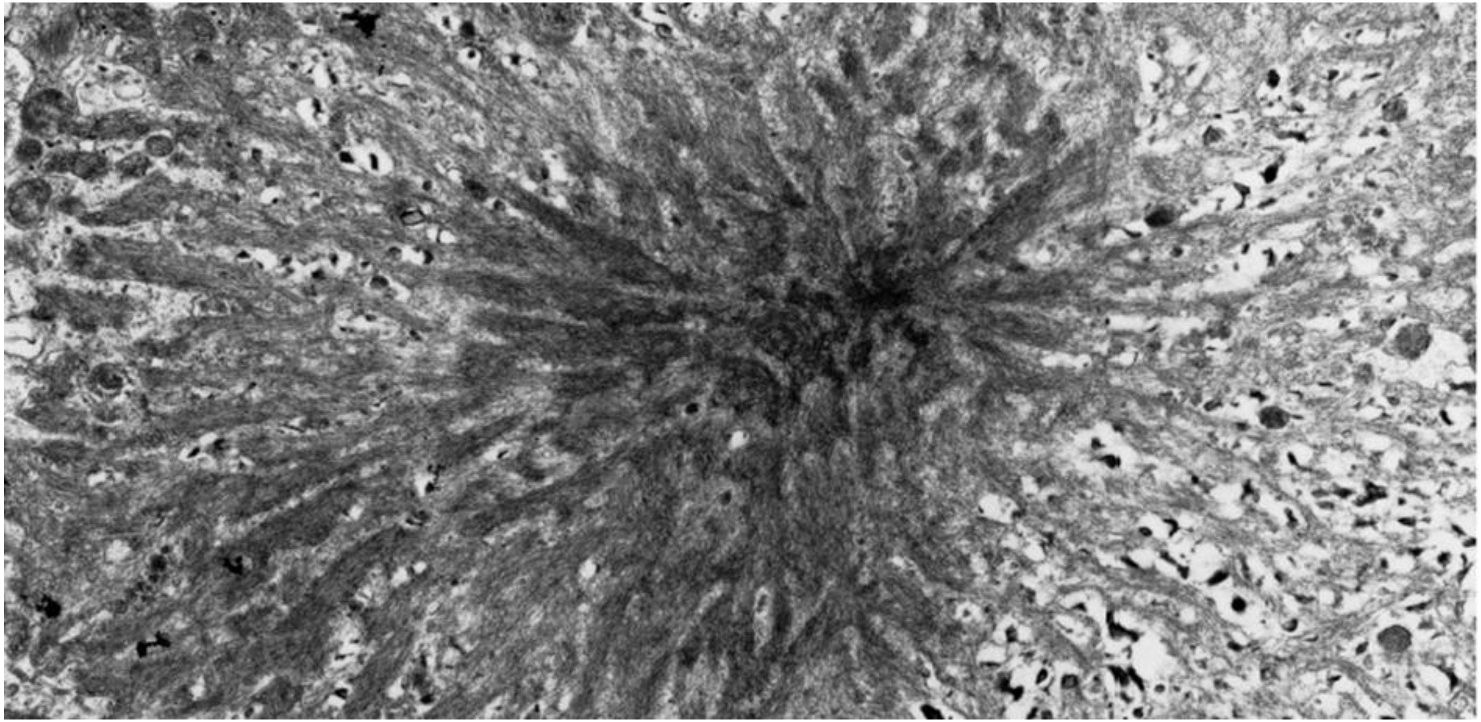
Other targets

The neocortex and archicortex in pathology

Alzheimer’s Disease

Alzheimer's Disease

- Commonest cause for dementia
- Can be sporadic, familiar, or associated to other syndromes (e.g. Down Syndrome)

