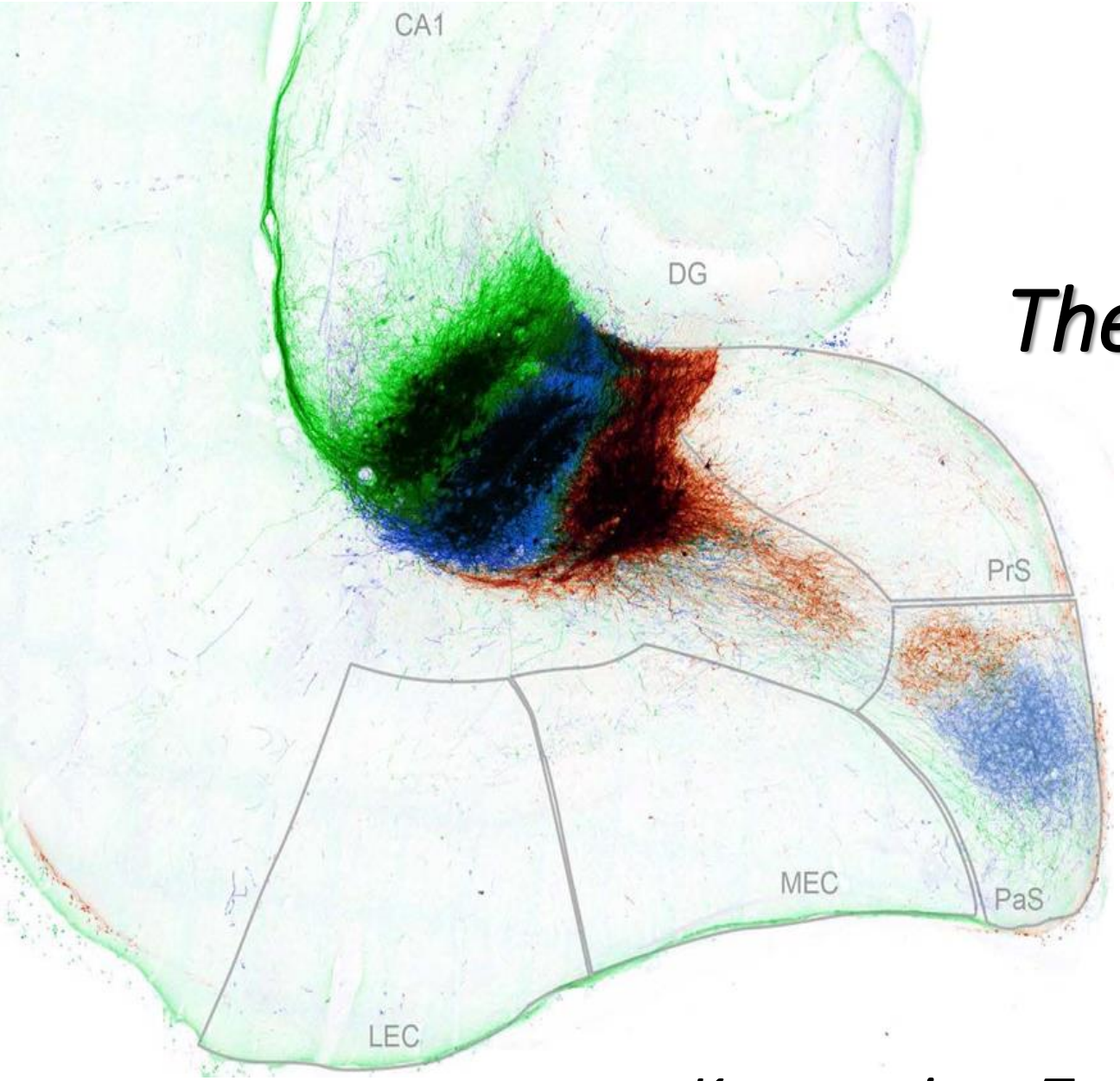
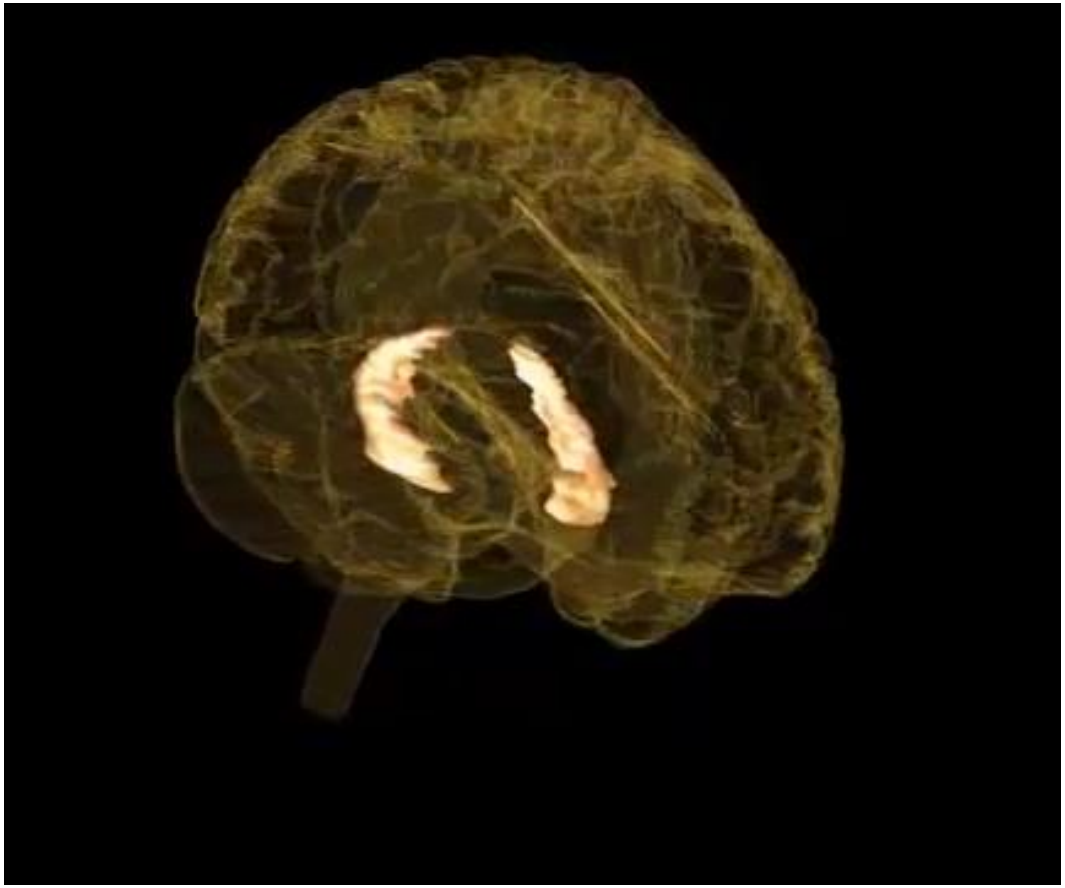


The Limbic System

Konstantinos Tsamis MD, PhD

Limbic System

Limbic (Latin) = margin, border, edge



*Limbic system was used to include a group of structures that **topographically** lie between the cerebral cortex & hypothalamus (or brainstem)*

Limbic System

Limbic (Latin) = margin, border, edge

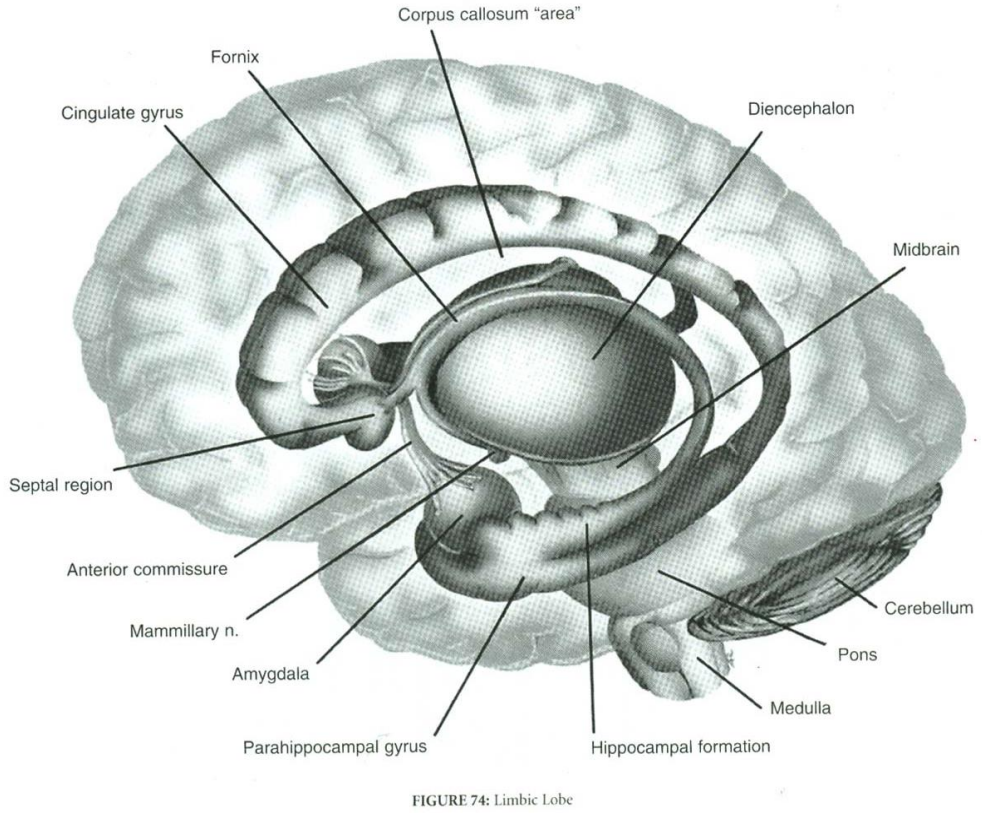
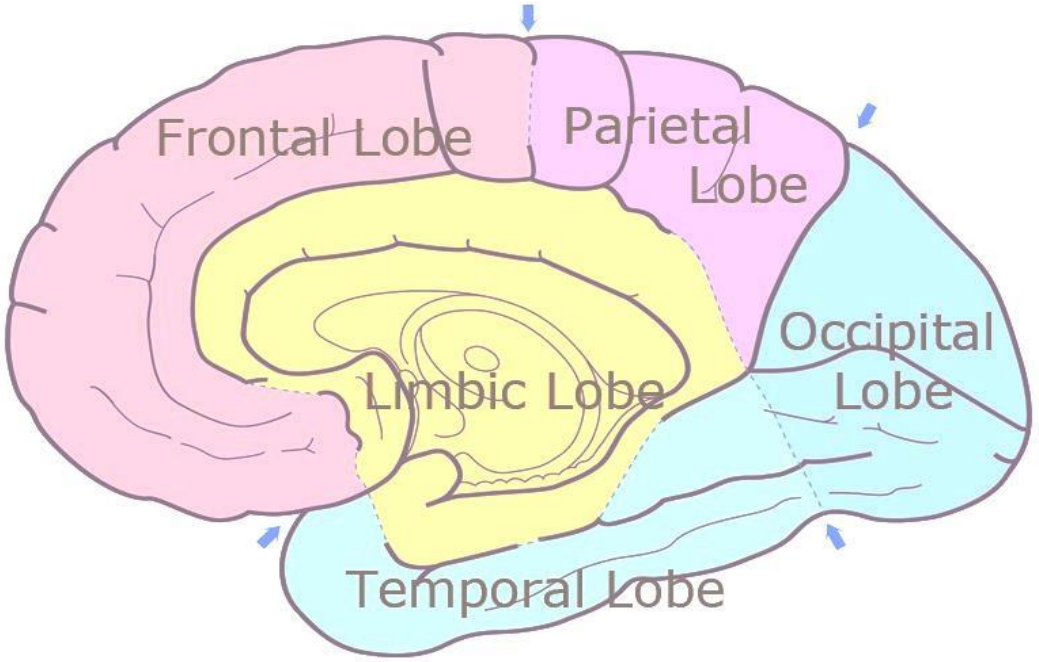


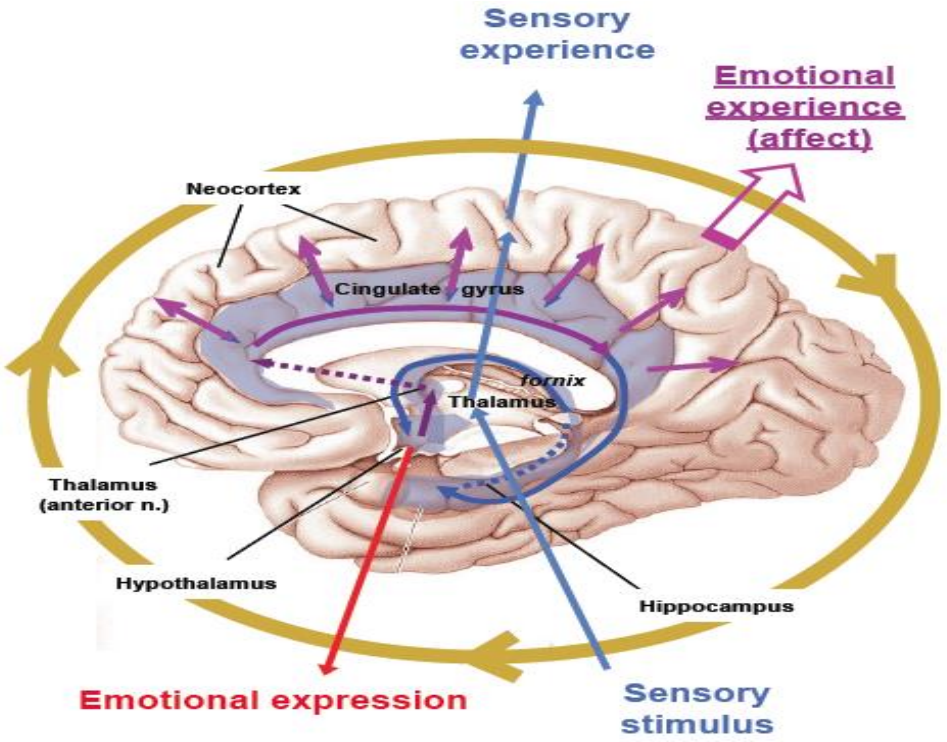
FIGURE 74: Limbic Lobe

*From a **<u>functional</u>** point of view the term limbic system includes the structures that are involved in emotional processing, behavioral expression, learning and memory.*

Limbic System

- Broca's Limbic System (1878)
- Papez Circuit (1930)
- MacLean's Limbic System (1950)
- Limbic Lobe





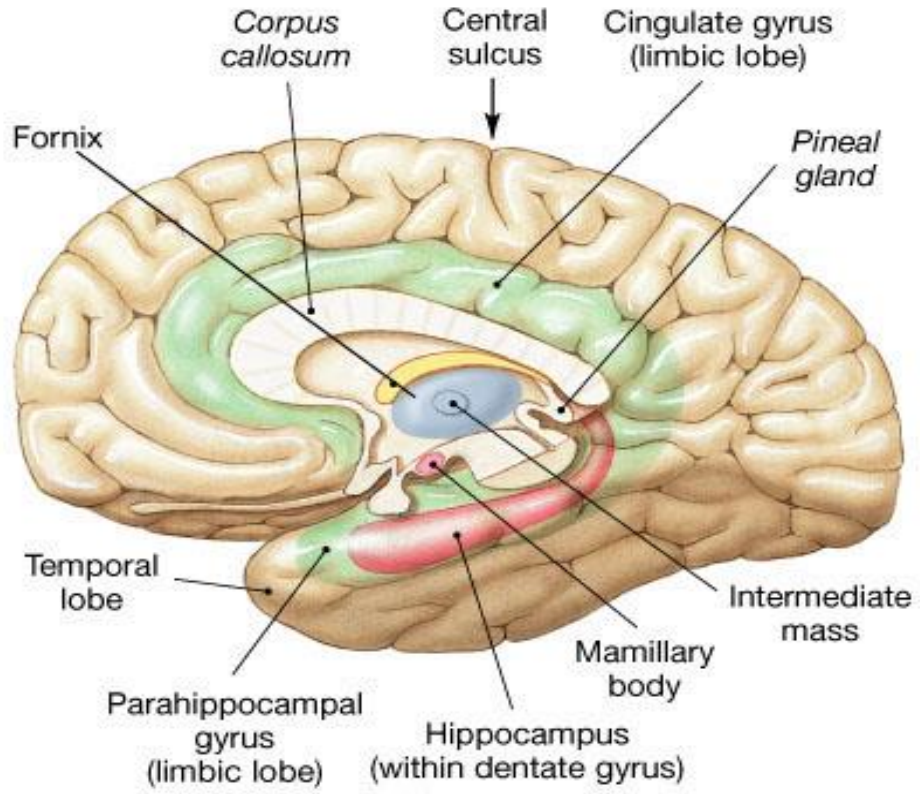
Today's Limbic System

Includes:

- Cortical Structures

- ✓ **Hippocampus**
- ✓ **Parahippocampal gyrus**
- ✓ **Cingulate gyrus**
- ✓ **Subcallosal gyrus**
- ✓ **Orbitofrontal cortex**

  (Prefrontal cortex)

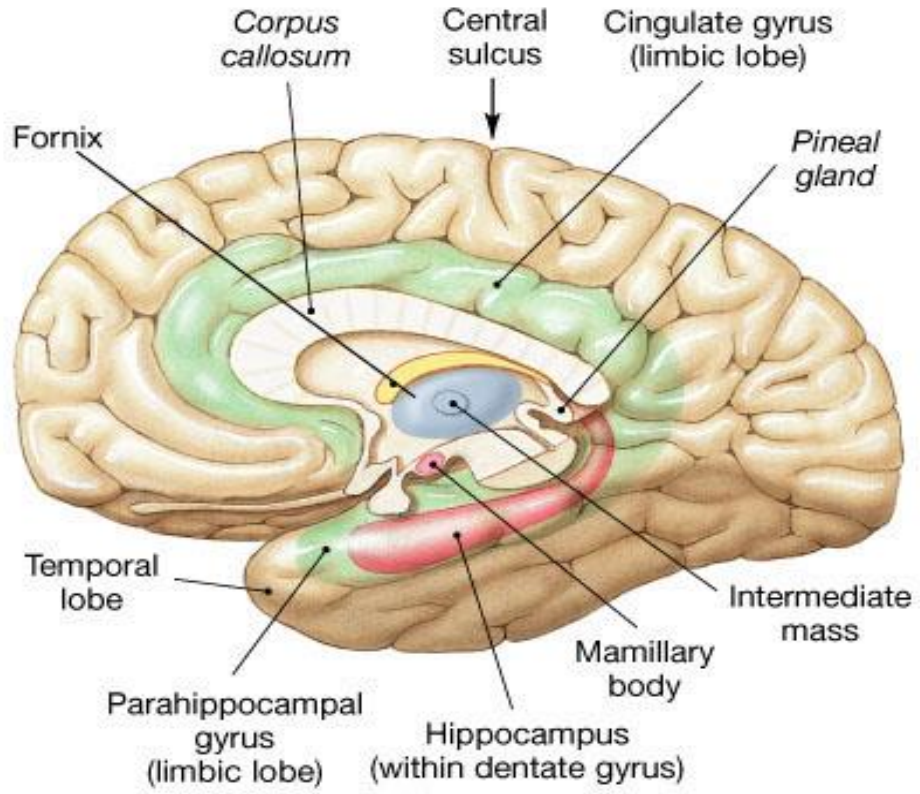


Today's Limbic System

Includes:

- Subcortical Nuclei

- ✓ **Amygdala**
- ✓ **Hypothalamic Nuclei (Mammillary Bodies)**
- ✓ **Thalamic Nuclei (Anterior nuclei)**
- ✓ **Nuclei of Septal Area**
- ✓ **Nucleus Accumbens**

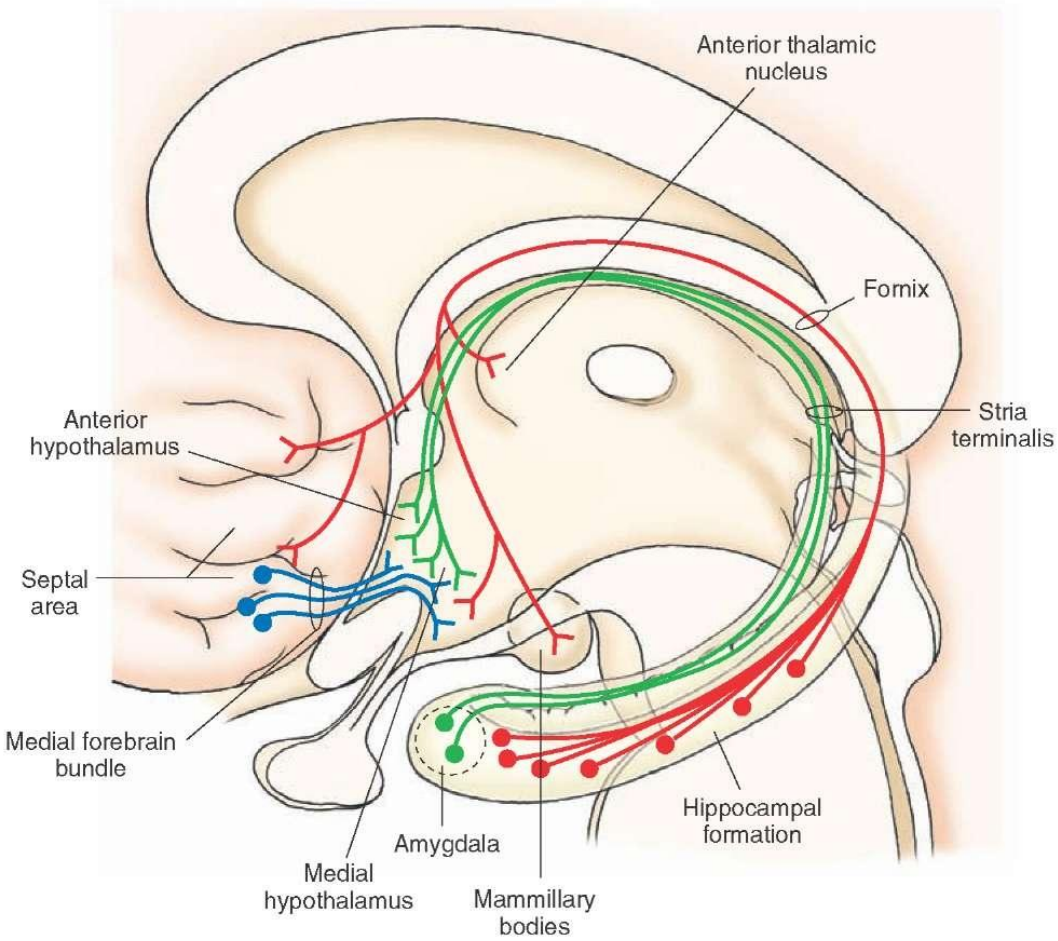


Today's Limbic System

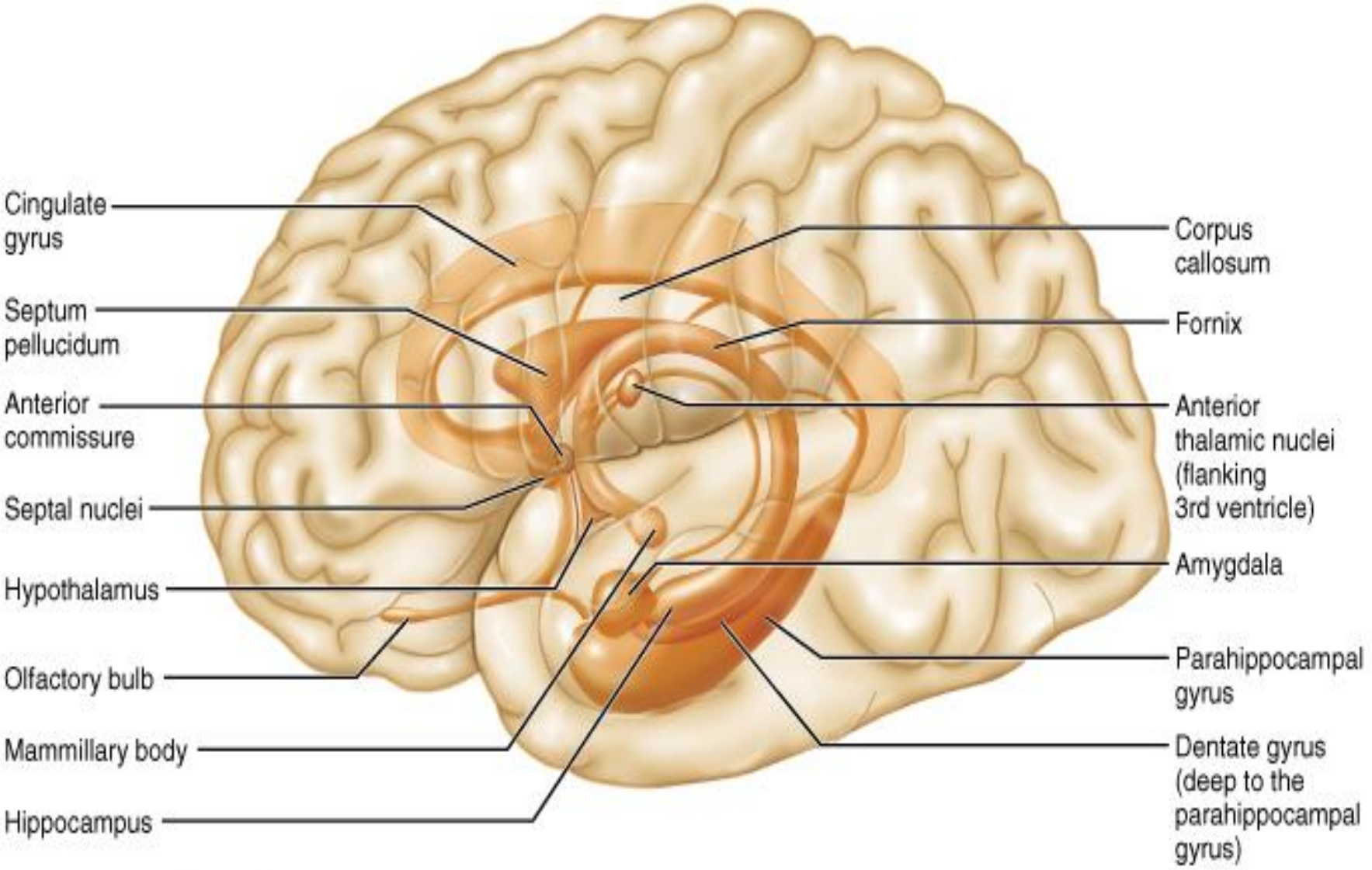
Includes:

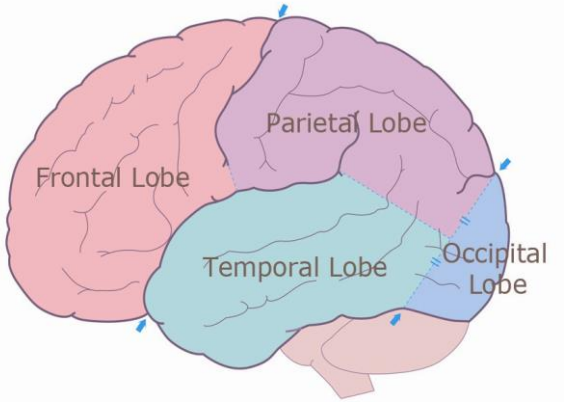
- Main Connections

- ✓ **Fimbria – Fornix**
- ✓ **Mammillothalamic Tract**
- ✓ **Stria Terminalis**
- ✓ **Medial Forbrain Bundle**

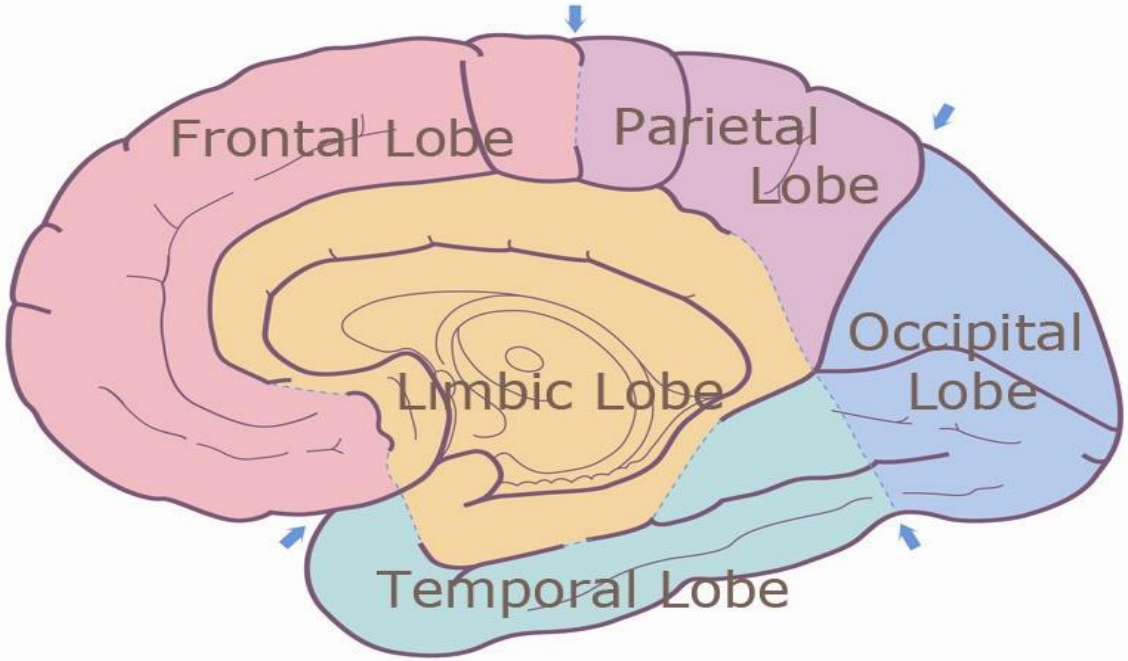


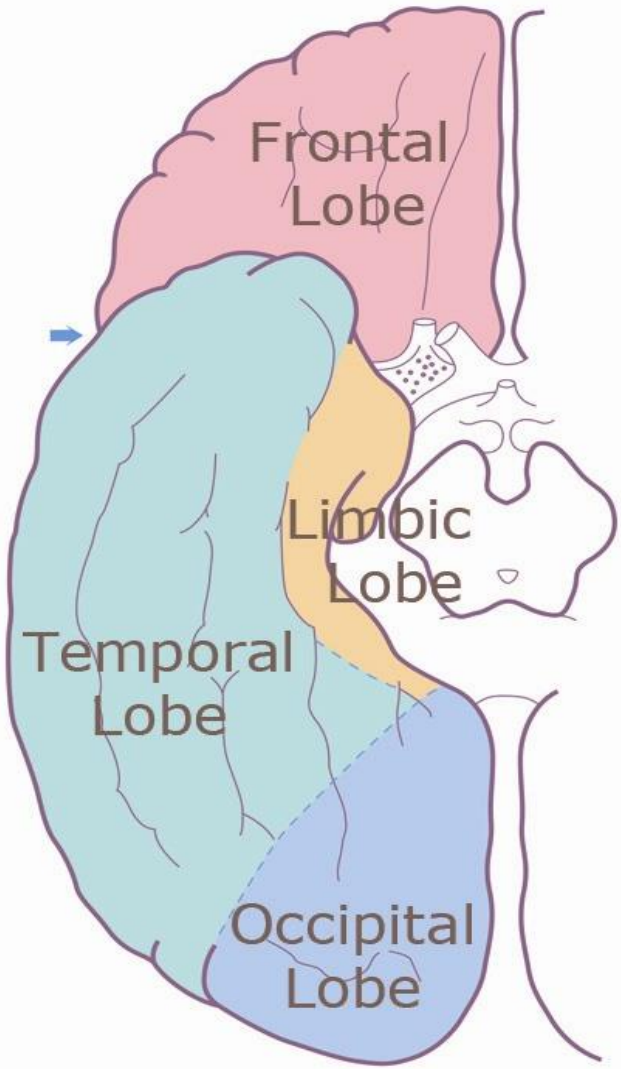
Neuroanatomy of the Limbic System





- Frontal Lobe
- Parietal Lobe
- Temporal Lobe
- Occipital Lobe
- *Limbic Lobe*





Function of the Limbic System

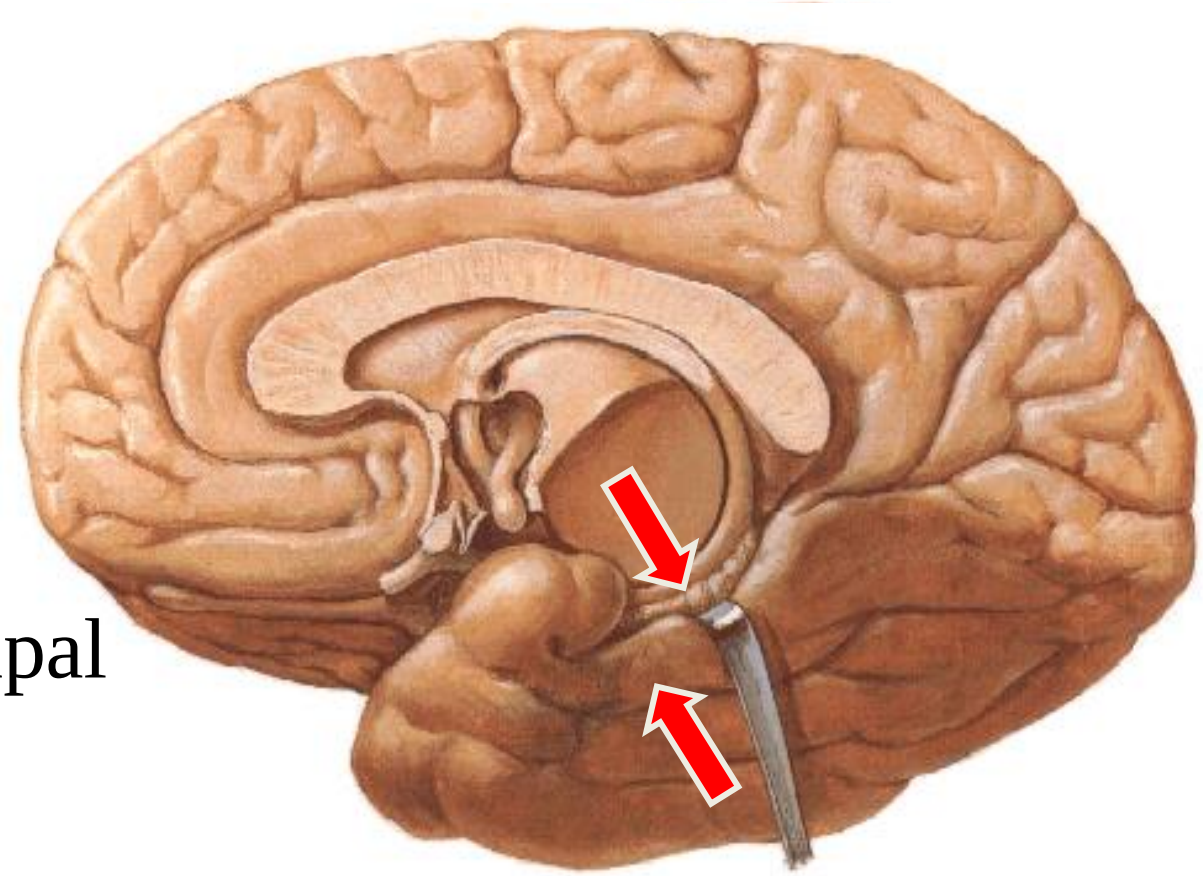
Core Limbic Structures
***Primary Functions*:**

