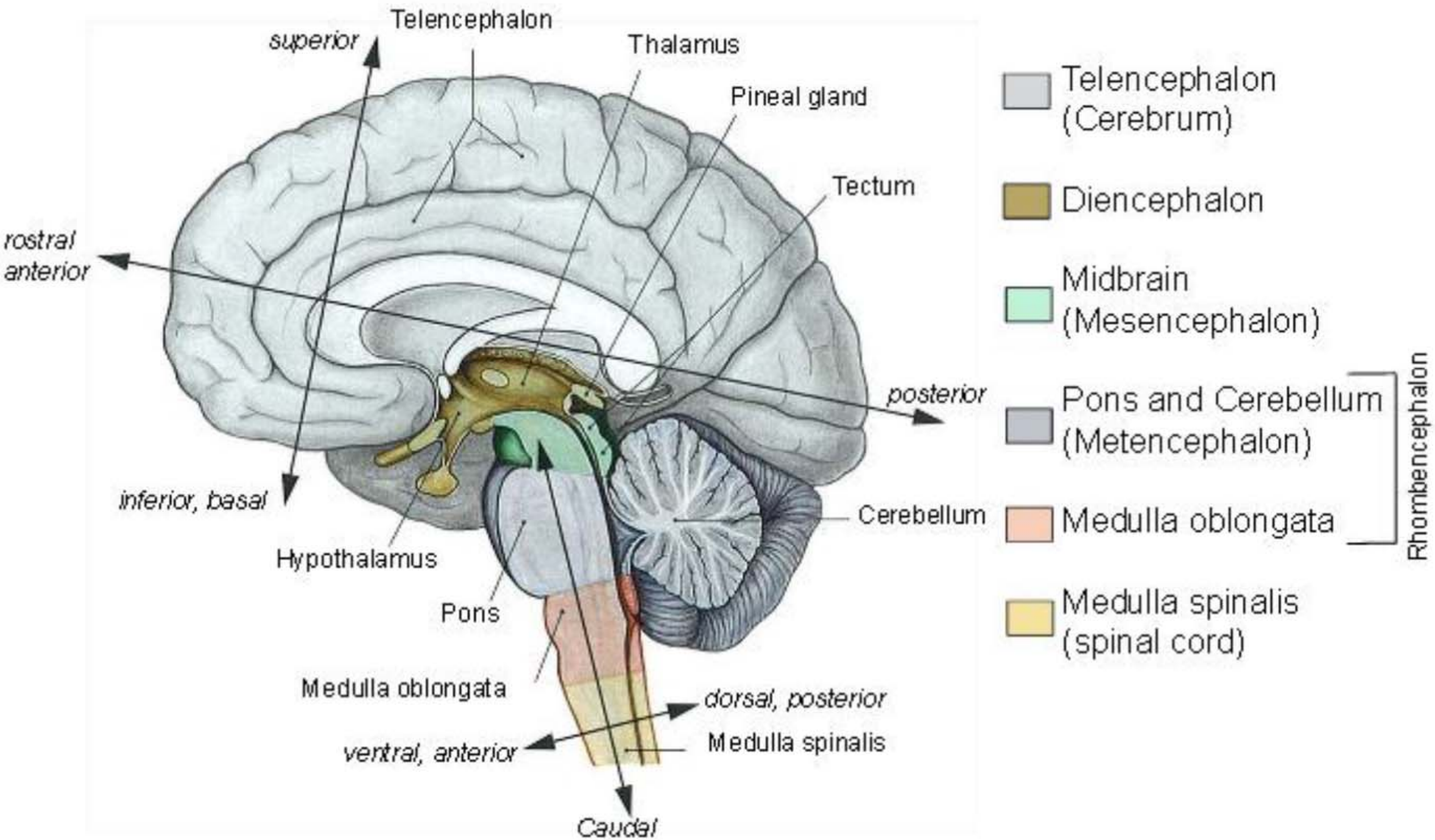
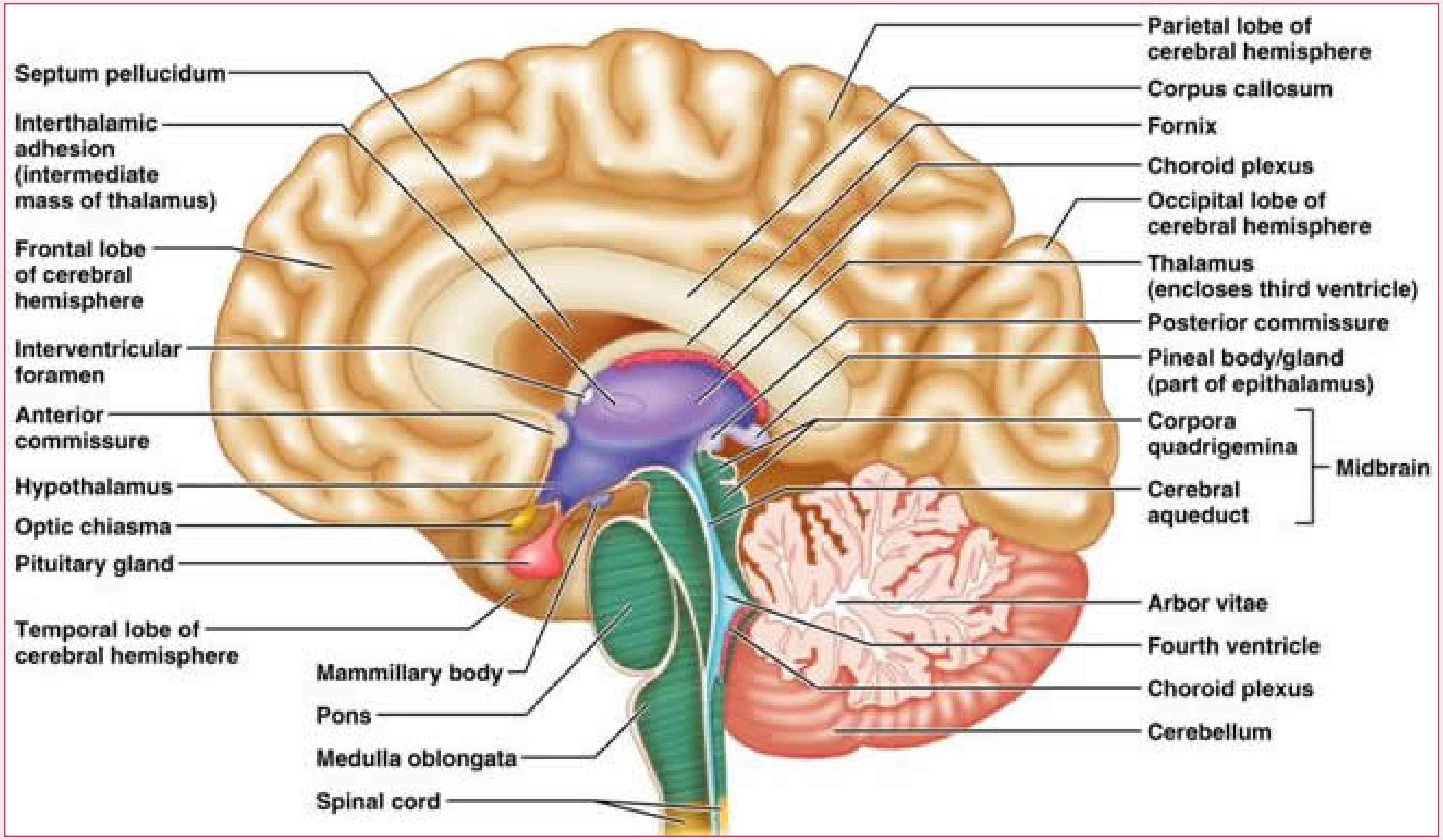
ORGANIZATION OF THE CNS
- TELENCEPHALON

Telencephalon

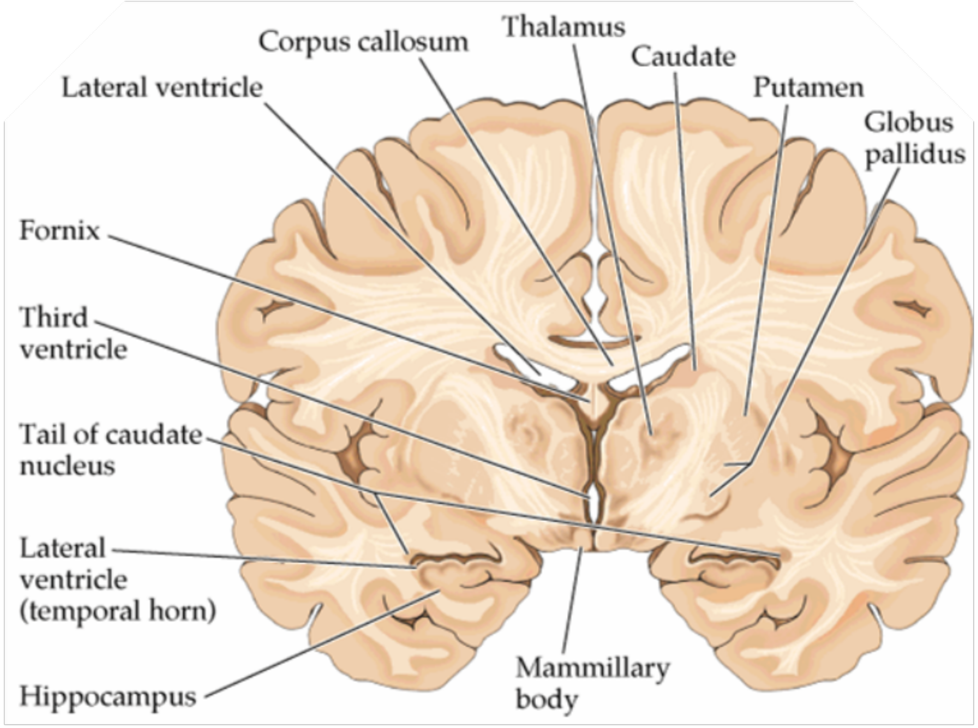


Schematics agittal section. Adapted from Sobotta 23 Ed.



Septum pellucidum
Interthalamic adhesion (intermediate mass of thalamus)
Frontal lobe of cerebral hemisphere
Interventricular foramen
Anterior commissure
Hypothalamus
Optic chiasma
Pituitary gland
Temporal lobe of cerebral hemisphere
Mammillary body
Pons
Medulla oblongata
Spinal cord
Parietal lobe of cerebral hemisphere
Corpus callosum
Fornix
Choroid plexus
Occipital lobe of cerebral hemisphere
Thalamus (encloses third ventricle)
Posterior commissure
Pineal body/gland (part of epithalamus)
Corpora quadrigemina
Cerebral aqueduct
Midbrain
Arbor vitae
Fourth ventricle
Choroid plexus
Cerebellum

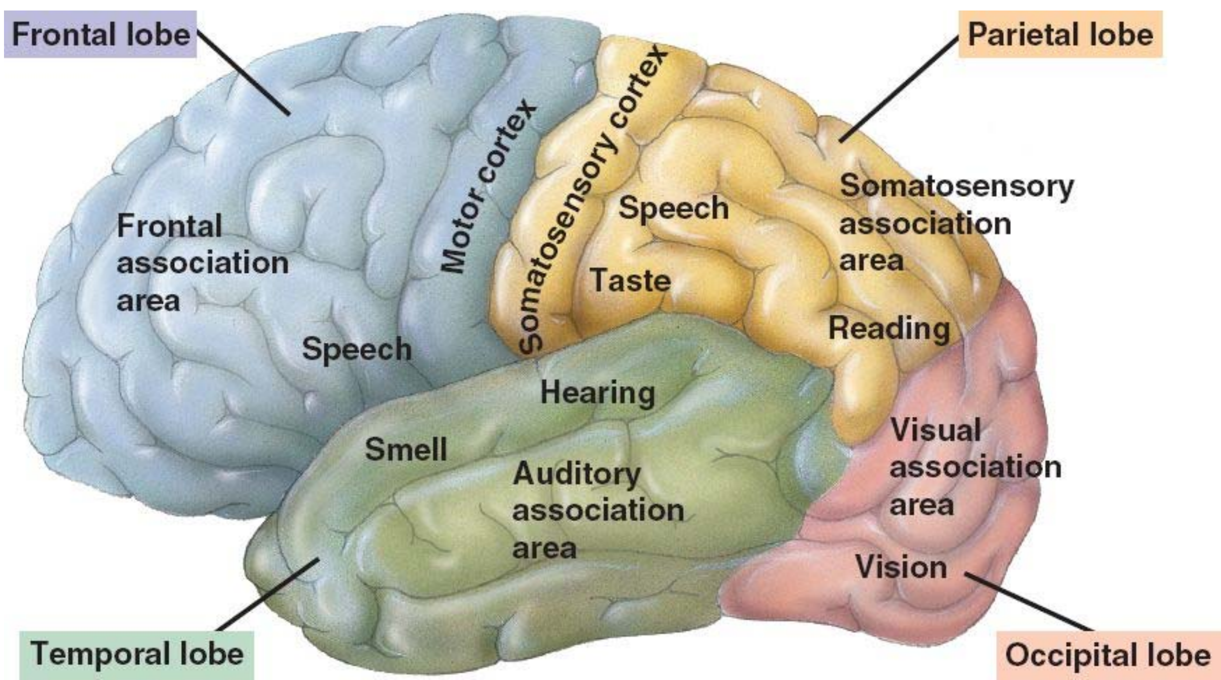
Telencephalon



- Cerebral cortex
- White matter
- Basal ganglia
- Limbic system
- Lateral cerebral ventricles

Cerebral cortex

- Contains 15 bilion neurons
- Area of 220 cm^2
- Histological arangement – functional units called **cortical columns**
- Sulcii and gyrii



Cerebral cortex

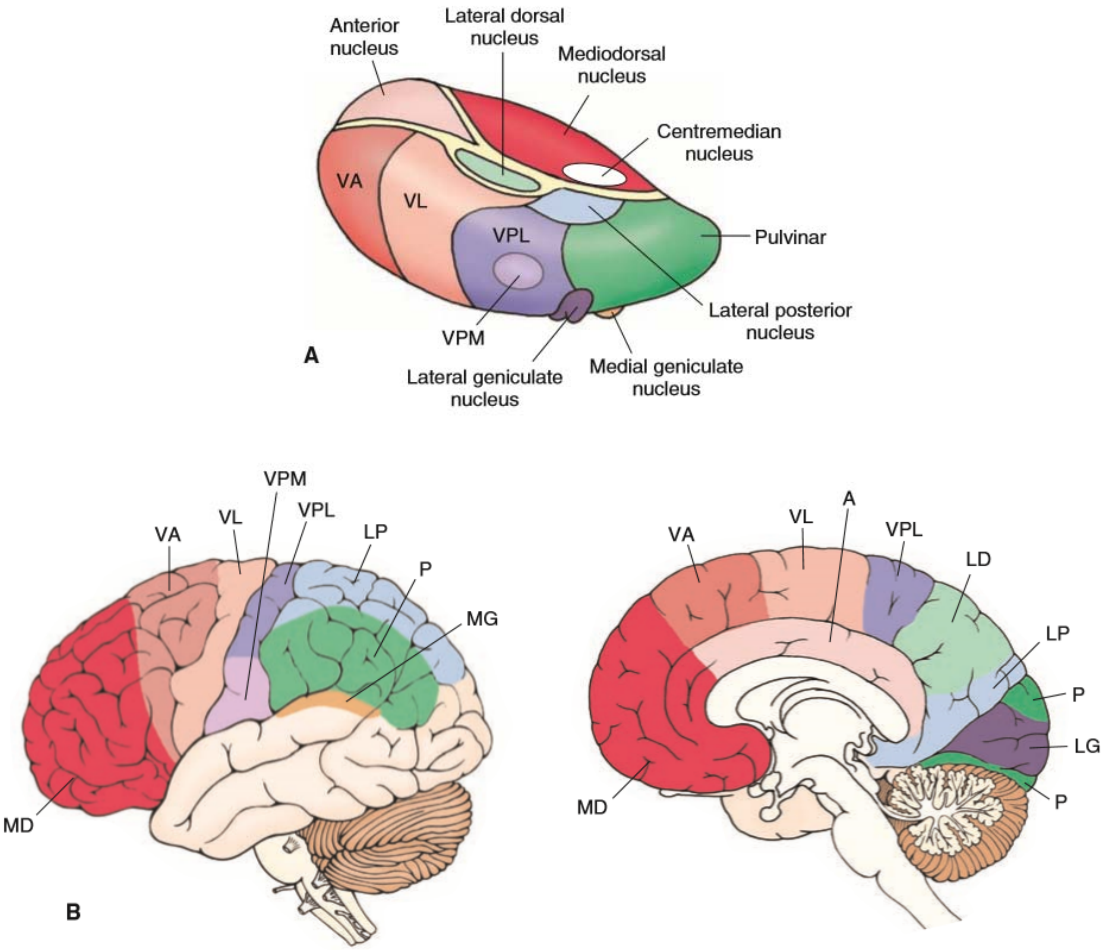
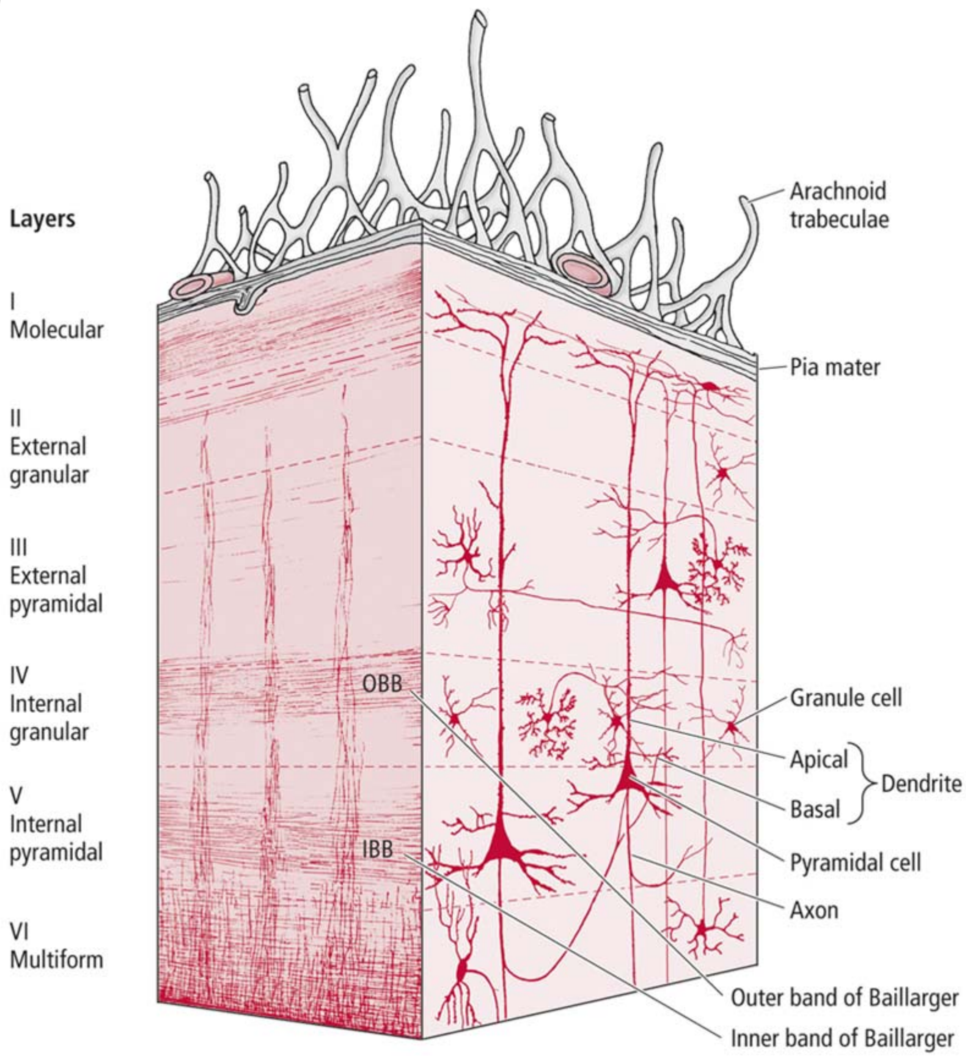
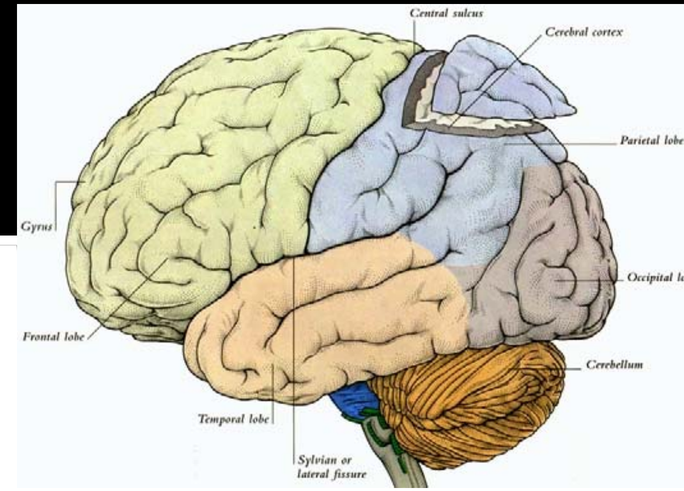


FIGURE 26–5 Thalamocortical relationships. **(A)** The relative positions of thalamic nuclei. **(B)** Lateral (*left*) and medial (*right*) views of the cerebral cortex that demonstrate the projection targets of thalamic nuclei. Color-coding is to facilitate visualization of the projection targets of thalamic nuclei on the cerebral cortex. VPM = ventral posteromedial nucleus; VPL = ventral posterolateral nucleus; VA = ventral anterior nucleus; VL = ventrolateral nucleus.

Cerebral cortex





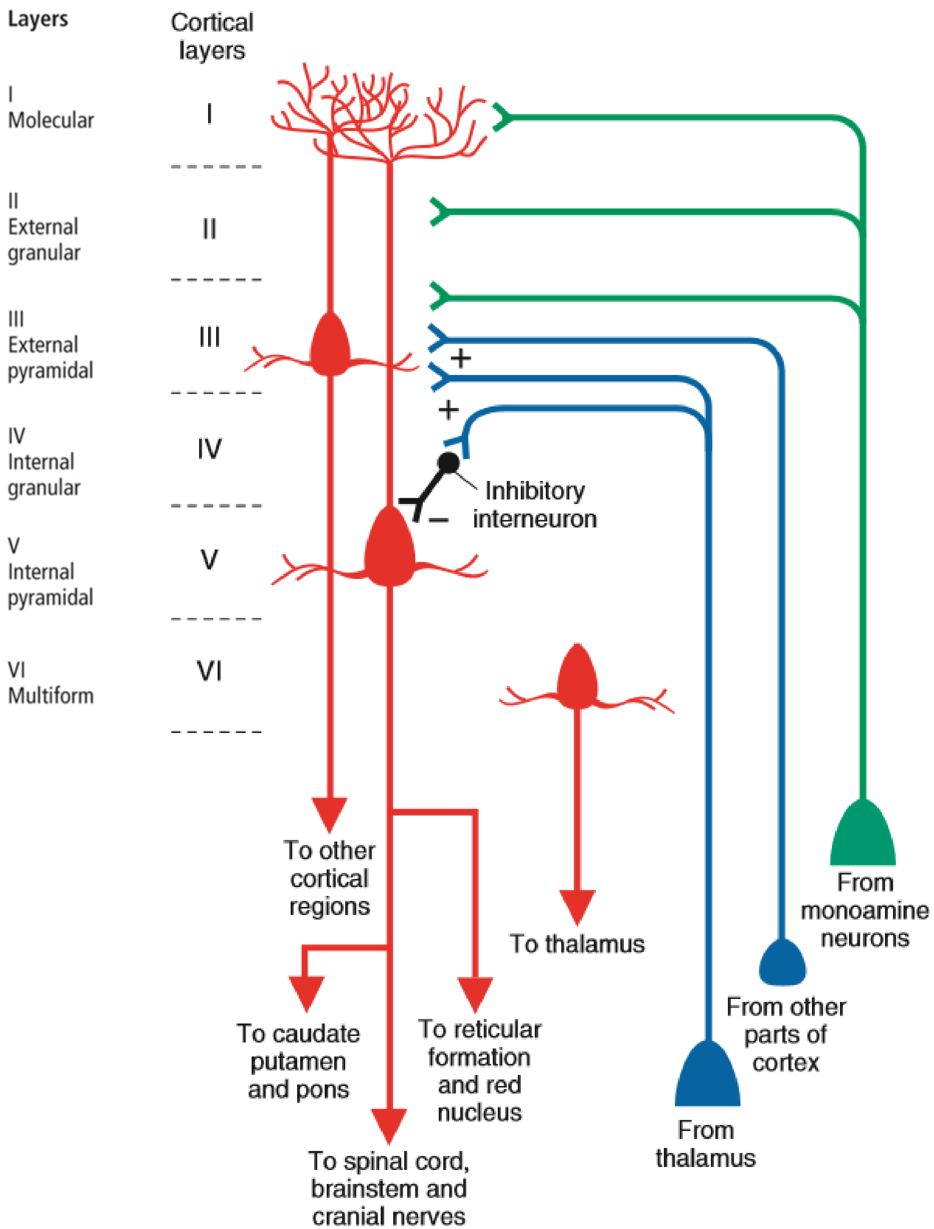
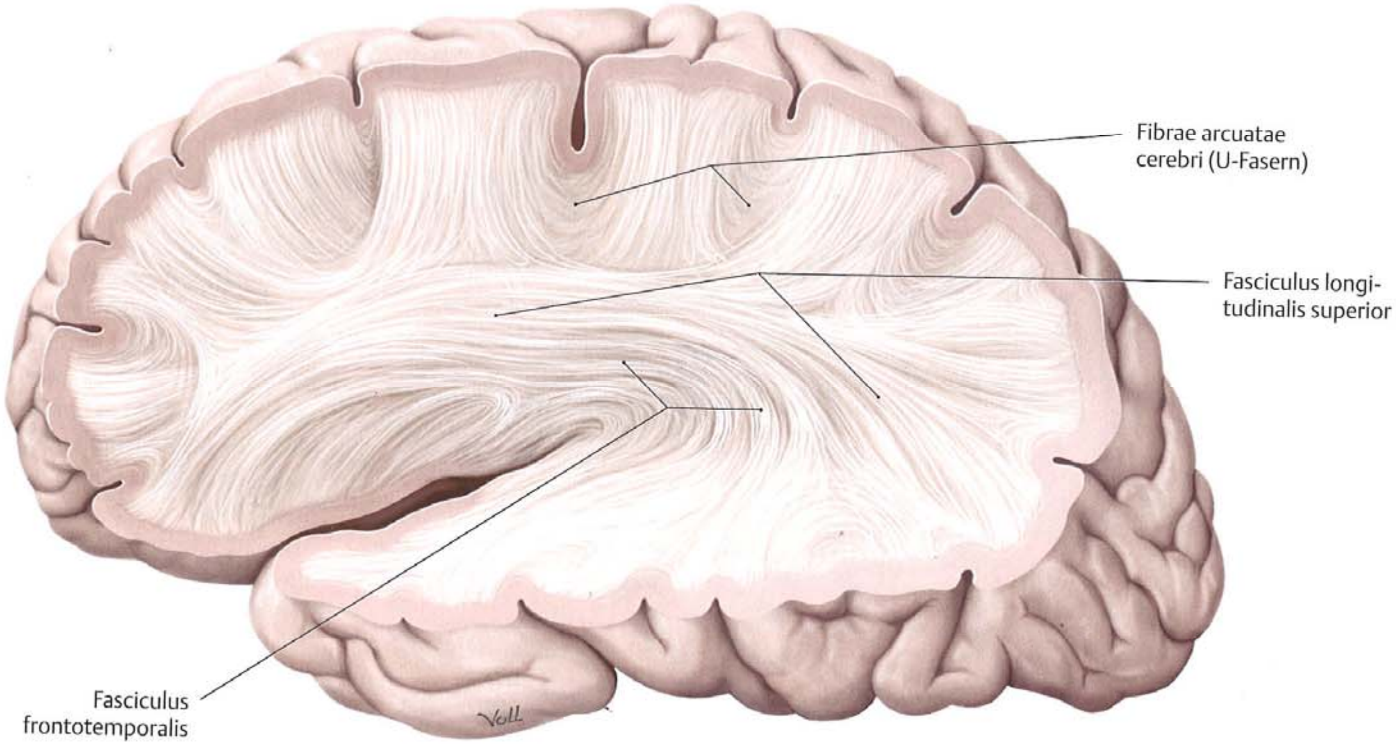
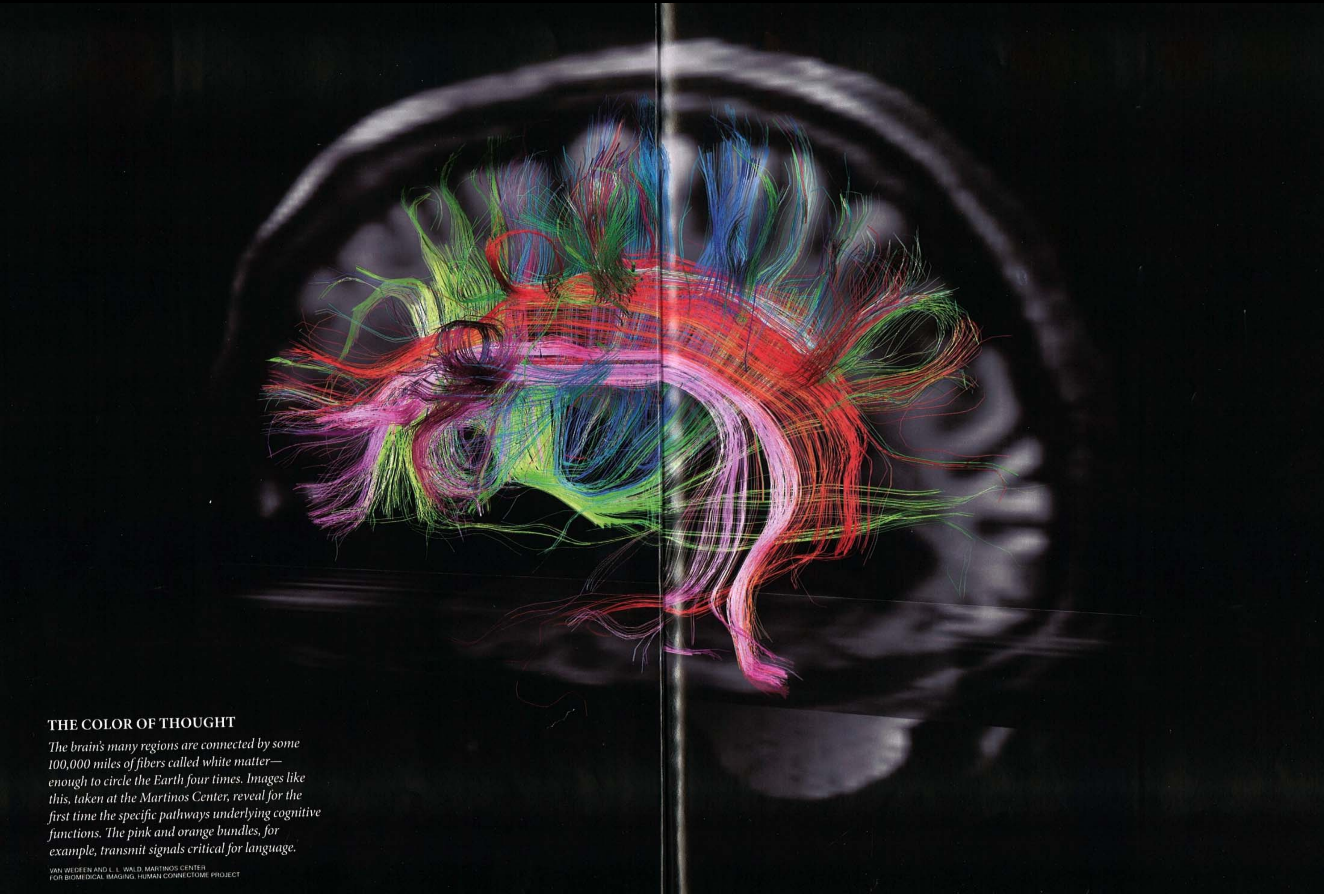


FIGURE 26–4 Input-output relationships of cortex. Schematic diagram depicts the intrinsic organization and input-output relationships of the cerebral cortex. Excitatory connections are indicated by (+), and inhibitory synapse is indicated by (–). Note that thalamocortical and intracortical projections terminate mainly in layer IV, and monoaminergic projections are distributed mainly to more superficial layers. Cortical afferents terminating in layer IV can either excite or inhibit pyramidal cells in layer V, which contribute significantly to the outputs of the cerebral cortex. The major outputs to the spinal cord, cranial nerve motor nuclei, other brainstem structures, thalamus, and neostriatum arise in layers V–VI, whereas projections to other regions of cortex either on the ipsilateral or contralateral side arise from layer III. (Adapted from Conn PM: Neuroscience in Medicine. Philadelphia: J.B. Lippincott, 1995, p. 316.)