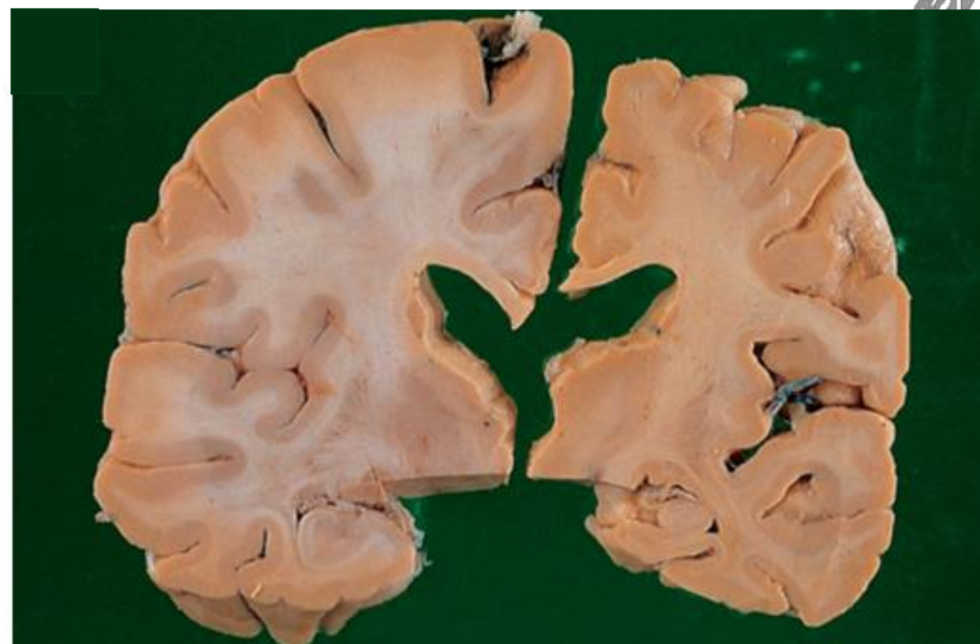


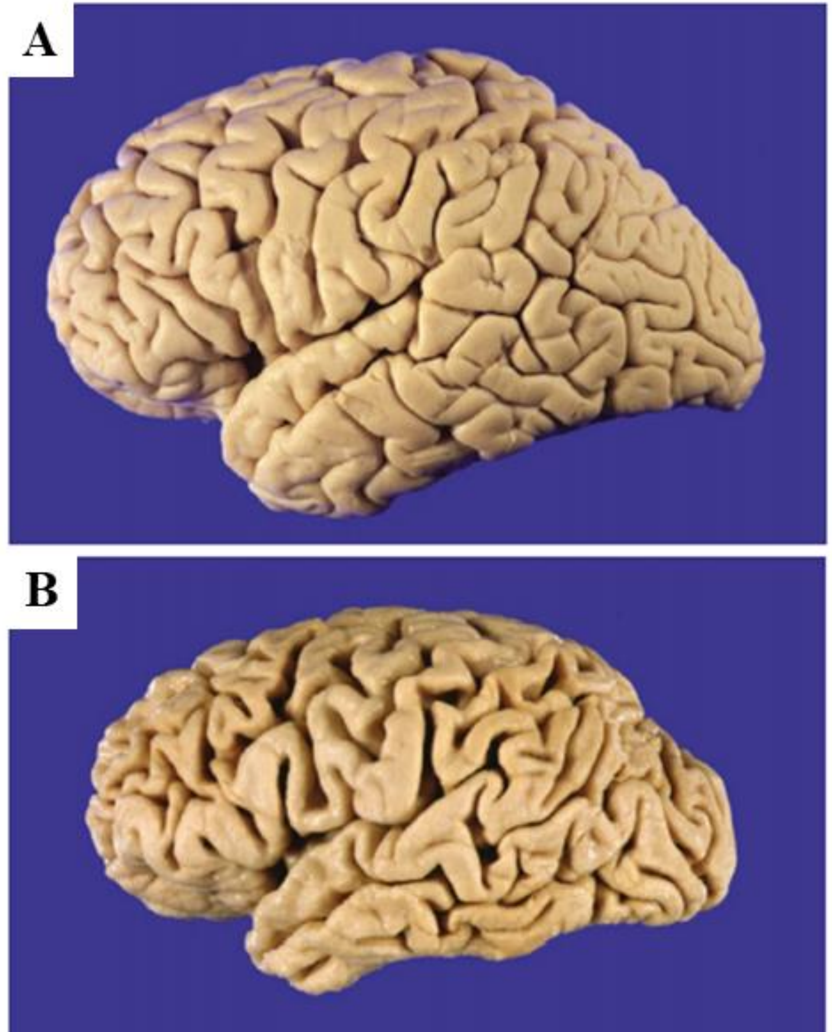
Alzheimer's Disease

- Commonest cause for dementia
- Can be sporadic, familiar, or associated to other syndromes (e.g. Down Syndrome)

MACROSCOPIC FEATURES

- **Global atrophy (weight > 1200g)**
- **Shrinkening of gyri, enlargement of sulci**
- **Ventricular dilation (hydrocephalus ex-vacuo)**