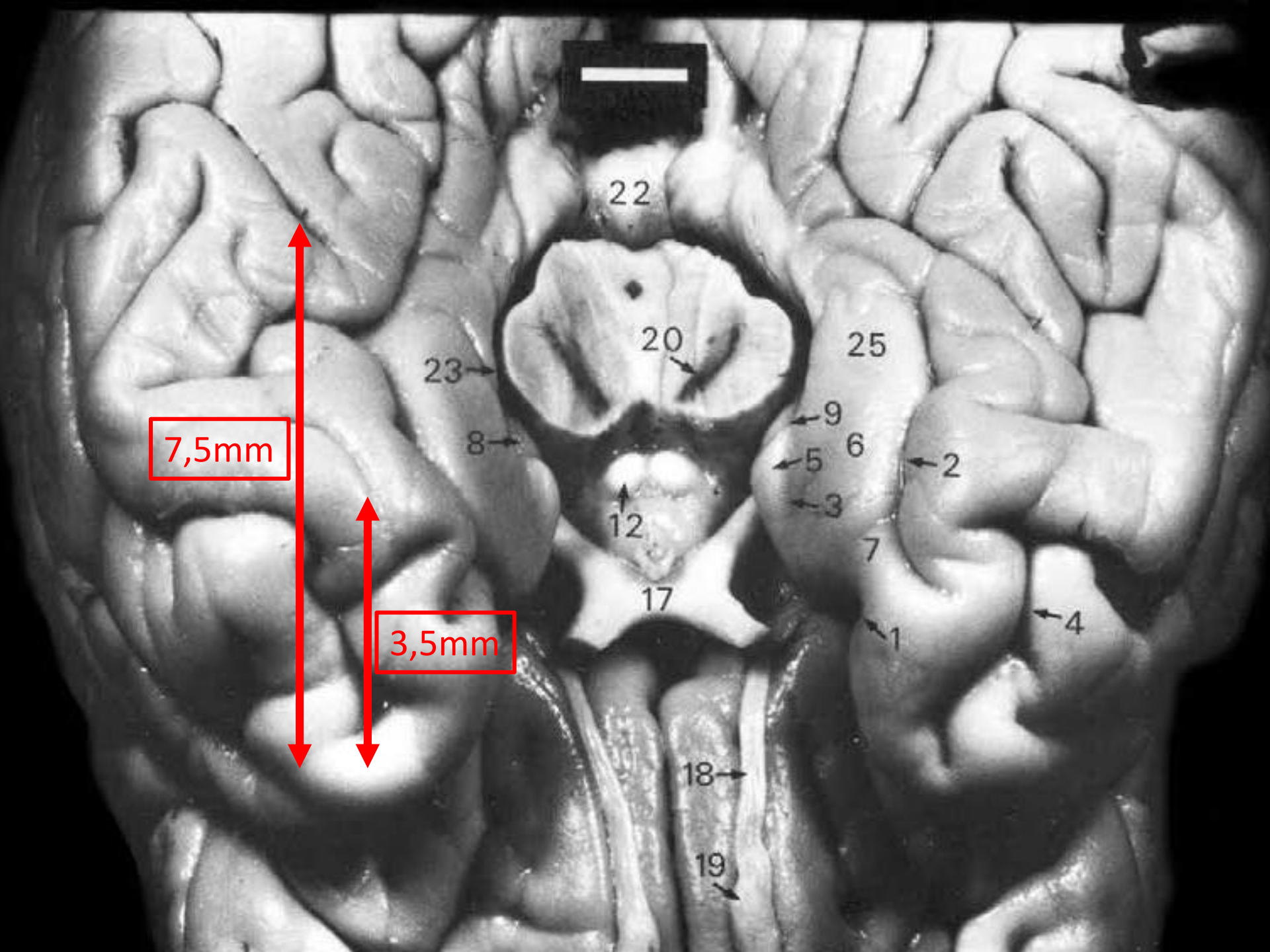
Hippocampus → memory

Amygdala → emotional processing

Hippocampal formation

- ✓ Hippocampus
- ✓ Dentate gyrus
- ✓ Parahippocampal gyrus

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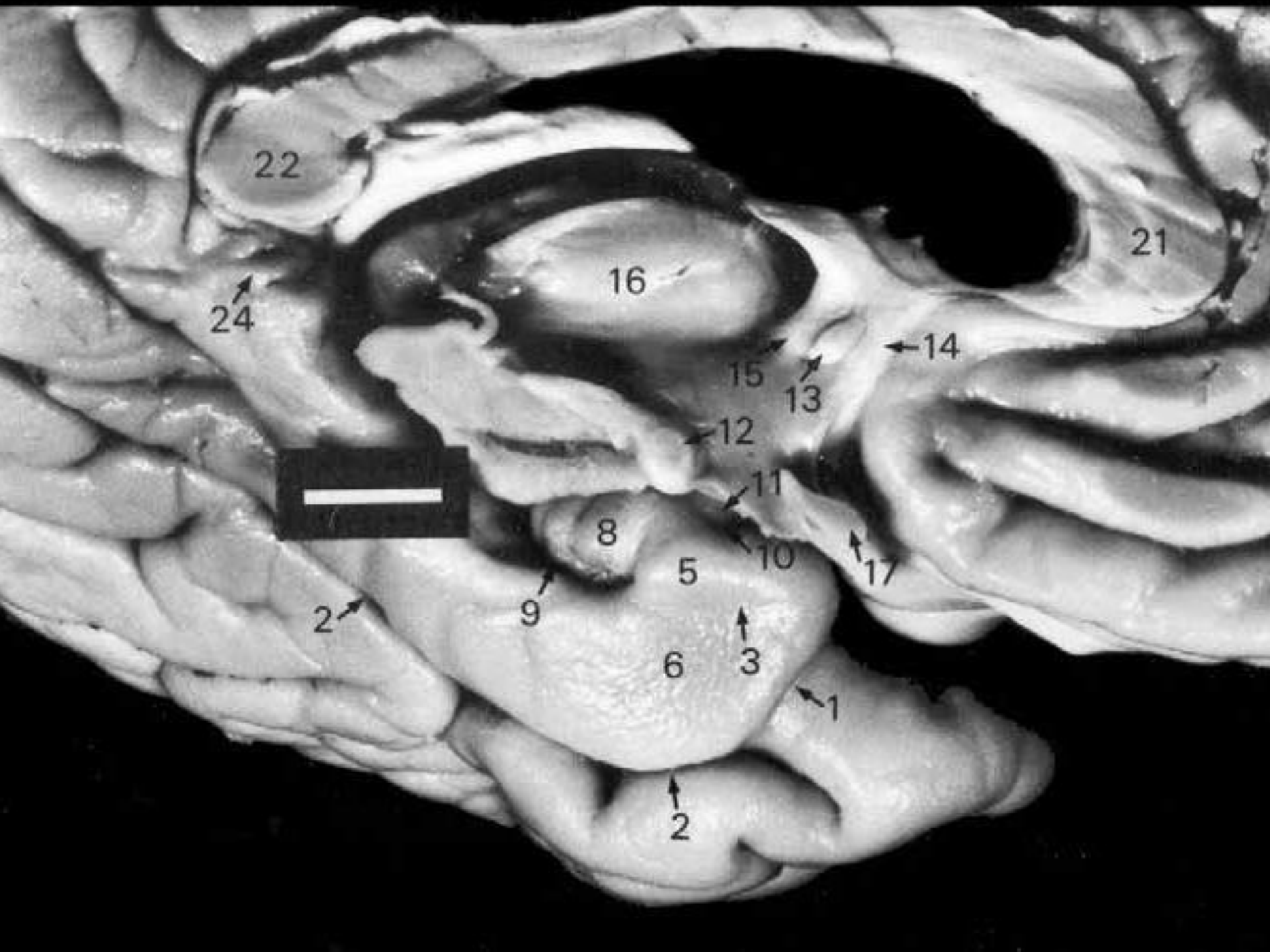
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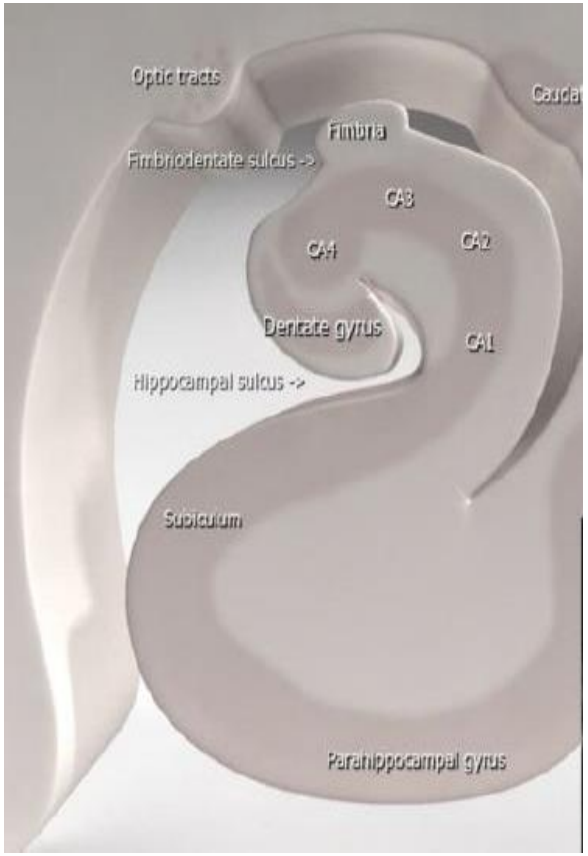
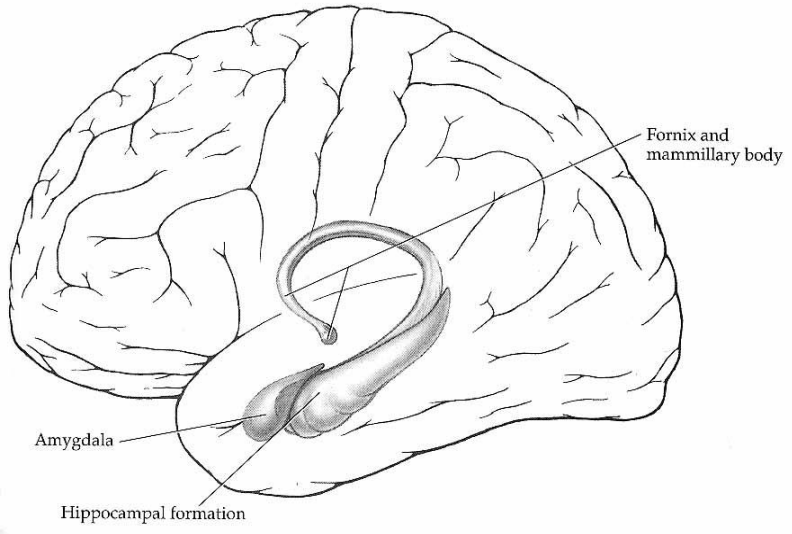
Hippocampus

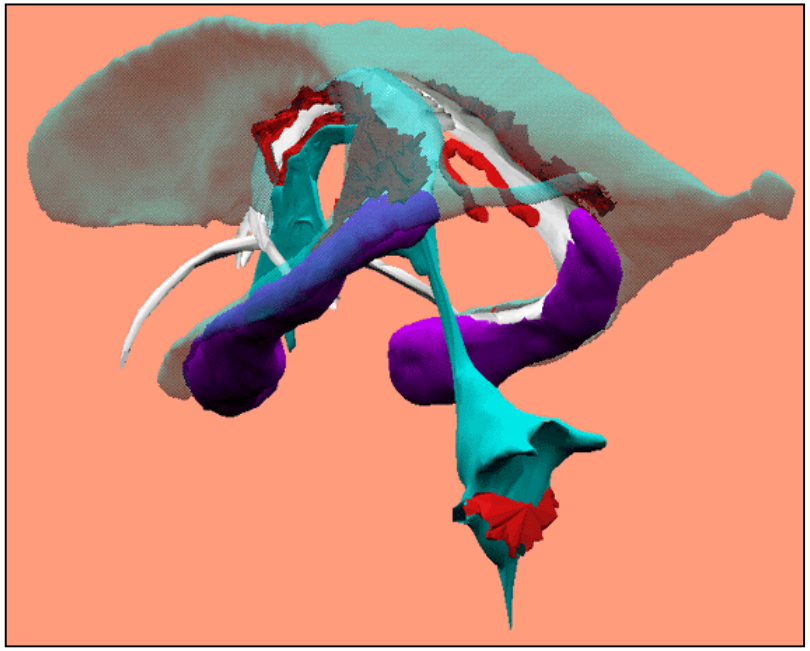


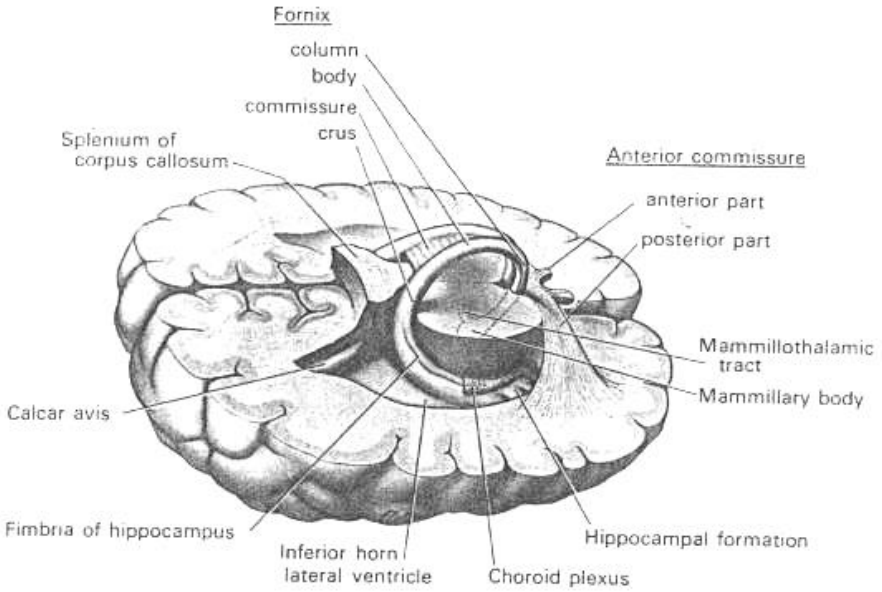
It is unclear if the name hippocampus derived from the overall longitudinal appearance of the structure or by it's appearance in coronal sections.

Hippocampus

- **located in medial temporal lobe**
- **C shaped**
- ***Cornu ammonis***

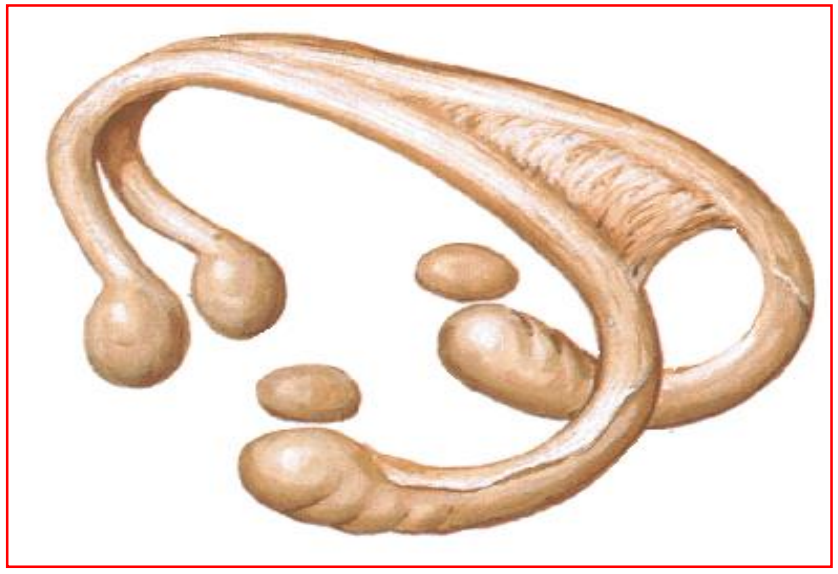


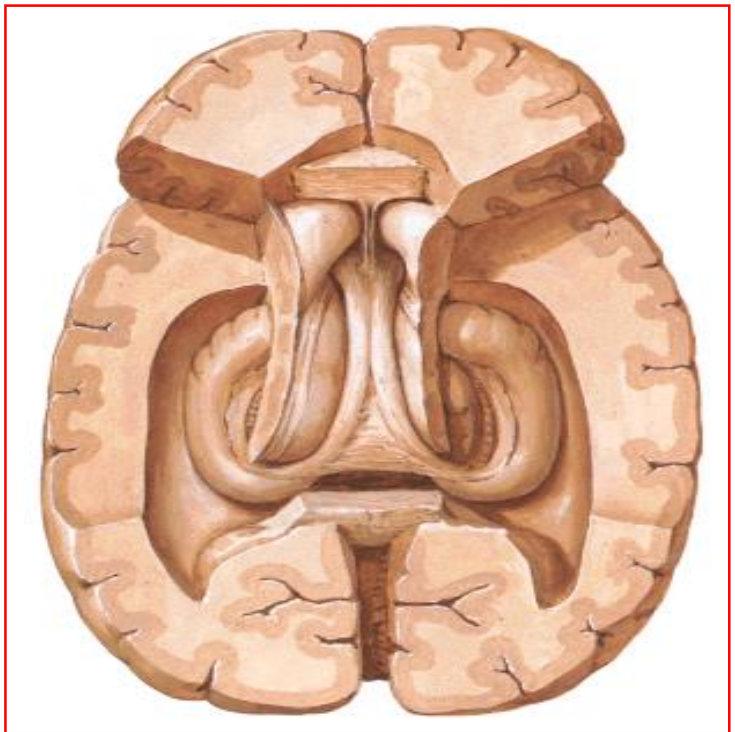


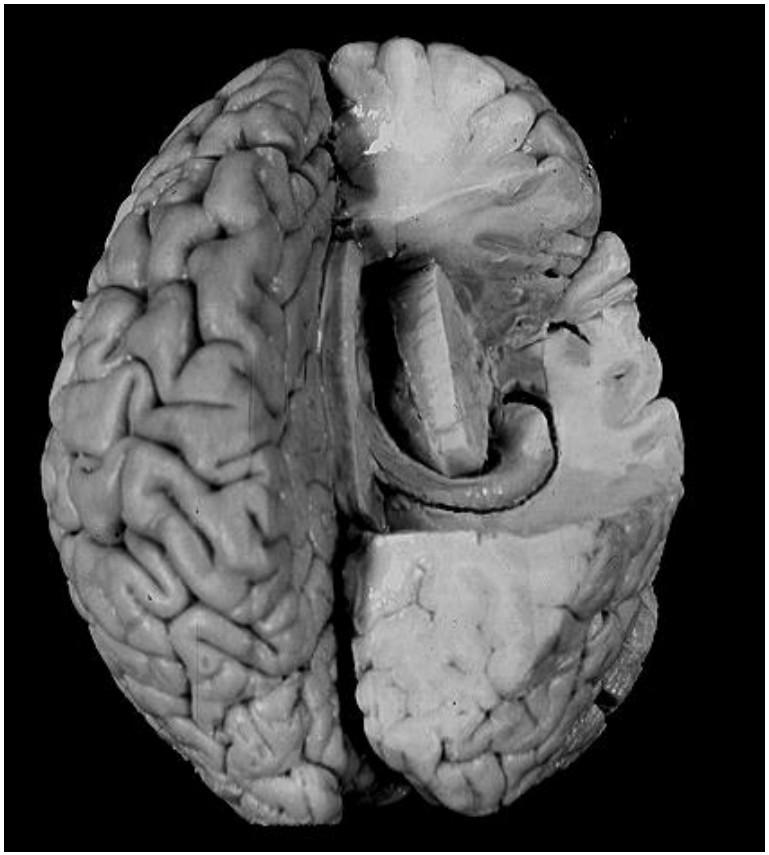


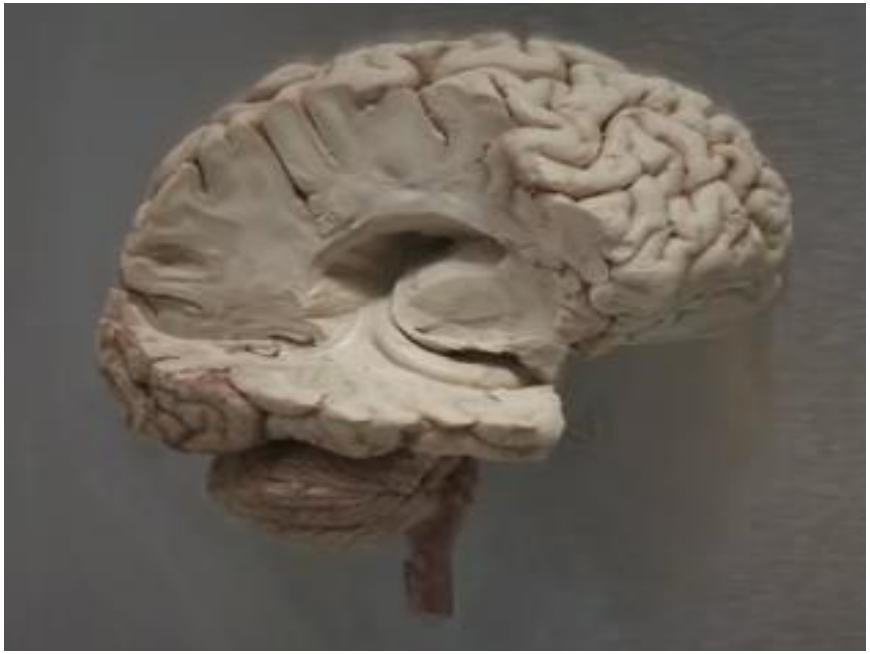
Hippocampus

- ✓ elongated elevation of grey matter
- ✓ extends throughout the entire length of the floor
  of the temporal horn
  of the lateral ventricles
- ✓ terminates at splenium of corpus callosum



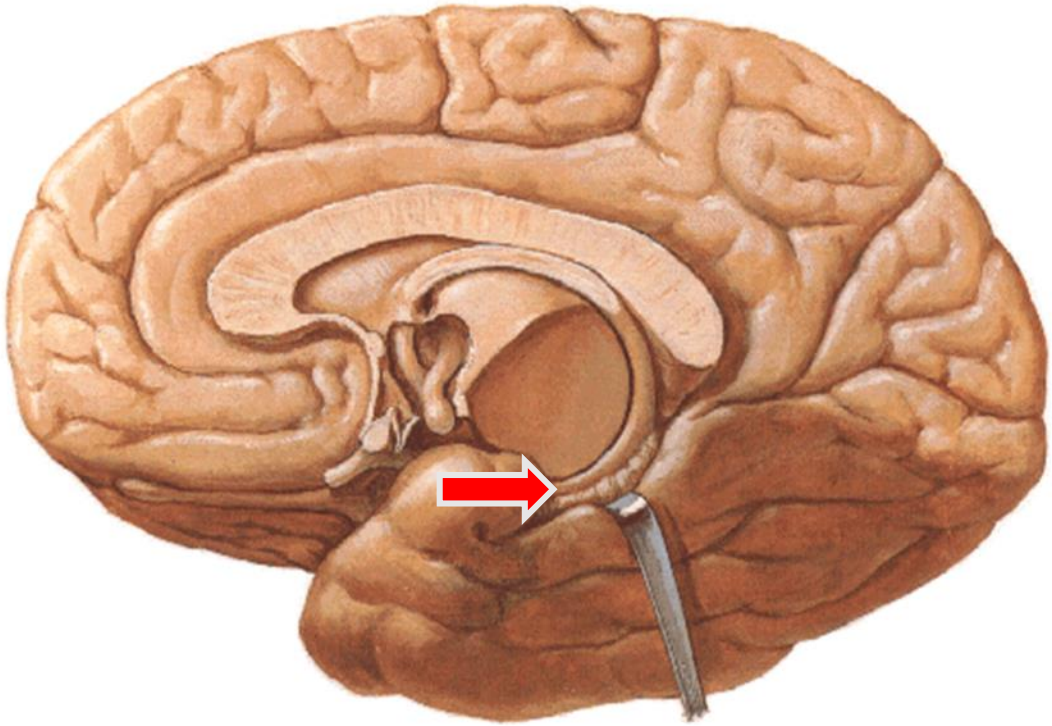


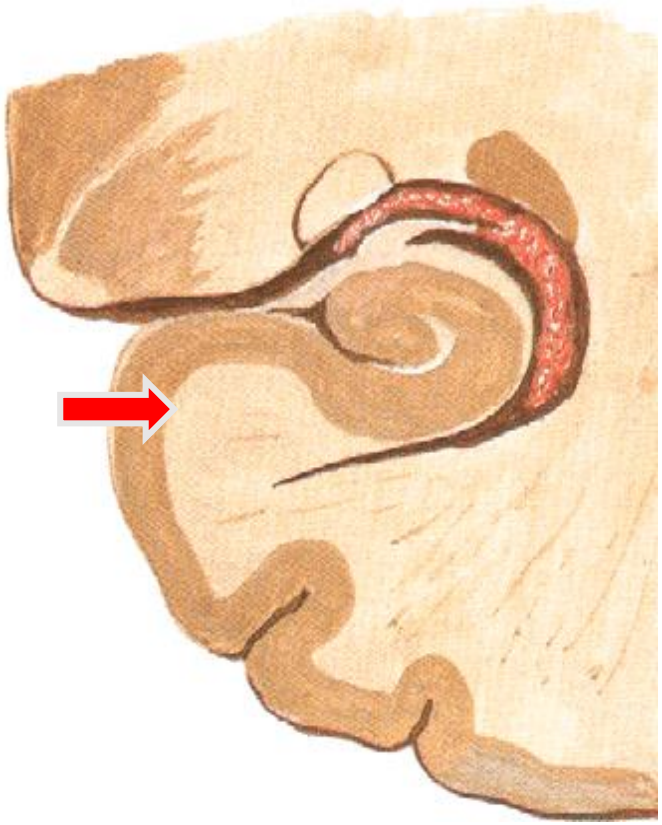




Hippocampus

- medial & inferior surface of the hemisphere
- continuous with parahippocampal gyrus

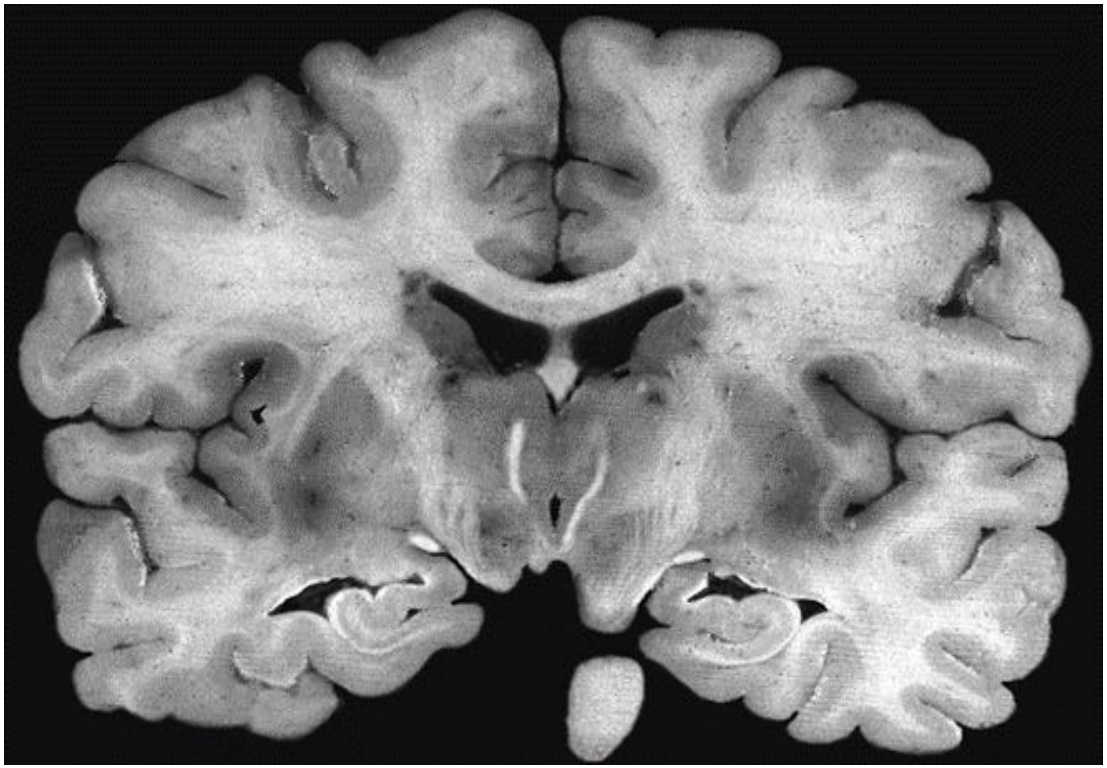


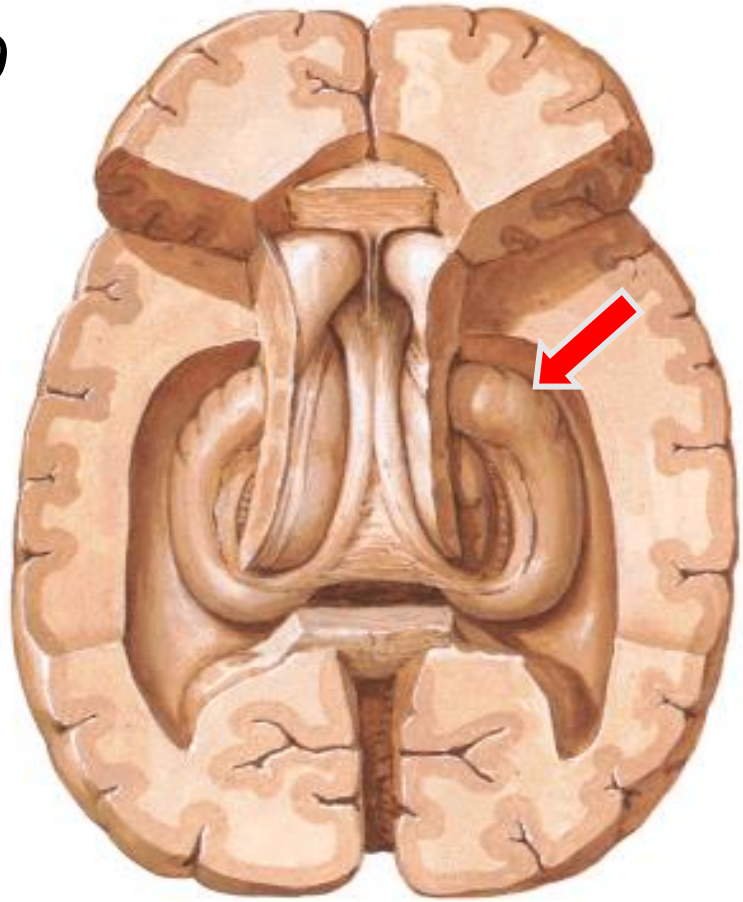


Hippocampus

- **anterior end – expanded**
- **pes hippocampus**

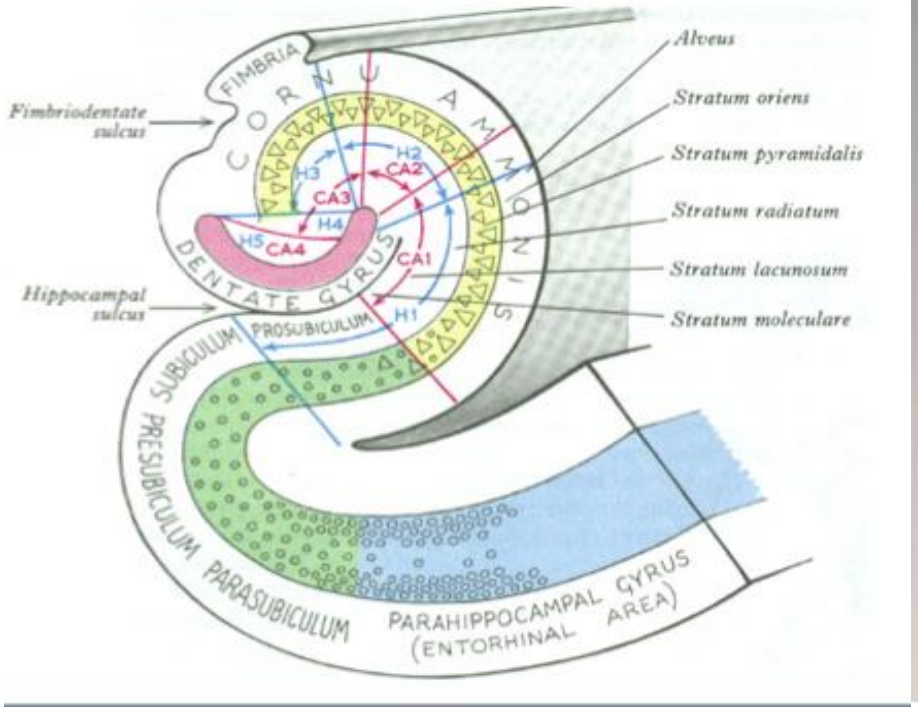
(shallow grooves – gives paw-like appearance)

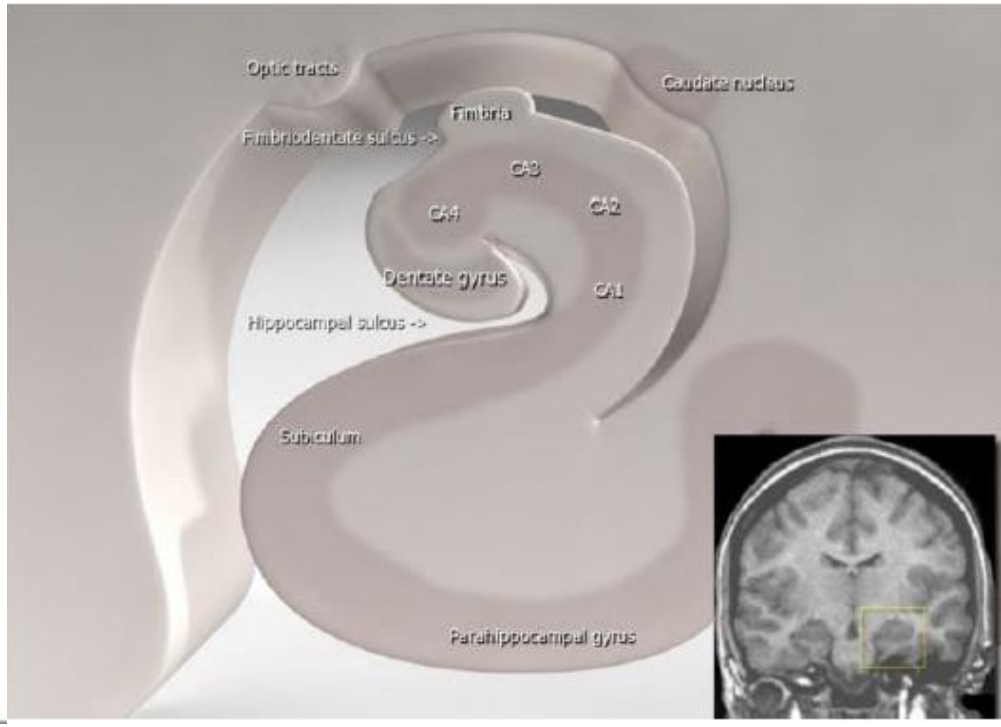




Hippocampal Regions

- ✓ **Cornu ammonis (CA regions - CA1, CA2, CA3 & ~~CA4~~)**
- ✓ **Subiculum**

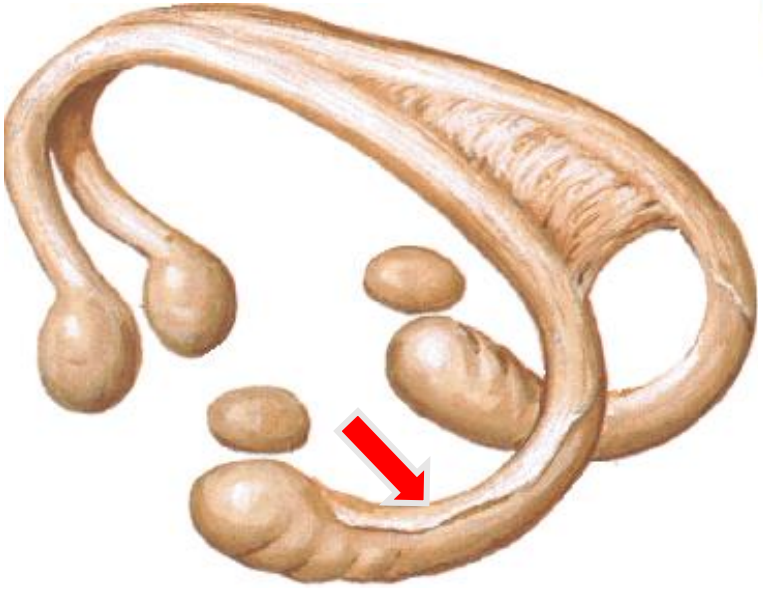


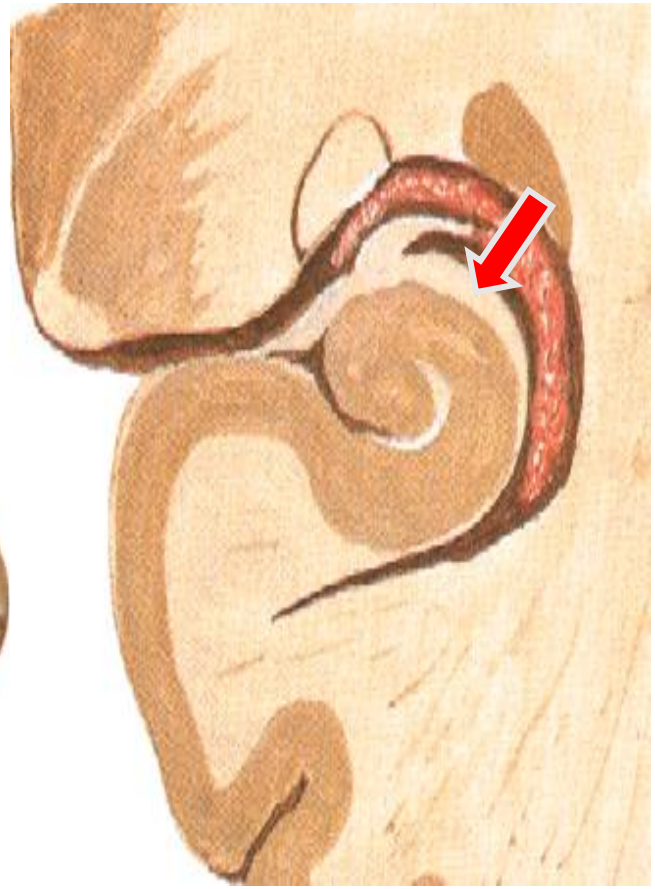


Hippocampus

Alveus

- ✓ white matter
- ✓ covers the ventricular surface
- ✓ afferent and efferent nerve fibers of the hippocampus