White matter

- ***Projection fibers*** (efferent or afferent: thalamocortical system and extrathalamic afferent fibers)
- ***Association fibers*** (axons of pyramidal neurons – II and III cortical layer)
- ***Commissural fibers*** (axons of pyramidal neurons – II and III cortical layer: corpus callosum, commissura anterior and commissura hippocampi)


Fibrae arcuatae
cerebri (U-Fasern)
Fasciculus longi-
tudinalis superior
Fasciculus
frontotemporalis
Voll

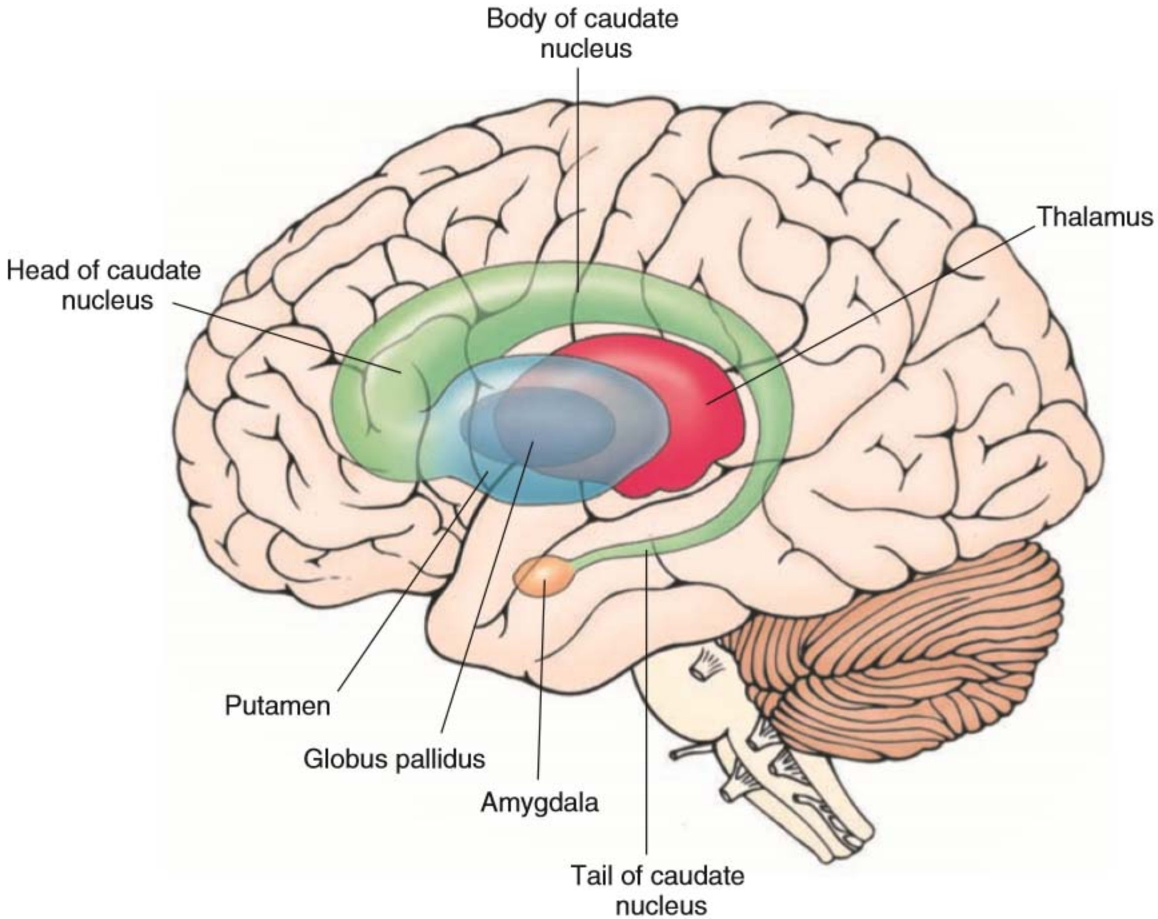


THE COLOR OF THOUGHT

The brain's many regions are connected by some 100,000 miles of fibers called white matter—enough to circle the Earth four times. Images like this, taken at the Martinos Center, reveal for the first time the specific pathways underlying cognitive functions. The pink and orange bundles, for example, transmit signals critical for language.

VAN WEDEEN AND L. L. WALD, MARTINOS CENTER FOR BIOMEDICAL IMAGING, HUMAN CONNECTOME PROJECT

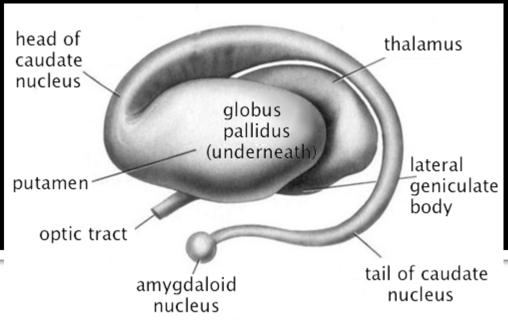
Basal ganglia



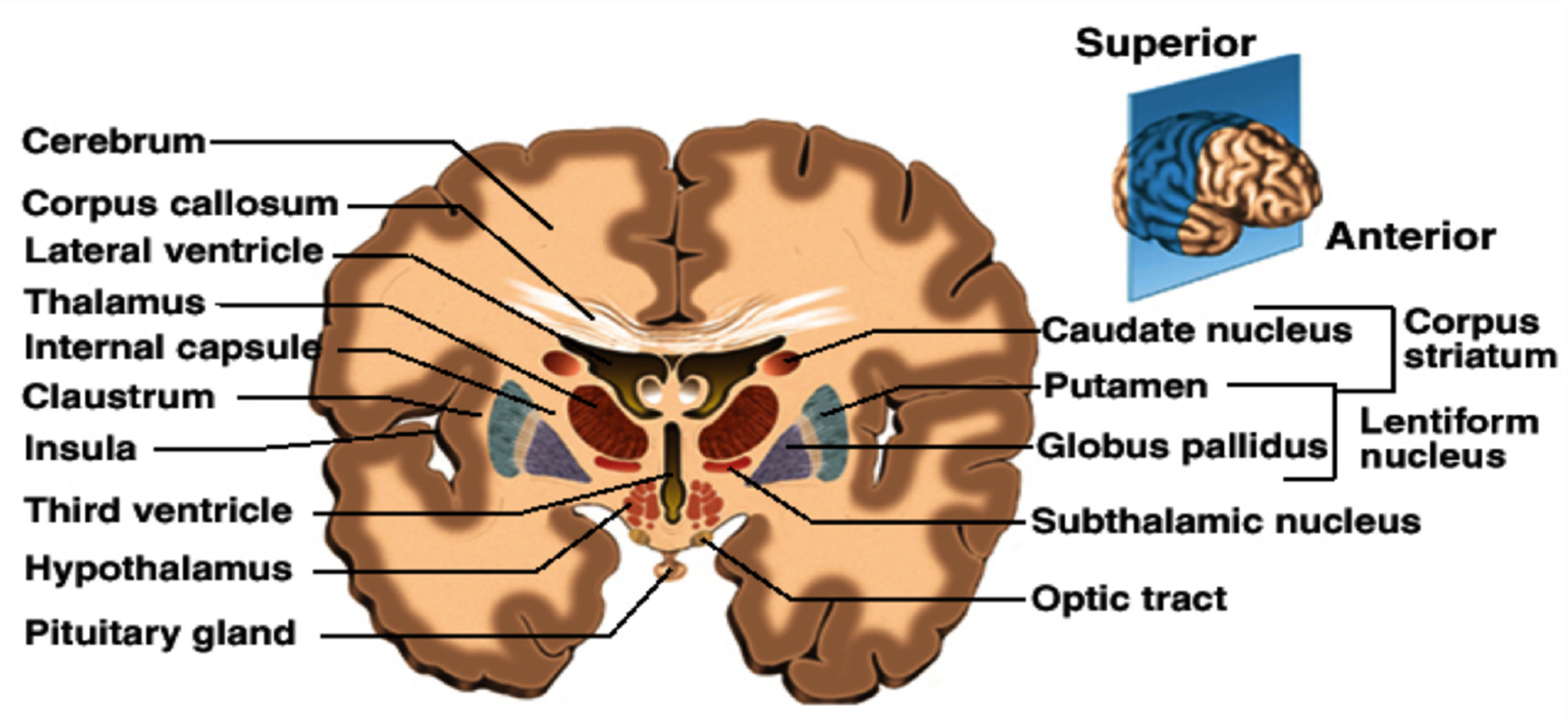
Nucleus caudatus
Putamen
Globus pallidus
(Claustrum)

FIGURE 13–11 The components of the caudate nucleus and their relationship to the thalamus, internal capsule, globus pallidus, putamen, and brainstem.

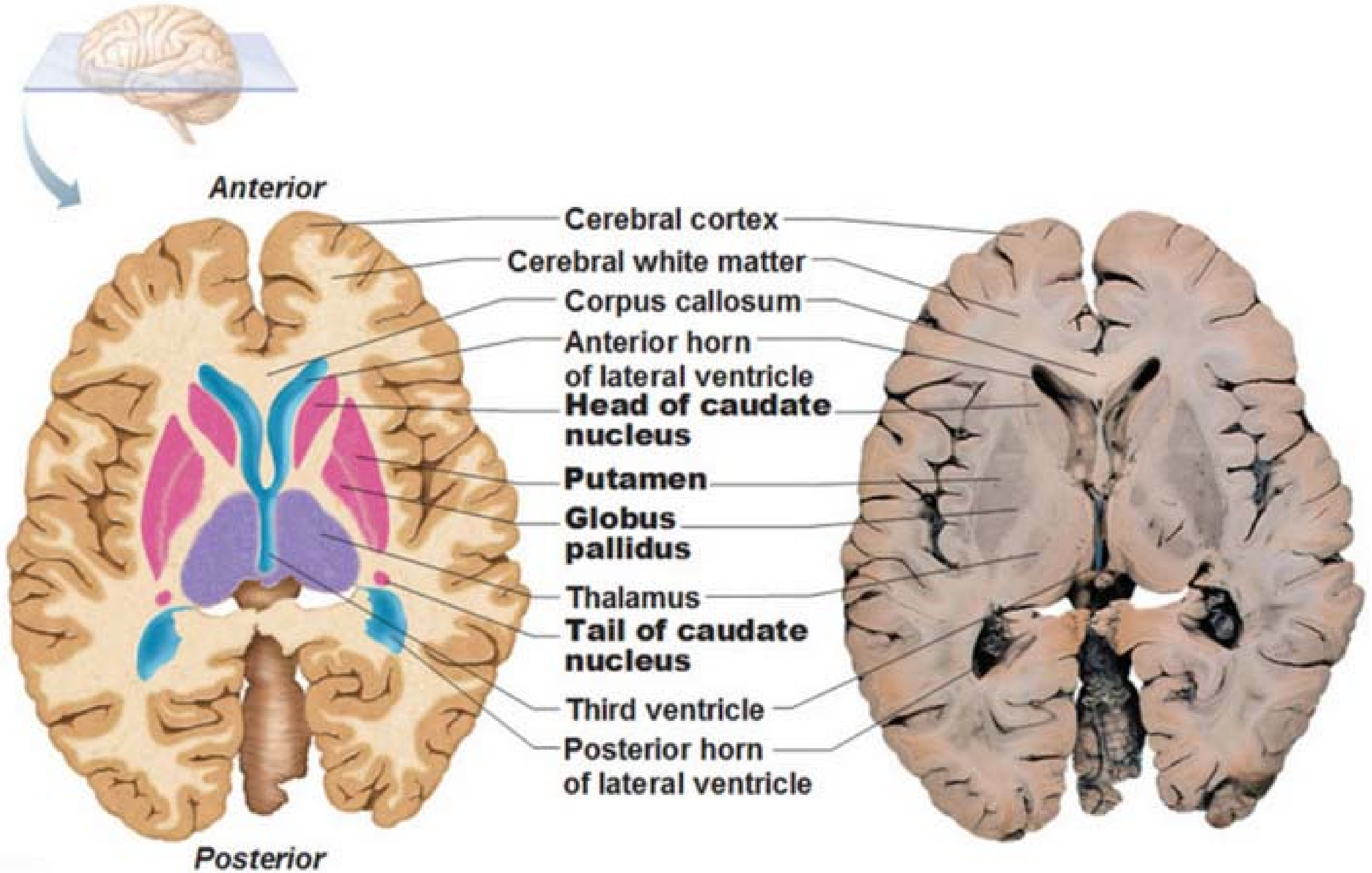
Basal ganglia



Regulation of motor functions!



Basal ganglia



Basal ganglia

- Nucleus caudatus
- Putamen
- Globus pallidus
- (Claustrum)

Nucleus caudatus + Putamen } Neostriatum

  - Substantia nigra
  - Subthalamic nucleus

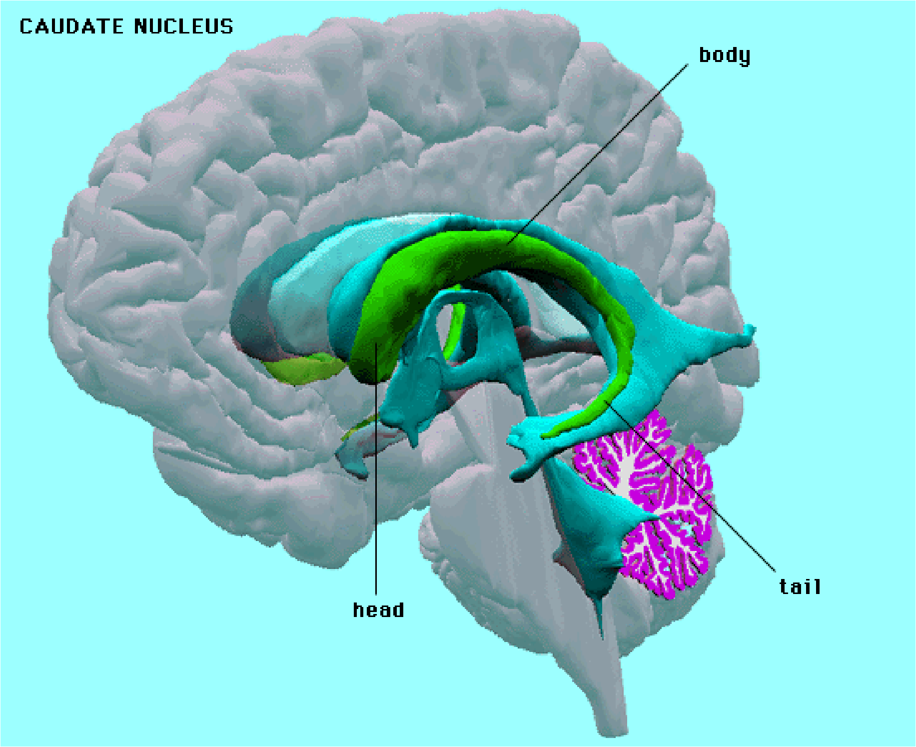
Substantia nigra + Subthalamic nucleus } **anatomical and functional relationships with neostriatum and globus pallidus**

Basal ganglia

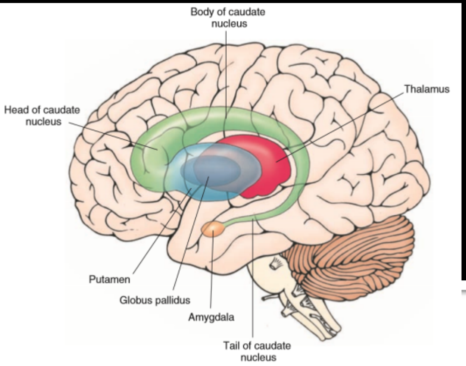
Neurological structure	*Basal nuclei*
Corpus striatum	Caudate nucleus + lentiform nucleus
Amygdala	Amygdaloid nucleus
Claustrum	Claustrum
Neostriatum	Caudate nucleus + putamen
Paleostriatum	Globus pallidus
Caudate nucleus	Caudate nucleus
Lentiform nucleus	Globus pallidus + putamen

Caudate nucleus

- C-shaped
- Follows the lateral ventricle for its entire lenght
  - Head
  - Body
  - Tail

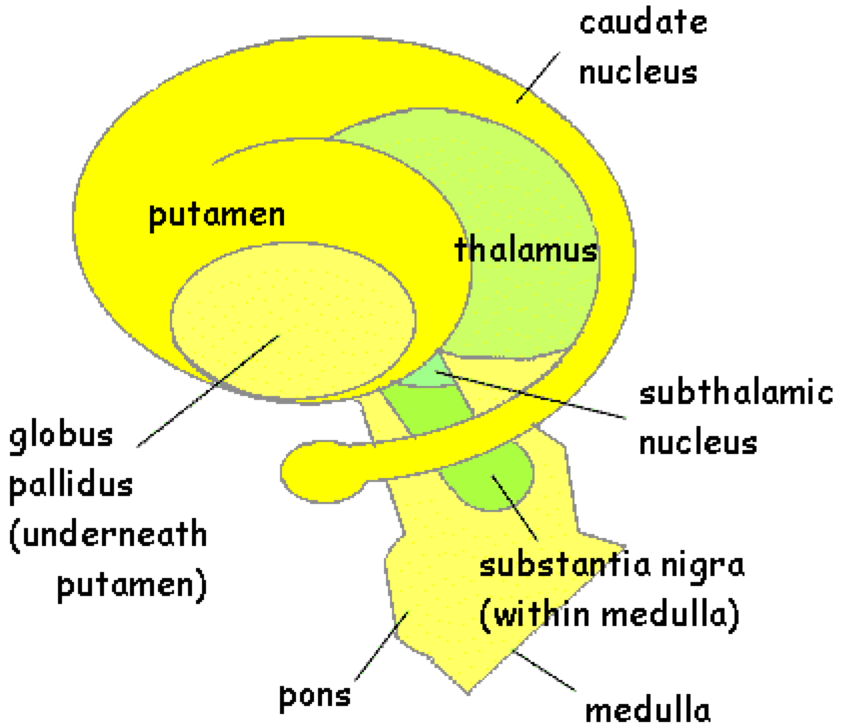


Putamen

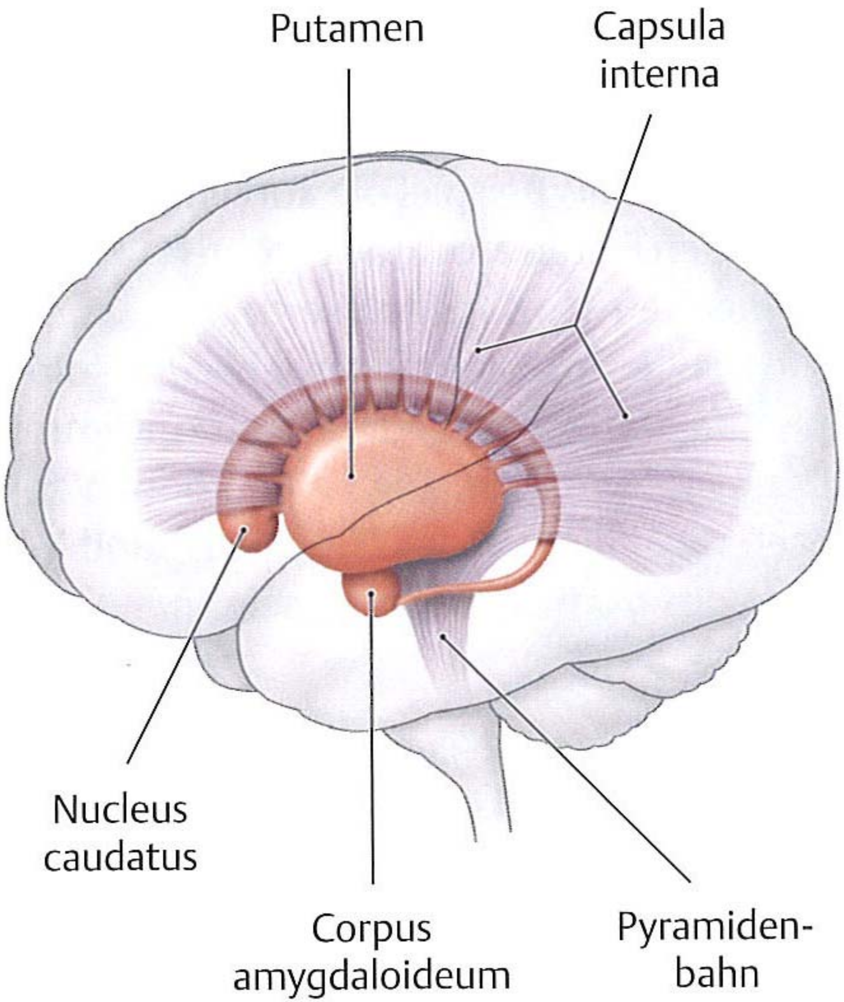


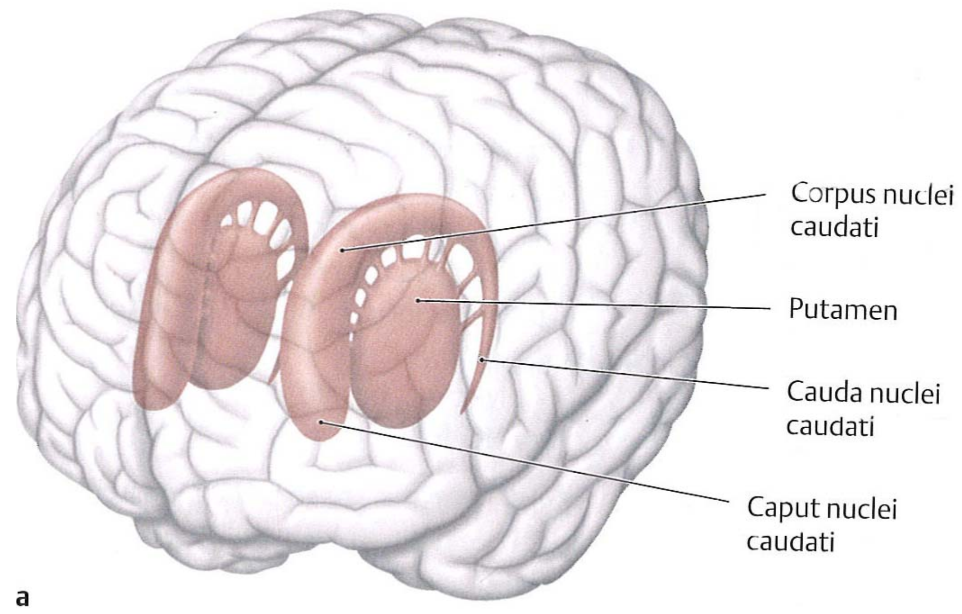
- Between globus pallidus and external capsule
- Lateral to the internal capsule

- Major **site of inputs** into the basal ganglia from cerebral cortex, thalamus, substantia nigra