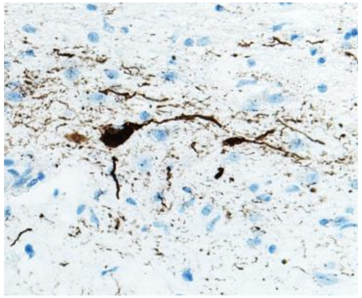


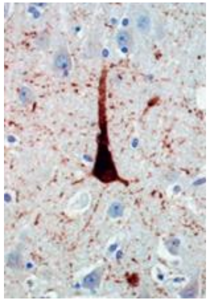

A
B

Alzheimer's Disease

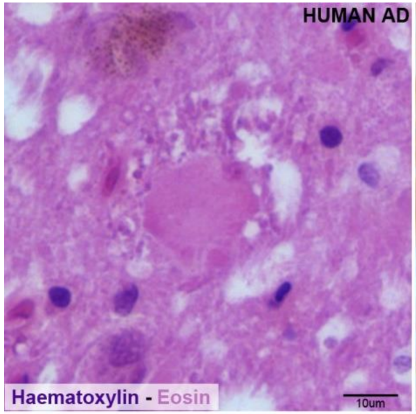
Microscopic Features

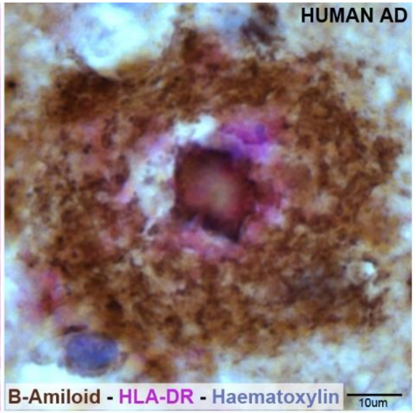
- Intracellular Neurofibrillary Tangles (TAU)