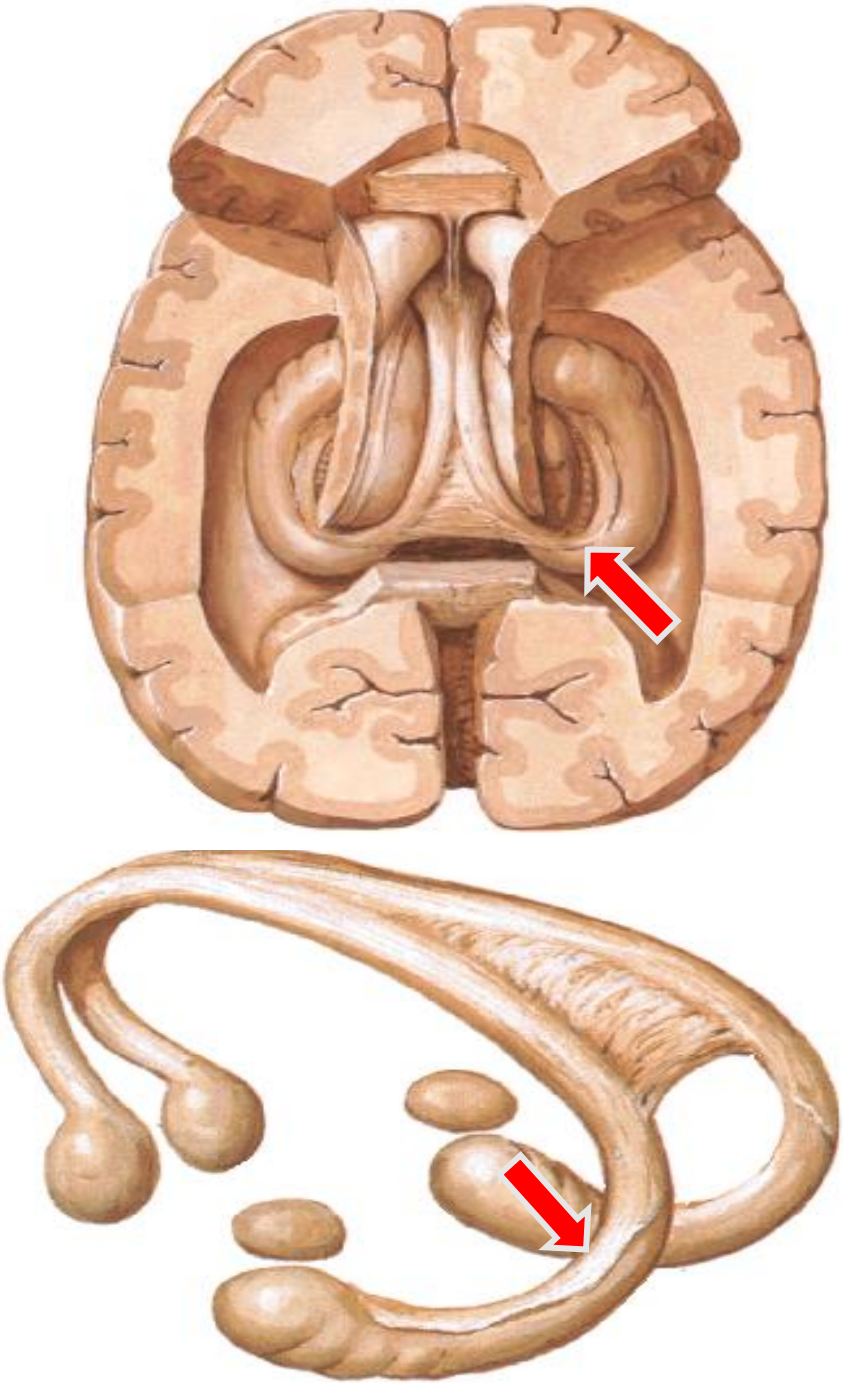




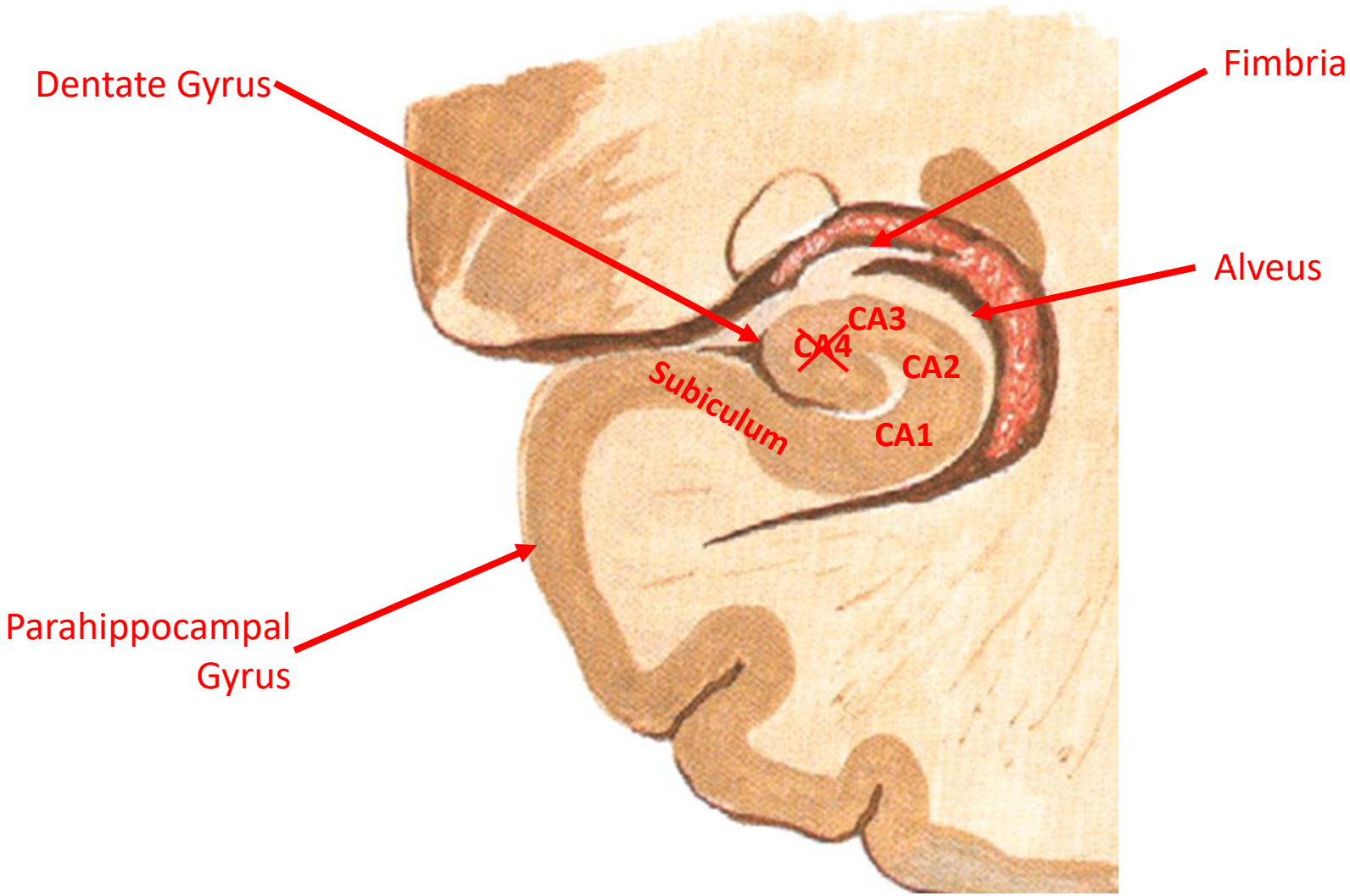
Hippocampus

Fimbria

- ✓ nerve fibers of alveus
- ✓ these converge medially & posteriorly
- ✓ fimbria is continuous with crus of fornix



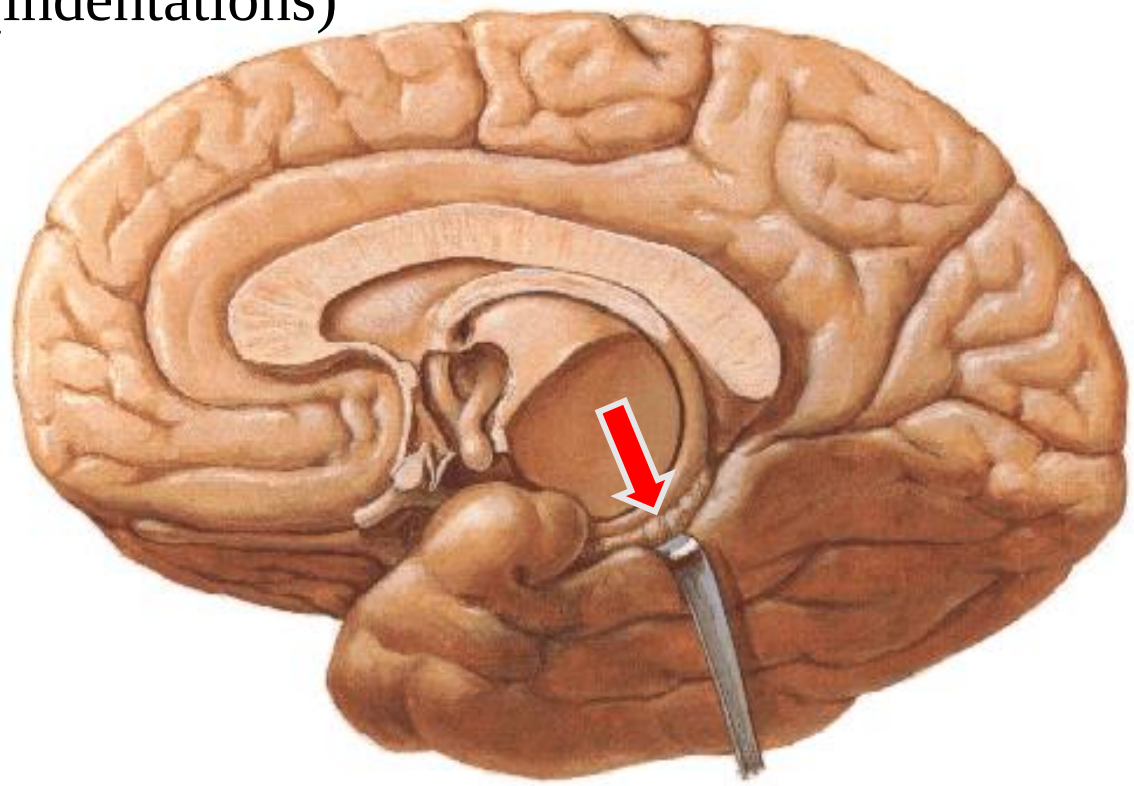
Hippocampal Formation



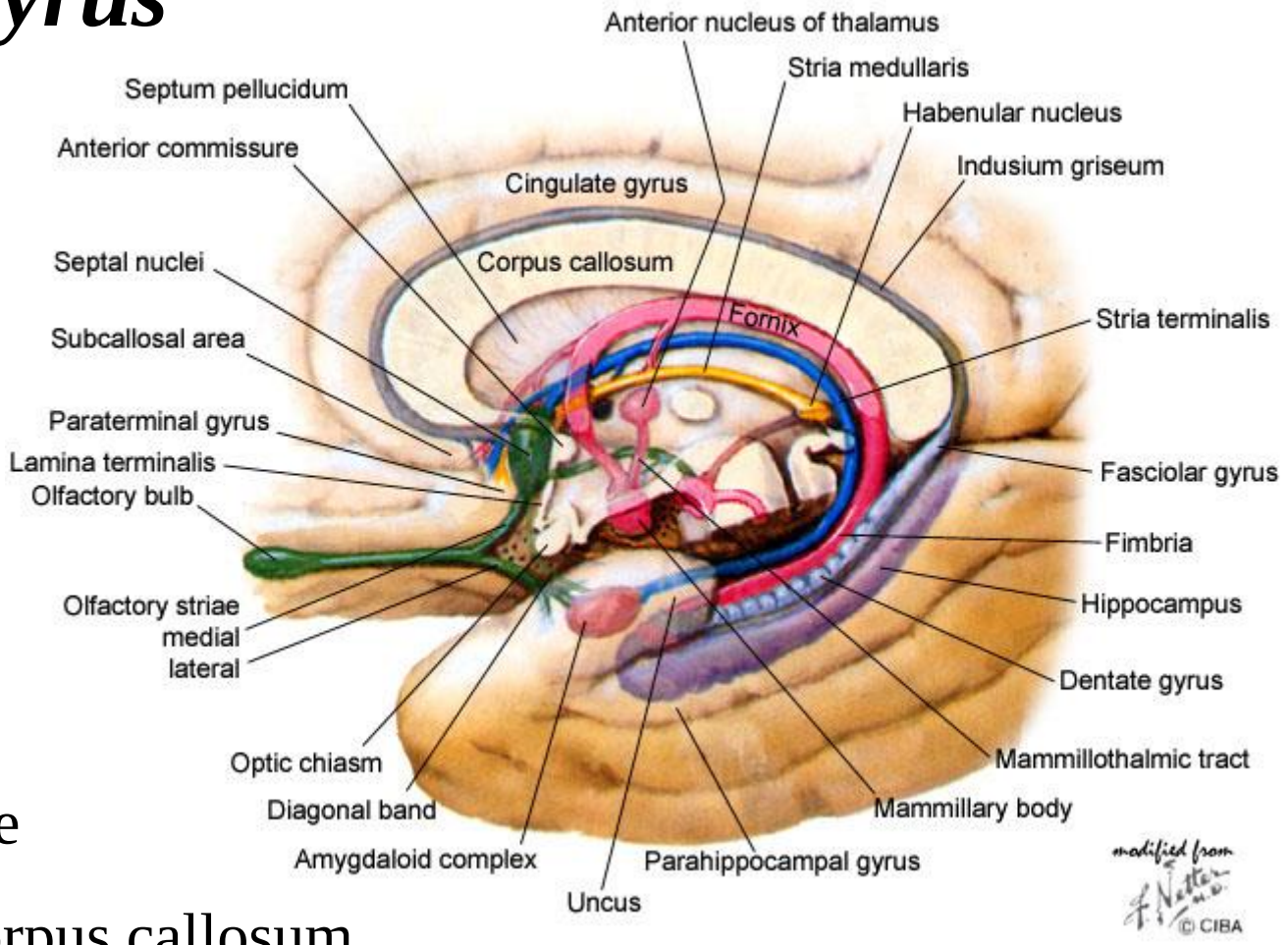
Dentate Gyrus

- ✓ narrow band of grey matter
- ✓ lies between fimbria & parahippocampal gyrus

  (separated by hippocampal fissure)
- ✓ shows notches (indentations)

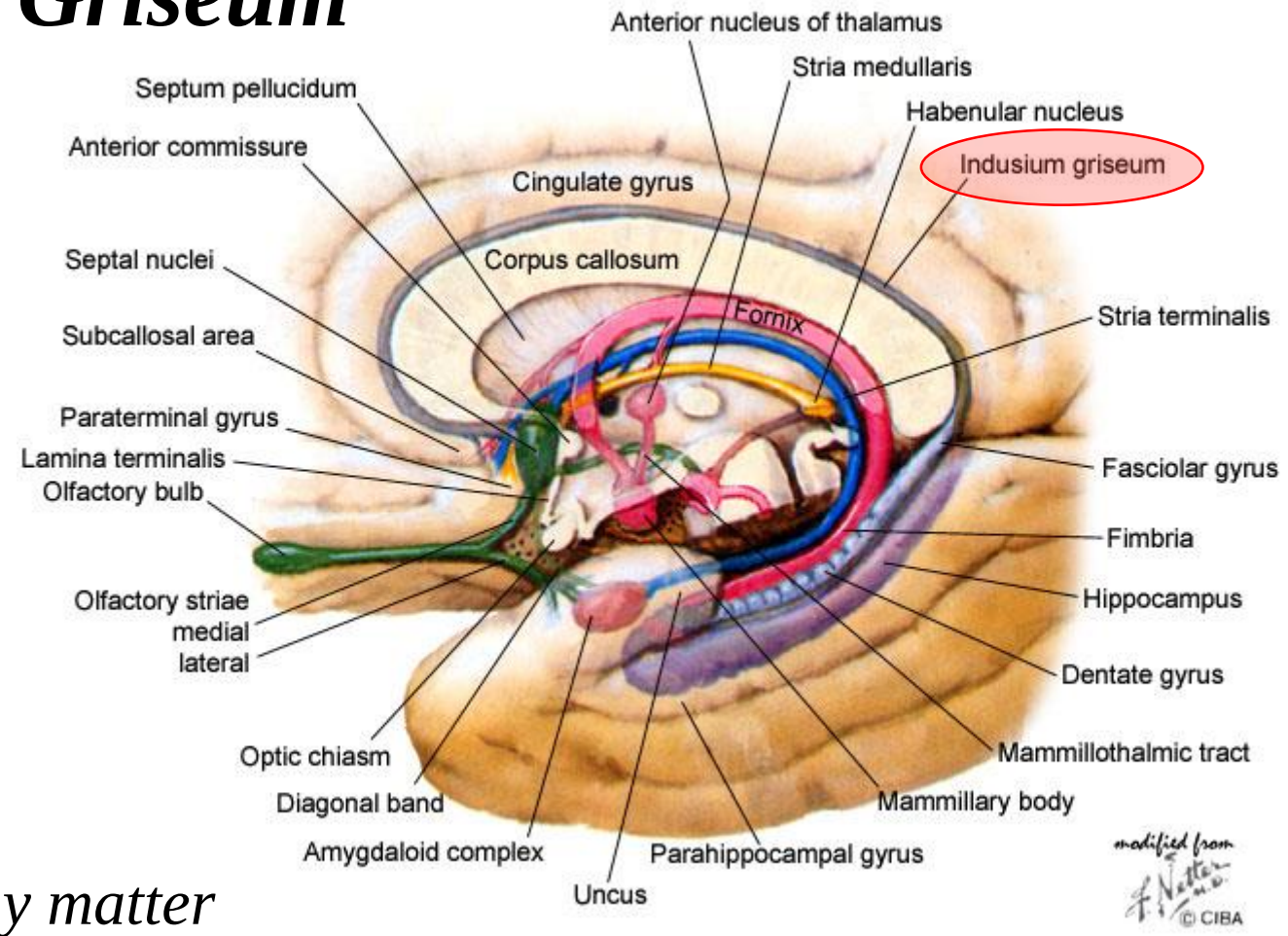


Dentate Gyrus

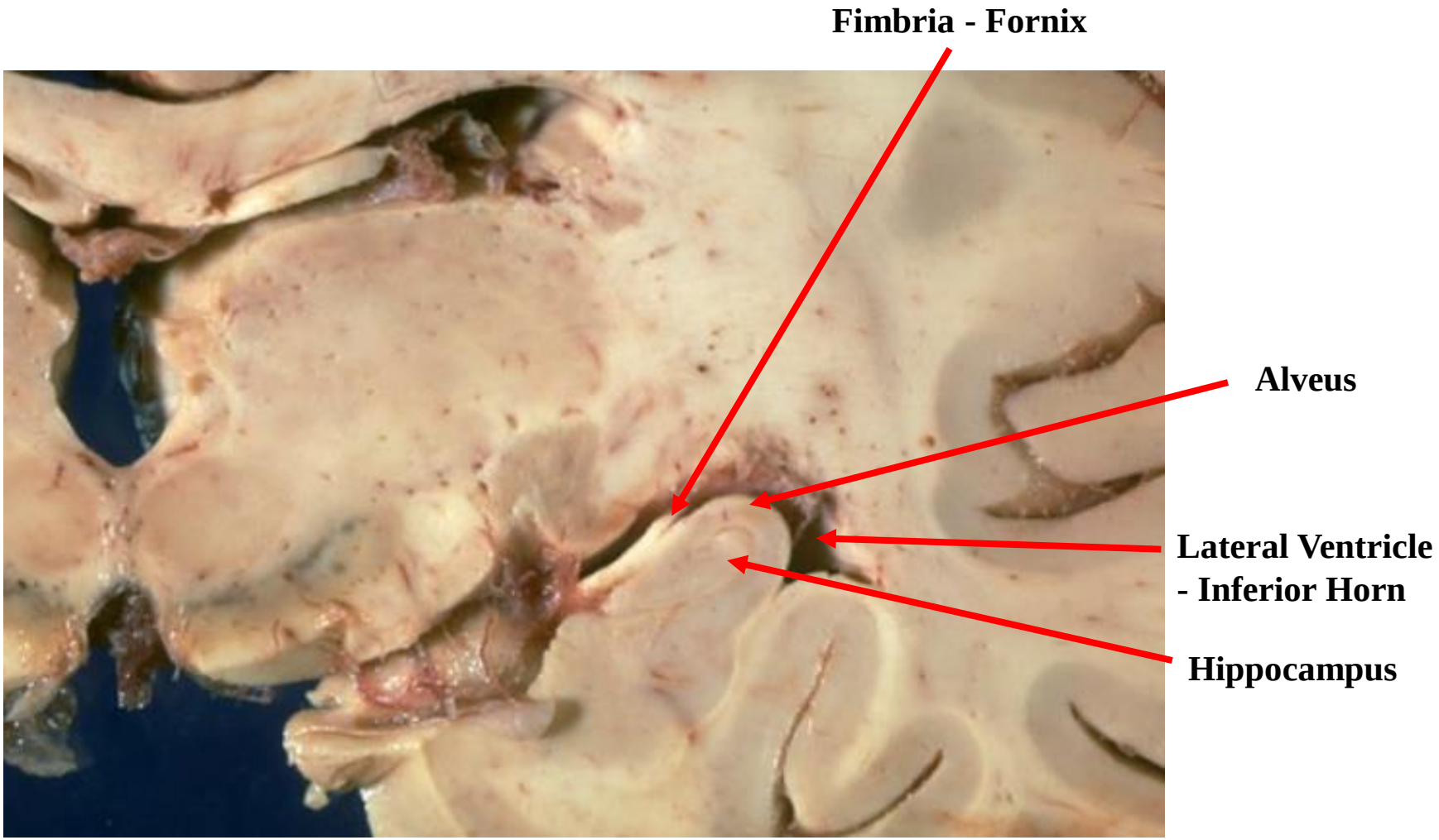


- ✓ extends back to the splenium of the corpus callosum
- ✓ dentate gyrus, CA3 and CA2 are enclosed at the rostral and caudal extremes by CA1 and the subiculum

Indusium Griseum



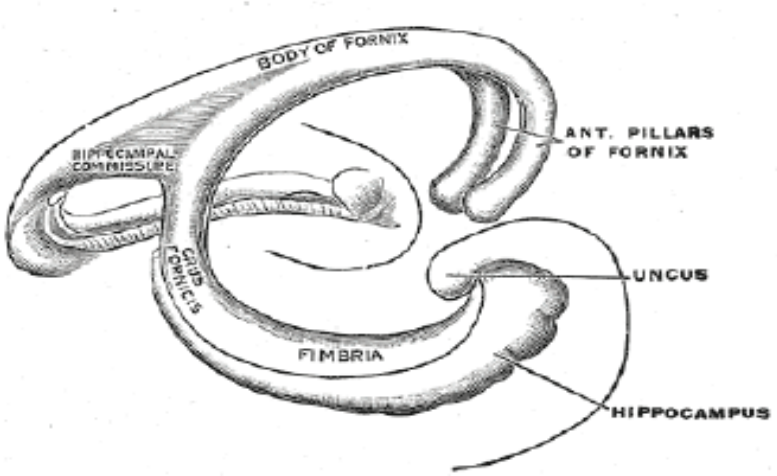
- ✓ *thin layer of gray matter*
- ✓ *covers superior surface of corpus callosum*
- ✓ *not clear which fields of the hippocampal formation generate it*

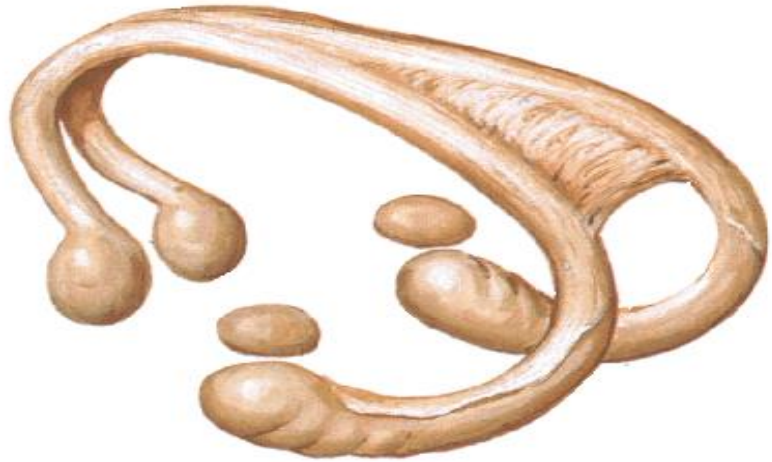

Fimbria - Fornix
Alveus
Lateral Ventricle
- Inferior Horn
Hippocampus

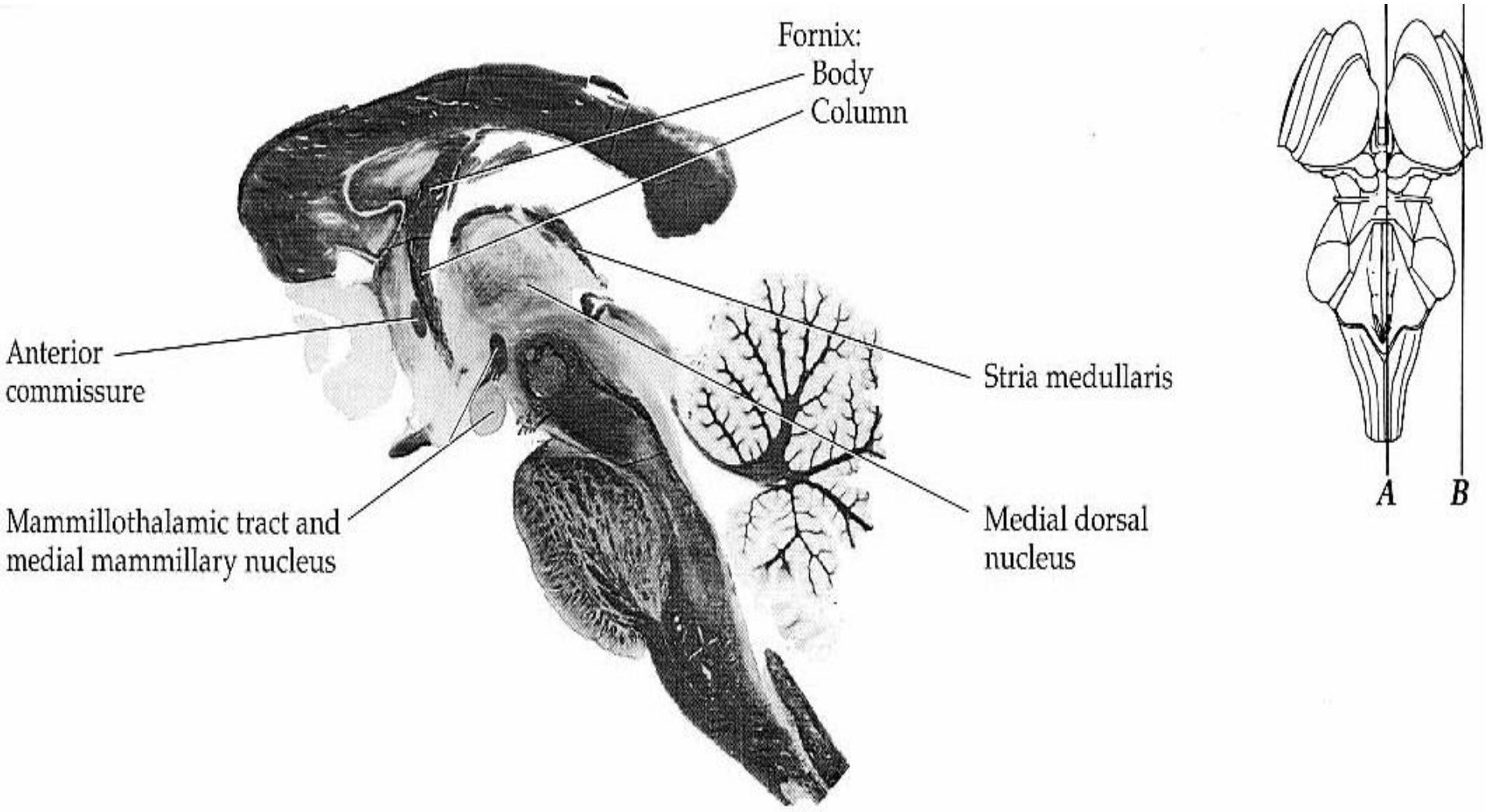
Hippocampus

Fornix

- ✓ lies below body of corpus callosum
- ✓ connects hippocampus with diencephalon & septal area
- ✓ fornix passes behind anterior commissure to reach mammillary body

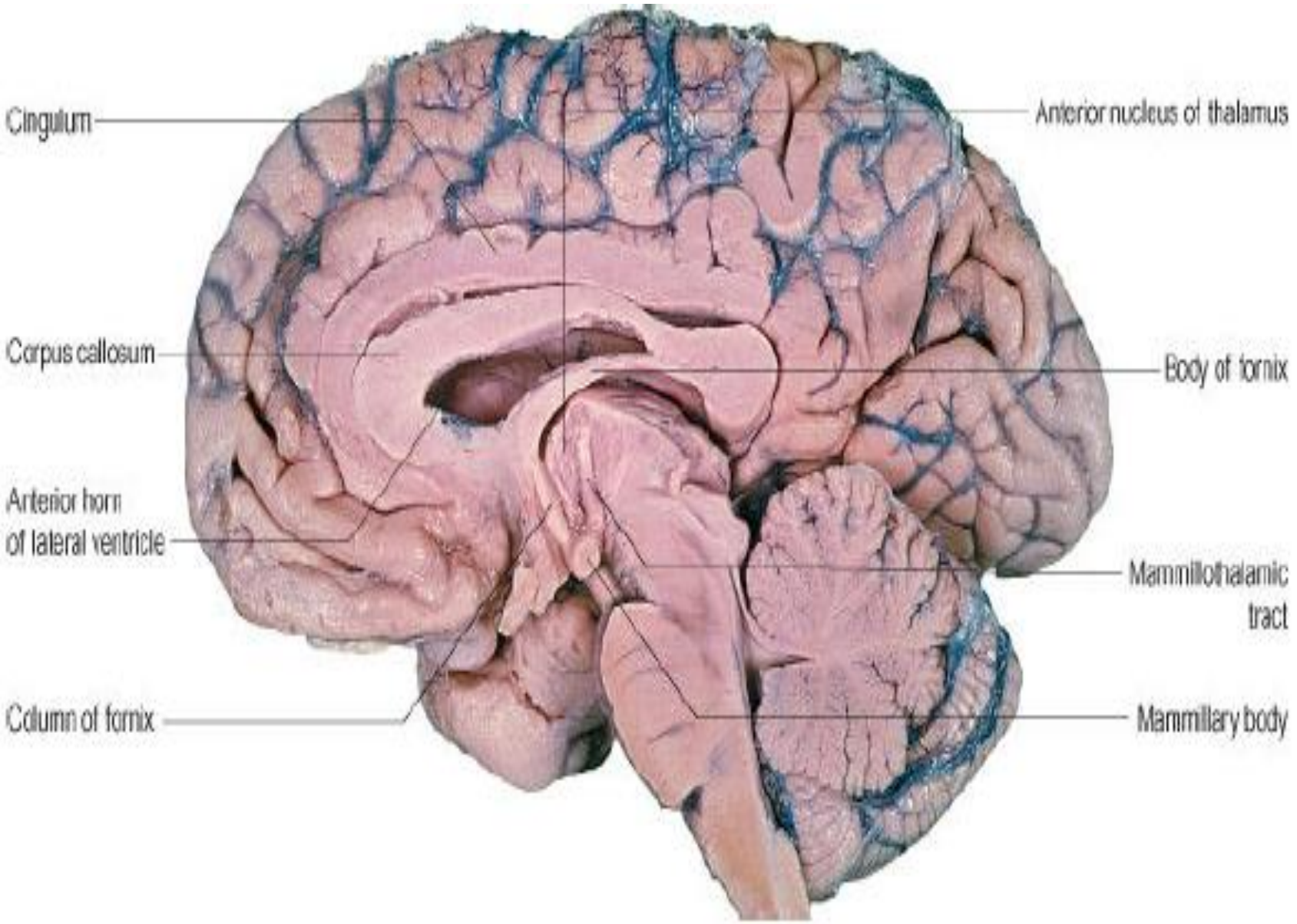


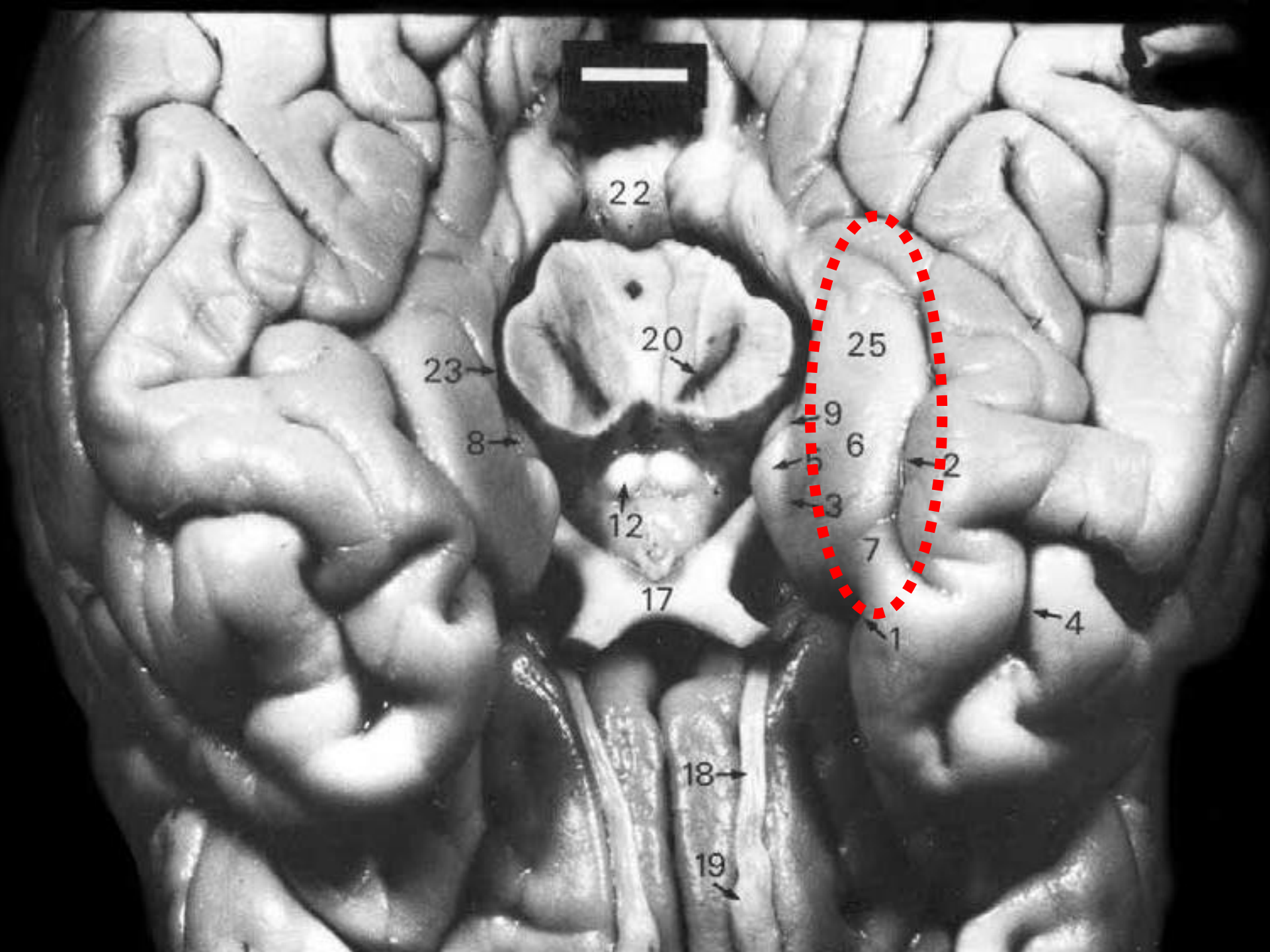




Note:

fornix – posterior to anterior commissure – mammillary body


Cingulum
Anterior nucleus of thalamus
Corpus callosum
Body of fornix
Anterior horn
of lateral ventricle
Mammillothalamic
tract
Column of fornix
Mammillary body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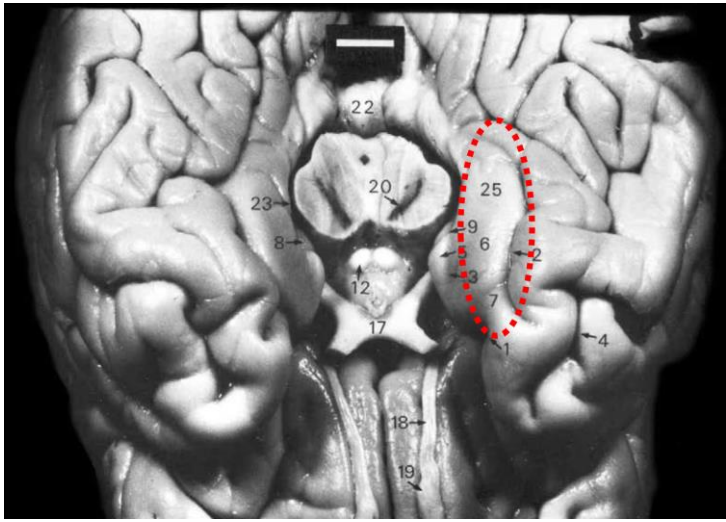
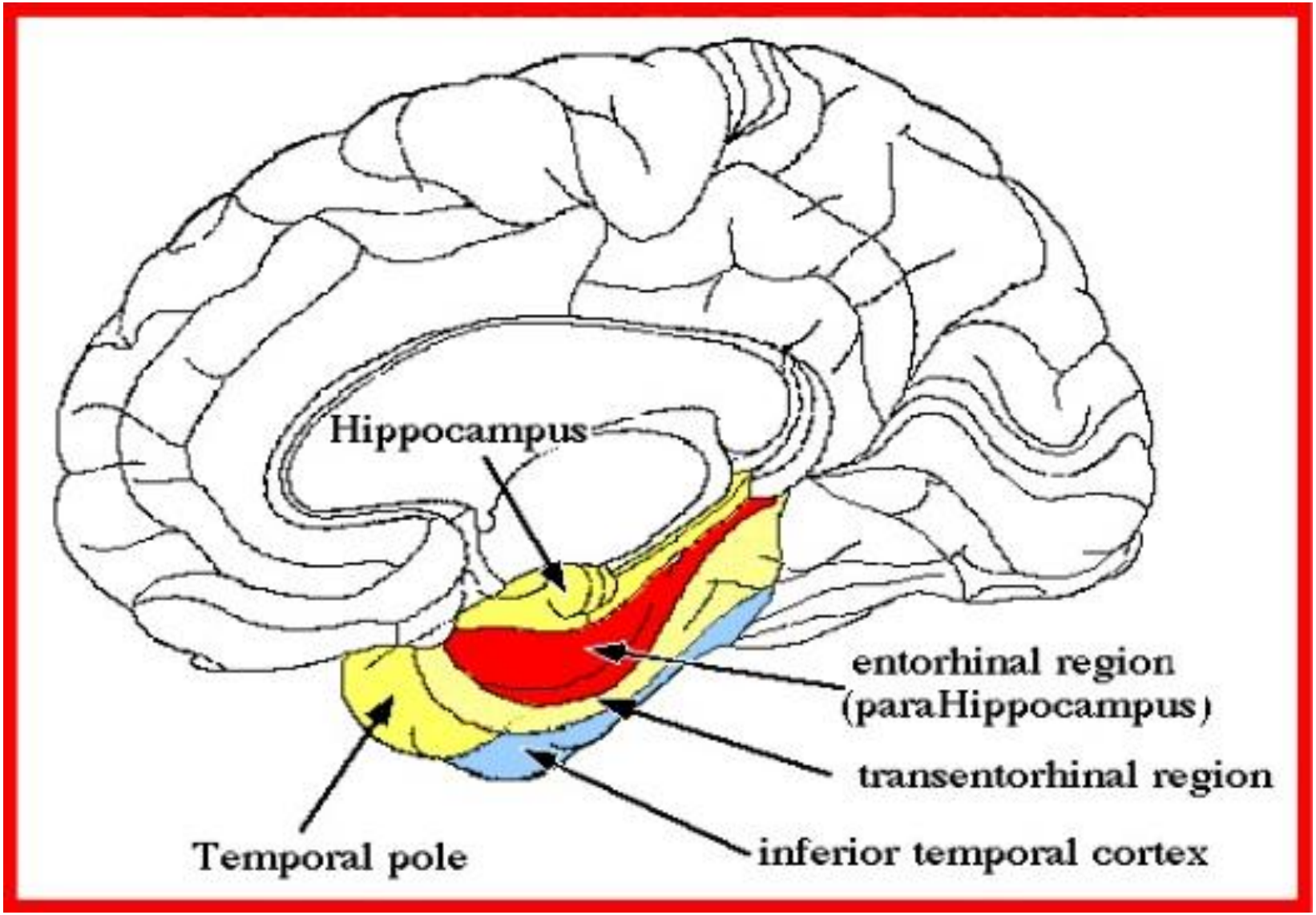
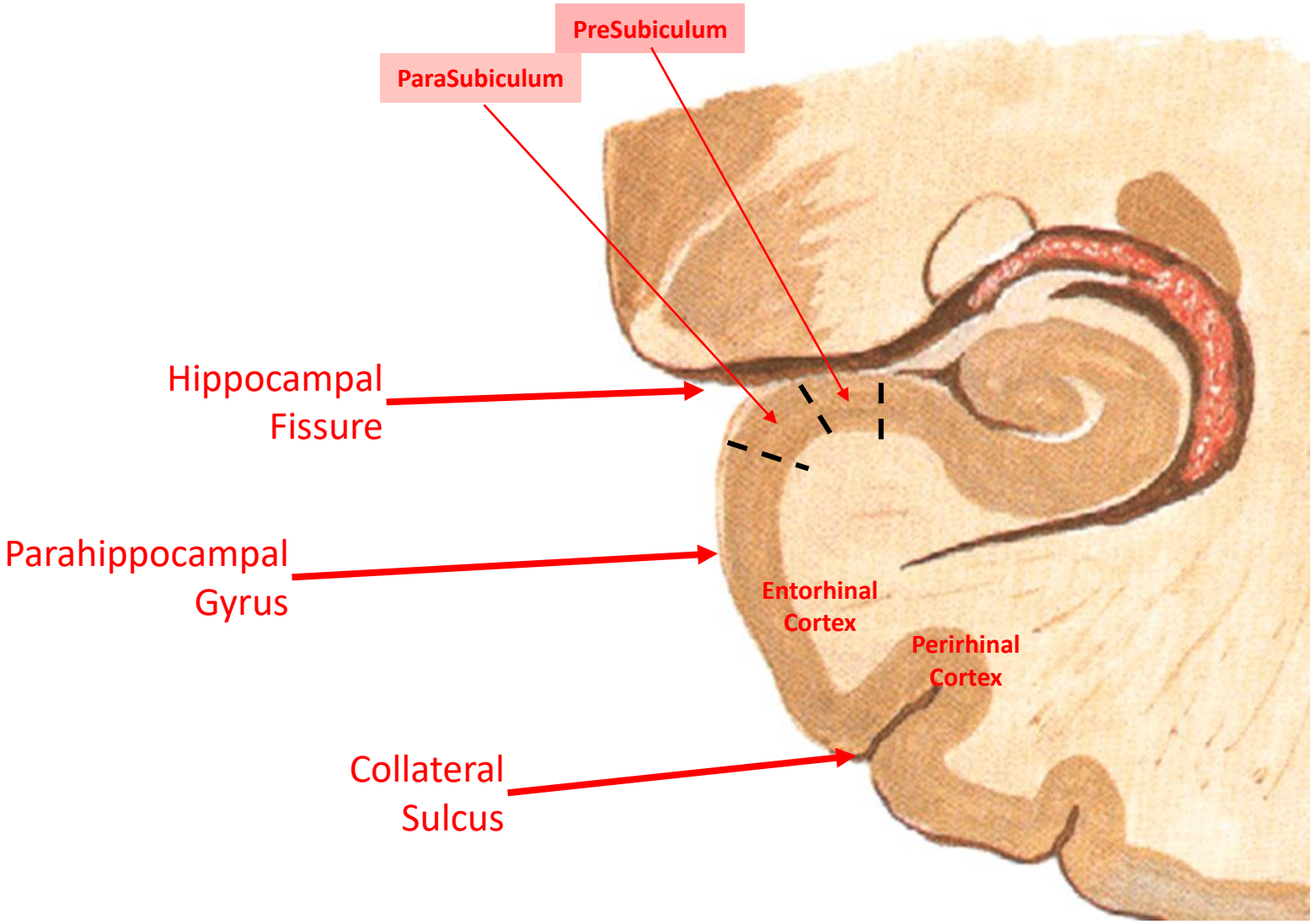
Parahippocampal Gyrus

