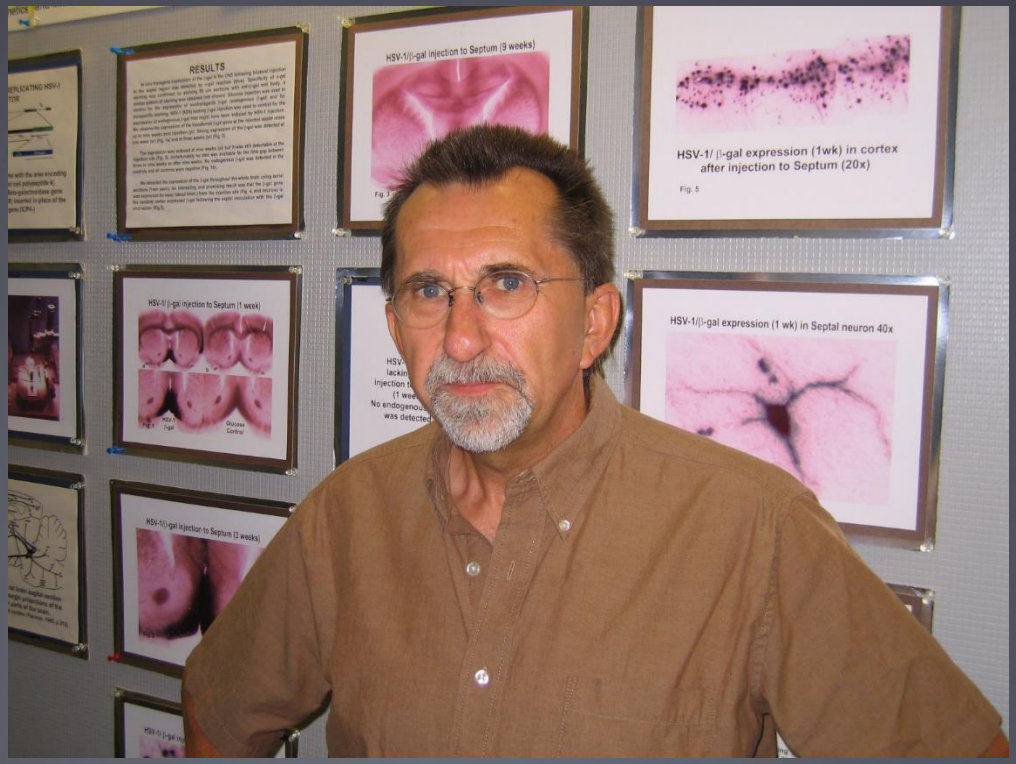

Michal K. Stachowiak

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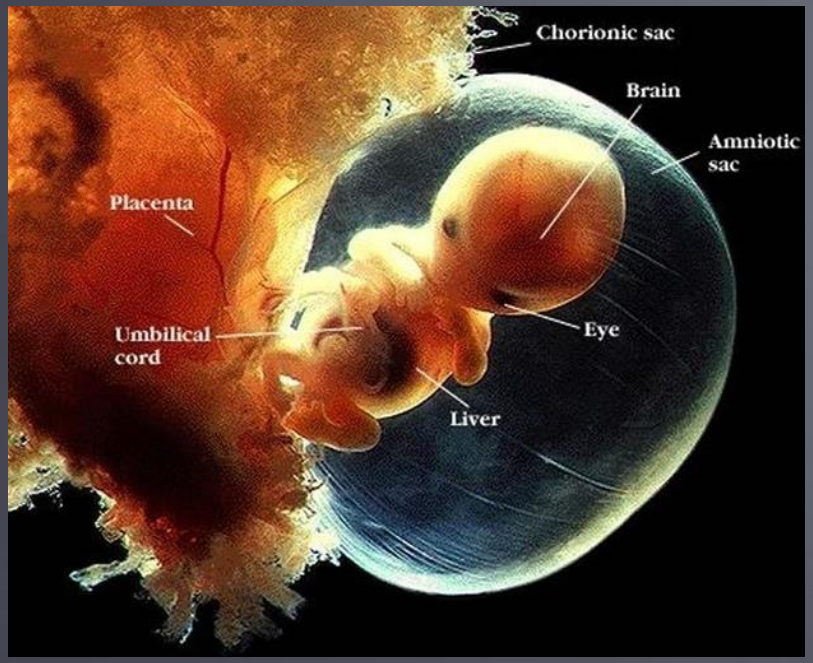
Professor, State University of New York at Buffalo
Pathology & Anatomical Sciences
Neuroscience Program
Genetics, Genomics and Bioinformatics
Biomedical Engineering

Fulbright project:

"Unravelling and combating neurodevelopmental disorders"



” Determining how the brain—an organ that perceives, thinks, loves, hates, remembers, changes, deceives itself, and coordinates all our conscious and unconscious bodily processes—is constructed is undoubtedly the most challenging of all developmental enigmas. A combination of genetic, cellular, and systems level approaches is now giving us a very preliminary understanding of how the basic anatomy of the brain becomes ordered”.

Gregor Eichele in 1992

“One ought to know that on the one hand pleasure, joy, laughter, and games, and on the other, grief, sorrow, discontent and dissatisfaction arise only from the brain. It is especially by it that we think, comprehend, see and hear, and distinguish the ugly from the beautiful, the bad from the good, the agreeable from the disagreeable……”

Hippocrates

Mechanisms and new Theory of (neuro) Ontogeny

SUNY, UB course PAS591 POL
Prof. Prof. Michal K. Stachowiak
Ewa K. Stachowiak

Mechanisms and new Theory of (neuro) Ontogeny

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http://www.brainmuseum.org/development/index.html

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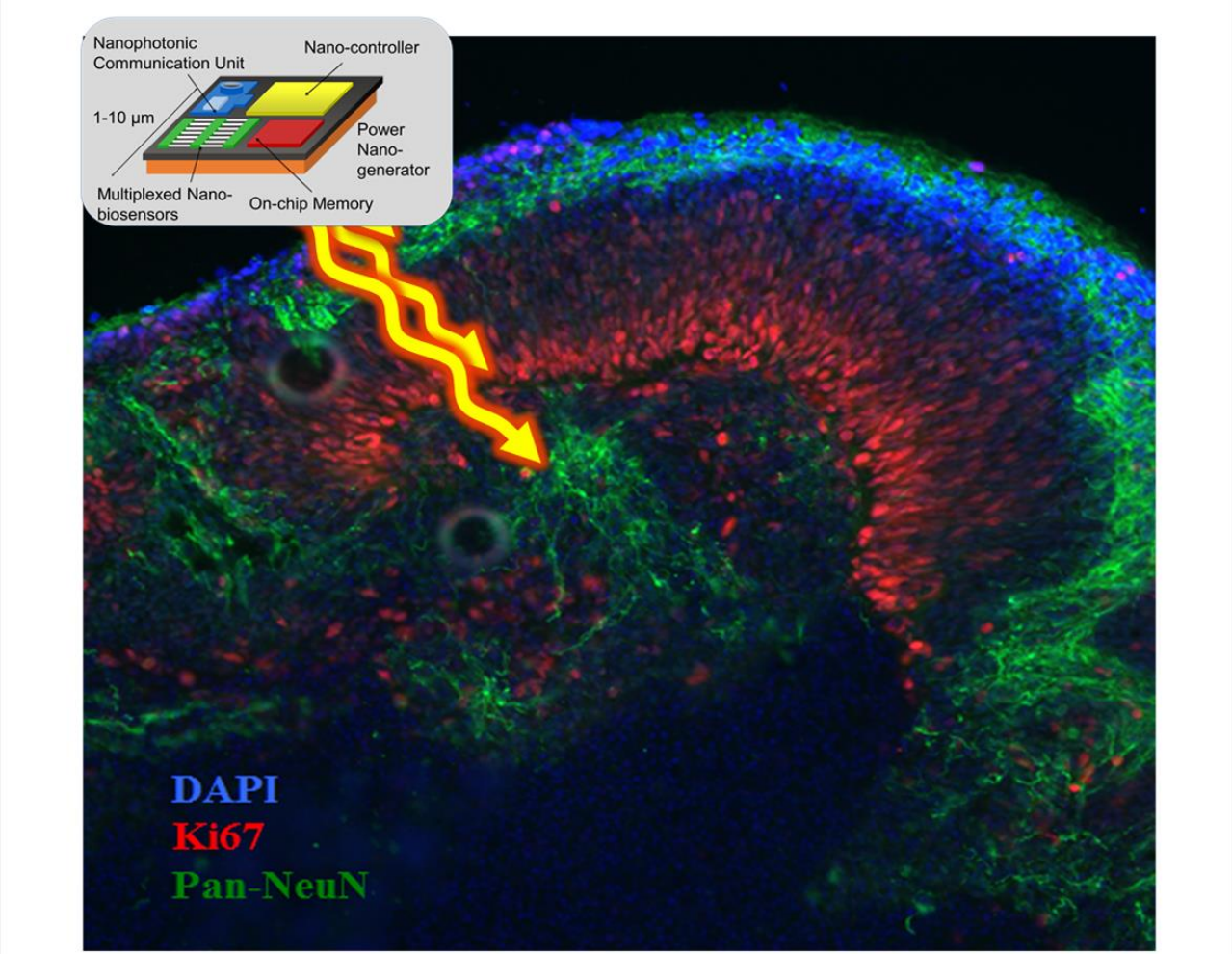

Mechanisms and new Theory of (neuro) Ontogeny

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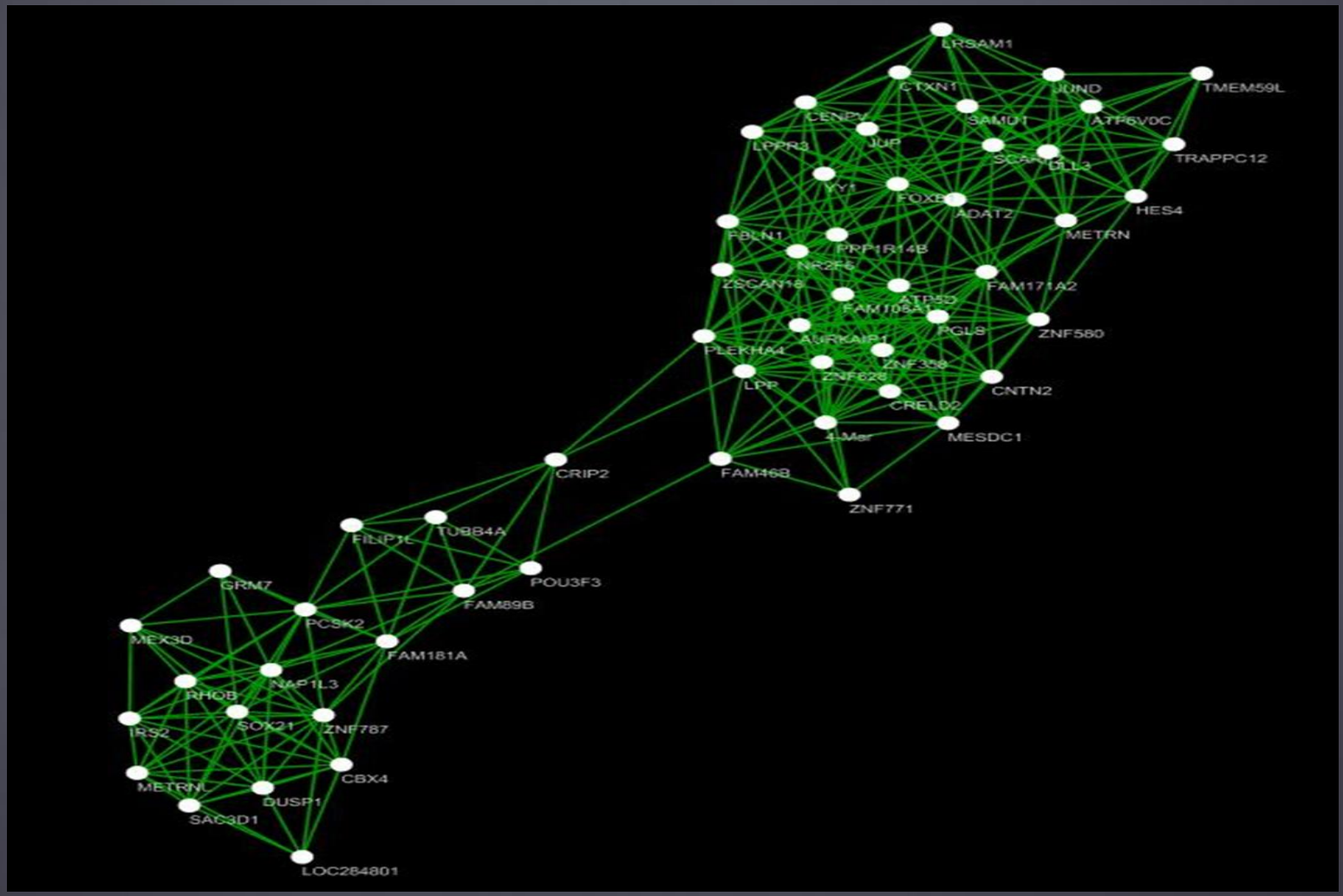


Textbook sources:

“The Human Brain – an Introduction to its Functional Anatomy”
6th edition,
author - John Nolte
Mosby/Elsevier

“Developmental Biology” 11th Edition,
authors - Scott Gilbert & Michael Barresi
Sinauer Associates Inc., Sunderland Massachusetts

Lecture 1:

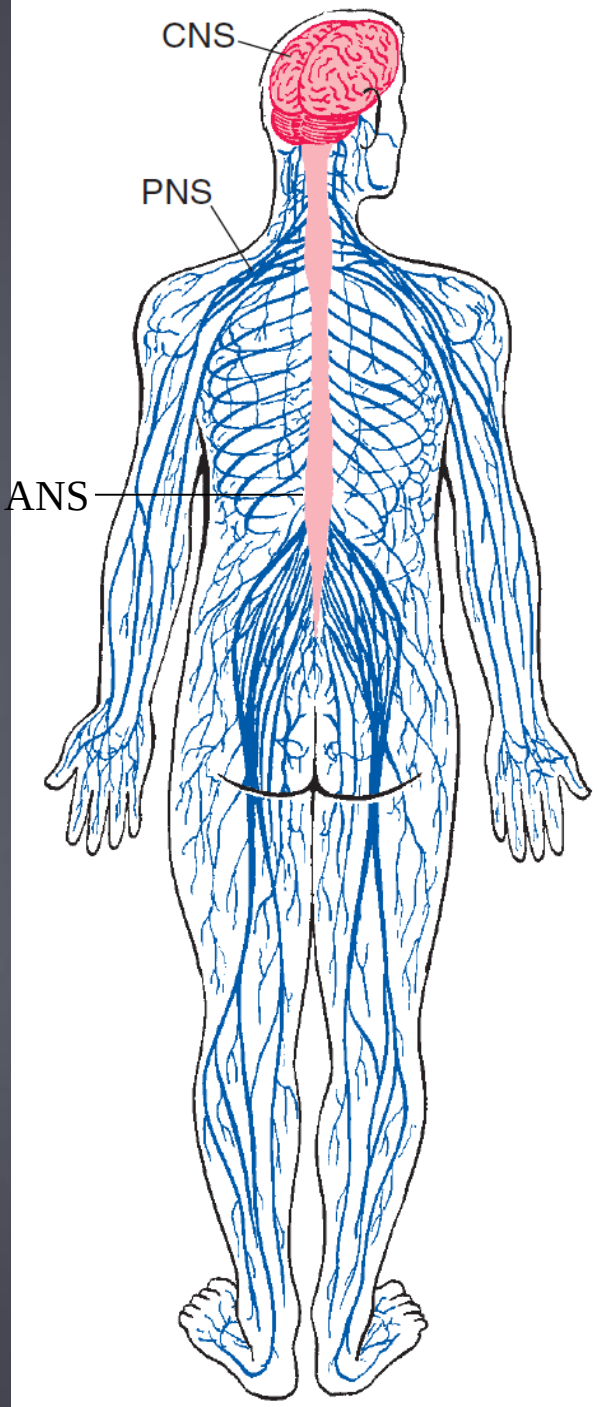
(1) Early embryogenesis, Neuro-ontology

(2) organization of adult Nervous System

(How things may go wrong early in development and what do diseases like Huntington, Parkinson, schizophrenia and cerebellar ataxia teach us how brain works)

General Organization of NS

- CNS
  - Brain
  - Spinal Cord
- PNS
  - Spinal nn.
  - Cranial nn.
- Autonomic Nervous System
  - Motor innervation
    - Cardiac and vascular mm.
    - Viscera
    - Glands
  - Sensory from organs and glands
  - Resides in both brain and spinal cord



"The Human Brain – an Introduction to its Functional Anatomy"
6th edition,author - John NoltebMosby/Elsevier

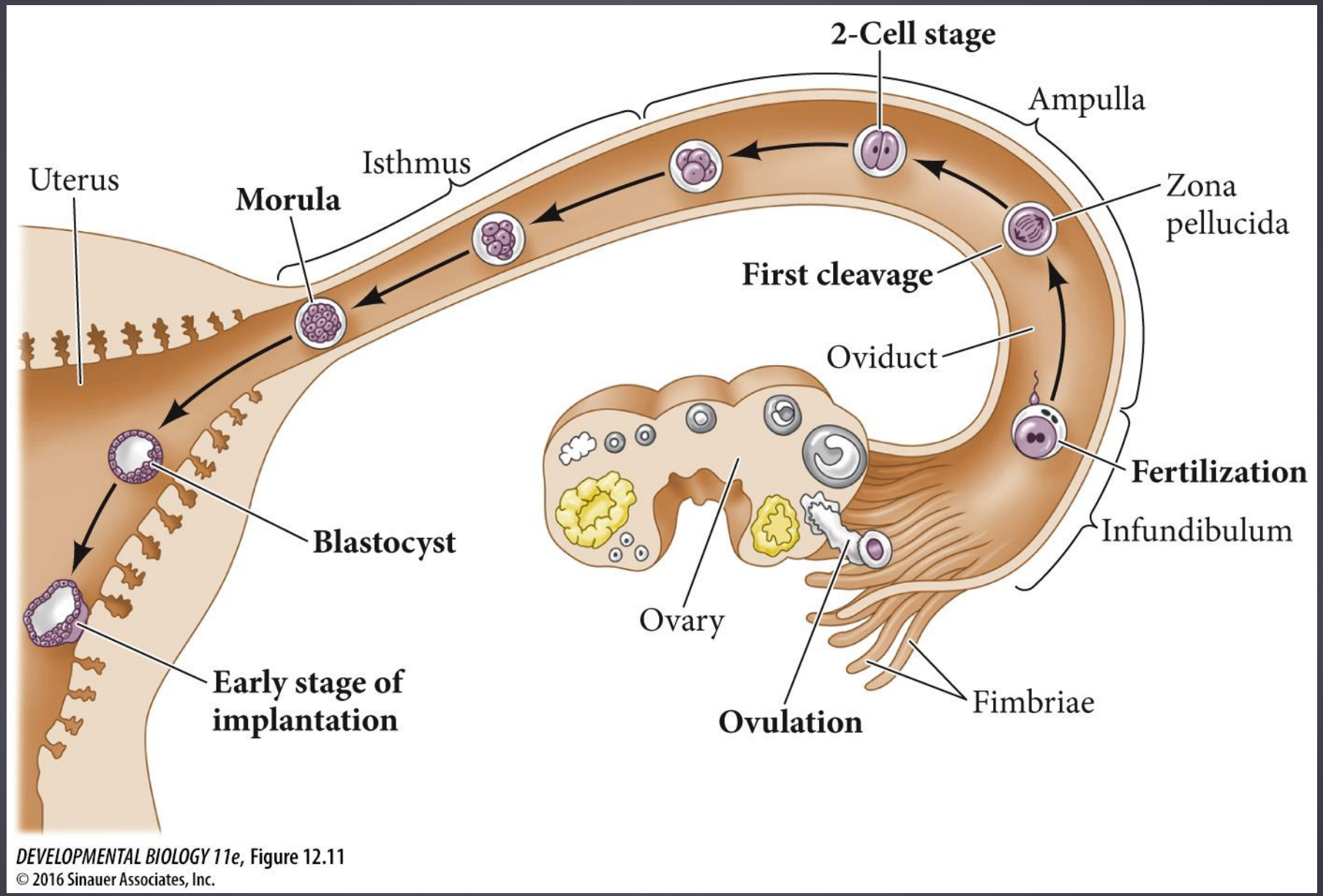
The **Central Nervous system (CNS)**

- Brain (1-3)
- Spinal cord (4)

<u>The brain is composed of</u>:

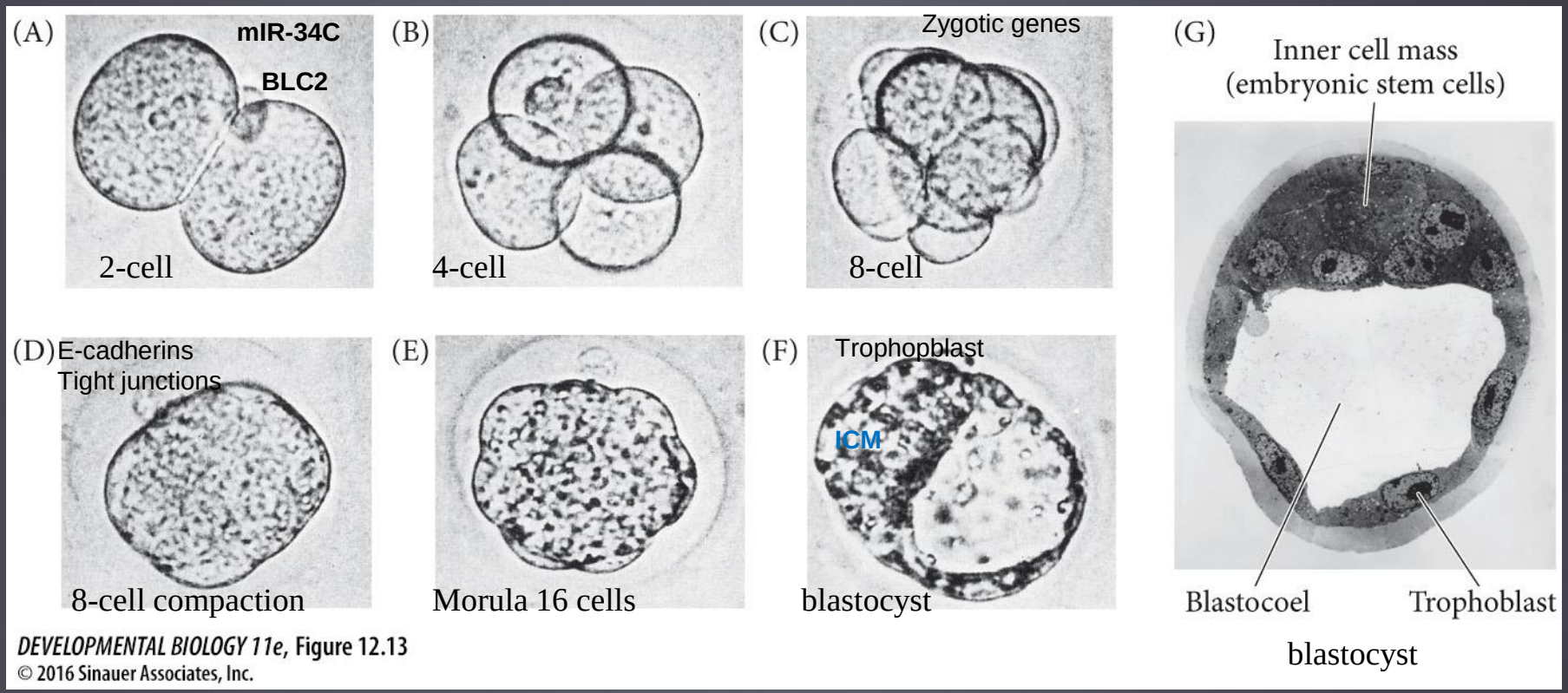
1. **Cerebrum** (cerebral hemispheres & diencephalon)
2. **Cerebellum**
3. **Brainstem (**between cerebrum and spinal cord).

Figure 12.11 Development of a human embryo from fertilization to implantation



DEVELOPMENTAL BIOLOGY 11e, Figure 12.11

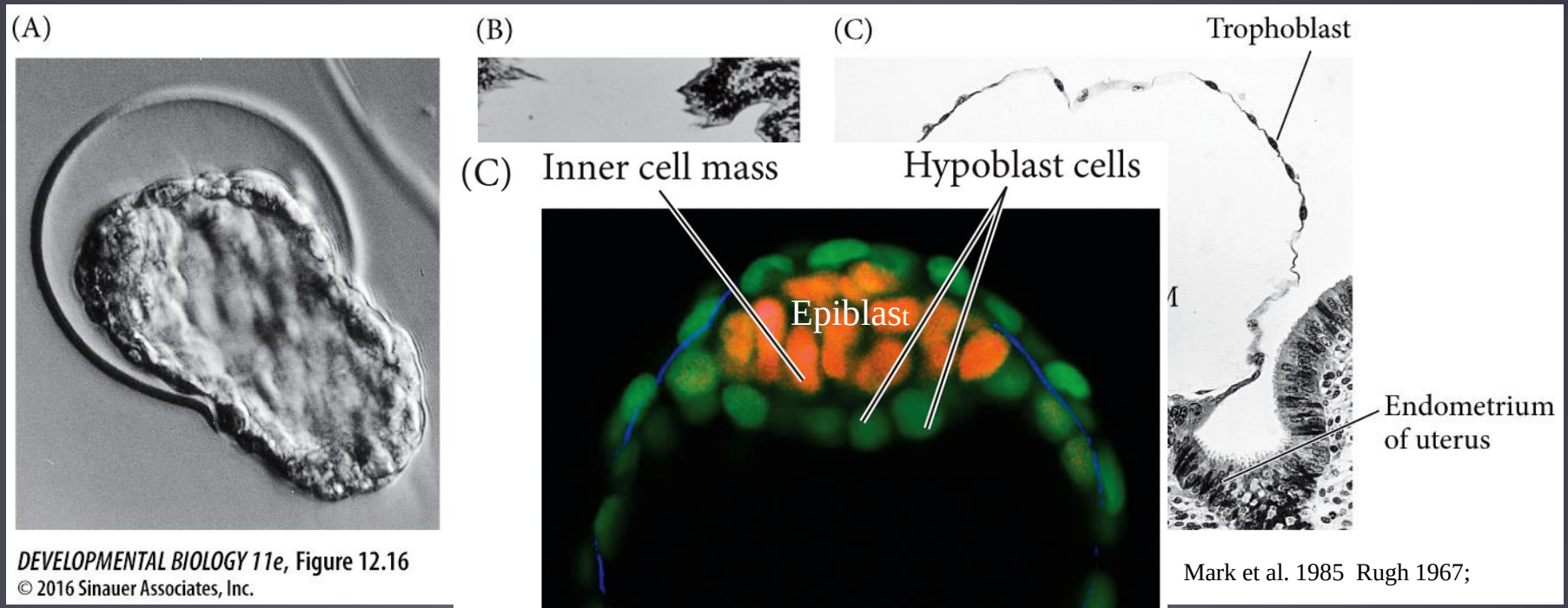
Figure 12.13 Cleavage of a single mouse embryo in vitro - (A) 2-Cell stage. (B) 4-Cell stage. (C) Early 8-cell stage. (D) Compacted 8-cell stage. (E) Morula. (F) Blastocyst. (G) Electron micrograph mouse blastocyst.



DEVELOPMENTAL BIOLOGY 11e, Figure 12.13

Piotrowska and Zernicka-Goetz 2001; Ducibella et al. 1975; Mulnard 1967,

Figure 12.16 (A) Hatching of the mouse blastocyst from the zona pellucida; (B) blastocysts entering the uterus; (C) Initial implantation of a rhesus monkey blastocyst .



DEVELOPMENTAL BIOLOGY 11e, Figure 12.16
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DEVELOPMENTAL BIOLOGY 11e, Figure 12.15 (Part 3)
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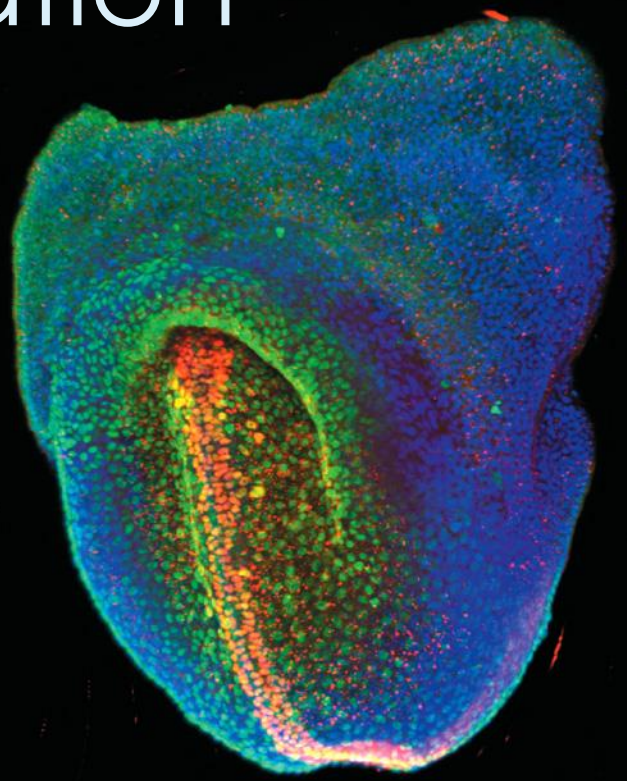
Mark et al. 1985 Rugh 1967;

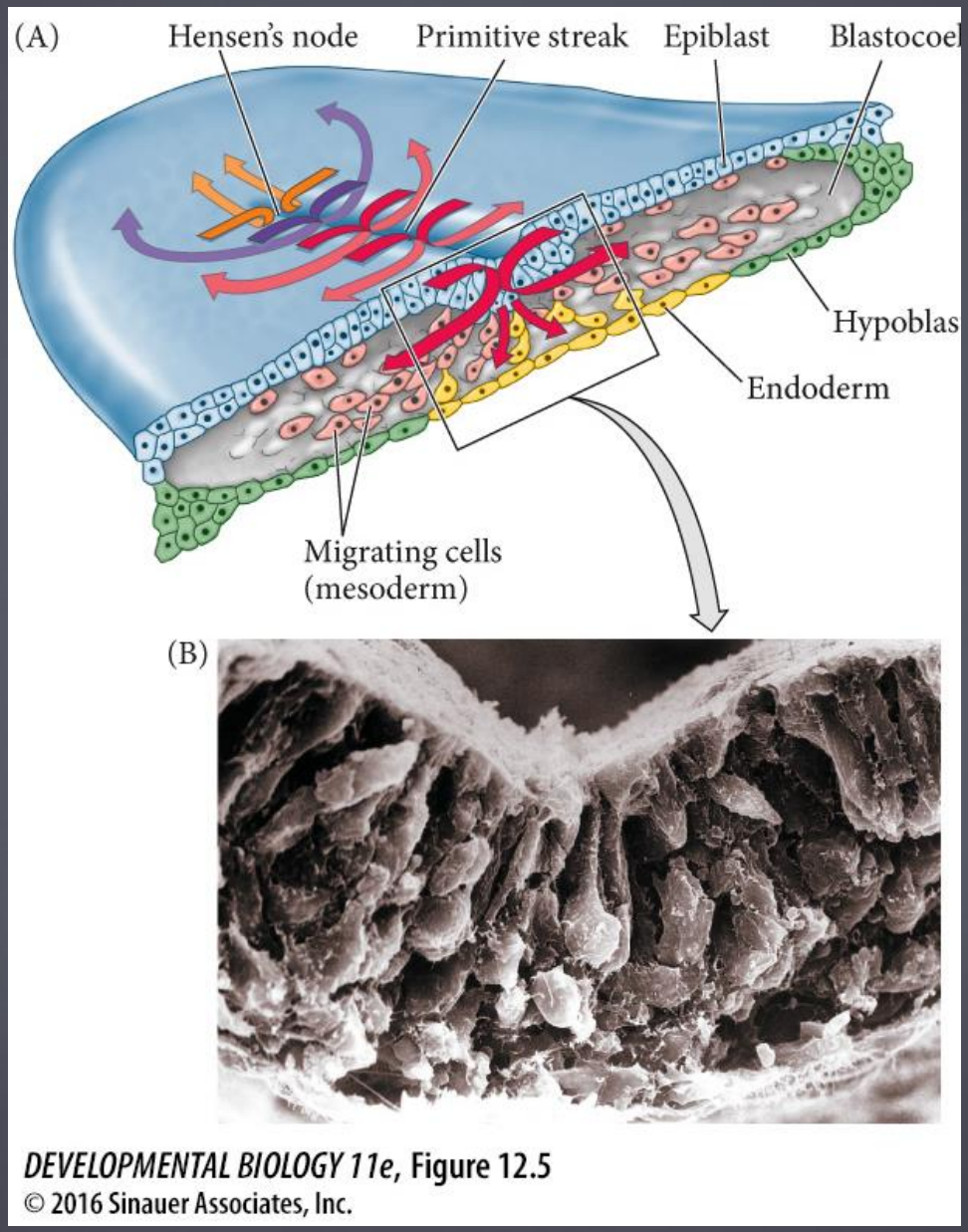
gastrulation



ectoderm,
mesoderm,
Endoderm

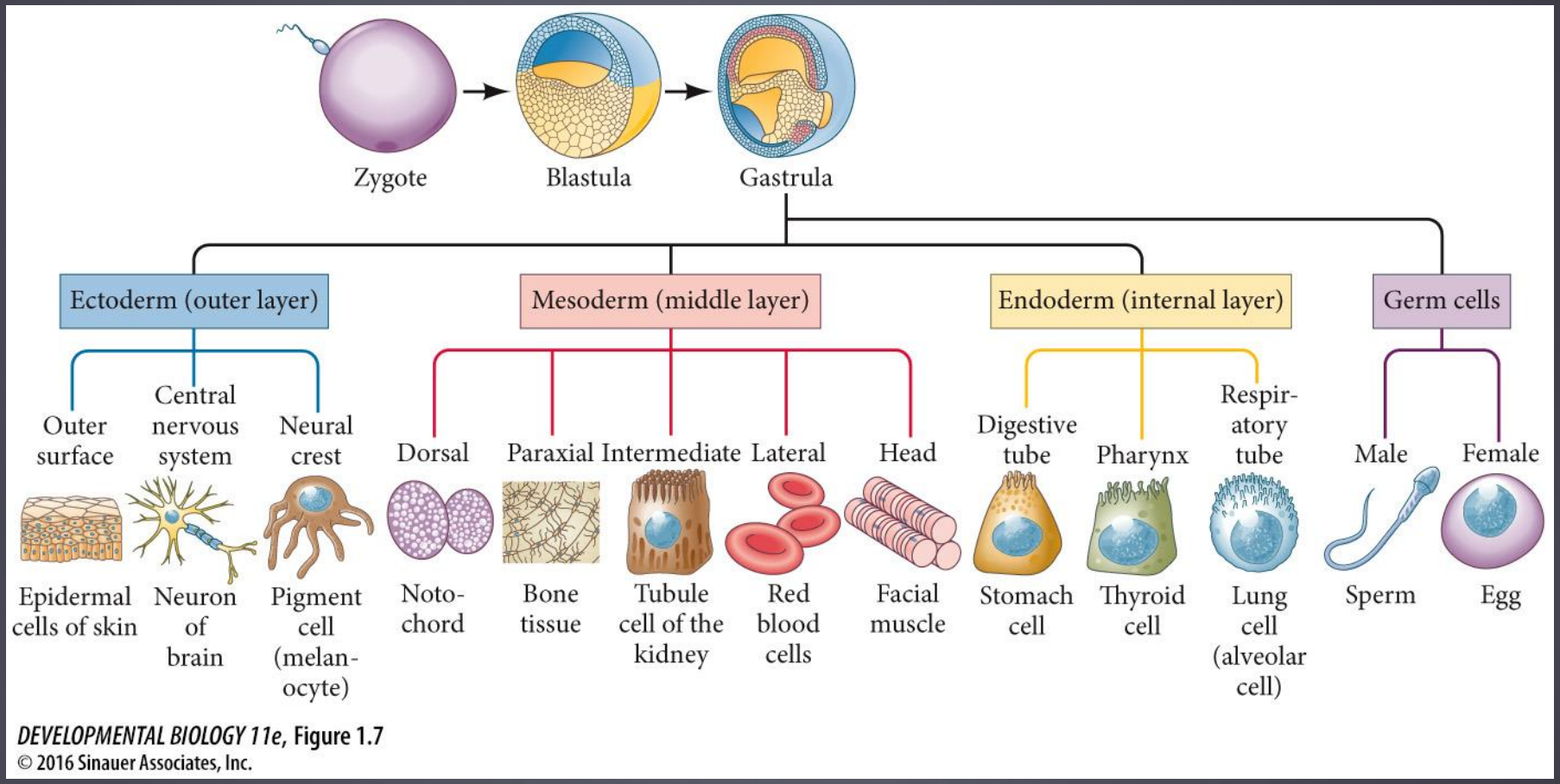
Primitive streak
Spemann organizer

Figure 12.17 Tissue and germ layer formation in the early human embryo.