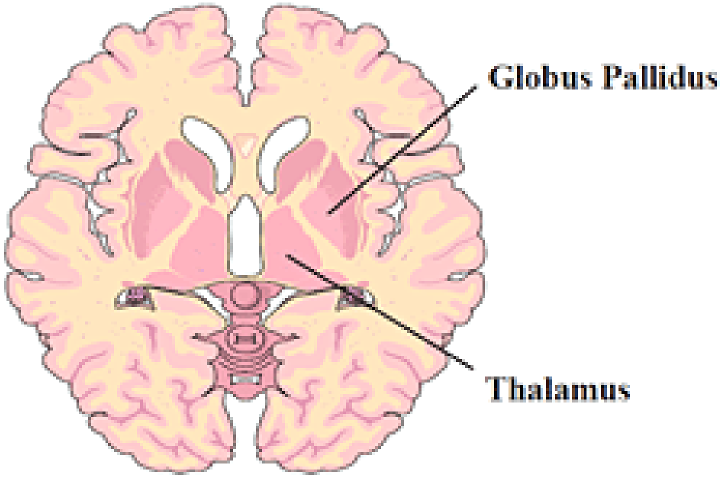
Putamen


Putamen
Capsula interna
Nucleus caudatus
Corpus amygdaloideum
Pyramidenbahn


Corpus nuclei caudati
Putamen
Cauda nuclei caudati
Caput nuclei caudati
a

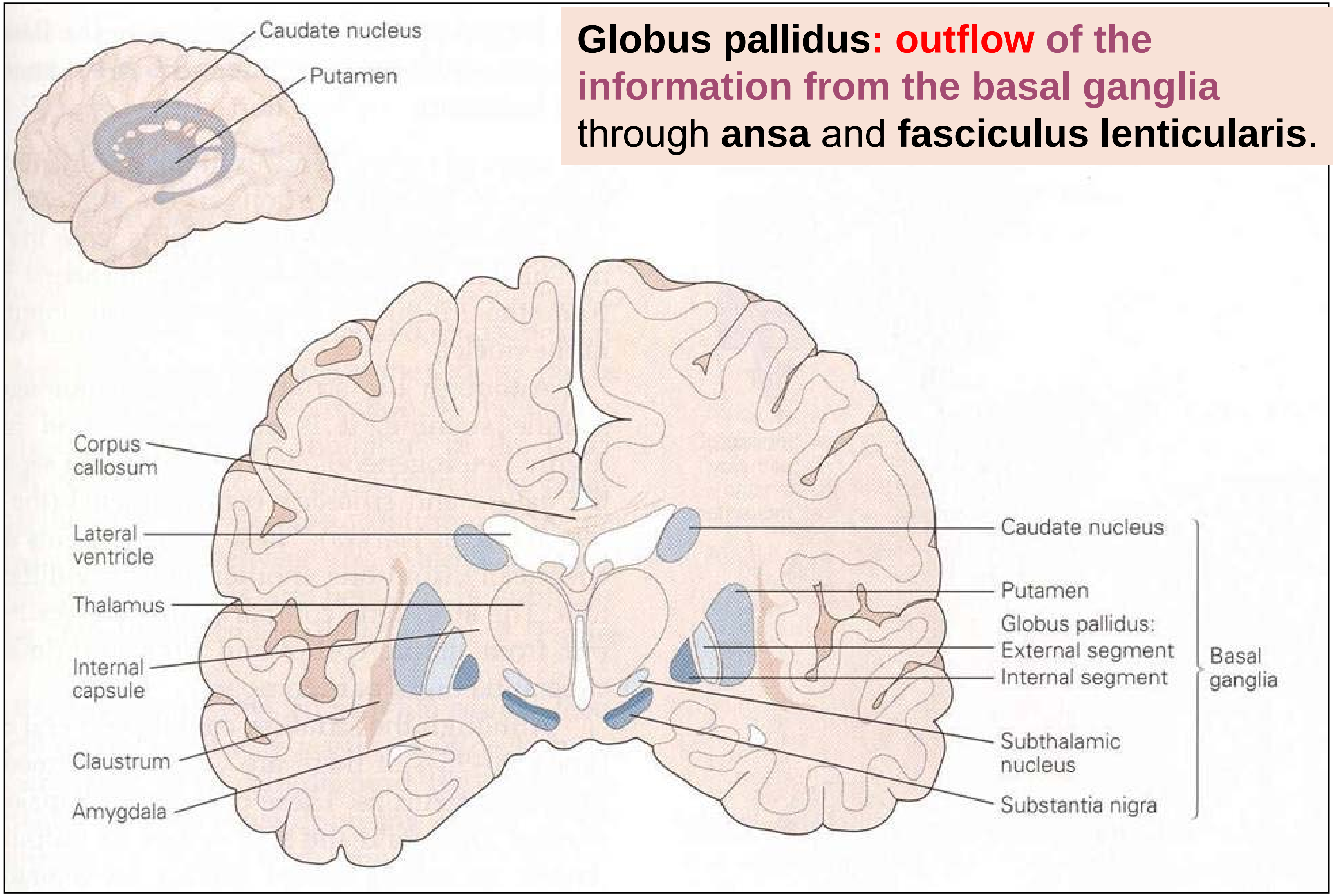
Globus pallidus

- Lateral to the internal capsule
- Medial to the putamen
- Lateral and medial segment (separated by medial medullary lamina)
- Primary region for the **outflow of the information from the basal ganglia** (ansa and fasciculus lenticularis)



Basal ganglia

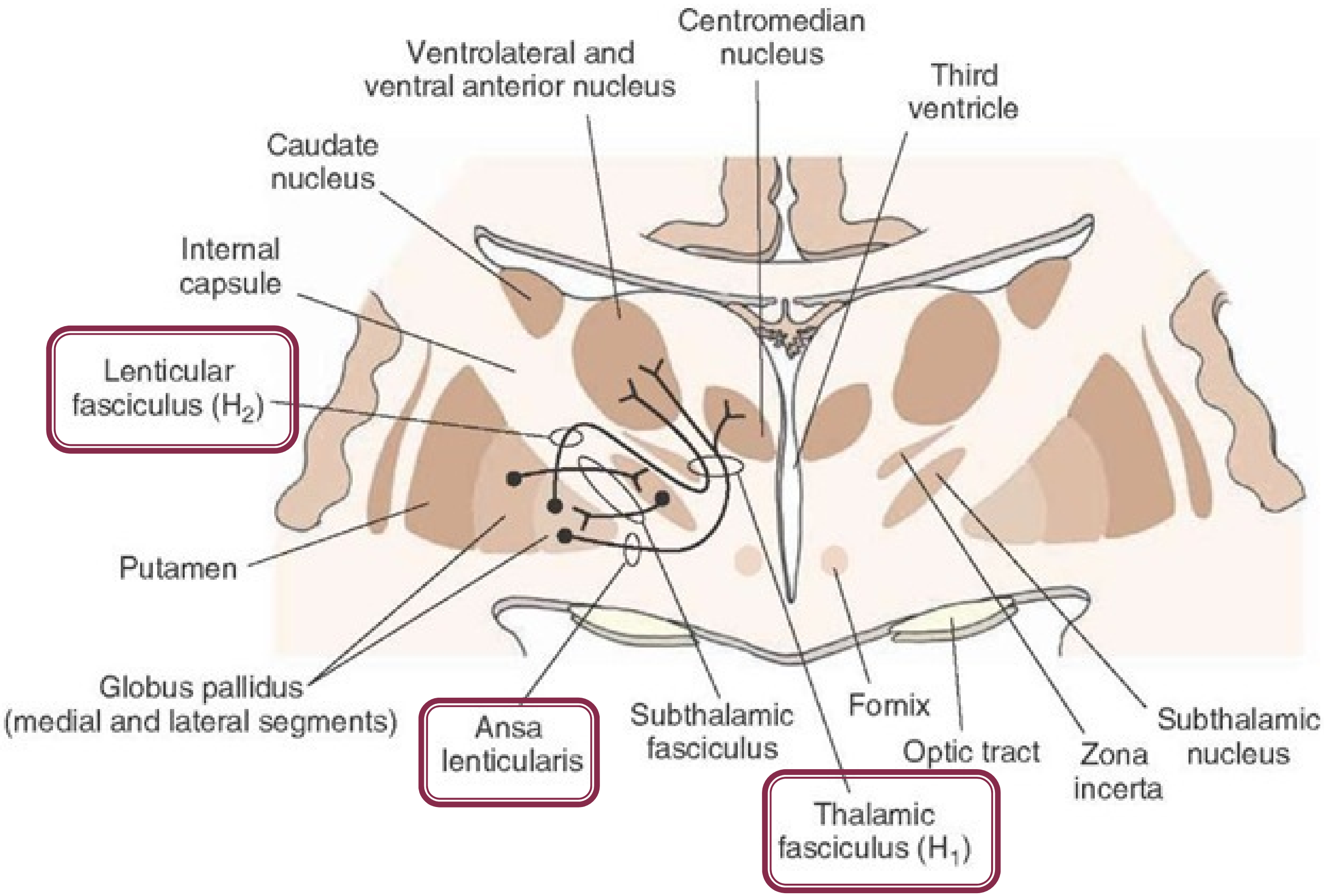
Globus pallidus: outflow of the information from the basal ganglia through **ansa** and **fasciculus lenticularis**.



Fiber pathways of the basal ganglia

- **Ansa lenticularis** – from medial segment of GP, ventromedial direction and caudally toward midbrain
- **Fasciculus lenticularis** – from pallidum, dorsomedial direction, around the dorsal surface of nucl. subth. and curve around the dorsal aspect of zona incerta, dorsolateral direction caudally toward midbrain
- Joined fibers form a **thalamic fasciculus** . Terminate in the VL and VA thalamic nuclei.

Fiber pathways of the basal ganglia



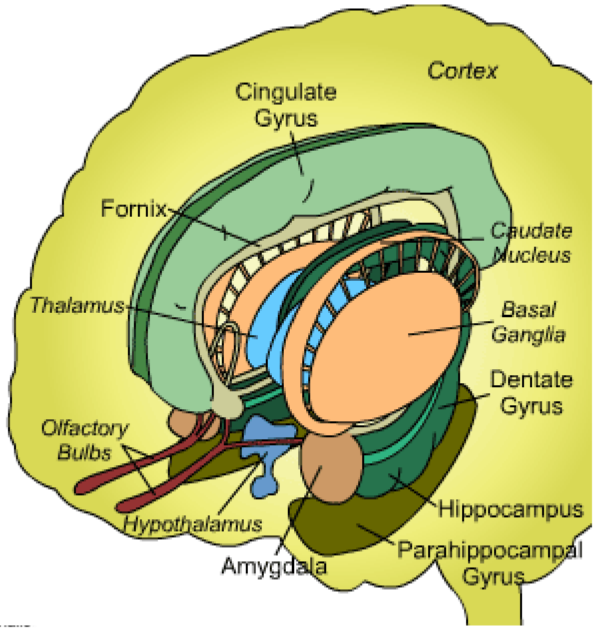
Fiber pathways of the basal ganglia

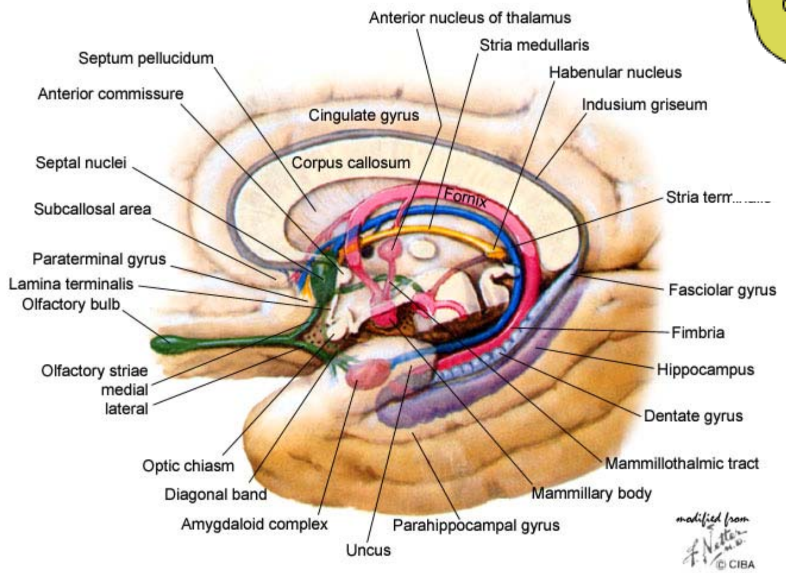
- Rostral to the red nucl. reverse course, rostral direction = **H field of Forel (pre-rubral field)**
- Joined by *dentatothalamic fibers* = **fasciculus thalamicus** (H1 field of Forel)
- Terminate in ventrolateral and ventral anterior thalamic nucl.
  - H2 field of Forel = fasciculus lenticularis

Limbic system

- Lobus limbicus
  - ***gyrus fornicatus***
  - ***formatio hippocampi***
- Rhinencephalon
- Mediobasal telencephalon

(paleocortex)

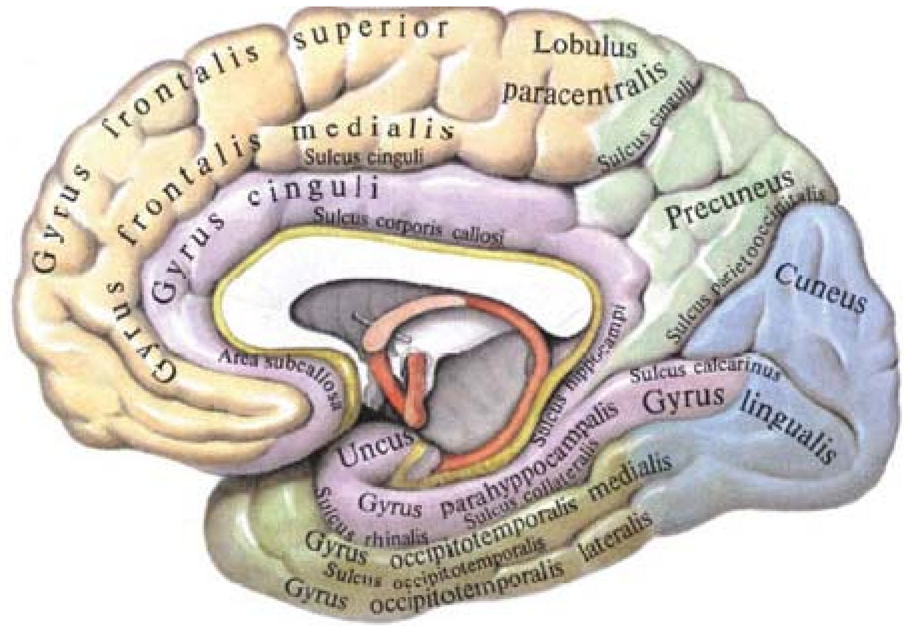




Lobus limbicus

- ***Gyrus fornicatus:***
  - Area subcallosa
  - Gyrus cinguli
  - Isthmus gyri cinguli
  - Gyrus parahippocampalis

Paralimbic cortical areas



Limbic system and associated structures of the basal forebrain

- LOBUS LIMBICUS described by Paul Broca in 1878

- Hippocampal formation
- Septal area
- Amygdala
- Adjoining regions of cortex (entorhinal, pyriform)
- Bed nucleus of the stria terminalis
- Nucleus accumbens
- Substantia innominata

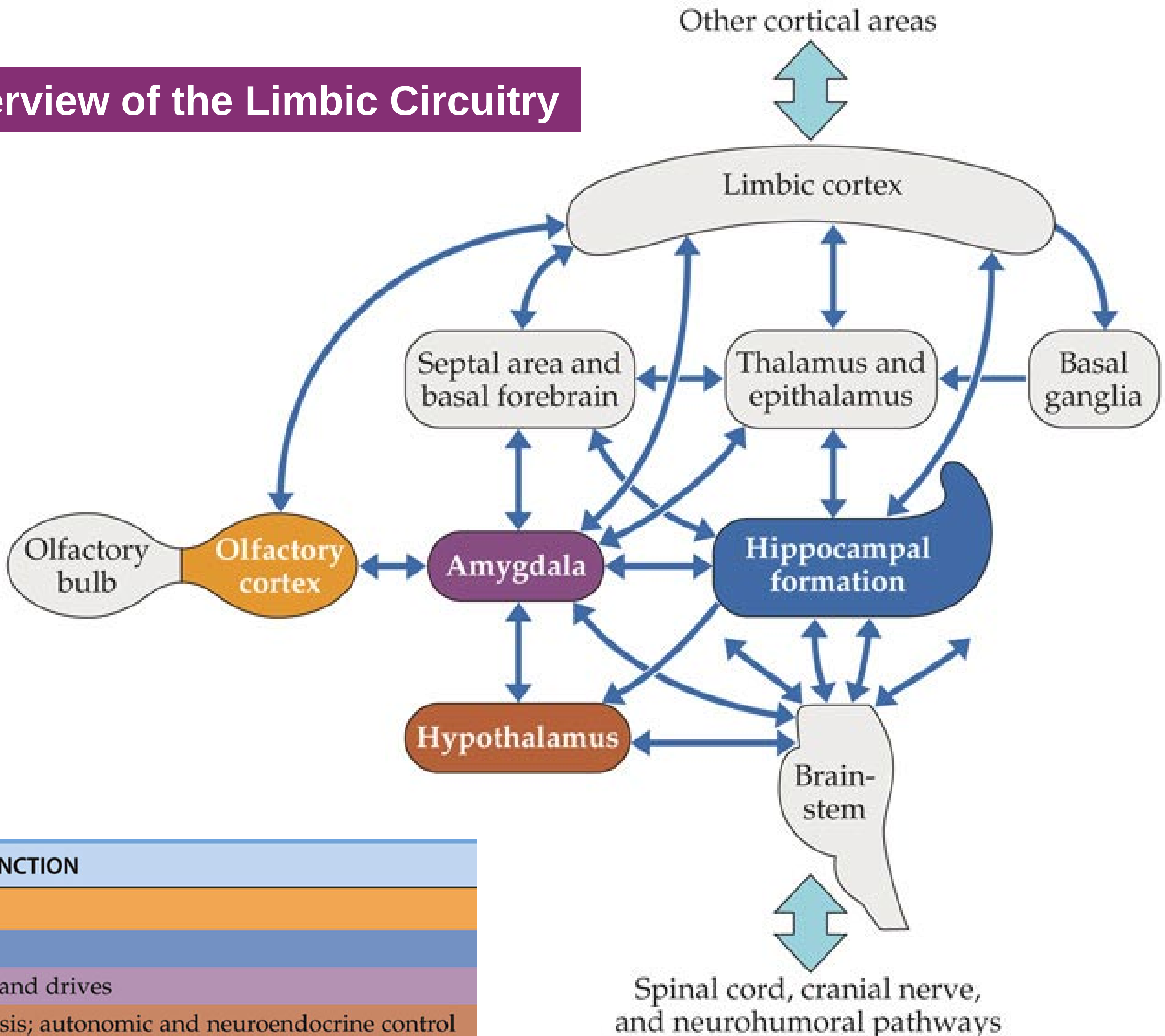
- Prefrontal cortex
- Cingulate gyrus

} Anatomical and functional relationships with processes in limbic system

Limbic system function

- **Olfaction**
- **Memory**
- **Emotions and drives**
- **Homeostatic functions, including autonomic and neuroendocrine control**
- An aid to remembering these functions is **HOME** (**H**omeostasis, **O**lfaction, **M**emory, and **E**motion).

Overview of the Limbic Circuitry

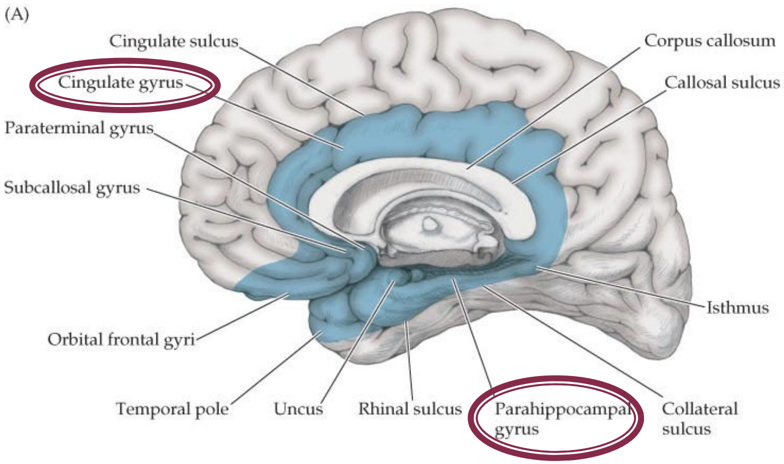


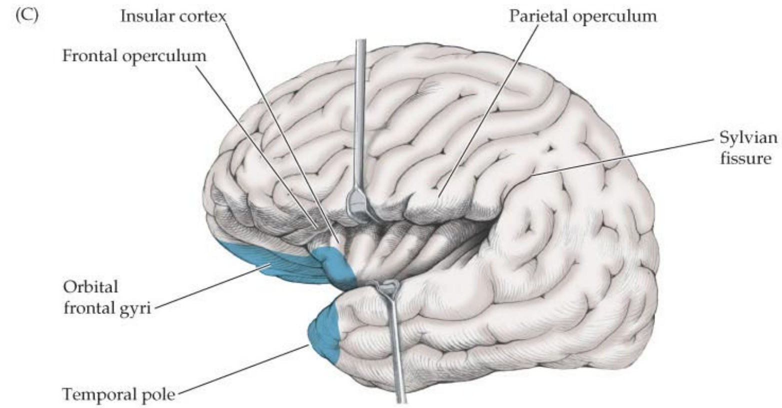
LIMBIC FUNCTION
Olfaction
Memory
Emotions and drives
Homeostasis; autonomic and neuroendocrine control

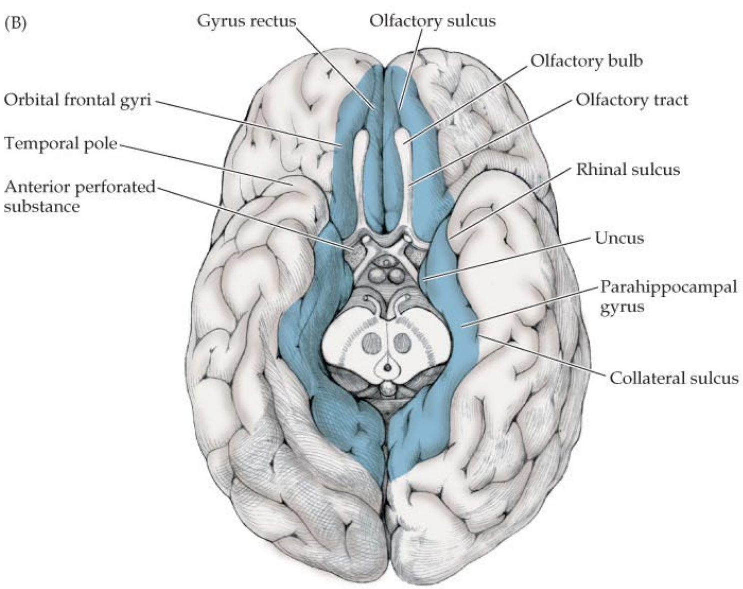
TABLE 18.2 Simplification of Limbic Functions and Corresponding Key Structures

LIMBIC FUNCTION	KEY STRUCTURE
Olfaction	Olfactory cortex
Memory	Hippocampal formation
Emotions and drives	Amygdala
Homeostasis; autonomic and neuroendocrine control	Hypothalamus

The main components of limbic cortex visible on a medial view are the **cingulate gyrus** (*cingulum* means "girdle" or "belt" in Latin) and the **parahippocampal gyrus**

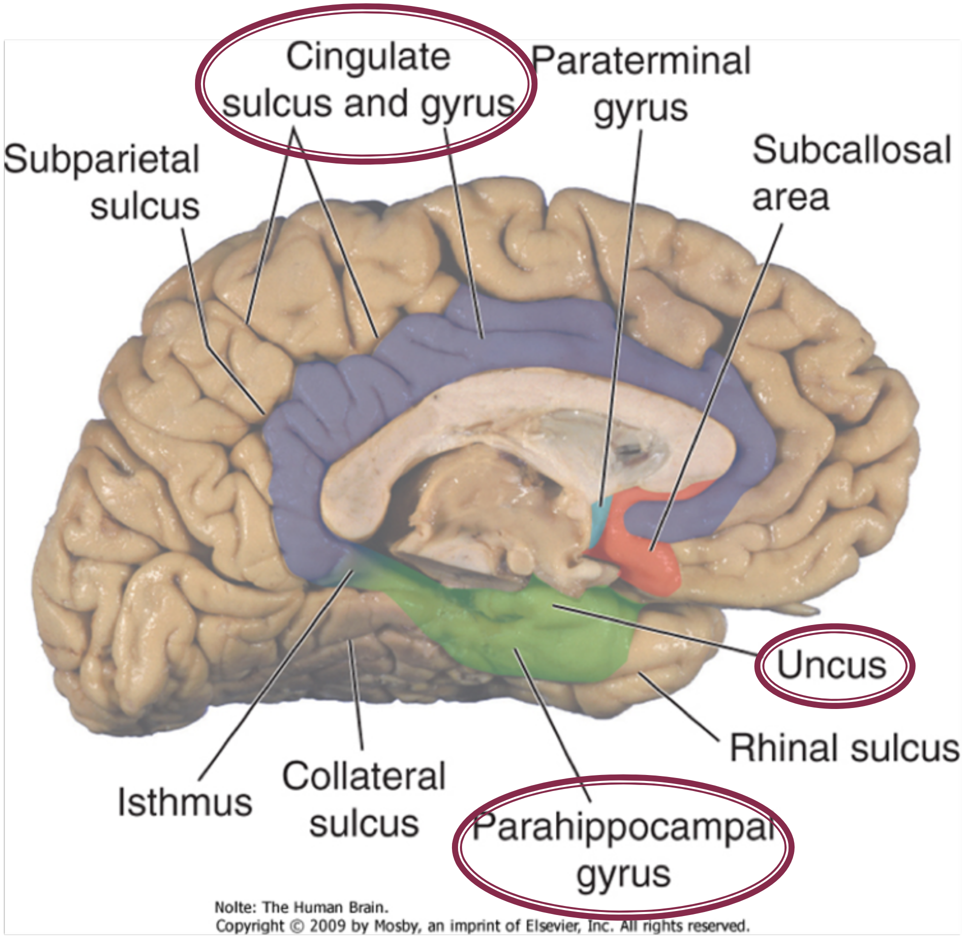


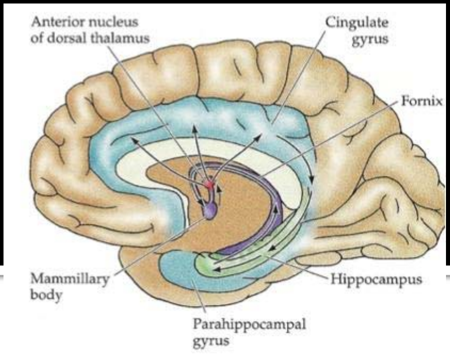




The **parahippocampal gyrus** is separated from the remainder of the temporal lobe by the **collateral sulcus**, which continues anteriorly as the **rhinal sulcus**

- The **uncus** is a bump visible on the anterior medial parahippocampal gyrus.
- The **cingulate gyrus** continues anteriorly and inferiorly as the subcallosal and paraterminal gyri. The cingulate gyrus joins the **parahippocampapal gyrus** posteriorly at the isthmus.

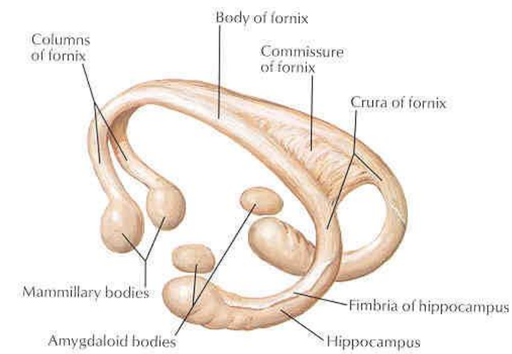




Papez's Circuit of Emotion

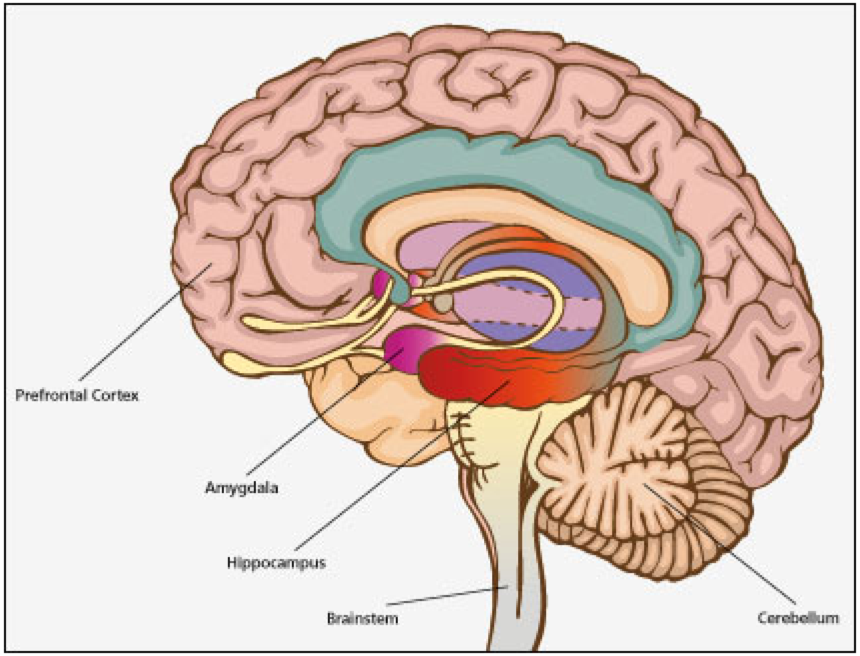
- The **hippocampal formation** is the medial and dorsal continuation of the parahippocampal gyrus. It is buried within the medial temporal lobe, forming the floor of the temporal horn of the lateral ventricle
- The hippocampal formation is one of several *C*-shaped structures in the limbic system.
- The hippocampal formation plays an important role in the ***memory functions*** of the limbic system.