- lies between hippocampal fissure & collateral sulcus
- continuous with hippocampus
- entorhinal cortex - the main interface between the hippocampus and neocortex




Hippocampus
entorhinal region
(paraHippocampus)
transentorhinal region
Temporal pole
inferior temporal cortex

Parahippocampal Gyrus



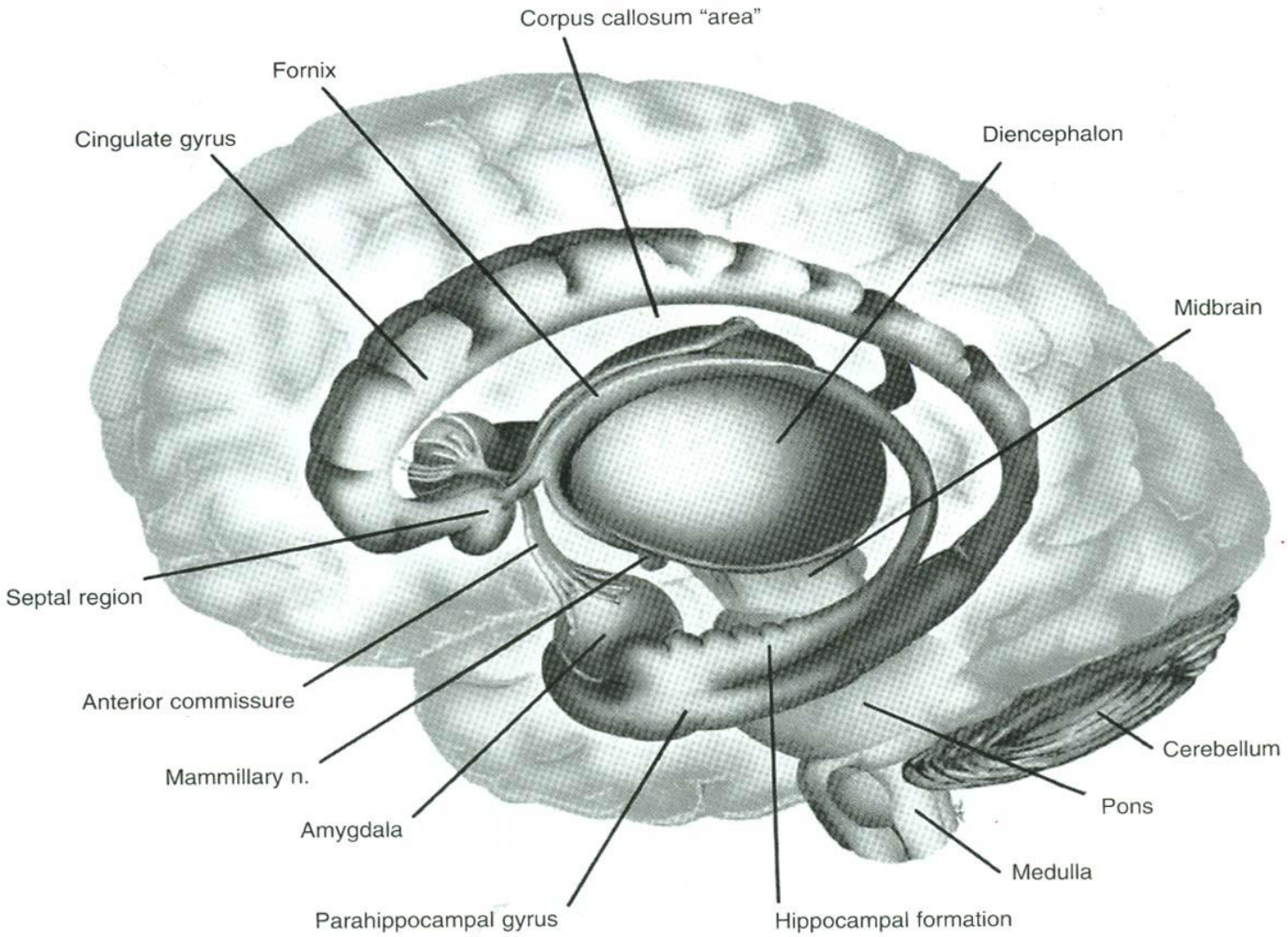
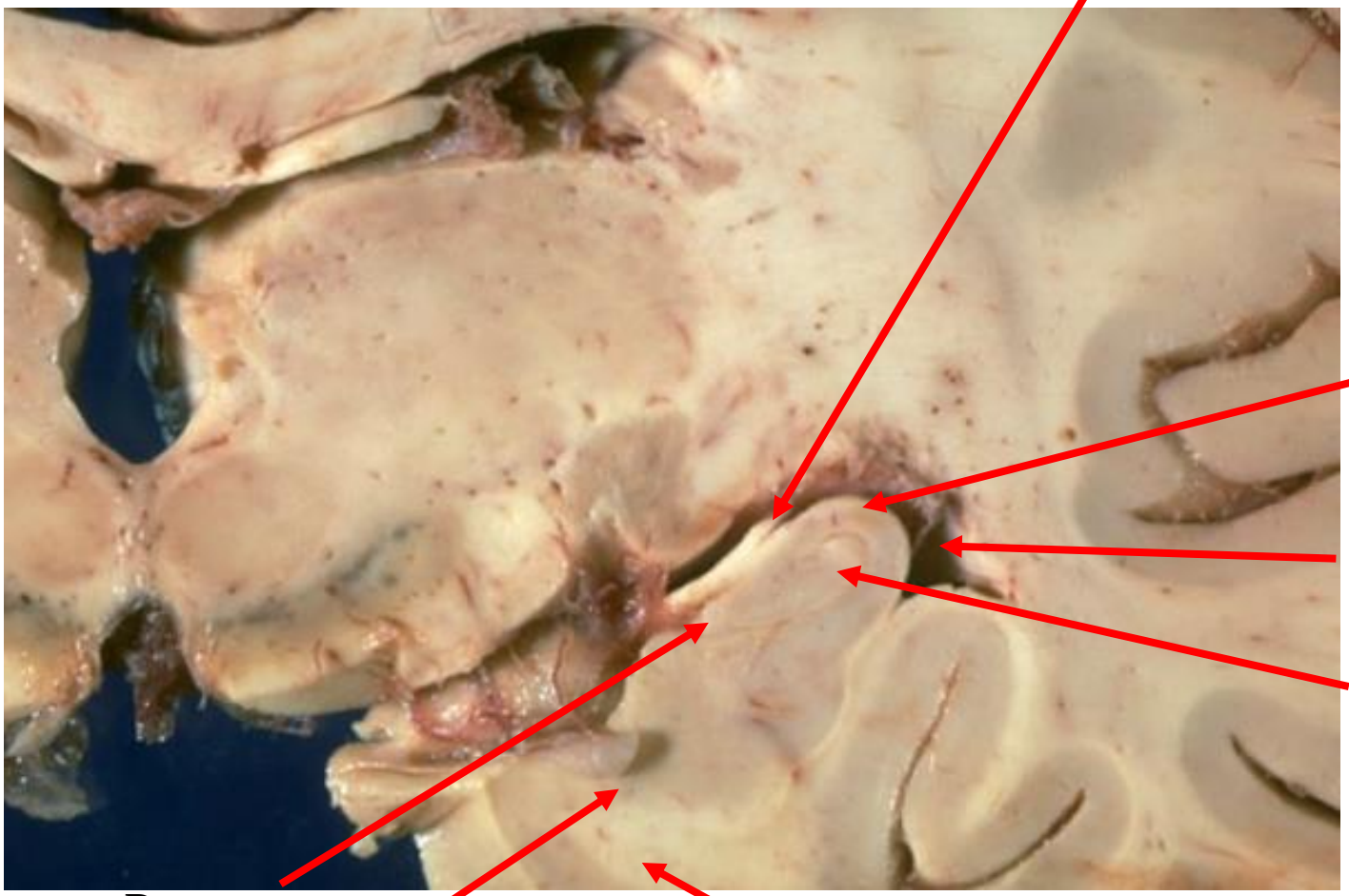
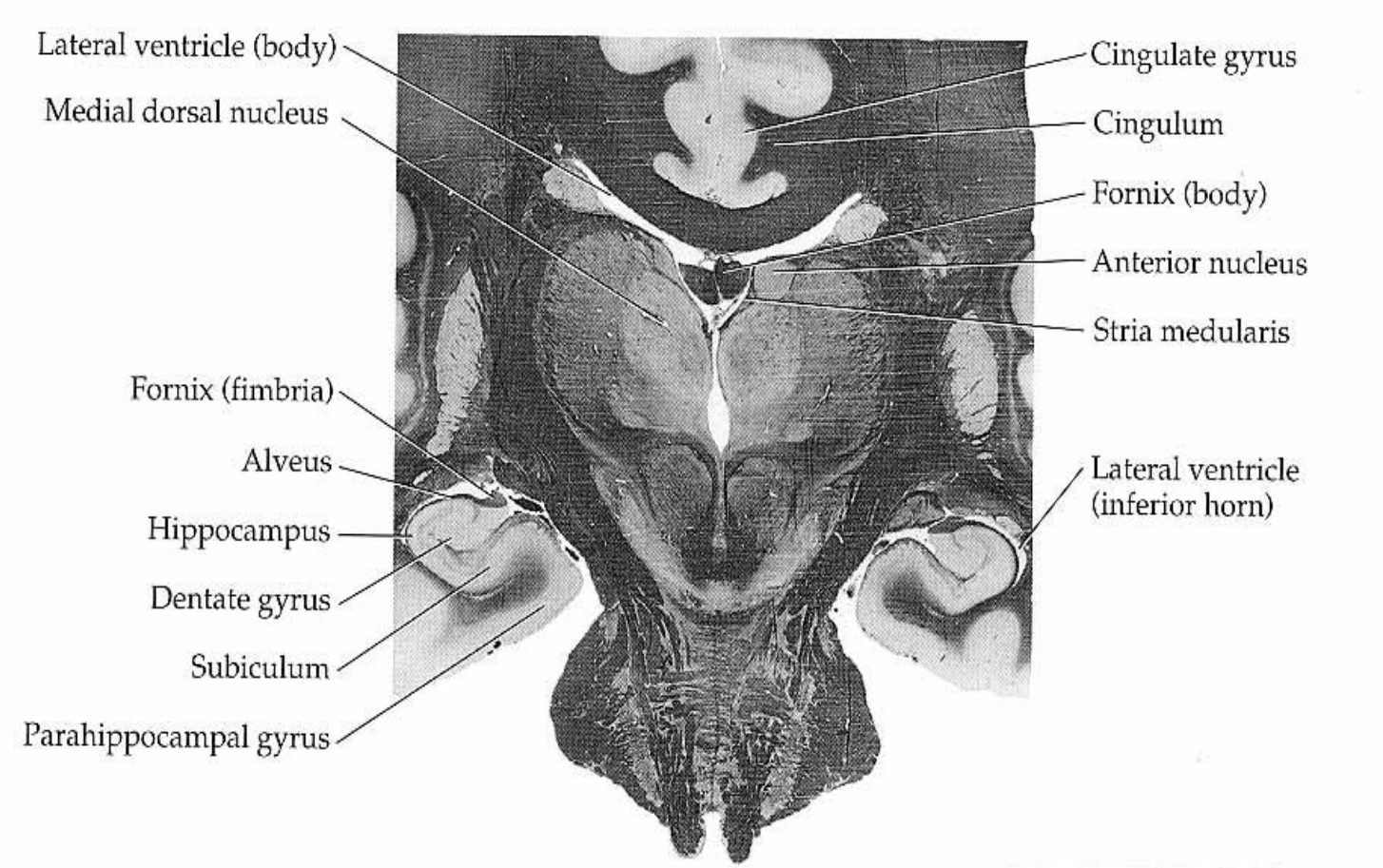
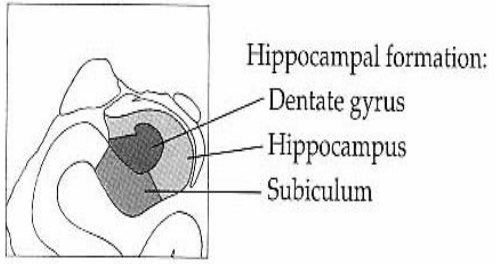


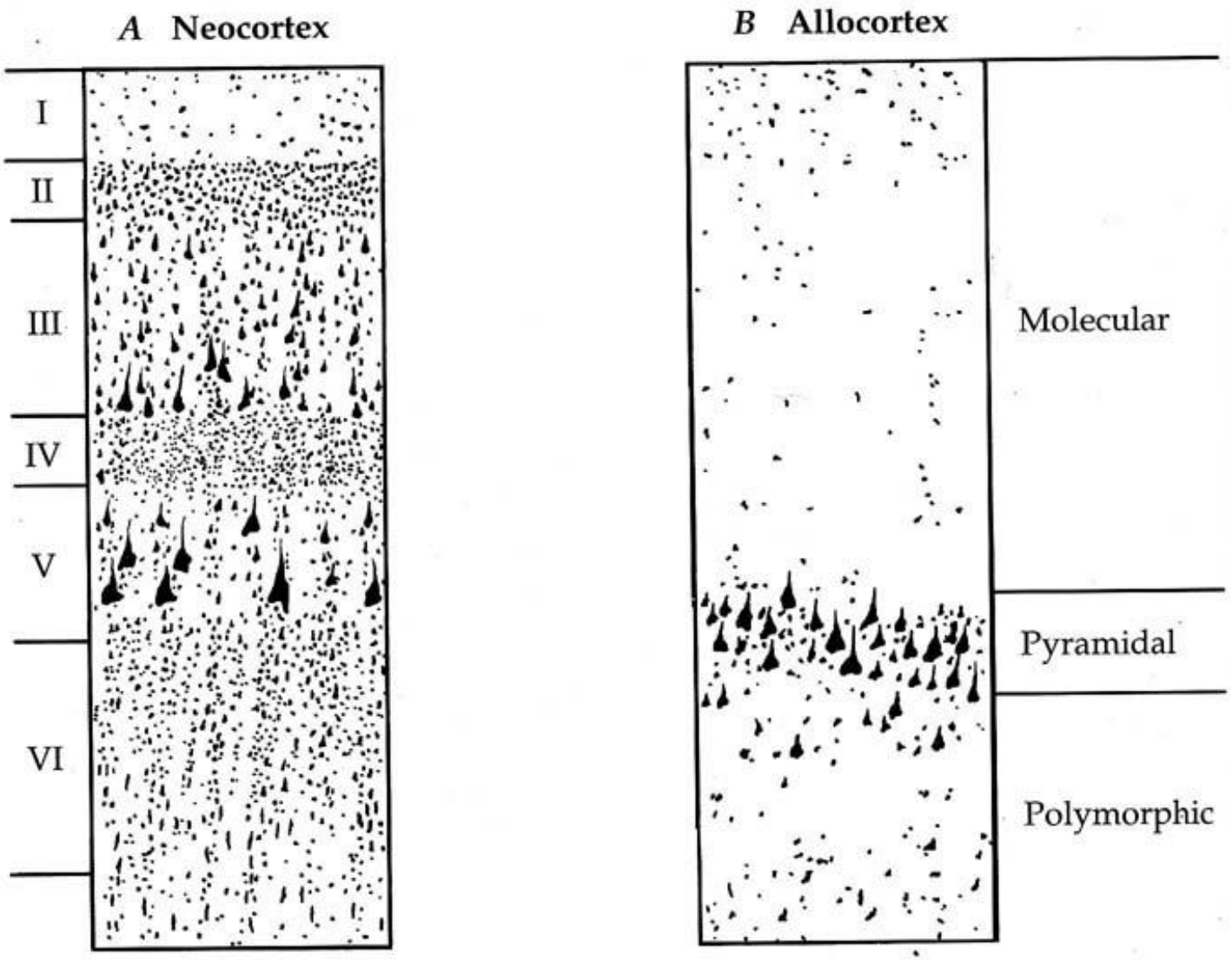
FIGURE 74: Limbic Lobe


Fimbria - Fornix
Alveus
Inferior horn
Lateral ventricle
Hippocampus
Dentate
gyrus
Subiculum
Parahippocampal
gyrus


Lateral ventricle (body)
Medial dorsal nucleus
Fornix (fimbria)
Alveus
Hippocampus
Dentate gyrus
Subiculum
Parahippocampal gyrus
Cingulate gyrus
Cingulum
Fornix (body)
Anterior nucleus
Stria medularis
Lateral ventricle (inferior horn)


Hippocampal formation:
Dentate gyrus
Hippocampus
Subiculum

Neocortex & Allocortex



Cytoarchitecture of the Hippocampus

- parahippocampal gyrus → ***6 layers***

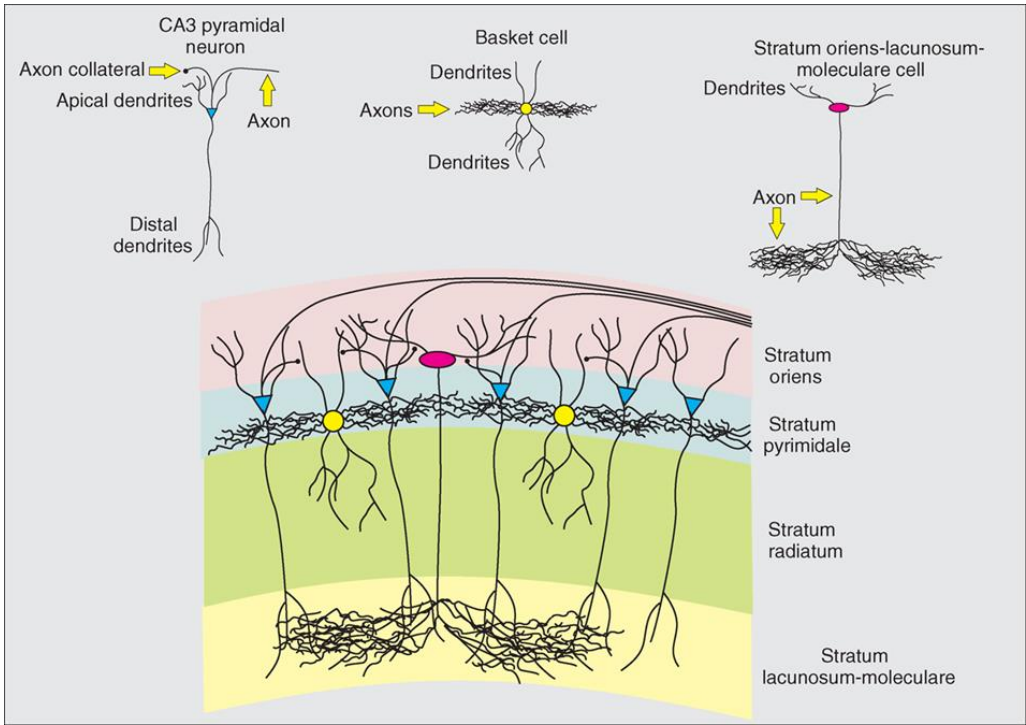
- 6 layers gradually decrease to **3 layers** as we move to hippocampus

Cytoarchitecture of the Hippocampus

- **Molecular Layer**
  - Stratum radiatum
  - Stratum lacunosum moleculare

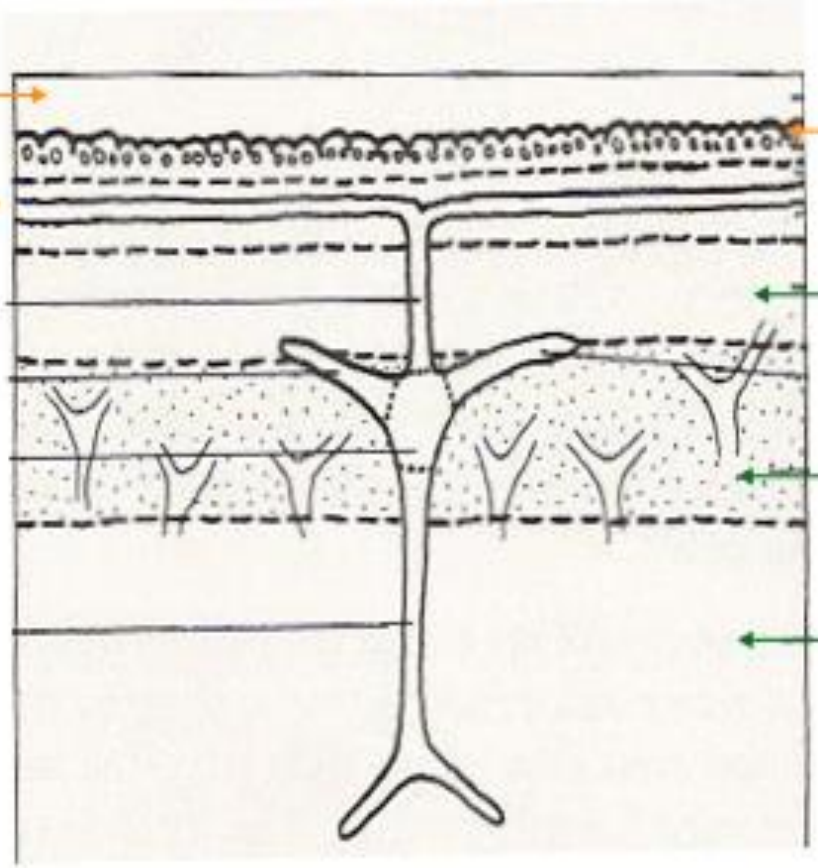
- **Pyramidal layer**
  - Stratum pyramidale
  - Large pyramidal cells

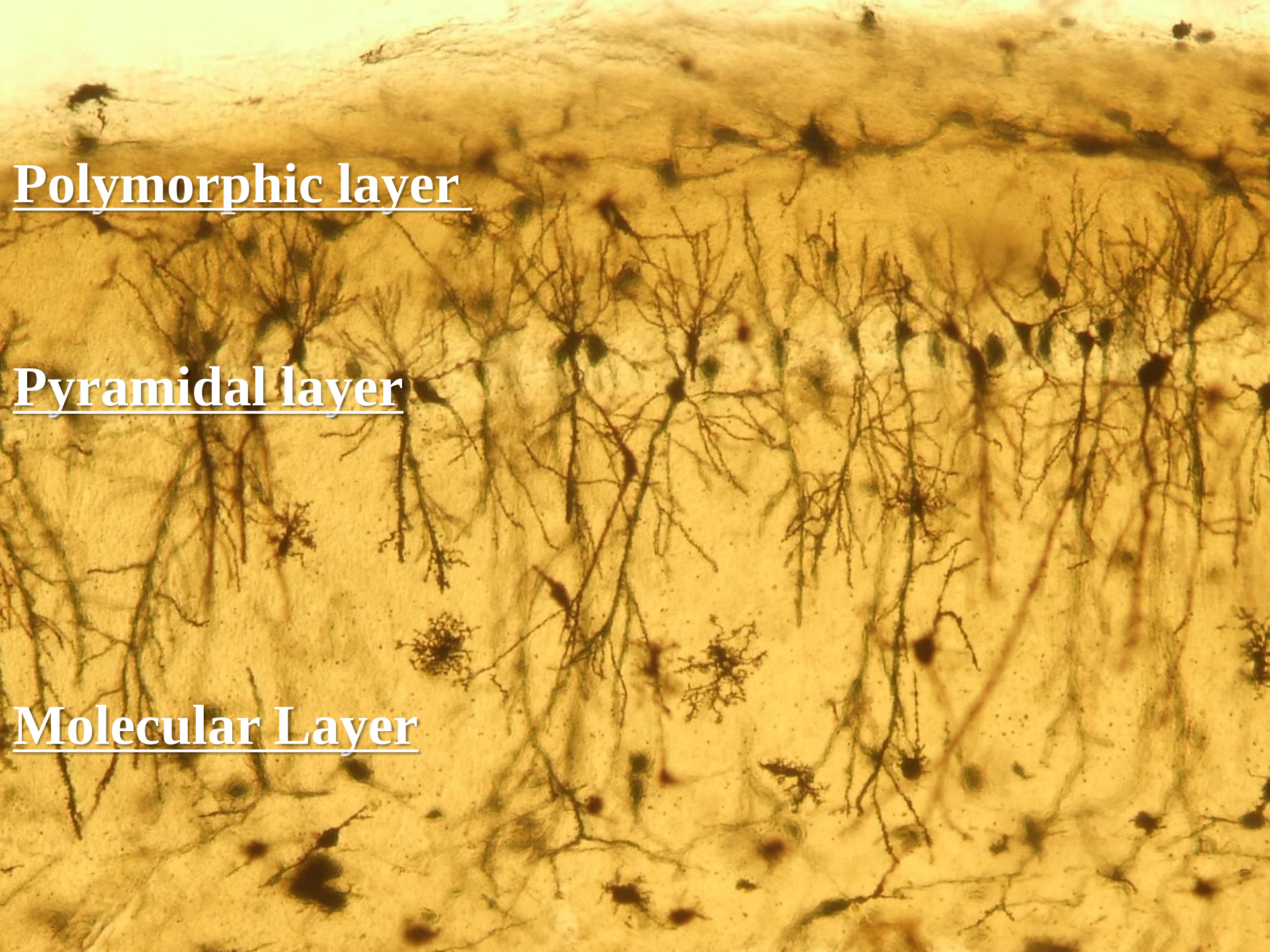
- **Polymorphic layer**
  - Stratum oriens
  - Polymorphic cells