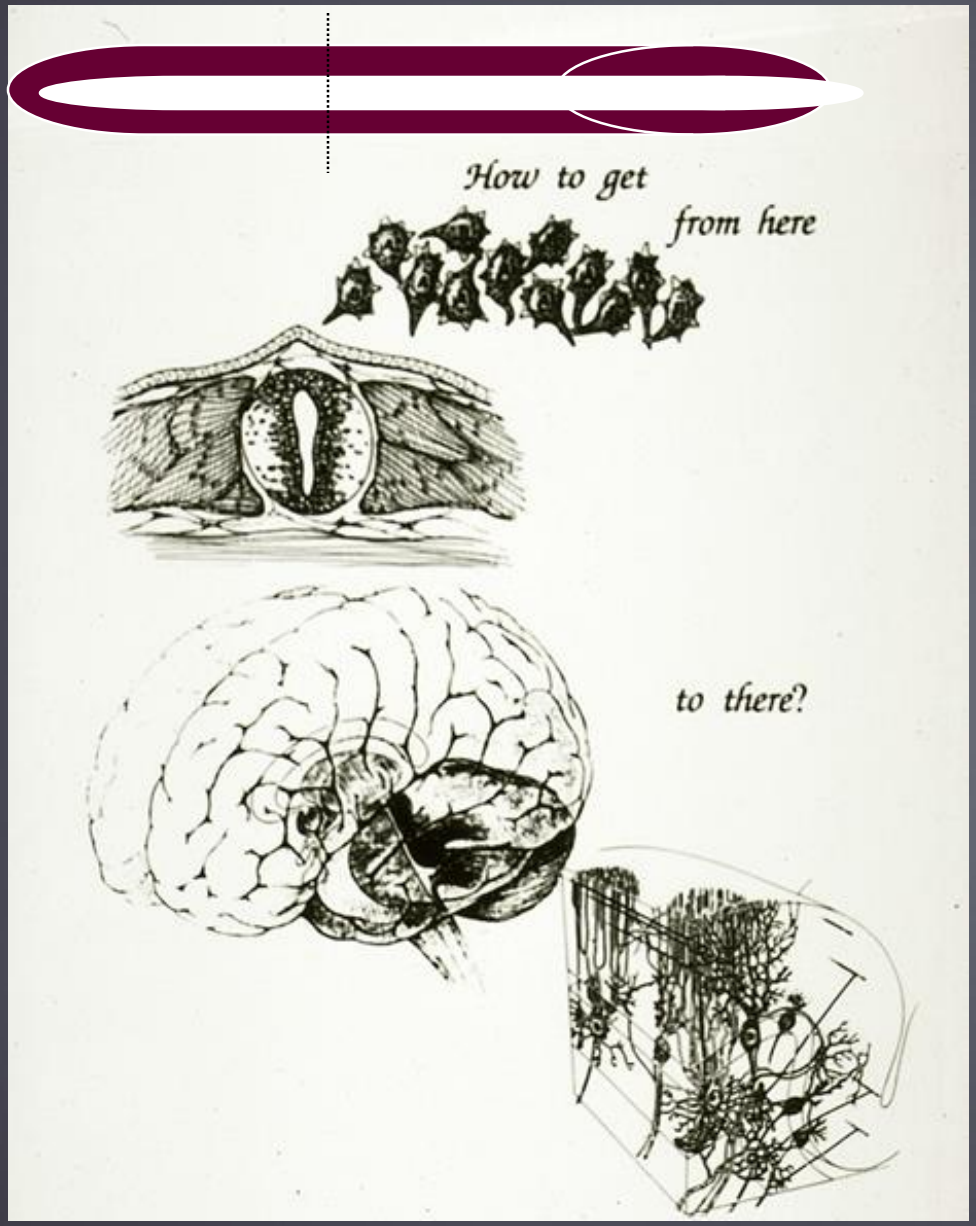
DEVELOPMENTAL BIOLOGY 11e, Figure 12.5

Figure 1.7 The dividing cells of the fertilized egg form three distinct embryonic germ layers



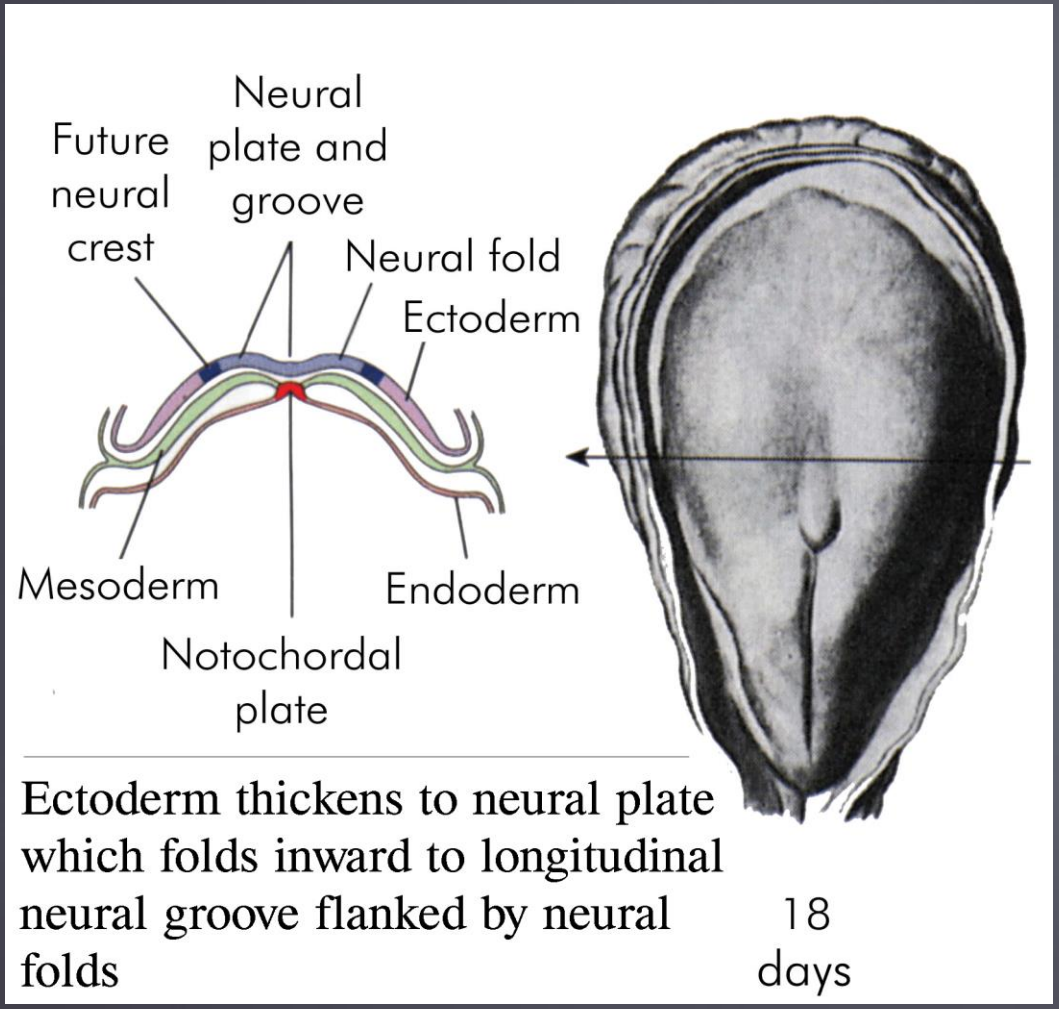
DEVELOPMENTAL BIOLOGY 11e, Figure 1.7

Development of the Nervous System



- Originates as a simple, ectoderm-derived tubular, structure.
- An understanding of CNS development helps make sense of adult organization and congenital malformations.
- Malformations also provide clues that aid in understanding normal development.

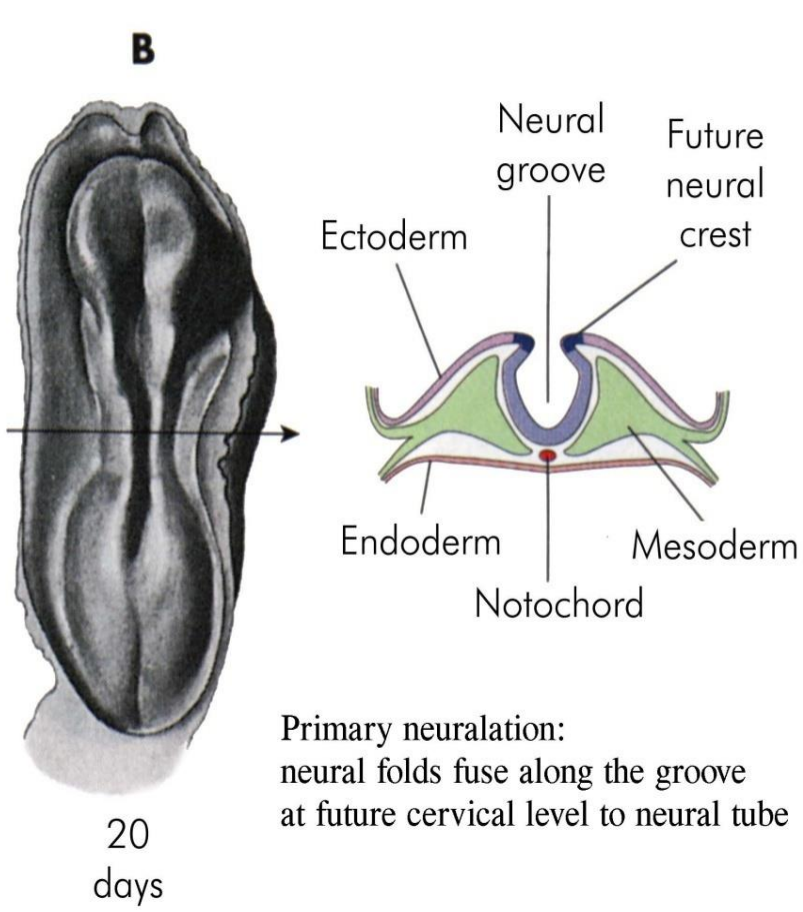
Dorsal Induction of the Neural Plate:



Ectoderm thickens to neural plate which folds inward to longitudinal neural groove flanked by neural folds

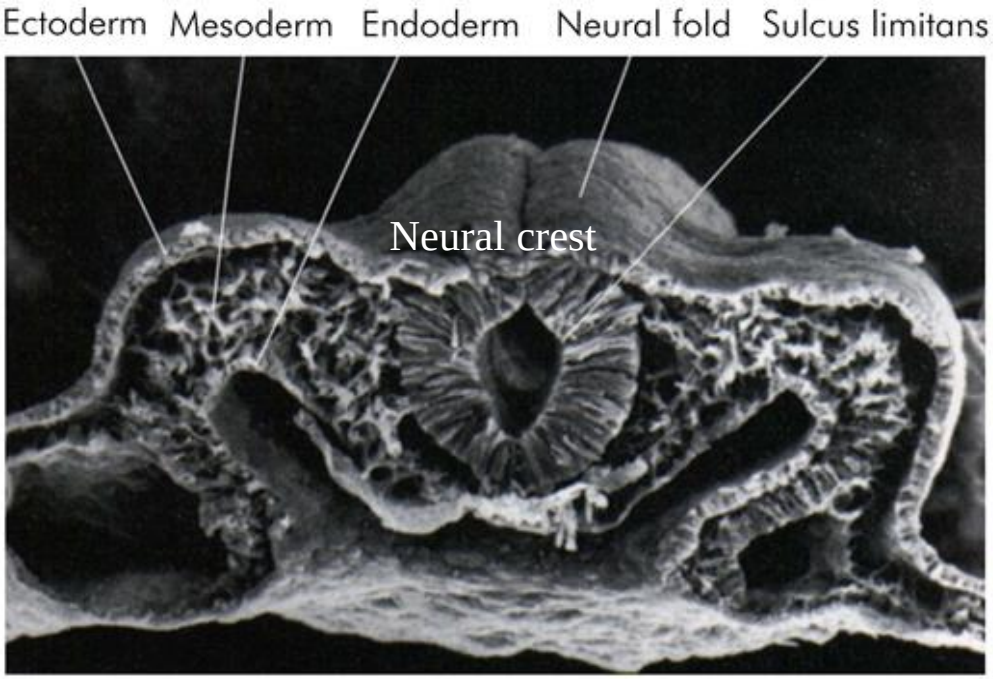
- 3rd week of development,
- **Neural plate** – induction underlying mesoderm.
- Plate folds in, forming **neural groove** flanked by **neural folds** .
- Under plate: specialized region of mesoderm, **notochord,** develops.
- Notochord stimulates further development of neural tube (ventral induction).

Primary neurulation - Formation of neural tube



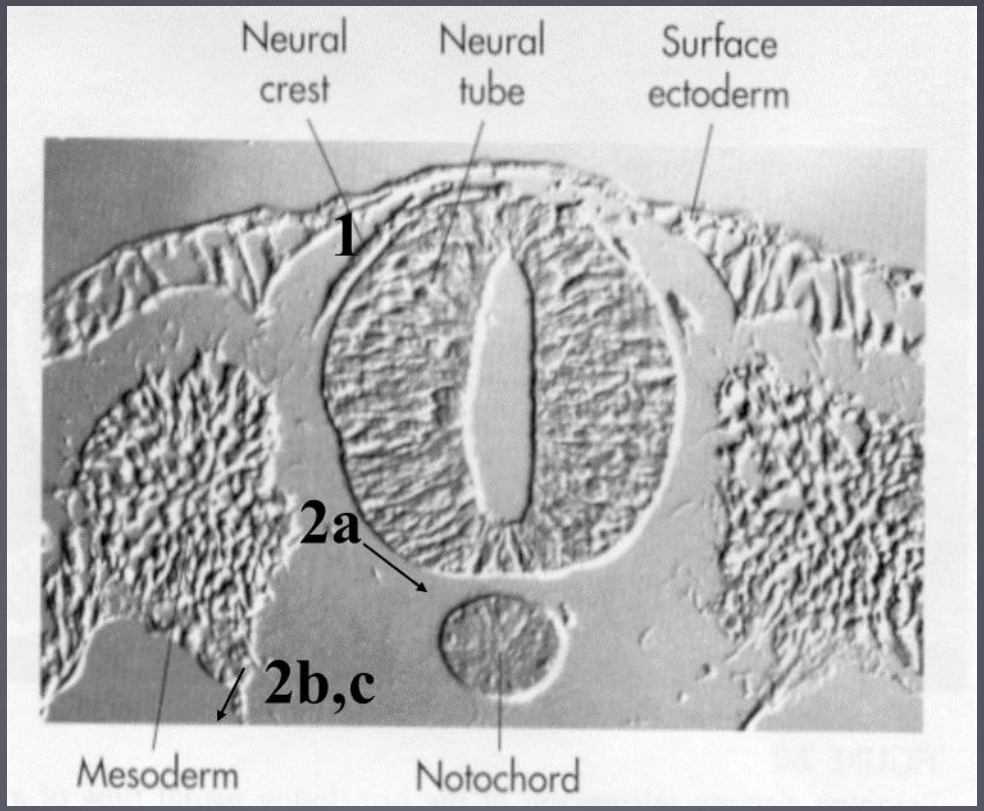
Primary neuralation:
neural folds fuse along the groove at future cervical level to neural tube

closing n. tube separates from ectoderm and becomes enclosed within the body



CHORDAMESODERM:

NEURAL CREST GIVES RISE TO THE PNS



Cells from the **crest** of each neural fold separate from the tube. These **neural crest cells** develop into the Peripheral somatic Nervous System (PNS 1) and peripheral Autonomic Nervous System ANS (2):

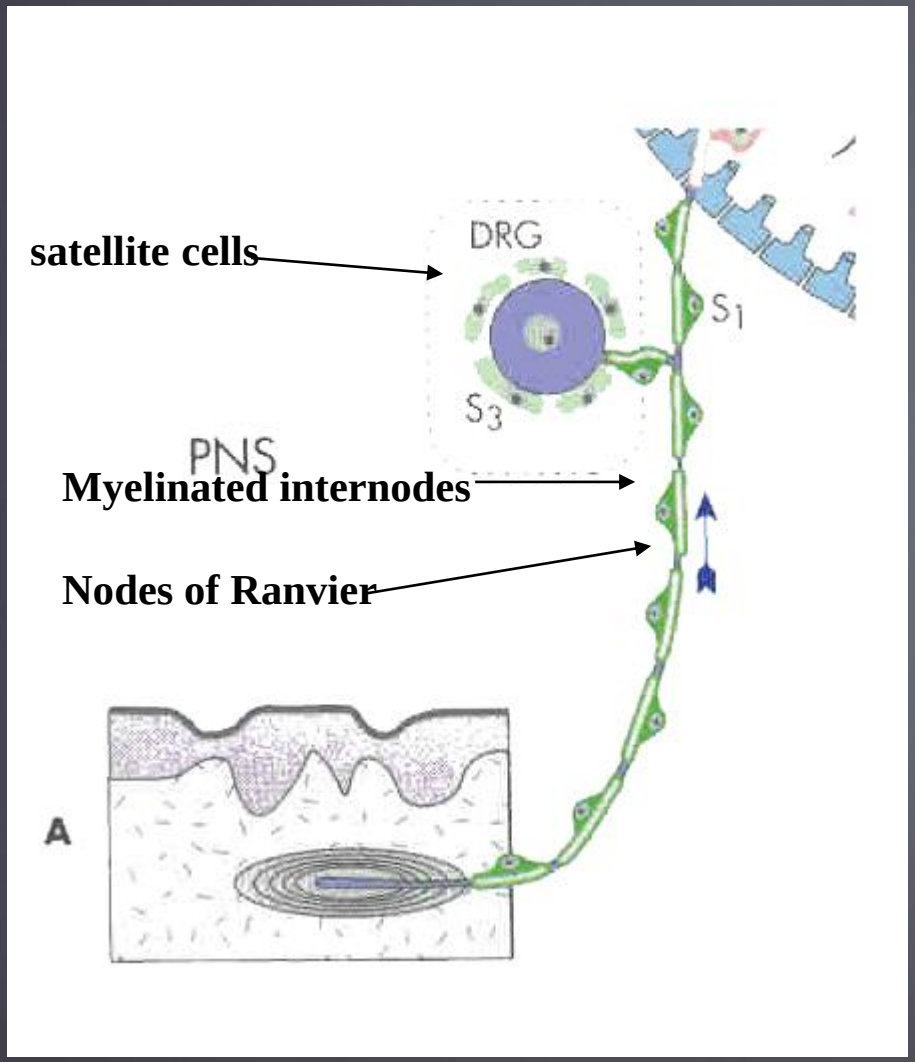
(1) sensory neurons of the spinal cord,

(2) postganglionic autonomic neurons (a) sympathetic, (b) parasympathetic, (c) cells in adrenal medulla

(3) Schwann cells (PNS glia)

(4) satellite cells of the PNS.

Schwann Cells Are the Principal PNS Glial Cells

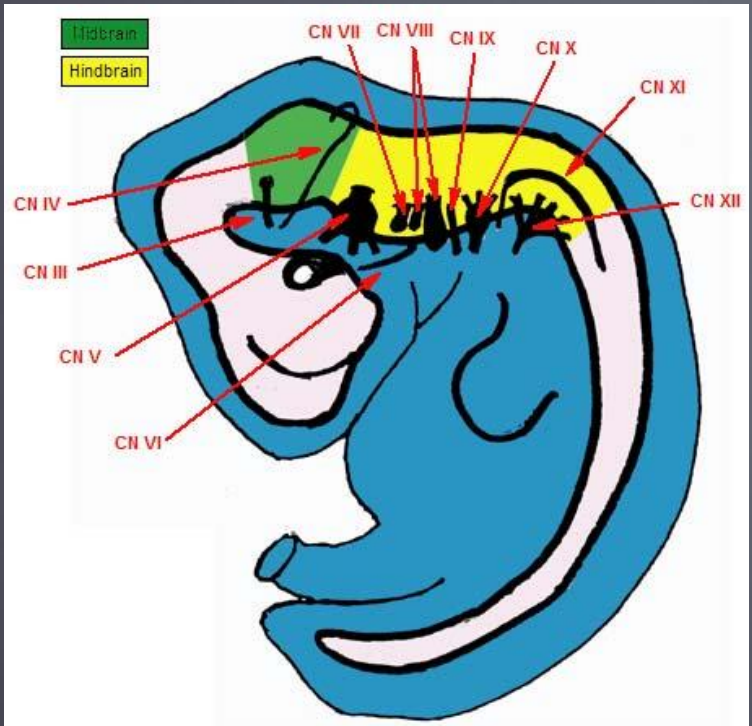


- Various supporting roles
- Some flattened SCHWANN Cells (**S_3 satellite cells)** surround neuronal cell bodies in PNS ganglia
- Most (**S_1**), **envelop axons,** some form **myelin sheath**
  - organized into myelinated internodes (0.2-2 mm)
  - separated by gaps (0.001 mm) in the myelin called nodes of Ranvier
- In image, axon is surrounded by processes of Schwann cells

Secondary Neural Crest

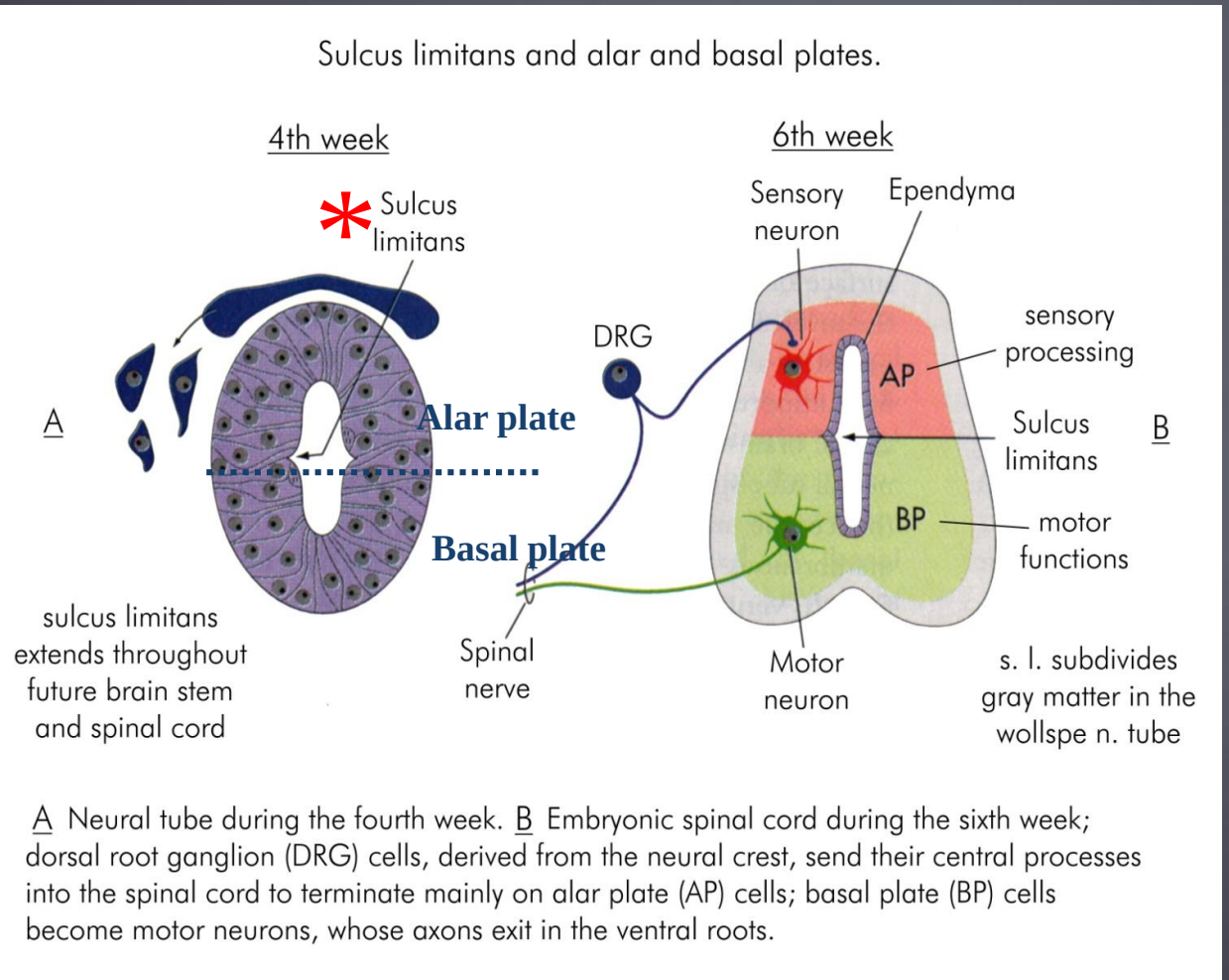
The neural tube induces thickening of the cranial epithelium (**placodes**) that generate **additional neural crest cells** giving rise to:

(1) some **cranial nerves (sensory: V,VII,VIII,IX,X**)
(2) olfactory epithelium,
(3) lens in the eye,
(4) hair cells of the inner ear.



8-10mm: In embryos at 5/6 weeks all cranial nerves are recognizable except for olfactory and optic. Sensory nerves have conspicuous ganglia near the brain the pure motor cranial nerves (III, IV, VI, and XII) have no external ganglia.

The Sulcus Limitans Separates Sensory and Motor Areas of the Spinal Cord and Brainstem



A Neural tube during the fourth week. B Embryonic spinal cord during the sixth week; dorsal root ganglion (DRG) cells, derived from the neural crest, send their central processes into the spinal cord to terminate mainly on alar plate (AP) cells; basal plate (BP) cells become motor neurons, whose axons exit in the ventral roots.

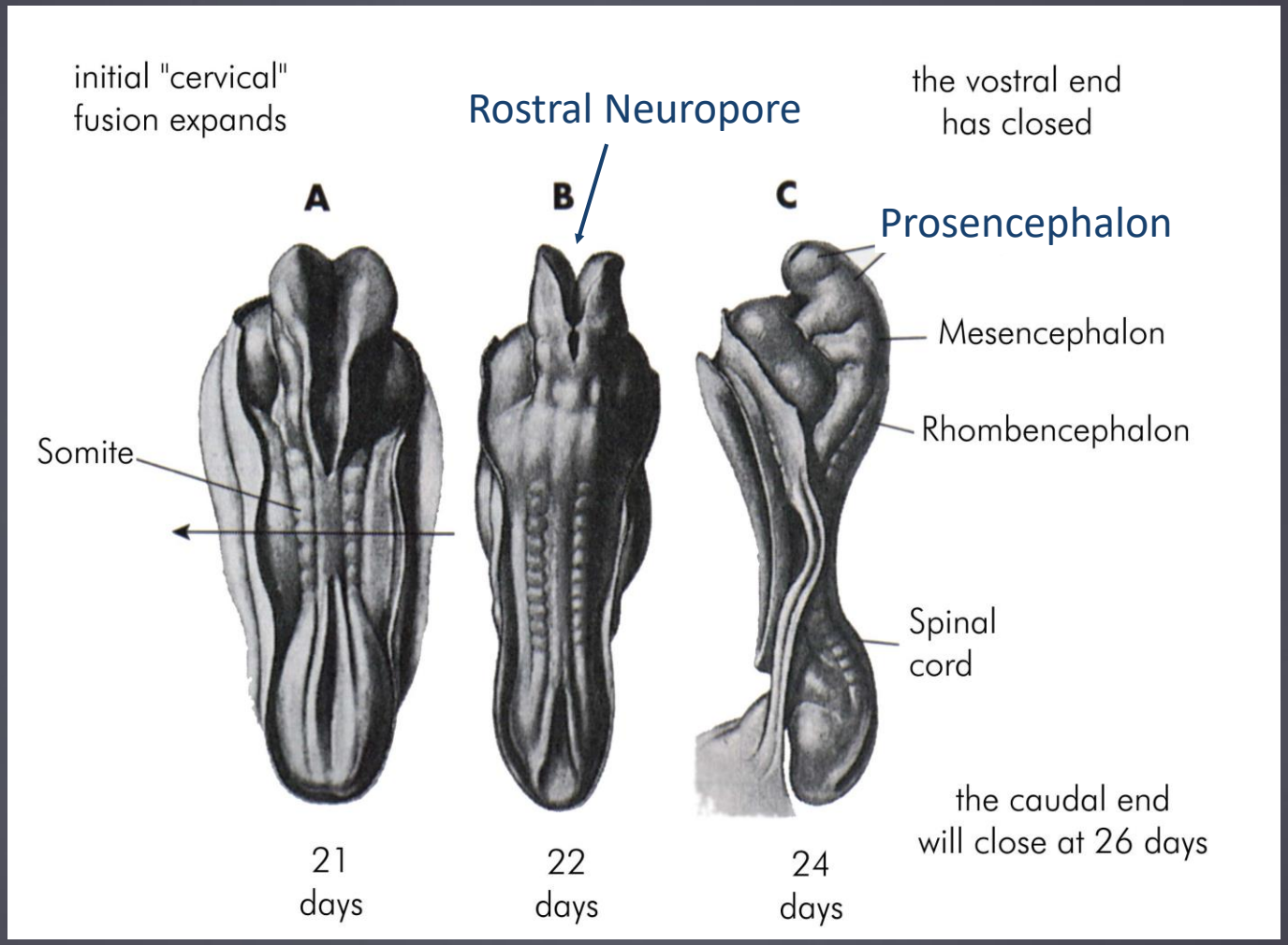
4th week:

Sulcus limitans - a longitudinal groove in the lateral wall of the neural tube appears and subdivides the gray matter in the walls into:

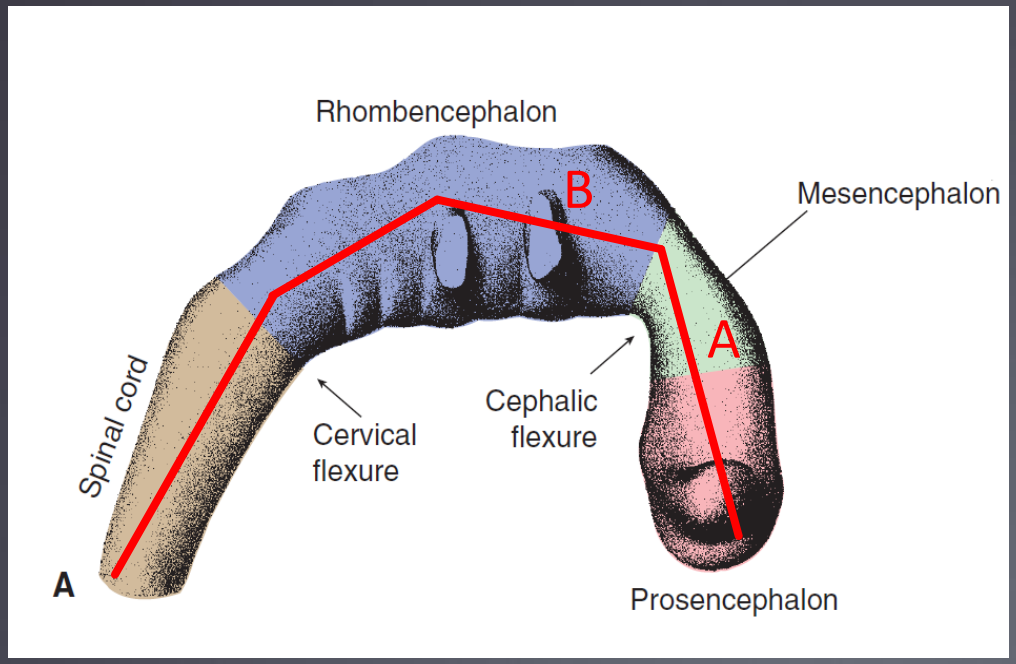
(1) **alar** (dorsal) **plate** (derivatives are primarily involved in sensory processing), and

(2) **basal** (ventral) **plate (**home for motor neurons).

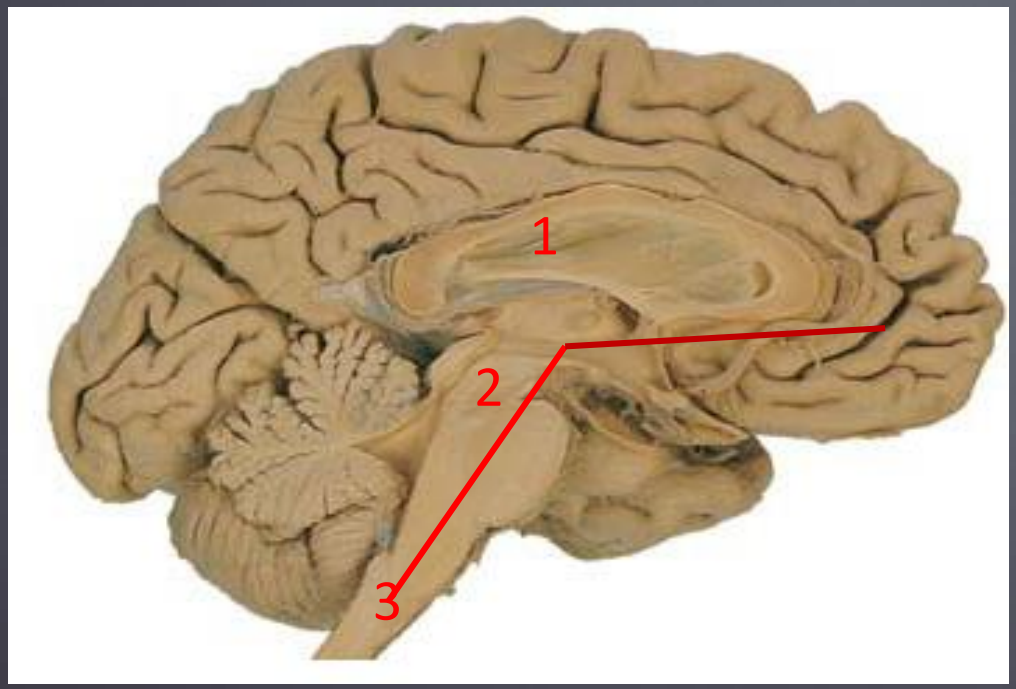
During the fourth week neural tube closes completely and develops a series of bulges and flexures



Secondary Neurulation –mass of neuromesodermal cells develops in closed caudal end (Sacral s. Cord) with a 2ndary cavity to form sacral s. cord and adjacent tissues.



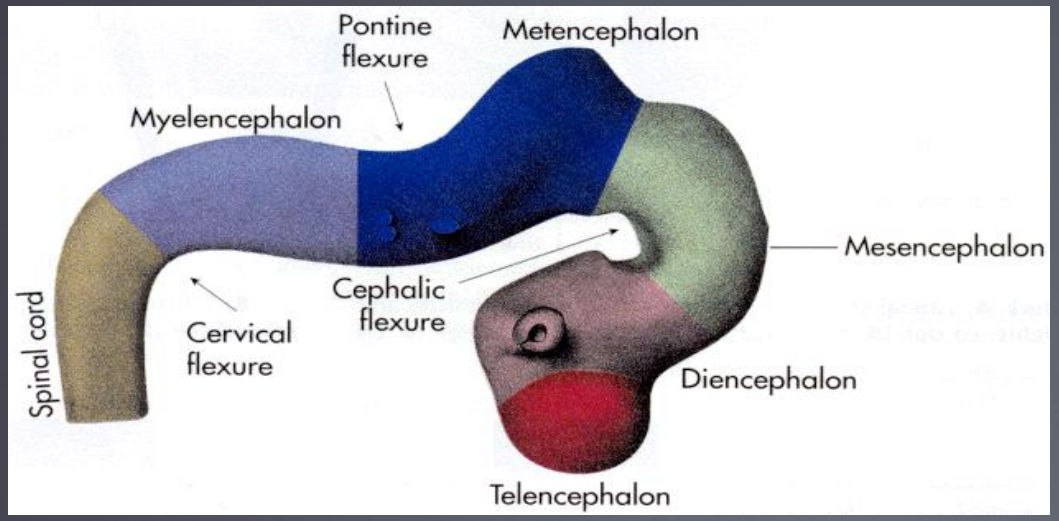
End of the 4th week - the 3 bulges become **primary vesicles:**

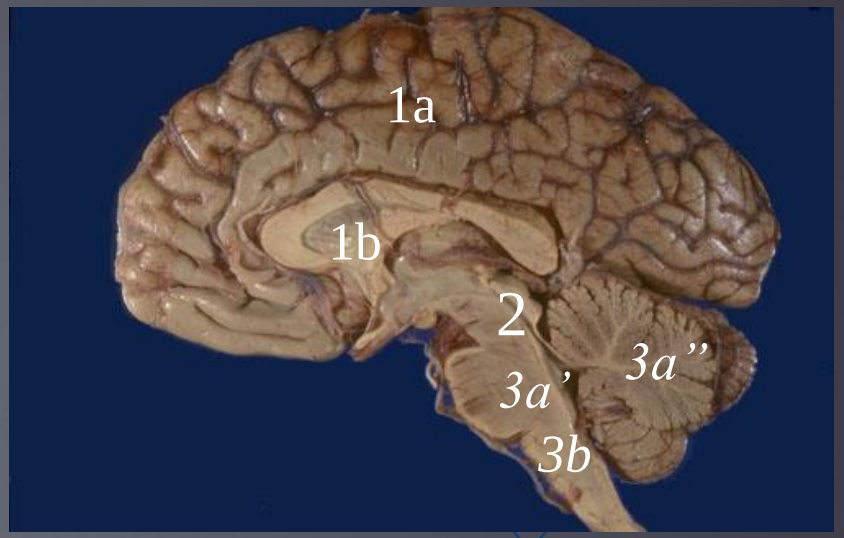


1. **Prosencephalon -** *forebrain*
2. **Mesencephalon-** *midbrain*
3. **Rhombencephalon -** *hindbrain*

Secondary Vesicles - 5th week

Formation of brain vesicles "ventral induction" by **notochord** **(Which also induces the allar and basal plates)**





Medial (sagittal)

1) Prosencephalon

a. Telencephalon ("end brain")

- Cerebral hemispheres

b. Diencephalon ("in-between-brain)

- Thalamus, hypothalamus, neural portion of eye

Both comprise the forebrain (cerebrum)

2) Mesencephalon remains undivided

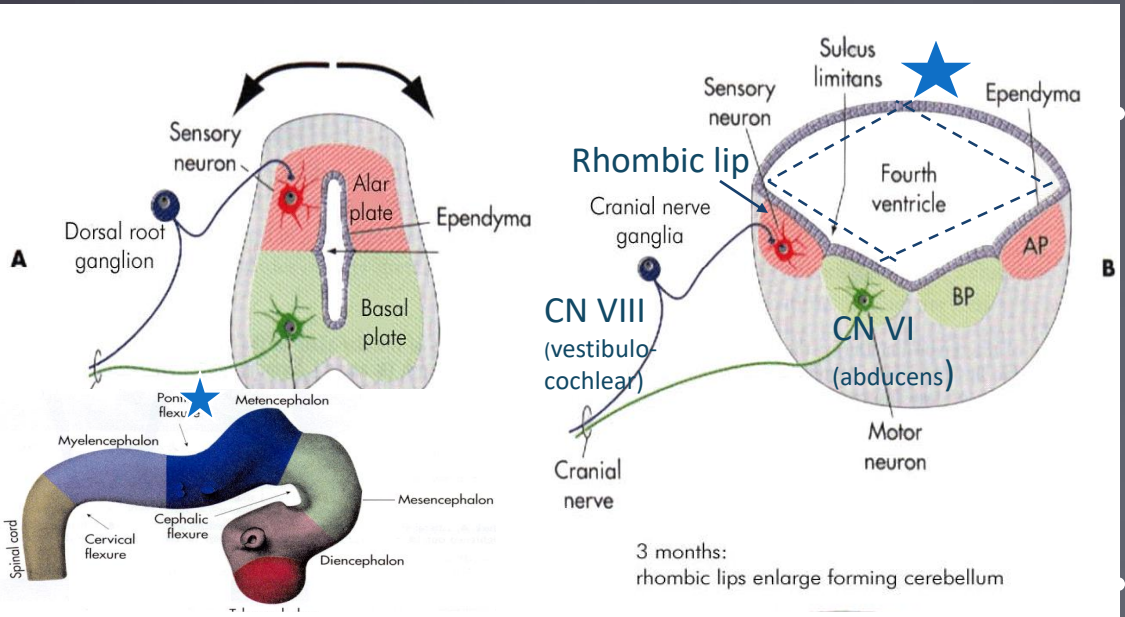
3) Rhombencephalon gives rise to:

a. Metencephalon (pons' + cerebellum)"

b. Myelencephalon (medulla)

B+C comprise the brain stem

5th week - transient **pontine flexure** develops that shapes the central cavity – future **4th ventricle**

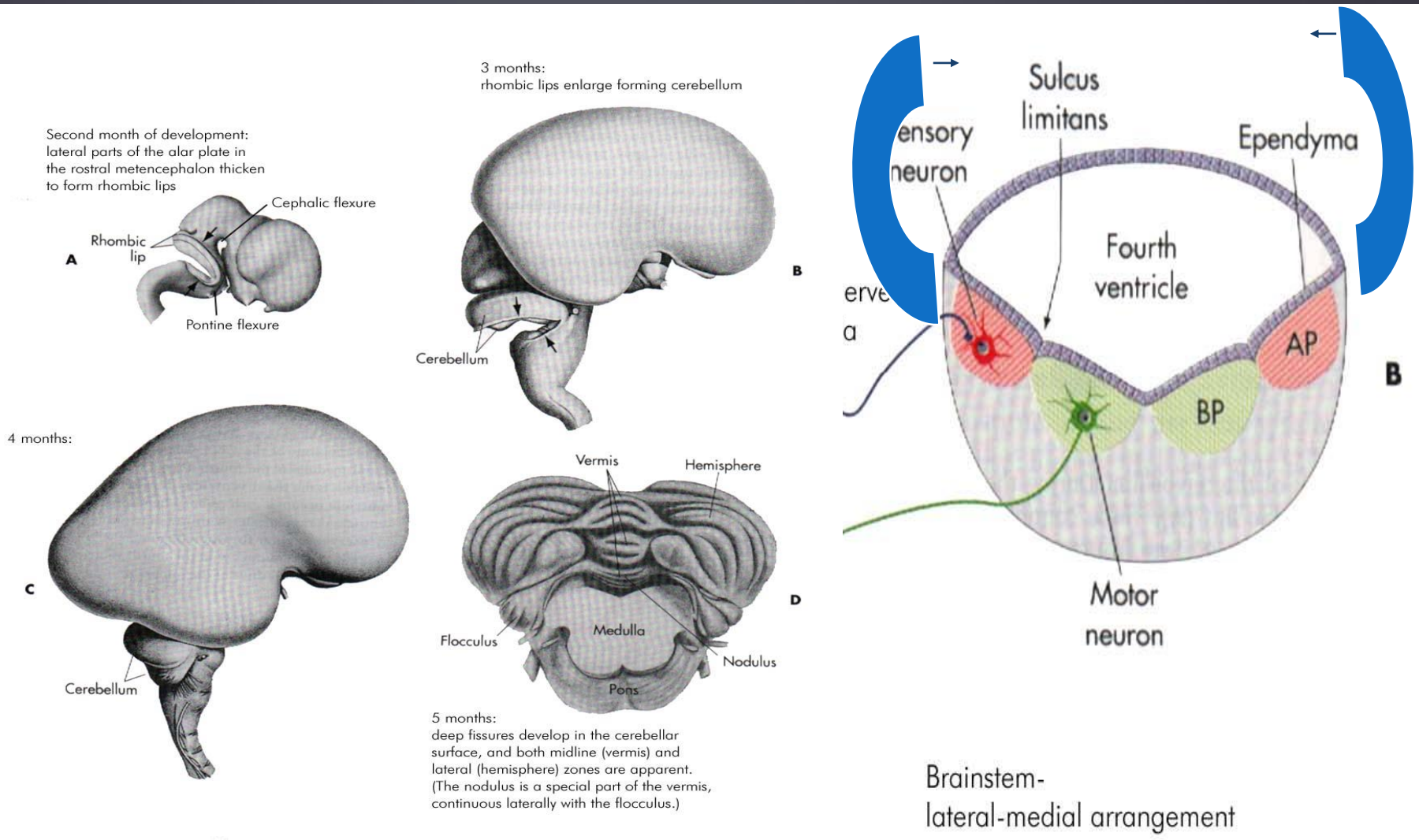


As pontine flexure develops on dorsal surface of metencephalon, side walls of tube spread apart to form rhomboidal cavity (covered with thin velum).