Hippocampal formation



Fornix: schema

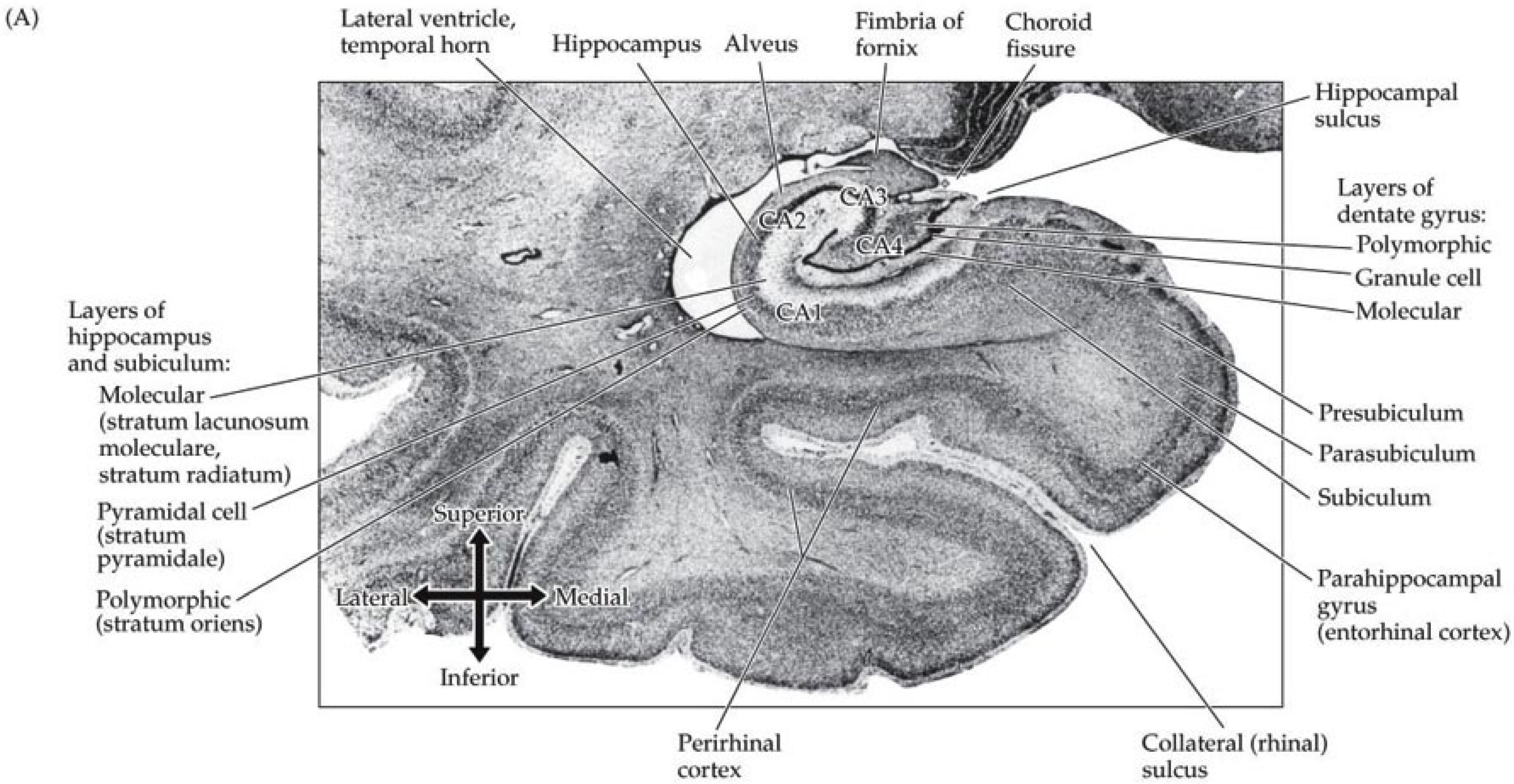
- Deep within the temporal lobe
- Medial wall of inferior horn of the lateral ventricle



Central regulation of:

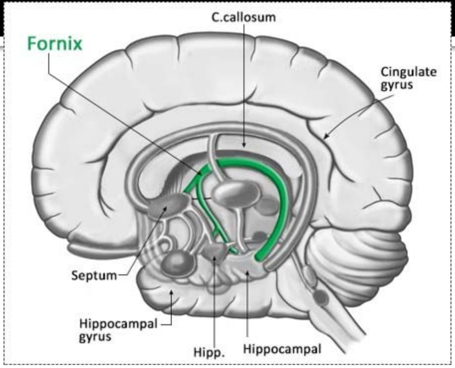
- *emotional behaviour*
- *motivational processes*
- *memory functions*
- *hormonal and autonomic regulation*

Unlike the **six-layered neocortex**, the hippocampal formation has only three layers and is called **archicortex**.



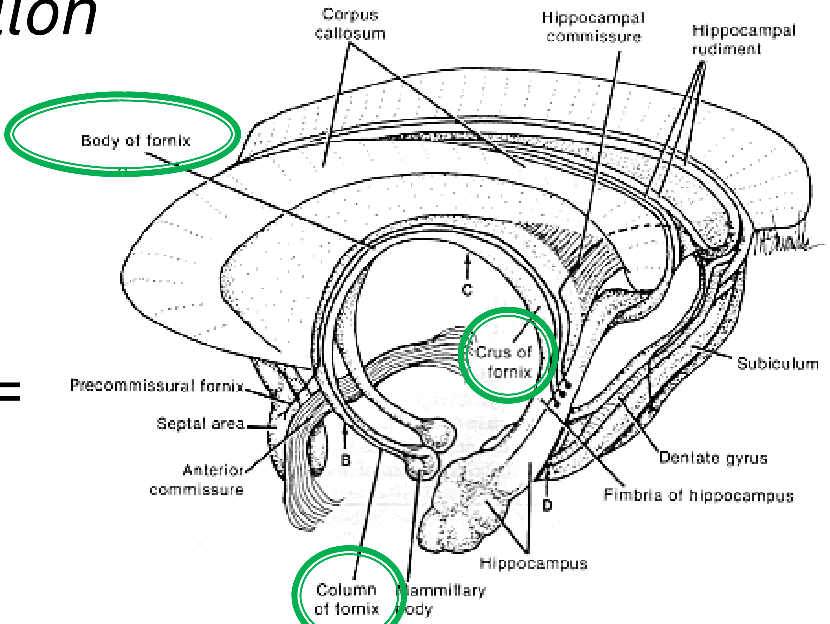
- About 95% of the cortex in humans is six-layered **neocortex** (meaning “new cortex”; also called isocortex, meaning “same cortex”)
- More phylogenetically ancient forms of cortex, which do not have six distinct layers, are referred to as **allocortex** (meaning “other cortex”).
- Allocortex includes the three-layered **archicortex** (meaning “first” or “original cortex”) of the hippocampal formation, as well as **paleocortex** (meaning “old cortex”), which is found predominantly in the piriform cortex of the **olfactory area**

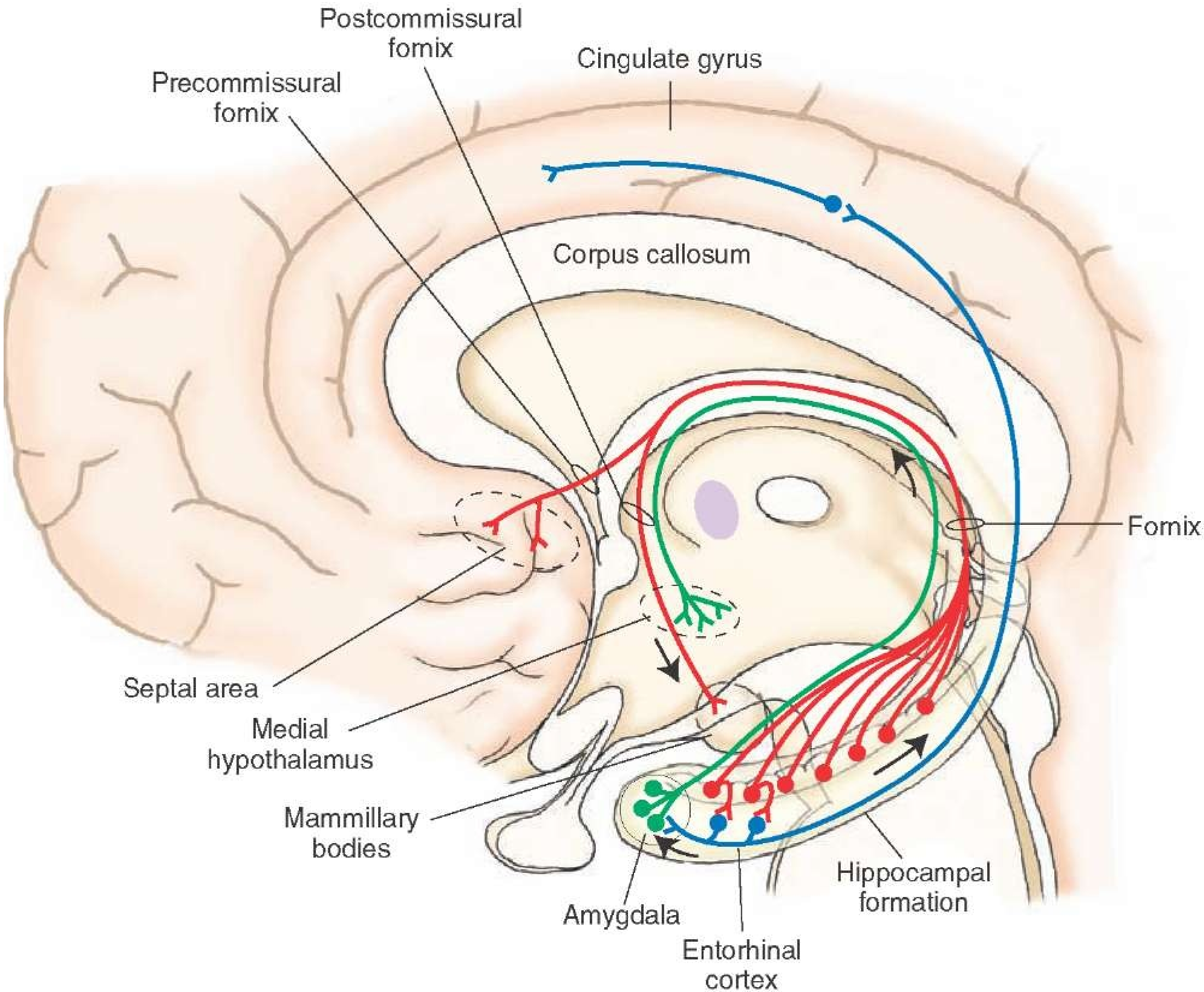
Fornix - major outflow pathway



Dorsomedial direction until corpus callosum, then rostral until anterior commissure,

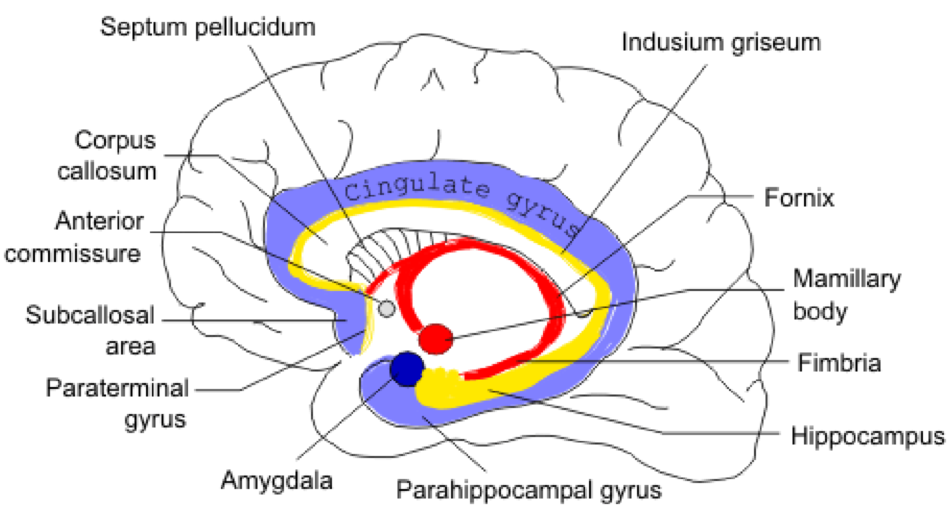
1. *then ventrally into diencephalon (ant. thalamic nucl. and mammillary bodies) =* ***postcommissural fornix***
2. *Then rostrally to septal area =* ***precommissural fornix***

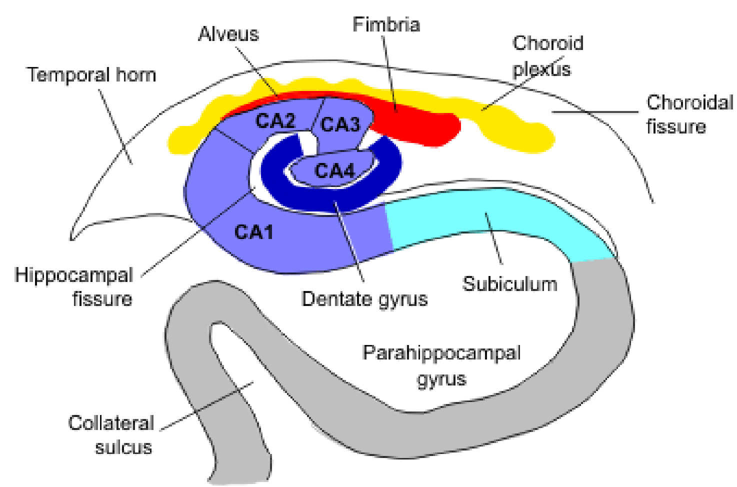



Postcommissural
fornix
Cingulate gyrus
Precommissural
fornix
Corpus callosum
Fornix
Septal area
Medial
hypothalamus
Mammillary
bodies
Amygdala
Entorhinal
cortex
Hippocampal
formation

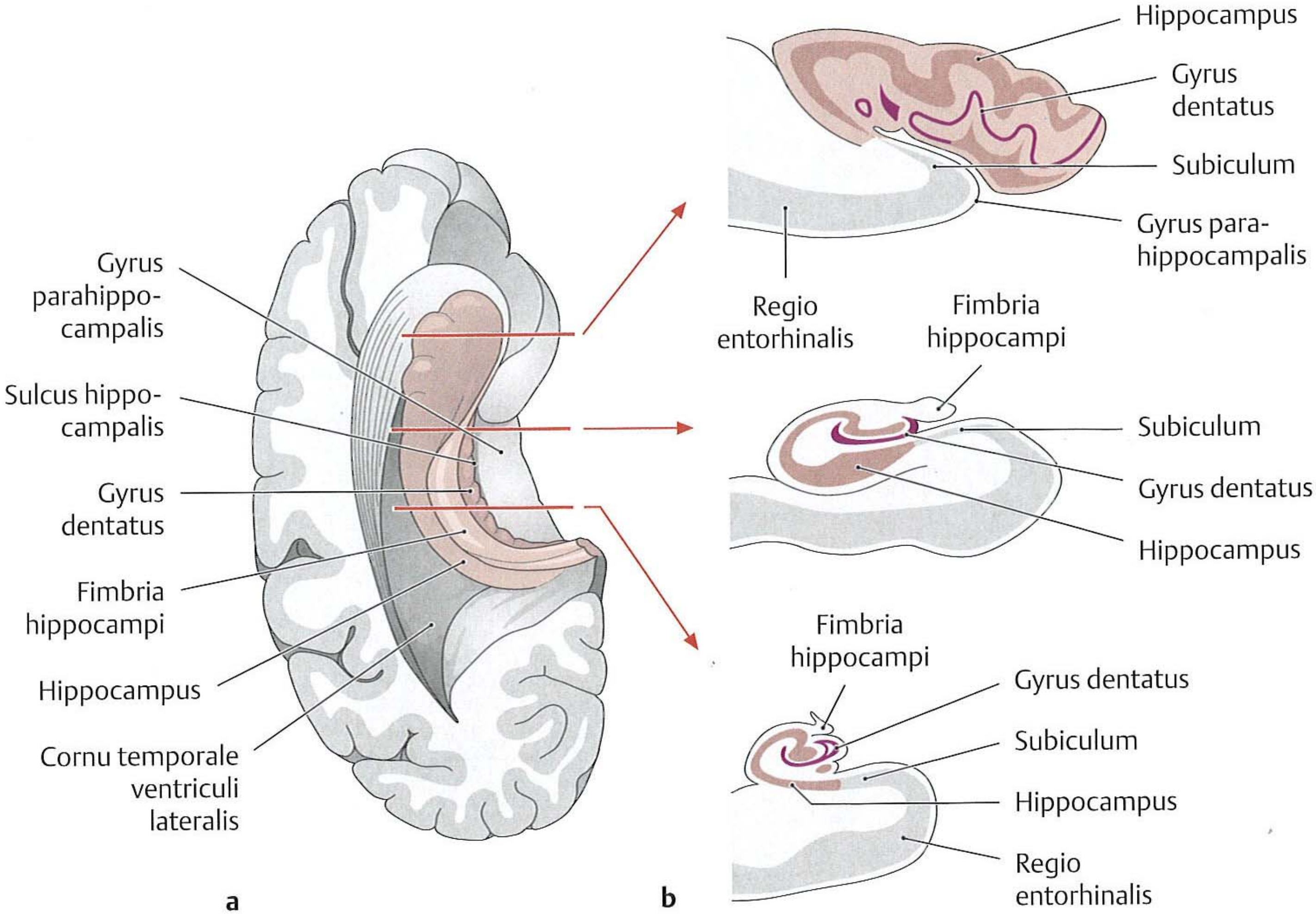
Formatio hippocampi

- Hippocampus praecommissuralis = gyrus paraterminalis
- Hippocampus supracommissuralis
- <u>Hippocampus retrocommissuralis:</u>
  - Cornu ammonis (=hippocampus proper)
  - Fascia dentata (=gyrus dentatus)
  - Subiculum

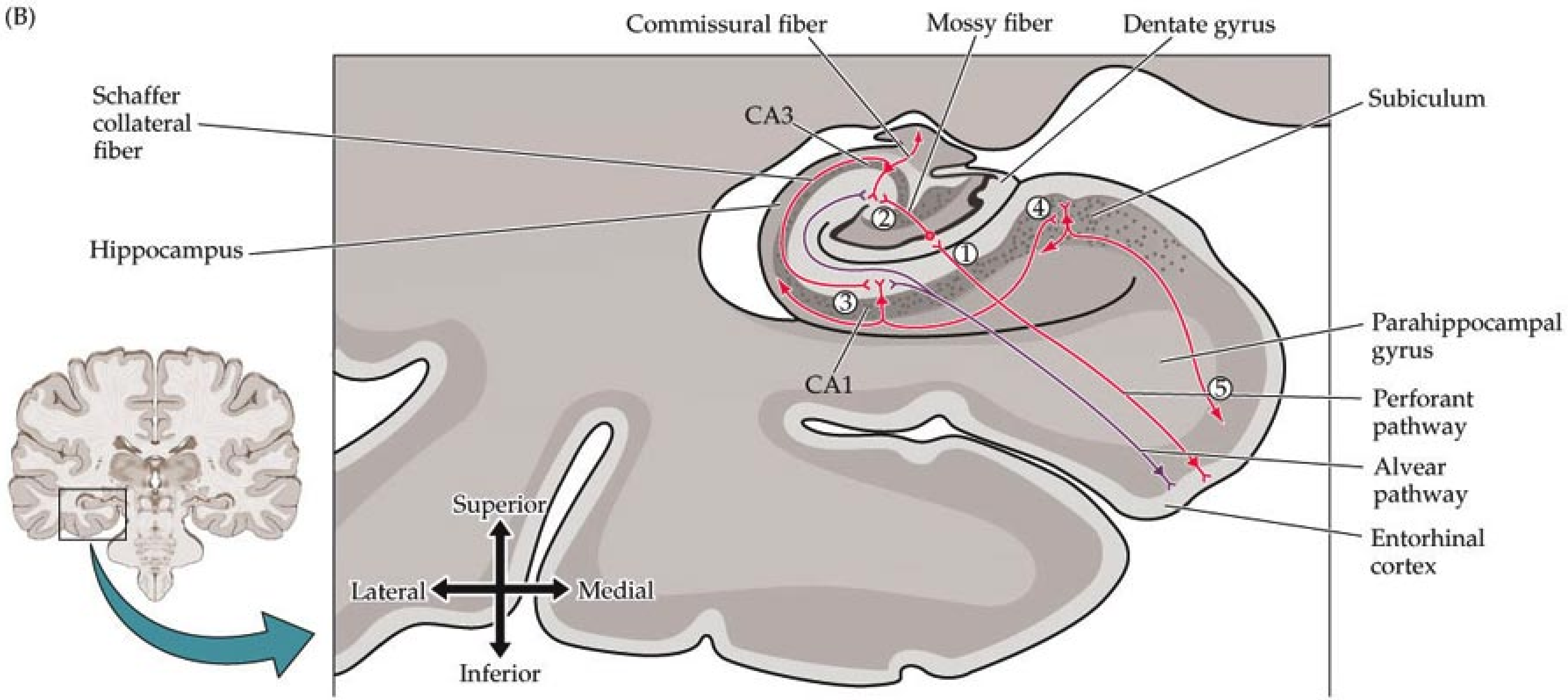




Hippocampal formation



Intrinsic Circuitry of the Hippocampal Formation



Tri-synaptic loop (The perforant pathway)

- Connecting hippocampus with cerebral cortex

  1. fasciculus perforans

  2. mossy cell fibers

  3. Schaffer collaterals

Tri-synaptic loop

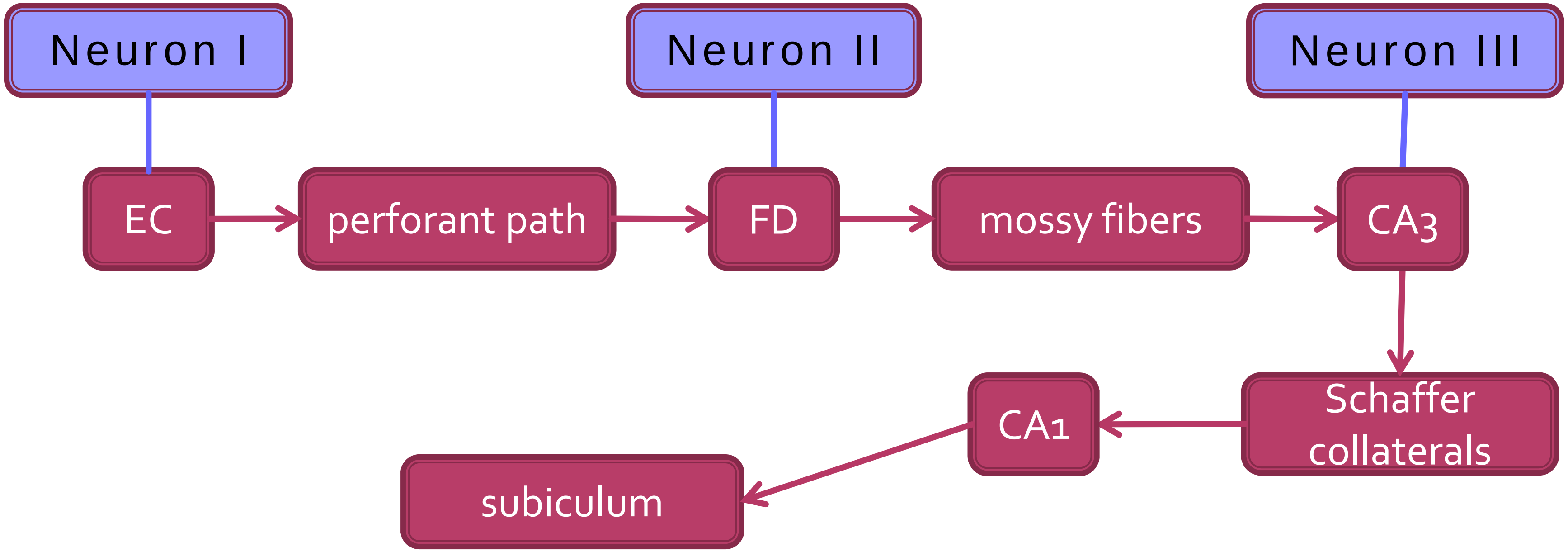
- **First order neuron:** pyramidal neurons in entorhinal cortex (layer II and III)
- their axons form ***tractus perforans***
- projects to dentate gyrus - granule cell fibers of fascia dentata (FD)

Trisynaptic loop

- **Second order neuron:** granule cells of fascia dentata
- their axons form ***Mossy fibers***
- pass through the *hilus* of FD
- synapses on pyramidal neurons in CA3

Trisynaptic loop

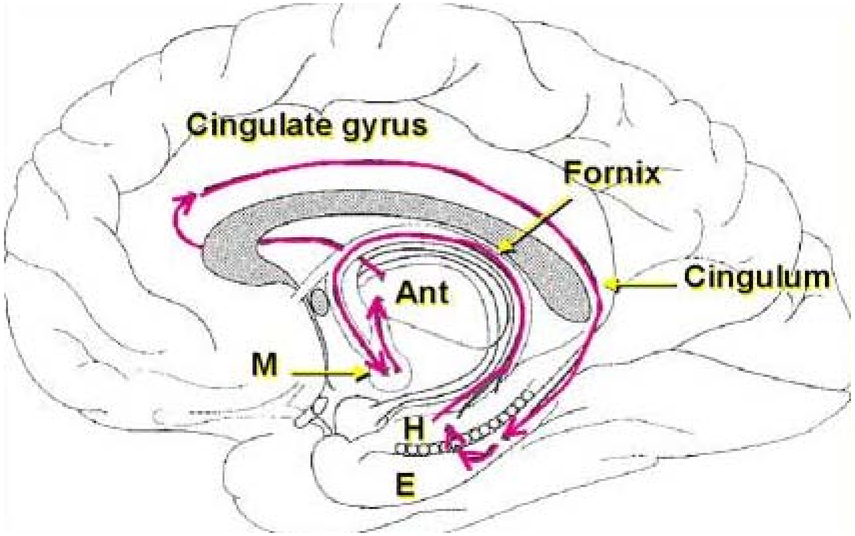
- <u>**Third order neuron:**</u> pyramidal neurons of CA3
- their axons form ***Schaffer collaterals***
- synapse in pyramidal neurons of CA1
- axons of CA1 neurons project to *subiculum*

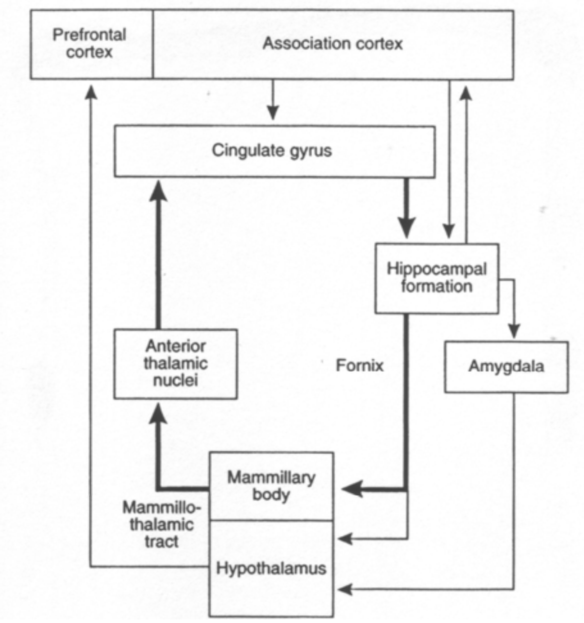


Papez circuit

- connects various structures of the telencephalon
- originates and ends in hippocampus
- average size of the circuit is 350 millimeters.

Hippocampal formation (subiculum) → fornix → mammillary bodies → mammillothalamic tract → anterior thalamic nucleus → cingulum → entorhinal cortex → hippocampal formation (FD).