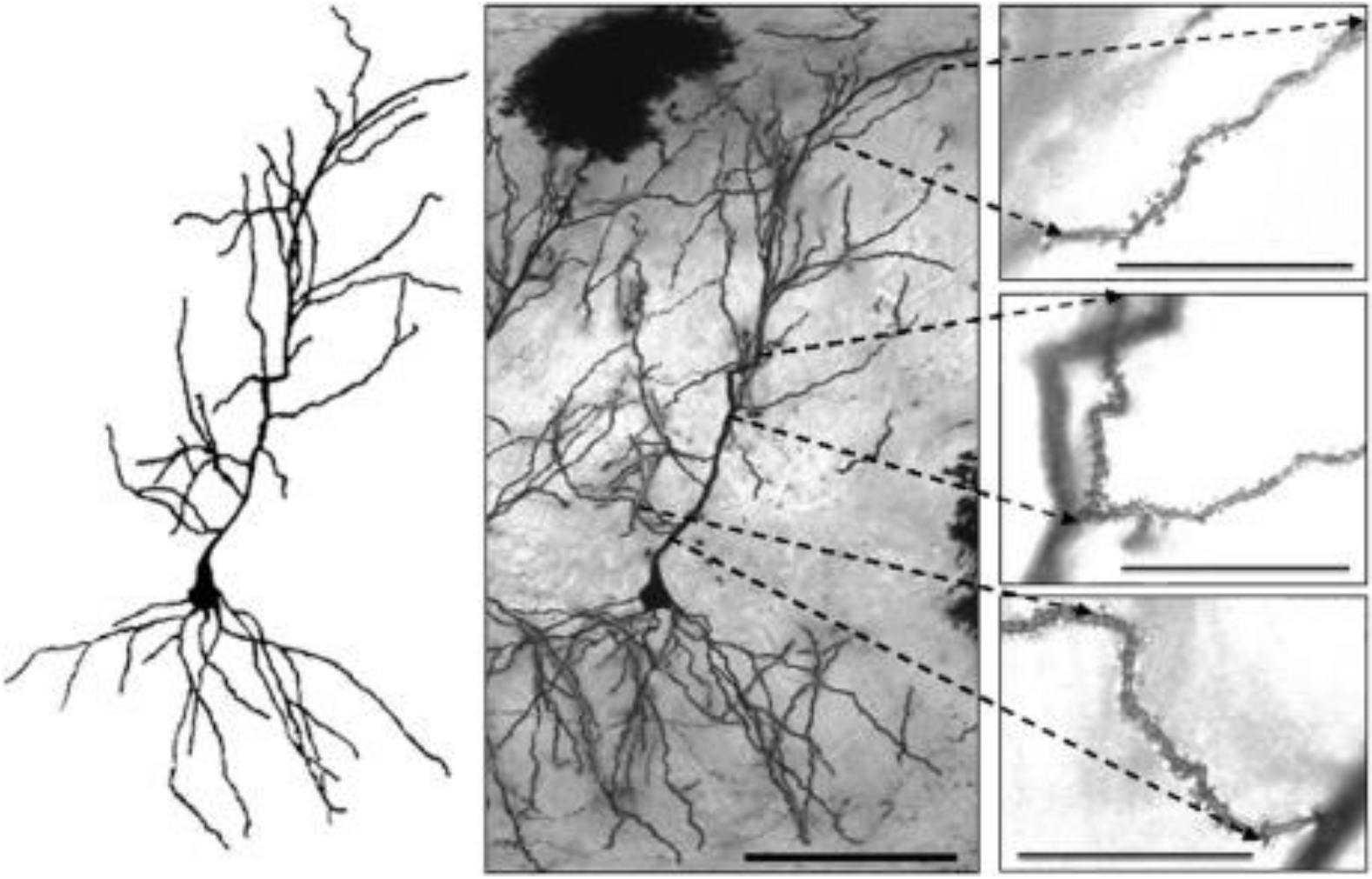
The Hippocampus

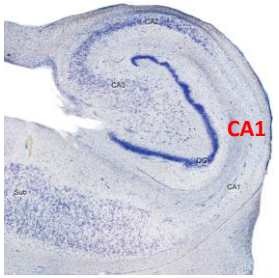
CA fields



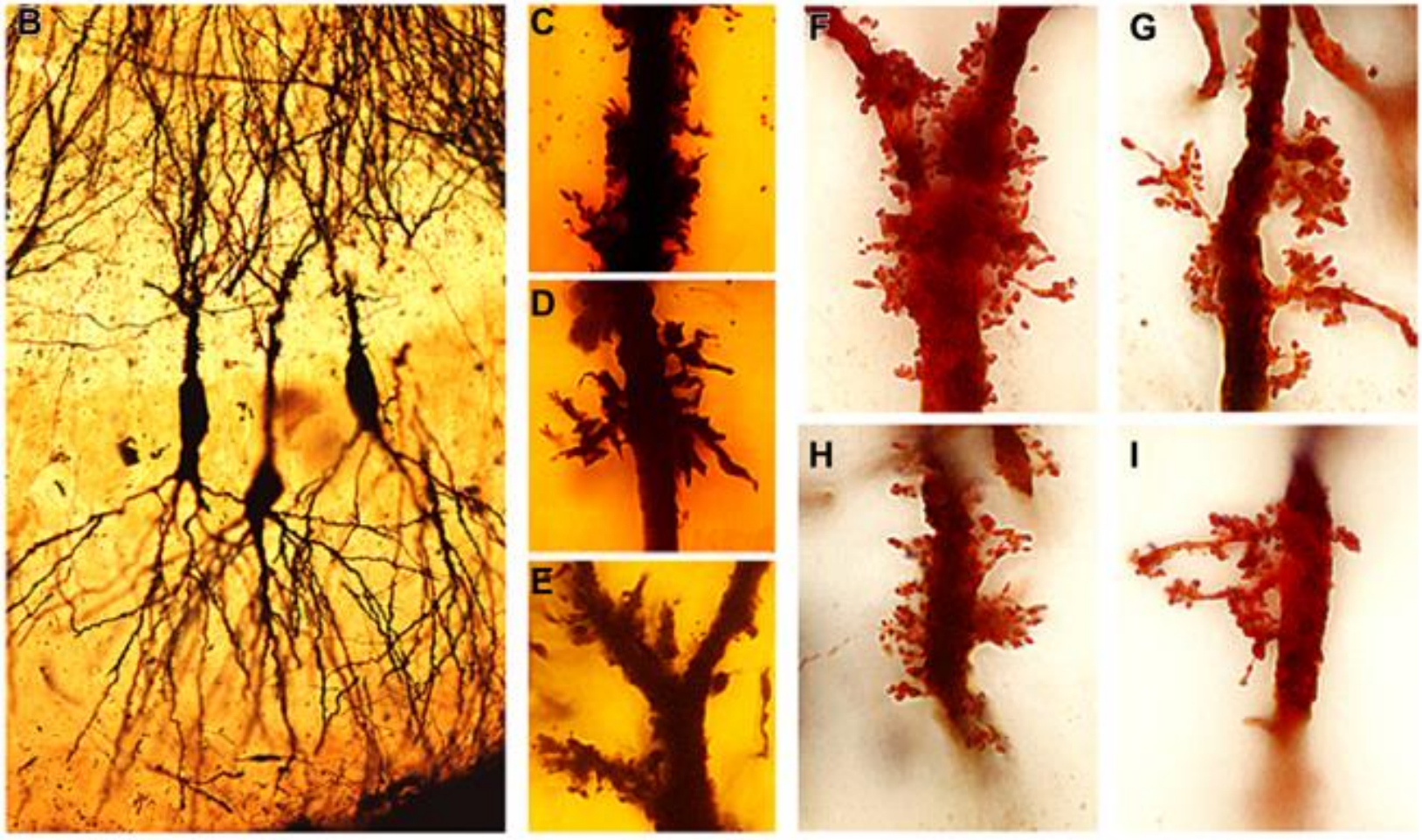

Polymorphic layer
Pyramidal layer
Molecular Layer

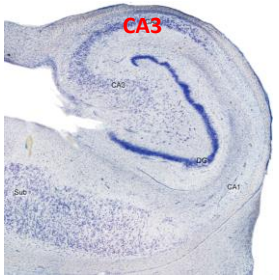
CA1 – Pyramidal Neuron



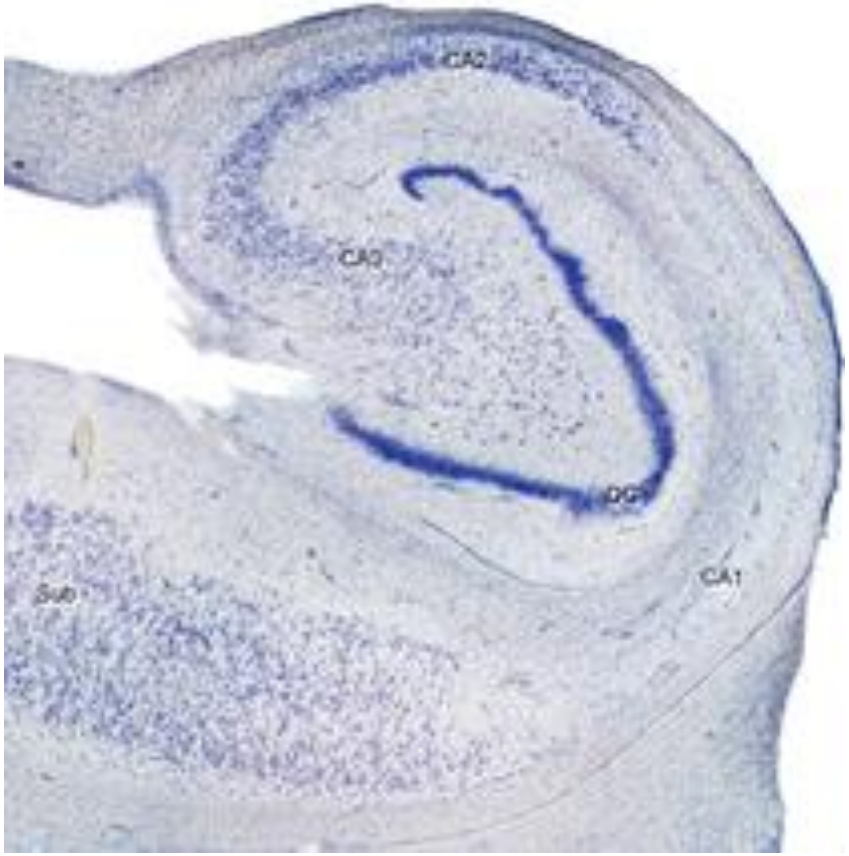


CA3 – Pyramidal Neuron



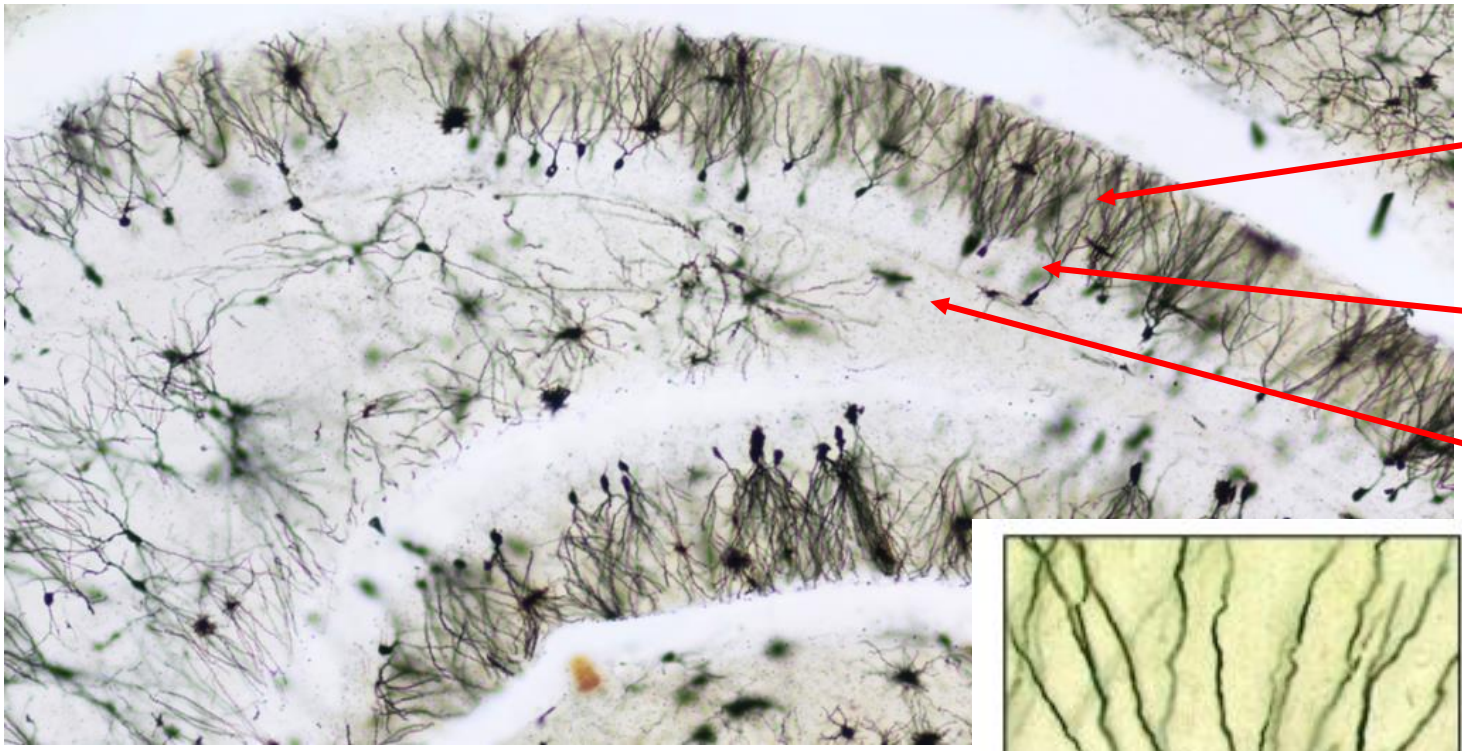


Dentate Gyrus



- ✓ **Molecular Layer**
  - **superficial layer**
  - **mostly fibers**
- ✓ **Granular layer**
  - **striatum granulosum**
  - **small granular cells**
  - **mossy fibers – axons from granule cells**
- ✓ **Polymorphic layer**
  - **hilus**
  - **polymorphic cells**

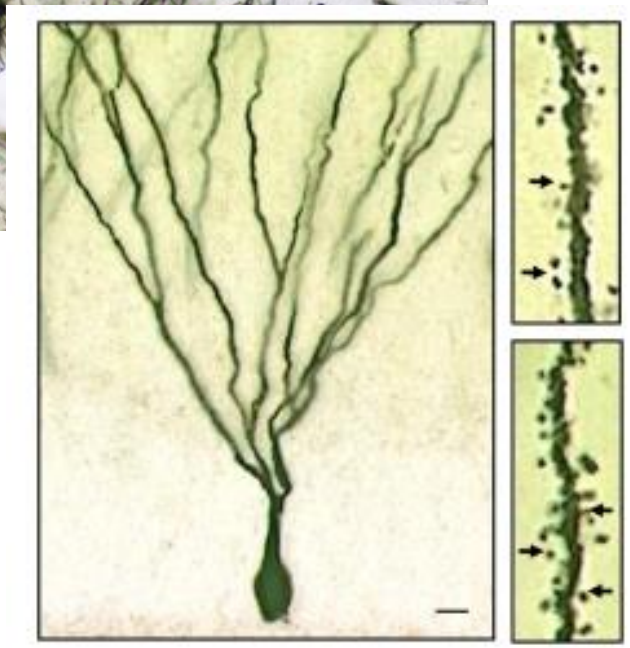
DG – Granule Neuron

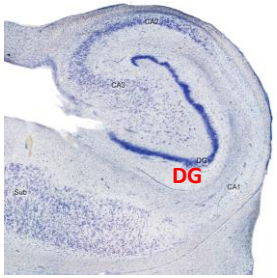


Molecular Layer

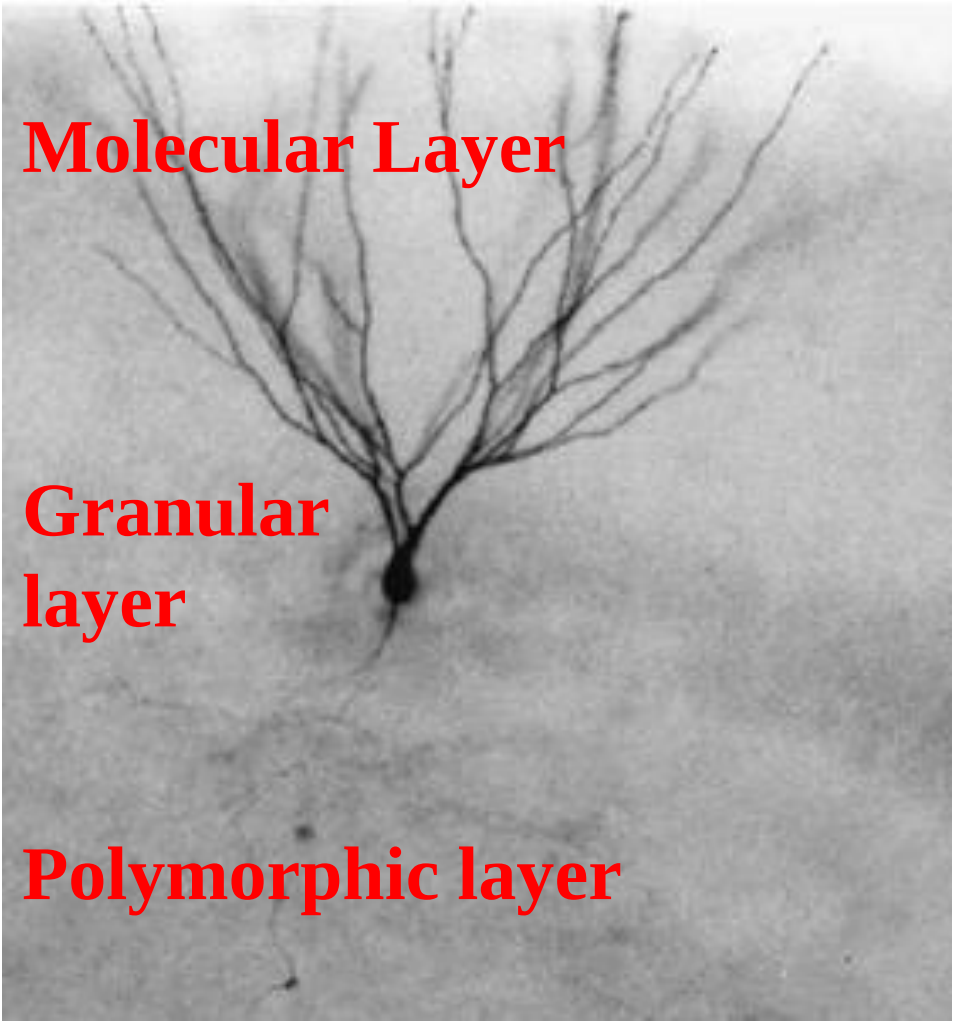
Granule Cell Layer

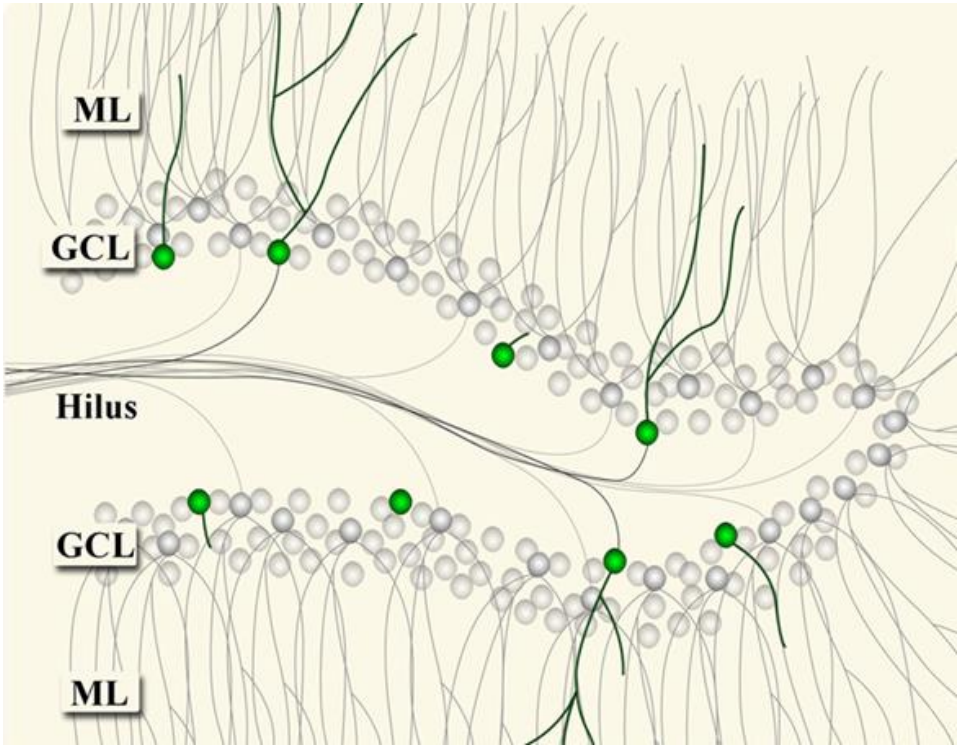
Polymorphic Layer / Hilus





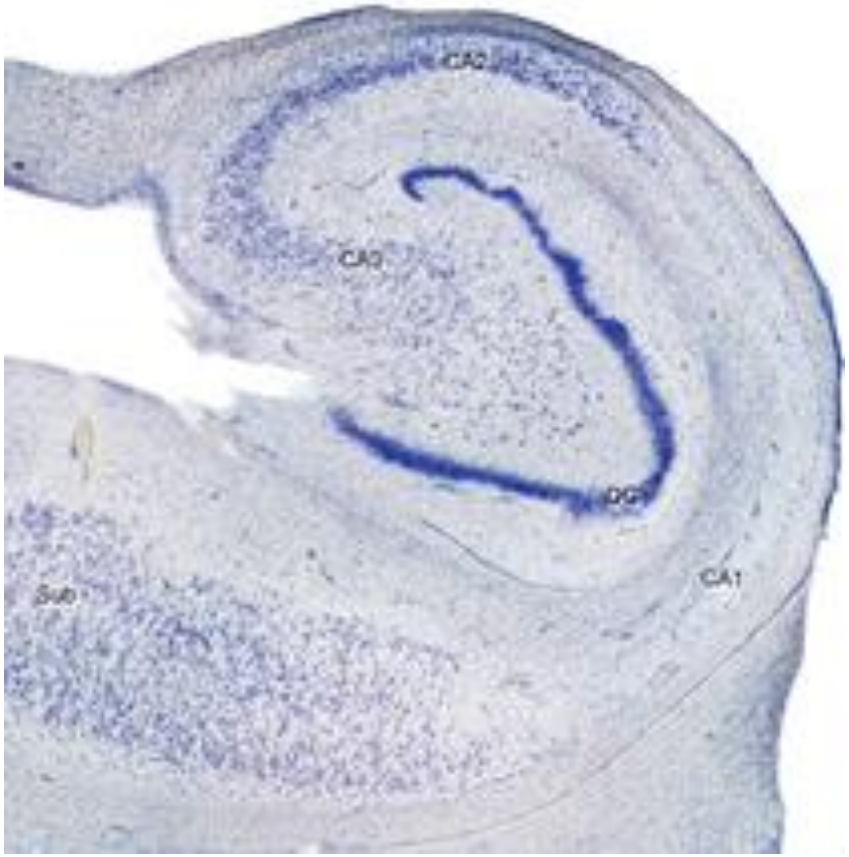
DG – Granule Neuron





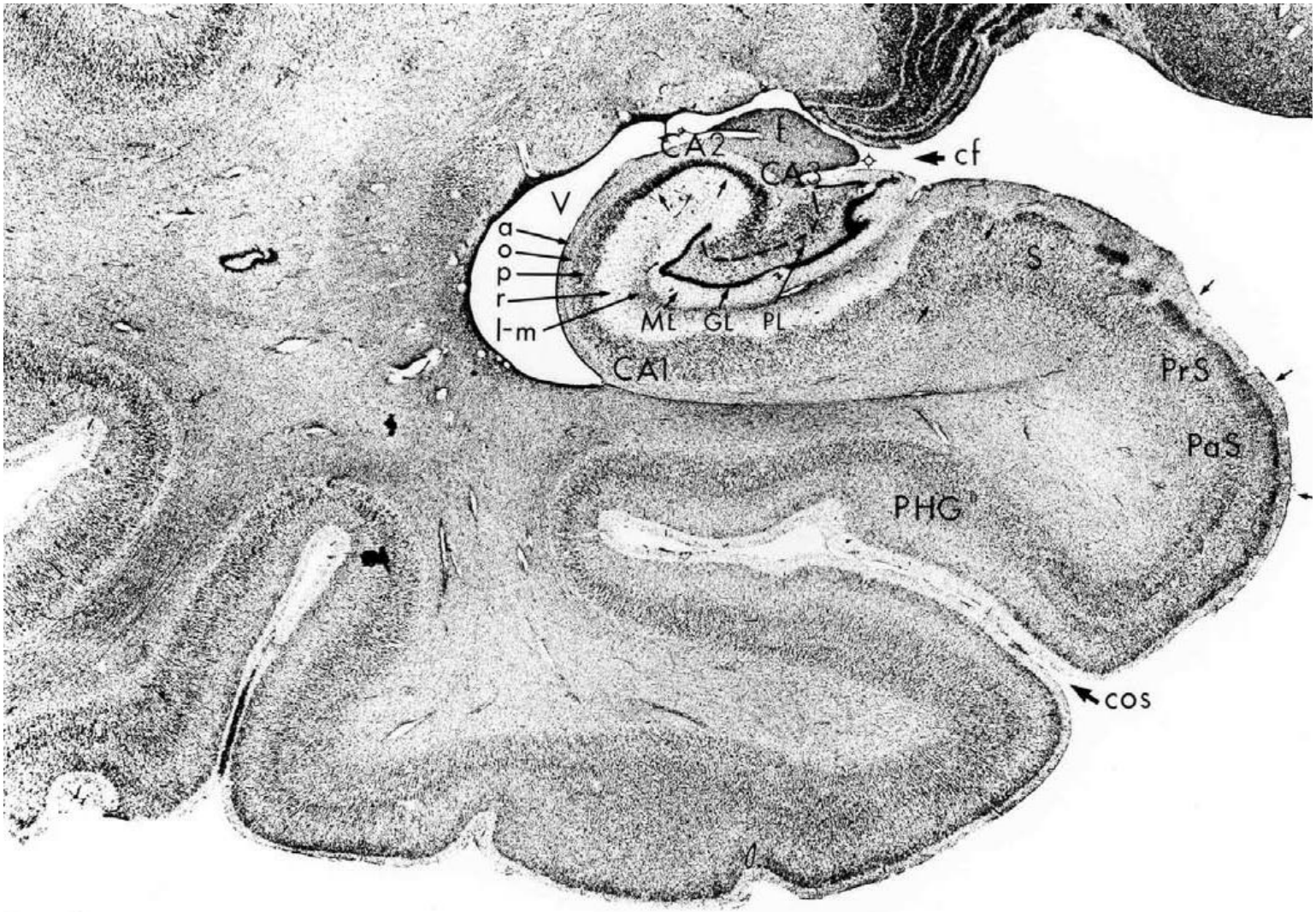
Subiculum

- ✓ Molecular Layer
- ✓ Superficial Pyramidal Layer
- ✓ Deep Pyramidal Layer



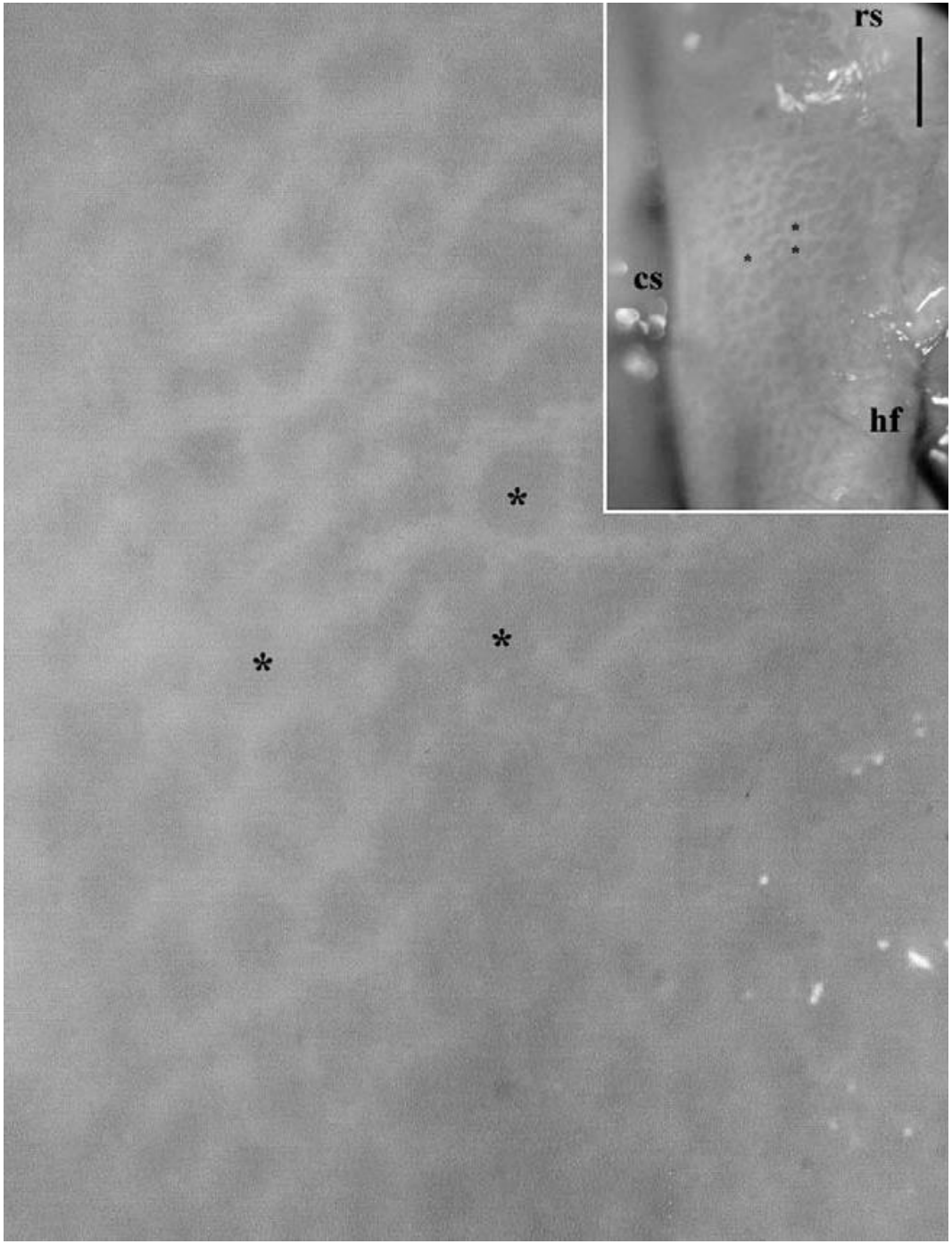
PreSubiculum & ParaSubiculum

✓ One Layer of Modified Pyramidal Neurons



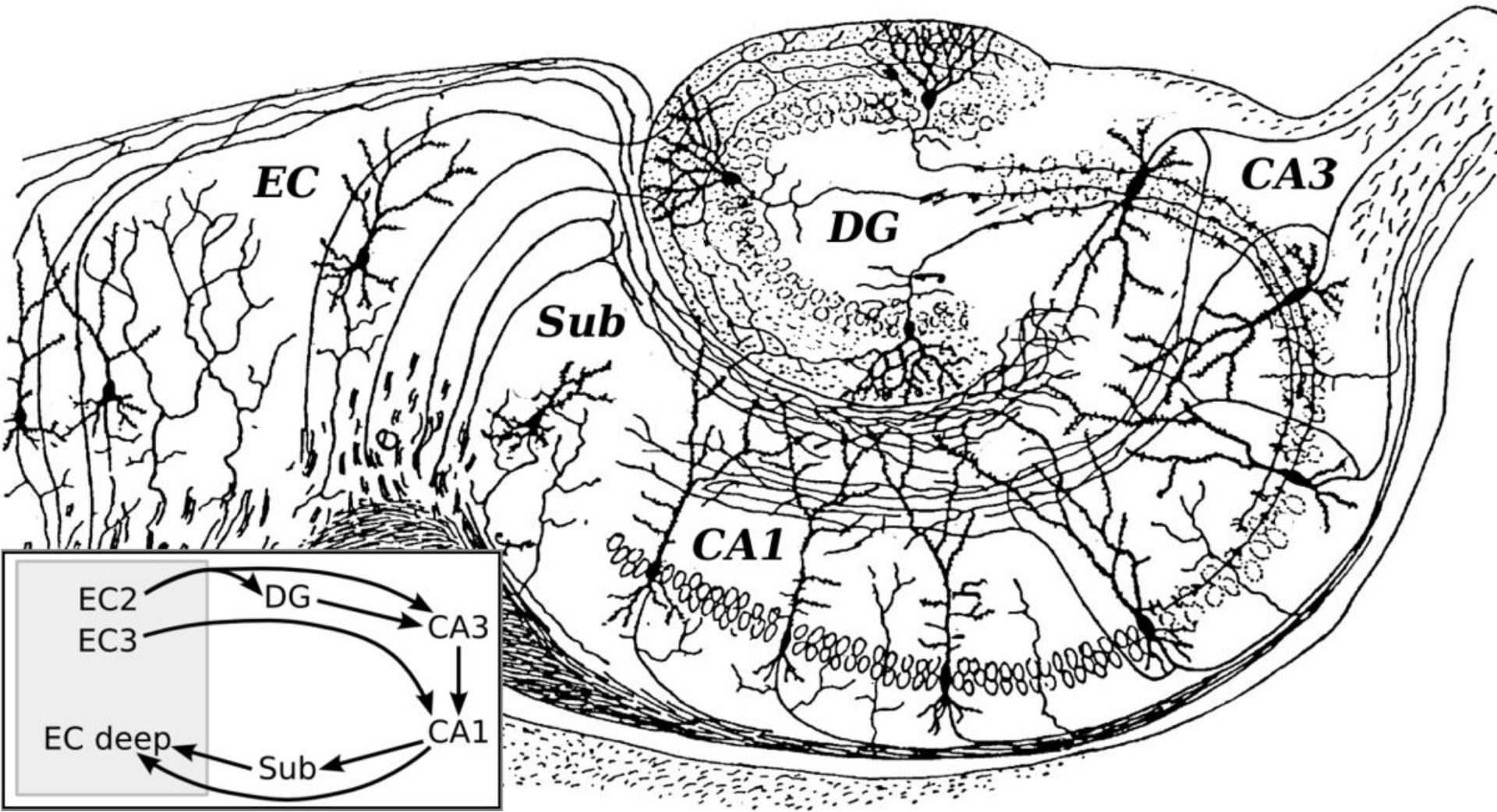
Entorhinal Cortex

- ✓ Six Layers
- ✓ Cell islands in 2nd layer

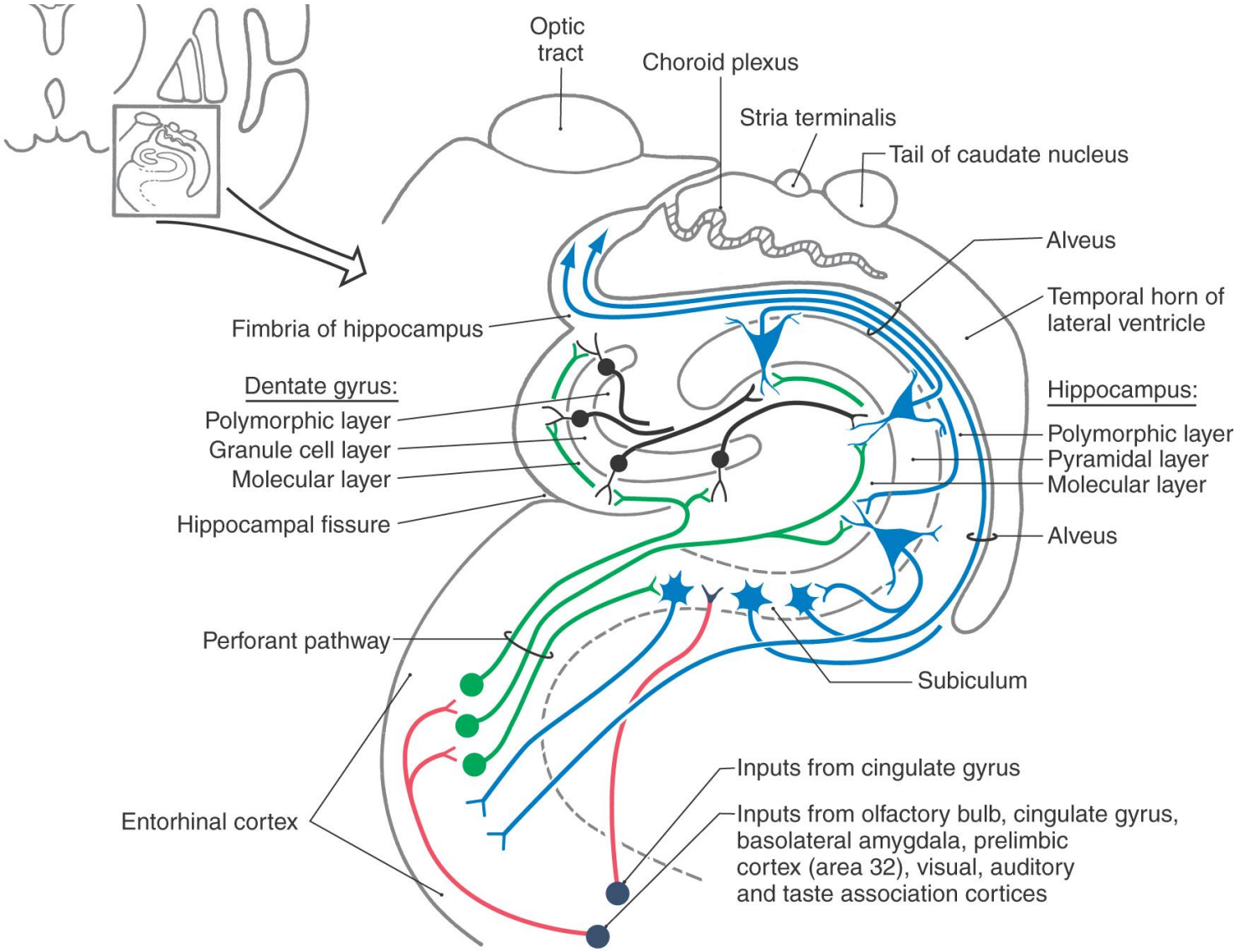


Hippocampal Circuitry

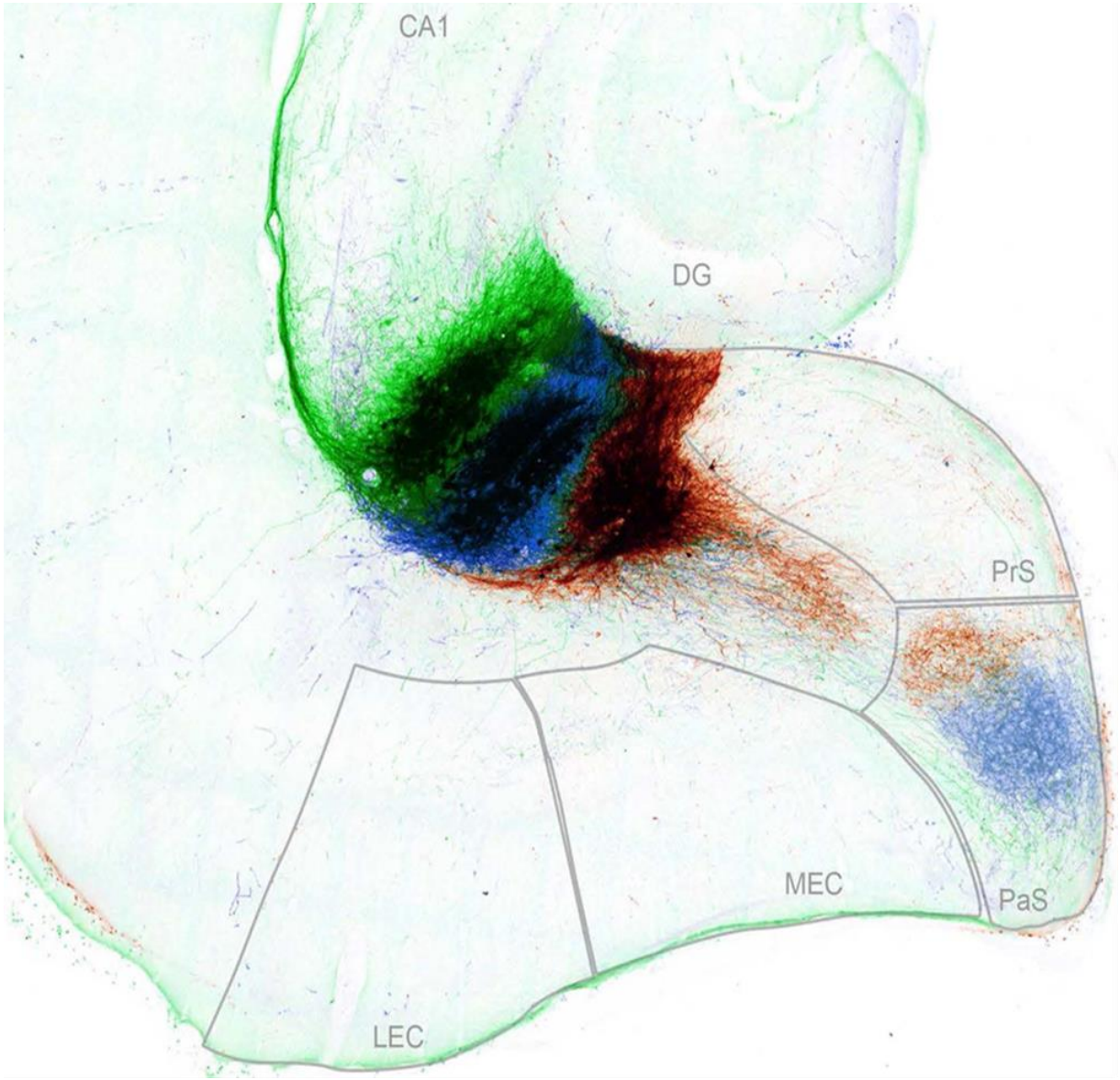
- **Inputs: from entorhinal cortex** ***(collects info from other association areas through perirhinal cortex)***
- **Outputs: to fornix & back to entorhinal cortex**