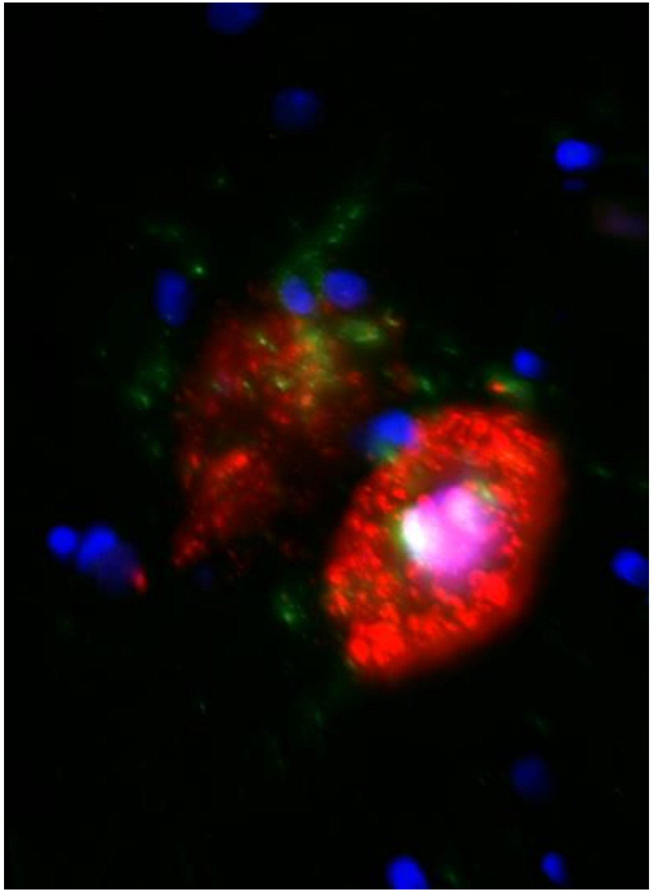


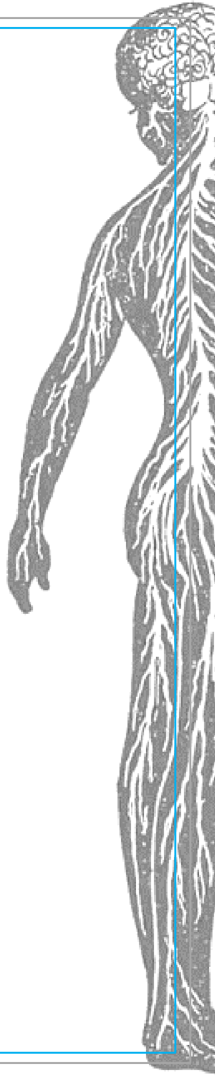


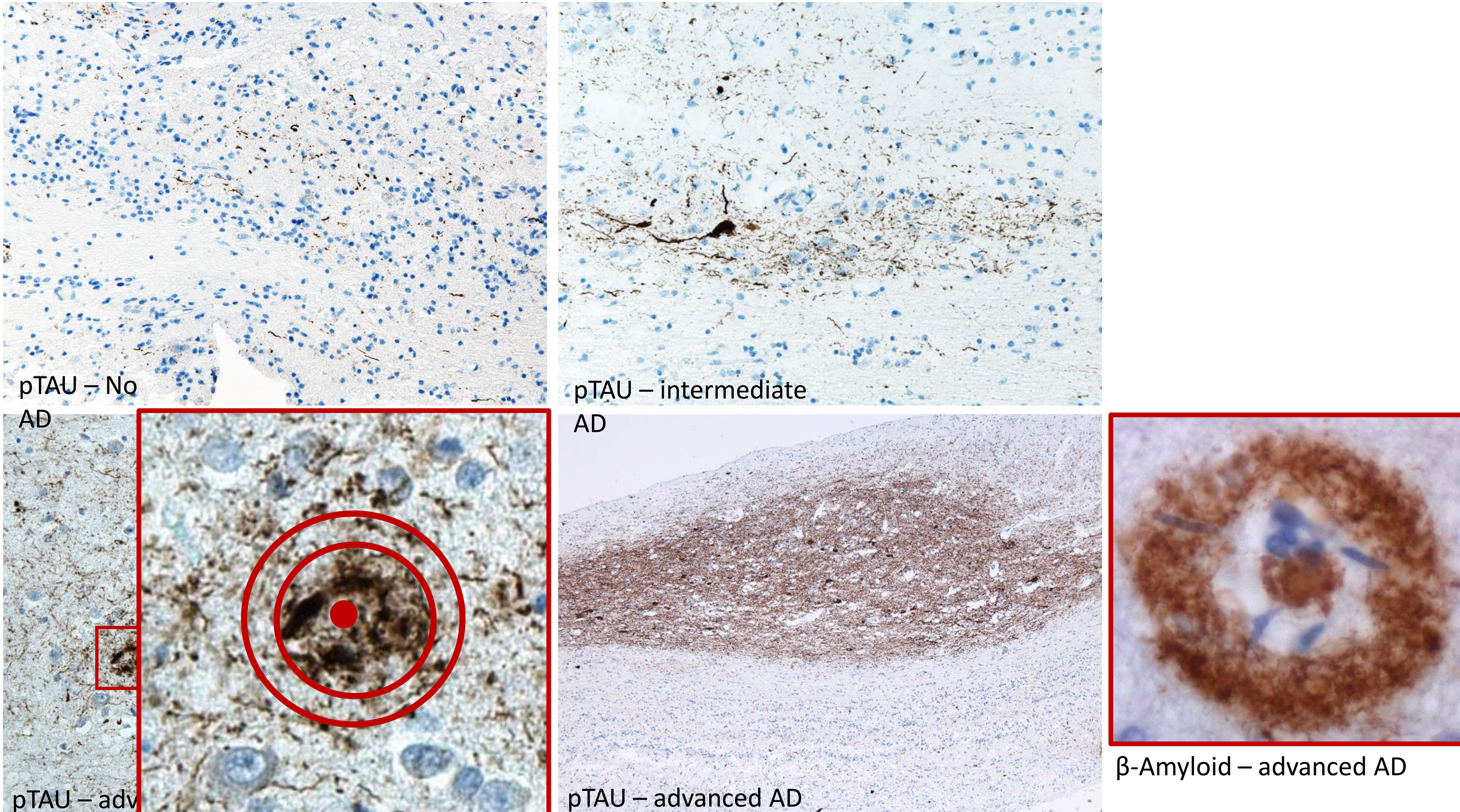
- Extracellular Senile Plaques (Beta-Amiloid Plaques)