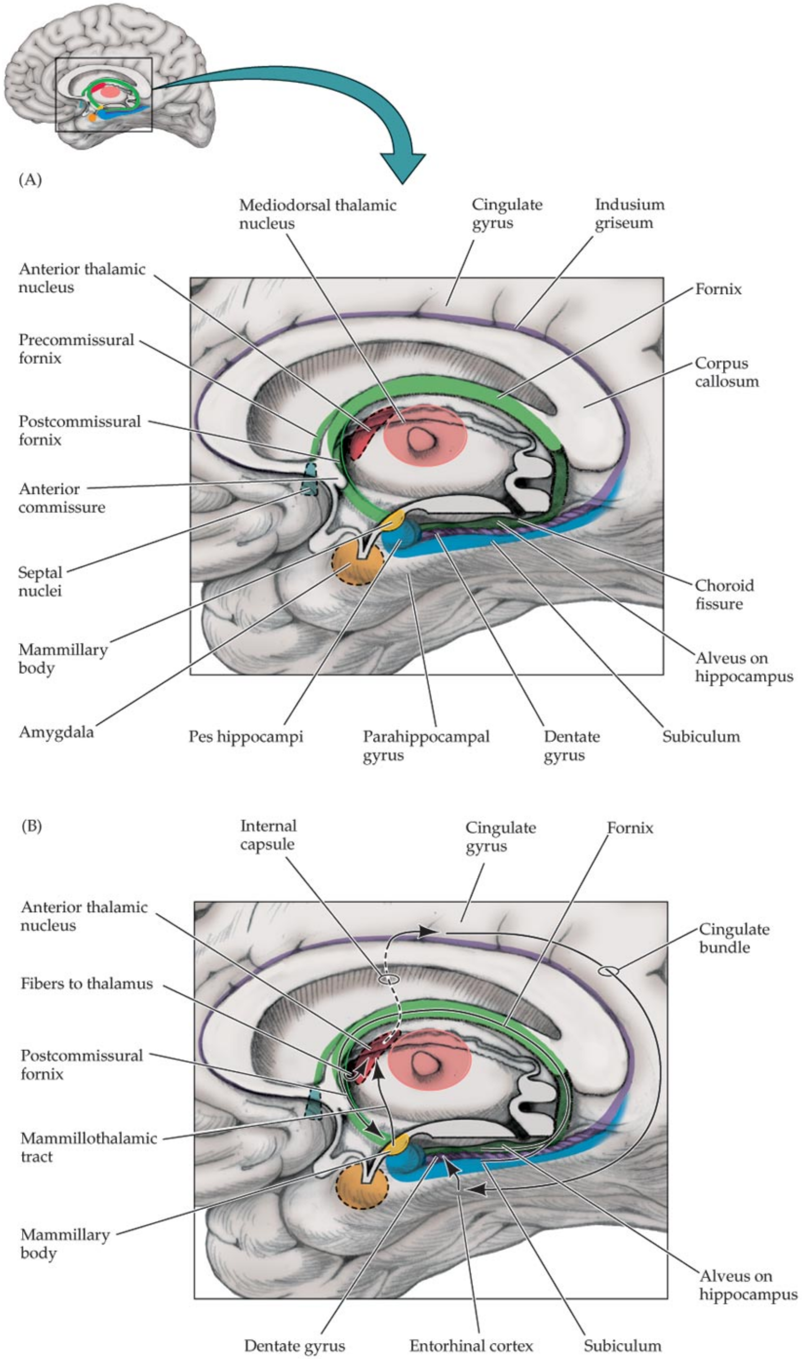
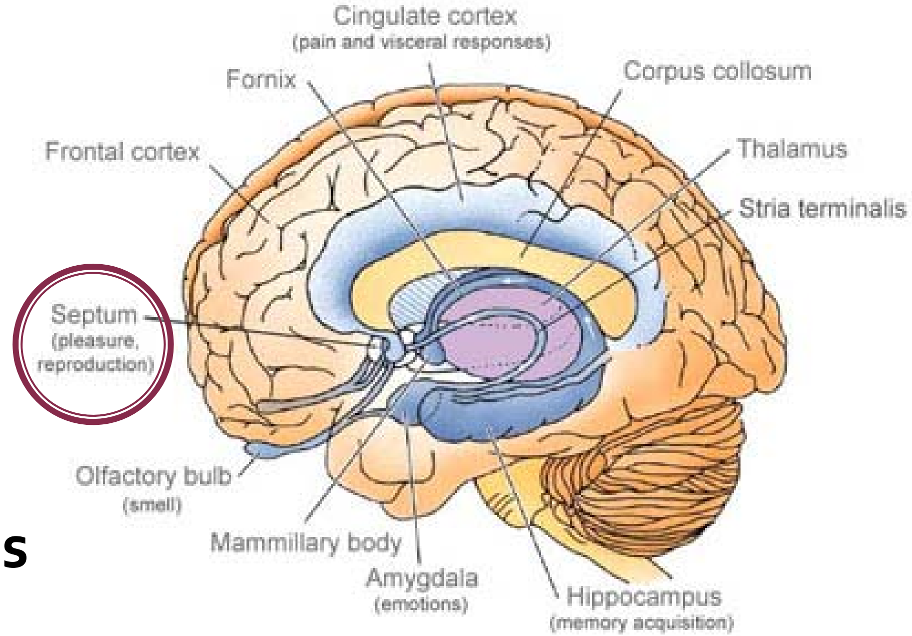


Figure 18.9 Circuit of Papez and Related Structures (A) Medial view showing the major structures participating in hippocampal circuits. (B) Although it is just one of many limbic circuits, the circuit of Papez provides a useful review of several limbic pathways.

Septal area

- The **septal region** lies just dorsal to the basal forebrain, near the septum pellucidum, and it also participates in limbic pathways
- The main septal nuclei lie within and just caudal to the subcallosal and paraterminal gyri and are named the **medial septal nucleus** and the **lateral septal nucleus**.
- The medial septal nucleus contains cholinergic neurons that project to the **hippocampal formation** and may play a role in modulation of memory function.

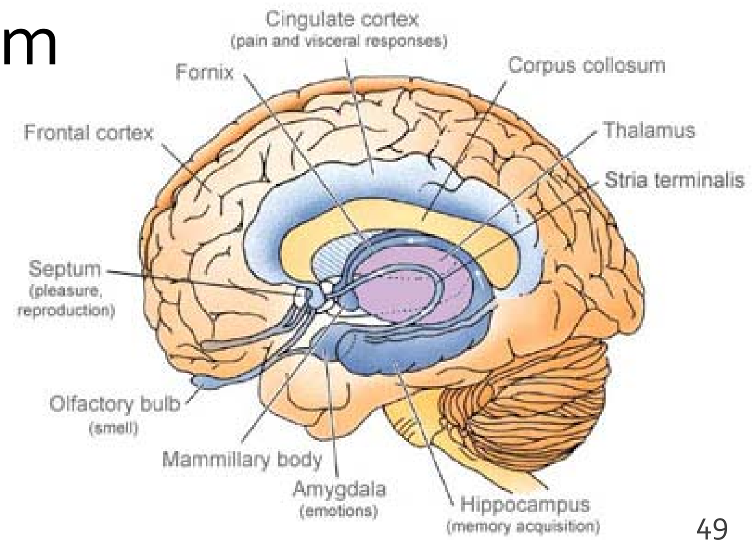


FUNCTION:
Aggression
Rage
Endocrine
Reproductive function

Septal area

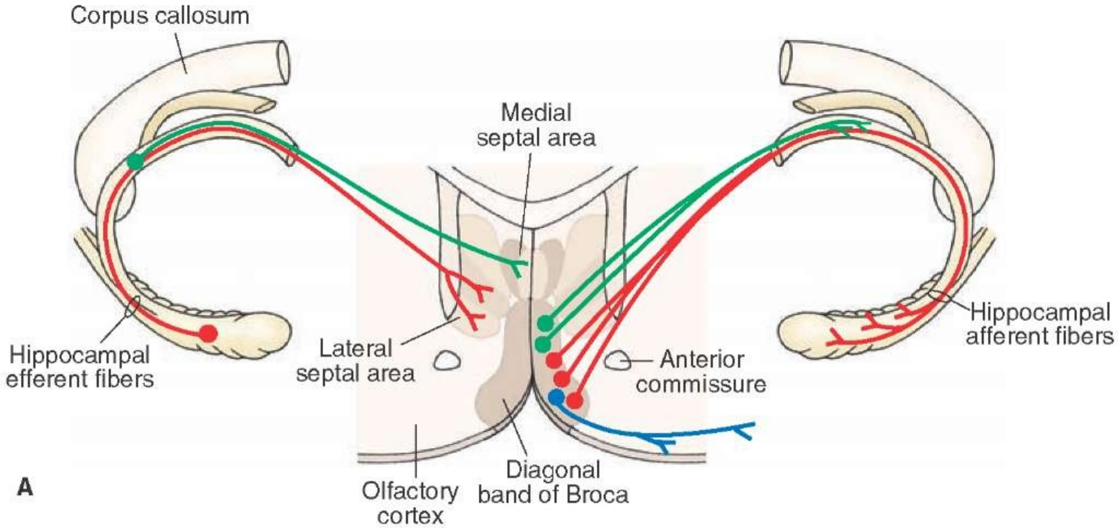
- Relay nucl. of the hippocamp. to hypothalamus (functional extension of the HF)
- Primary receiving area (precommissural fornix)
- Projects to hypothalamus

o Dorsal region – septum pellucidum
o Ventral region – large in humans



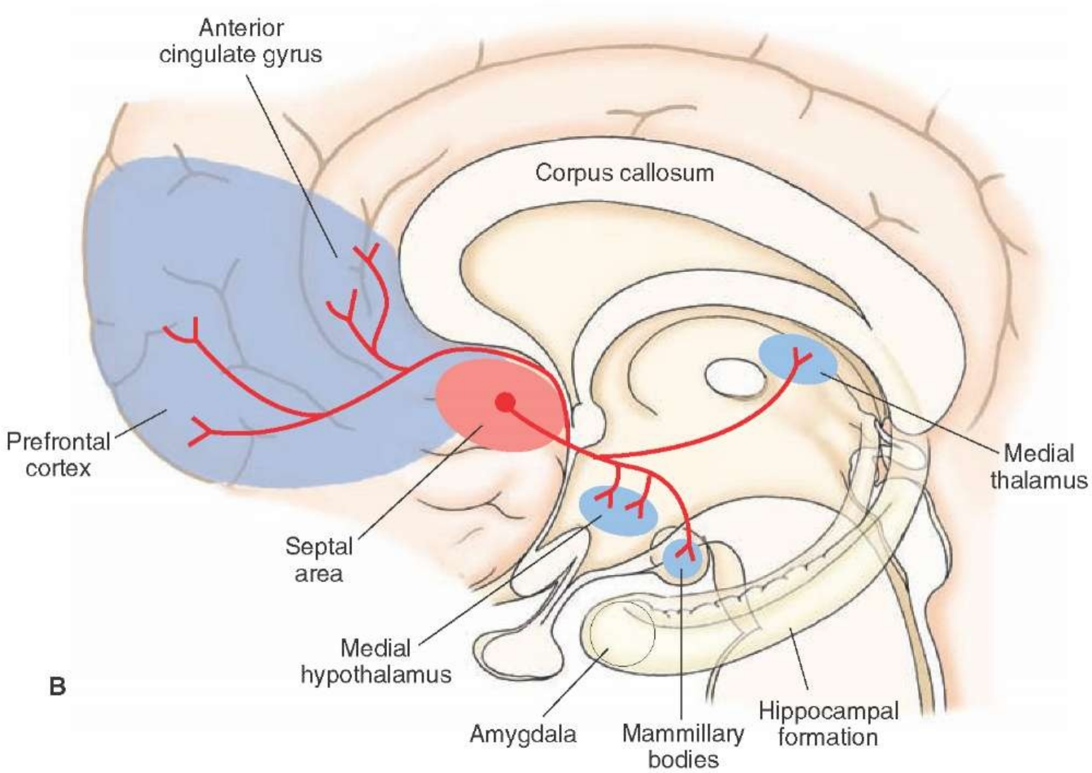
- **Inputs from** the hippocampal formation are mainly to the **lateral septal nucleus**,
- **Outputs** are mainly from the **medial septal nucleus**.
- The lateral septal nucleus has a large projection to the medial septal nucleus, completing this circuit.

- The **nucleus accumbens** is sometimes included in the septal region or basal forebrain and is involved in basal ganglia–limbic circuitry
- Another nearby nucleus with limbic connections is the **bed nucleus of the stria terminalis**



Corpus callosum
Medial septal area
Hippocampal efferent fibers
Lateral septal area
Anterior commissure
Hippocampal afferent fibers
Olfactory cortex
Diagonal band of Broca

A



Anterior cingulate gyrus
Corpus callosum
Prefrontal cortex
Medial thalamus
Septal area
Medial hypothalamus
Amygdala
Mammillary bodies
Hippocampal formation

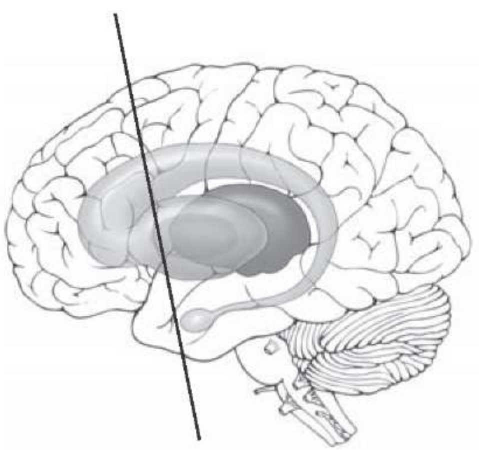
B

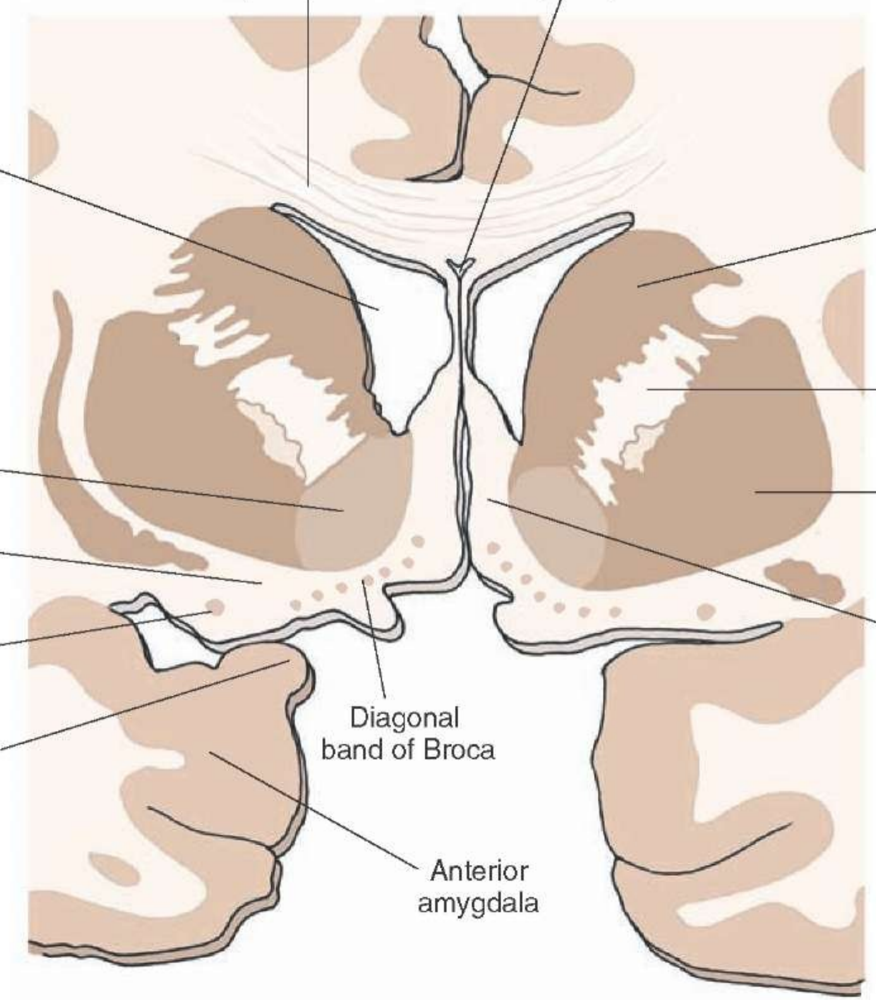
Bed nucleus of the stria terminalis

- Location: Ventrolateral to the fornix at the level of anterior commissure
- Recieves fibers from amygdala, sents fibers to hypothalamus and autonomic centres of the brainstem
- Regulates autonomic, endocrine, and affective processes associated with amygdala

Nucleus accumbens

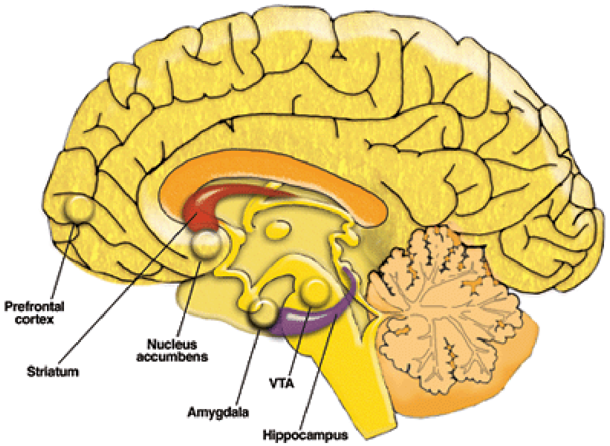
Between septal area, SI, putamen, caudatus

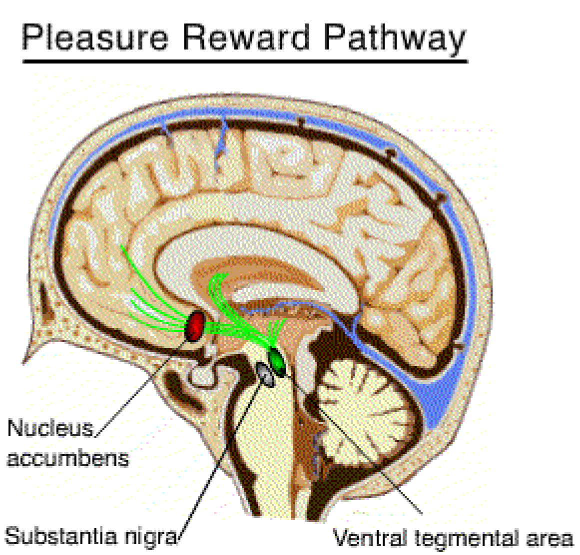


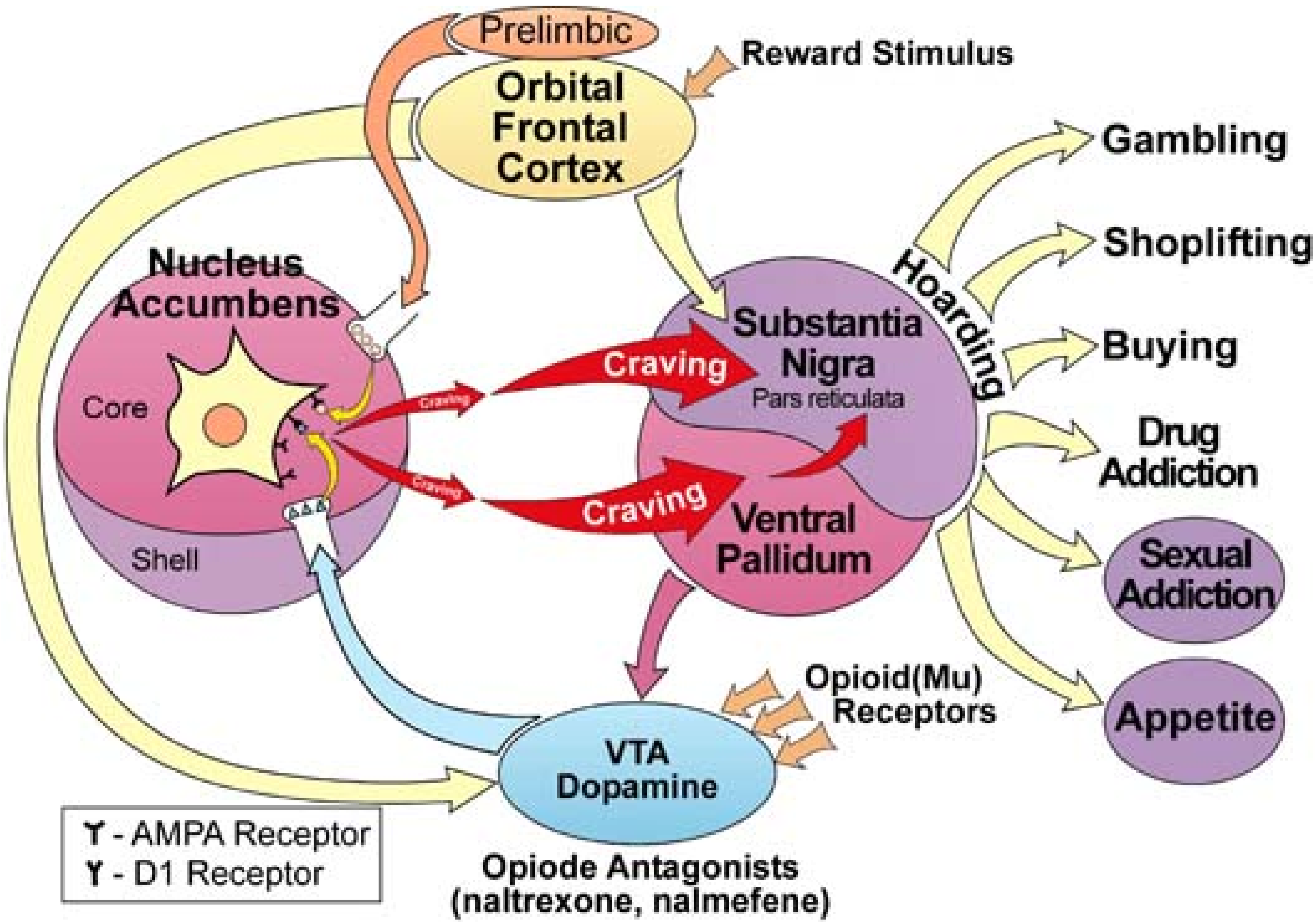


Nucleus accumbens

- Inputs from brainstem (DA), amygdala, hippocampal formation
- Projects to substantia innominata, SN, VTA
- Integrates the sequencing of motor responses associated with affective processes (and addictive – hedonic system).





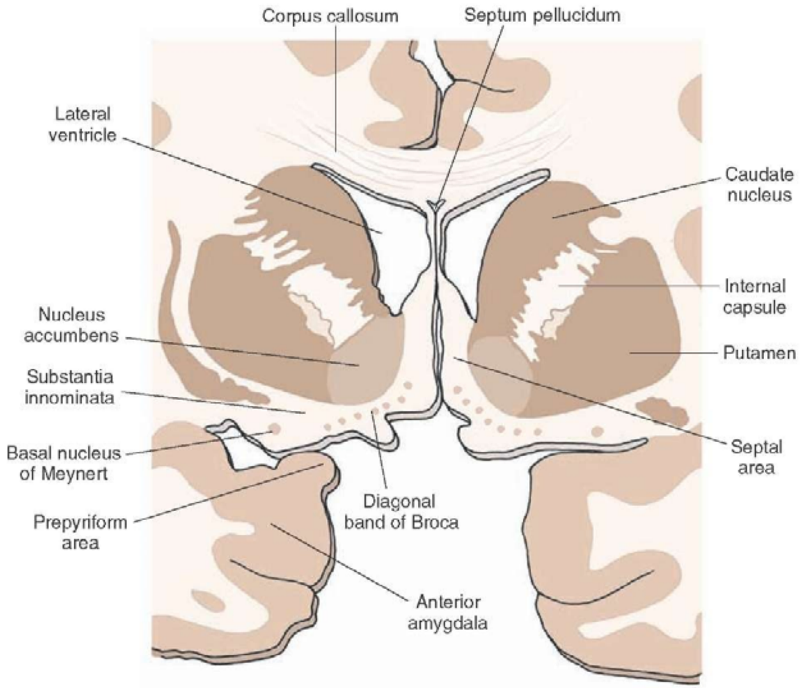

Prelimbic
Reward Stimulus
Orbital Frontal Cortex
Gambling
Shoplifting
Hoarding
Buying
Drug Addiction
Sexual Addiction
Appetite
Nucleus Accumbens
Core
Shell
Craving
Craving
Substantia Nigra
Pars reticulata
Ventral Pallidum
Opioid(Mu) Receptors
VTA Dopamine
- AMPA Receptor
- D1 Receptor
Opiode Antagonists
(naltrexone, nalmefene)

Substantia innominata

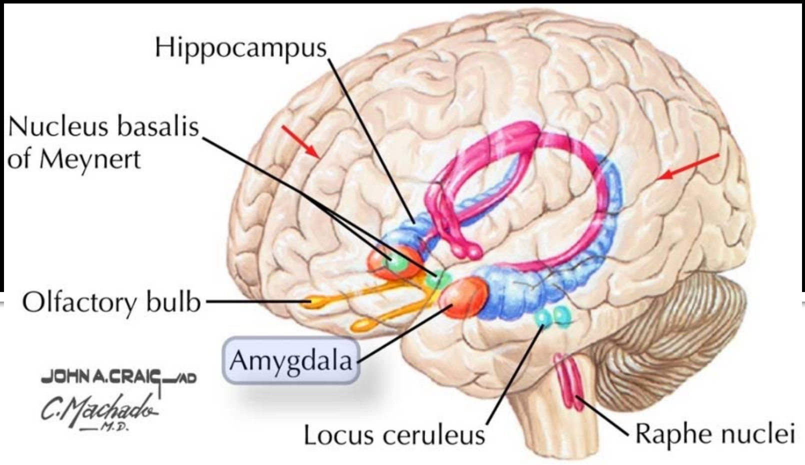
- Between diagonal band of Broca, preoptic region, prepyriform area, striatum
- Reciprocal connections with the amygdala, projects to lateral hypothalamus *(relay from A to lat.hypoth.)*

Basal nucelus of Meynert

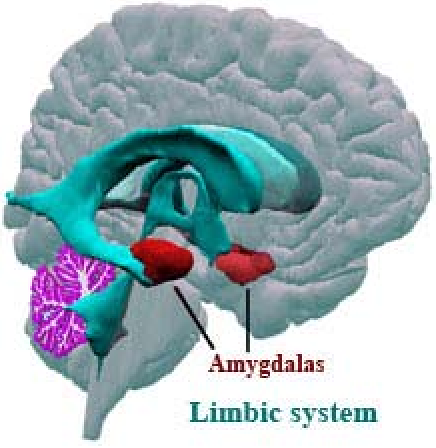
- Projects to cortex and limbic structures
- Etiology of Alzheimer's disease (ACh)

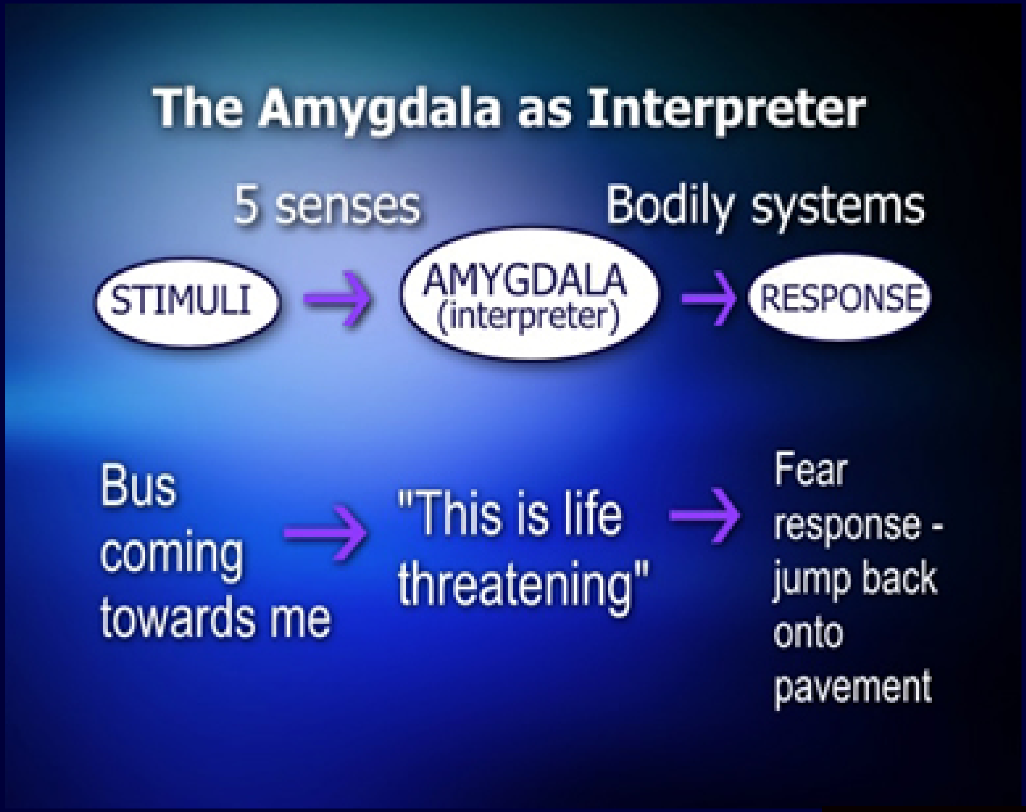


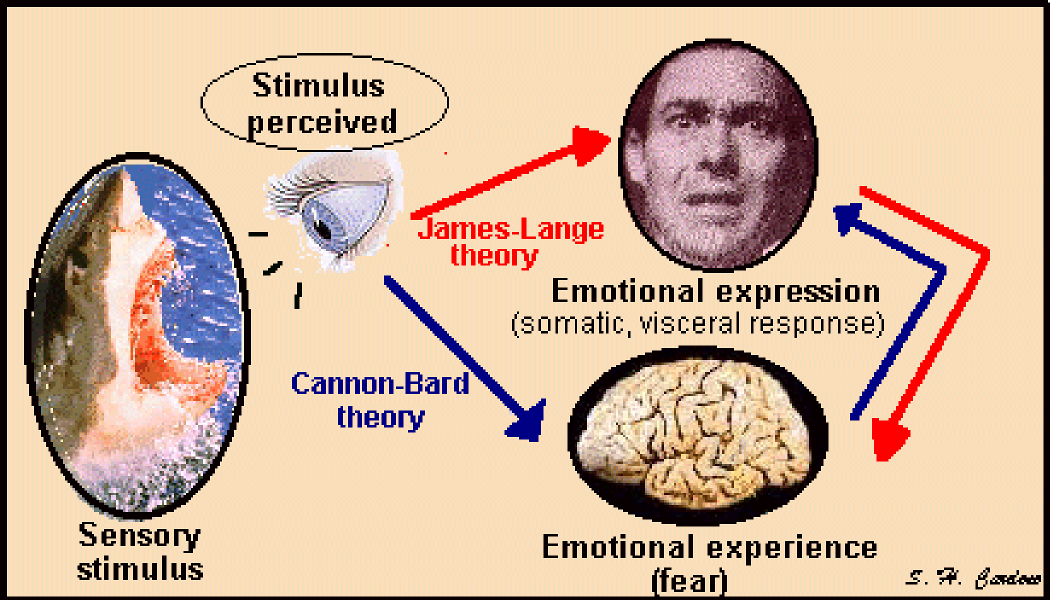
Amygdala



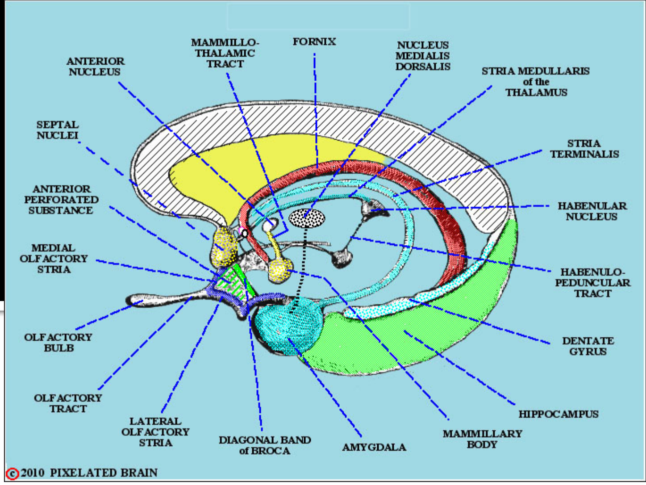
- Deep within temporal lobe
- Lateral, medial, central and basal nucleus
- Modulate processes associated with hypothalamus and midbrain PAG:
  - rage and aggression,
  - flight and other affective processes,
  - feeding behaviour,
  - endocrine adn hormonal activity,
  - sexual behavior,
  - autonomic control