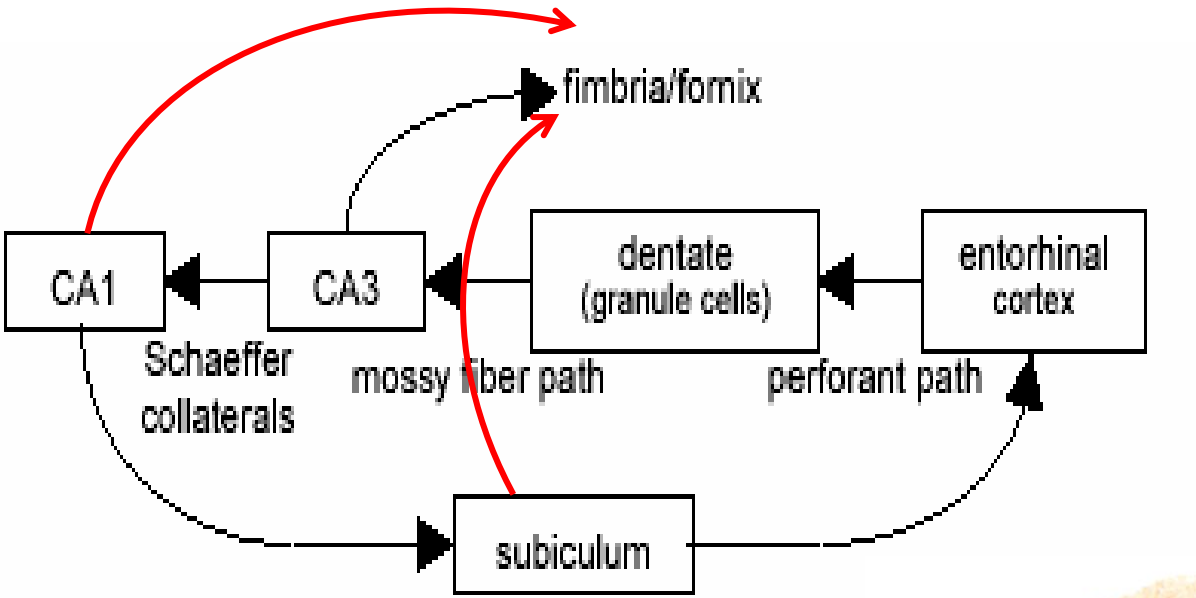


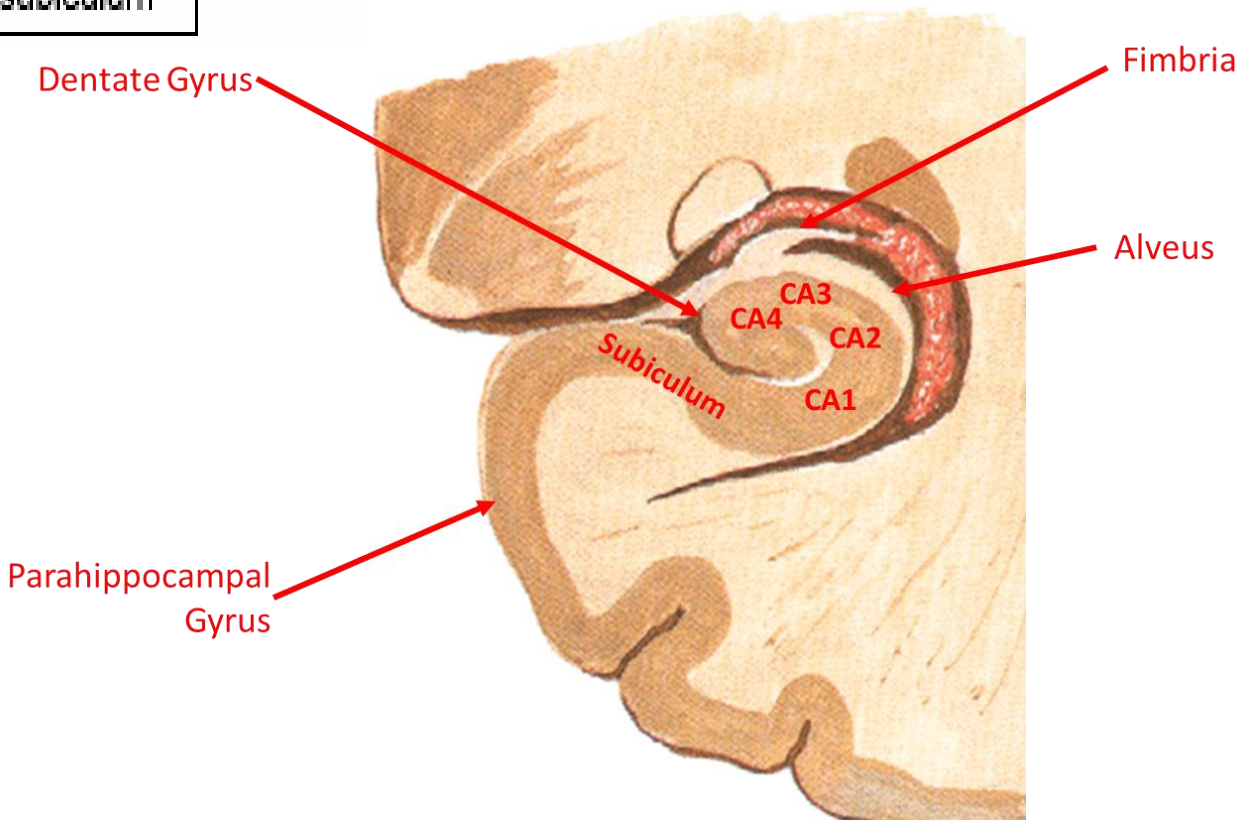
Hippocampal Circuitry

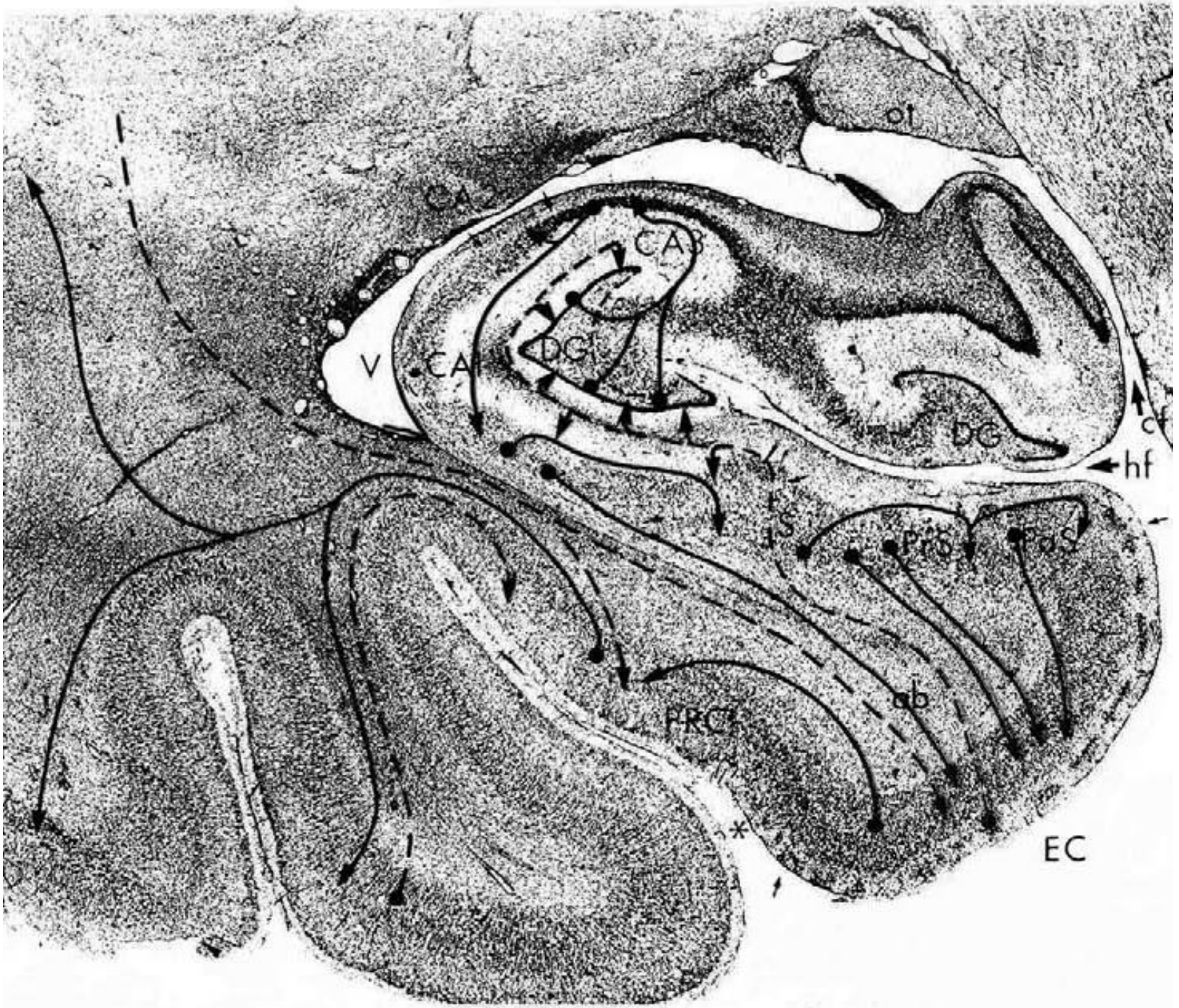


Hippocampal Circuitry




fimbria/fornix
CA1
CA3
dentate
(granule cells)
entorhinal
cortex
Schaeffer
collaterals
mossy fiber path
perforant path
subiculum


Dentate Gyrus
Fimbria
Alveus
CA3
CA4
CA2
Subiculum
CA1
Parahippocampal
Gyrus

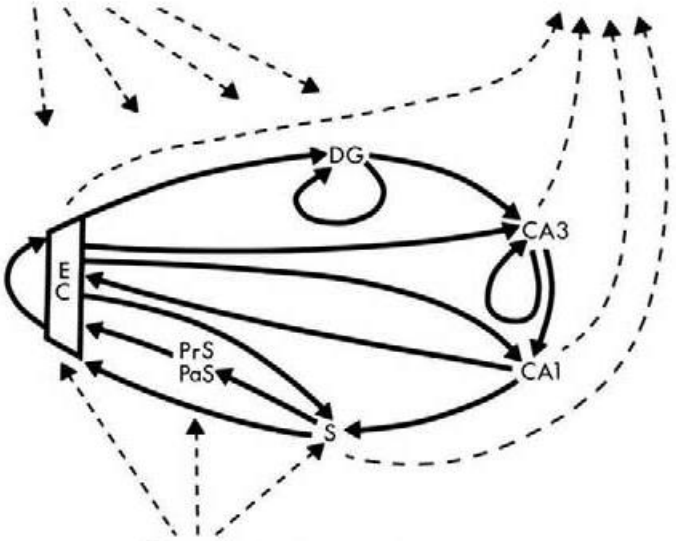

ot
CA
CA3
fp
V
CA1
DG
DG
cf
hf
S
Pro
Pros
ab
PRC
EC

Subcortical Input

AMYGDALA
CLAUSTRUM
SEPTAL NUCLEI
BASAL NUCLEUS (MEYNERT)
SUPRAMAMMILLARY NUCLEUS
ANTERIOR THALAMUS
MIDLINE THALAMUS
VENTRAL TEGMENTAL AREA
RAPHE NUCLEI
LOCUS COERULEUS

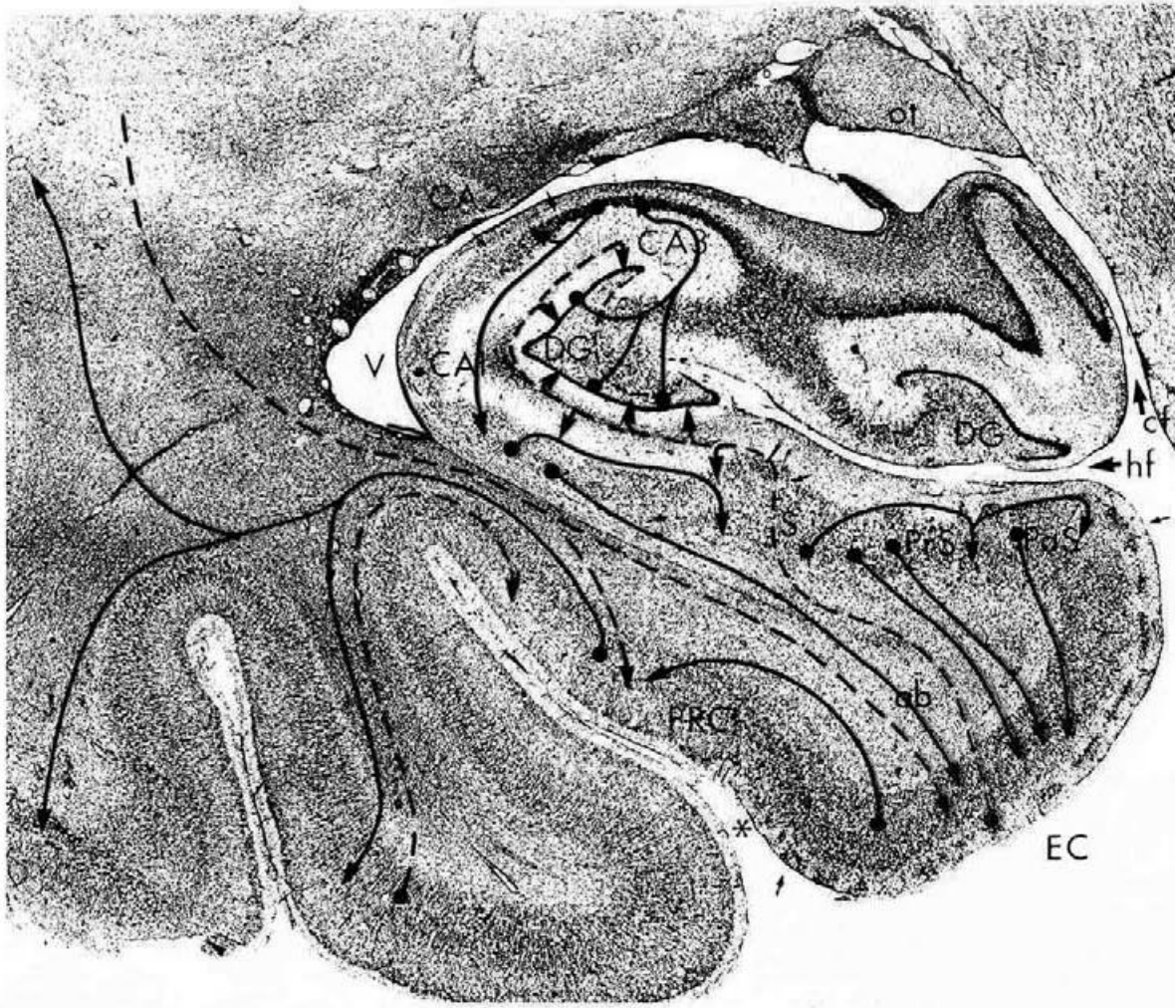
Subcortical Output

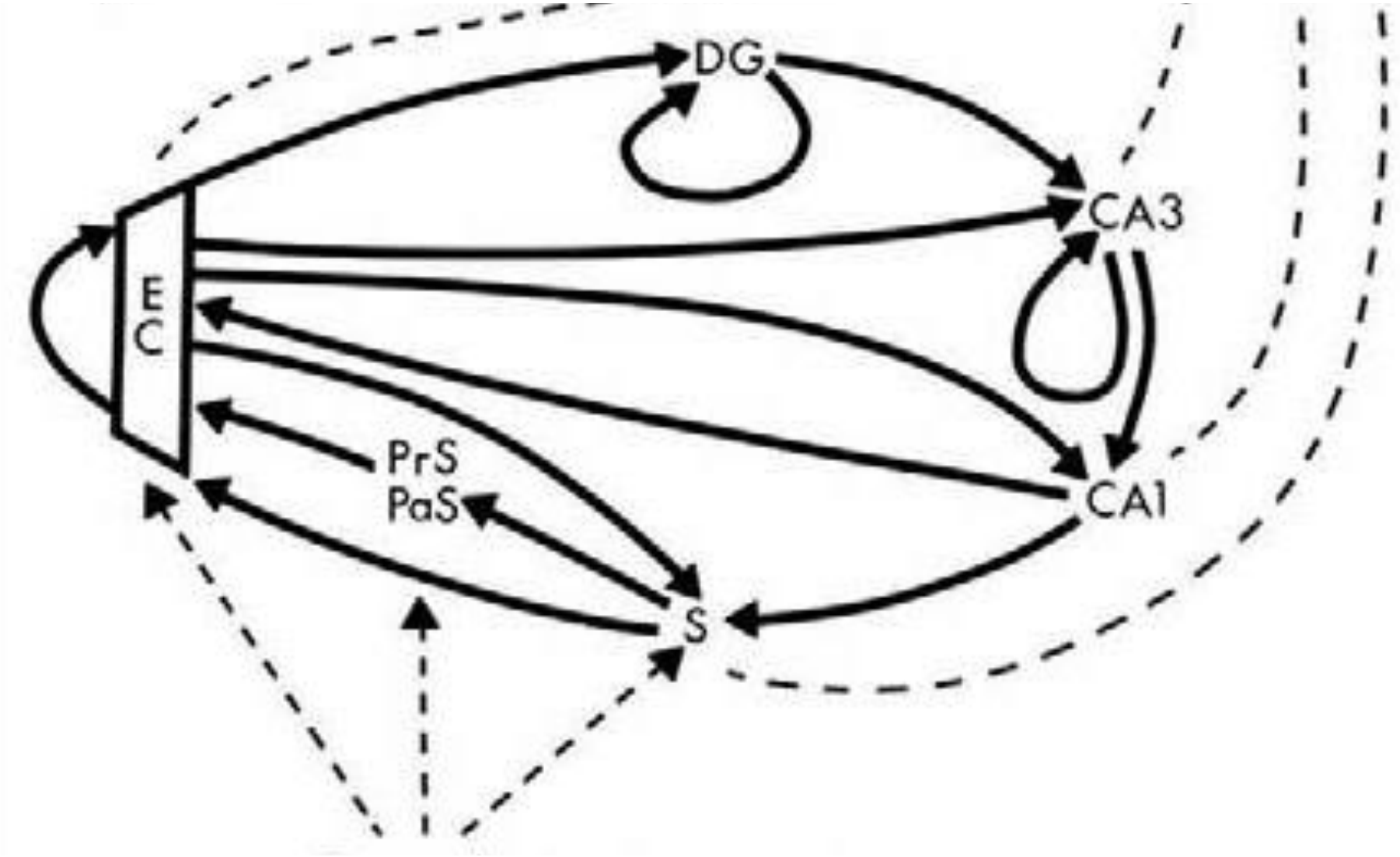
OLFACTORY REGIONS
CLAUSTRUM
AMYGDALA
SEPTAL NUCLEI
NUCLEUS ACCUMBENS
CAUDATE/PUTAMEN
HYPOTHALAMUS
ANTERIOR THALAMUS
MAMMILLARY NUCLEI

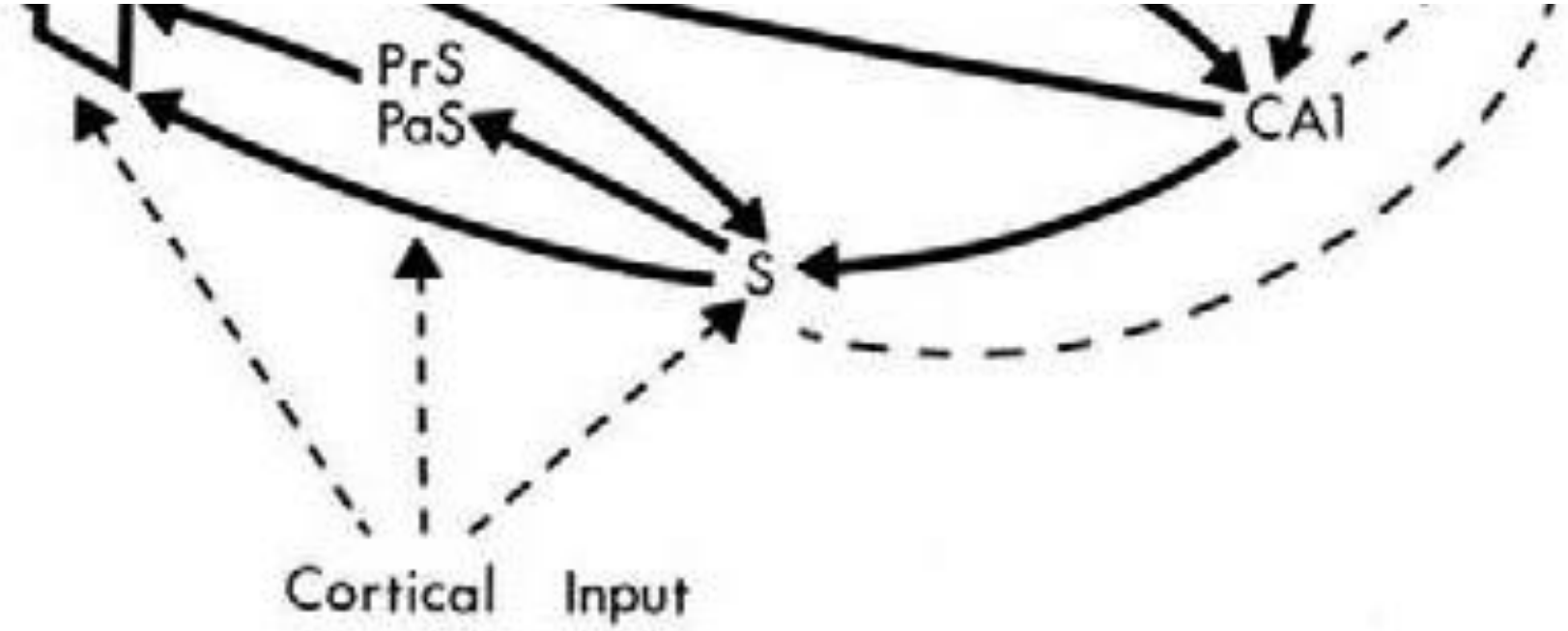


Cortical Input

PERIRHINAL CORTEX (AREAS 35 AND 36)
PARAHIPPOCAMPAL GYRUS (AREAS TF AND TH)
CINGULATE CORTEX
PIRIFORM CORTEX
INSULAR CORTEX
ORBITOFRONTAL CORTEX
SUPERIOR TEMPORAL GYRUS




DG
CA3
EC
PrS
PaS
CA1
S



PERIRHINAL CORTEX (AREAS 35 AND 36)
PARAHIPPOCAMPAL GYRUS (AREAS TF AND TH)
CINGULATE CORTEX
PIRIFORM CORTEX
INSULAR CORTEX
ORBITOFRONTAL CORTEX
SUPERIOR TEMPORAL GYRUS

Subcortical Input

- Amygdala
- Claustrum
- Septal nuclei
- Basal nucleus (Meynert)
- Supramammillary nucleus
- Anterior thalamus
- Midline thalamus
- Ventral tegmental area
- Raphe nuclei
- Locus coeruleus

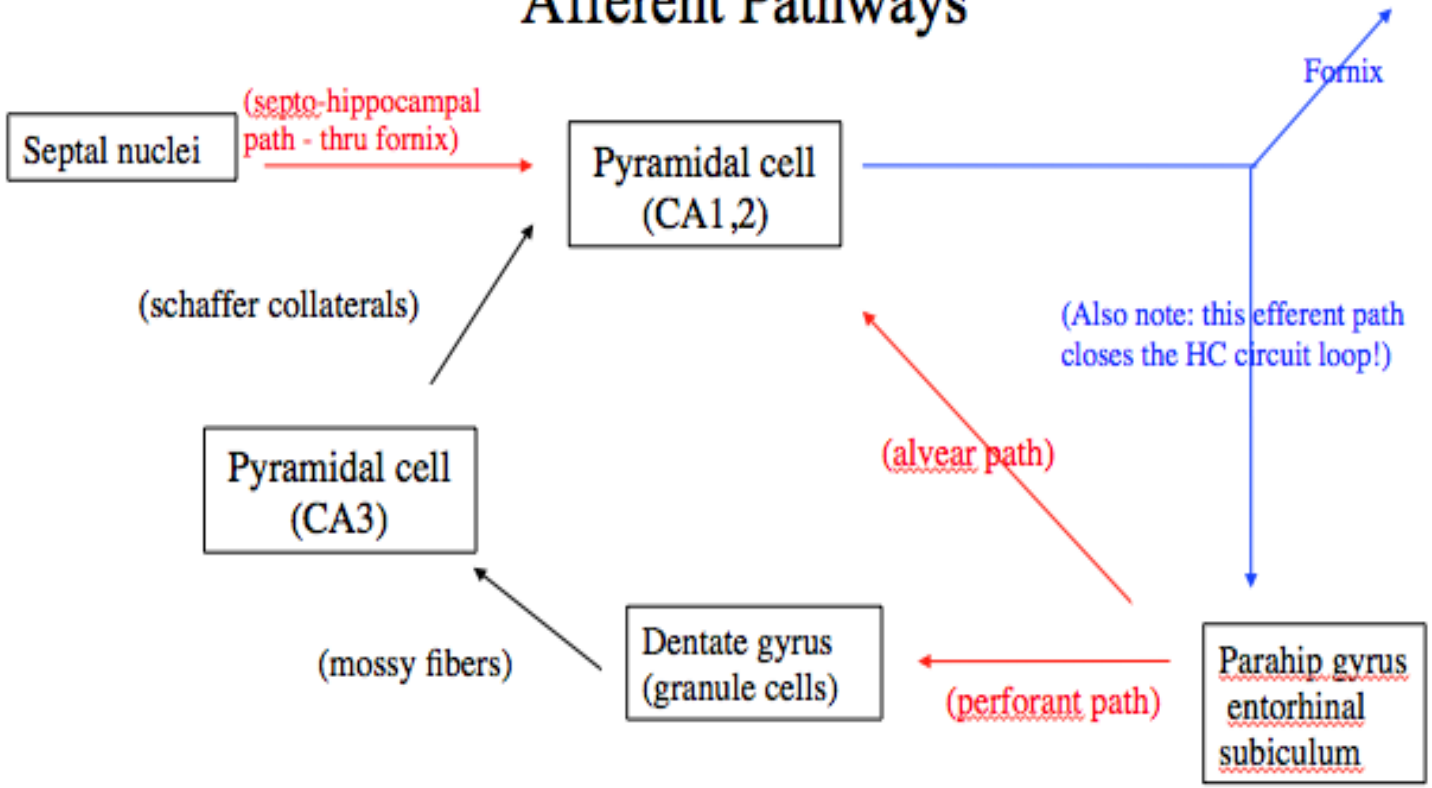
Subcortical Output

- Olfactory regions
- Claustrum
- Amygdala
- Septal nuclei
- Nucleus accumbens
- Caudate/Putamen
- Hypothalamus
- Anterior thalamus
- Mammillary nuclei

The Hippocampus Dentate Complex

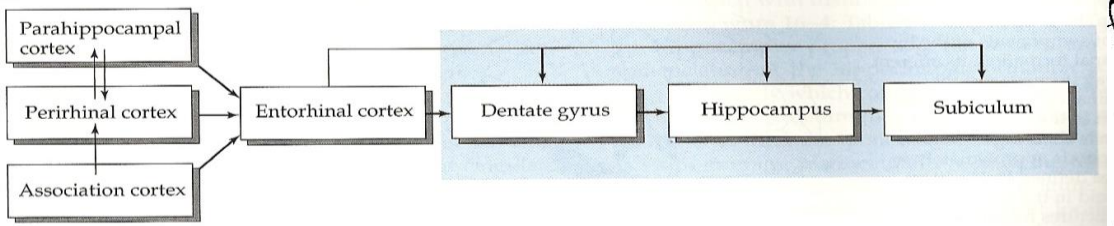
(HC-DG)

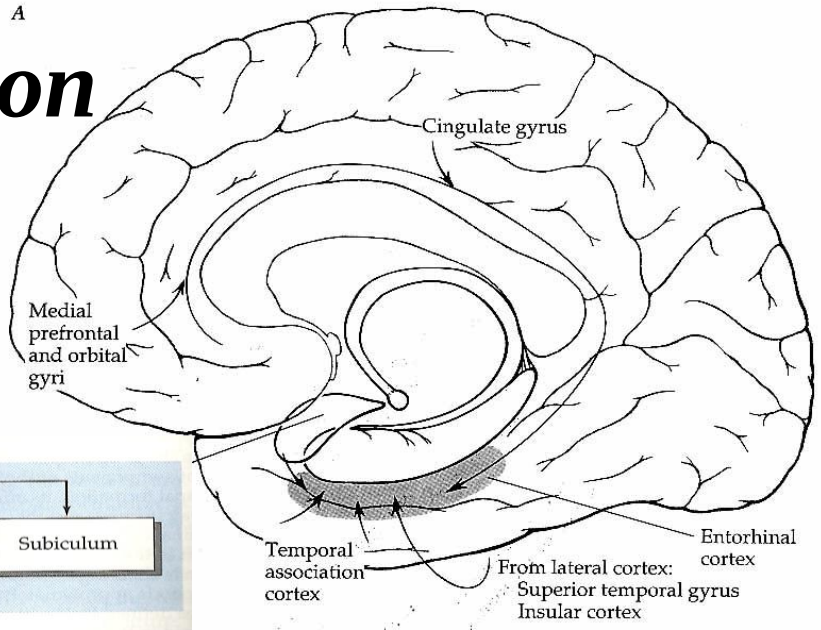
Afferent Pathways



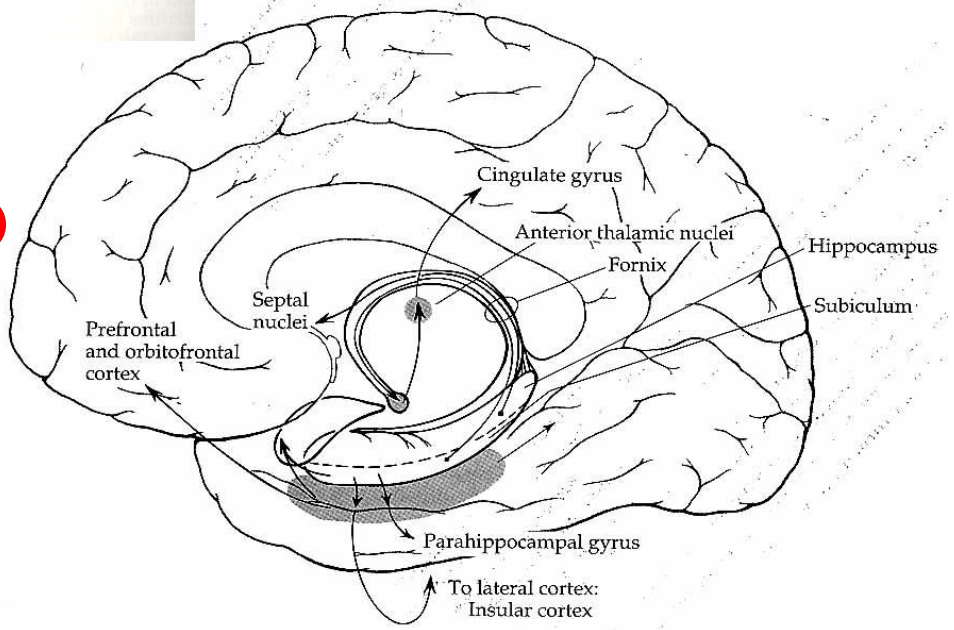
Circuitry of the Hippocampal Formation

Afferent (Input)



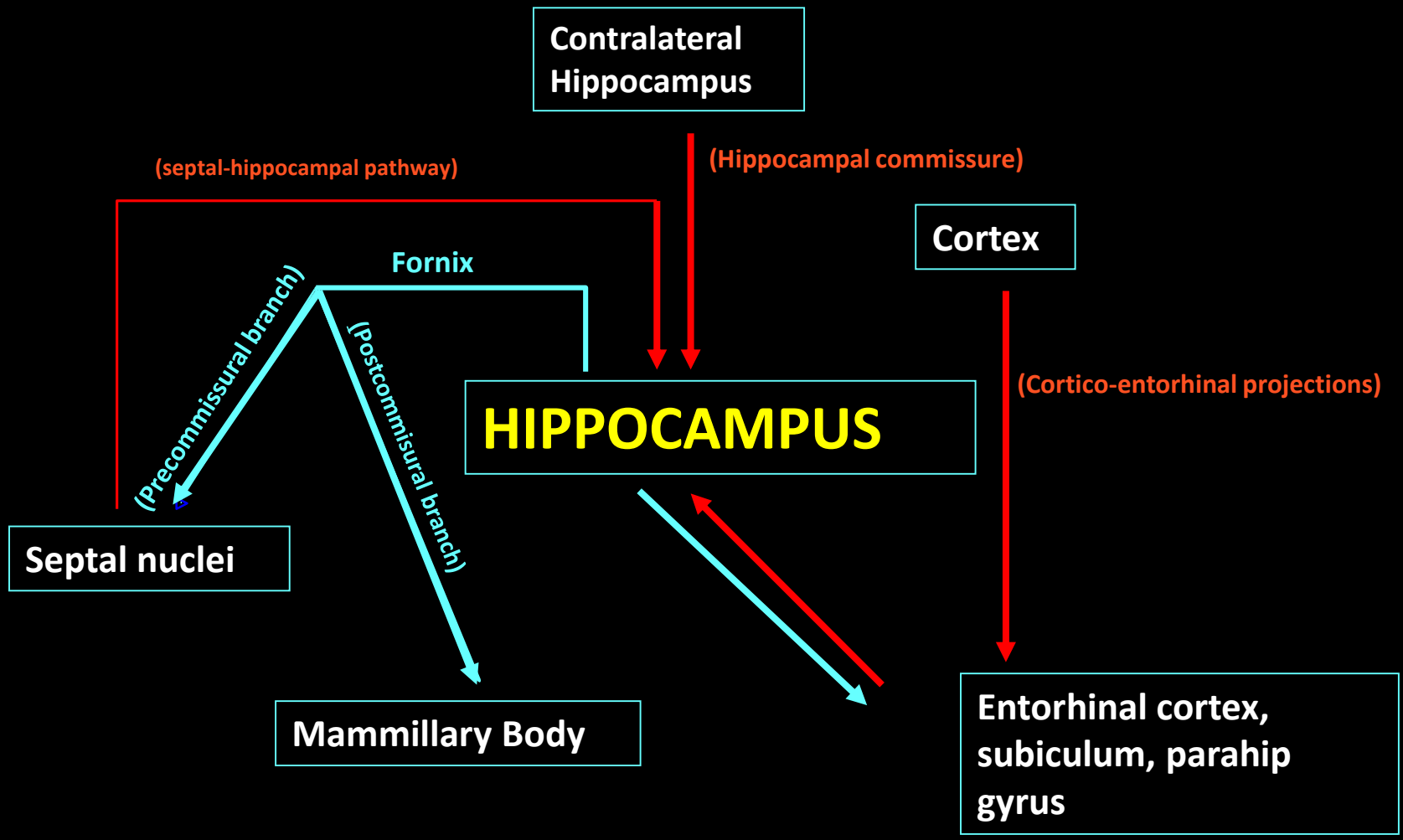


Efferent (Output)



Circuitry of the Hippocampal Formation

Afferents
Efferents

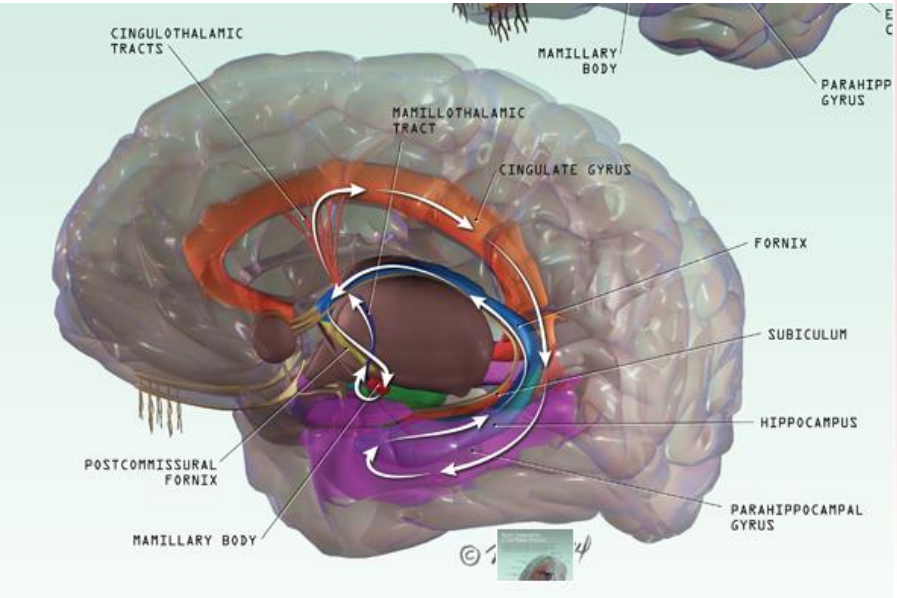


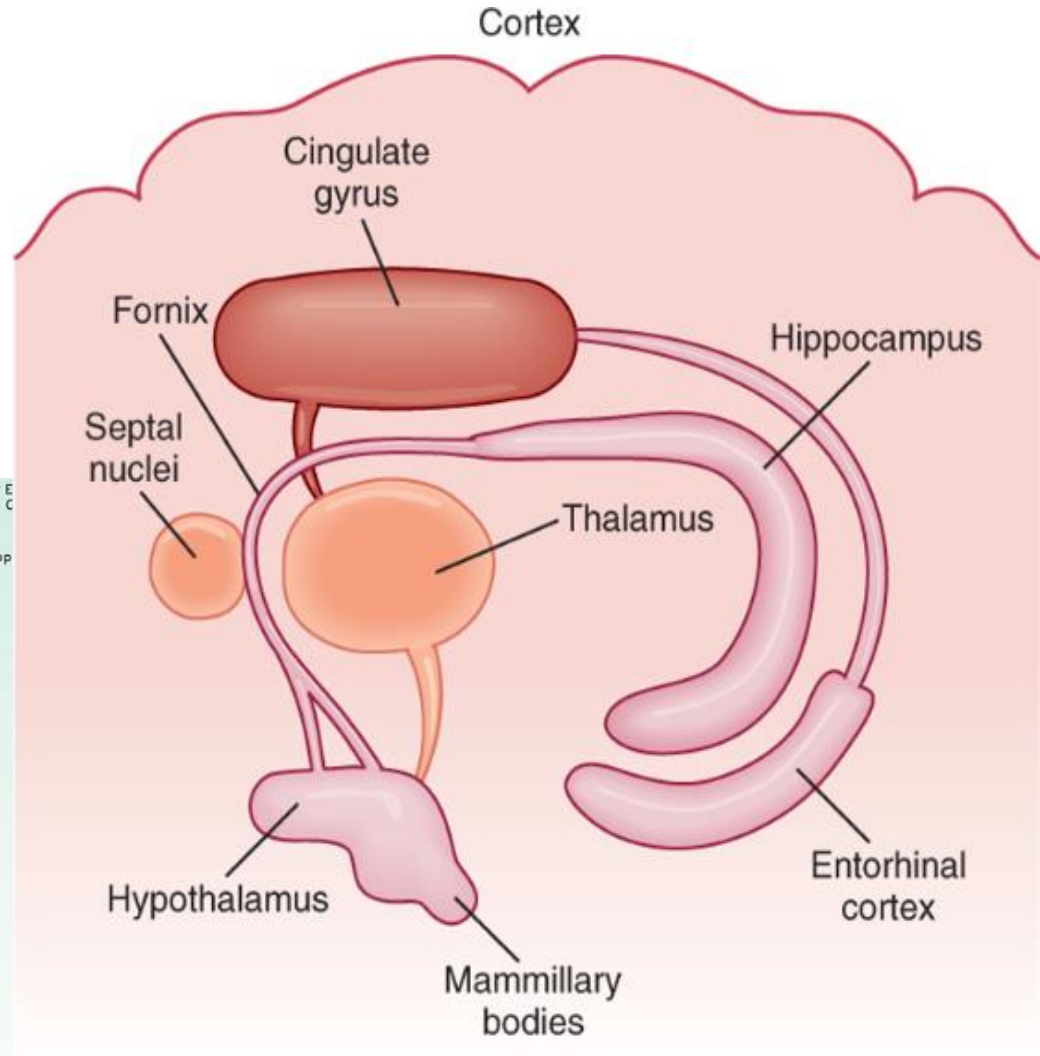
Papez Circuit

Provides a bridge between:

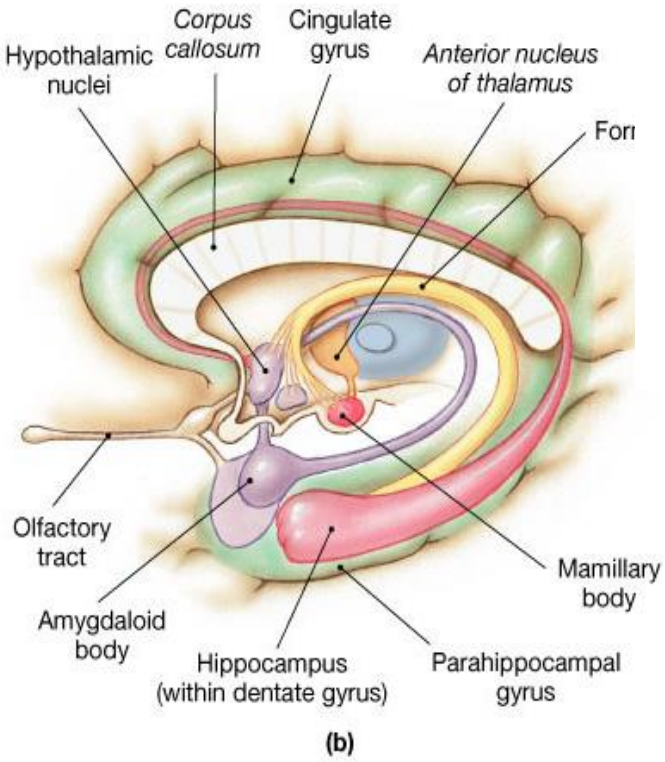
- endocrine
- visceral
- emotional
- voluntary