Alar (sensory) and **basal** (motor) plates and the **sulcus limitans** lie on the floor.

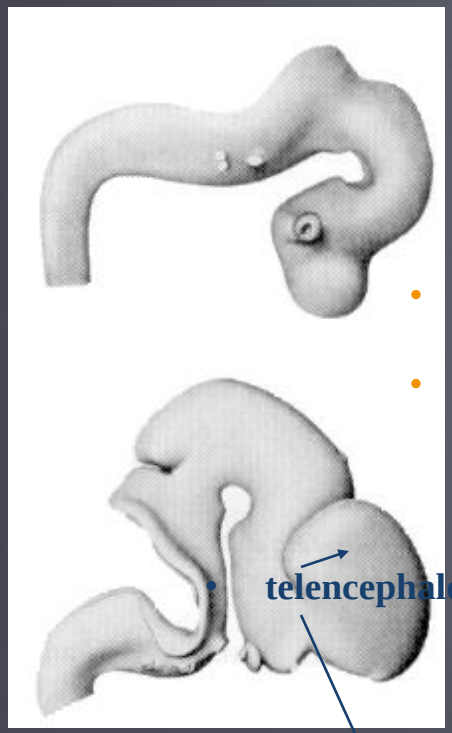
Localization of some cranial nerves reflects this arrangement.

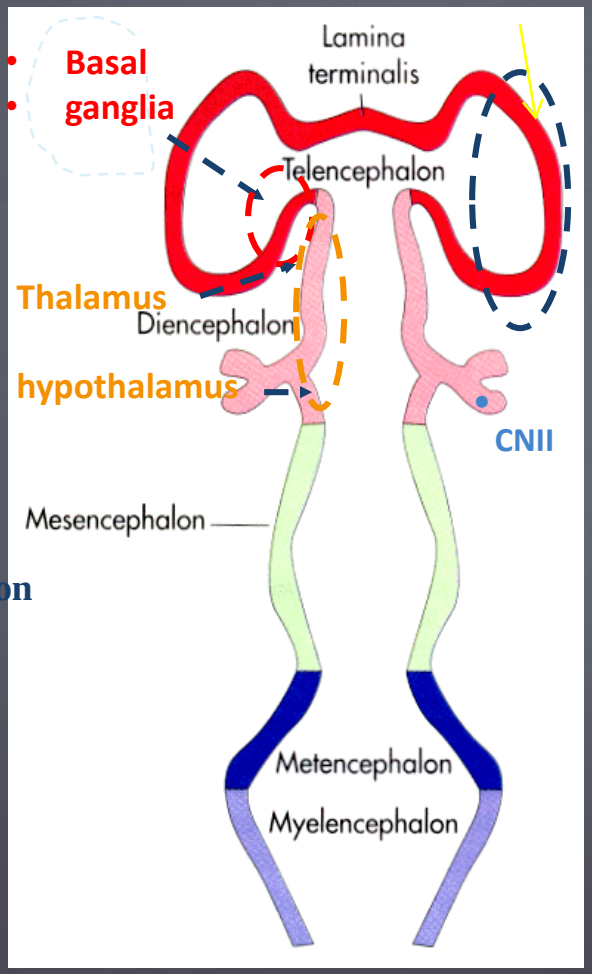
Development of Cerebellum initiated by Pontine Flexure



Lateral portions of the alar plate form thick **rhombic lips** that become the **cerebellum**.

- Growth of Telencephalon overshadows the rest of the Human Brain





- Telencephalon: 2 swellings in prosencephalon
- Lateral wall → Hemispheres
- Lamina Terminalis
- Basal telencephic wall → Basal Ganglia (basal nuclei)
- Diencephalon walls → Thalamus, Hypothalamus (separated by hypothalamic sulcus and remained fused) and CN II

"Fusion between telencephalic Basal Ganglia (BG), diencephalic Thalamus (T) and Hypothalamus (H) with continued growth of cerebral hemispheres"

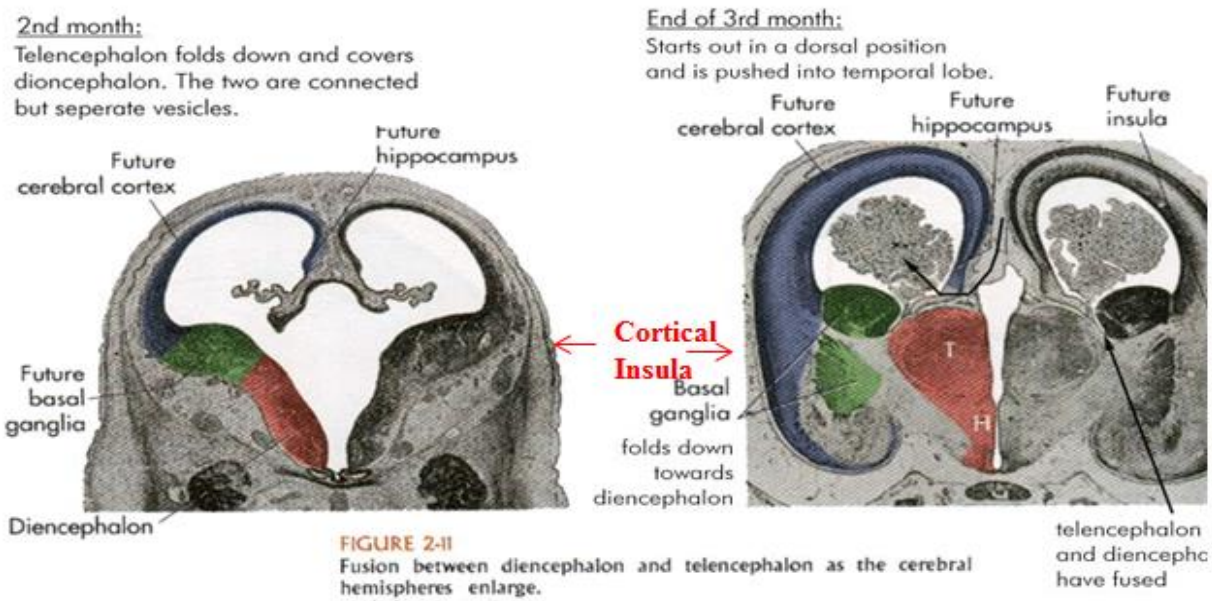
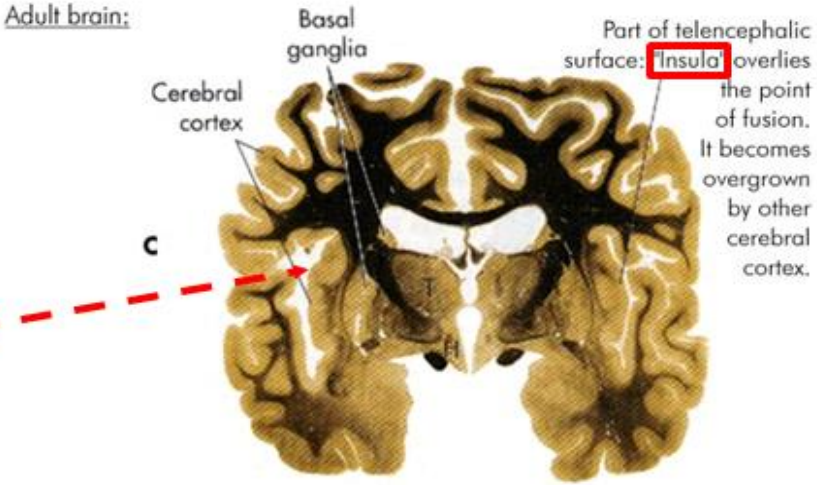
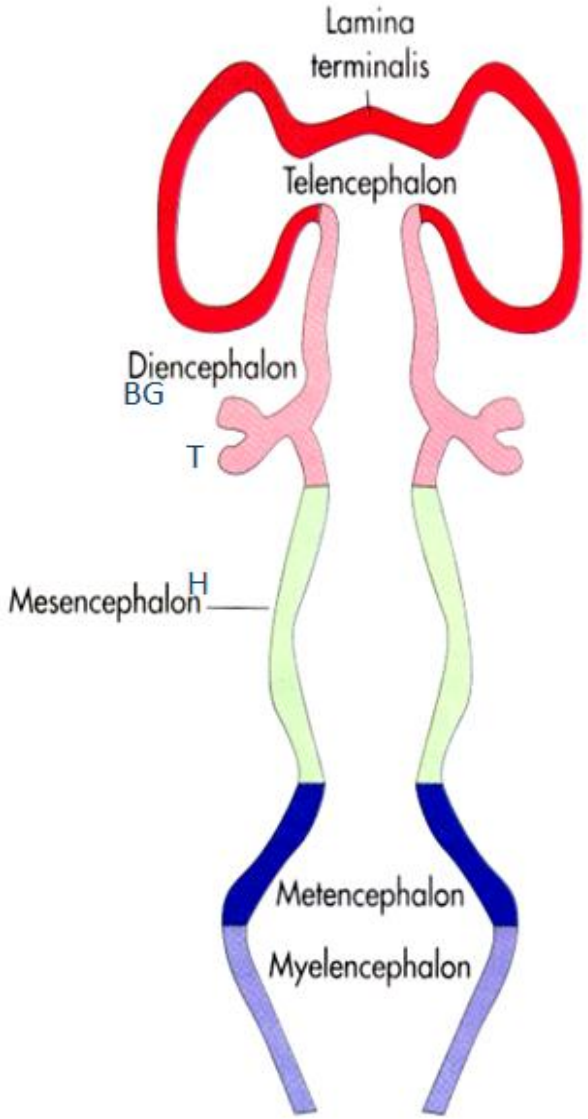


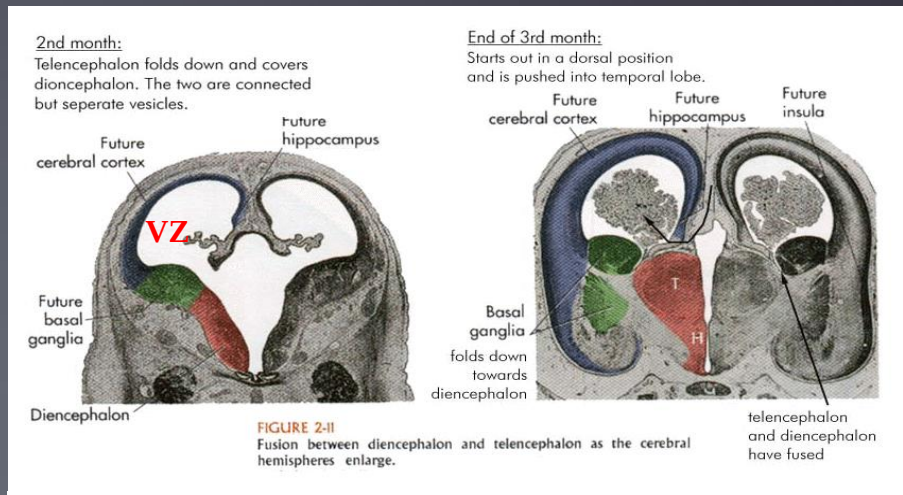
FIGURE 2-11
Fusion between diencephalon and telencephalon as the cerebral hemispheres enlarge.

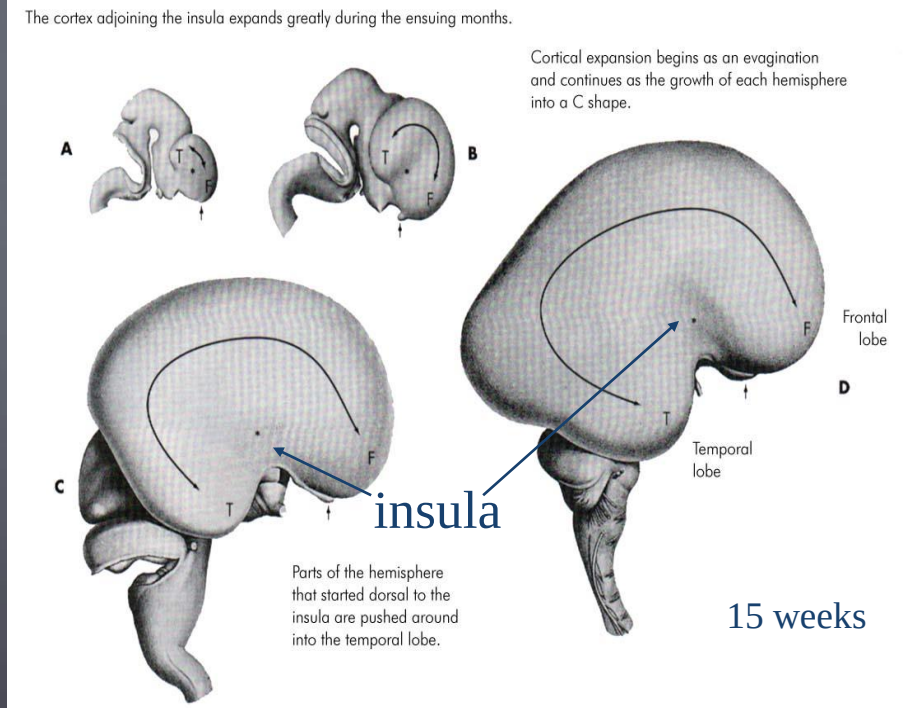




Proliferation/Migration of neurons and glial cells

- Growth of the cerebral cortex, cerebellum and other parts of the CNS:
  - Proliferation of stem cells,
  - migration and differentiation of neuronal and glial cells.
- Most neuronal production/migration - 3rd through 5th month
- Cells migrate from ventricular zone (VZ) to cortex (surface dorsal to insula)





The cortex adjoining the insula expands greatly during the ensuing months hiding the insula completely from view

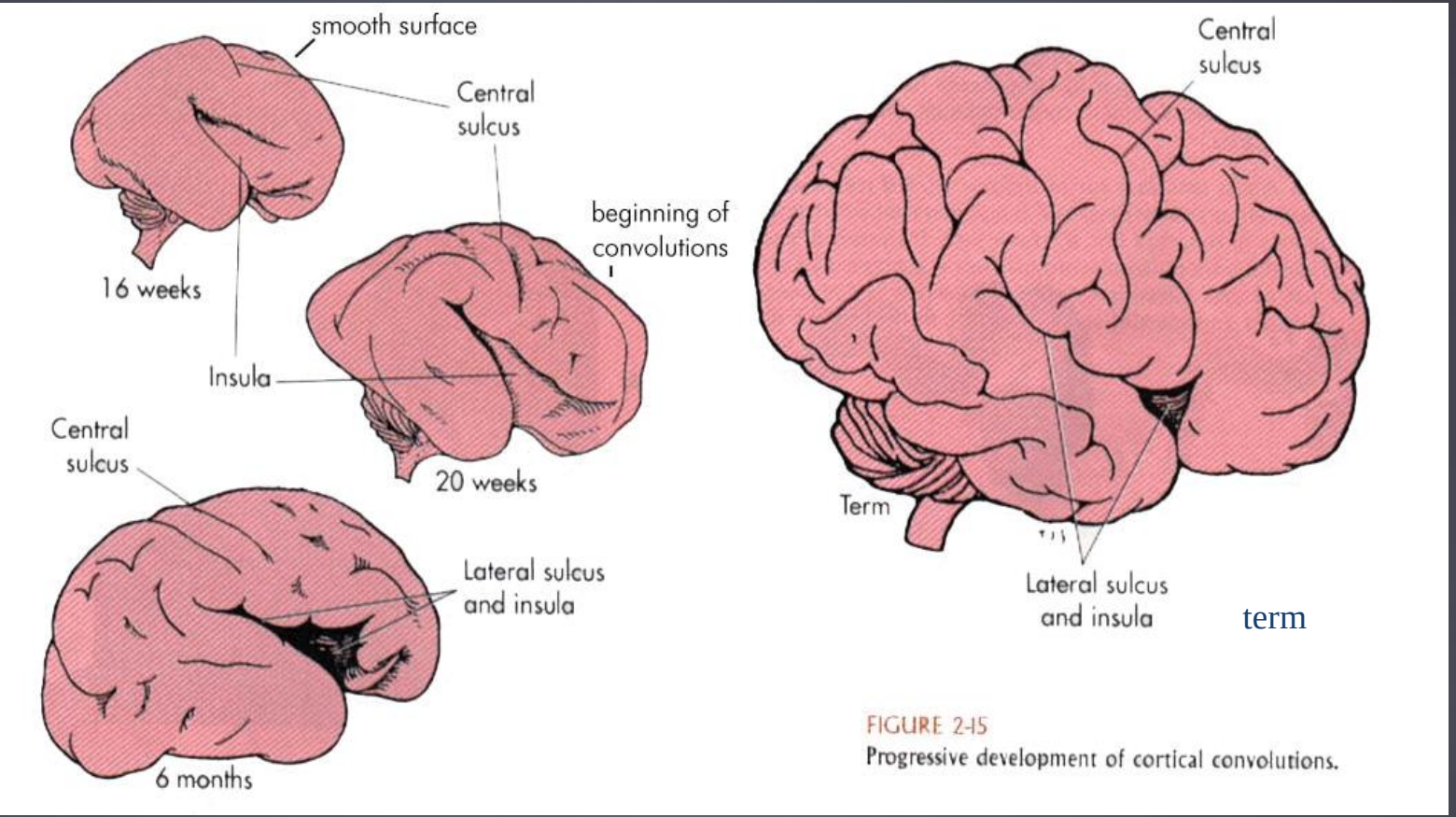
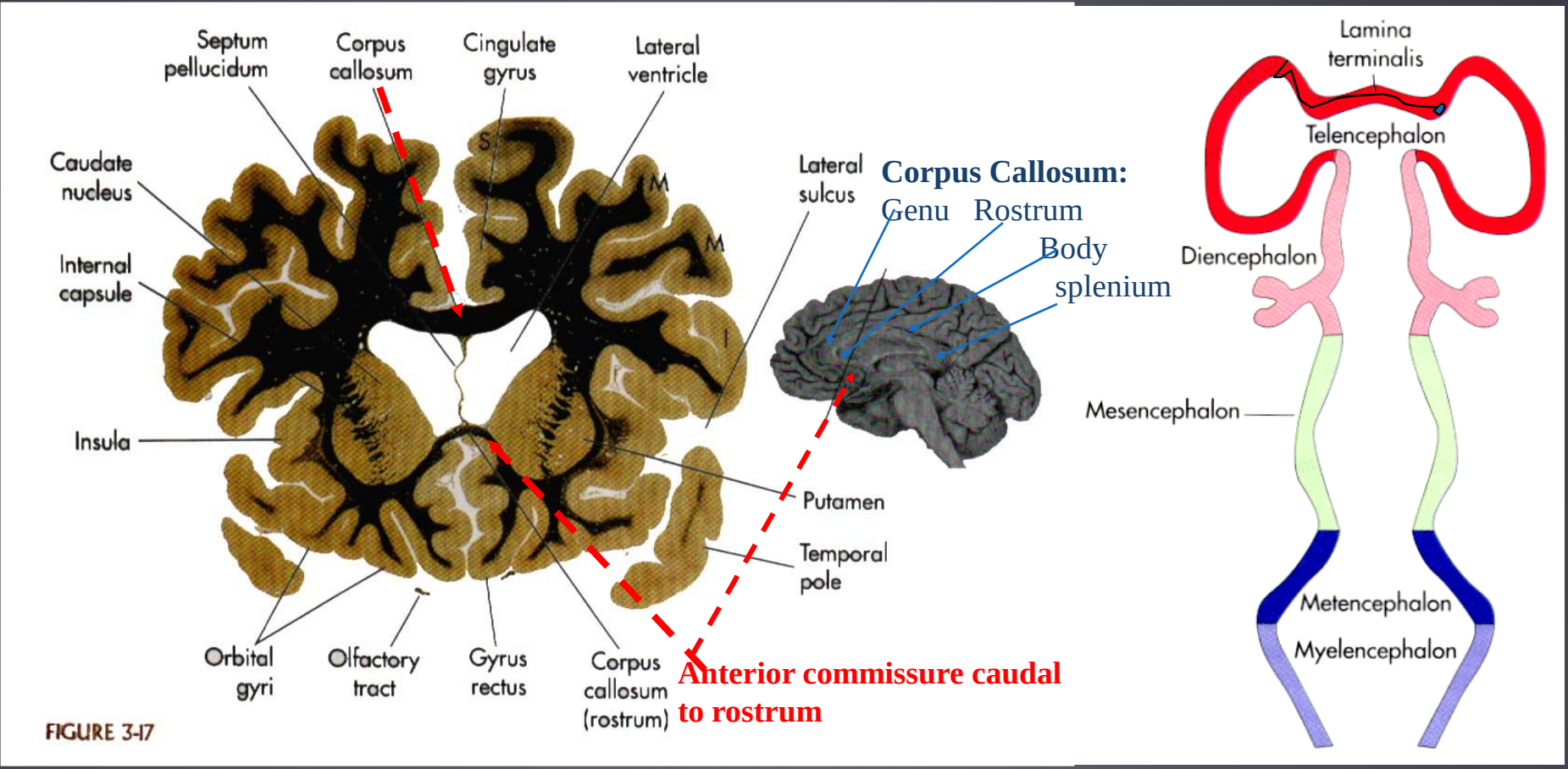


FIGURE 2-15
Progressive development of cortical convolutions.

Cortical expansion concludes with development of extensive surface folds. The sulci (valleys) and gyra (ridges) are formed.

The **lamina terminalis** sticks out as a bridge between the two cerebral hemispheres



Through the lamina terminalis bundles of fibers interconnecting the hemispheres begin to grow. In the adult brain they form two most prominent commissures: **anterior commissure and corpus callosum** still attached to the lamina terminalis.(*Fig. 2.8B & 3.17)*

“Construction” Neurogenesis: mostly completed before birth

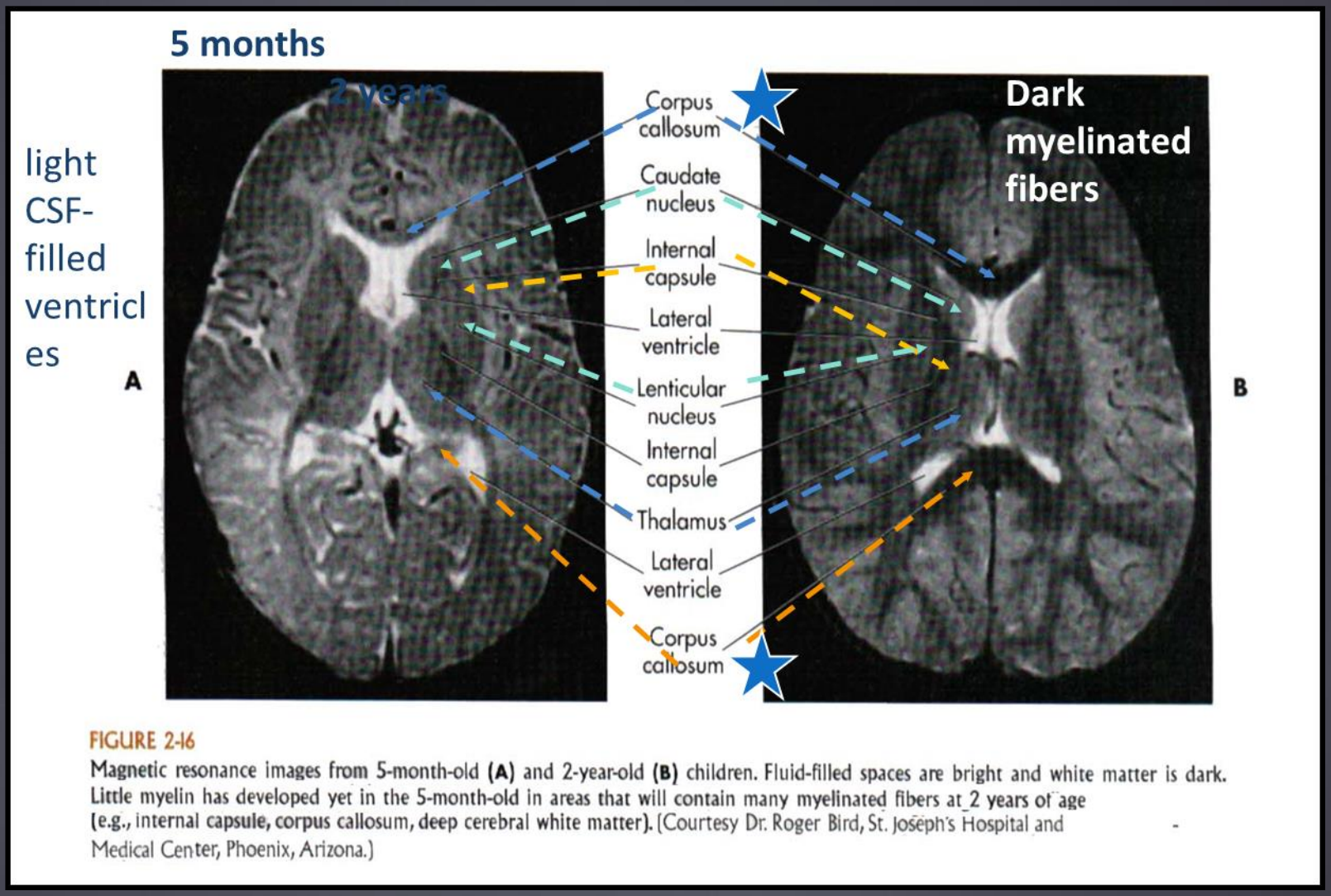
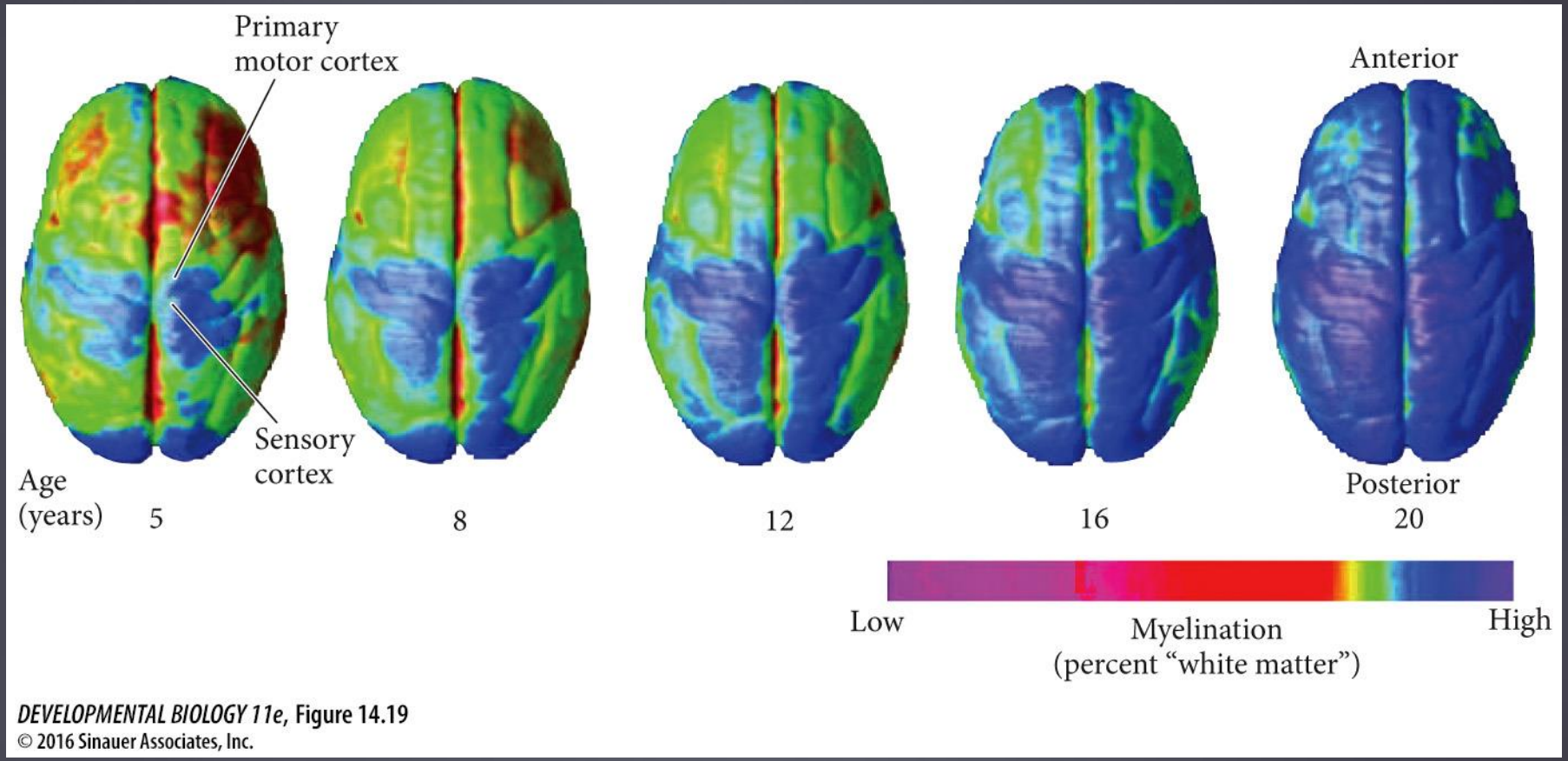


FIGURE 2-16

Magnetic resonance images from 5-month-old **(A)** and 2-year-old **(B)** children. Fluid-filled spaces are bright and white matter is dark. Little myelin has developed yet in the 5-month-old in areas that will contain many myelinated fibers at 2 years of age **(e.g., internal capsule, corpus callosum, deep cerebral white matter).** (Courtesy Dr. Roger Bird, St. Joseph's Hospital and Medical Center, Phoenix, Arizona.)

Figure 14.19 Dorsal view of the human brain showing the progression of myelination ("white matter") over the cortical surface during adolescence

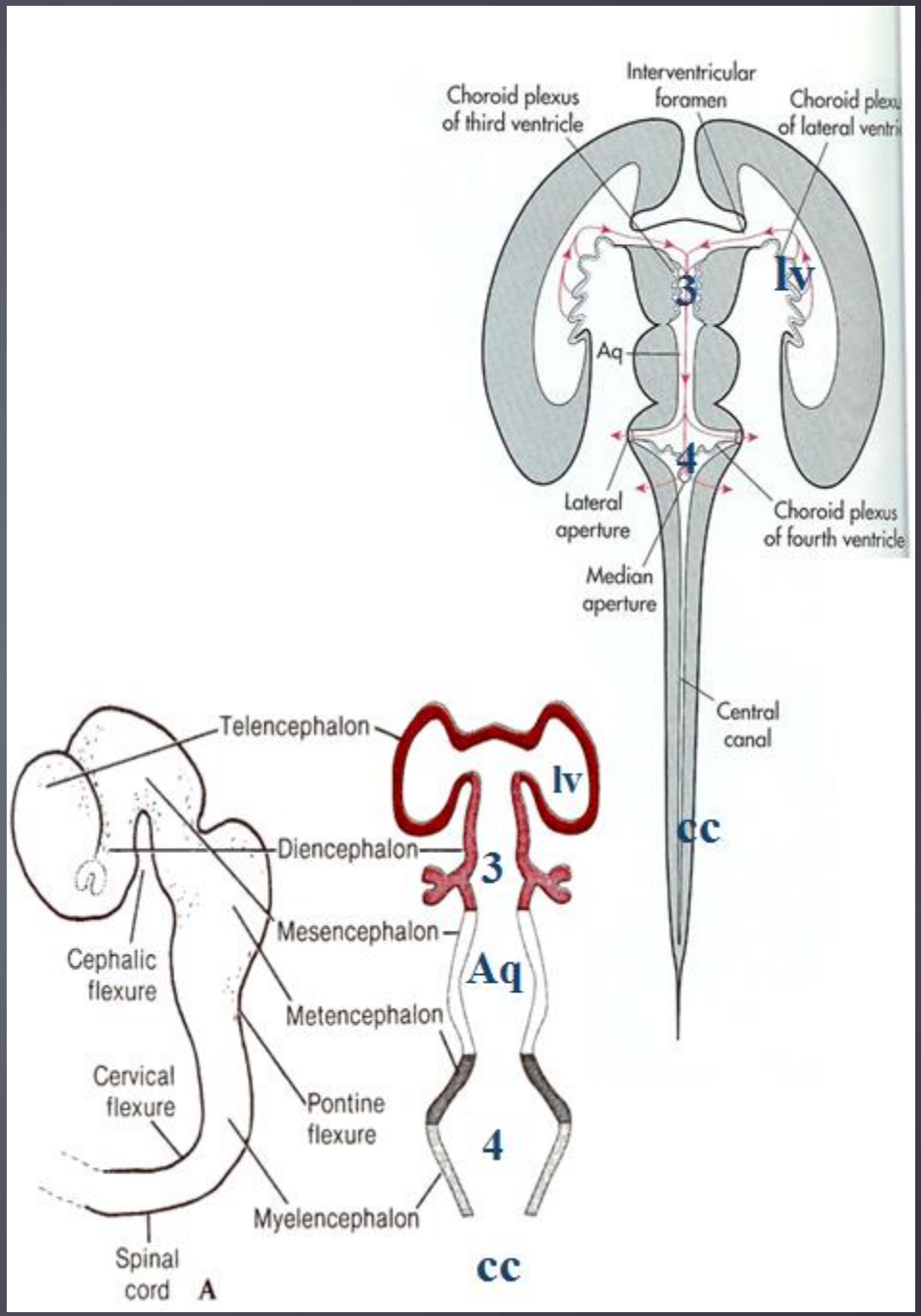


DEVELOPMENTAL BIOLOGY 11e, Figure 14.19

Neural Tube Cavity Persists in adult CNS as Ventricles/canals filled with Cerebro-spinal Fluid (CSF) pp.99-110

Vesicles:	**Ventricles:**
Telencephalon:	lateral ventricles (lv)
Diencephalon:	3rd ventricle (3)
Mesencephalon:	*cerebral aqueduct (Aq)*
Metencephalon:	part of 4th ventricle (4)
Myelencephalon	
- rostral:	4th ventricle
- caudal:	central canal (cc)
Sspinal cord:	spinal canal

Sacral spinal cord: a secondary cavity extends into the caudal mass of cells after the neural tube closes (**secondary neurulation**).



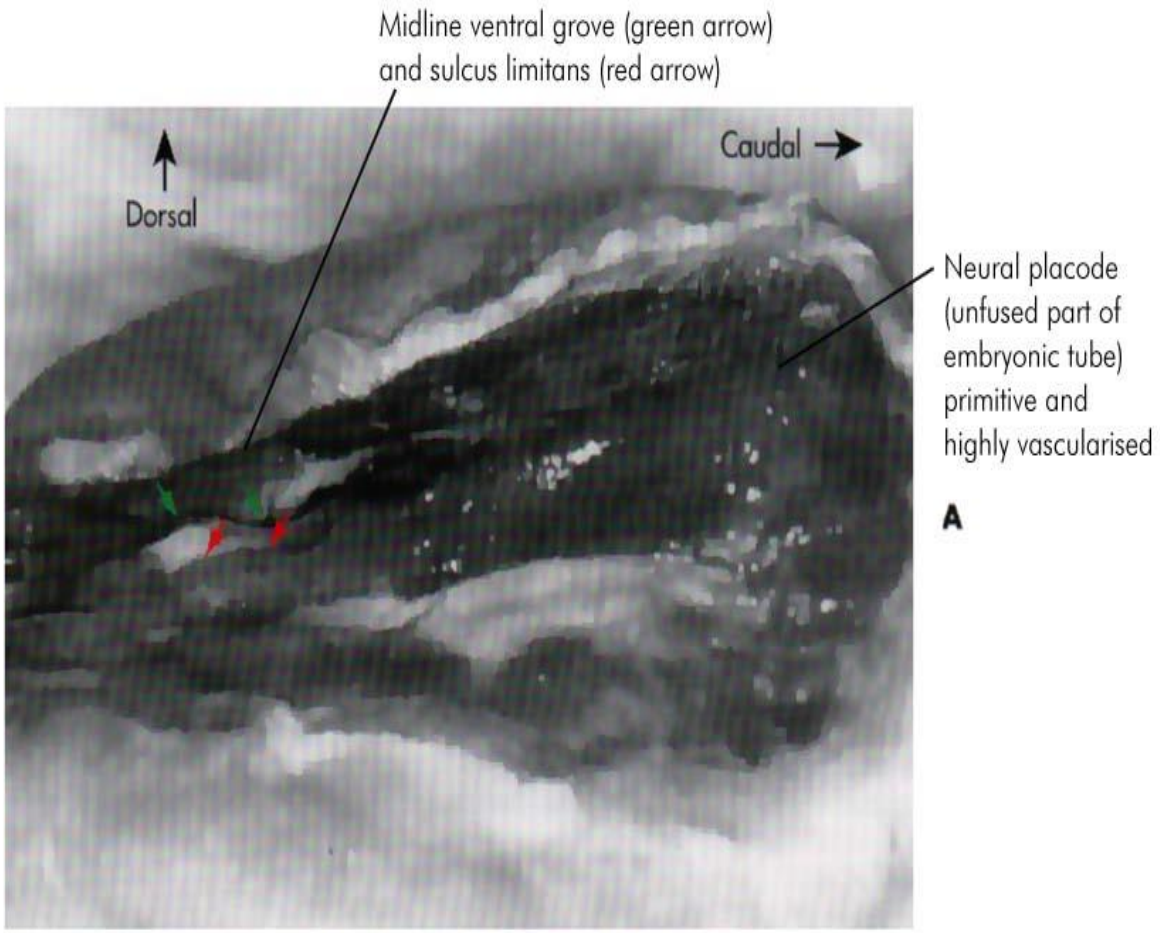
CONGENITAL MALFORMATIONS
pp49-51

Precisely coordinated events occur during the NS development. A flaw in the process causes **congenital malformations**.

Malformations may be caused by chromosomal disorders, viruses or environmental toxins.
Their nature suggests the timing of the defect.