The Amygdala as Interpreter
5 senses
Bodily systems
STIMULI
AMYGDALA
(interpreter)
RESPONSE
Bus coming towards me
"This is life threatening"
Fear response - jump back onto pavement


Stimulus perceived
James-Lange theory
Emotional expression
(somatic, visceral response)
Cannon-Bard theory
Sensory stimulus
Emotional experience (fear)

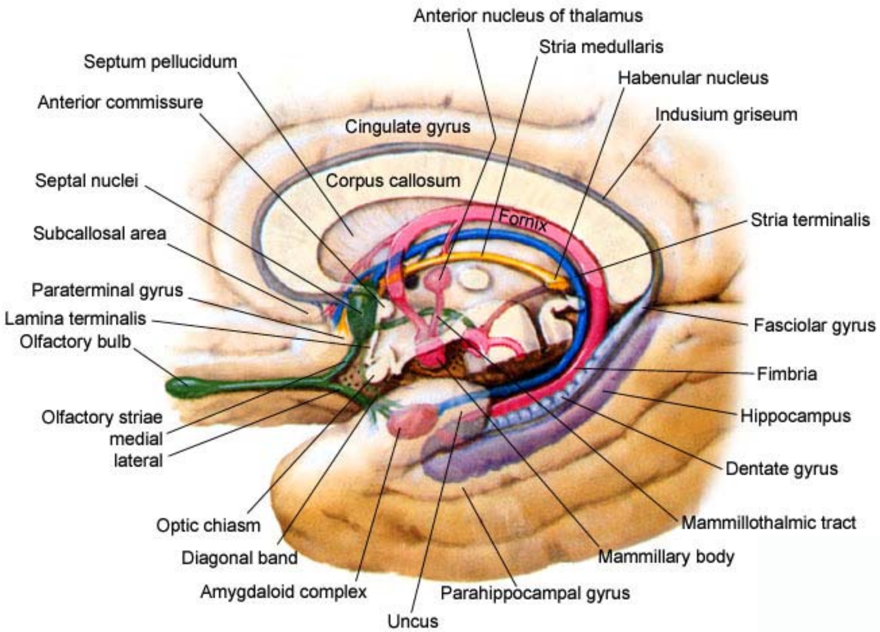
Amygdala

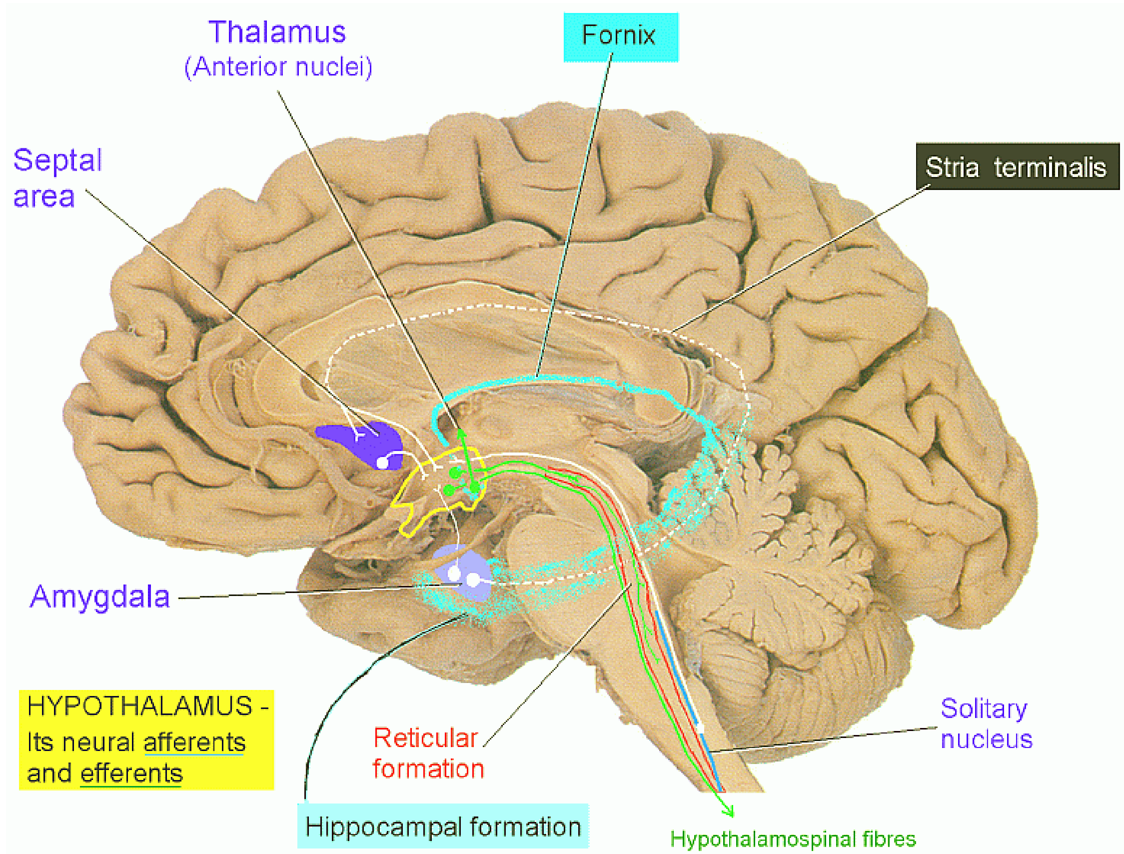


Major pathway: ***stria terminalis***

1. *from medial amygdala,*
2. *dorsally around post.thalamus,*
3. *then follow the tail of caudate nucleus rostrally (located ventromedially)*
4. *at the level of ant.commissure, descend ventromedially through bed nucleus*
5. *end in the medial hypothalamus*

Stria terminalis
major output from amygdala





Other major pathways of the forebrain

- Internal capsule
- Anterior commissure
- Tri-synaptic loop
- Papez circuit

Internal capsule

- **Descending**: corticospinal, corticopontine, corticobulbar pathways
- **Ascending**: thalamocortical fibers
  - ***Sensorimotor functions!***

- Genu (corticobulbar)
- Anterior limb (frontopontine)
- Posterior limb (corticospinal)
- Separates thalamus from GP, and caudate nucl. from putamen

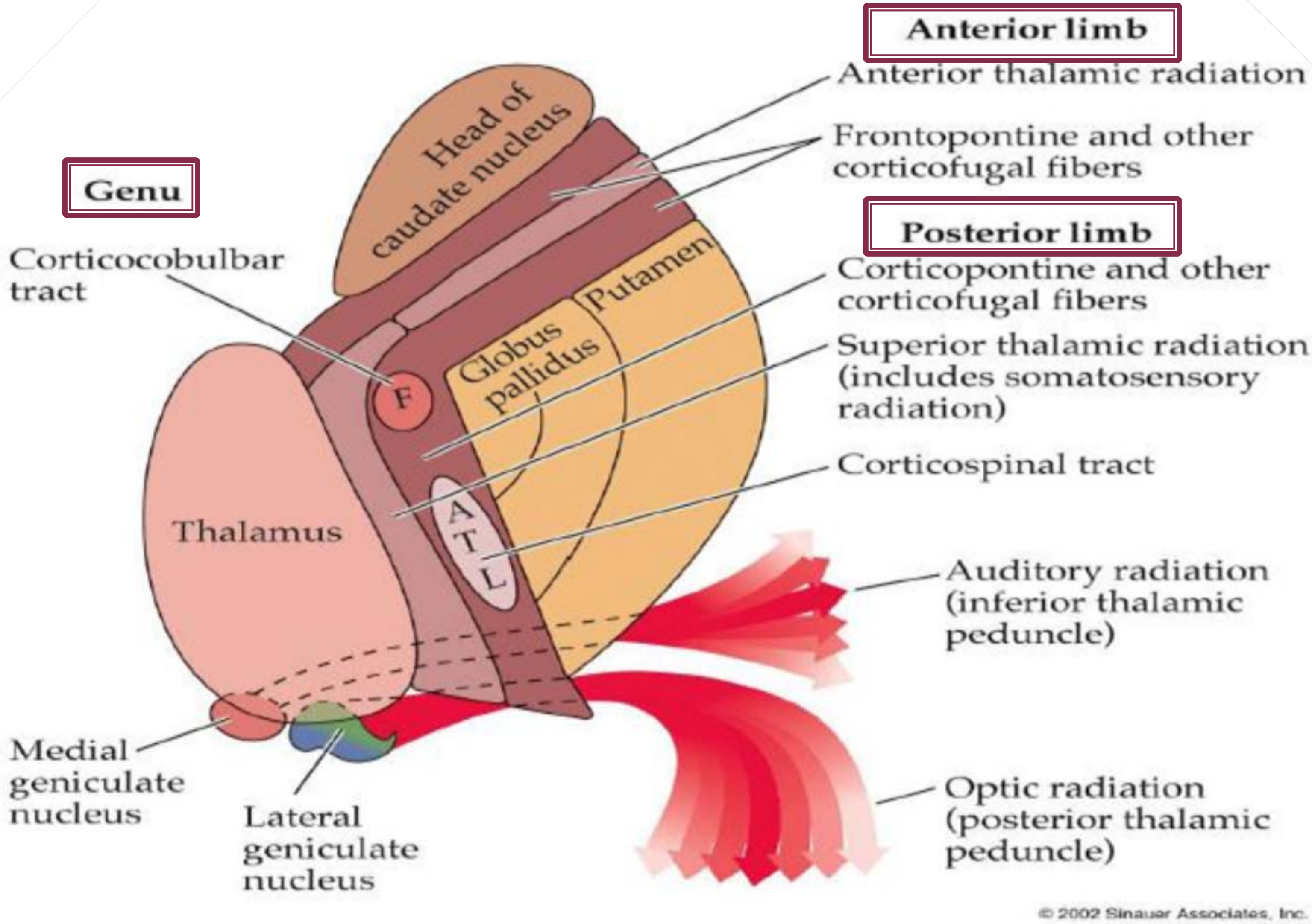
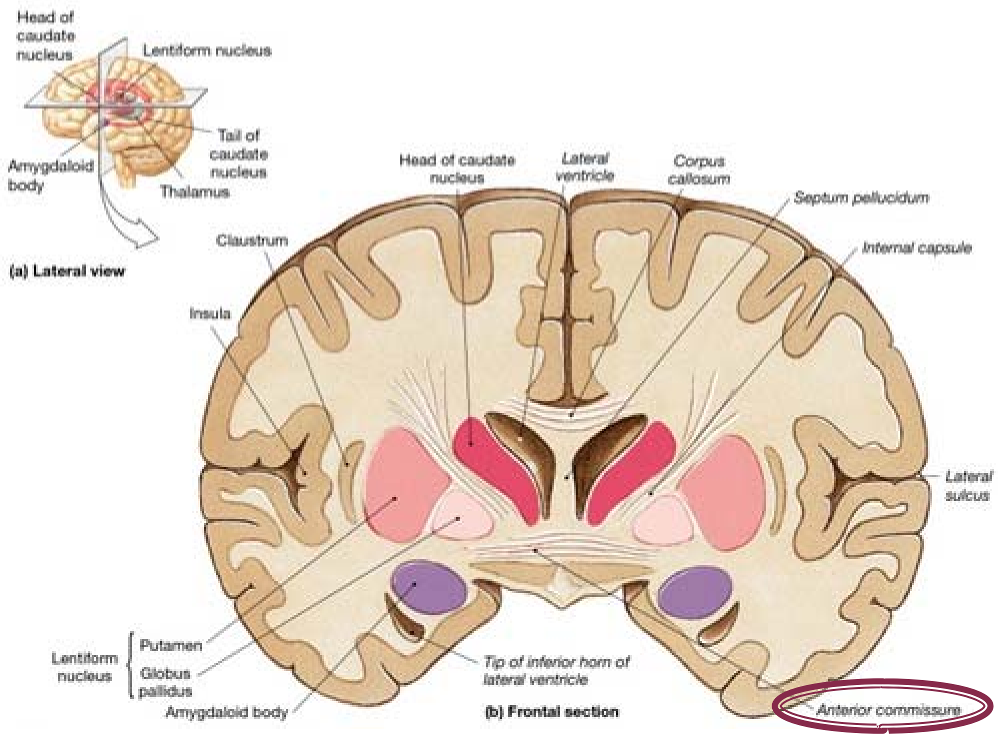


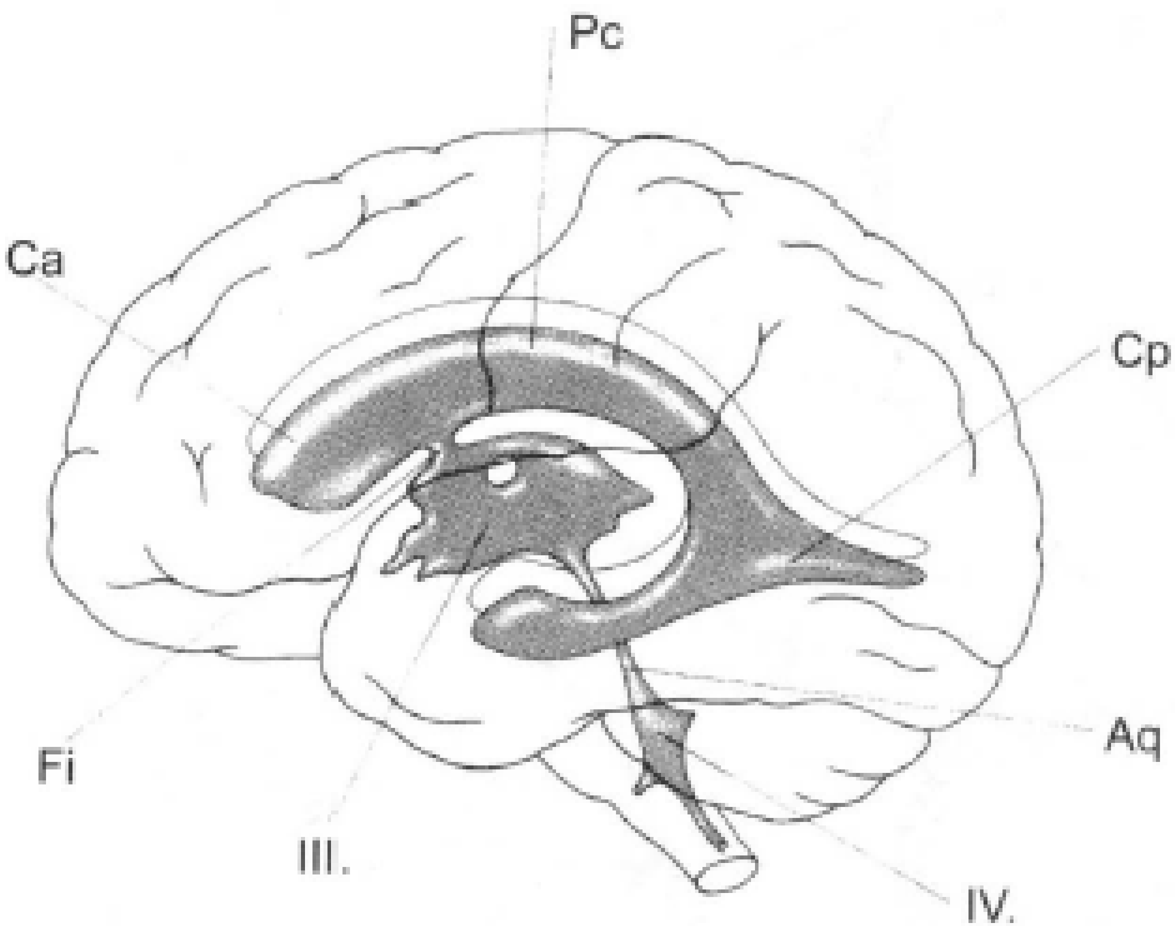
Figure showing Corticospinal & Corticobulbar Fibers in Internal capsule

Anterior commissure

- Rostral to the descending column of the fornix
- Olfactory fibers from anterior olfactory bulb
- Fibers that originate in temporal lobe (amygdala)



Lateral cerebral ventricles

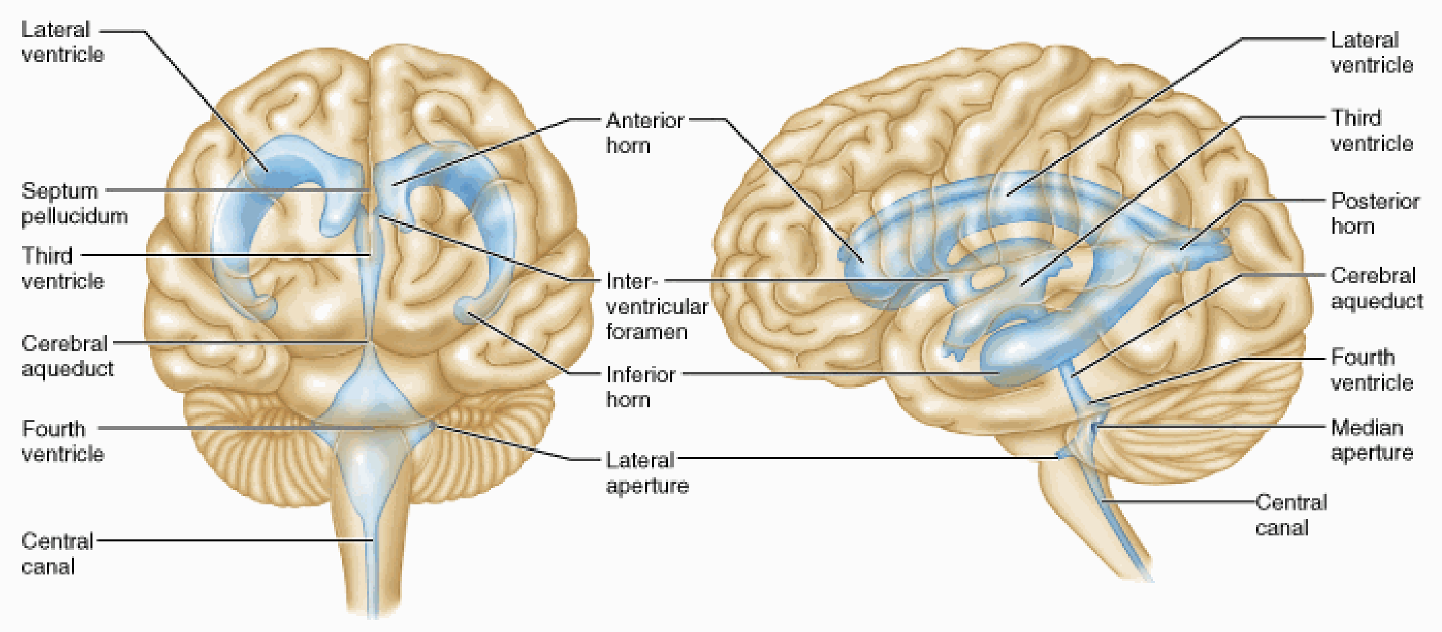


Lateral cerebral ventricles

- Contain CSF
  - secreted primarily from choroid plexus (specialized epithelial cells)
  - Source of electrolytes, protective and supportive medium
  - Conduit for neuroactive and metabolic products
  - Removes neuronal metabolic products from brain

Lateral cerebral ventricles

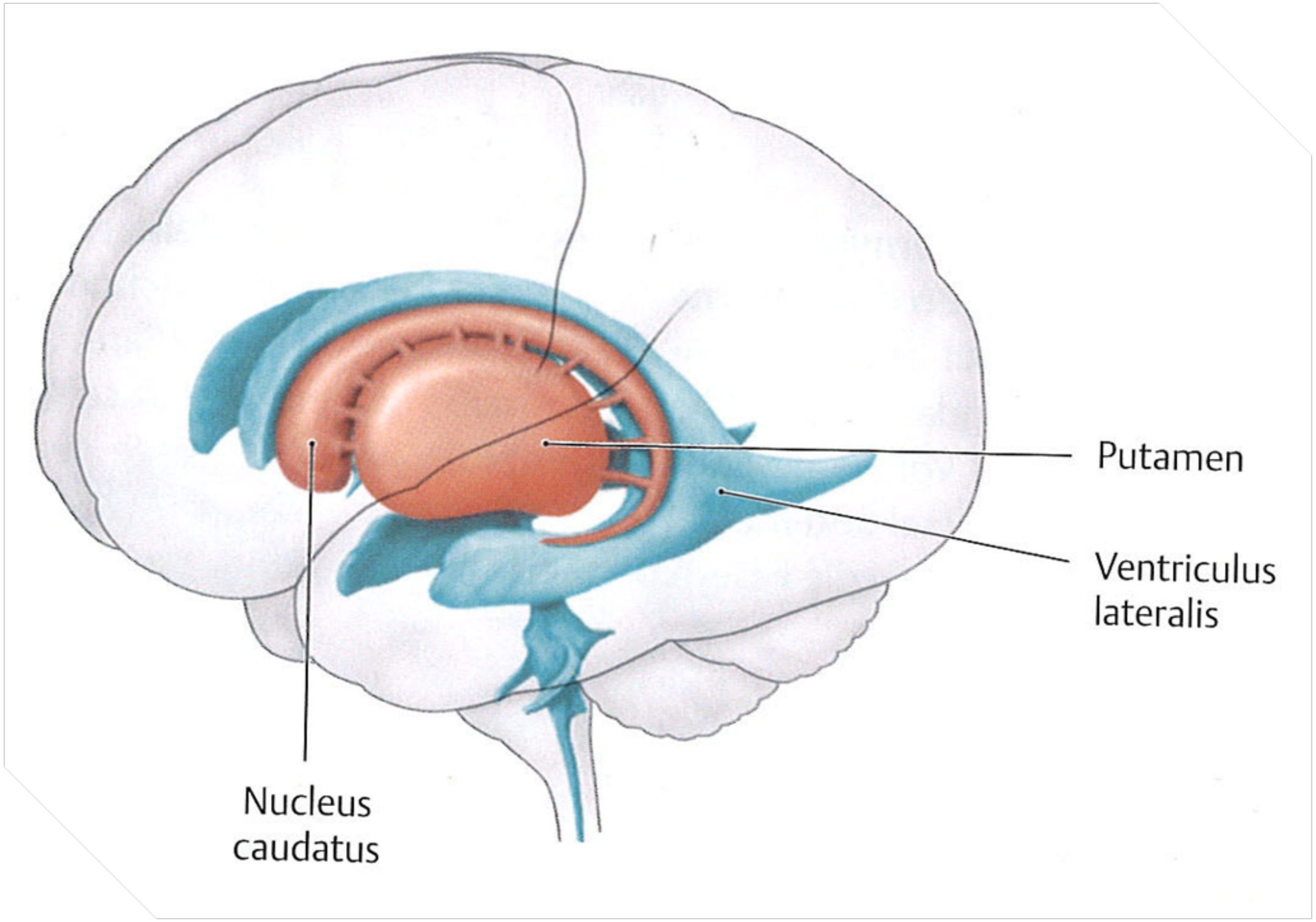
- Anterior horn (in frontal lobe)
- Posterior horn (extends into occipital lobe)
- Inferior horn (in temporal lobe)
- Body (between interventricular foramen and posterior horn)



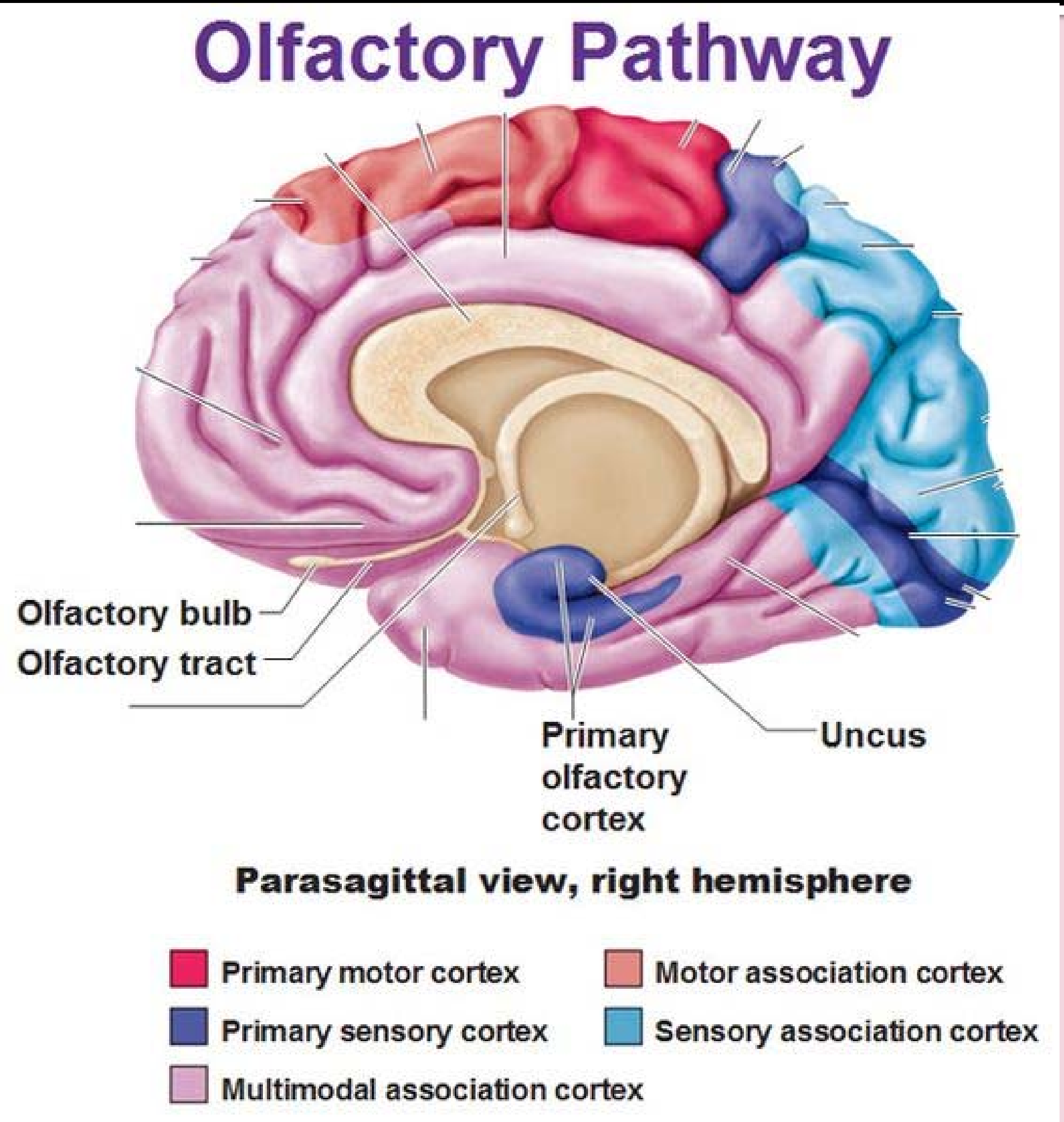
(a) Anterior view

(b) Left lateral view

Cerebral ventricles



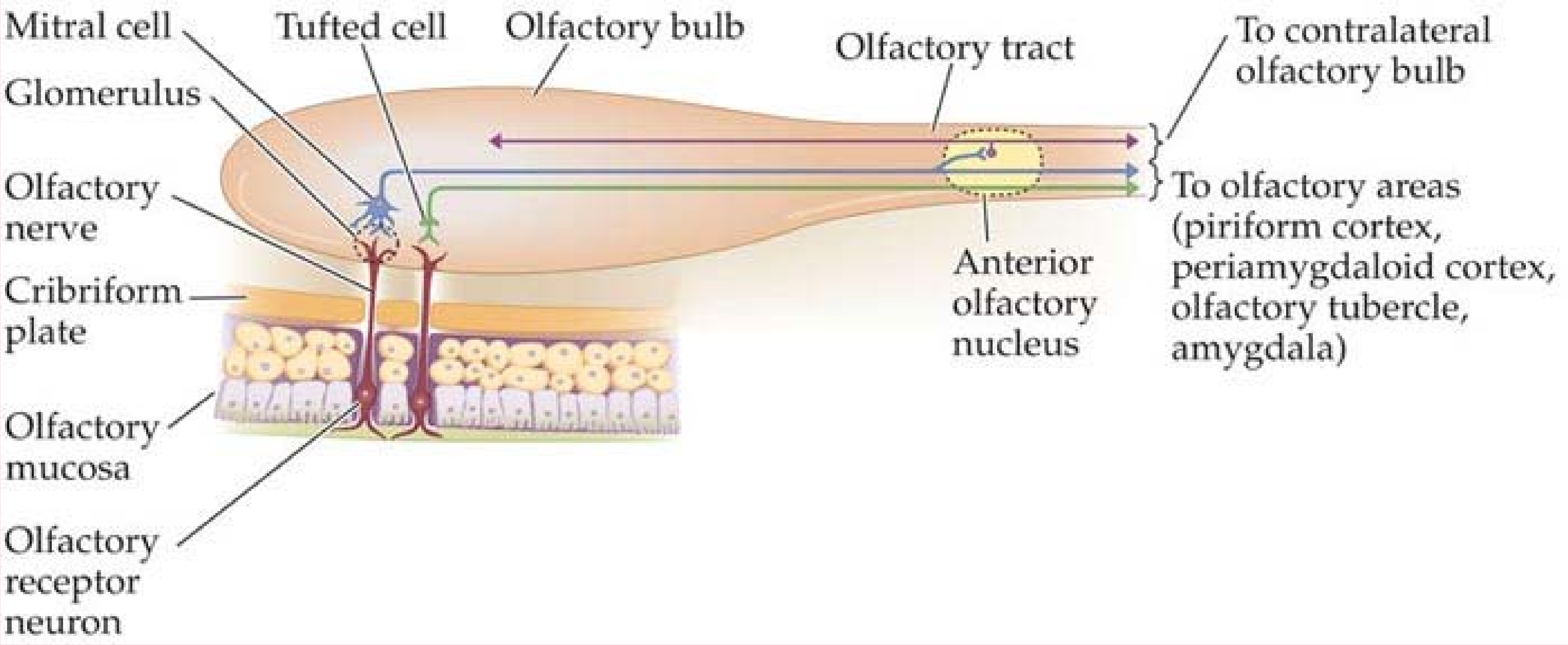
Olfactory system



Olfactory system

- Bipolar **olfactory receptor neurons** in the **olfactory mucosa** express the products of several hundred recently discovered olfactory receptor genes.
- A single **odor molecule** usually activates several olfactory receptors, enabling a virtually infinite number of different odors to be identified through combinatorial processing.
- Olfactory receptor neurons send unmyelinated axons in the **olfactory nerves** through the **cribriform plate** to reach the **olfactory bulb**.