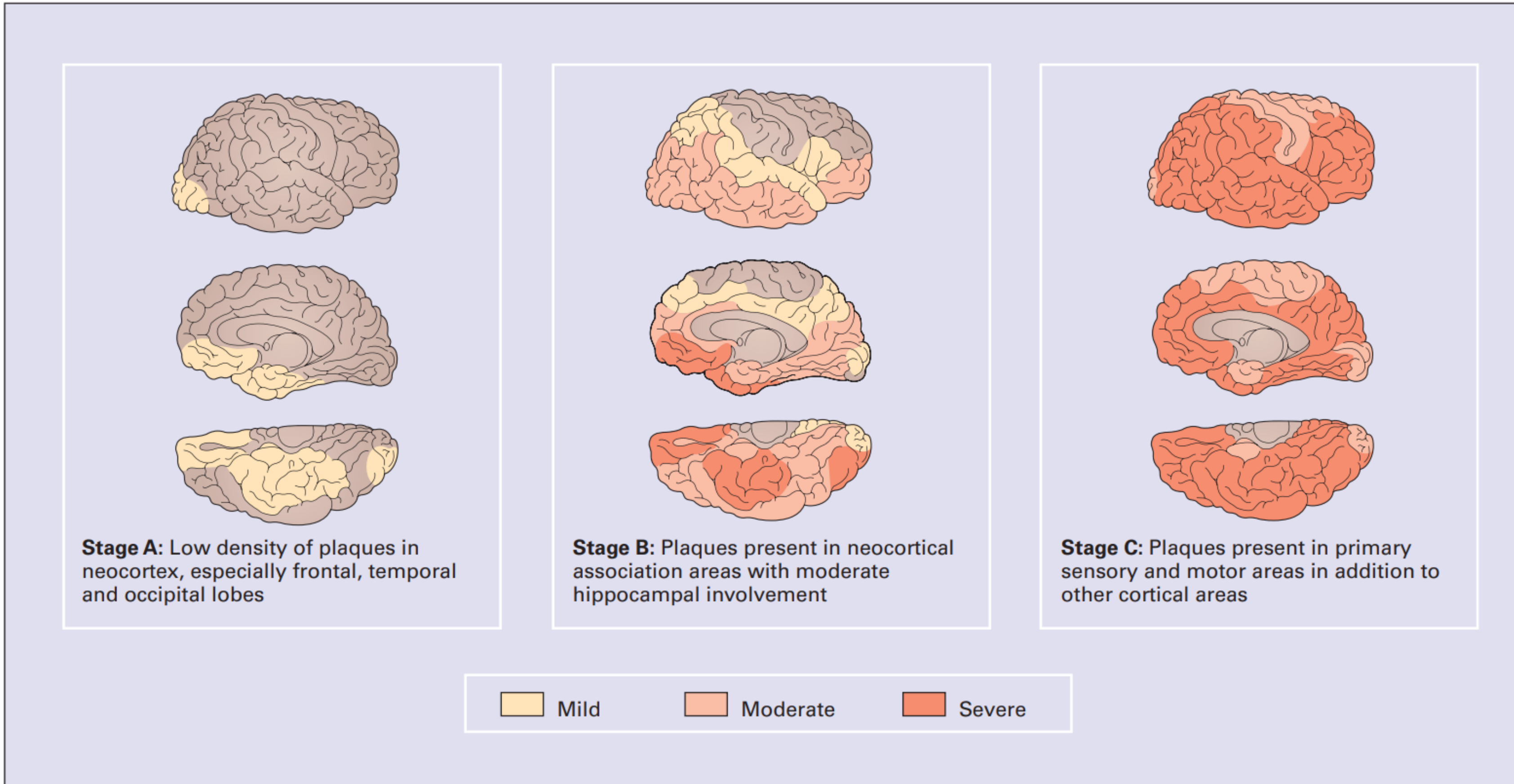




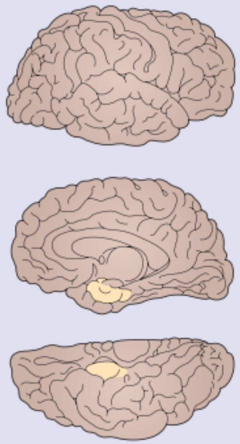



pTAU – No AD
pTAU – intermediate AD
pTAU – adv
pTAU – advanced AD
β-Amyloid – advanced AD

AD Amyloid Plaque Staging



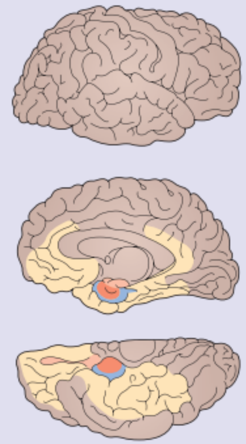
AD NFT Staging



TRANSENTORHINAL
(Clinically asymptomatic)

Stage I: NFTs and NTs in small density, confined to transentorhinal cortex in pre-α cells

Stage II: Tangles present in moderate density in pre-α cells of entorhinal cortex. Small numbers develop in CA1 region of hippocampus

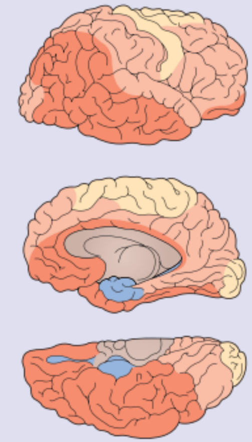


LIMBIC
(Incipient AD)

Stage III: There are modest numbers of NFTs and NTs throughout CA1 and in pyramidal cells in the subiculum. Small numbers appear in the fusiform gyrus lateral to the transentorhinal cortex as well as in the nucleus basalis of Meynert and amygdaloid complex

There is now severe involvement of pre-α cells with neuronal loss and gliosis

Stage IV: Severe involvement of areas affected in stage 3. Large numbers of ghost tangles in entorhinal and transentorhinal regions. Mild involvement of isocortex with sparing of primary sensory and motor cortices