Defects of Dorsal Induction/Primary Neurulation

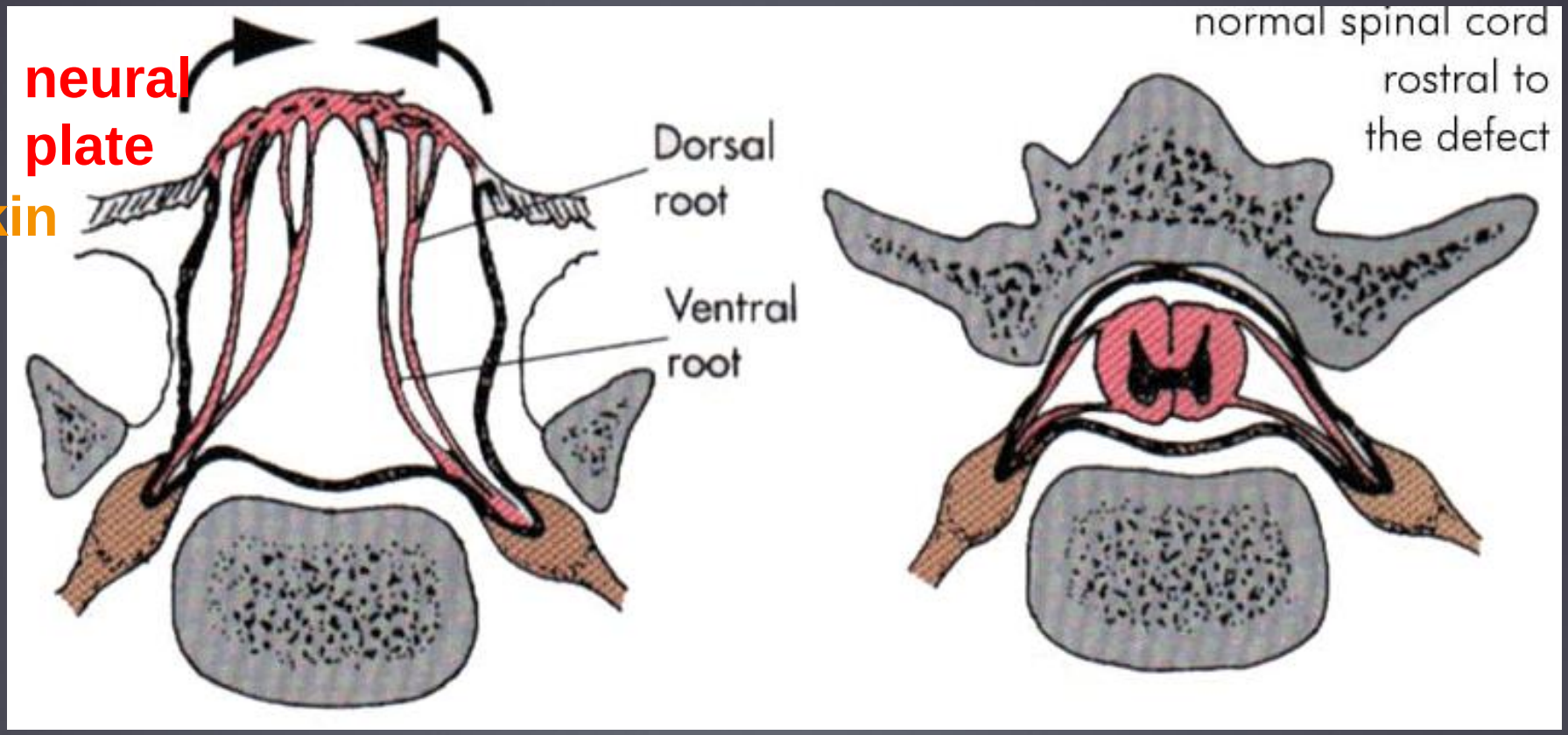
1. **Craniorachischisis** ("cleft skull and spine"; 3-4 weeks fatal) complete failure of tube to close. The CNS is an open dorsal furrow on the head and the body.



(Figure 2-19A).

2. Spina bifida - caudal neuropore does not close. The sulcus limitans o each side of the midline ventral groove, the alar and basal plates are visible as four distinct bands on the exposed neural plate.

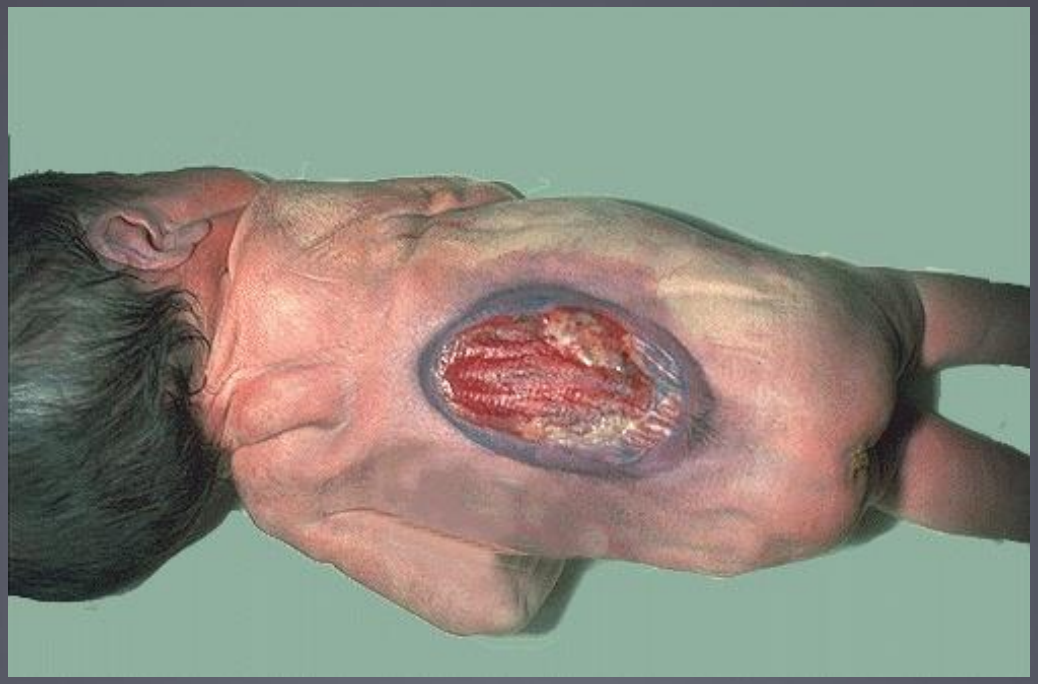
Spina bifida (cont.)



The caudal walls of the **neural plate** are continuous with the skin, rootlets are attached to the ventral surface of this placode. Vertebrae fail to form over the defect.
(The cord and meninges are displaced into a saclike cavity on the back.) (Fig. 2-19B)

Defects of Dorsal Induction/Primary Neurulation

meningomyelocele



- This large mid-thoracic meningomyelocele is another form of neural tube defect (NTD). The genetic polymorphisms due to mutations in the methylene tetrahydrofolate reductase gene may increase the risk for NTDs.. The C677T and the A1298C mutations are associated with elevated maternal **homocysteine** concentrations and an increased risk for NTDs in fetuses. Folate is a cofactor for this enzyme, which is part of the pathway of homocysteine metabolism in cells . Mothers who supplement their diets with **folate** prior to and during pregnancy can often reduce this risk.

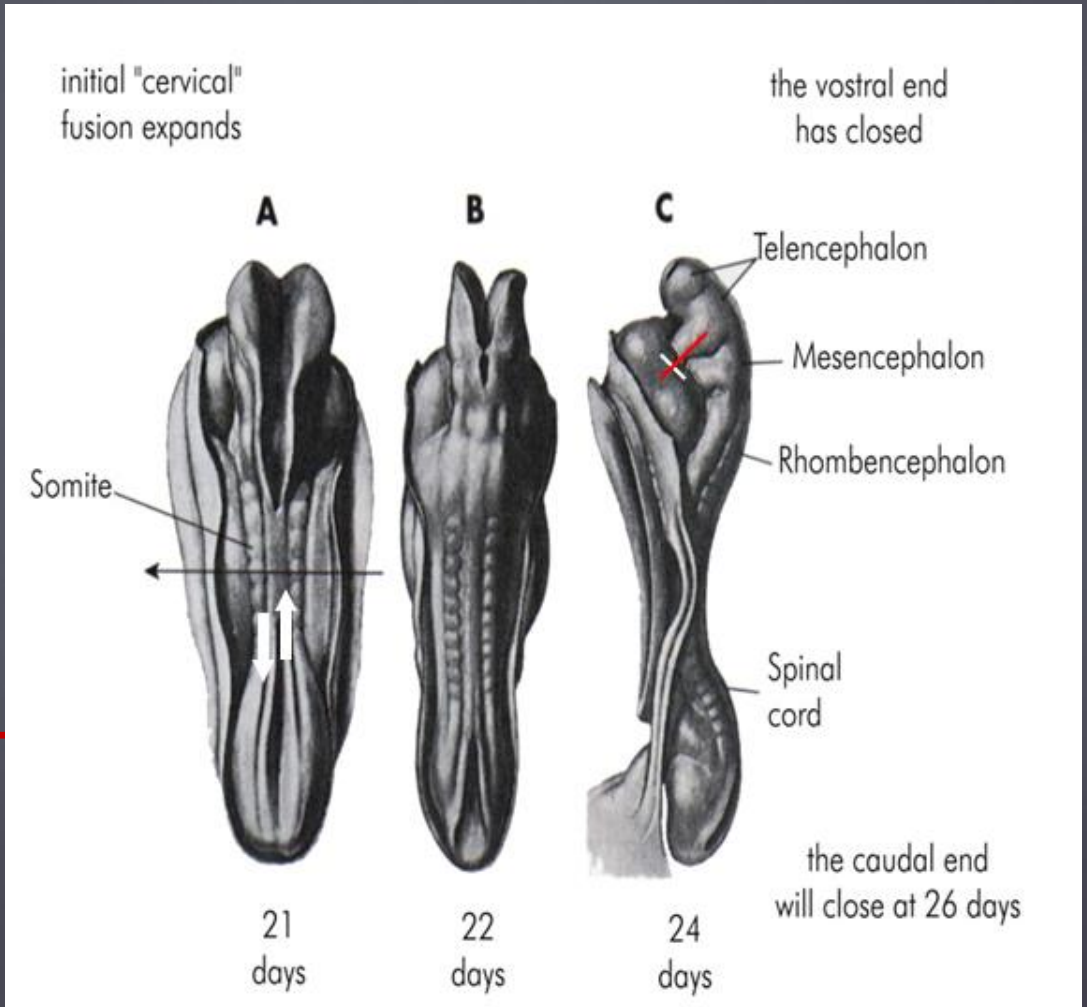
Defects of Dorsal Induction/Primary Neurulation

Anencephaly

The rostral neuropore fails to close - absence of much of cerebral hemispheres. The neural tube walls are continuous with the skin, and it's central cavity may be open to the outside. The absence of the fetal cranial vault in anencephaly is shown here. Anencephaly is typically an isolated birth defect that is not related to chromosomal abnormalities. Exposure of cerebral tissue to **amniotic fluid** precludes brain development.

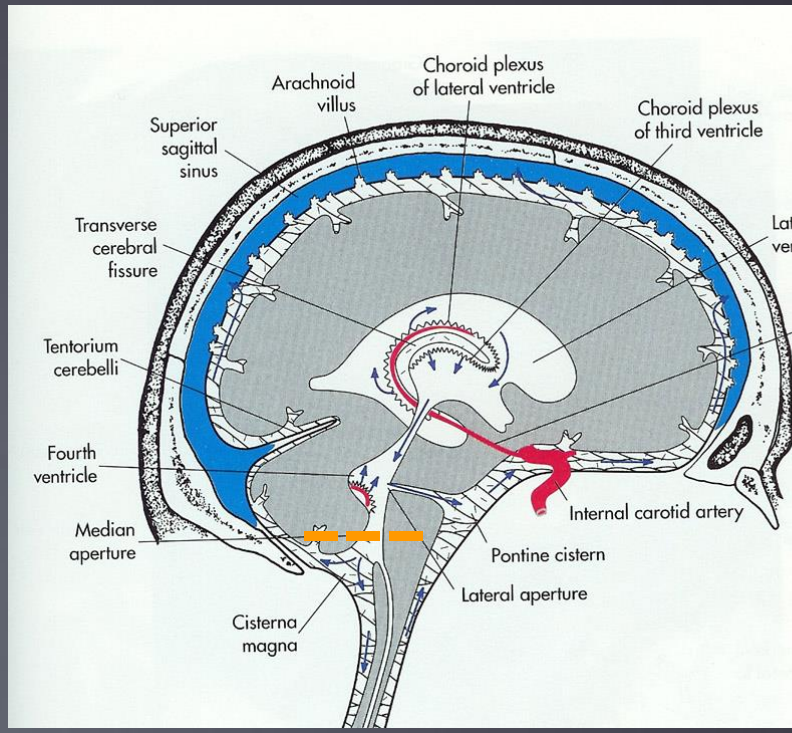
Arnold-Chiari malformation:

1. A single misalignment at the site where the neural tube begins to close may cause tw deformities: (i) Elongated **cerebellum** and (ii) elongated **caudal brainstem**. They are pushed down into the foramen magnum**.**



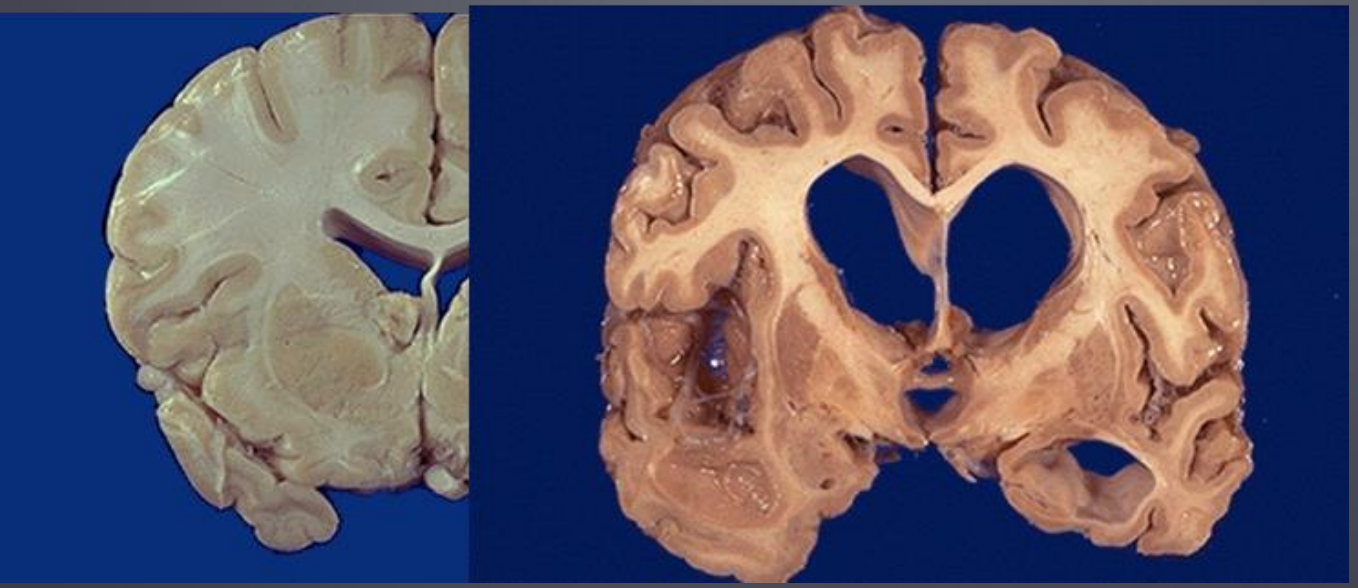
Arnold-Chiari malformation:

The flow of CSF may be obstructed (----) causing hydrocephalus.



Normal Size Lateral ventricle

Hydrocephalus



Defects of Secondary Neurulation

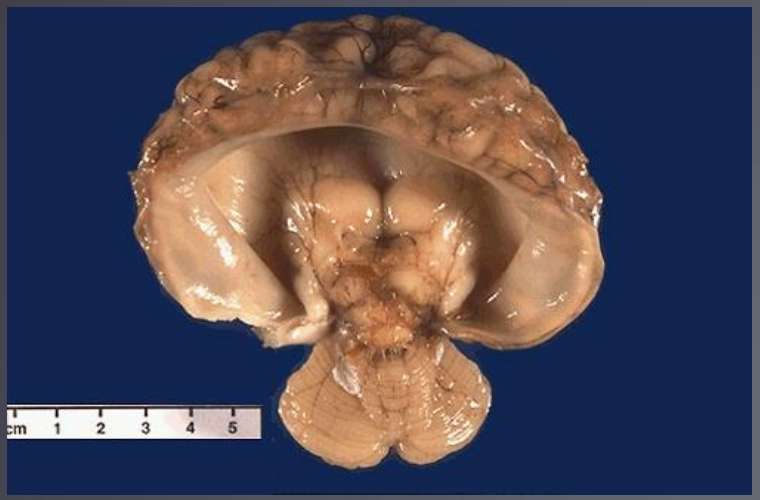
The cell mass at the caudal end of the neural tube gives rise to sacral S.C. and adjacent tissues.

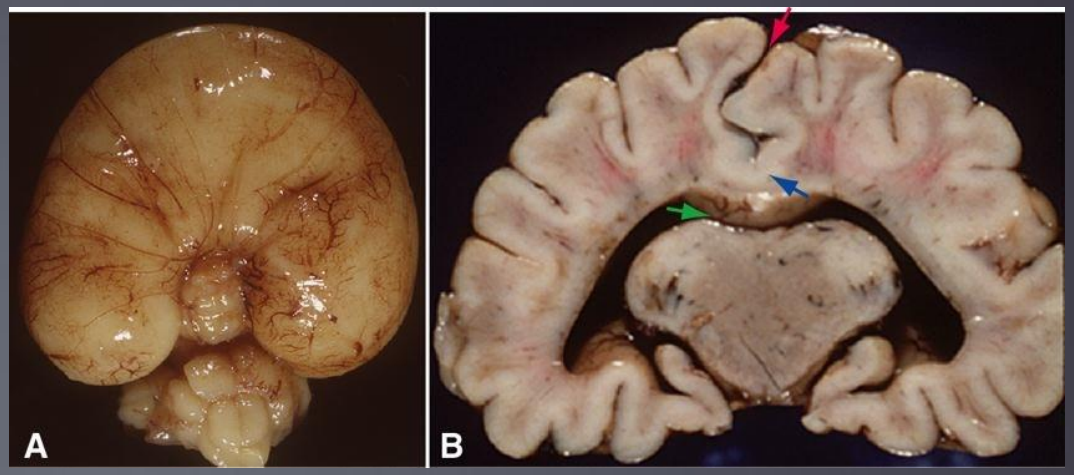
Abnormal tethering of the S.C. may cause traction injuries.

Warning signs: dimpling, hairiness, discoloration of the overlying skin.

Defects of Ventral Induction by Notochord

holoprosencephaly

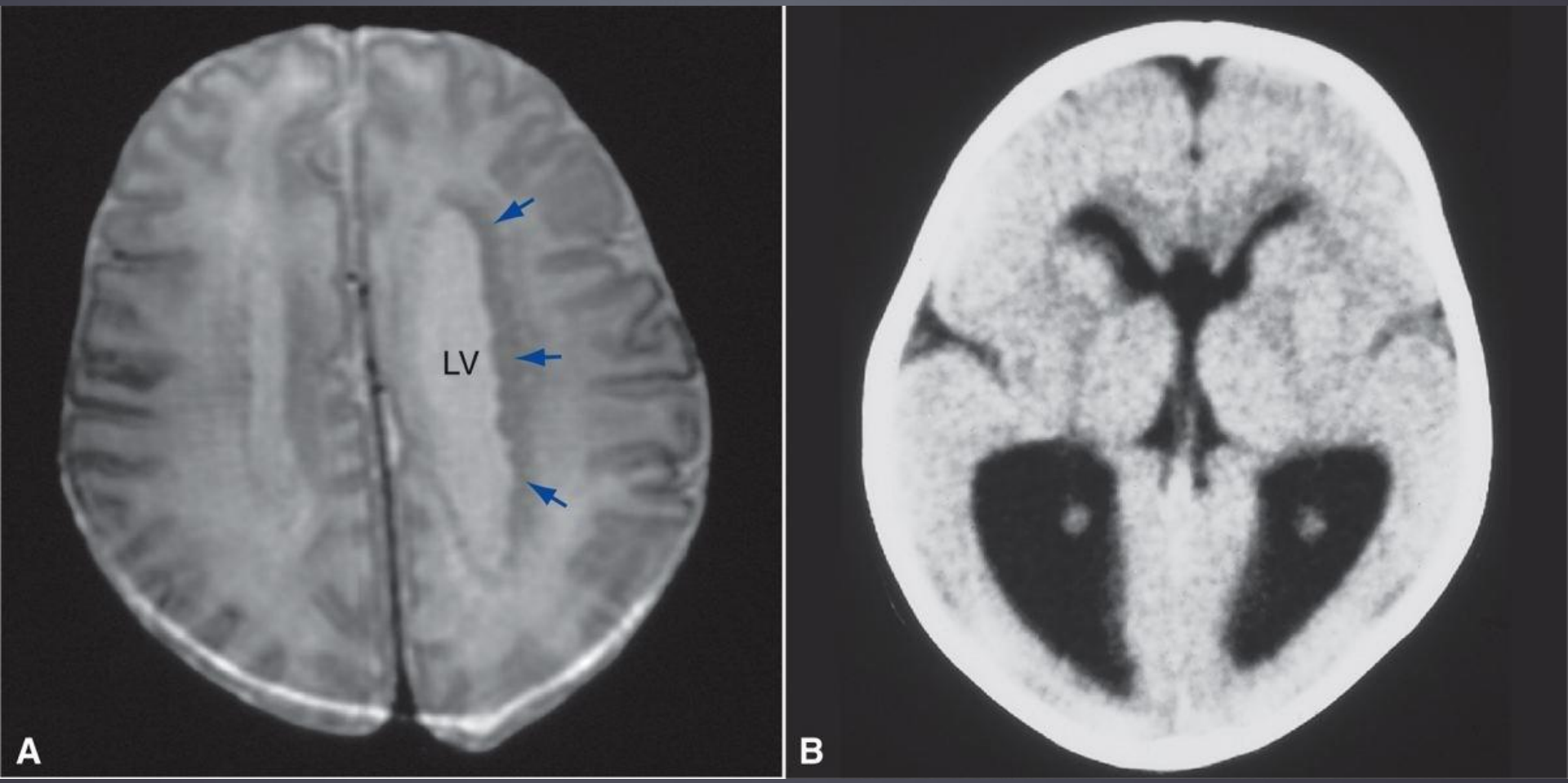




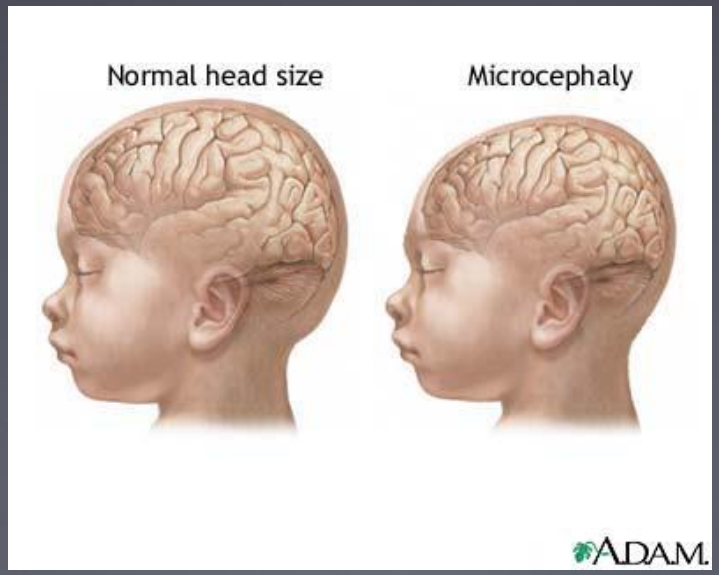
- Failure of prosencephalon to develop into diencephalon and paired telencephalon. The large **single ventricle** seen here inside a **single hemisphere** represents the "alobar" form of holoprosencephaly in which there was no division of hemispheres.
- There is a range of findings, including **facial abnormalities**, that can occur with holoprosencephaly, many of which can be seen in a fetus by ultrasound, so prenatal diagnosis is possible. (See also Figs. 2-20A,B –Nolte textbook)

Disruption in neuronal proliferation and migration :

- (A) Heterotopias (ectopic areas of gray matter – blue arrows) also abnormal surface
- Gyri pattern
- (B) Lyssencephaly – absence of gyri
- (Fig. 2-22A, –Nolte textbook)



Genes involved in Brain Development have undergone recent evolution.



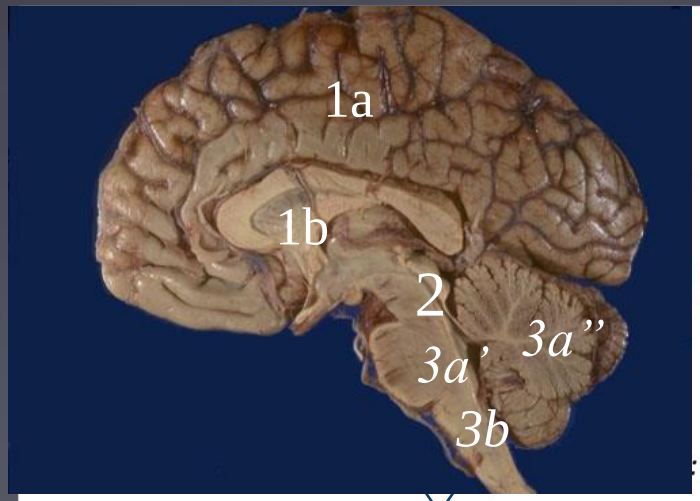
Pathological Mutations in MCPH1 (Microcephalin) gene are associated with smaller brain size.

Recent history of this gene:

***Microcephalin*, a Gene Regulating Brain Size, Continues to Evolve Adaptively in Humans**

Patrick D. Evans,[1,2] Sandra L. Gilbert,[1] Nitzan Mekel-Bobrov,[1,2] Eric J. Vallender,[1,2] Jeffrey R. Anderson,[1] Leila M. Vaez-Azizi,[1] Sarah A. Tishkoff,[4] Richard R. Hudson,[3] Bruce T. Lahn[1*]
Science 9 September 2005:Vol. 309. no. 5741, pp. 1717 - 1720DOI: 10.1126/science.1113722

(2) organization of adult Nervous System

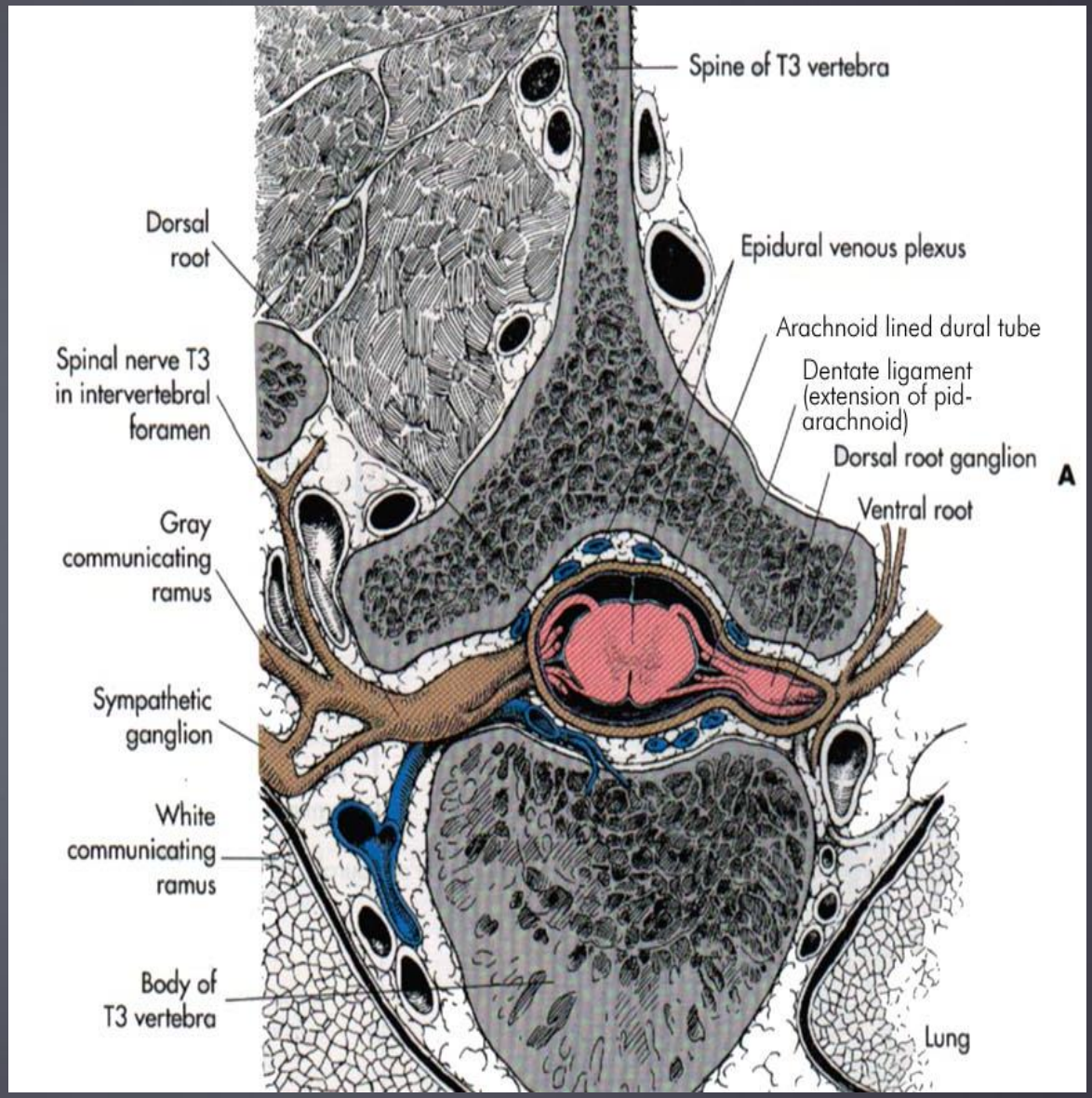


Central nervous system
Neural Tube
Dorsal Induction:
Brain
Spinal cord
Cerebrum
Brainstem
Mesencephalon + Rhombocephalon
Telencephalon:
Cerebral hemisphere
1a
Diencephalopn:
Diencephalon
1b
Mesencephalon:
Midbrain (2)
Metencephalon:
Pons (3a), cerebellum (3b)
Myencephalon:
Medulla
Cerebral cortex
Frontal lobe (9)
(motor cortex)
Parietal lobe (10)
(somatosensory cortex)
Occipital lobe (11)
(visual cortex)
Temporal lobe (12)
(auditory cortex)
Limbic lobe (13)
(drives, emotions, memory)
Basal ganglia
(movement control; related structures in brainstem)
Caudate nucleus (14)
Lenticular nucleus
(putamen [15] and globus pallidus [16])
Hippocampus (5), amygdala (6)
(limbic structures; drives, emotions, memory)
Thalamus (7)
(relay to cortex)
Hypothalamus (8)
(control of autonomics)

FIGURE 3-23

Overview of the subdivisions of the CNS. The major structures listed here, as well as many related structures, are the subjects of subsequent chapters.

The cord is suspended within arachnoid-lined dural tube by the denticulate ligaments (extensions of the pia-arachnoid in between nerve roots).



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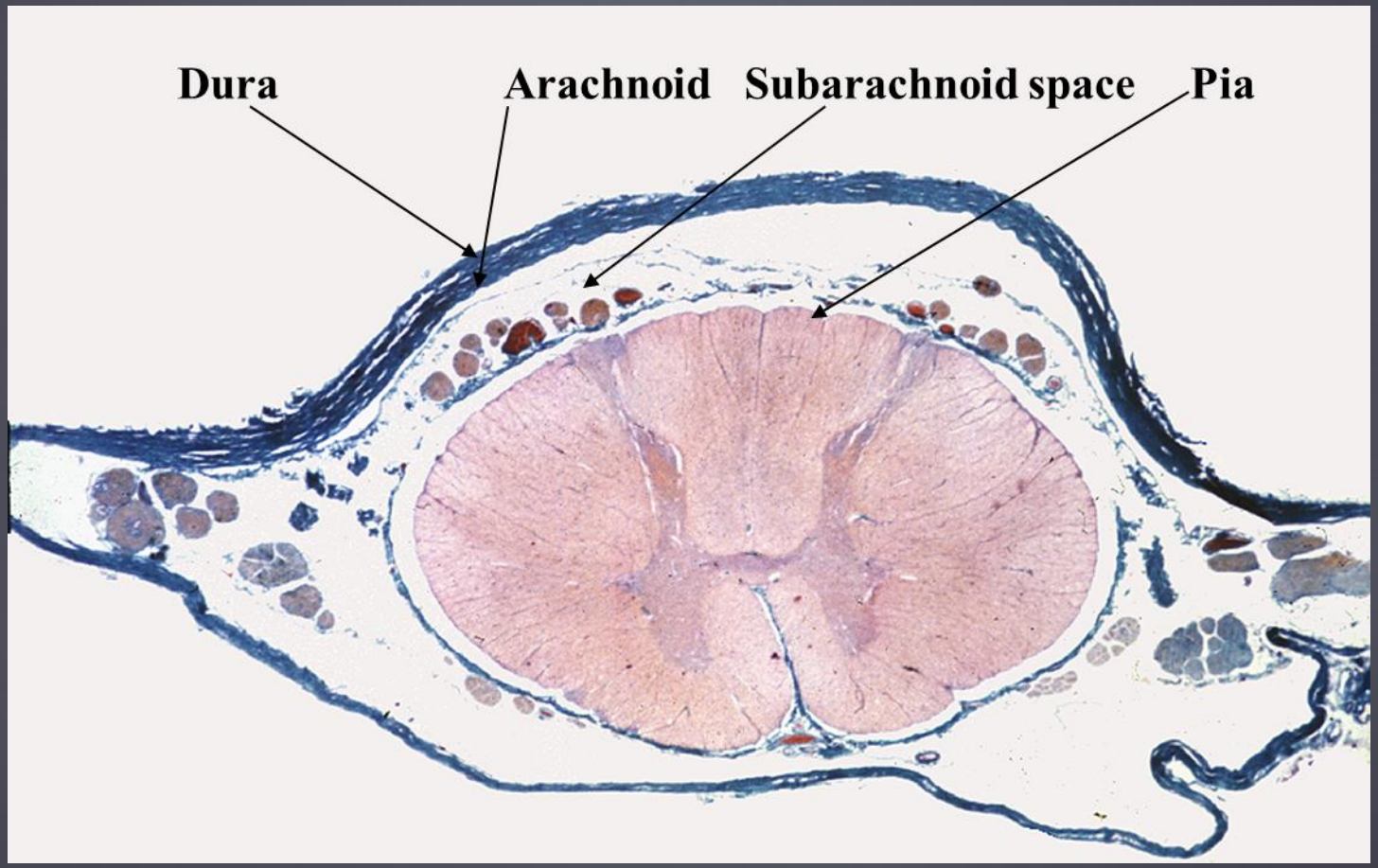
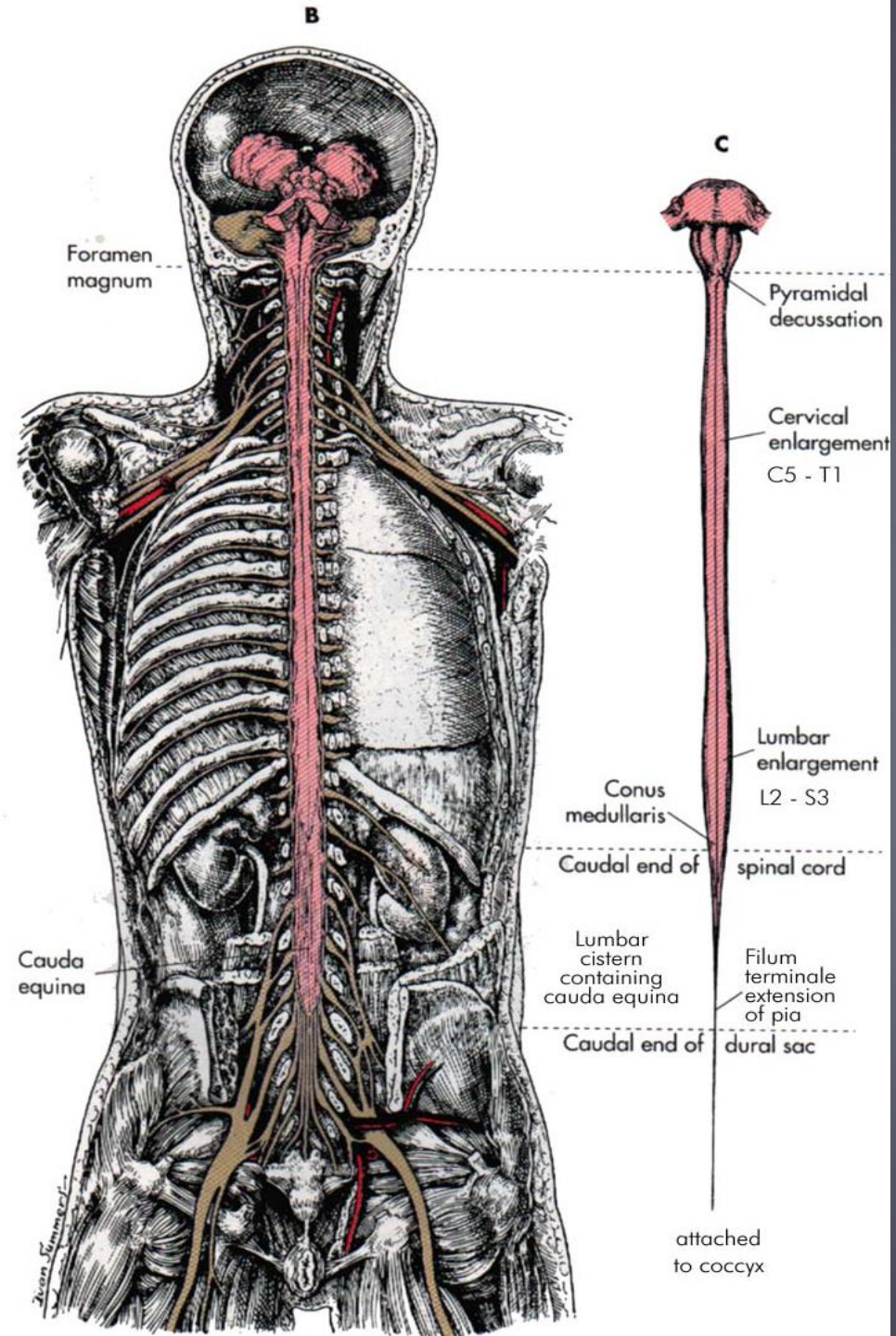




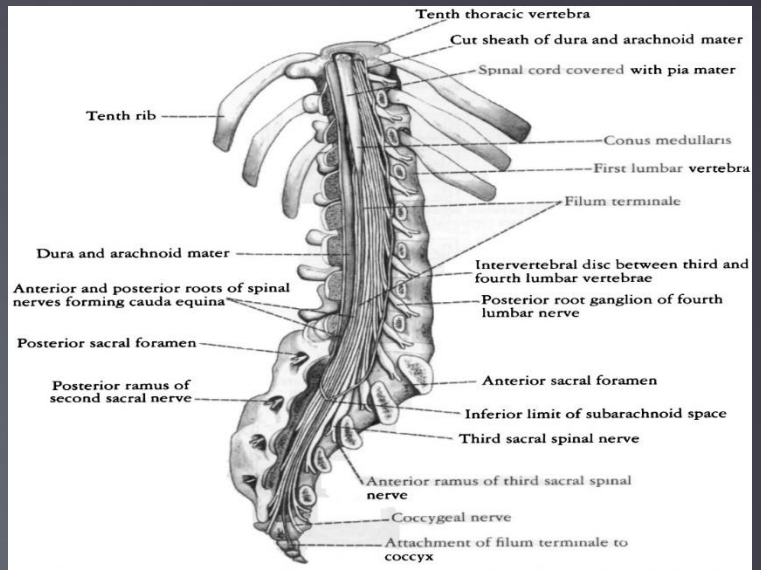


FIGURE 1-27 Oblique posterior view of the lower end of the spinal cord and the cauda equina. On the right, the laminae have been removed to expose the right half of the spinal cord and the nerve roots.