Olfactory system



Olfactory system

- In the **glomeruli** of the olfactory bulb olfactory receptor neurons synapse onto **mitral cells** and **tufted cells,** both of which have long axons that enter the **olfactory tract** to reach the **olfactory cortex.**
- Collaterals in the olfactory tract synapse onto scattered neurons, forming the **anterior olfactory nucleus**.

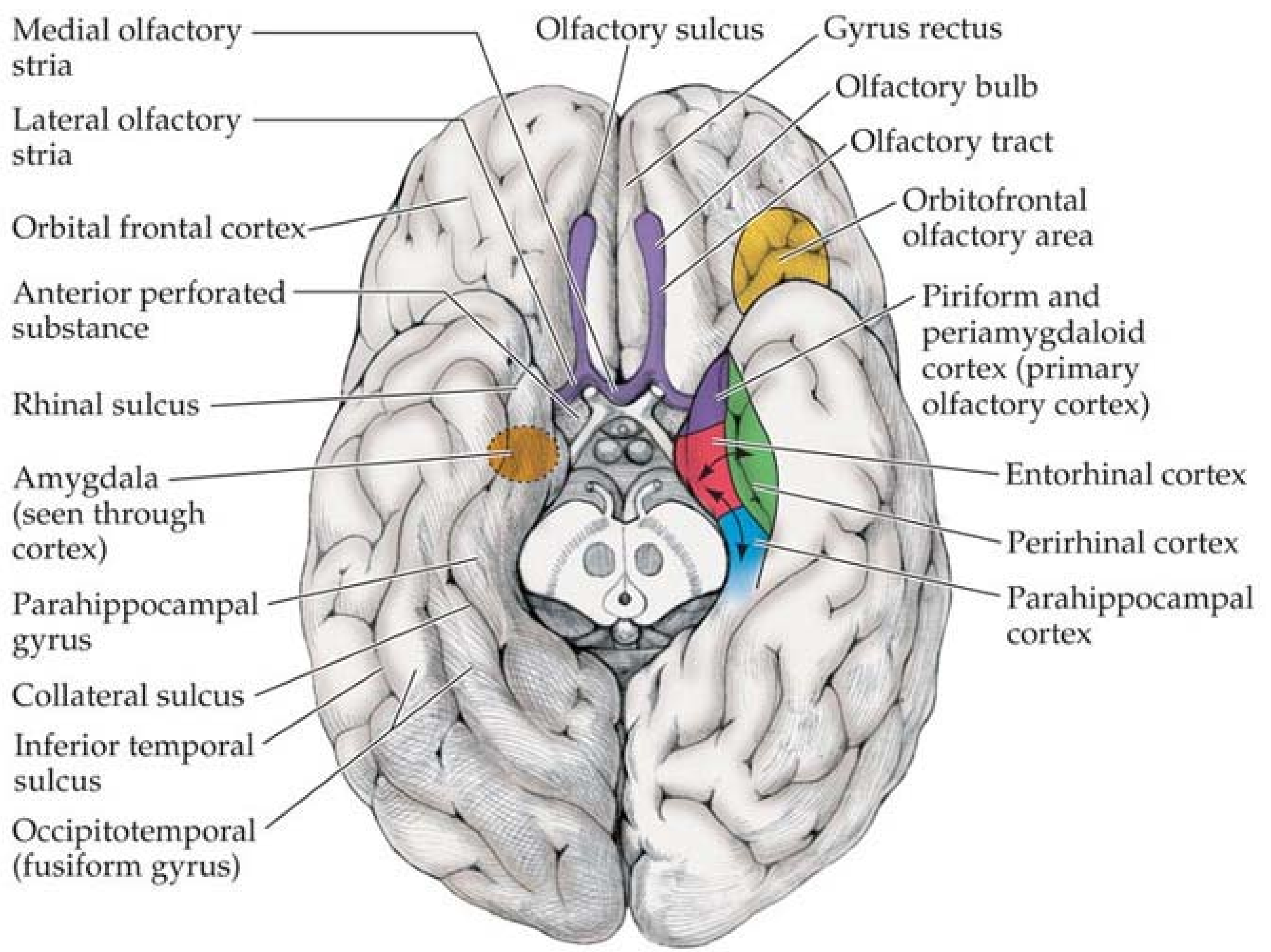
Olfactory system

- Neurons of the anterior olfactory nucleus, in turn, feed back both to the ipsilateral olfactory bulb and to the contralateral olfactory bulb, which is reached via the **medial olfactory stria** and the anterior part of the **anterior commissure**
- Atrophy of the anterior olfactory nucleus may be responsible for impaired olfaction seen in Alzheimer's disease.
- In addition to mitral cells and tufted cells, the olfactory bulb contains interneurons called **periglomerular cells** and **granule cells**.

Olfactory system- Rembember!

- The primary olfactory cortex is unique among sensory systems in that it receives direct input from secondary sensory neurons without an intervening thalamic relay.

Olfactory system: The primary olfactory cortex consists of the piriform cortex and the periamygdaloid cortex, which are located near the medial anterior tip of the temporal lobe



Olfactory system-

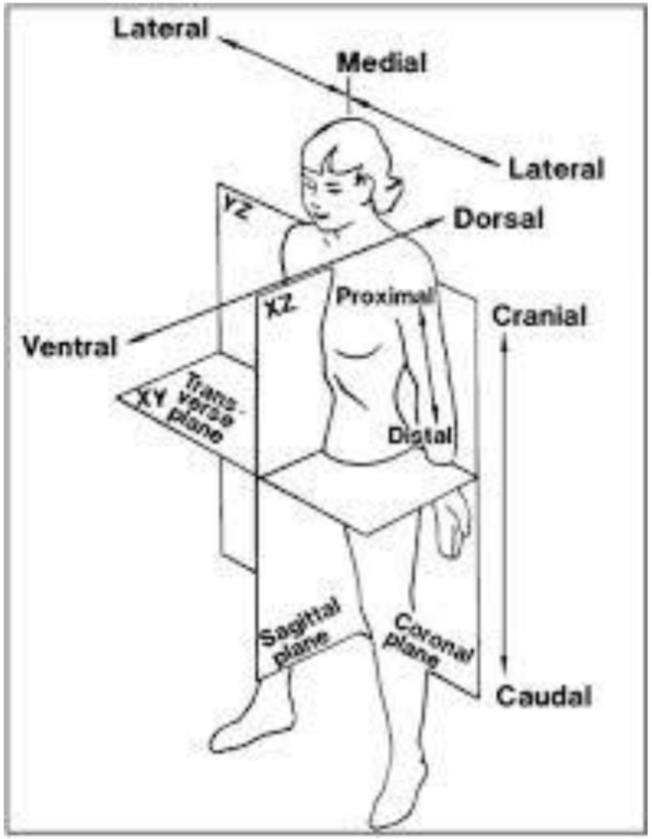
- The primary olfactory cortex projects to several secondary olfactory areas. The **anterior entorhinal cortex** receives projections from the piriform cortex.
- Given the role of the entorhinal cortex in memory this projection may explain the occasional ability of odors to evoke vivid memories.
- The piriform cortex projects to the **orbitofrontal olfactory area** both directly and indirectly via relays in the entorhinal cortex, or in the **mediodorsal nucleus of the thalamus**.

Olfactory system

- Interestingly, there are no direct projections from the piriform cortex to the hippocampal formation, and the hippocampal formation does not appear to have a significant role in olfactory processing.

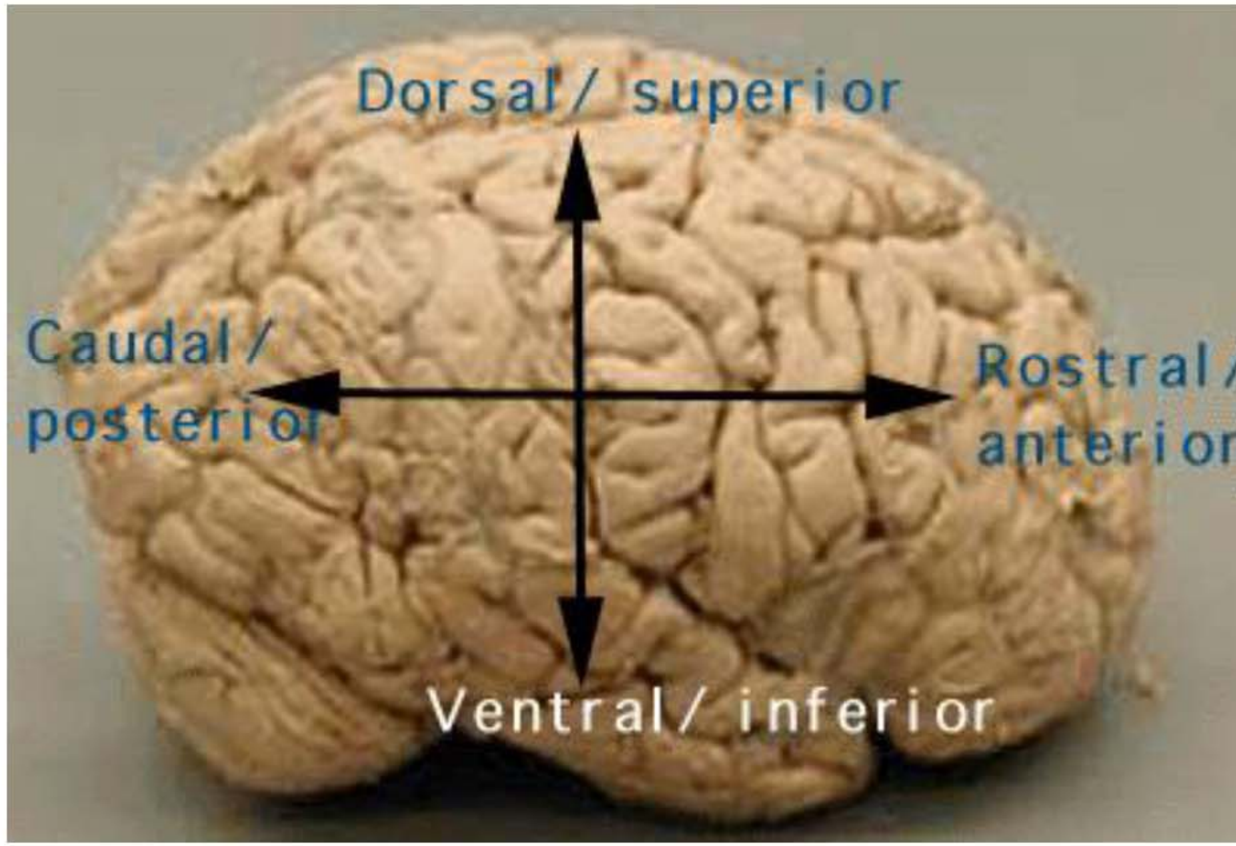
Neuroanatomical terms

- Superior (cranial)
- Inferior (caudal)
- Anterior (ventral)
- Posterior (dorsal)
- Medial
- Lateral
- Intermediate

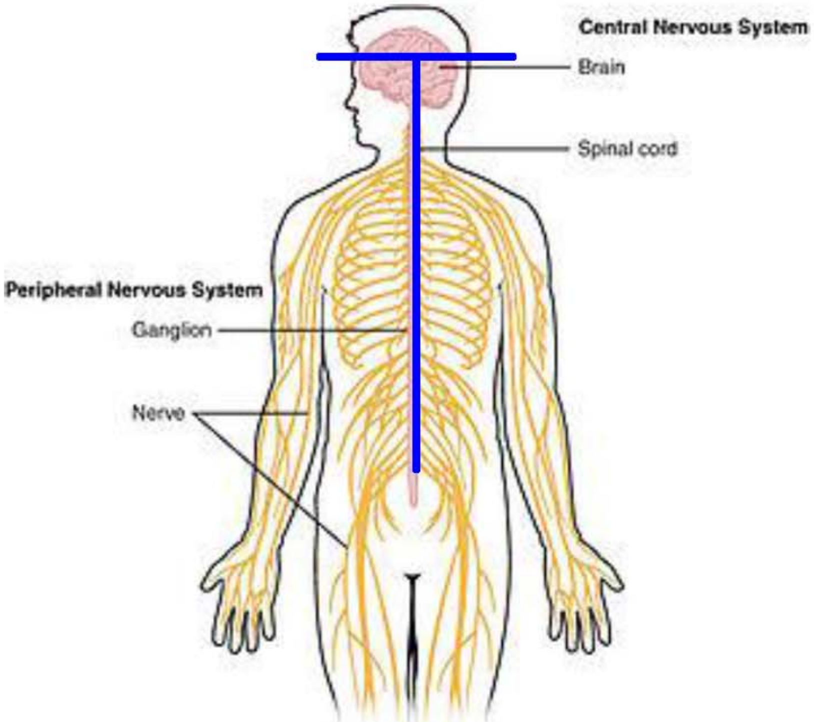


Neuroanatomical directions

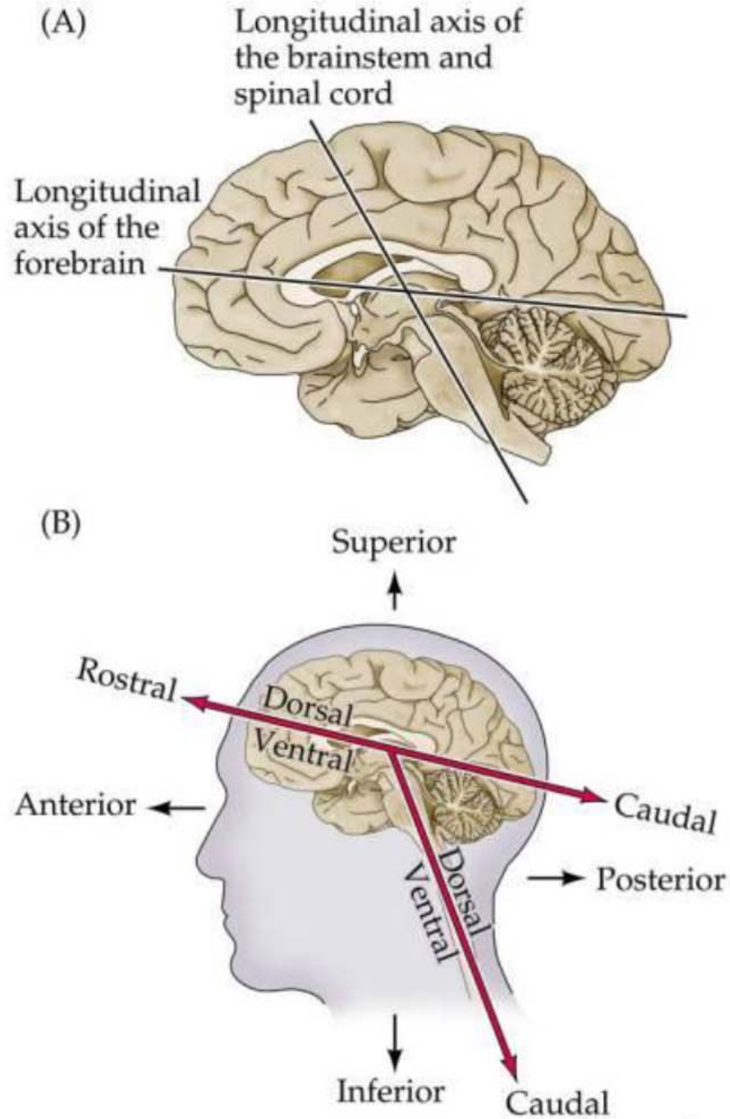
- Rostral vs. caudal
- Dorsal vs. ventral
- Medial vs. lateral
- Superior vs. inferior



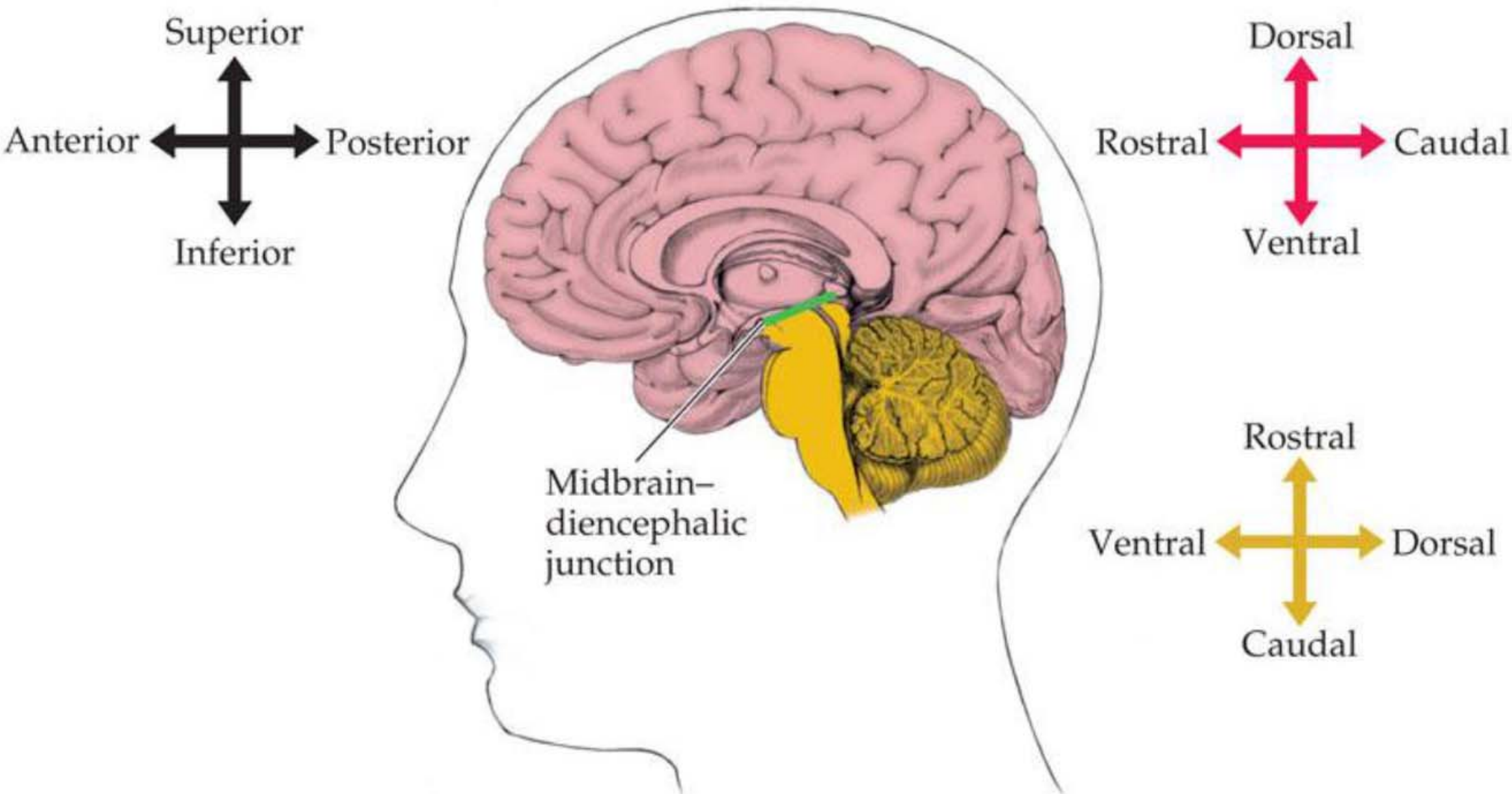
Neuroaxis



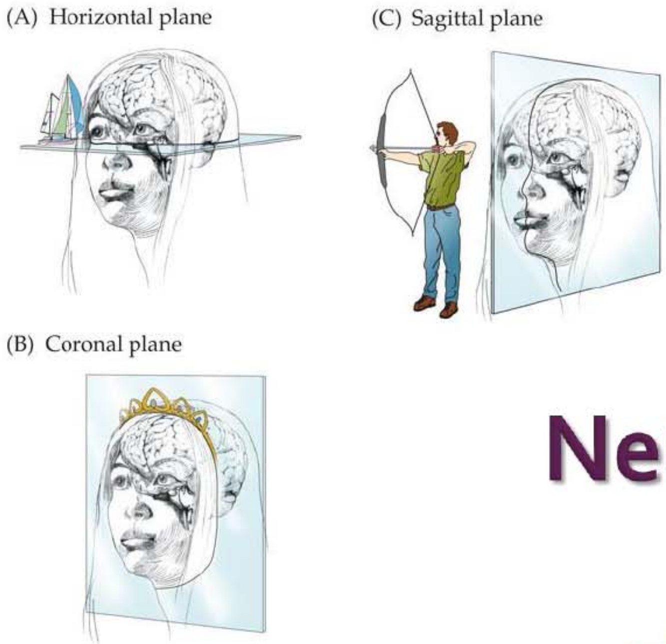
Central Nervous System
Brain
Spinal cord
Peripheral Nervous System
Ganglion
Nerve



(A)
Longitudinal axis of the brainstem and spinal cord
Longitudinal axis of the forebrain
(B)
Superior
Rostral
Dorsal
Ventral
Anterior
Caudal
Posterior
Dorsal
Ventral
Inferior
Caudal

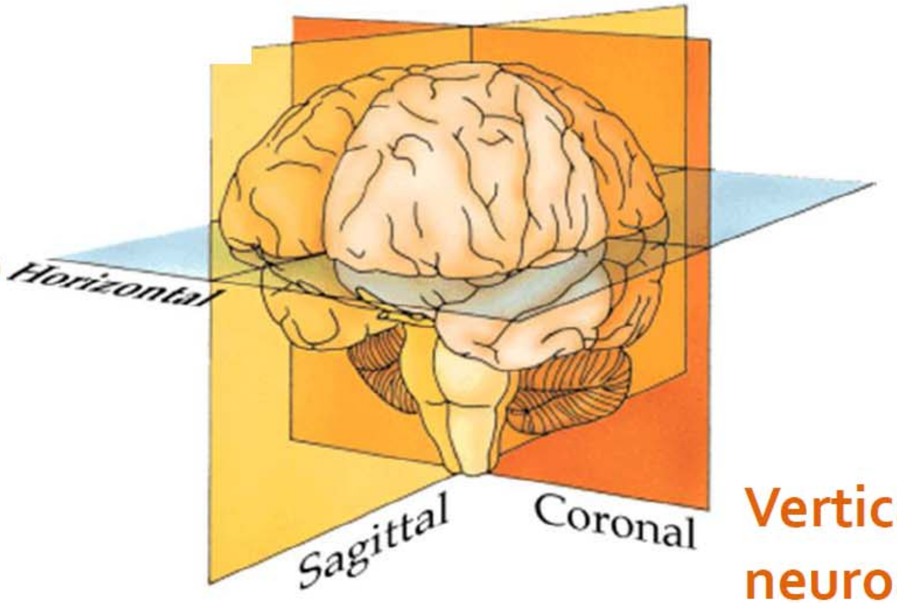


The meaning of some terms (dorsal, ventral, rostral, caudal) changes at the midbrain–diencephalic junction.