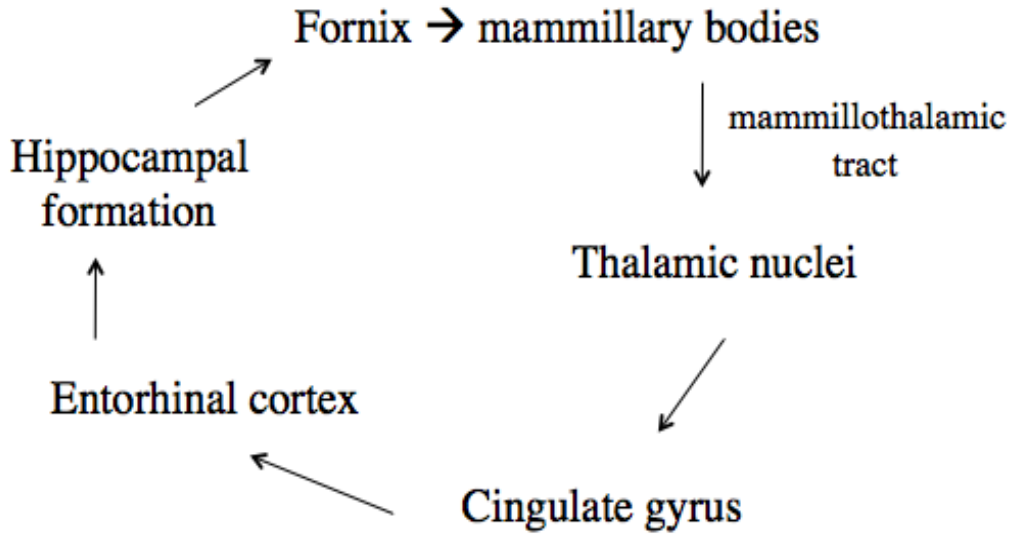
responses to environment





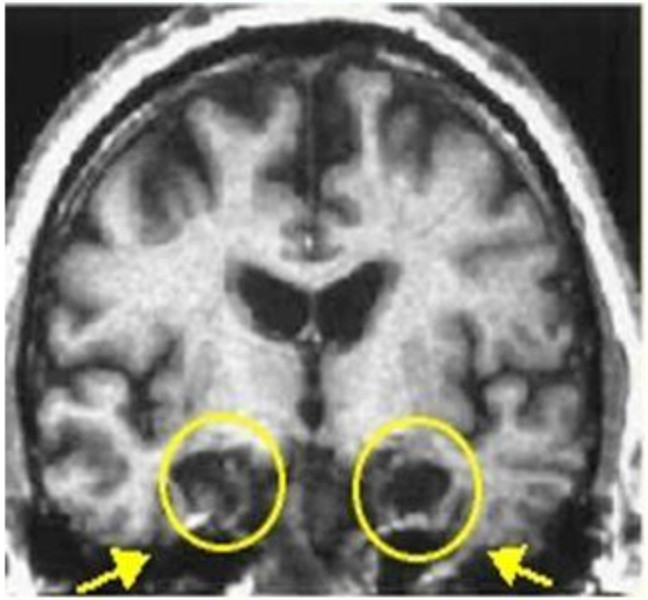
Papez Circuit





Input for memory consolidation

Henry Gustav Molaison



Patient HM

Born: February 26, 1926
Surgery: September 1, 1953 (age 27)
Died: December 2, 2008 (age 82)

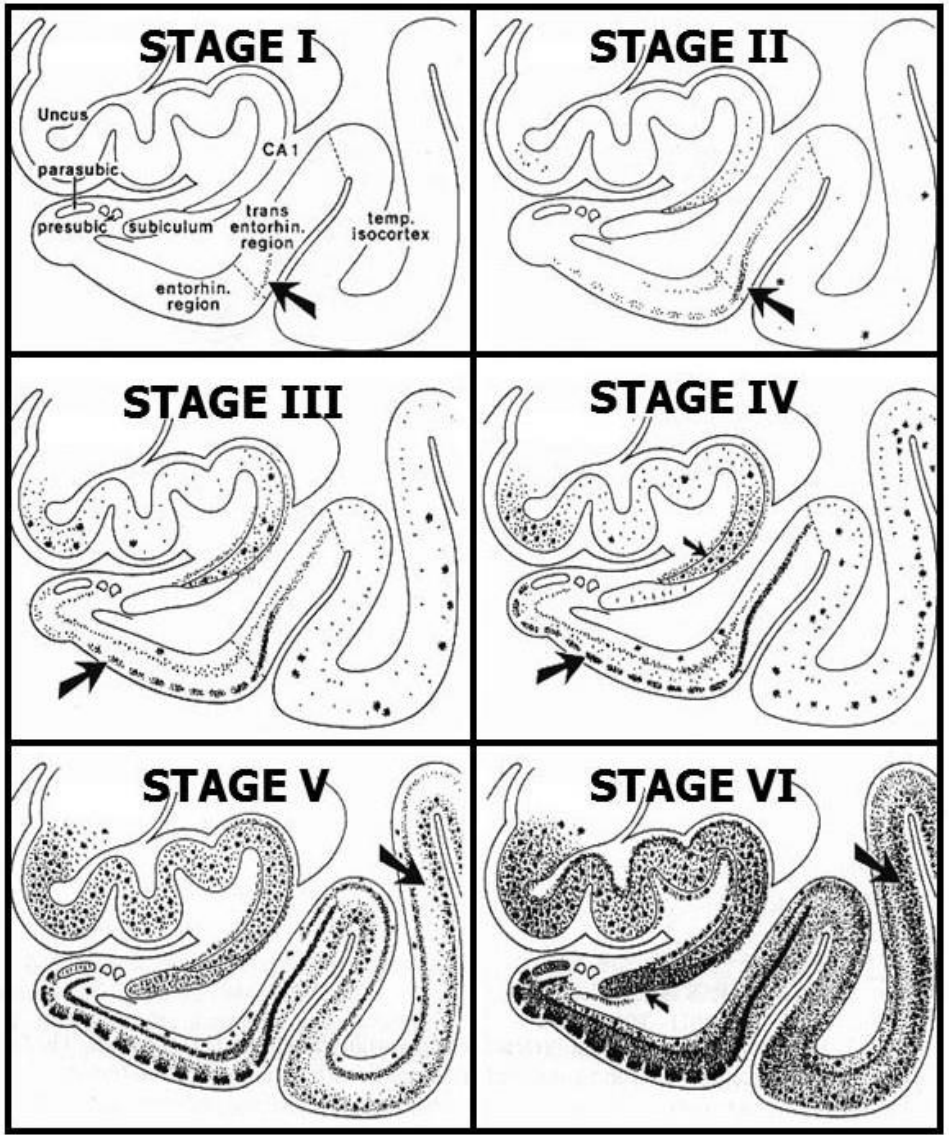
- Severe anterograde declarative memory disorder
- Retrograde memory disorder back 11 years
- Intact: immediate memory, procedural memory, priming, & release from proactive interference

Scoville WB, Milner B. Loss of recent memory after bilateral hippocampal lesions. J Neurol Neurosurg Psychiatr 1957;20:11-21.

Hippocampal Formation ***Functions***

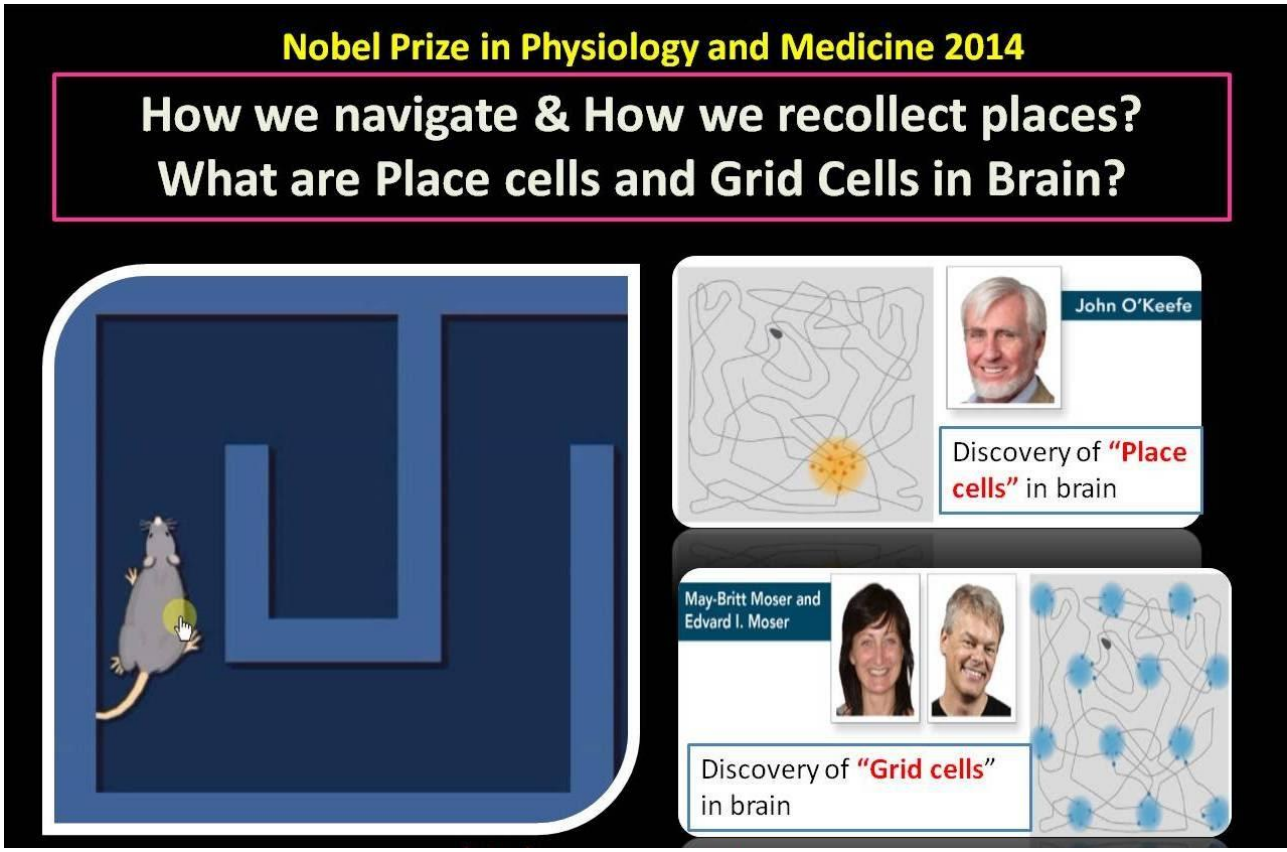
- ✓ **Learning & Memory**
- ✓ **Spatial Memory & Navigation**
- ✓ **Behavior**

Alzheimer's Disease



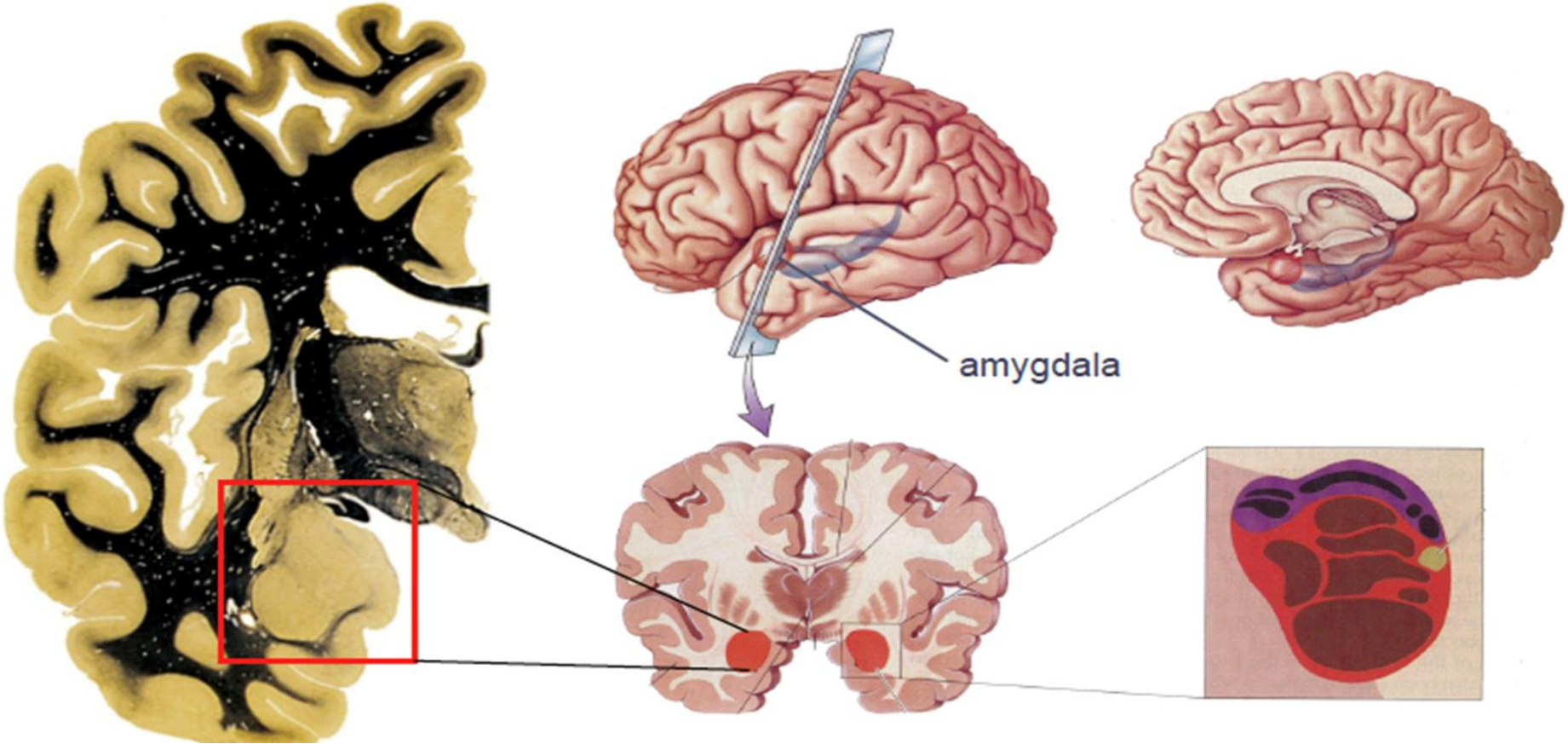
Hippocampal Formation
Functions

- ✓ **Learning & Memory**
- ✓ **Spatial Memory & Navigation**
- ✓ **Behavior**

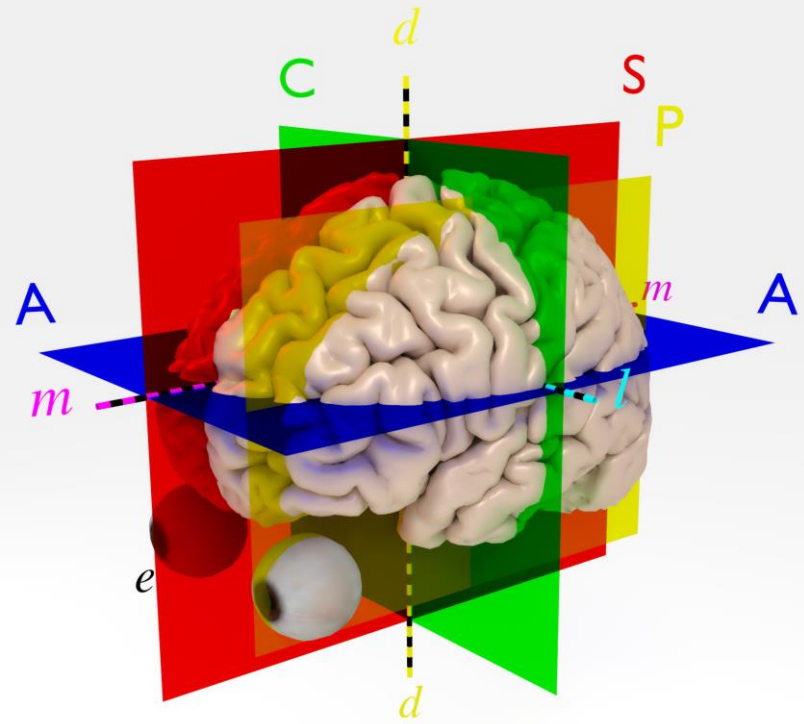


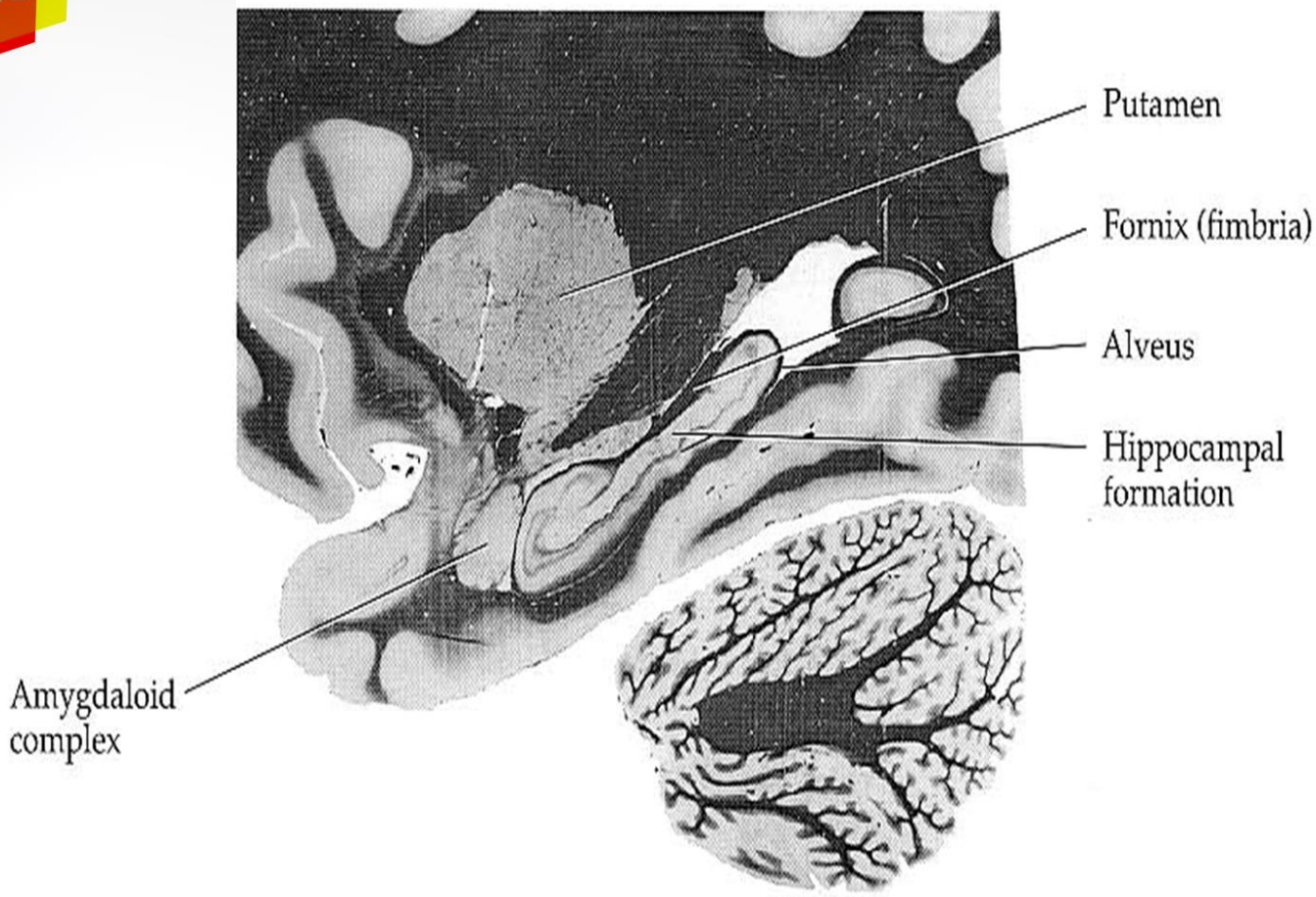
Amygdala

- ✓ **Almond shape**
- ✓ **Anterior – superior to tip of temporal horn of lateral ventricle**



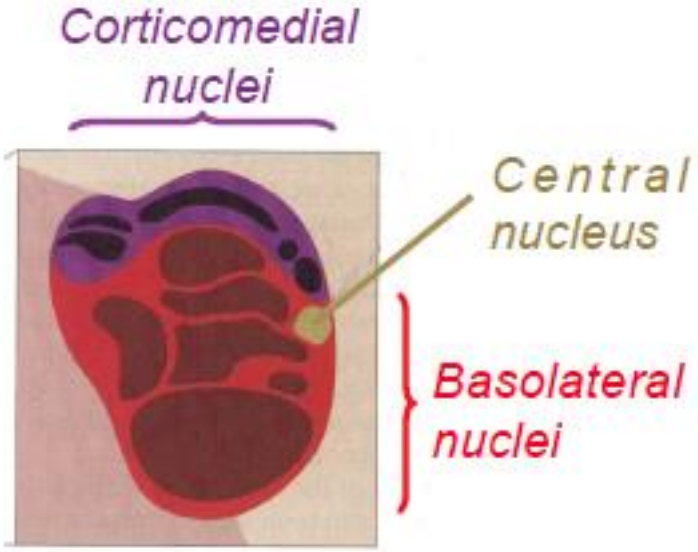
Parasagittal plane

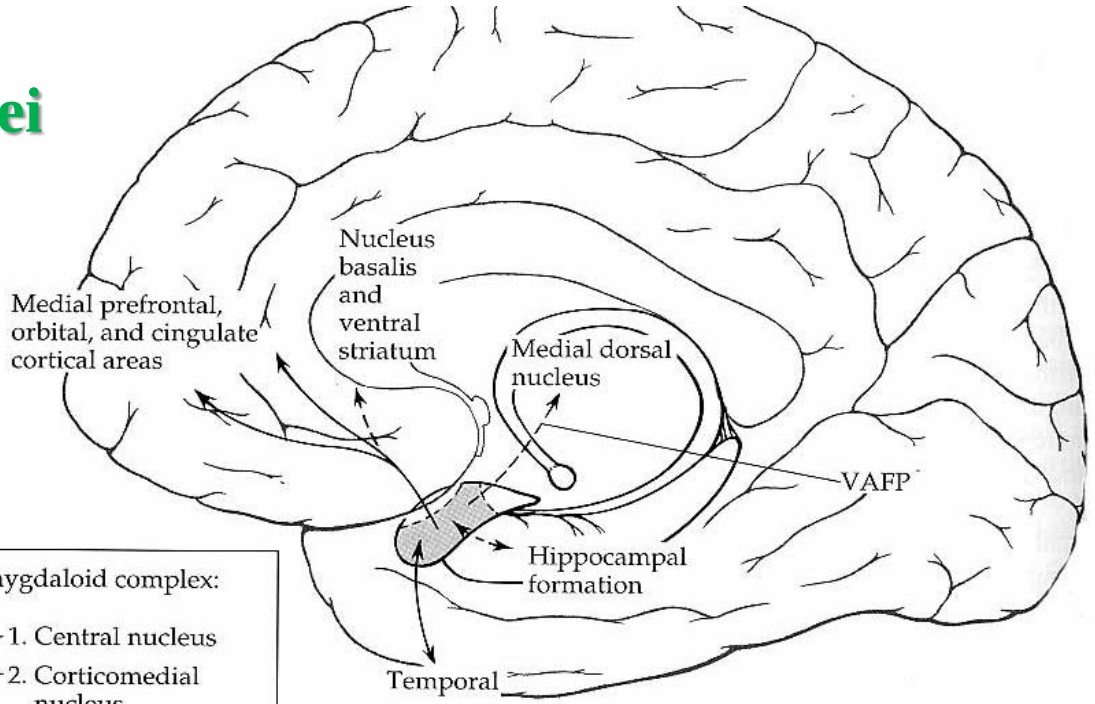


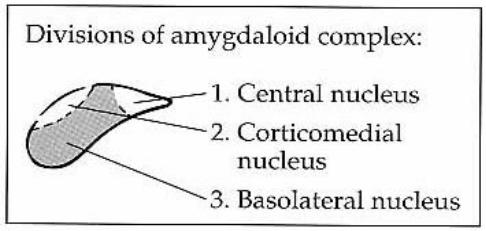


Amygdala

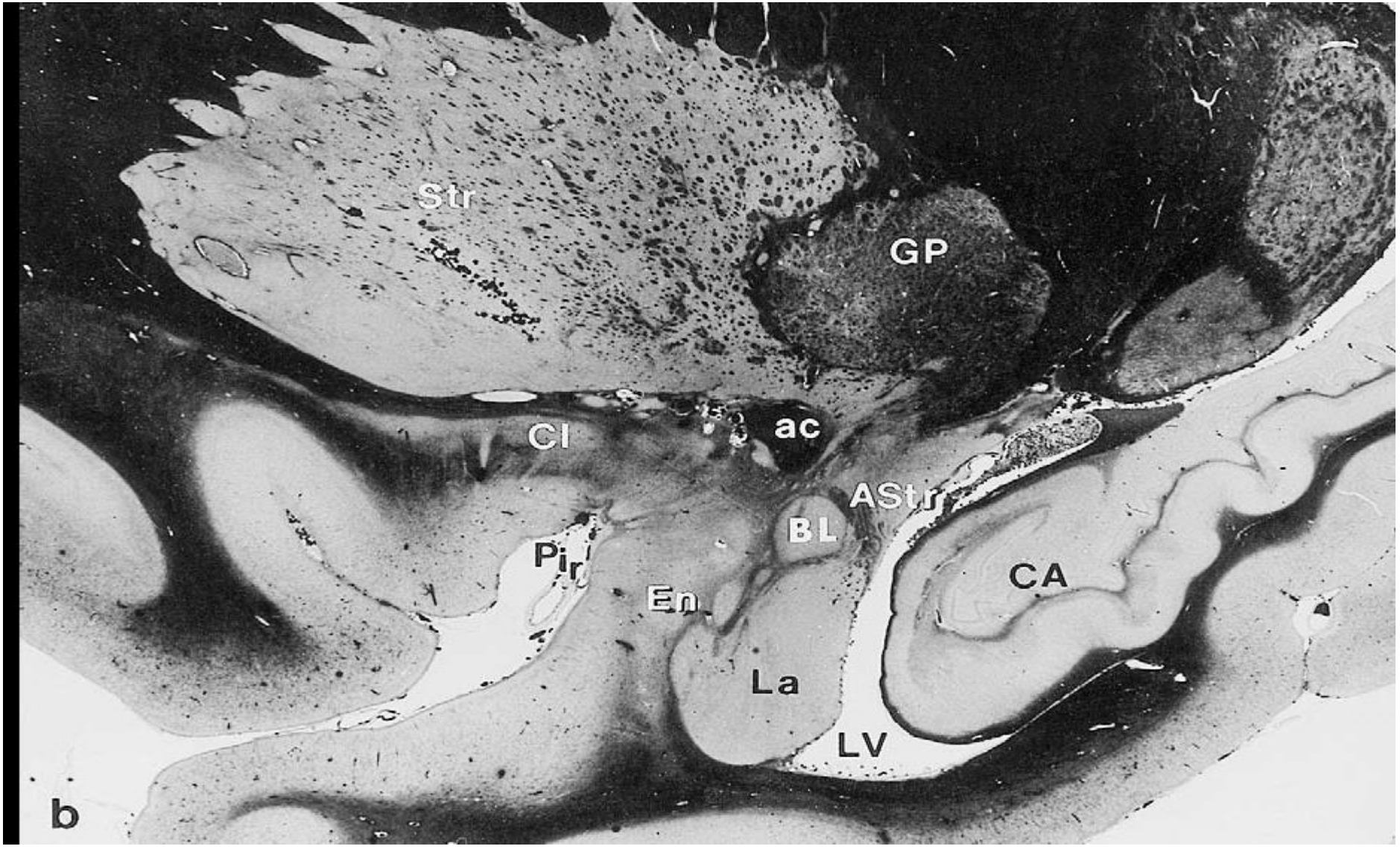
- ✓ **About 27 subnuclei**
- ✓ **Major function: responding to stimuli with an *emotional component***
- ✓ **Grouped:**
  - **Corticomedial nuclei**
  - **Basolateral nuclei**
  - **Central nucleus**





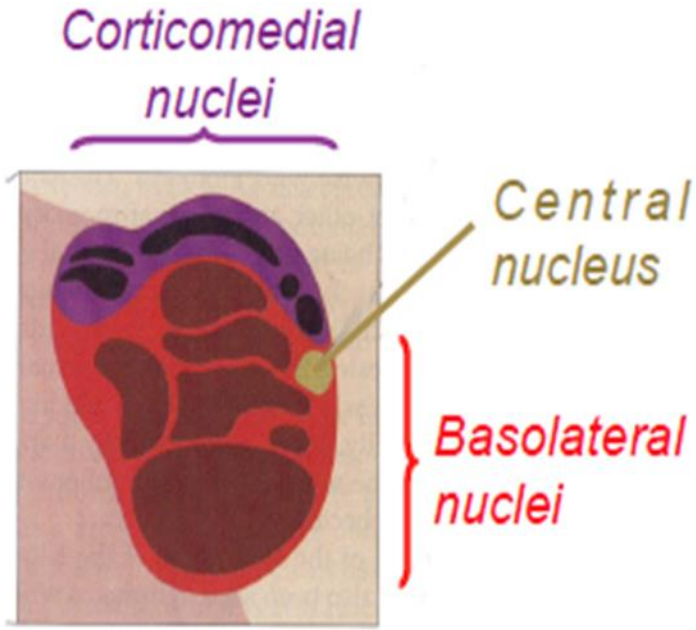


Amygdala
Basolateral nuclei



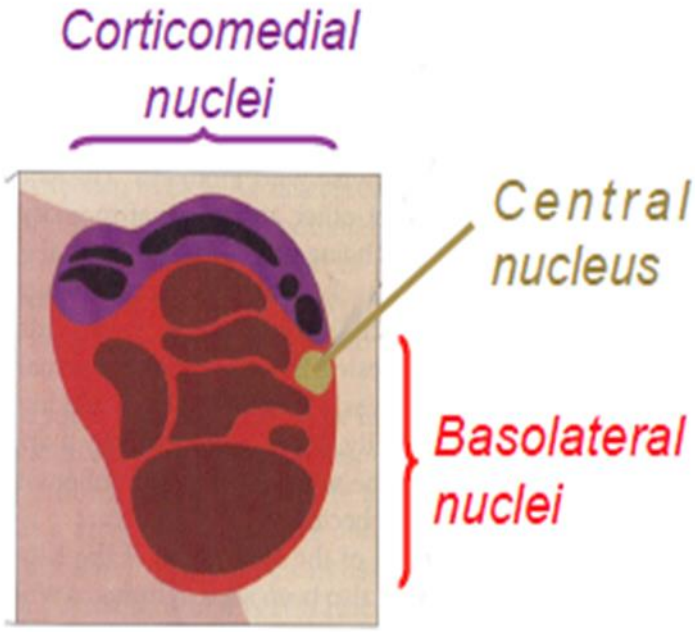
Amygdala
Basolateral nuclei

- ✓ **Attaches emotional significance to a stimulus**
- ✓ **Receives input from sensory cortices**
- ✓ **Sends output to limbic association cortex, prefrontal cortex & hippocampal formation**
- ✓ **Learning emotional significance**

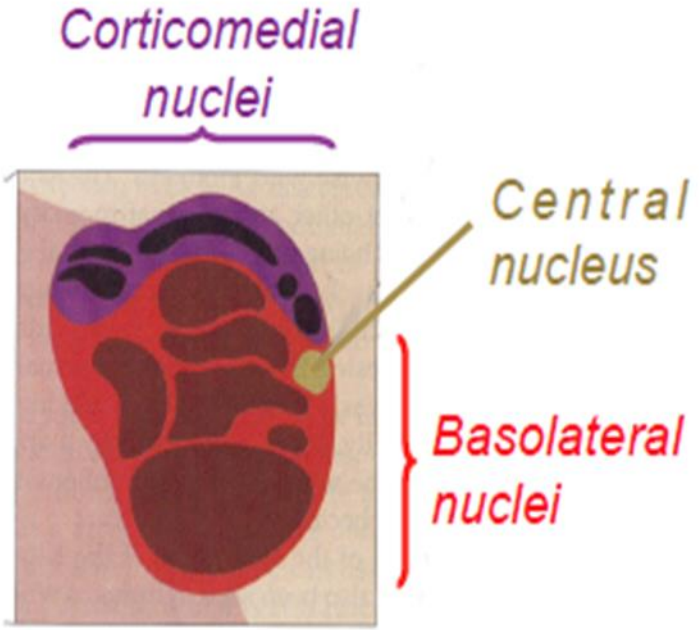


Amygdala
Central nucleus

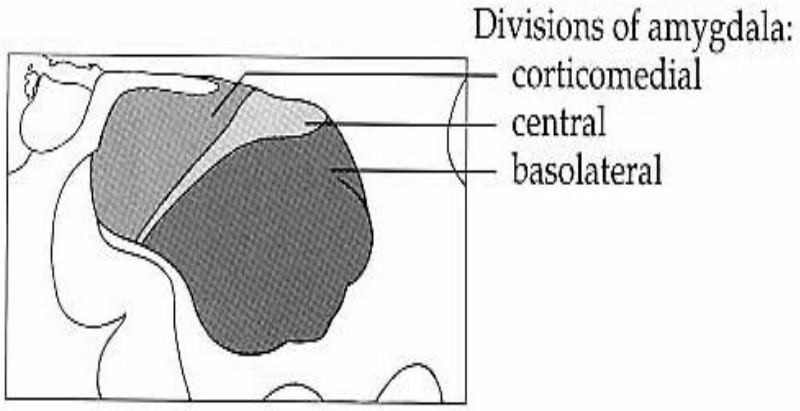
- ✓ **Mediates emotional and autonomic responses**
- ✓ **Receives input from solitary, parabrachial nuclei**
- ✓ **Sends output to dorsal motor nucleus of vagus nerve (X), other parasympathetic nuclei, reticular formation & hypothalamus**



Amygdala
Corticomedial nuclei

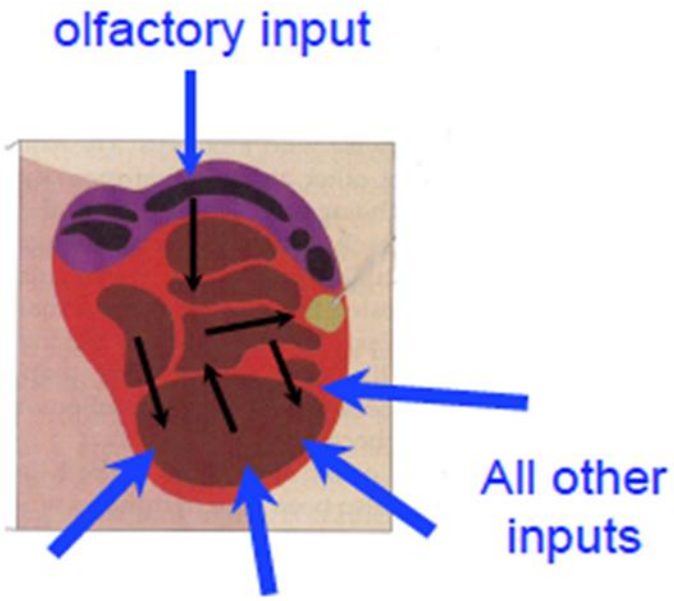


- ✓ **Mediates behaviors triggered by olfactory stimuli**
- ✓ **Receives input from olfactory bulb**
- ✓ **Sends output to hypothalamus**
- ✓ **Regulates "appetitive behaviors" (eg eating in response to smells)**