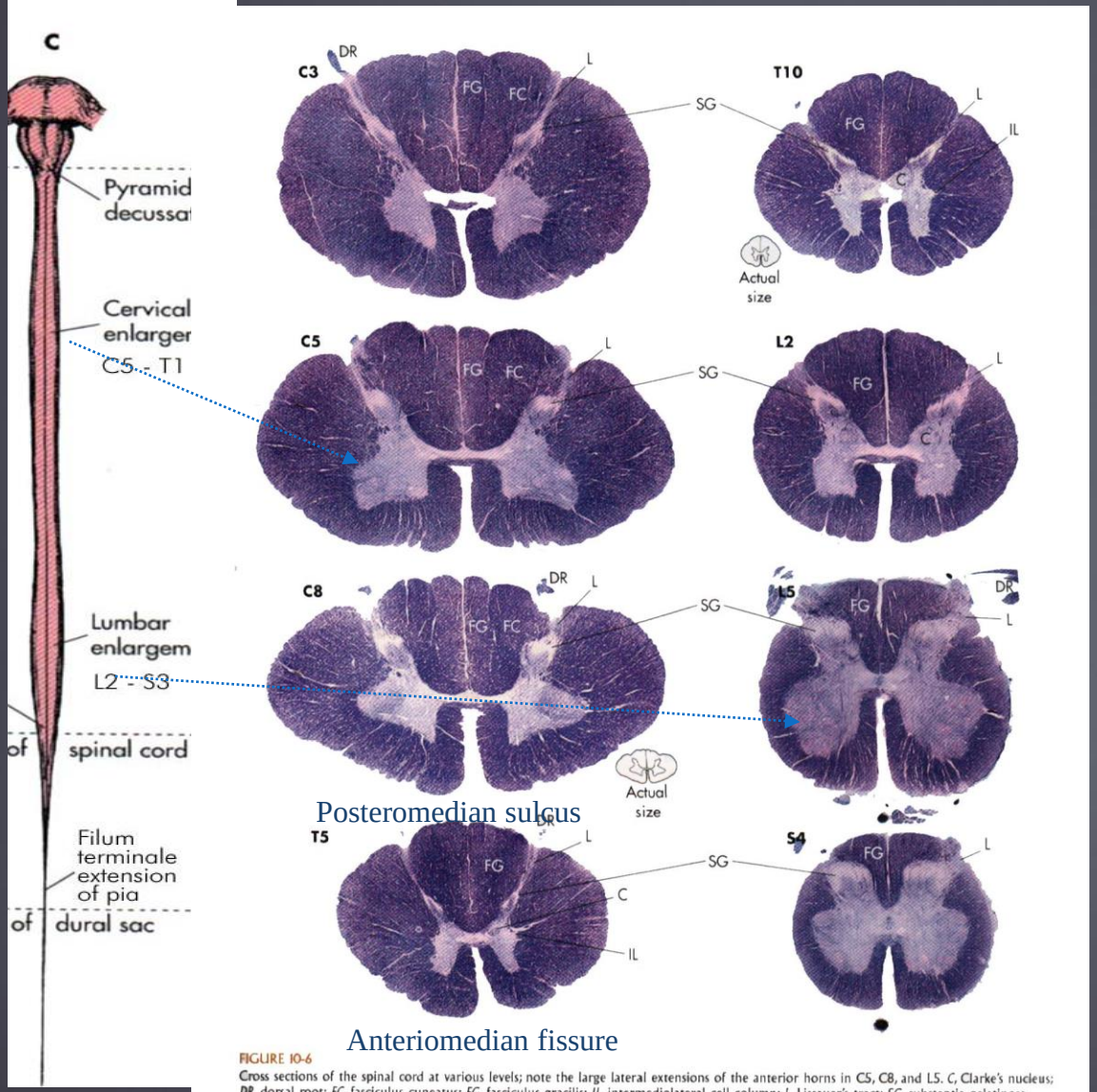


FIGURE 10-6
Cross sections of the spinal cord at various levels; note the large lateral extensions of the anterior horns in C5, C8, and L5. C, Clarke's nucleus; DR, dorsal root; FC, fasciculus cuneatus; FG, fasciculus gracilis; IL, intermediolateral cell column; L, Lissauer's tract; SG, substantia gelatinosa.

Cross sections of the spinal cord:

- butterfly-shaped gray matter: (1) anterior and (2) posterior horns, (3) intermediate gray, (4) pericentral canal gray.

- White matter surrounds GM and is organized into large Funiculi (F) cords: Posterior (PF), lateral(LF) and anterior funiculi (AF) with long ascending sensory tracts , descending motor tracts (mostly anterior and lateral funiculi) and local interconnecting axons (e.g. coordinating withdrawal reflexes - *fasciculus proprius).*

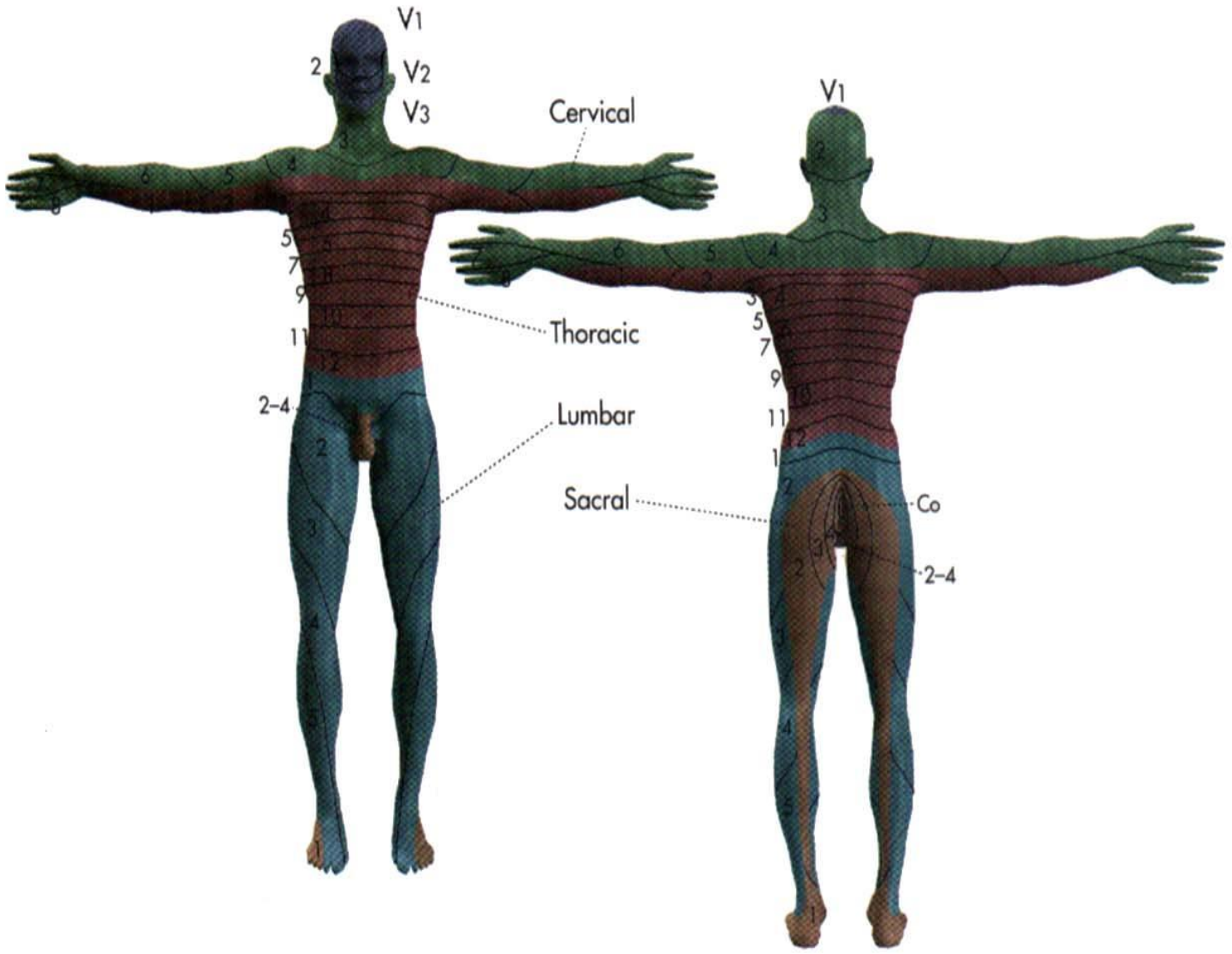
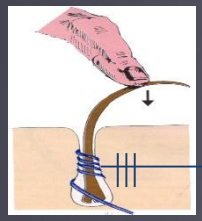
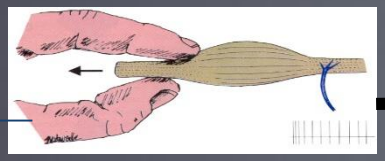


FIGURE 10-3
Cutaneous territories innervated by spinal nerves (dermatomes) and the trigeminal nerve *(V1, V2, V3)*. *Co*, Coccygeal segment.

Definition: *Afferent (to)* and *efferent (from) (lower, upper moto-neurons) fibers:* refer to the direction of information flow in an axon, relative to a given structure.

- The Bell-Magendie law: *"the dorsal root contains afferent fibers and the ventral root only efferent fibers"*



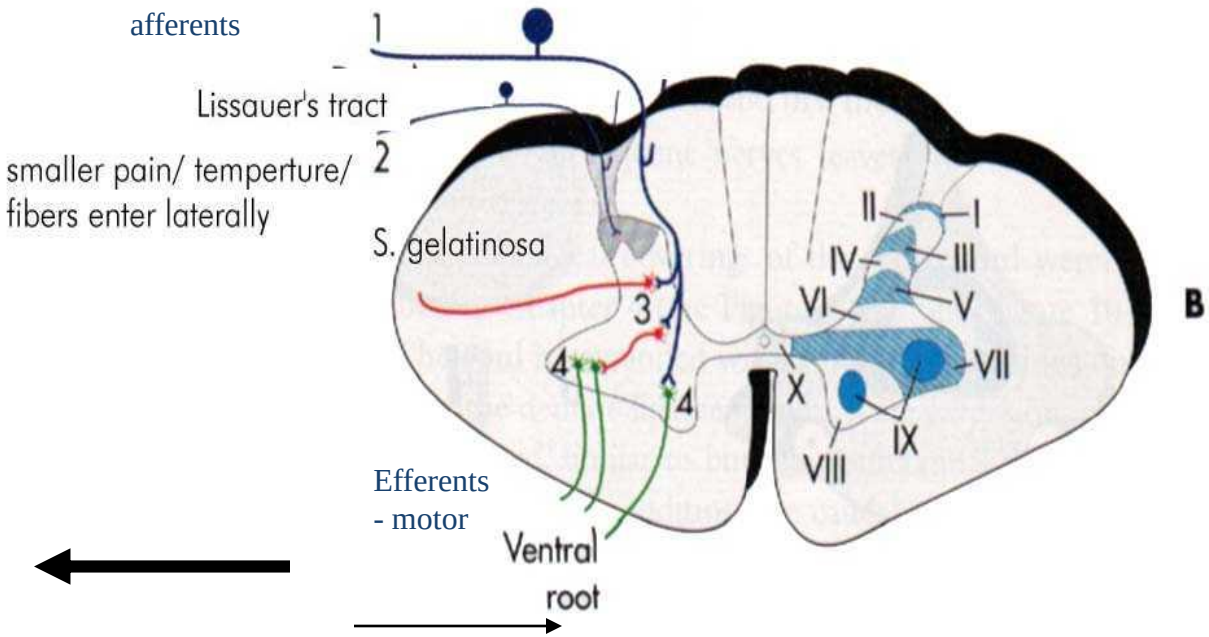


Afferents
- sensory
  Myelinated afferents
  enter via posterior funiculus

afferents

Lissauer's tract

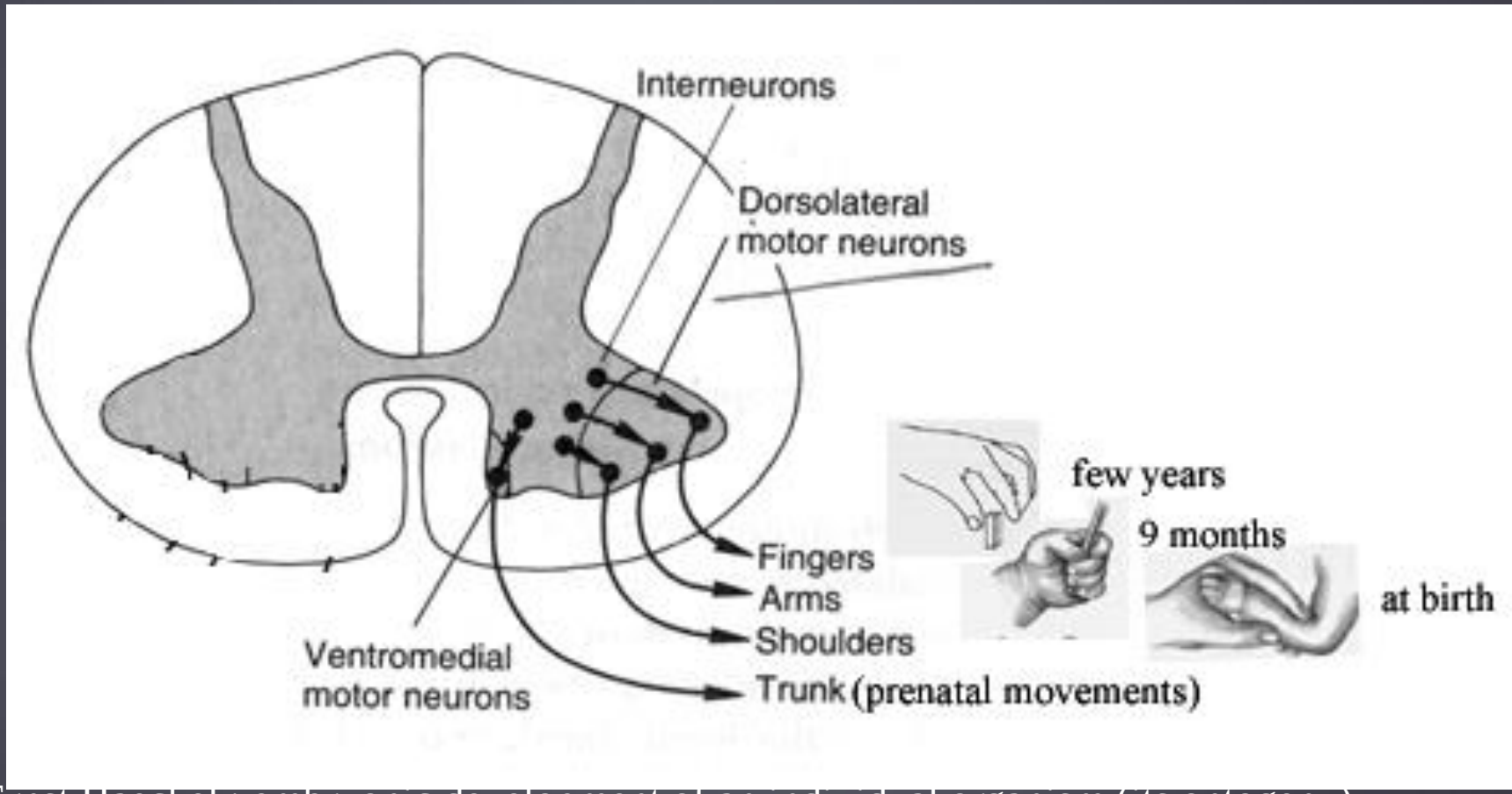
smaller pain/ temperture/
fibers enter laterally



Efferents
- motor

Ventral
root

Ontogenesis & localization of lower Motoneurons and Movements

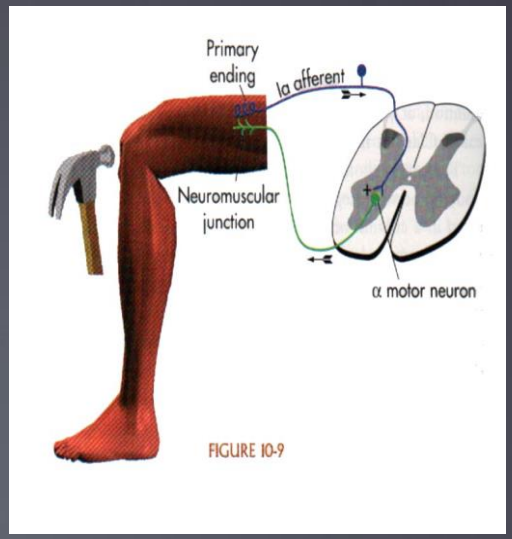


Ernst Haeckel : embryonic development of an individual organism (its ontogeny) followed the same path as the evolutionary history of its species (its phylogeny).

Stretch monosynaptic reflexes

Myotatic reflexes (Deep Tendon Reflexes elicited from muscle stretch receptors):

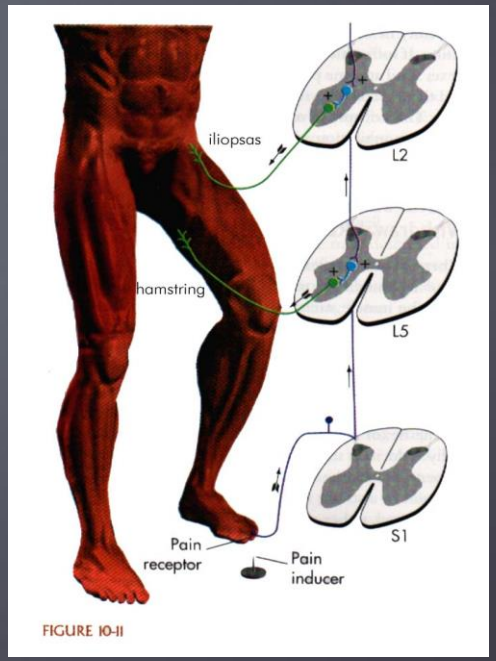
Knee jerk reflex – stretching patellar tendon and the quadriceps activates Primary Ia spindle afferents in the muscle that directly stimulate alpha motor neurons at L4> femoral n. >quadriceps contraction.



L4

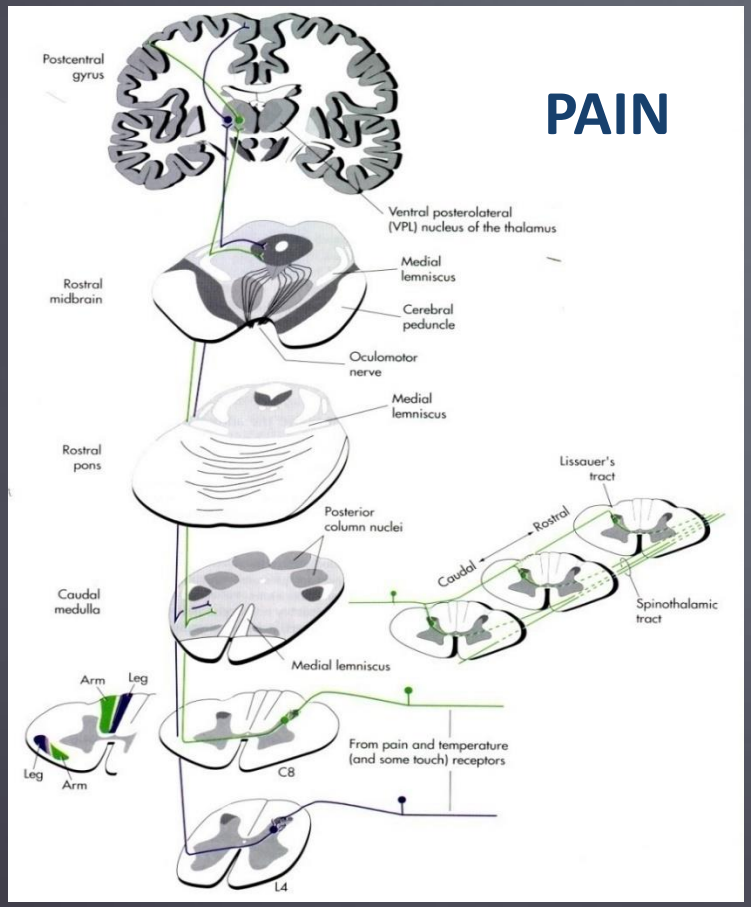
Inherent capabilities of the spinal cord motor apparatus:

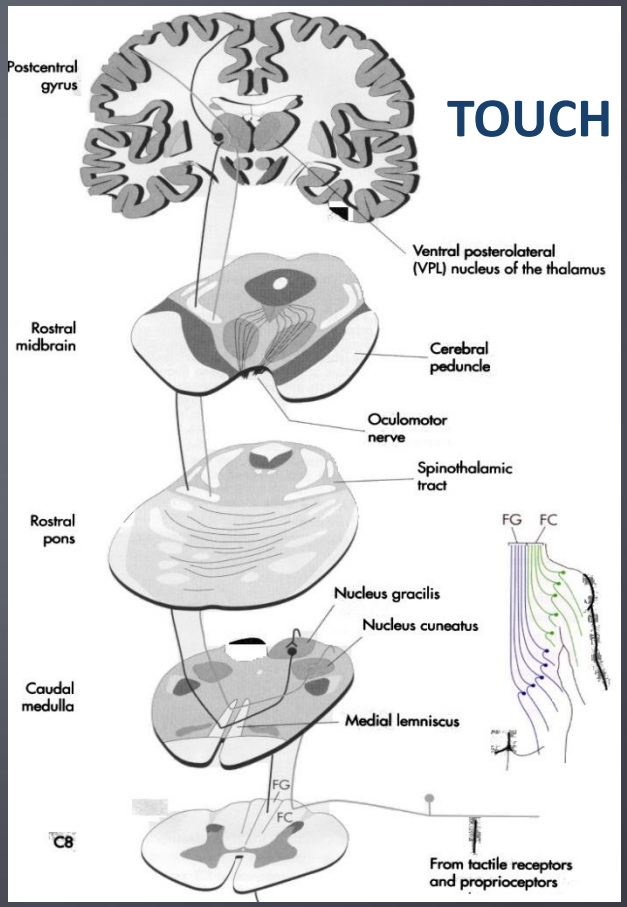
1. **Mediates a variety of reflexes (example withdrawal reflex).**
2. **Is sufficient for rhythmic movements (stepping and other locomotor patterns).**



Separate CNS pathways for touch/proprioception and for pain

Modality (nature) of sensation - determined by type of stimulated receptors
Information about the nature of a stimulus is preserved in CNS, as specific wiring patterns are maintained from receptors through specific ascending sensory pathways to separate regions of cerebral cortex. Electrical stimulation at any level of pathway generates sensation characteristic to its receptor. (Rare cases of crossed modalities: **synesthesia** – i.e., hearing in color).





Voluntary precision movements

- corticospinal tracts

Involuntary movements – (Brain Stem)

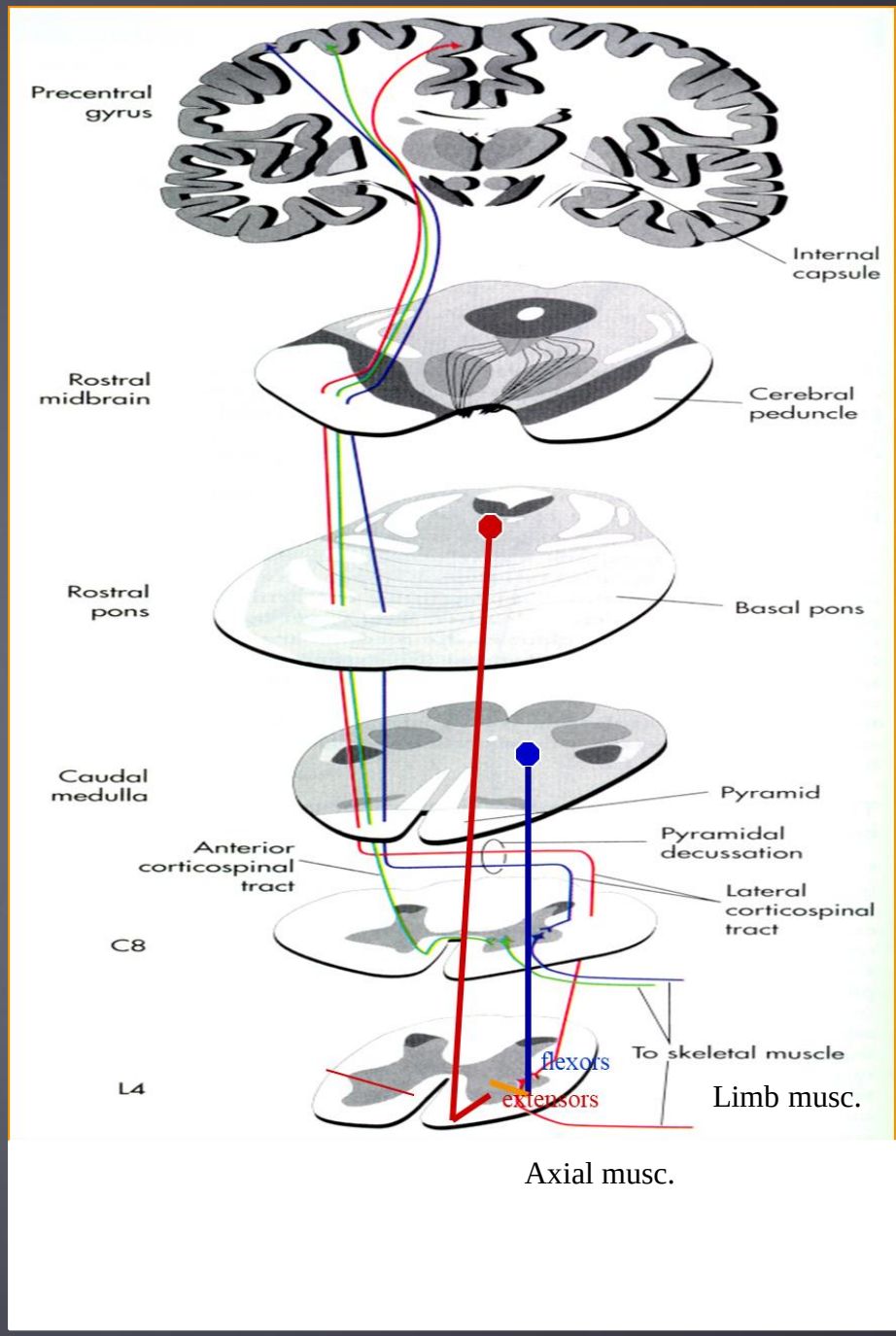
Bulbo-Spinal systems

(tecto-(visual signals),

vestibulo-(equilibrium),

reticulo-(postural),

rubro-spinal (gripping).



BRAIN STEM IS A RELAY TO THE SPINAL CORD AND TO CORTEX

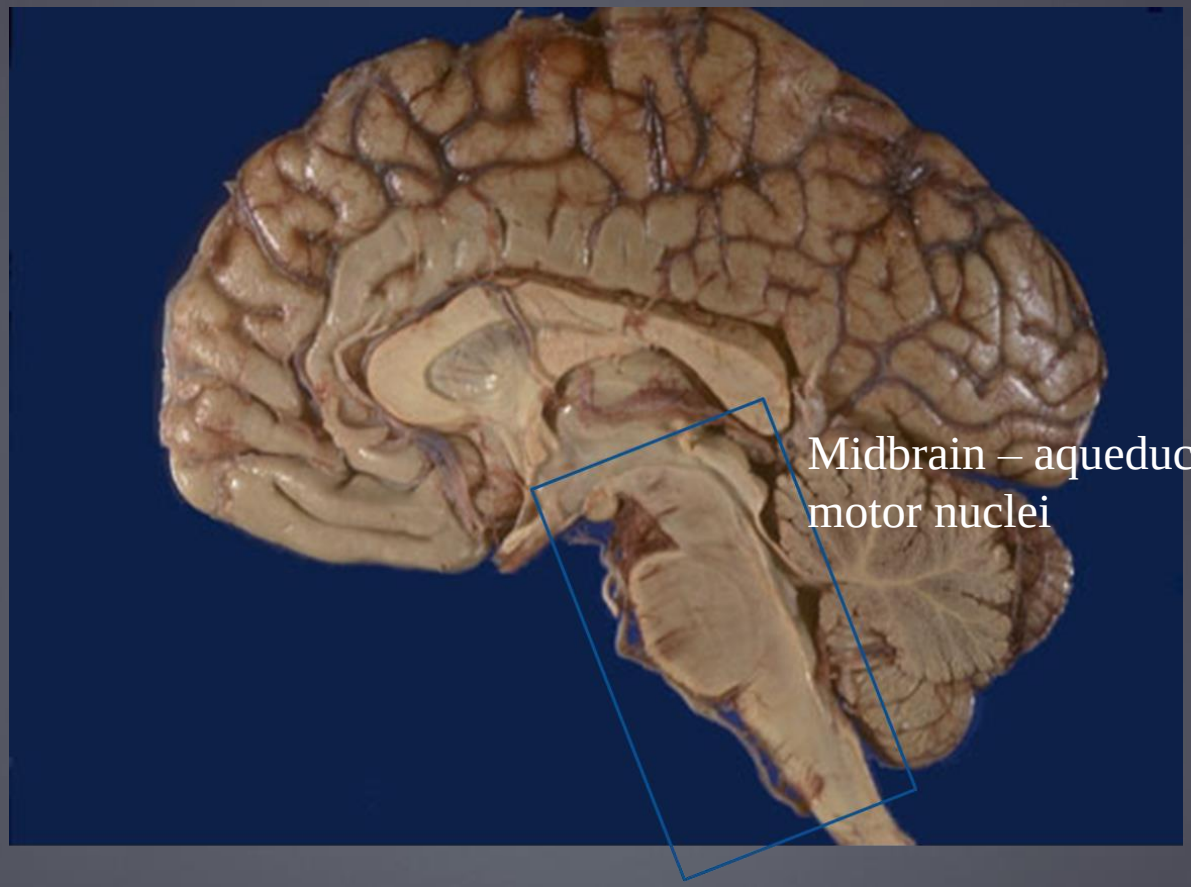
Conveys information to/from cerebrum, cerebellum, cranial nerve functions,
Nuclei with special functions (heart rate, respiration, movement, attention ,reward, pain control)

BRAIN STEM IS A RELAY TO THE SPINAL CORD AND TO CORTEX

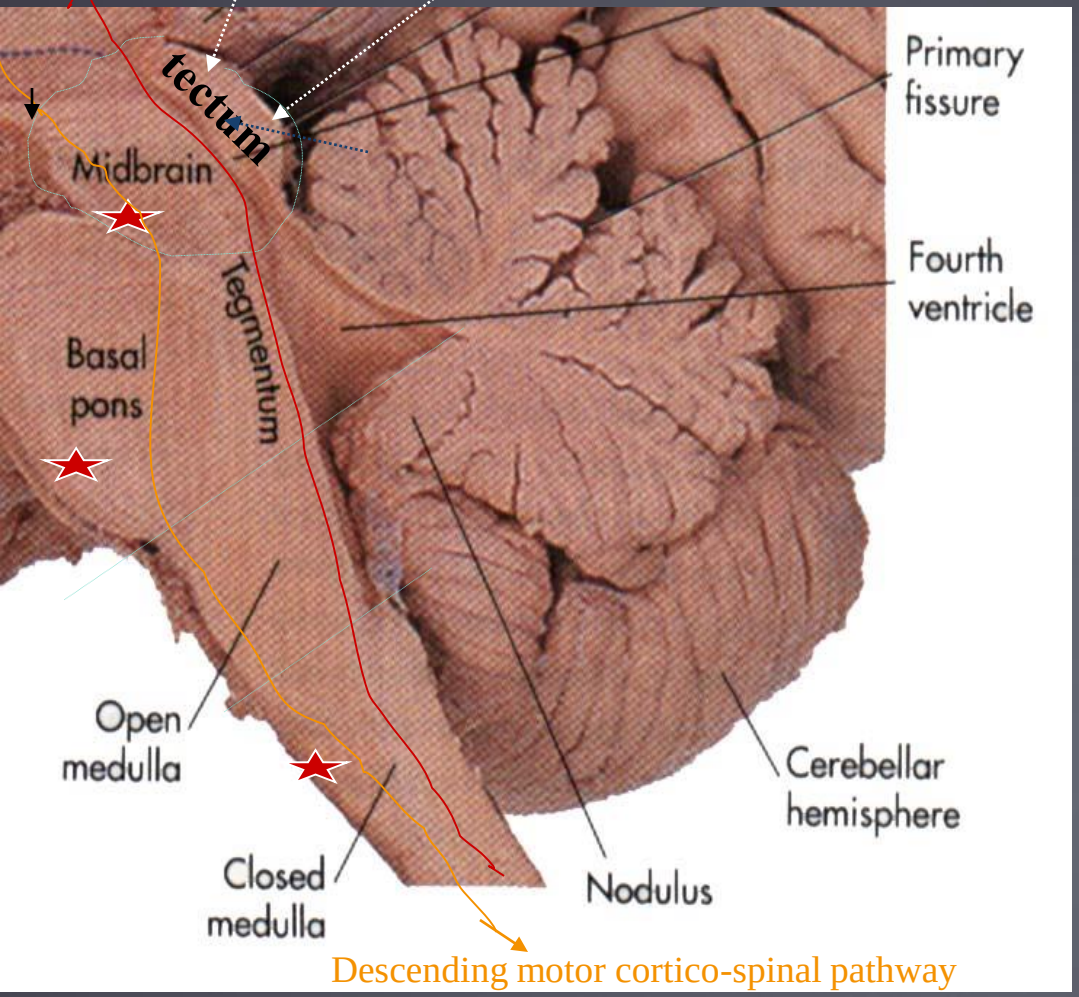
BRAIN STEM IS A RELAY TO THE SPINAL CORD AND TO CORTEX

Pons: (I) basal pons, (ii) Tissue under the, 4th ventricle).

BRAIN STEM IS A RELAY TO THE SPINAL CORD AND TO CORTEX

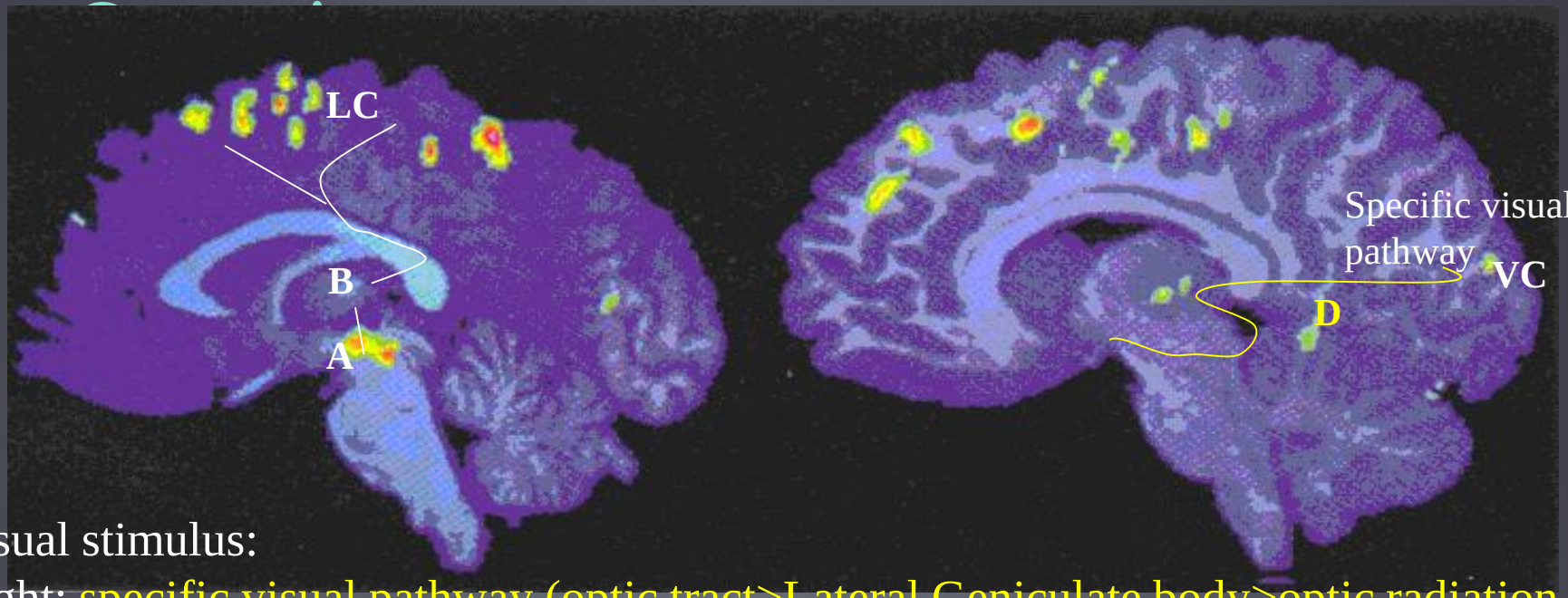


THE BRAIN STEM:



Internal anatomy:
(i) tectum "roof", dorsal to the aqueduct, paired superior and inferior colliculi (sensory nuclei) ;
(ii) tegmentum sensory & motor nuclei.
(iii) Appended structures (tracks):
- cerebral peduncles (midbrain)
- basal pons,
- pyramids

Ascending Reticular Activating System (ARAS) Controls Arousal and

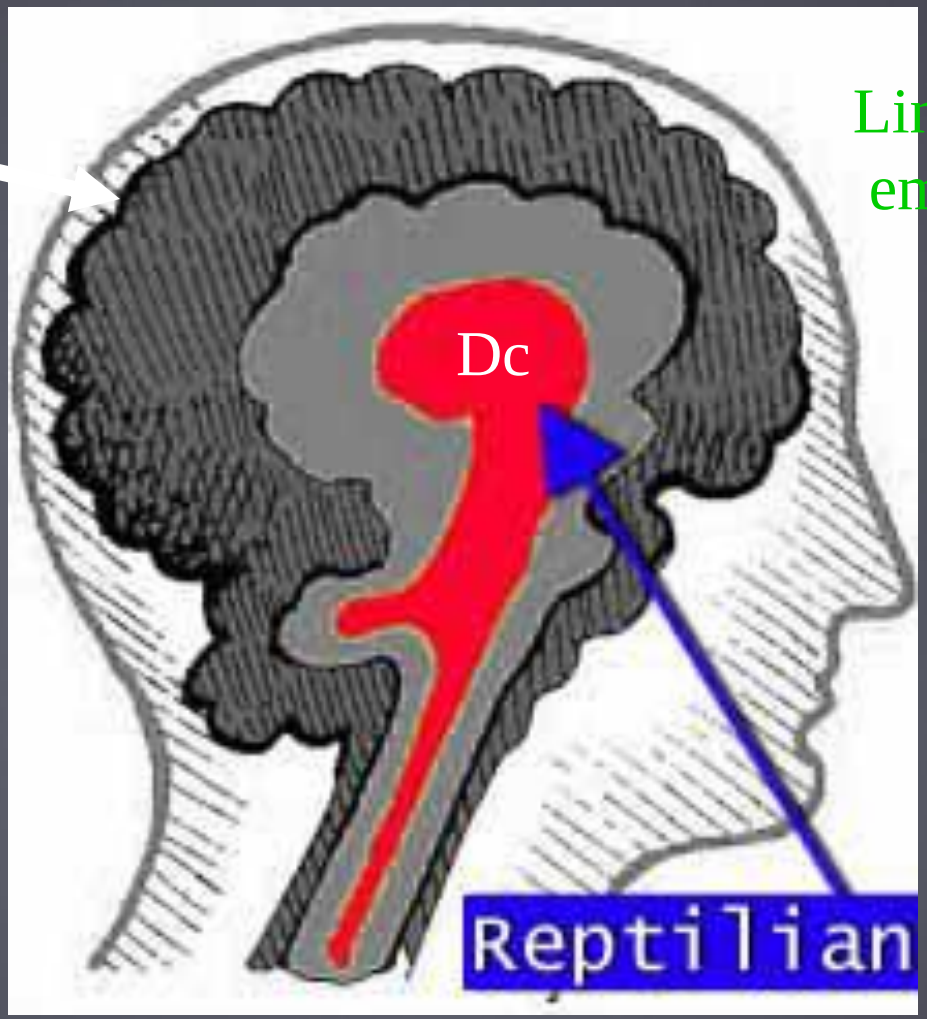


-Visual stimulus:

-Right: specific visual pathway (optic tract>Lateral Geniculate body>optic radiation (D)> visual cortex.

-Left: nonspecific pathway Neurons in the reticular formation (A) collect sensory information and project via the intralaminar thalamic nuclei (B) to cortex (C), causing **arousal** in response to sensory stimuli or attention-demanding tasks. Here PET shows increased blood flow in midbrain reticular formation (**A**) and (B) thalamic intralaminar nuclei and limbic cortex (L**C**) in response to the visual stimulus. Pain transmitted by spino-reticular track has similar thalamo-cortical distribution. Bilateral damage to reticular formation results in **coma**.