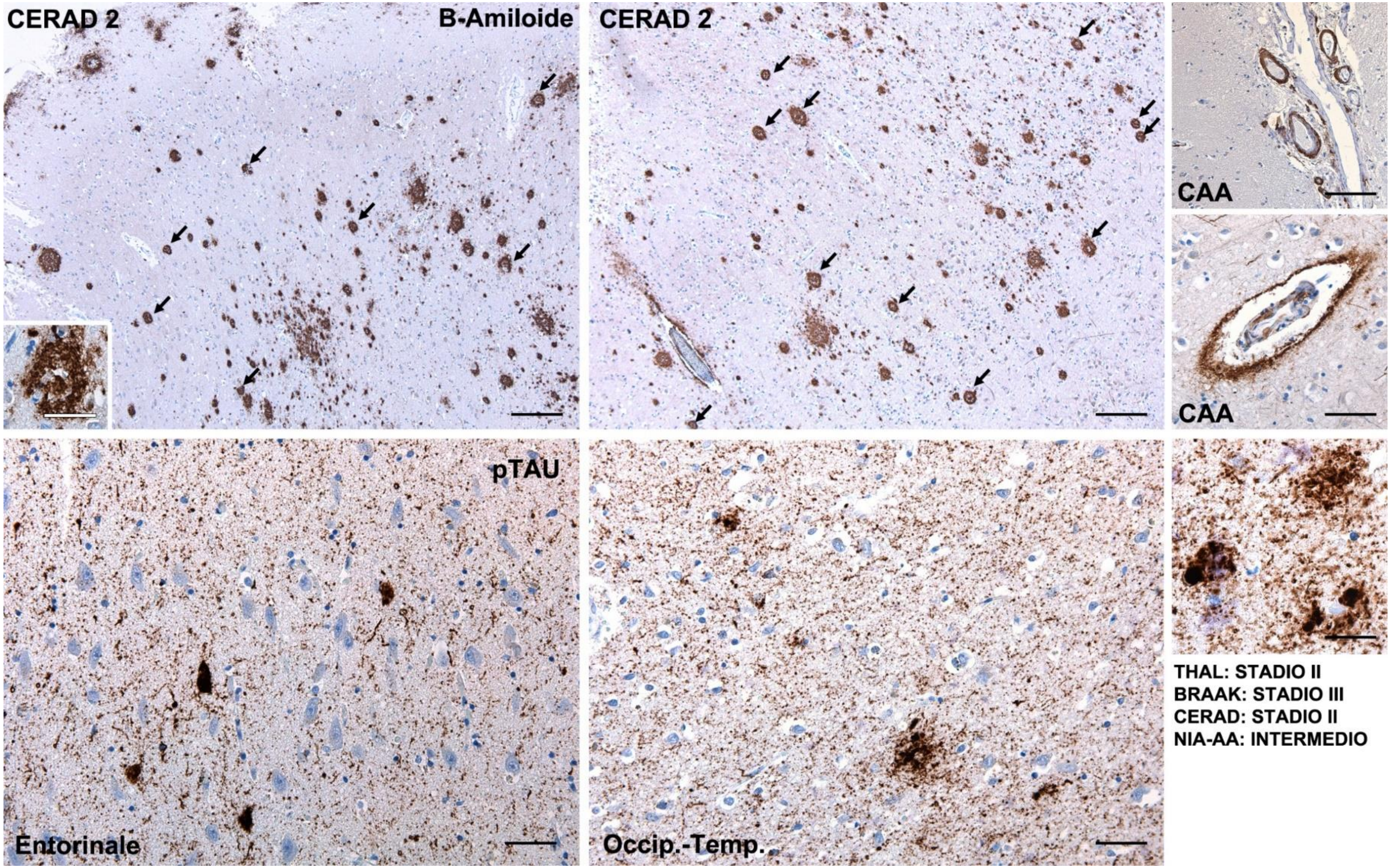


ISOCORTICAL
(Symptomatic AD)

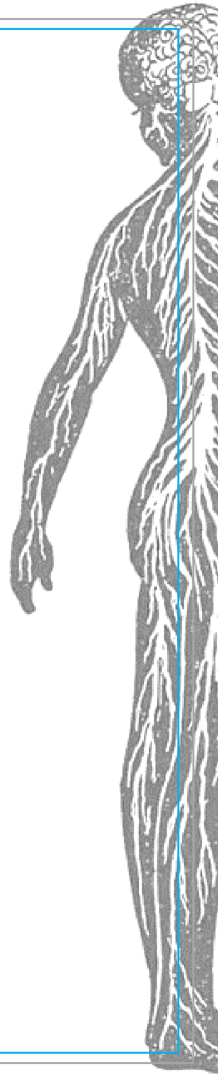
Stage V: Tangles in all sectors of hippocampus and subiculum. Widespread, moderate to severe isocortical involvement but still relative sparing of primary sensory and motor cortices. Tangles in claustrum, thalamus, hypothalamus. Ghost tangles with neuronal loss and astrocytic gliosis involving pre-α cells, CA1, antero-dorsal thalamic nucleus