Neuroanatomical planes

Parallel to neuroaxis



Vertical to neuroaxis

Information flow - terminology

Afferents / efferents

Ascedent / descedent

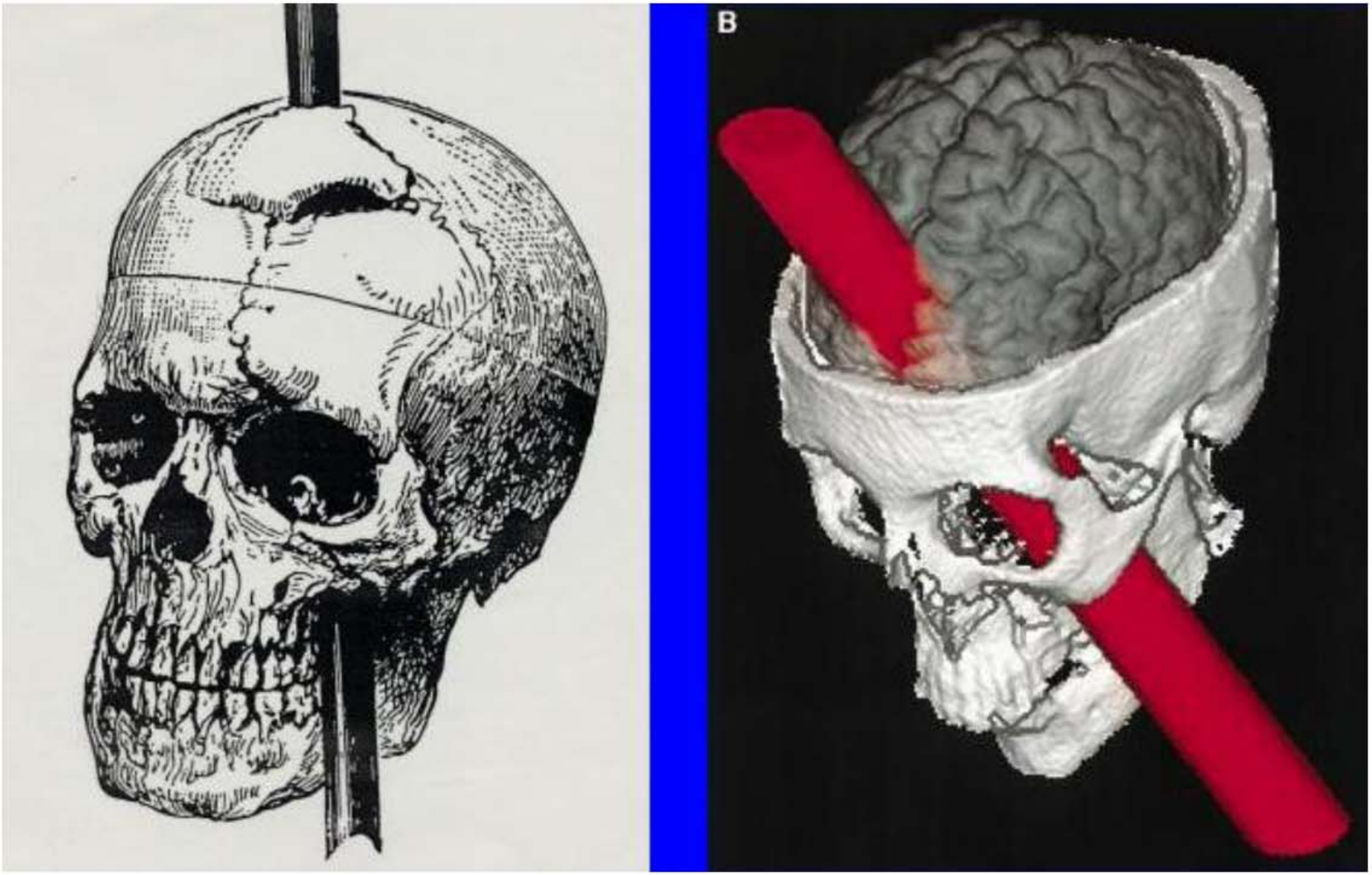
convergence (many→one) / divergence (one → many)

nuclei (containers of DNA) / nuclei (collections of neurons)

Brain research - Methods

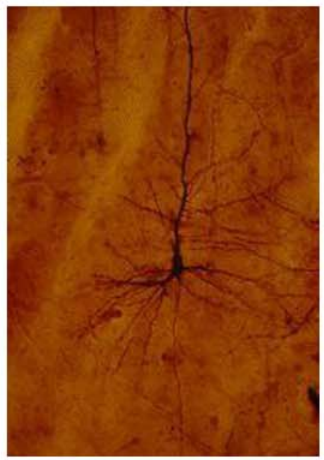
- Lesion studies
- Special stains (Golgi, Nissel) and histology
- Tract tracing
- Surface-, Intracortical microstimulation
- PET, (f)MRI, CT, EEG, TMS

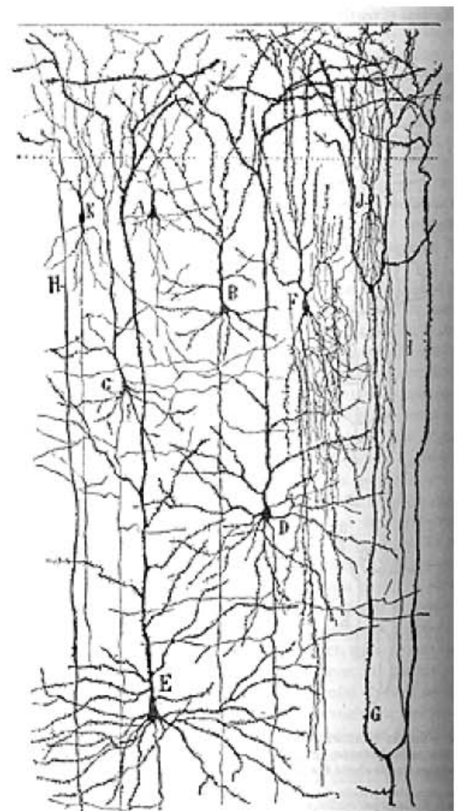
Phineas Gage--1848



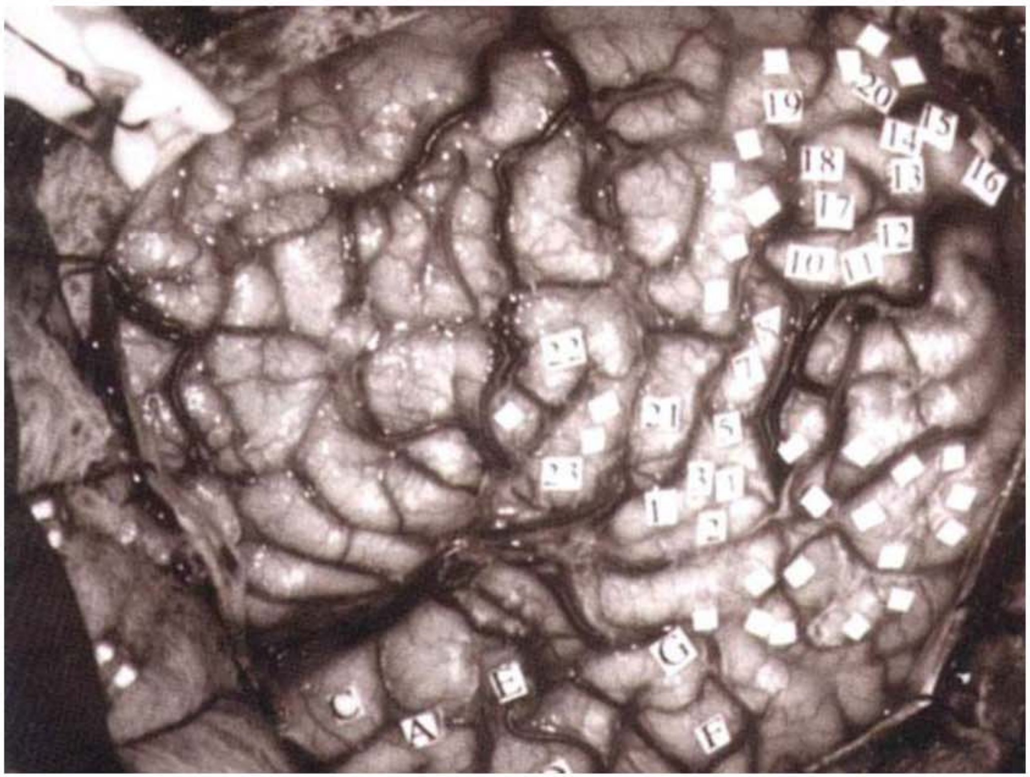
Neurons are signaling elements

- Late nineteenth century: Golgi and Ramon y Cajal





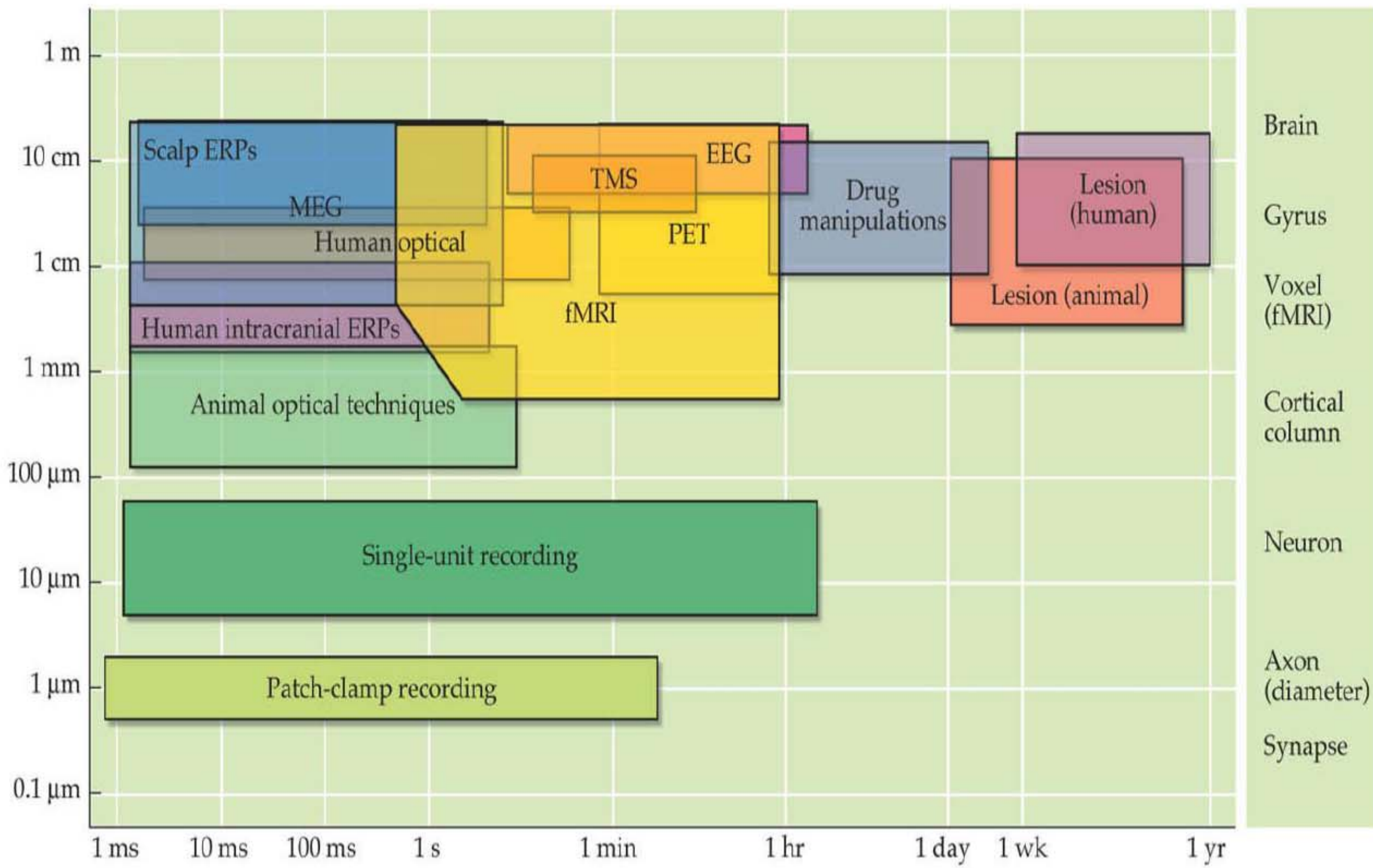
Mapping brain regions



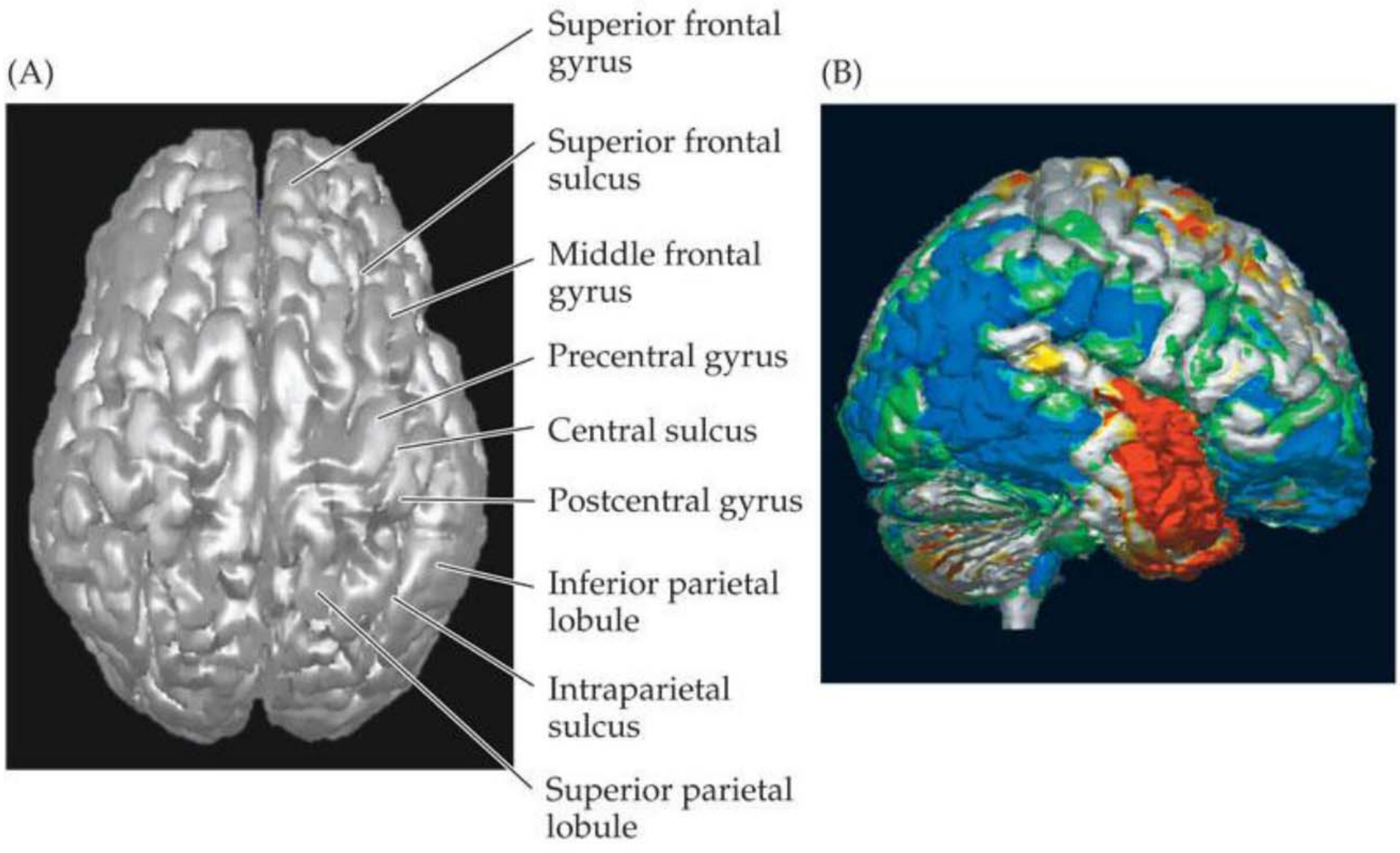
Wilder Penfield, 1940's

Electrical stimulation of exposed human cortex during surgery

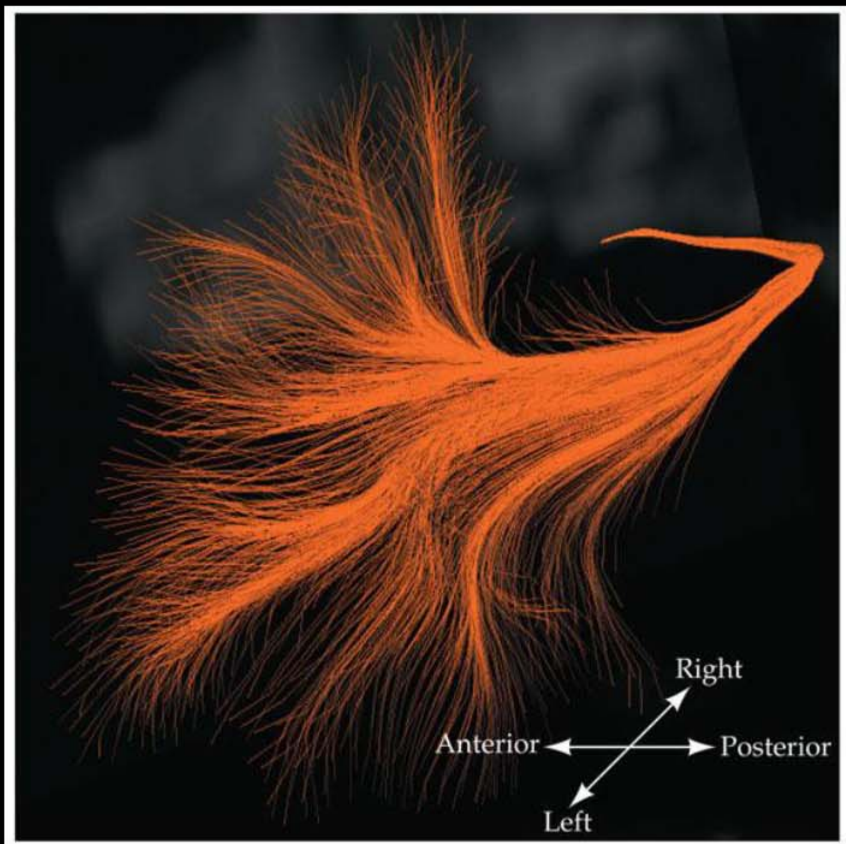
Methods for functional studies



Three-dimensional surface reconstructions

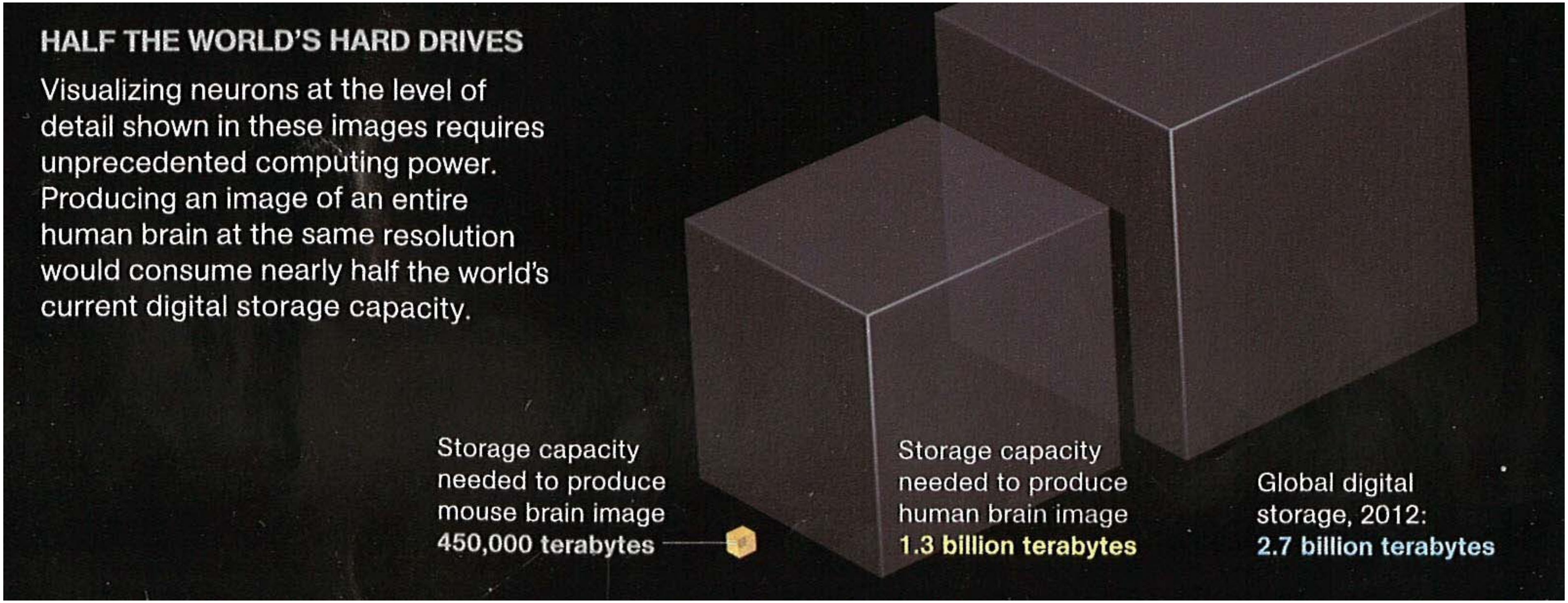


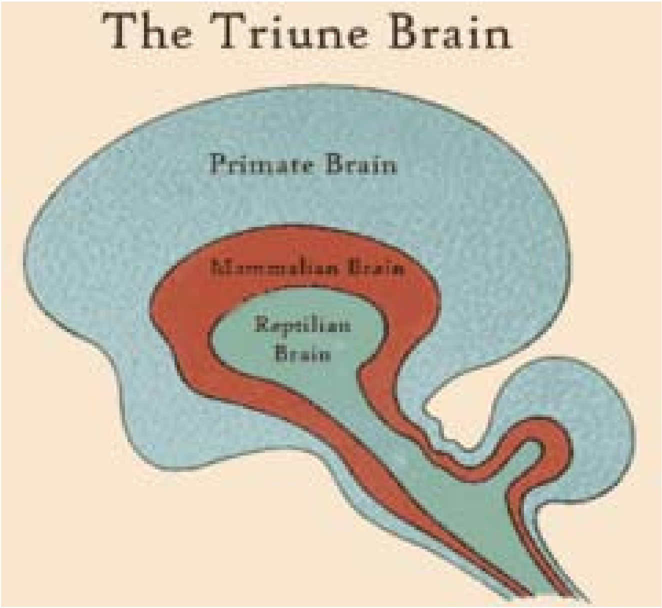
DTI: Diffusion Tensor Tractography

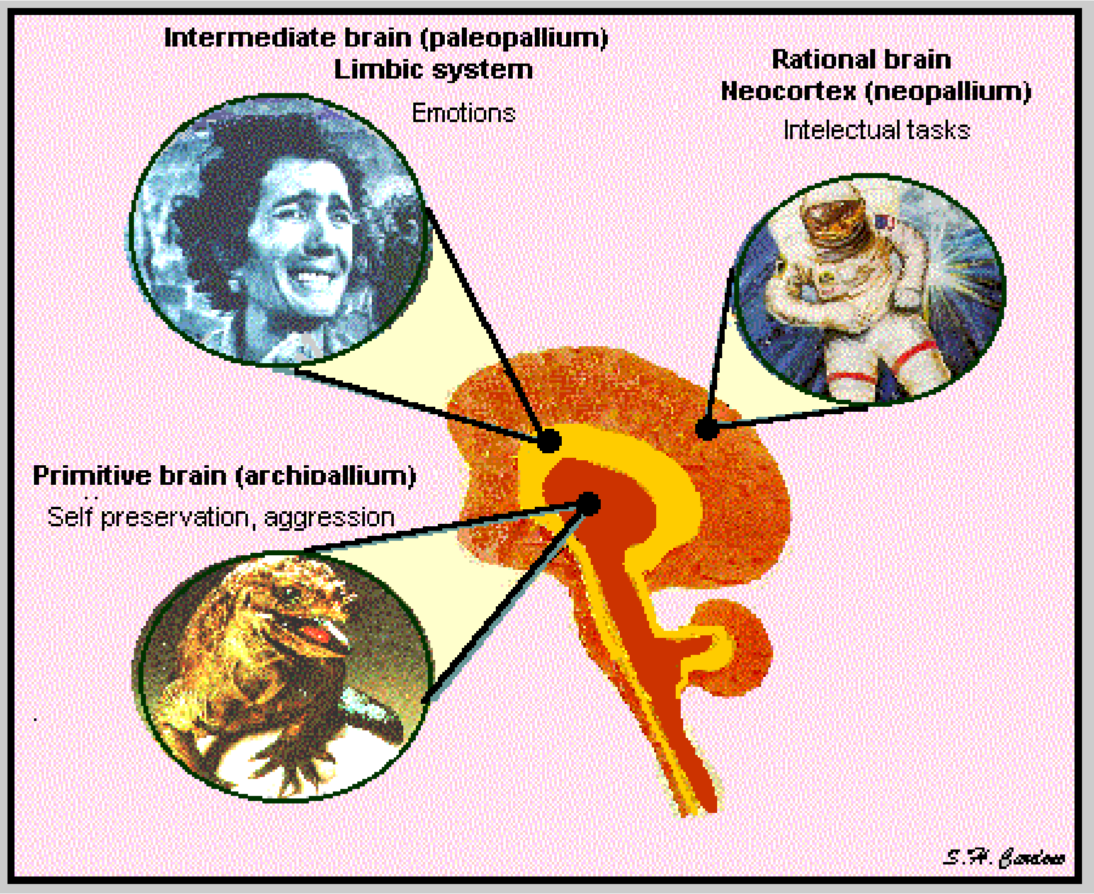


Fiber tracts through anterior corpus callosum (from seed point in right frontal lobe, to left frontal cortex areas).

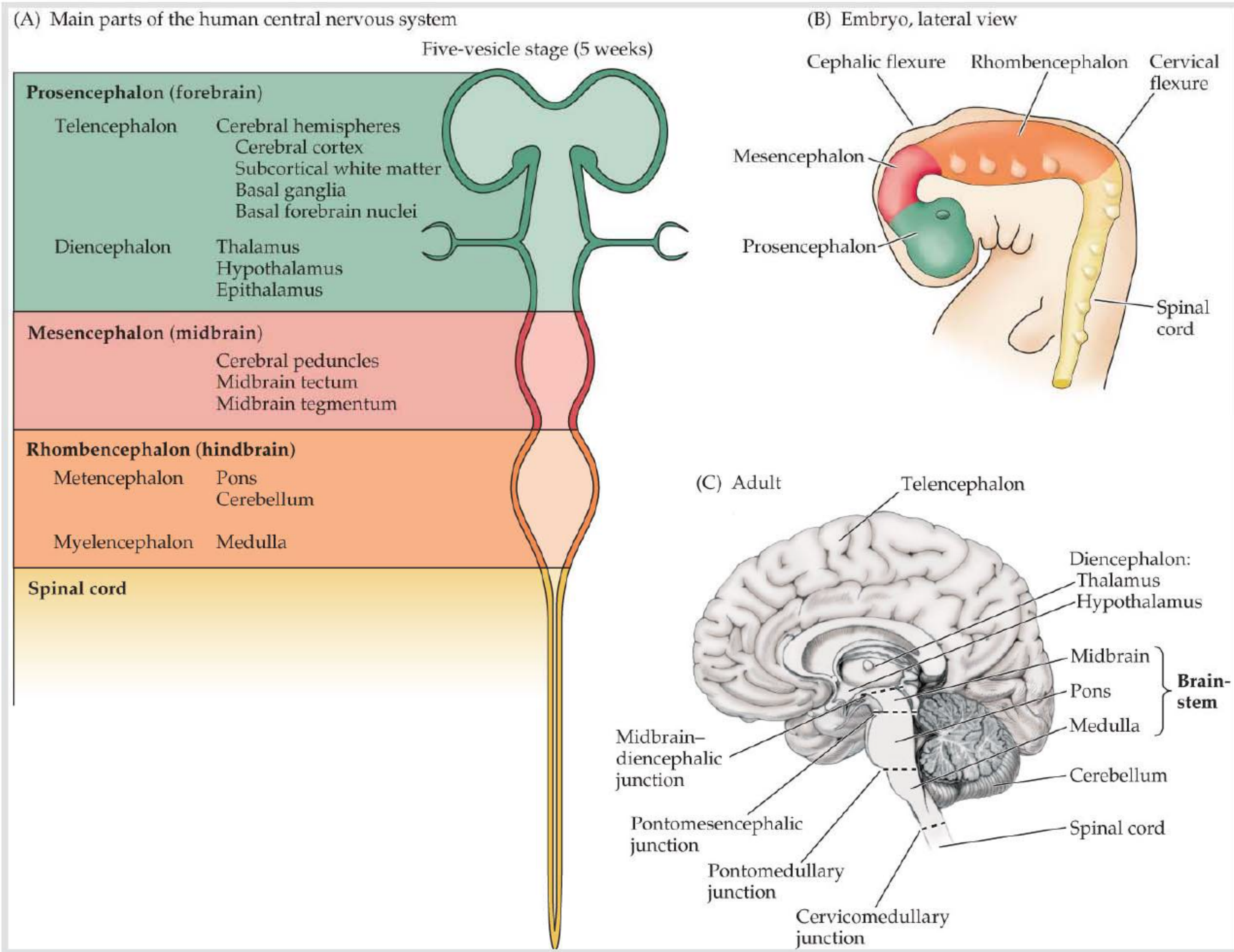
This technique traces the direction of maximal water diffusion, constrained by white matter architecture, to follow major fiber tracts.


HALF THE WORLD'S HARD DRIVES
Visualizing neurons at the level of detail shown in these images requires unprecedented computing power. Producing an image of an entire human brain at the same resolution would consume nearly half the world's current digital storage capacity.
Storage capacity needed to produce mouse brain image 450,000 terabytes
Storage capacity needed to produce human brain image 1.3 billion terabytes
Global digital storage, 2012: 2.7 billion terabytes


The Triune Brain
Primate Brain
Mammalian Brain
Reptilian
Brain


Intermediate brain (paleopallium)
Limbic system
Emotions
Rational brain
Neocortex (neopallium)
Intelectual tasks
Primitive brain (archipallium)
Self preservation, aggression
S.H. Cardoso

EMBRYOLOGICAL DEVELOPMENT OF THE CNS



22

MAJOR DIVISIONS OF THE BRAIN