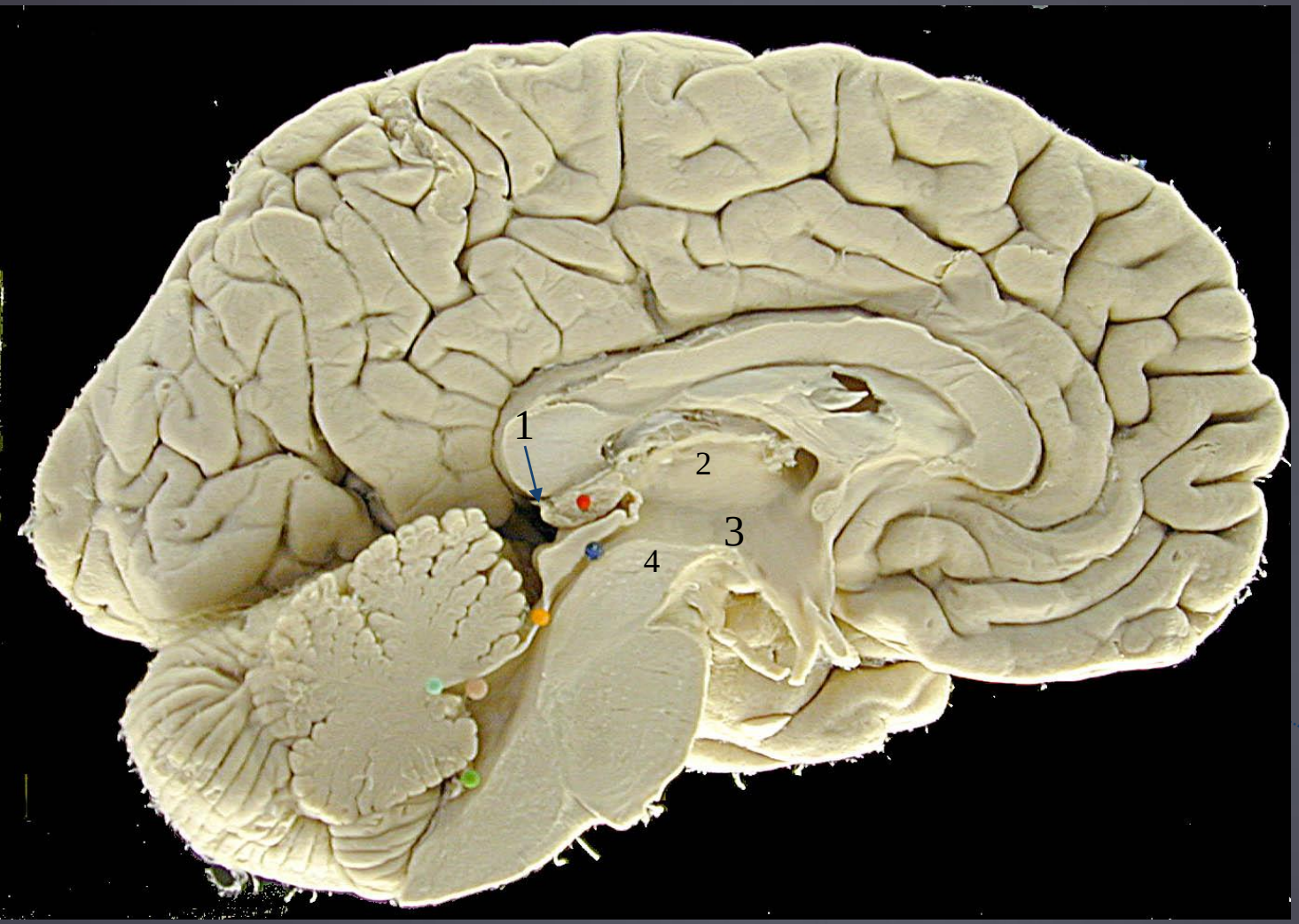
DIENCEPHALON (Dc)– tops the reptilian brain



Limbic functions – emotions, learning

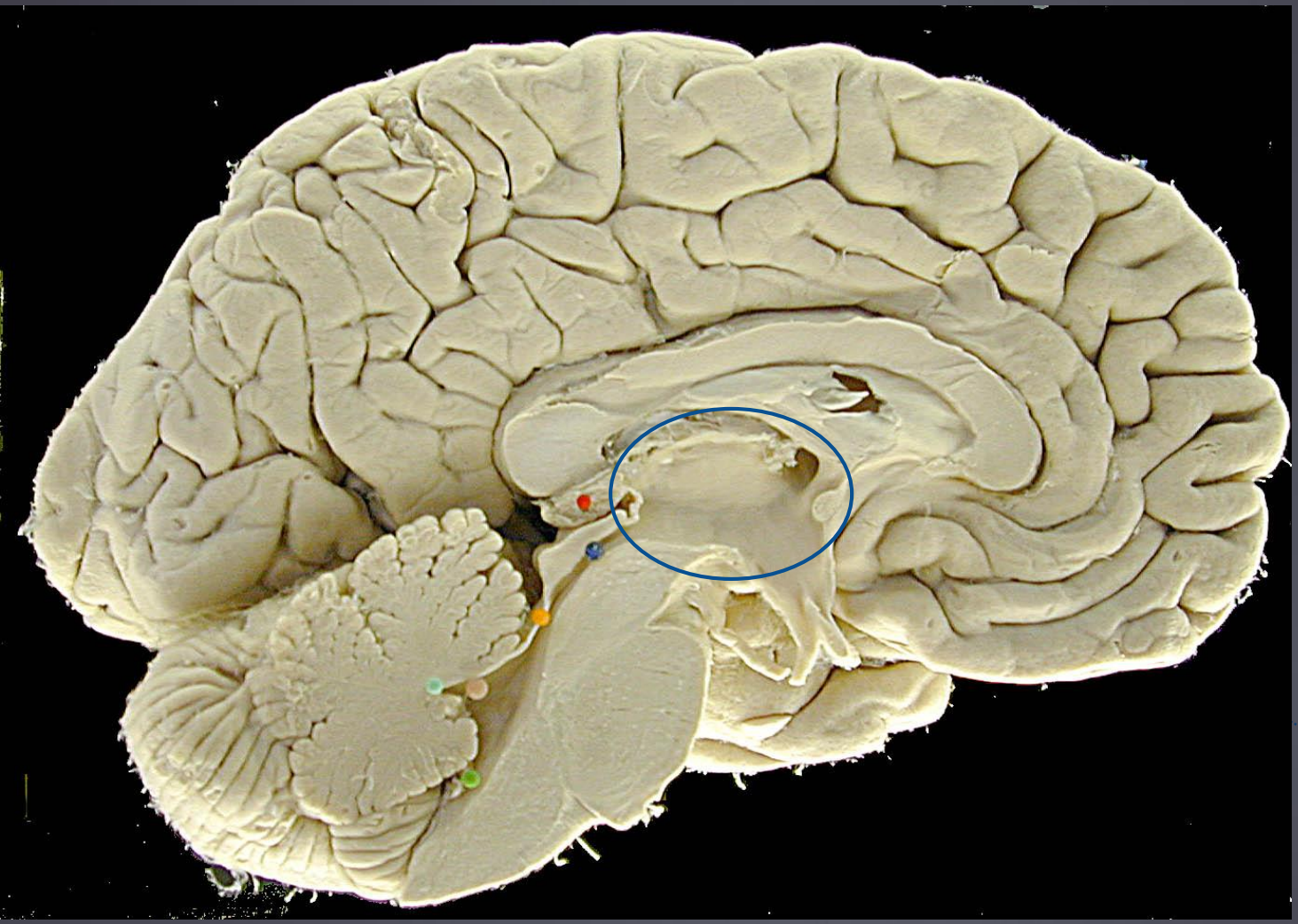
Self-preservation, aggression, instincts,

The diencephalon has four divisions:



1. Epithalamus (pineal gland, small nearby structures;
2. thalamus
(3) hypothala-mus,
(4) subthalamus
(All have less than 2% of the brain weight.

The diencephalon has four divisions:

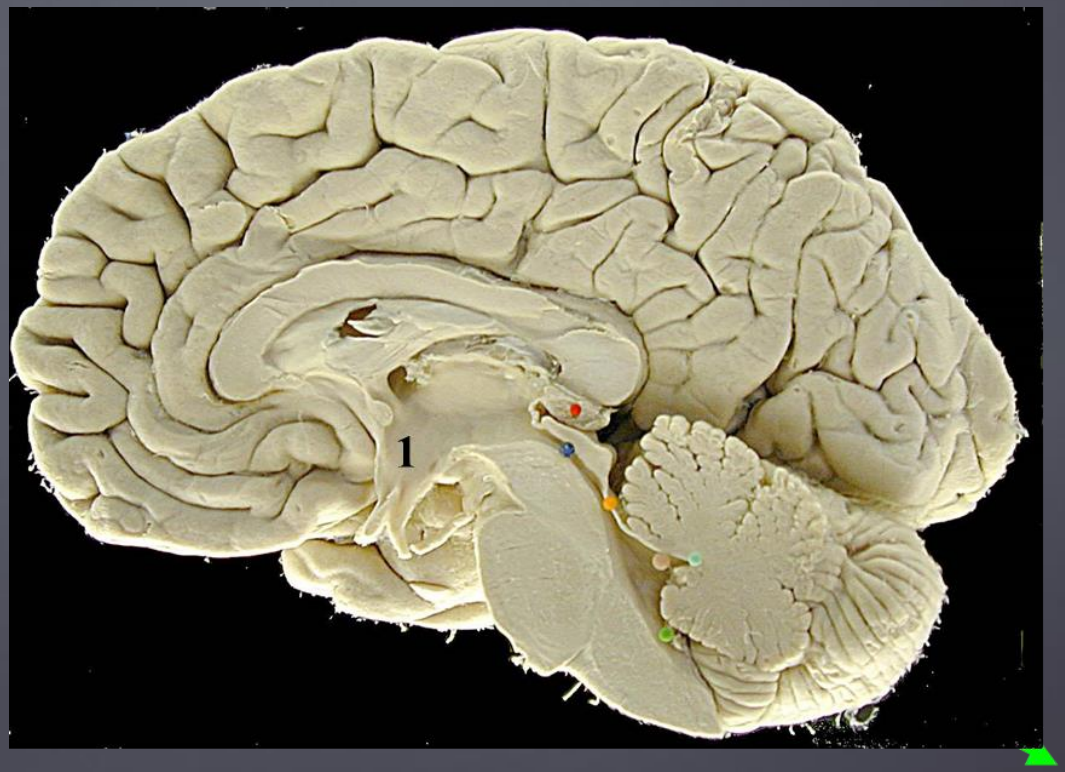


Thalamus - a relay station to cortex: (i) for all sensory information, except smell,
(ii) for motor loops between the cerebellum or basal ganglia and the cerebral cortex go
(iii) drive, emotion, learning – limbic functions

Hypothalamus

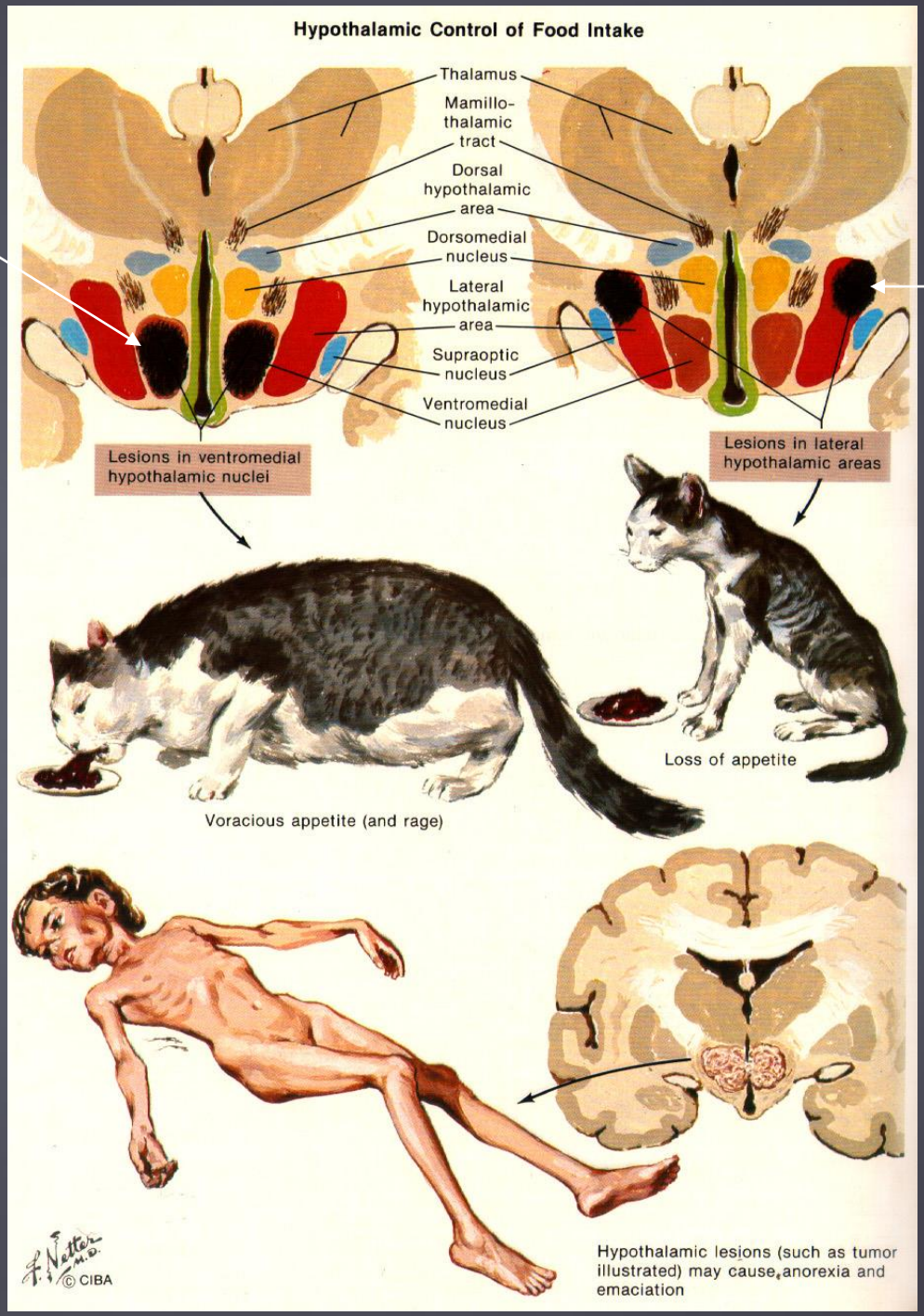
A IS A "VISCERAL CENTER" – RECEIVES "INTERNAL AND EXTERNAL" SENSORY INFORMATION,

CONTROLS AUTONOMIC, MOTOR AND LIMBIC SYSTEM FUNCTIONS



“Satiety center”

“hunger center”



Suprachiasmatic Nucleus – Master Clock

free running 25h cycle; reset by signals from the retina)

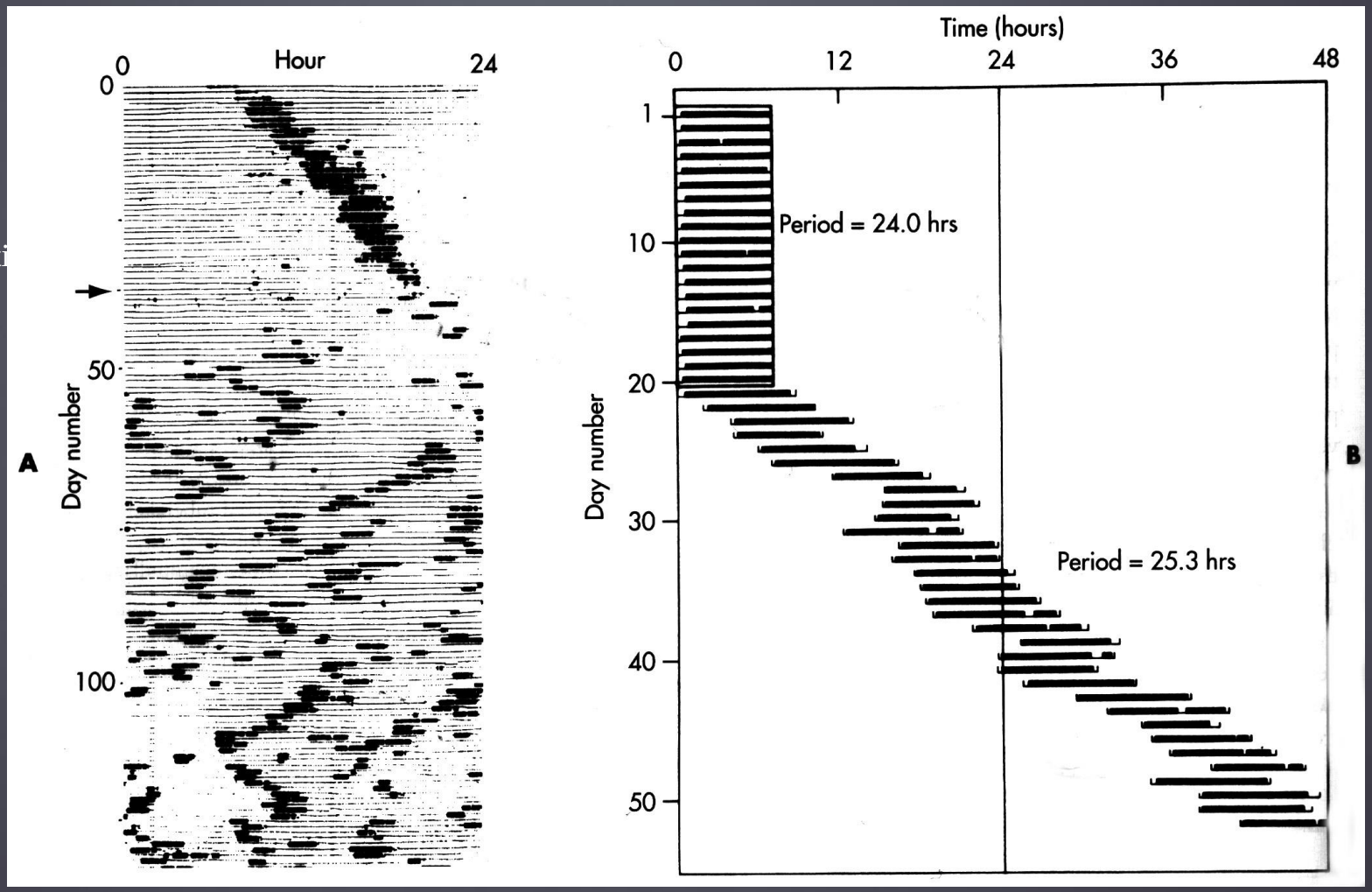
Human subject:

enforced self-selected sleep time

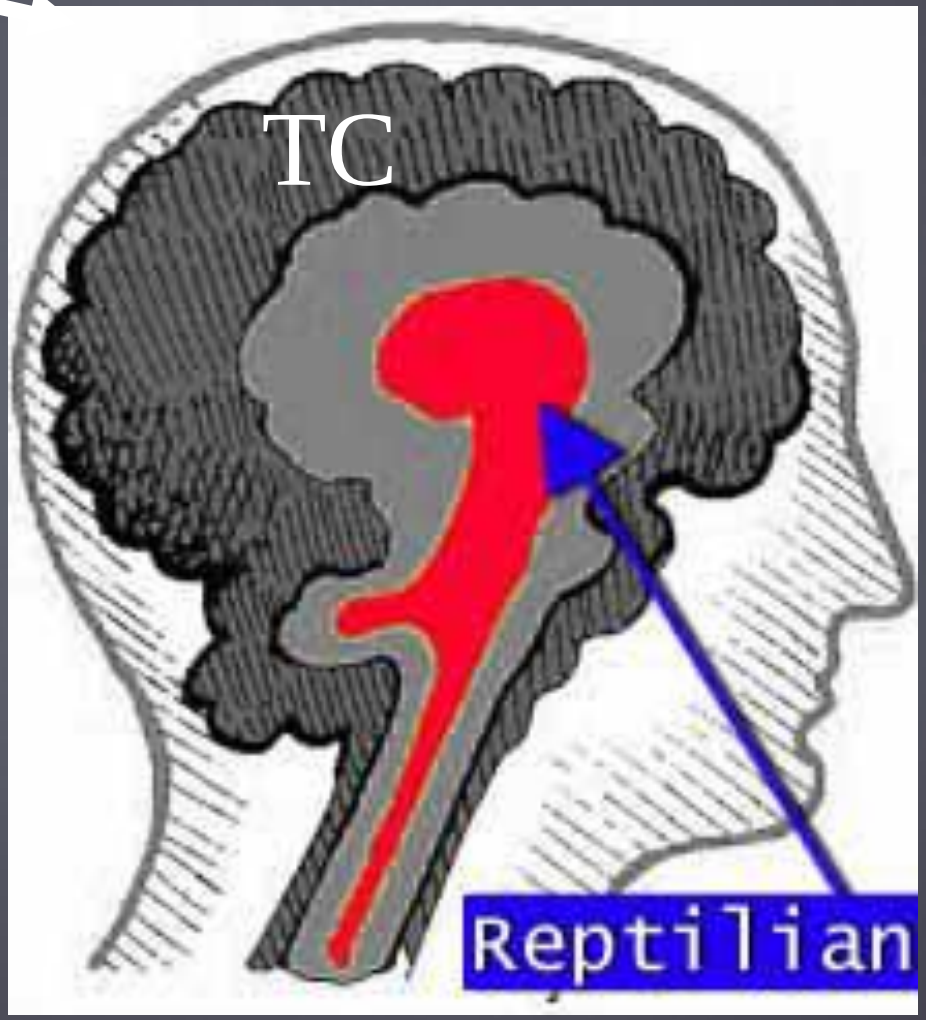
Hamster:

Wheel running behavior in constant light

Lesion of suprachiasmati nucleus



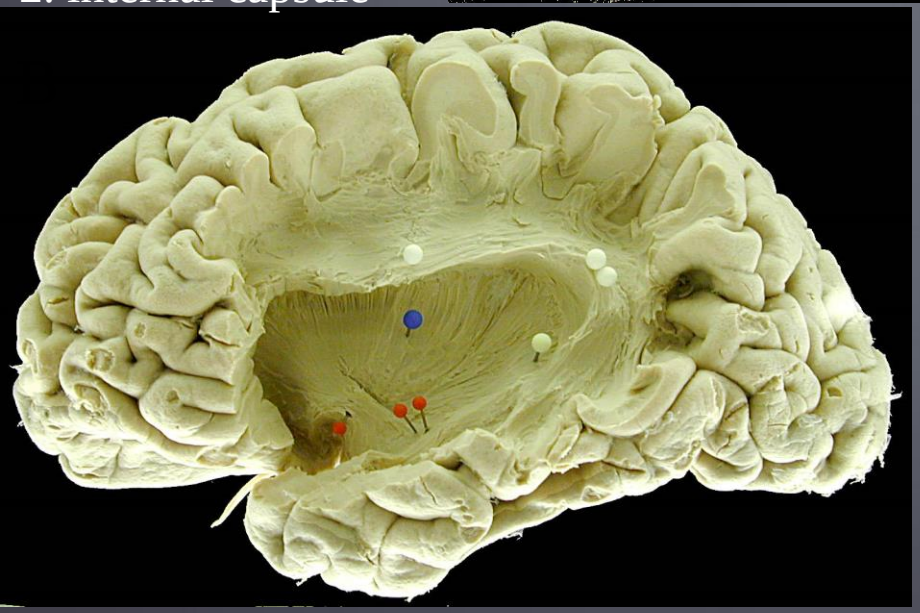
TELENCEPHALON (TC) – precision, flexibility, learning



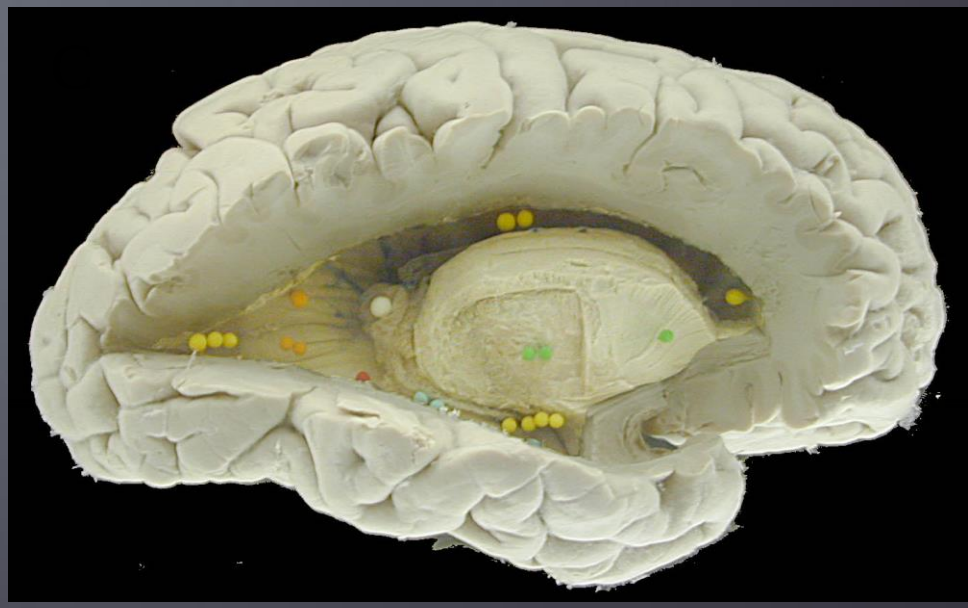
Self-preservation, aggression, instincts,

Telencephalon: (A) cortex, (B) subcortical white matter and (C) basal ganglia

Section revealing
1. Corona radiata,
2. internal capsule



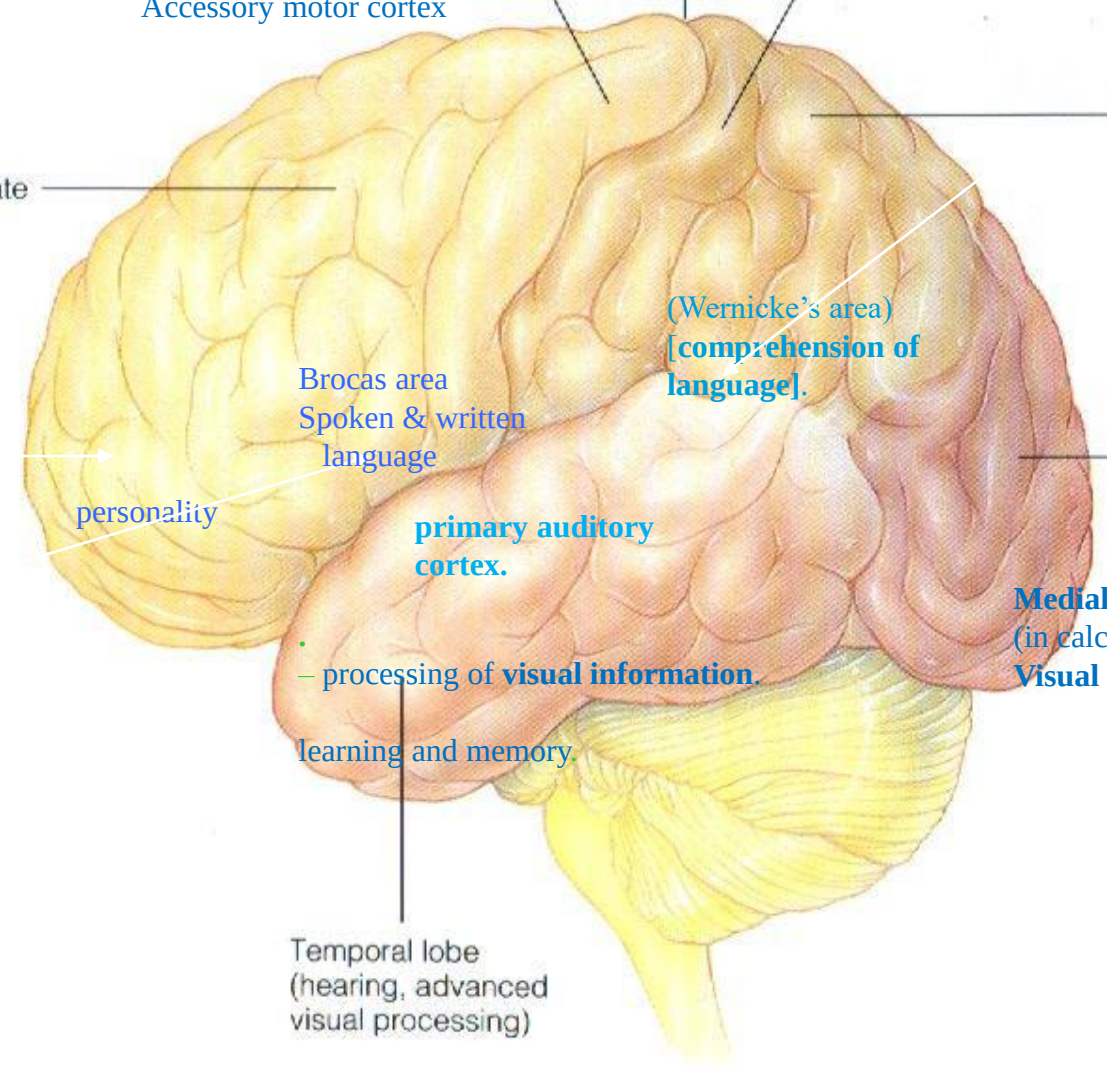
Section revealing Basal ganglia [lentiform nucleus)].



Transparency 18

Figure 4.20

Lobes of the cerebral cortex



Precentral gyrus (primary motor cortex)

Central sulcus

Postcentral gyrus (primary somatosensory cortex)

Initiation of voluntary movements

[initial cortical processing of tactile and proprioceptive information].

Accessory motor cortex

Frontal lobe (planning of movements, some aspects of memory, inhibition of inappropriate behaviors)

Parietal lobe (body sensations)

(Wernicke's area) **[comprehension of language]**.

Brocas area Spoken & written language

personality

Occipital lobe (vision)

primary auditory cortex.

Medialy:Primary visual cortex – (in calcarine sulcus)

Visual association cortex

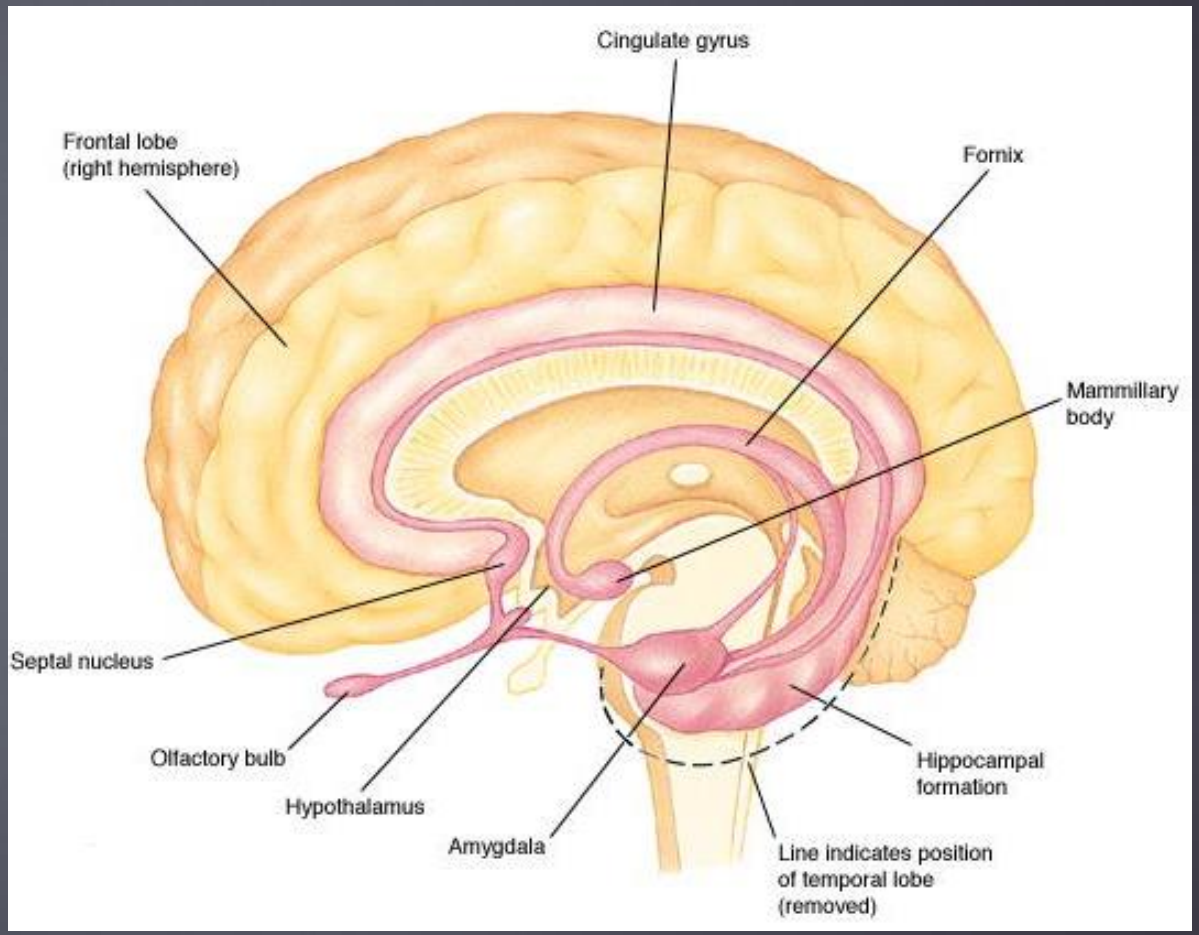
– processing of **visual information**.

learning and memory.

Temporal lobe (hearing, advanced visual processing)

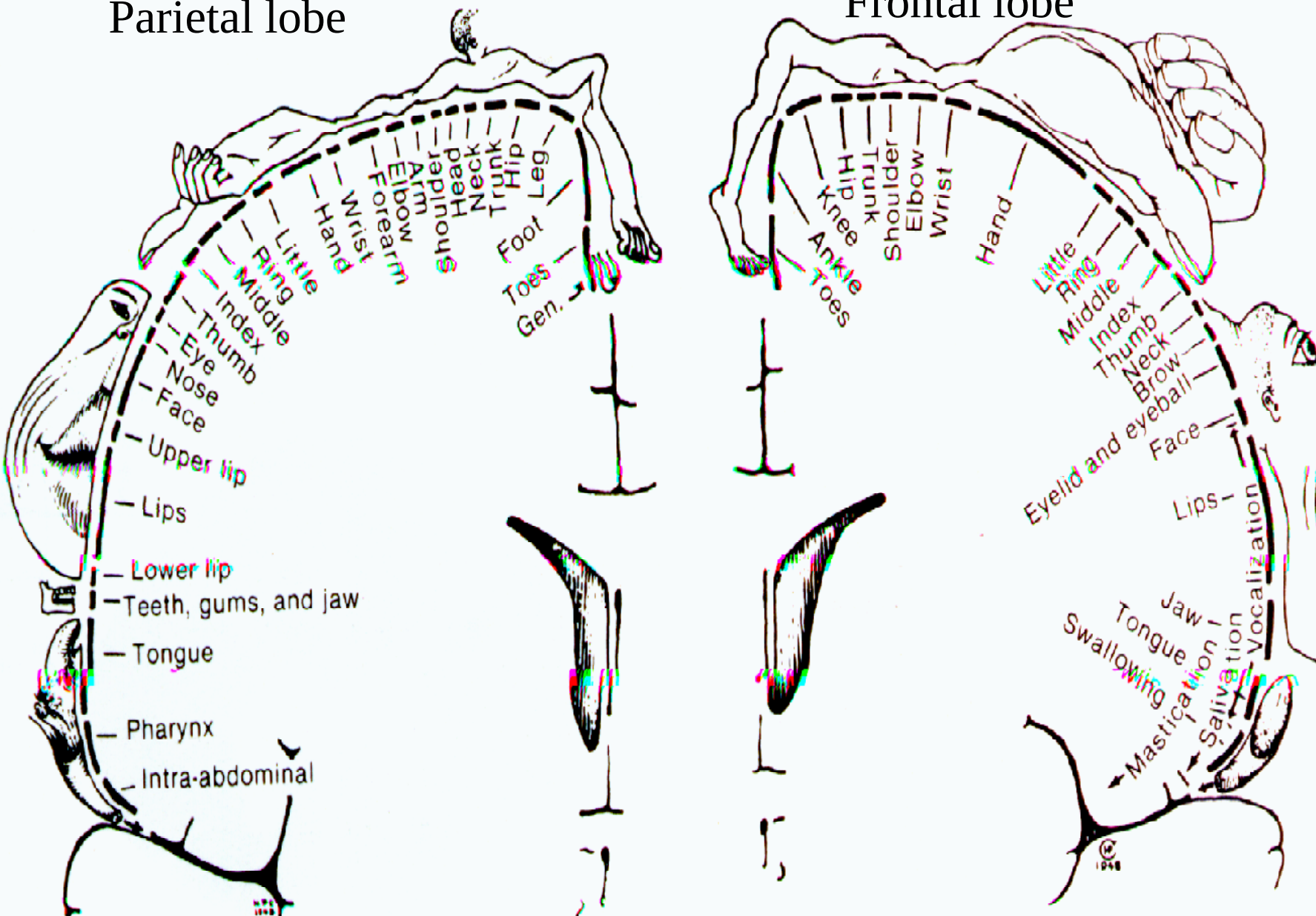
The limbic lobe, hippocampus and other interconnected structures make up the limbic system (emotional responses, motivation, and memory).

- Limbic System:
  - Amygdala – aggression and emotional memory
  - Hippocampus - memory
  - Cingulate - emotion
  - Olfactory - smell



Sensory homunculus
Parietal lobe

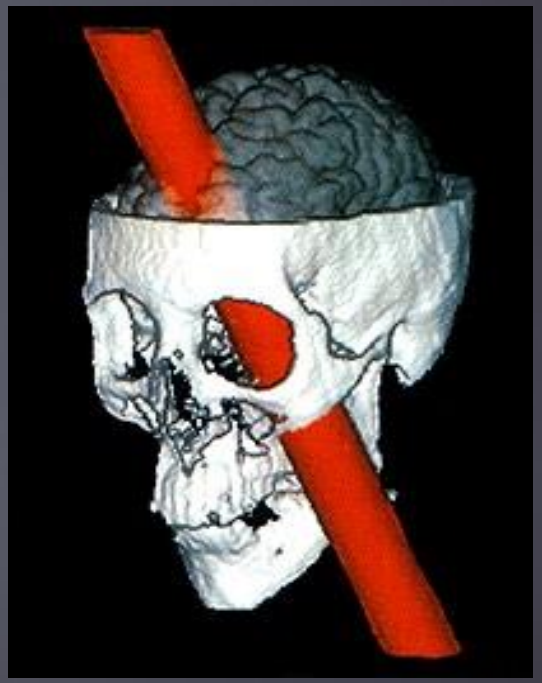
Motor homunculus
Frontal lobe



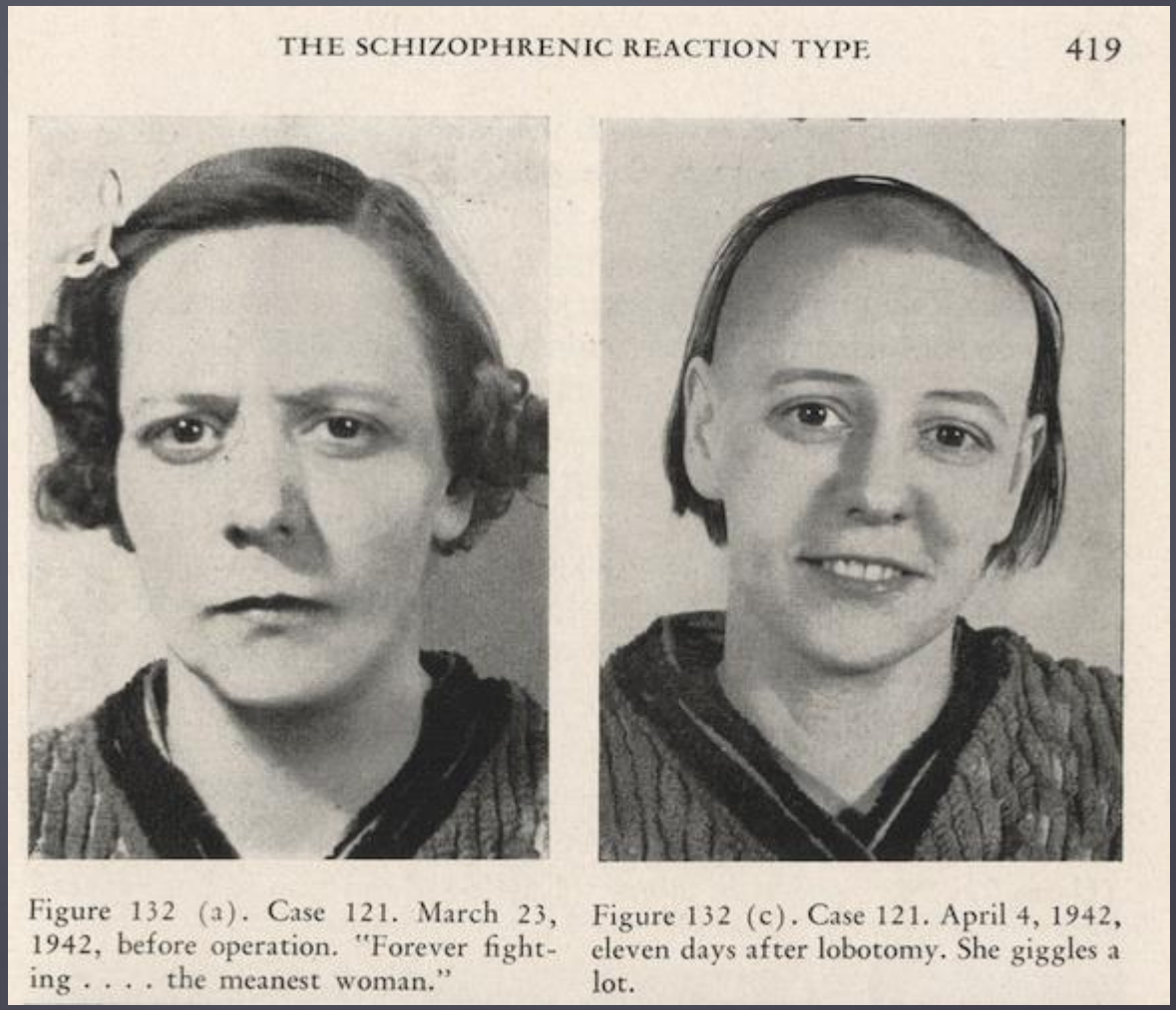
Phineas Gage, classic example of frontal lobotomy

"Within two months, the physical organism that was Phineas Gage had completely recovered--he could walk, speak, and demonstrate normal awareness of his surroundings. But the character of the man did not survive the tamping rod's journey through his brain. In place of the diligent, dependable worker stood a foulmouthed and ill-mannered liar given to extravagant schemes that were never followed through. "Gage," said his friends, "was no longer Gage."

http://www.mc.maricopa.edu/academic/cult_sci/anthro/origins/phineas.html



In 1949, Dr. **Antônio Egas Moniz** was awarded the Nobel Prize for Medicine and Physiology, in recognition of his creation of the prefrontal leucotomy, This had the effect of making **lobotomy** a respectable procedure, and as a result, in the ensuing three years, more **lobotomies** were performed than in all previous years.