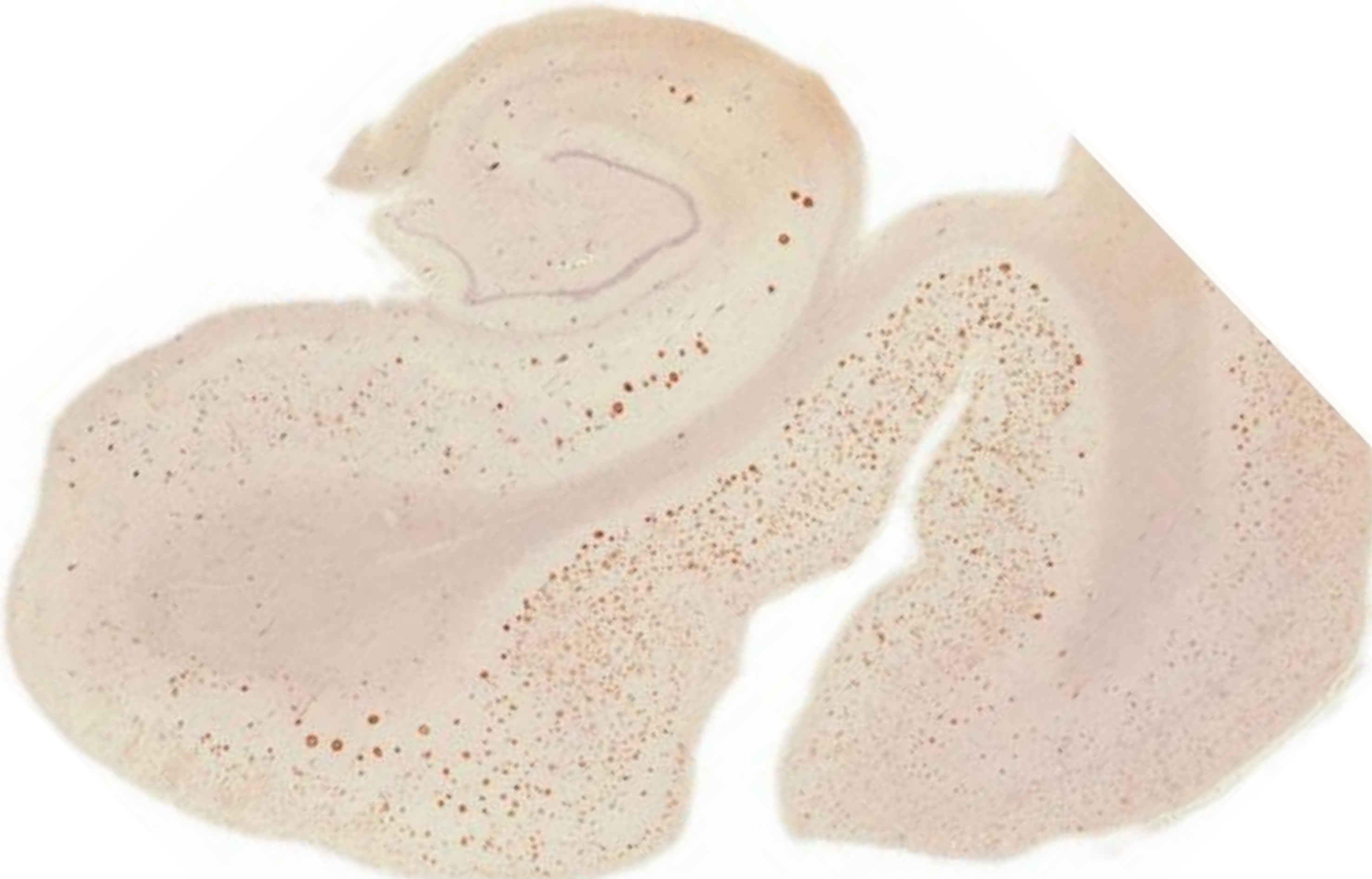
Stage VI: Increased densities of tangles in regions affected in earlier stages. Tangles in dentate granule cell layer. Marked involvement of claustrum, thalamus, hypothalamus, substantia nigra