THE SCHIZOPHRENIC REACTION TYPE 419

Figure 132 (a). Case 121. March 23, 1942, before operation. "Forever fighting . . . . the meanest woman."

Figure 132 (c). Case 121. April 4, 1942, eleven days after lobotomy. She giggles a lot.

Parietal association cortex mediates spatial orientation

Agnosia--lack of knowledge. Can't recognize object even though senses are intact.

Apraxia--lack of action. Unable to perform an action even though muscles are intact and the action could be performed under other circumstances.

Large lesions in the non-dominant parietal lobe results in spatial neglect, as seen below.

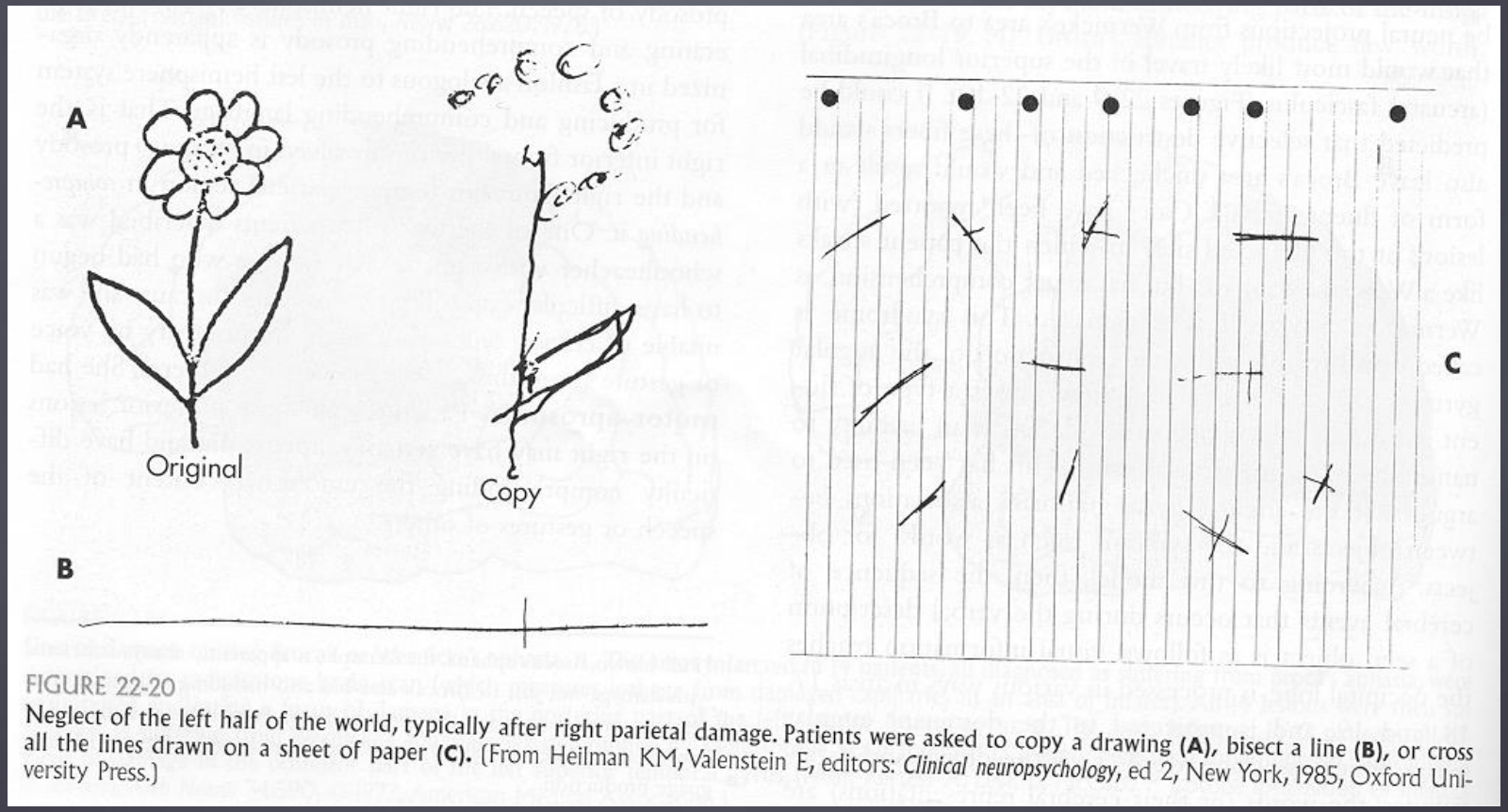


FIGURE 22-20
Neglect of the left half of the world, typically after right parietal damage. Patients were asked to copy a drawing **(A)**, bisect a line **(B)**, or cross all the lines drawn on a sheet of paper **(C)**. (From Heilman KM, Valenstein E, editors: *Clinical neuropsychology*, ed 2, New York, 1985, Oxford University Press.)

Association bundles interconnect areas within each cerebral hemisphere

Arcuate fasciclus: connects the frontal lobe with the parietal, occipital, and temporal lobes.
Superior and Inferior occipitofrontal fasciculi: connects occipital and frontal lobes.
(superior occipitofrontal is also called the **subcallosal bundle** because it runs under the corpus callosum.
Uncinate fasciculus: "hooks" around the lateral sulcus to connect the orbital (frontal) cortex with the anterior temporal cortex.

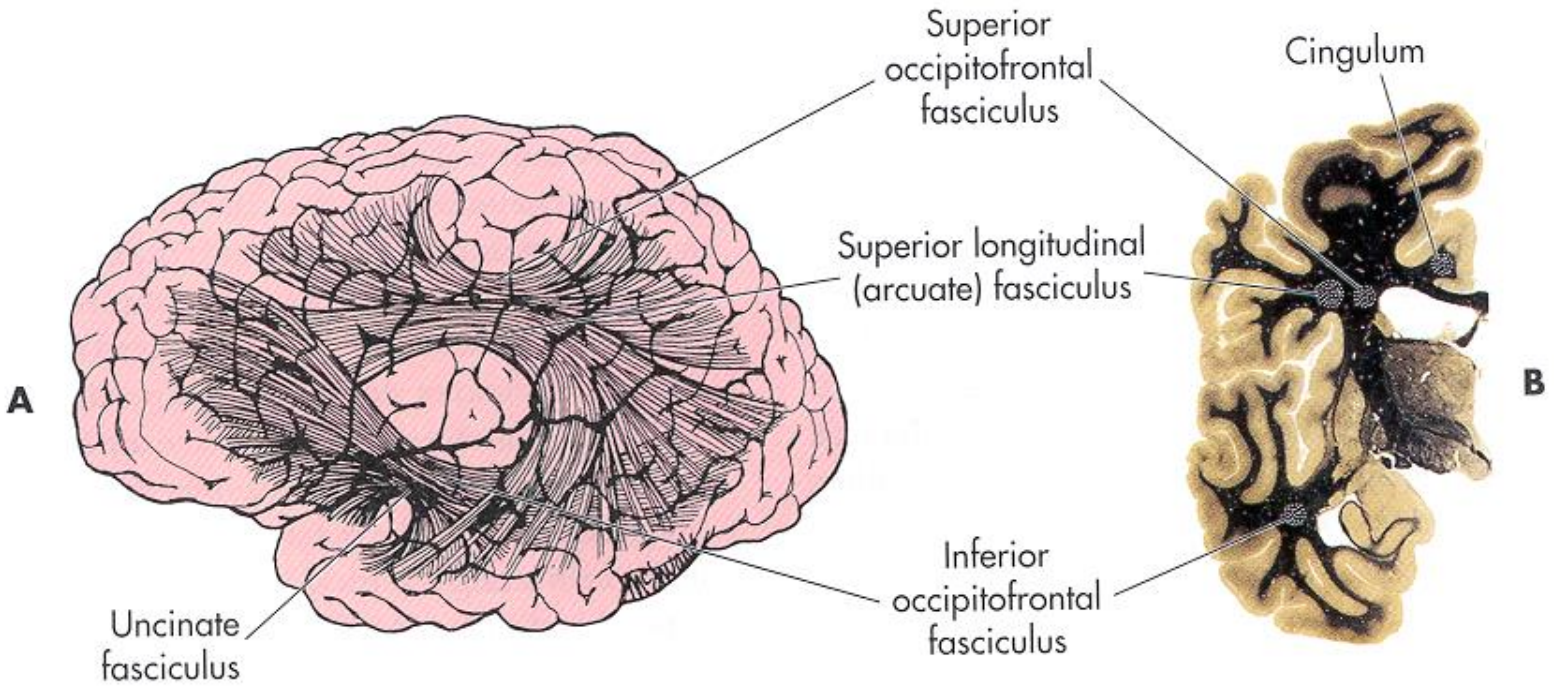
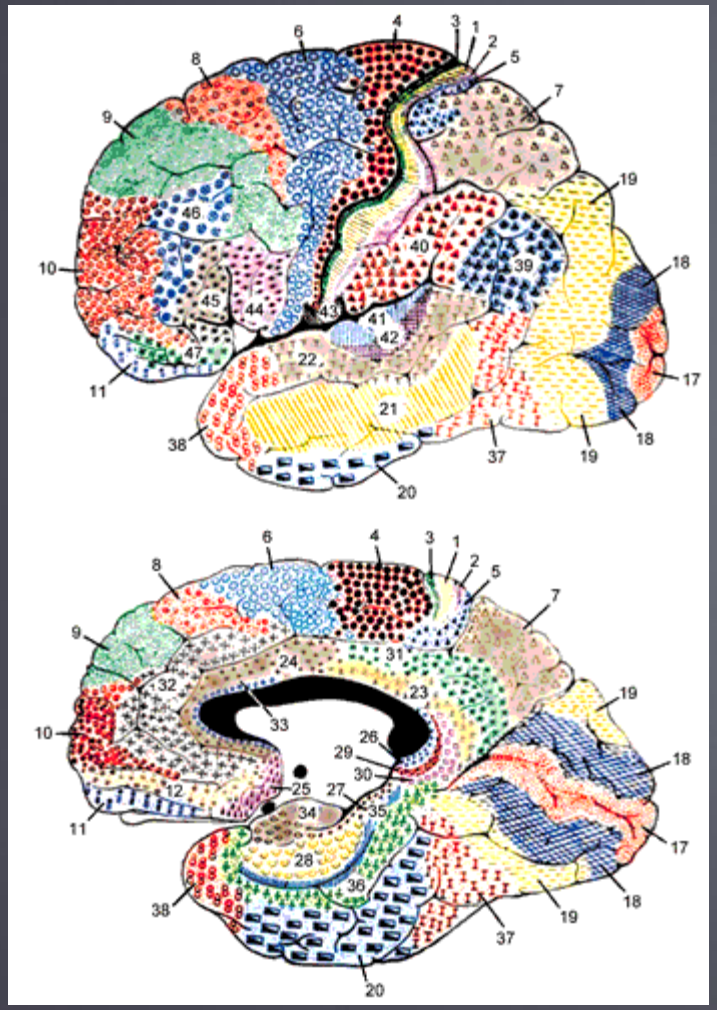
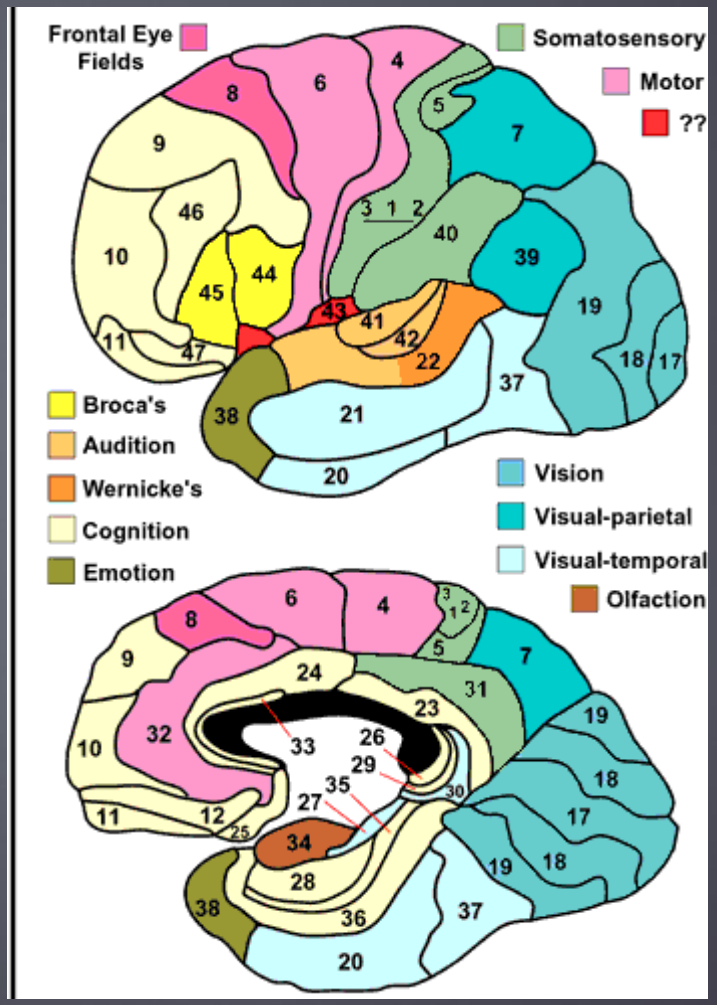


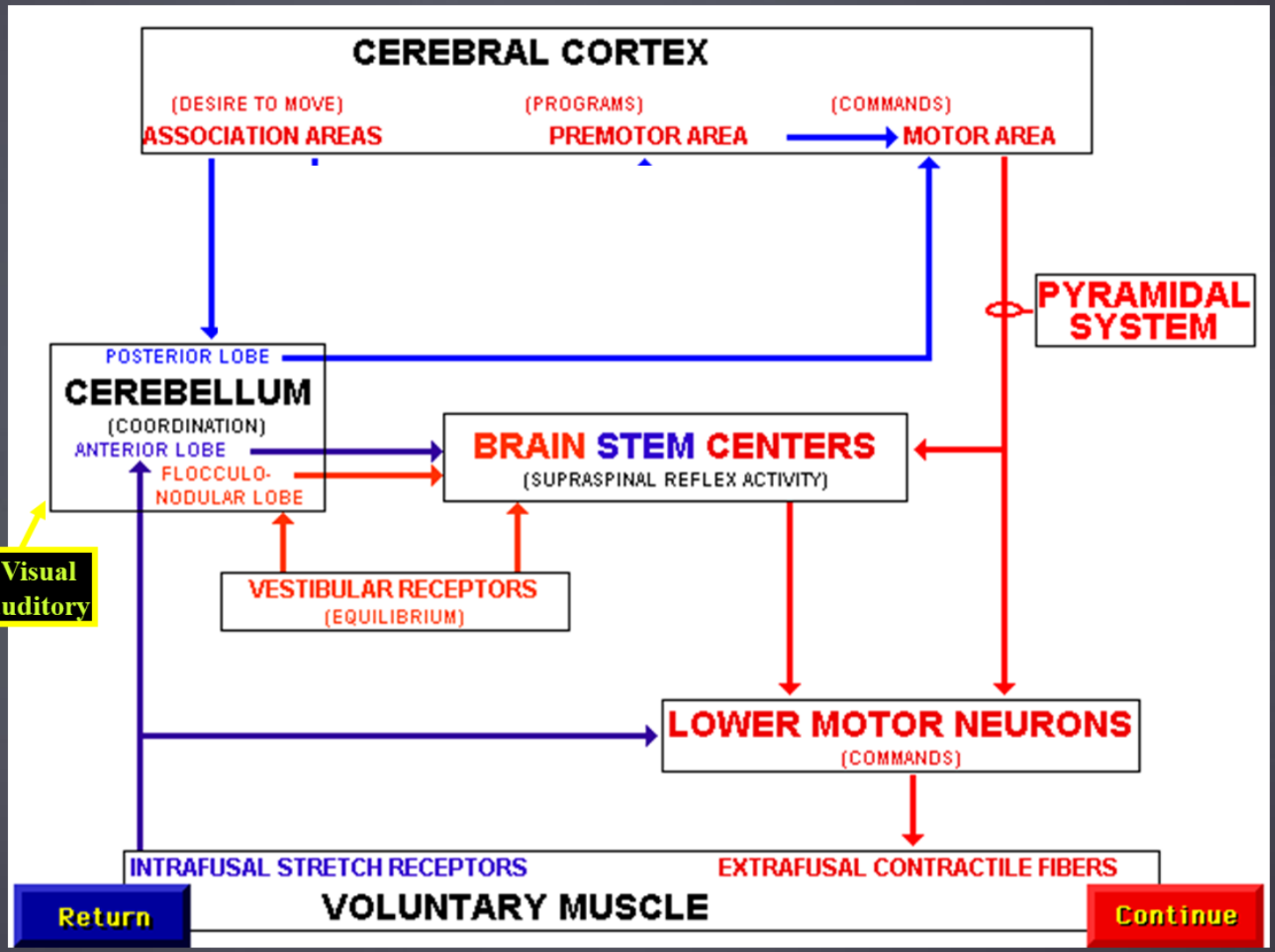
FIGURE 22-9
Long association bundles interconnecting cortical areas. **A,** Major bundles projected onto a lateral view of a cerebral hemisphere. **B,** Position of association bundles in a coronal section through one cerebral hemisphere.

Brodmann divided cortex into 52 **structurally distinct** regions. These regions correspond well with **functional** anatomy, and so his numbering system has stayed popular.

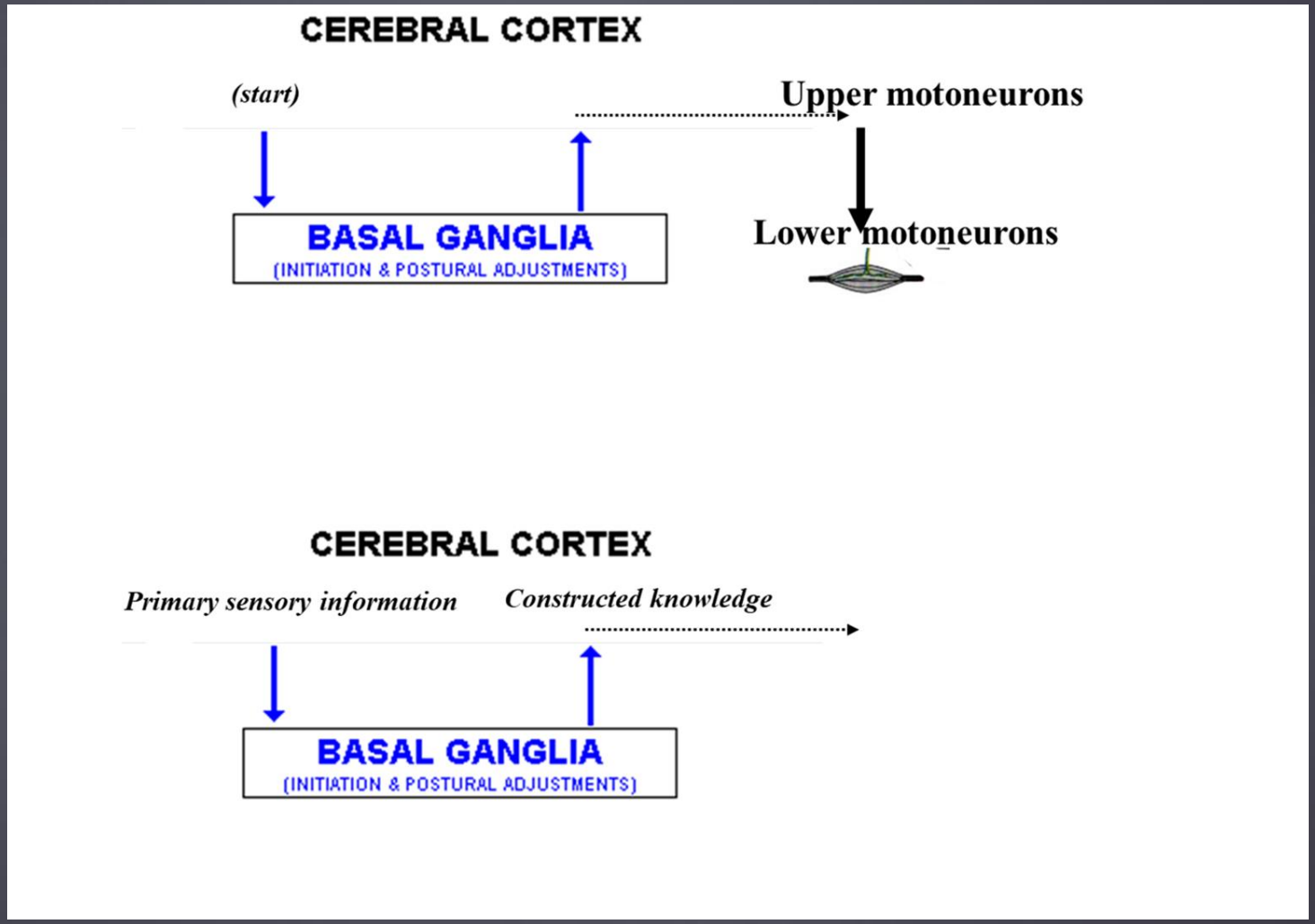


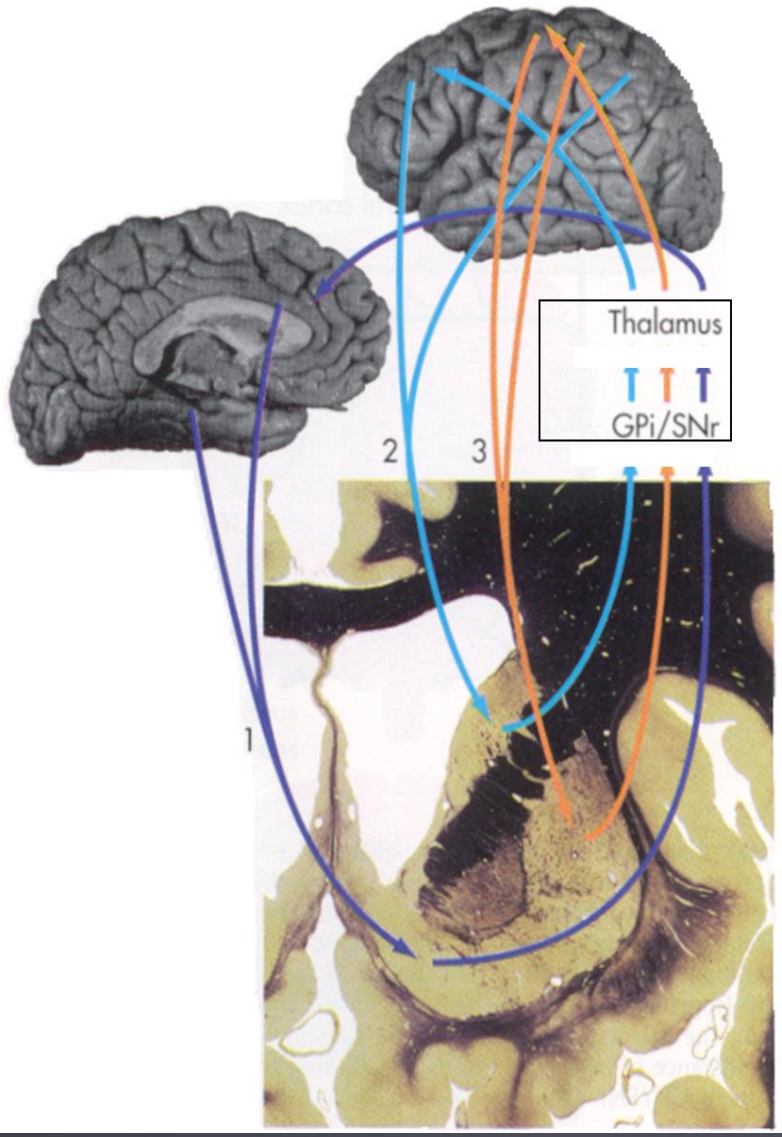


Computational brain – integrating inputs and plans in cerebellum



Computational brain – gating principle, basal ganglia



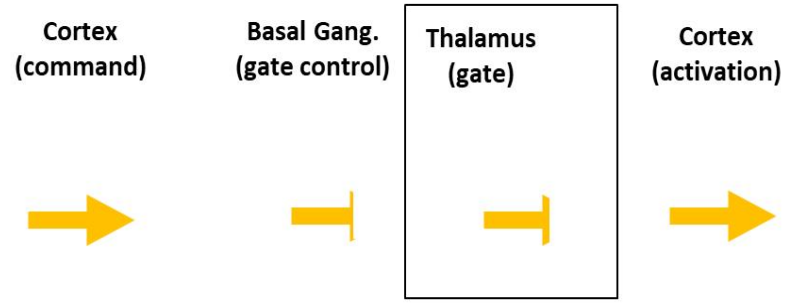


Brain computational circuits

Basal Ganglia loops execute motor functions (3) Somatosensory processing (2) & (3) cognition &drive (3) using information gating system

Deficits in Basal Ganglia functions affect:

1. Drive – *excessive gating depression, psychoses*
2. Somatosensory processing - *reduced gating - hallucination, schizophrenia*
3. Motor behavior - *excessive gating – Parkinson Dsease;*
   - abolished gating – Huntington, Balismus, Tourrette's



Diseases of the information processing

Closed gate – PD

Open gate – HD, Tourrete's

Schizophrenia

Computational errors – lack of sensory input - spino cerebellar ataxias

http://www.youtube.com/watch?feature=player_embedded&v=i4b-_bNsajY

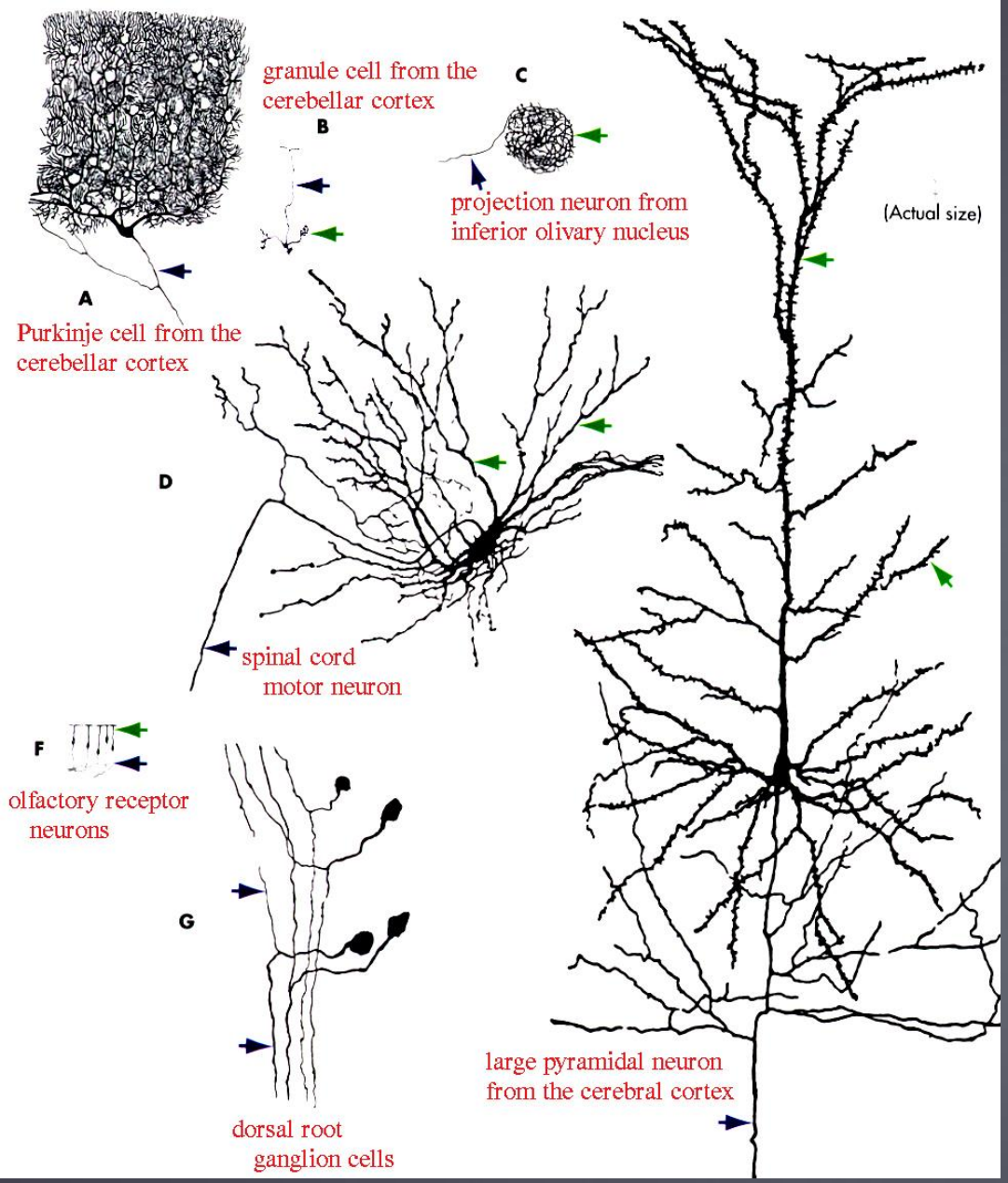
The End

- **Supplement:**

Cellular elements in the Nervous system and their basic functions

-

Review past material from the Histology & Neurophysiology courses



"The Human Brain – an Introduction to its Functional Anatomy"
6th edition,author - John NoltebMosby/Elsevier

Morphological types of neurons (arrows > **dendrites**, **axons** 1mm - >1 m; soma 5-100 micrometers):

1. **Multipolar:**
multiple dendrites and almost always an axon *(A-E)*

2. Bipolar *(F)*

3. Unipolar *(pseudounipolar with two fused processes)*

Functional classification:

- 1%:
  - sensory neurons- (connected to, or serving as receptors)
  - motor neurons
- 99%:
  - interneurons
  - projection neurons

Non-neuronal cells in the CNS:

1. **Glial Cells:**

A. Protoplasmic Astrocytes (gray matter, mechanical and metabolic support, response to injury).

B. Fibrous Astrocytes (white matter, mechanical and metabolic support, response to injury).

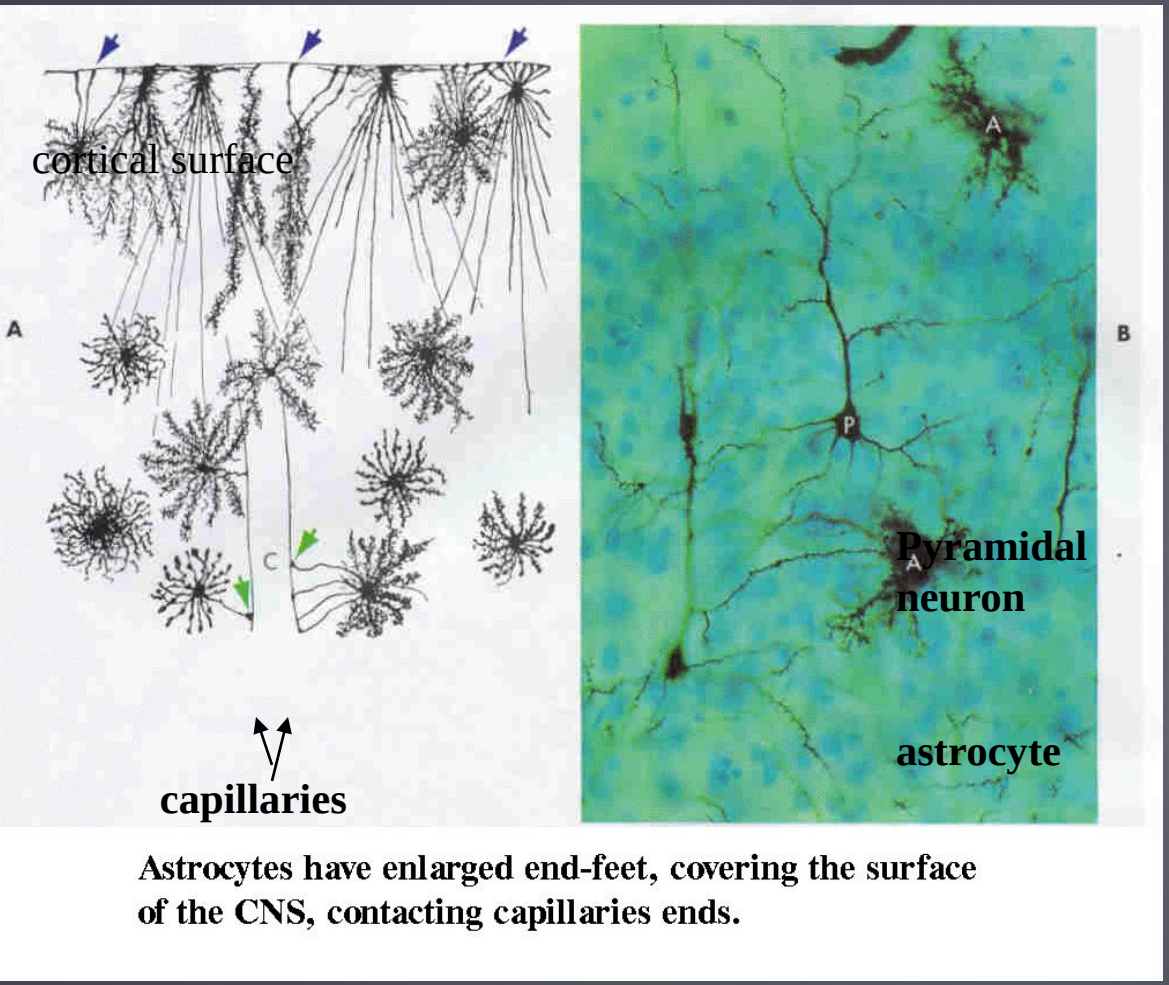
C. Radial Glia (developmental form)

D. Oligodendrocytes (white matter, form myelin sheath).

2. PNS glia:

Schwann Cells (Principal PNS Glial Cells)

Protoplasmic Astrocytes:



Astrocytes have enlarged end-feet, covering the surface of the CNS, contacting capillaries ends.

Protoplasmic Astrocyte processes have enlarged **end-feet** that are applied to CNS capillaries, CNS surface (protective membrane – "pia matter"), or neurons.

Fibrous Astrocytes are associated with some axons. All provide structural, metabolic, ionic, and trophic support to neurons. Form gliotic scars.

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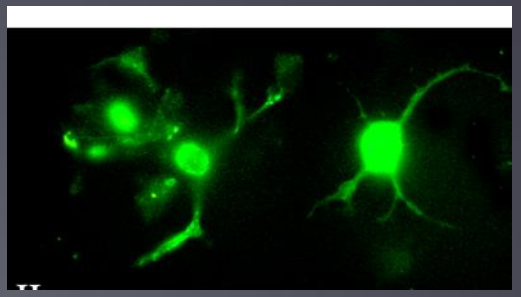
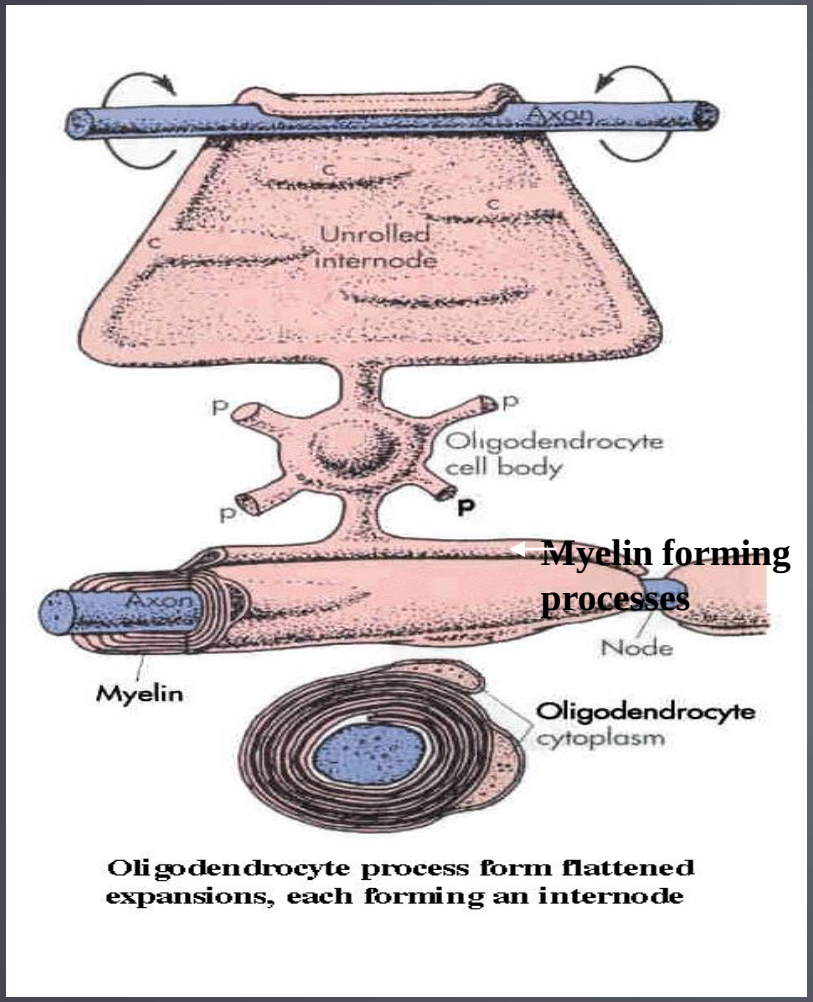
6th edition,author - John NoltebMosby/Elsevier

Oligodendrocytes form myelin sheath in the CNS.