Mild	Moderate
Severe	Very severe



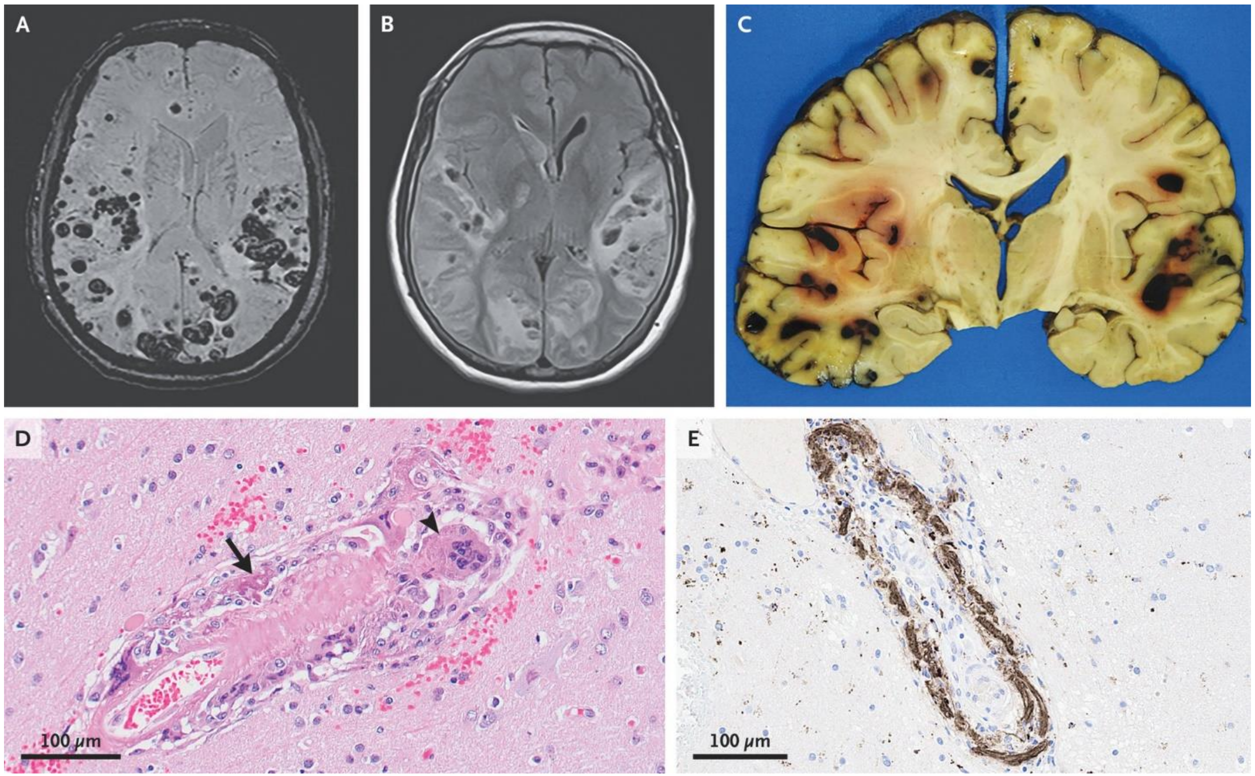
THAL: STADIO II
BRAAK: STADIO III
CERAD: STADIO II
NIA-AA: INTERMEDIO





Alzheimer’s Disease

Lecanemab trial…. a monoclonal antibody against Beta-Amyloid



CLINICAL CASE 1

83-year-old Male

Reported 4 years of worsening memory impairment, following retirement. Initially the patient was unable to remember new information, especially events occurring recently, and reported loss of smell (anosmia). No difficulties in recalling distant memories. Family reports disorientation and inability to find the way back home. Started displaying signs of irritability and was easy to anger.

Neurological examination:
Alert. MoCA score: 22/30.
MRI: mild global atrophy.
Progressive worsening of cognitive status on follow-up examinations.

Mild atrophy of the cerebral hemispheres. Cored amyloid plaques are found in the associative cortices of the parietal and temporal lobe and,
less diffusely, in the limbic regions.
pTAU is mainly found in the limbic regions and in the temporal cortex.

Parietal Cortex
- Beta Amyloid IHC

CLINICAL CASE 2

86-year-old Female

Housewife. 7 years of worsening memory impairment; admitted to hospice. Marked cognitive decline, abulia and anhedonia.

MRI moderate global atrophy.

Neuropathological evaluation revealed global cortical atrophy, more pronounced frontally, and reduced hippocampal volume. Neurofibrillay tangles and cored neuritic plaques are found throughout the limbic and associative cortices.

Anterior Hippocampus

- pTAU (Pink)
- Beta Amyloid (Brown)