Oligodendrocyte process form flattened expansions, each forming an internode

In the CNS the myelin sheath is formed by oligodendrocytes (glial cells with few processes)**. Using these processes individual oligodendrocytes** produce **multiple internodes** (0.2-2 mm) on multiple axons. Areas not covered by myelin - ”nodes of Ranvier” (0.001).

Oligodendrocytes **do not envelop nonmyelinated axons** (in CNS such axons are exposed to the extracellular environment; poor regeneration).

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6th edition,author - John NoltebMosby/Elsevier

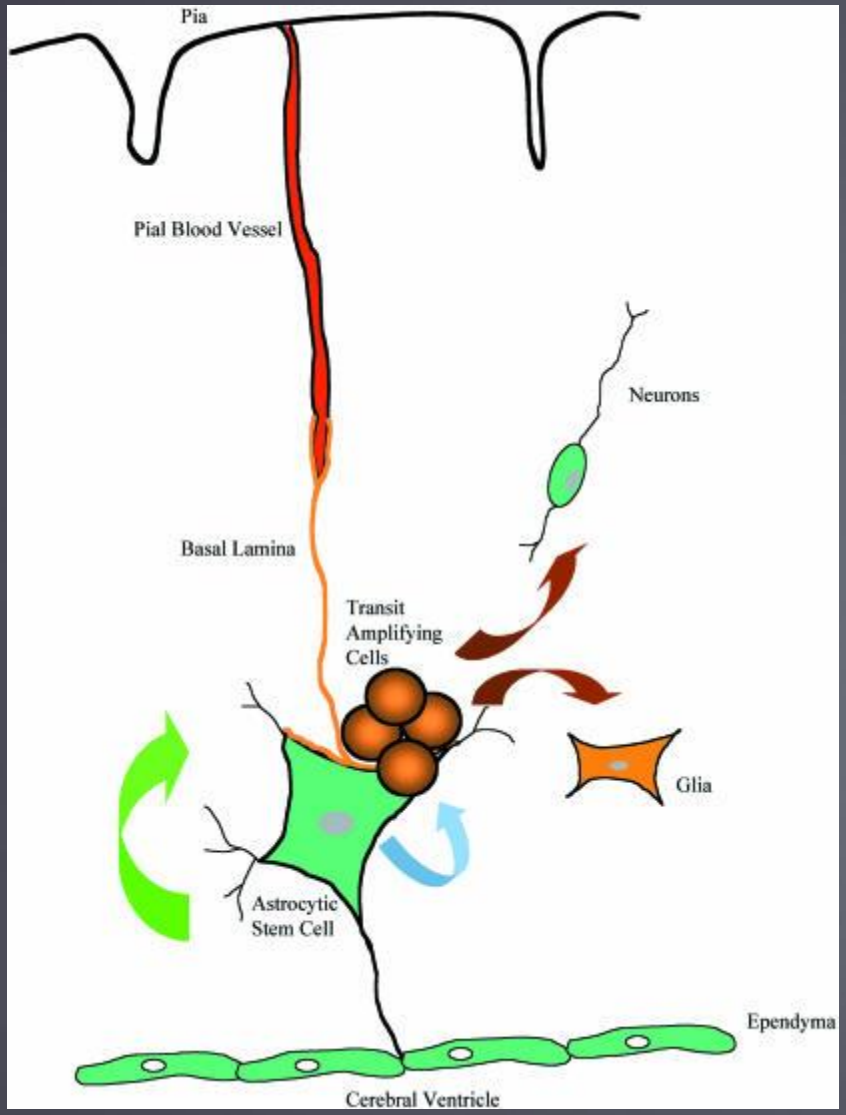
Other cells in CNS:

2. **Microglia** (gray and white matter, phagocytosis).

3. **Ependymal cells** (walls of ventricles, choroid plexus; secrete CSF)

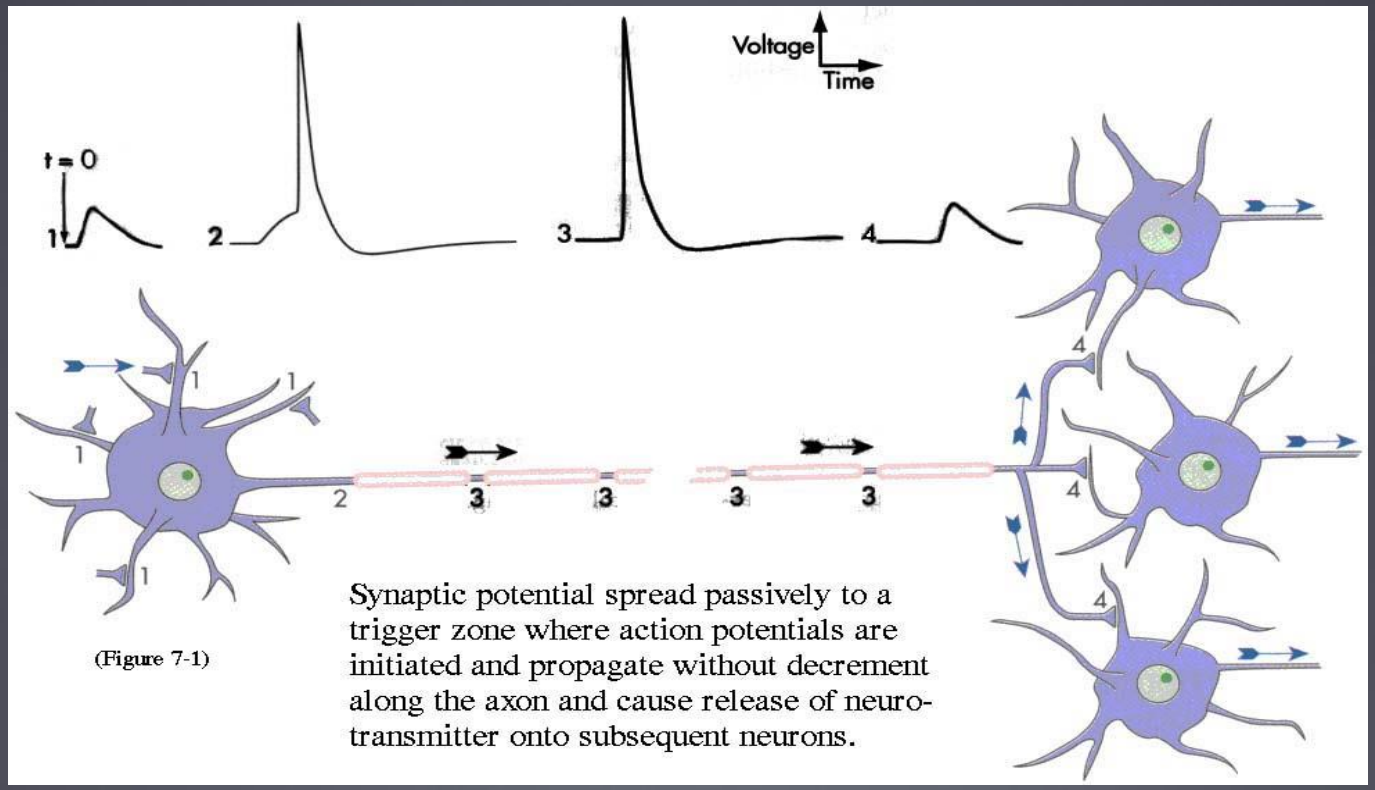
4. **Brain stem cells** related to astrocytes (under ependymal layer - walls of ventricles)

Brain stem cells are related to astrocytes



The multipotent stem cell-like astrocytes are closely opposed to the ventricular lining and basal lamina associated with the pial microvasculature. Asymmetric division gives rise to self-renewal (green arrow) and a transit amplifying population (blue arrow). These cells can migrate out of the germinal niche and differentiate into neurons and glia (astrocytes or oligodendrocytes).

In the NS Information is carried out by multi-neuronal chains (pathways) in which neurons are separated by synapses.



(Figure 7-1)

Synaptic potential spread passively to a trigger zone where action potentials are initiated and propagate without decrement along the axon and cause release of neuro-transmitter onto subsequent neurons.

In the Neurons the information is encoded in **electrical impulses** and in synapses by chemicals – **neurotransmitters.** At every synaptic junction chemical signals are converted into **postsynaptic potentials** (PP), which are in turn converted into and carried as **action potentials** (AP) – velocity increases with the size of axon and myelinization). At the axon terminal AP causes release of neurotransmitter which transmits excitation across synaptic cleft to regenerate PP.

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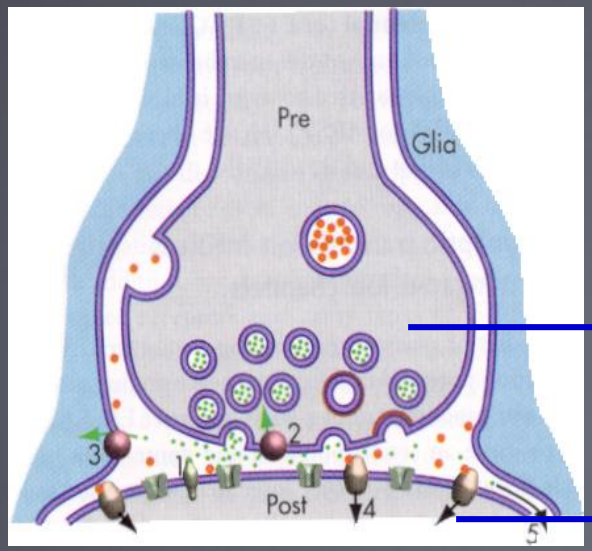
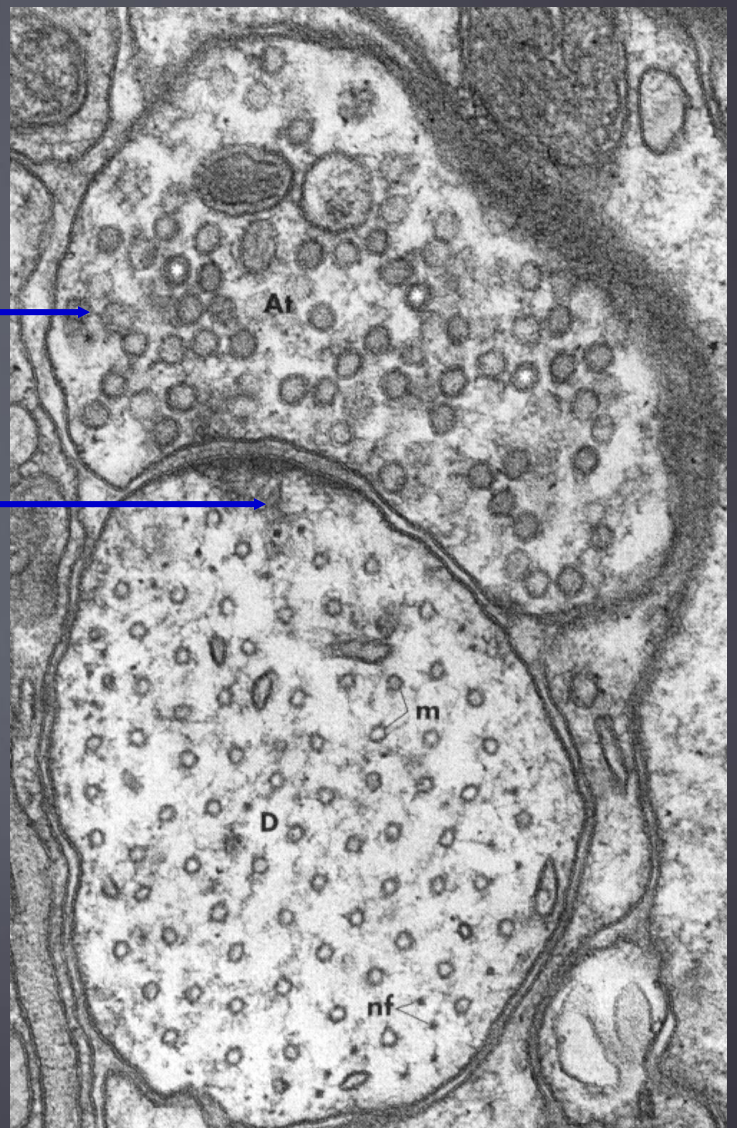
ANATOMICAL ASYMETRY OF CHEMICAL SYNAPSES DETERMINES UNIDIRECTIONAL TRANSMISSION

presynaptic endings – terminal buttons at the tip of the axon. Neurotransmitter-filled **vesicles** have only presynaptic localization.

a.





synaptic cleft 10 to 20 nm**, postsynaptic element** – a thickened postsynaptic membrane with receptors (on dendrites, soma, axon initial segment, or another synaptic terminal). Fig. 1-19.

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Table 8-1 Major Neurotransmitters

Type	Major Transmitters
Amines	Acetylcholine
	Cetecholamines
	Dopamine
	Norepinephrine
	Serotonin
Amino Acids	Glutamate (and asparate)
	GABA (γ-aminobutyric acid)
	Glycine
Neuropeptides	Angiotensin II
	β-Endorphin
	Cholecystokinin
	Enkephalin
	Neuropeptide Y
	Neurotensin
	Somatostatin
	Substance P
	And many others

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Supplemental Information

Neoplasms (NRSIII):

1. Medulloblastoma

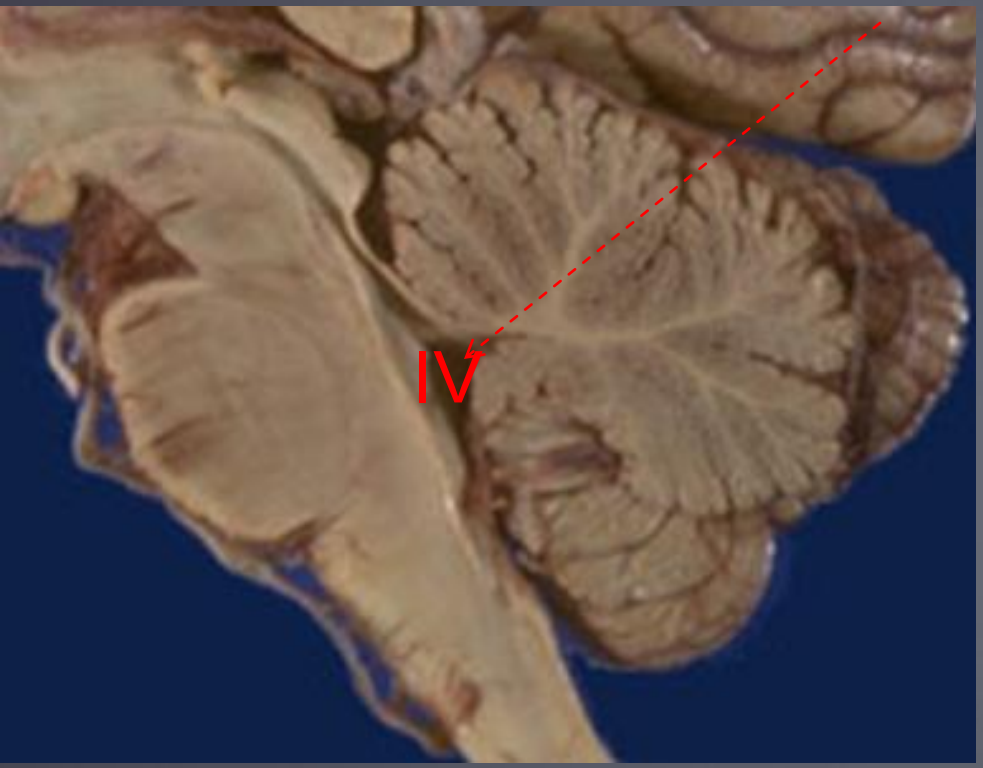
Progenitors of Cerebellar neurons (granule cells) continue to proliferate and mature in early postnatal life. Uncontrolled proliferation may lead to medulloblastoma tumors.
Medulloblastoma tumors in the cerebellum can cause loss of functioning of cerebellum, leading to uncoordinated movement - cerebellar ataxia

Medulloblastoma affects other brain structures

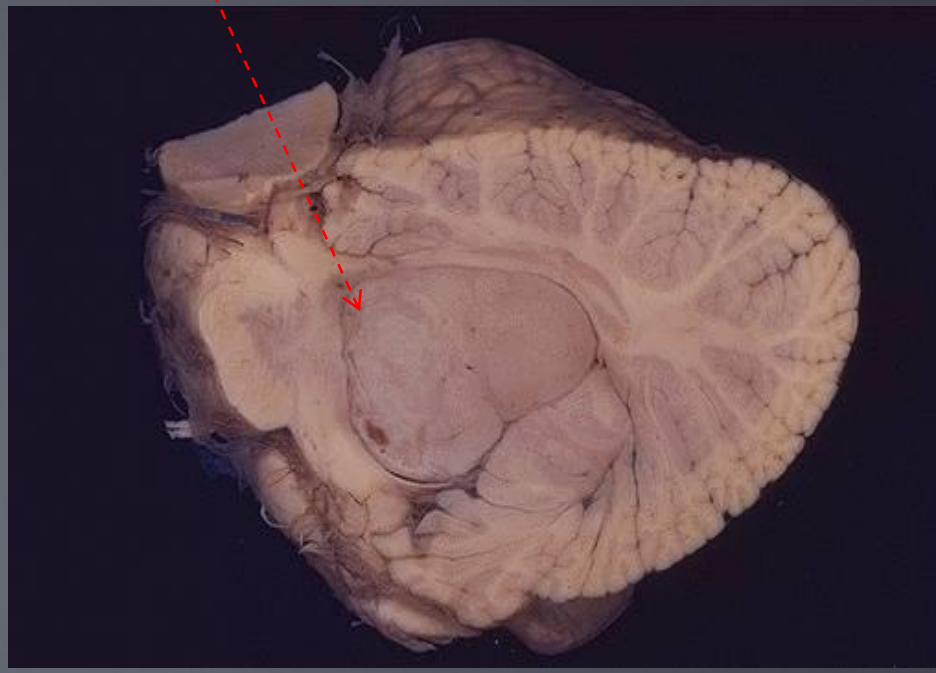
- The irregular posterior fossa mass that is seen here near the midline of the cerebellum and extending into the fourth ventricle above the brainstem is a medulloblastoma. This is one of the "small round blue cell" tumors and it most often occurs in children.
- Large tumors invade other brain structure in addition to the cerebellum (here medulla), other regions may include midbrain or upper spinal cord

2. ependymoma

Normal



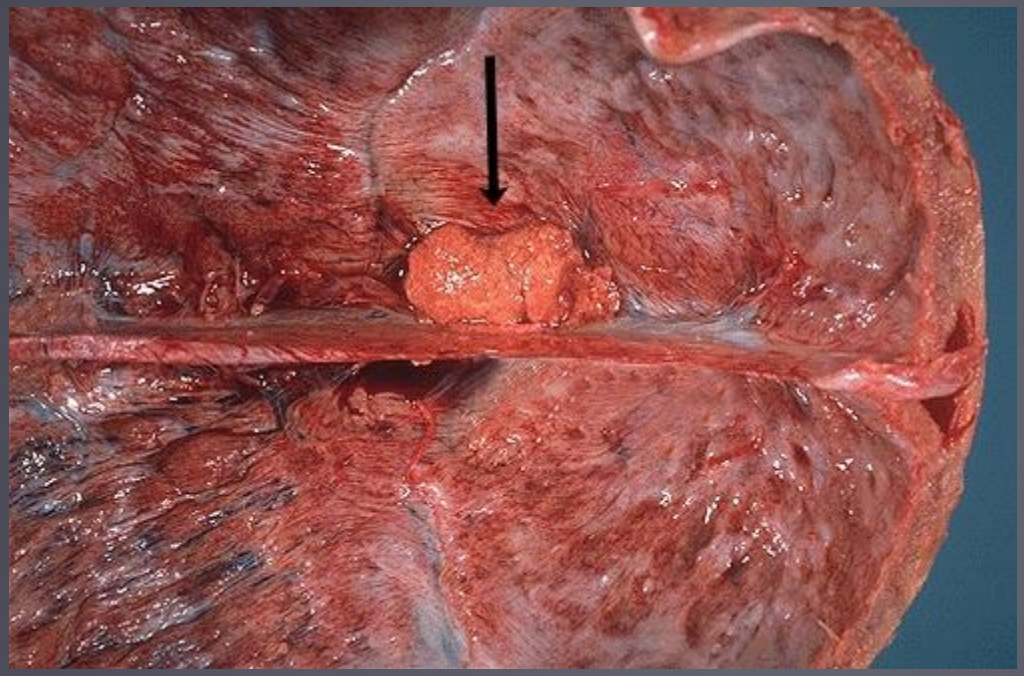
disease



- Here is an ependymoma arising from the ependymal lining of the fourth ventricle (IV) above the brainstem and bulging toward the cerebellum. Ependymomas are benign histologically

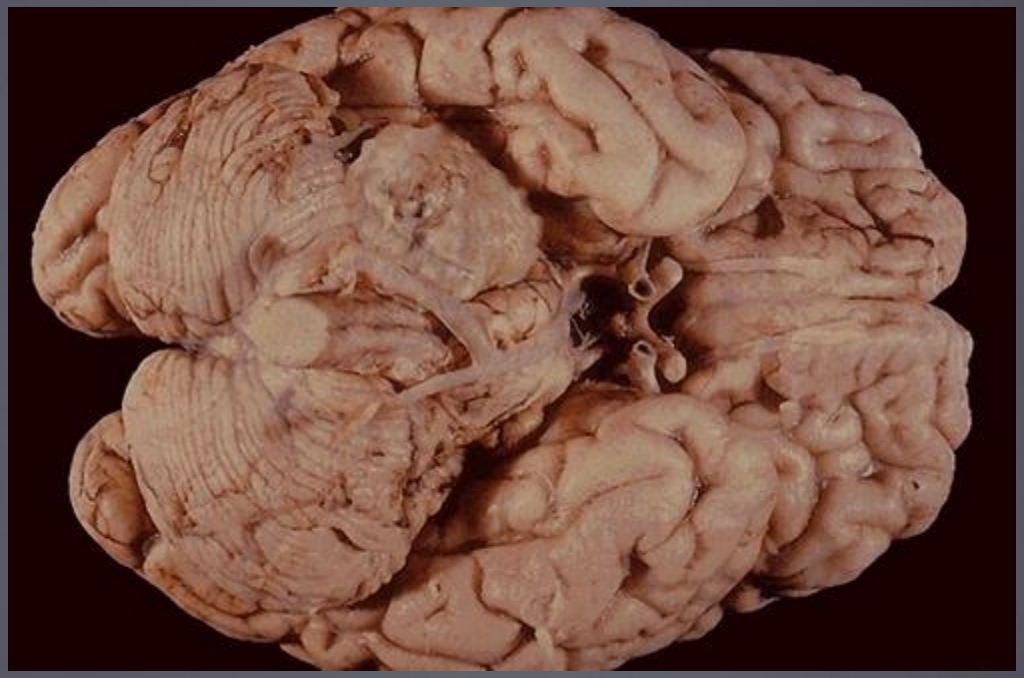
3. Meningioma.

Meningiomas arise from arachnoidal cells, often in the vicinity of the venous sinuses. This circumscribed reddish-yellow firm neoplasm beneath the dura next to the falx is a meningioma. The superior parasagittal location is quite common.



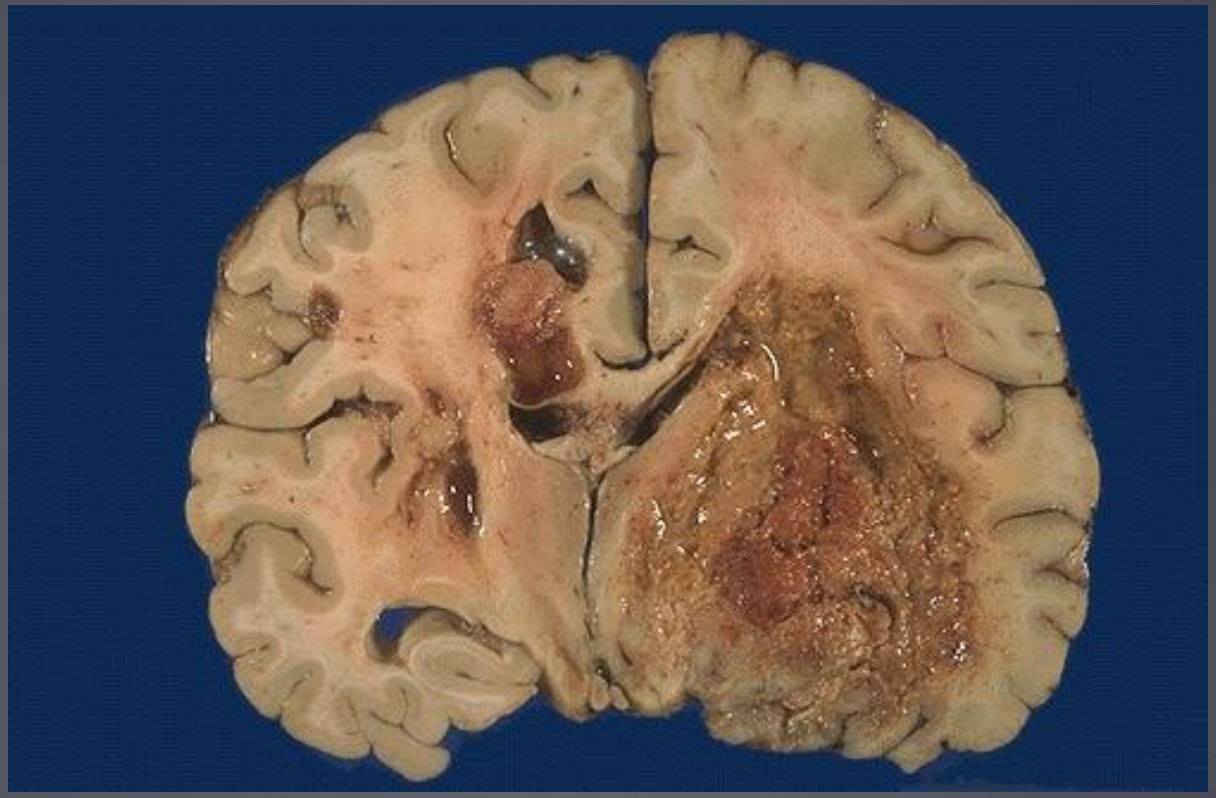
Typically benign slow growing, some cancerous faster growing can cause neurological problems, swelling in the brain. Benign usually don't cause problems unless they are pushing on the brainstem and/or compressing structures such as optic and cranial nerves.

4. Acoustic schwannoma



- The mass lesion here is arising in the vestibulo-cochlear (eighth cranial) nerve at the cerebellopontine angle. Patients may present with hearing loss. These benign neoplasms can be removed.

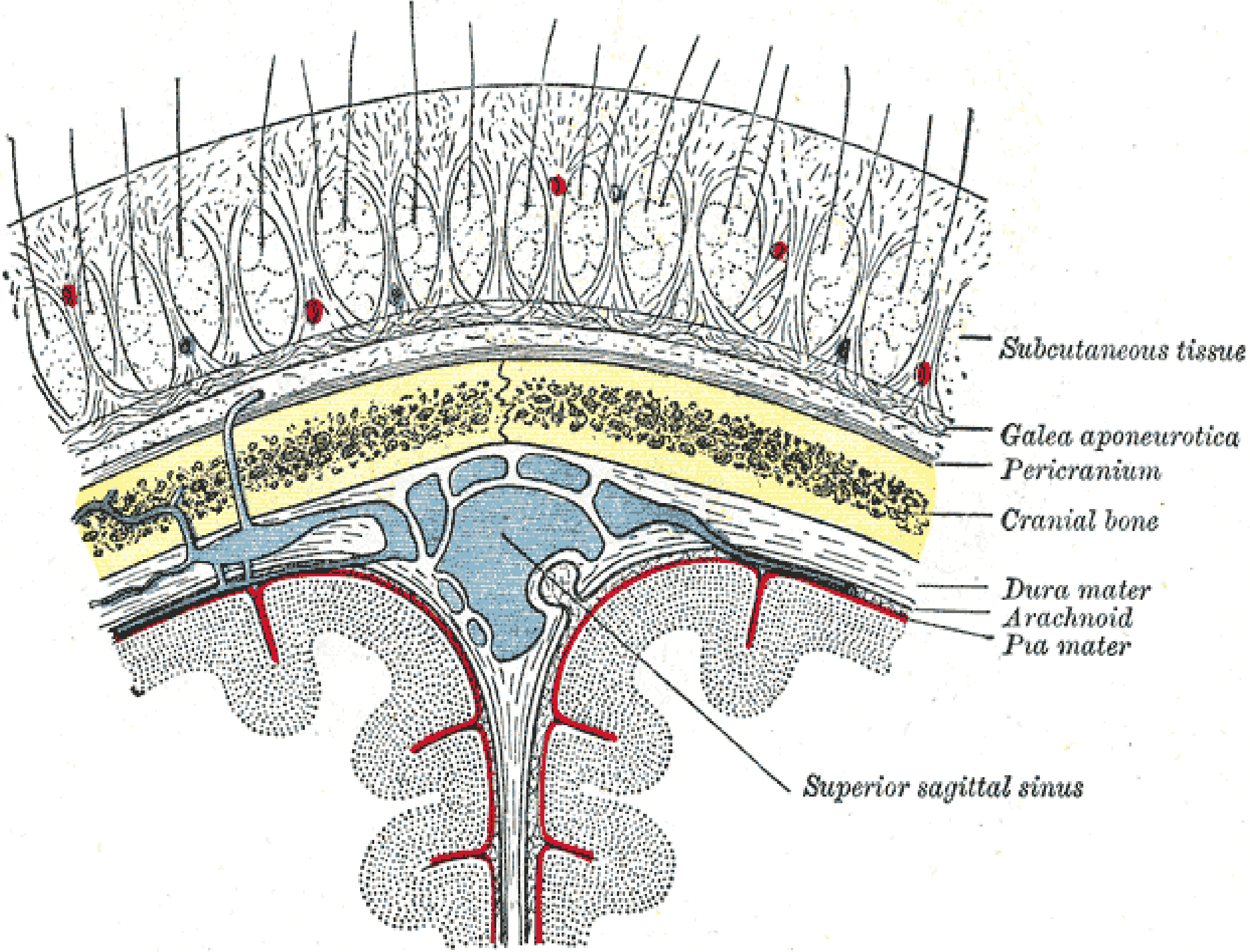
5. glioblastoma multiforme



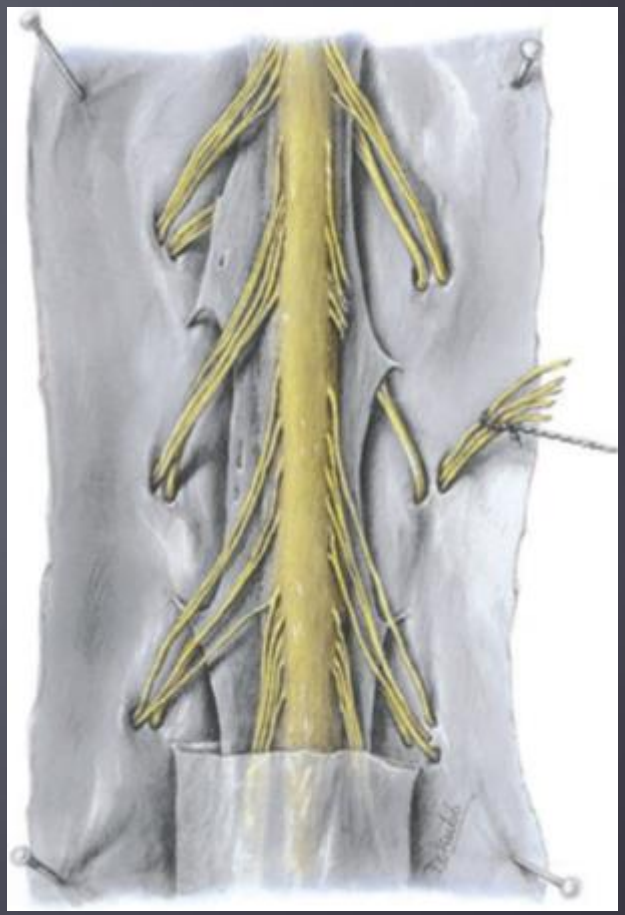
- Adult astrocytic tumor - This is the worst possible form of glioma--a glioblastoma multiforme (GBM). These neoplasms are quite vascular with prominent areas of necrosis and hemorrhage. Note how this one has crossed the midline to the opposite hemisphere

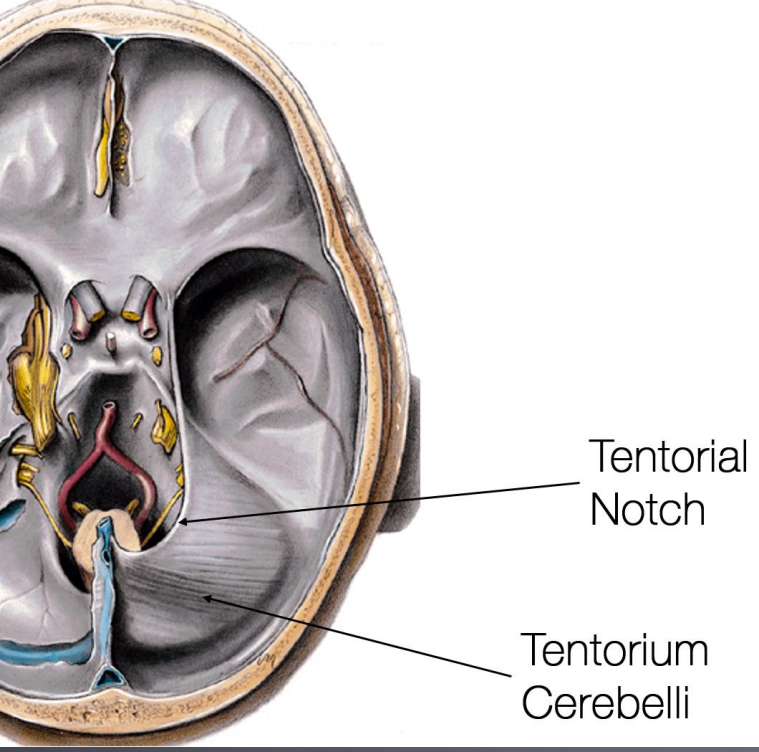
SUPPLEMENT – MENINGES

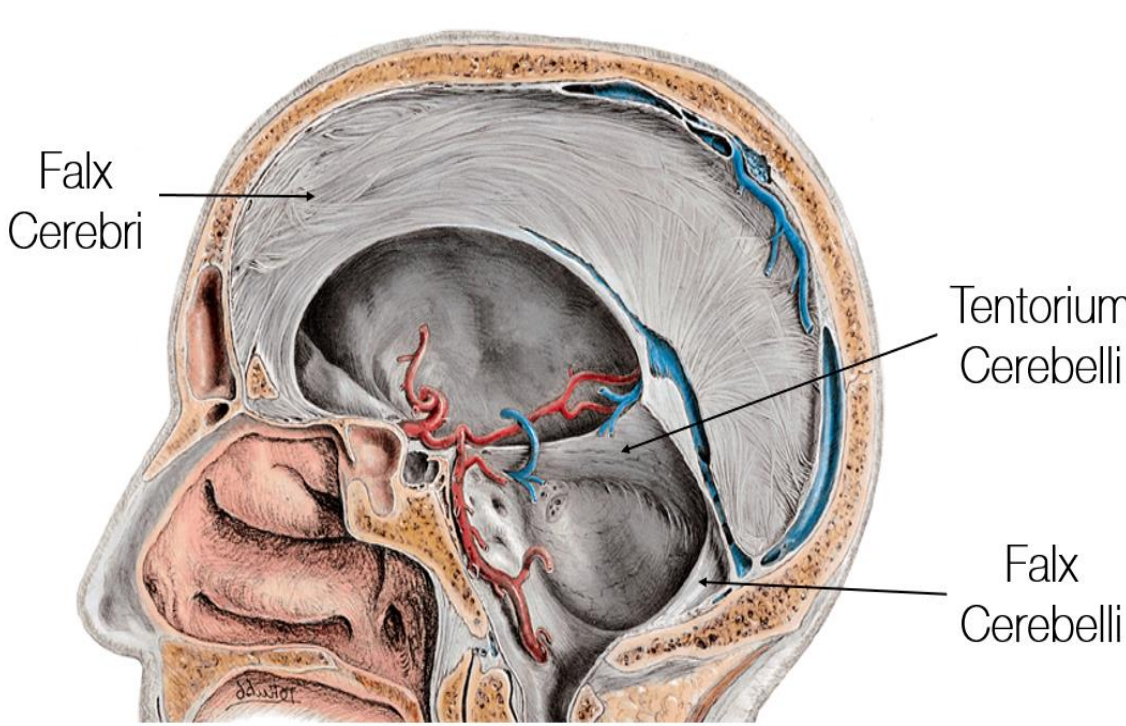
http://en.wikipedia.org/wiki/Meninges


Subcutaneous tissue
Galea aponeurotica
Pericranium
Cranial bone
Dura mater
Arachnoid
Pia mater
Superior sagittal sinus

Spinal Cord meninges







The dura has four areas of infolding:

- Falx cerebri, the largest, sickle-shaped; separates the cerebral hemispheres.
- Tentorium cerebelli, second largest, crescent-shaped; separates the occipital lobes from cerebellum. The falx cerebri attaches to it giving a tentlike appearance.
- Falx cerebelli, vertical infolding; lies inferior to the tentorium cerebelli, separating the cerebellar hemispheres.
- Diaphragma sellae, smallest infolding; covers the pituitary gland and sella turcica.

Arachnoid mater

The middle element of the meninges is the arachnoid mater, so named because of its spider web-like appearance. It cushions the central nervous system. This thin, transparent membrane is composed of fibrous tissue and, like the pia mater, is covered by flat cells also thought to be impermeable to fluid.

The shape of the arachnoid does not follow the convolutions of the surface of the brain and so looks like a loosely fitting sac. A large number of fine filaments called arachnoid trabeculae pass from the arachnoid through the subarachnoid space to blend with the tissue of the pia mater. The arachnoid is composed of an outermost portion (arachnoid barrier cell layer) with tightly packed cells which represent an effective morphological and physiological meningeal barrier between the cerebrospinal fluid and subarachnoid space and the blood circulation in the dura.

The pia mater [Latin: 'soft mother'] is a very delicate membrane. It is the meningeal envelope that firmly adheres to the surface of the brain and spinal cord, following the brain's minor contours (gyri and sulci). It is a very thin membrane composed of fibrous tissue covered on its outer surface by a sheet of flat cells thought to be impermeable to fluid. The pia mater is pierced by blood vessels to the brain and spinal cord, and its capillaries nourish the brain.

Spaces[edit]

The subarachnoid space is the space that normally exists between the arachnoid and the pia mater, which is filled with cerebrospinal fluid.

Normally, the dura mater is attached to the skull, in the spinal cord, the dura mater is separated from the bone (vertebrae) by a space called the epidural space, which contain fat and blood vessels. The arachnoid is attached to the dura mater, while the pia mater is attached to the central nervous system tissue. When the dura mater and the arachnoid separate through injury or illness, the space between them is the subdural space. There is a subpial space underneath the pia mater that separates it from the glia limitans.

Clinical significance:

There are three types of hemorrhage involving the meninges:[7]

•A subarachnoid hemorrhage is acute bleeding under the arachnoid; it may occur spontaneously or as a result of trauma.

•A subdural hematoma is a hematoma (collection of blood) located in a separation of the arachnoid from the dura mater. The small veins that connect the dura mater and the arachnoid are torn, usually during an accident, and blood leaks into this area.

•An epidural hematoma may arise after an accident or spontaneously.

Other medical conditions that affect the meninges include meningitis (usually from fungal, bacterial, or viral infection) and meningiomas that arise from the meninges, or from meningeal carcinomatoses (tumors) that form elsewhere in the body and metastasize to the meninges.

Sagittal View

1. Telencephalon (a. hemispheres; b. c. callosum) (CNI)
2. Diencephalon (b. hypothalamus,a. thalamus) (CNII)
3. **Mesencephalon (Midbrain) (CNIII,IV)**
4. **Metencephalon**
   a. Pons (CNV,VI,VII,VIII),
   b. cerebellum
1. **Myencephalon (Medulla)** (CNIX,X,XI)

Ventricles:

Telencephalon (lateral vntricles)
Diencephalon – 3rd ventricle
Midbrain – aquedcut
Pons, medulla – 4th ventricle
Medulla – central canal