✓ Corticomedial nuclei

- **Receive olfactory input**

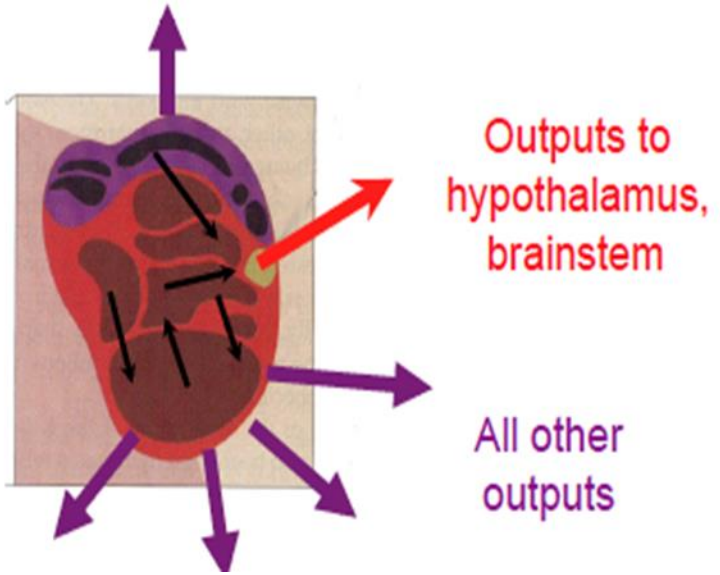


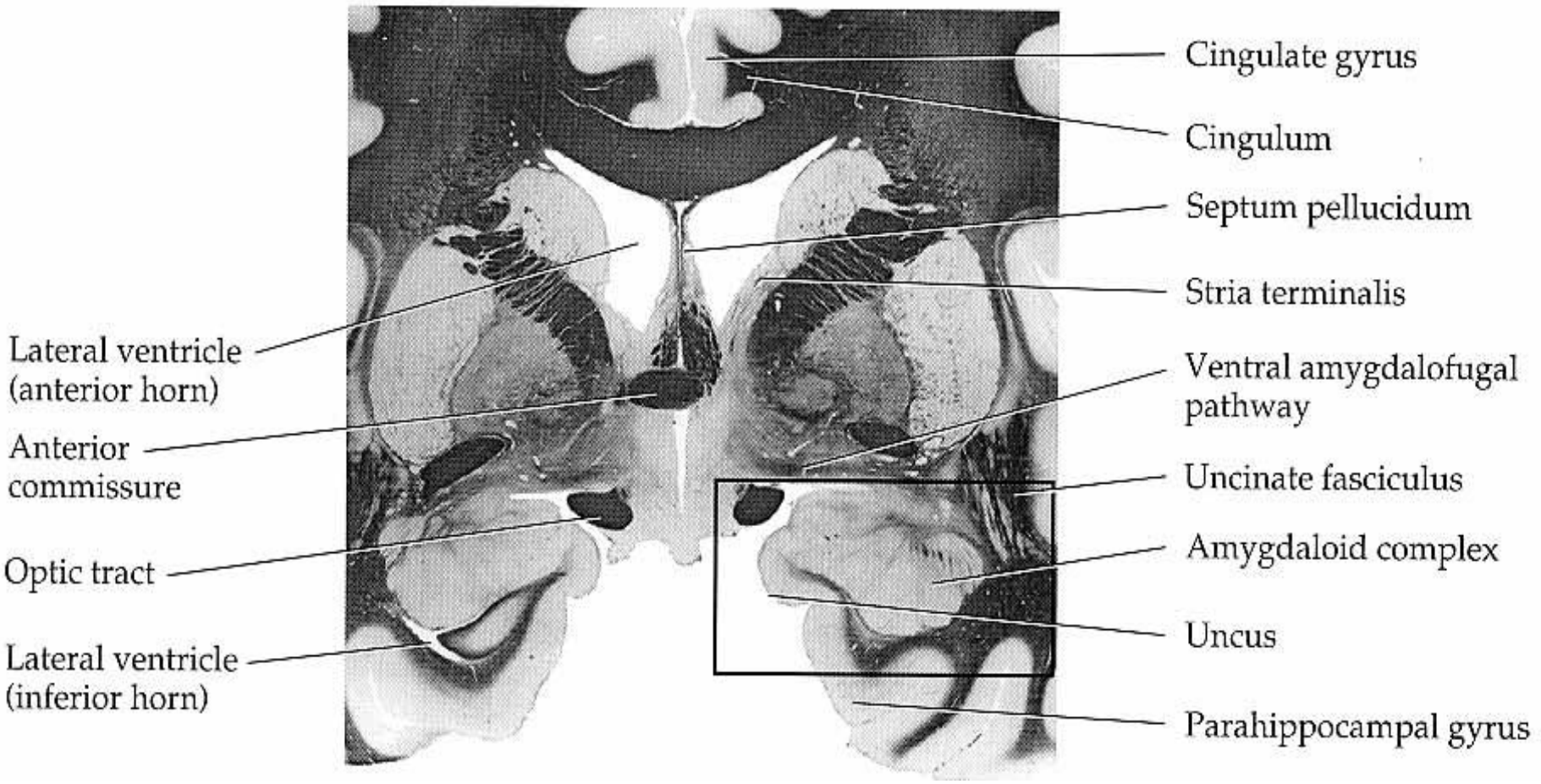
✓ Basolateral nuclei

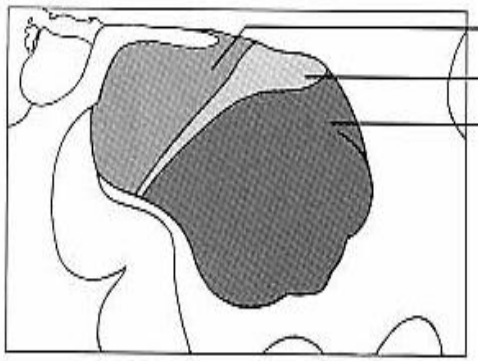
- **Receive all other inputs**
- **Process information**
- **Sends processed info to central nucleus or back to cortex**

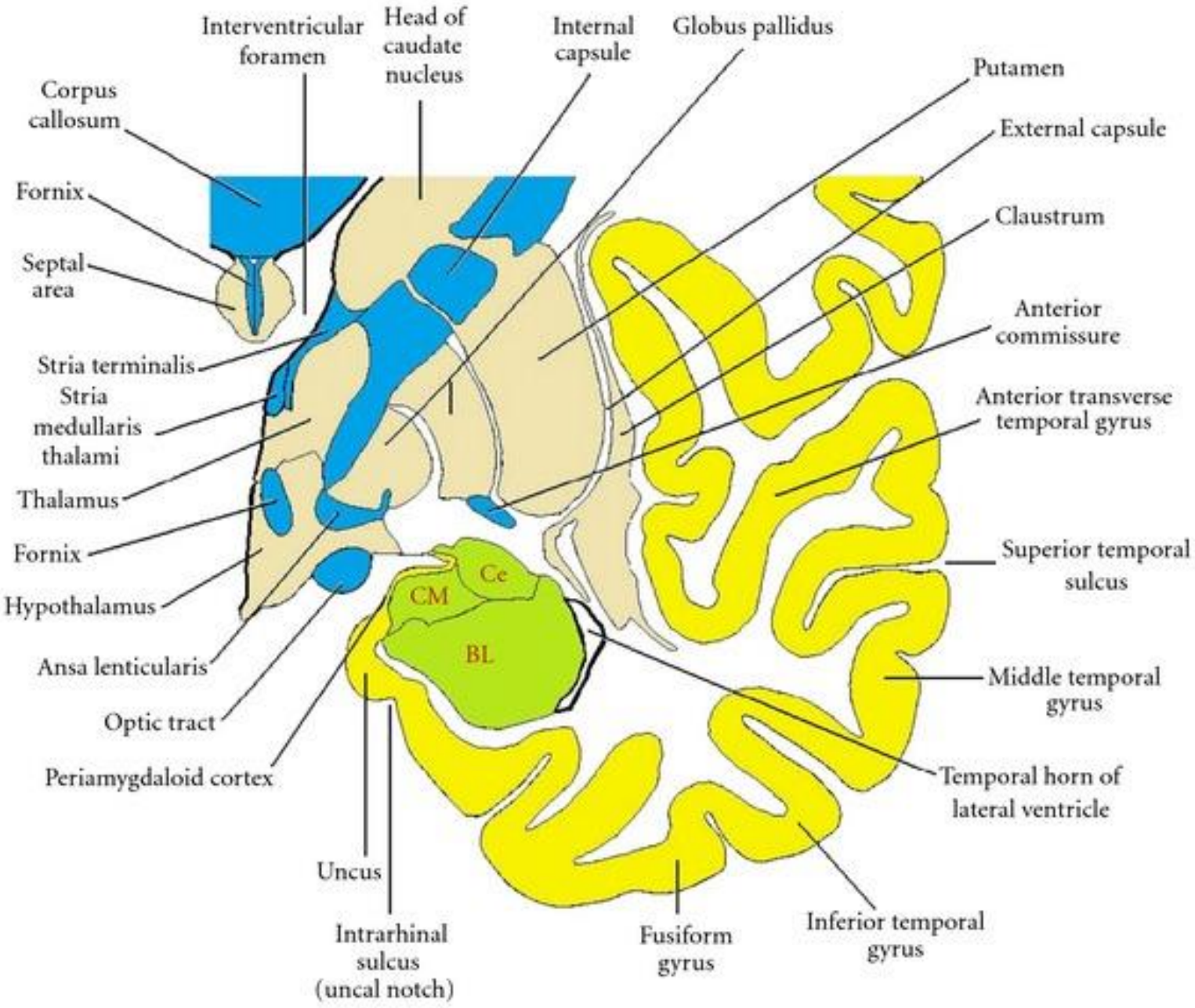
✓ Central nucleus

- **Main output nucleus to hypothalamus & brainstem**

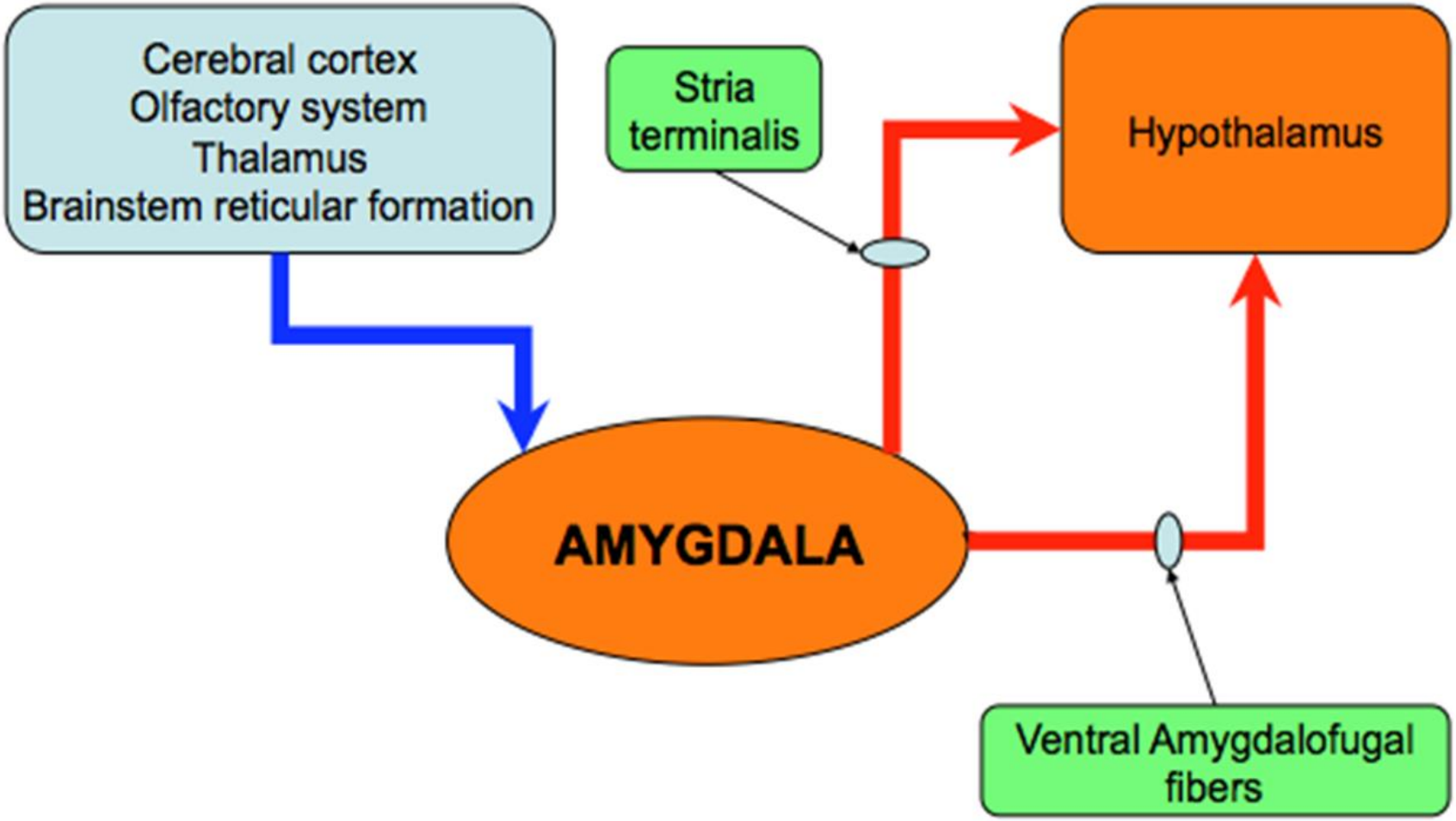



Cingulate gyrus
Cingulum
Septum pellucidum
Stria terminalis
Lateral ventricle (anterior horn)
Ventral amygdalofugal pathway
Anterior commissure
Uncinate fasciculus
Amygdaloid complex
Optic tract
Uncus
Lateral ventricle (inferior horn)
Parahippocampal gyrus


Divisions of amygdala:
corticomedial
central
basolateral


Interventricular foramen
Head of caudate nucleus
Internal capsule
Globus pallidus
Putamen
Corpus callosum
External capsule
Fornix
Claustrum
Septal area
Anterior commissure
Stria terminalis
Stria medullaris thalami
Anterior transverse temporal gyrus
Thalamus
Fornix
Superior temporal sulcus
Ce
CM
Hypothalamus
BL
Ansa lenticularis
Middle temporal gyrus
Optic tract
Periamygdaloid cortex
Temporal horn of lateral ventricle
Uncus
Intrarhinal sulcus (uncal notch)
Fusiform gyrus
Inferior temporal gyrus

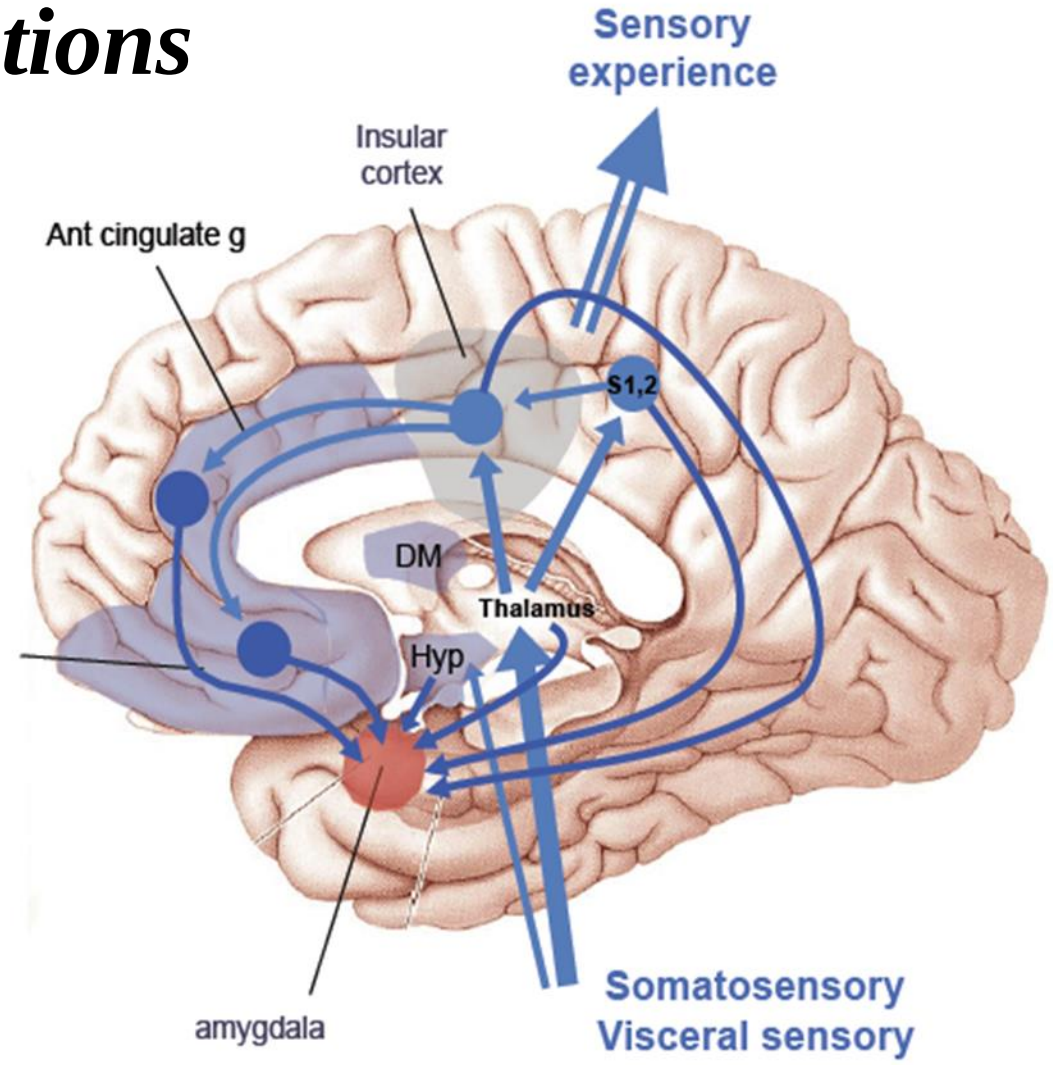
Amygdala Connections



Amygdala Connections Input

Somatosensory & Visceral Sensory Input From:

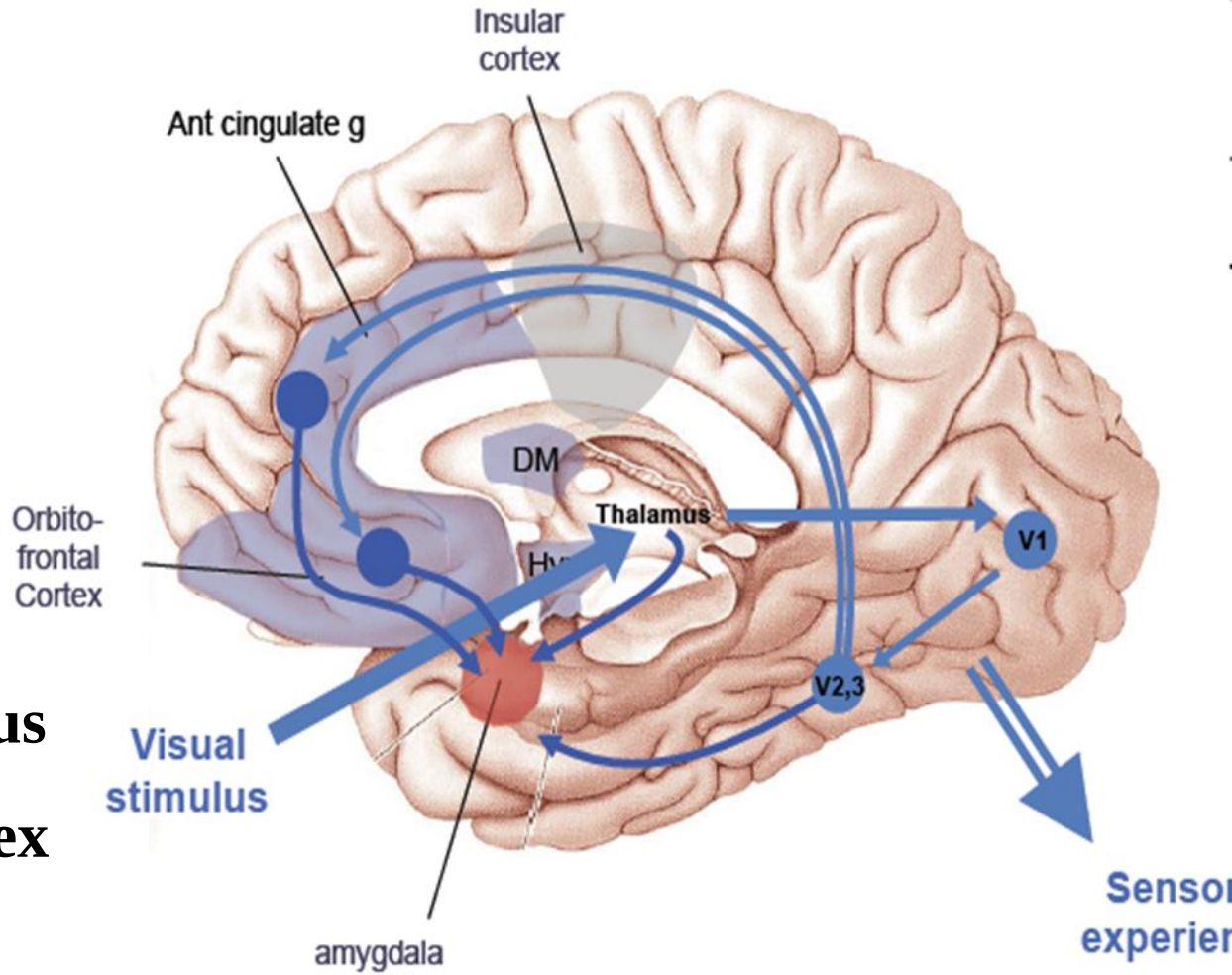
- ✓ **thalamus**
- ✓ **primary somatosensory cortex**
- ✓ **insula**
- ✓ **ant. cingulate gyrus**
- ✓ **orbitofrontal cortex**
- ✓ **hypothalamus**



Amygdala Connections Input

Visual & Auditory Sensory Input From:

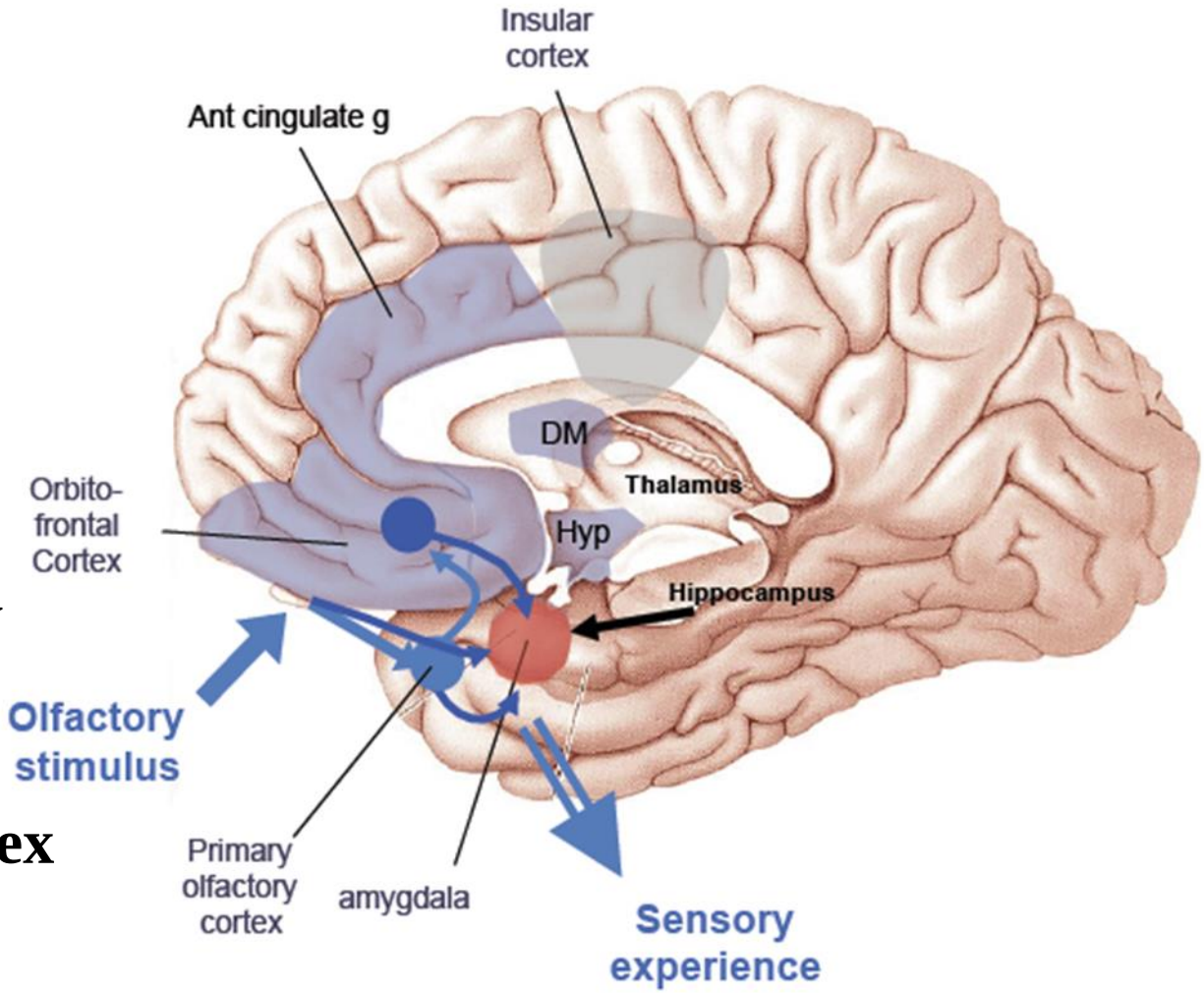
- ✓ **thalamus**
- ✓ **visual cortex**
- ✓ **ant. cingulate gyrus**
- ✓ **orbitofrontal cortex**
- ✓ **temporal lobe**



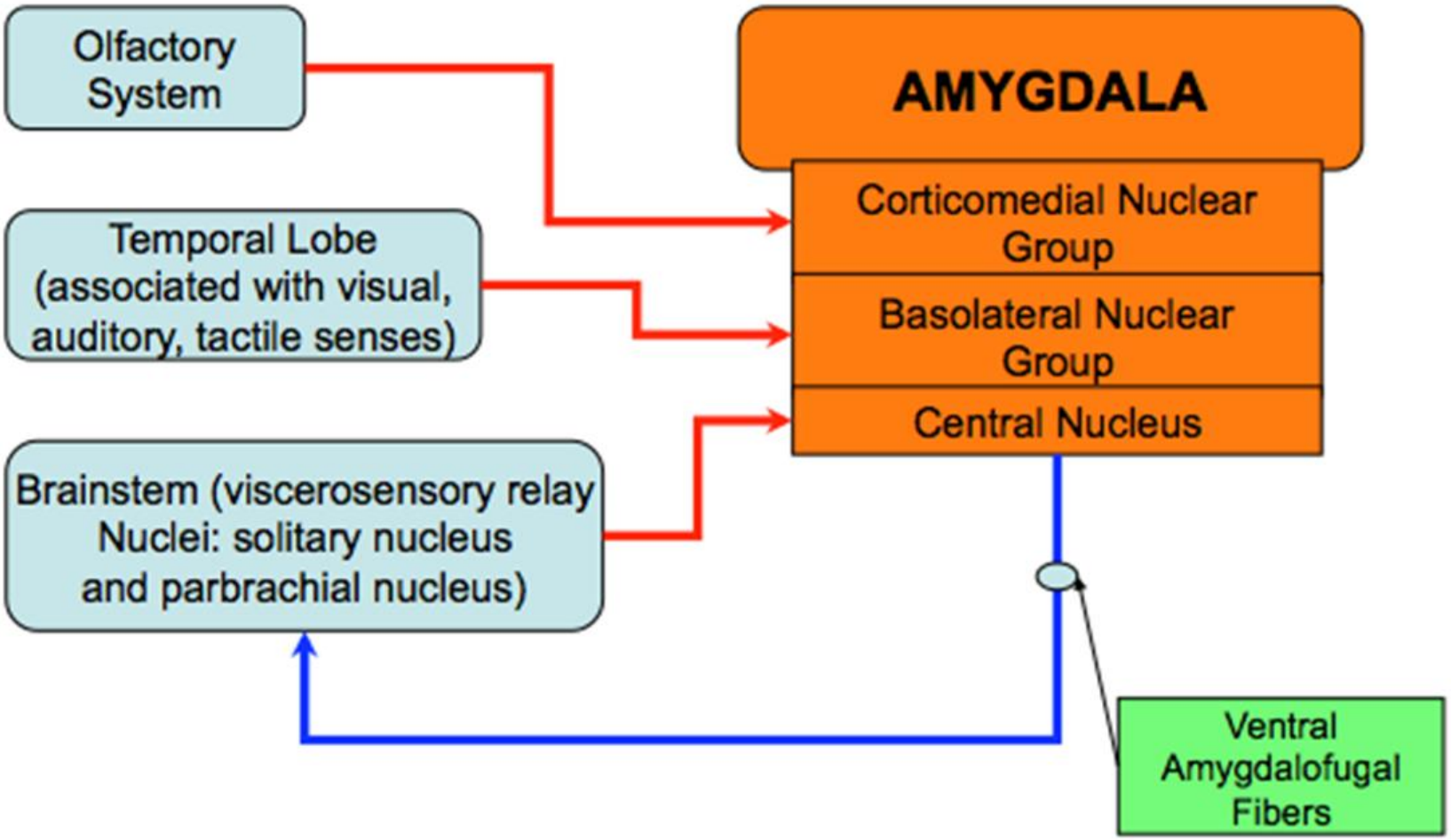
Amygdala Connections Input

Olfactory Sensory Input From:

- ✓ **olfactory bulb**
- ✓ **primary olfactory cortex**
- ✓ **orbitofrontal cortex**
- ✓ **hippocampus**
- ✓ **parahippocampal gyrus**



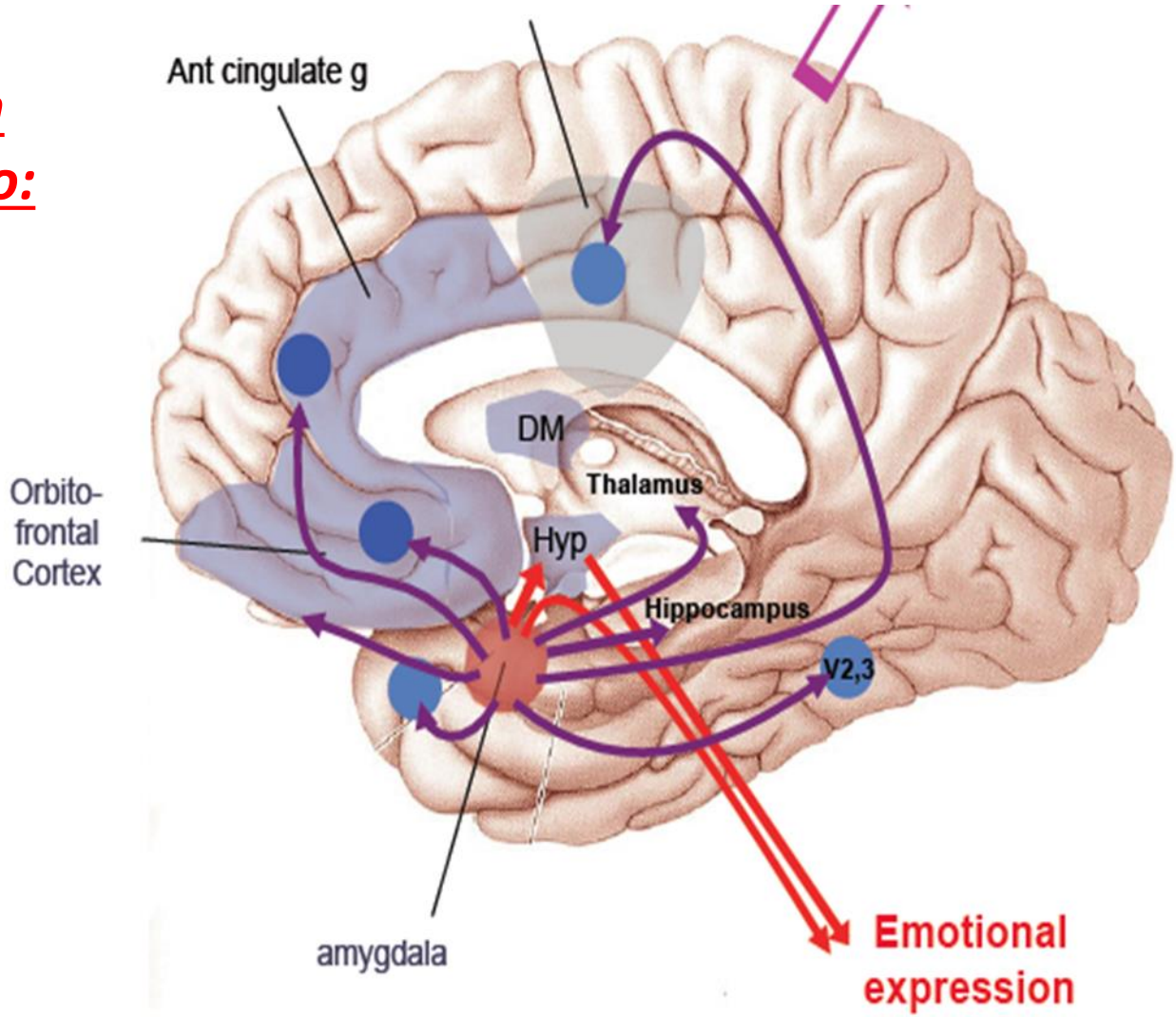
Amygdala Inputs



Amygdala Connections Output

Emotional Expression Descending Output To:

- ✓ **hypothalamus**
- ✓ **brainstem**

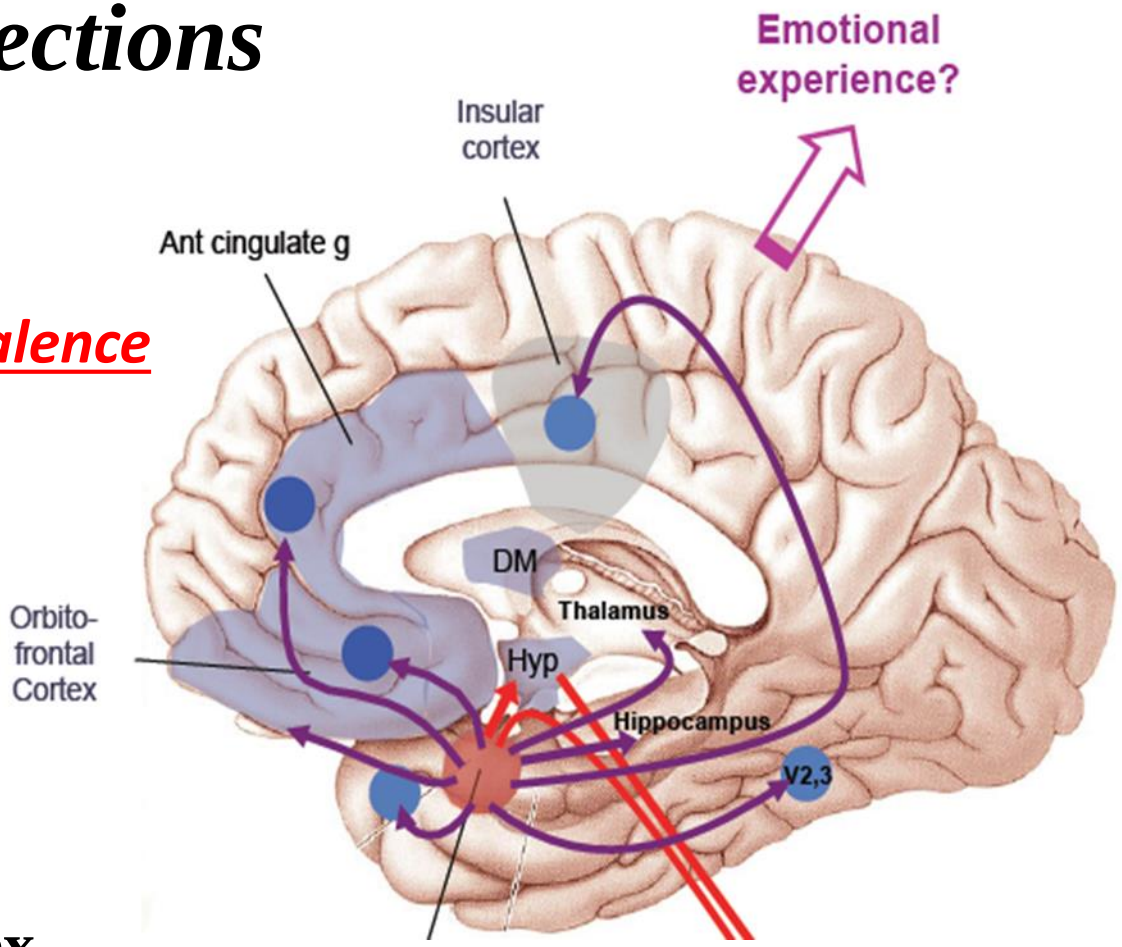


Amygdala Connections Output

Emotional Experience
Feedback with affective valence

Feedback Output To:

- ✓ **orbitofrontal cortex**
- ✓ **ant cingulate cortex**
- ✓ **insular cortex**
- ✓ **visual - auditory cortex**
- ✓ **primary olfactory cortex**
- ✓ **thalamus**
- ✓ **hippocampus**

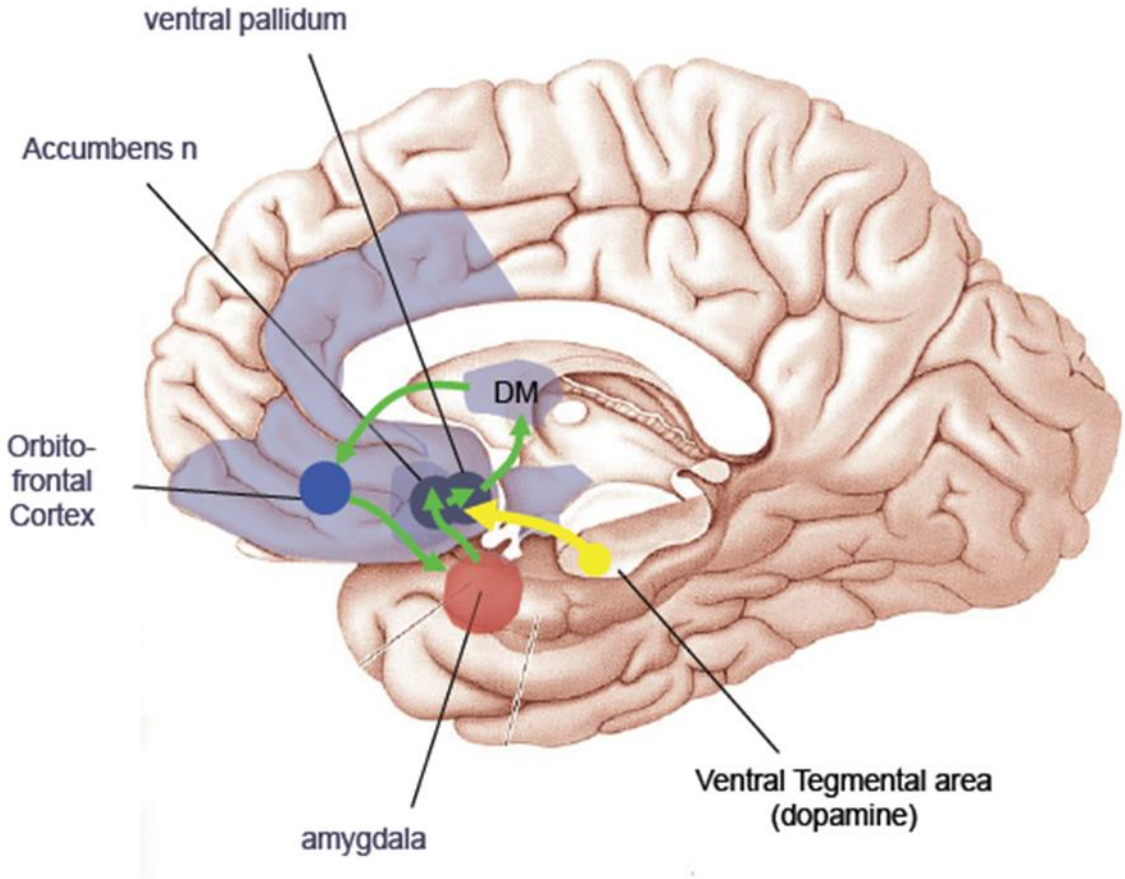


Amygdala Connections Output

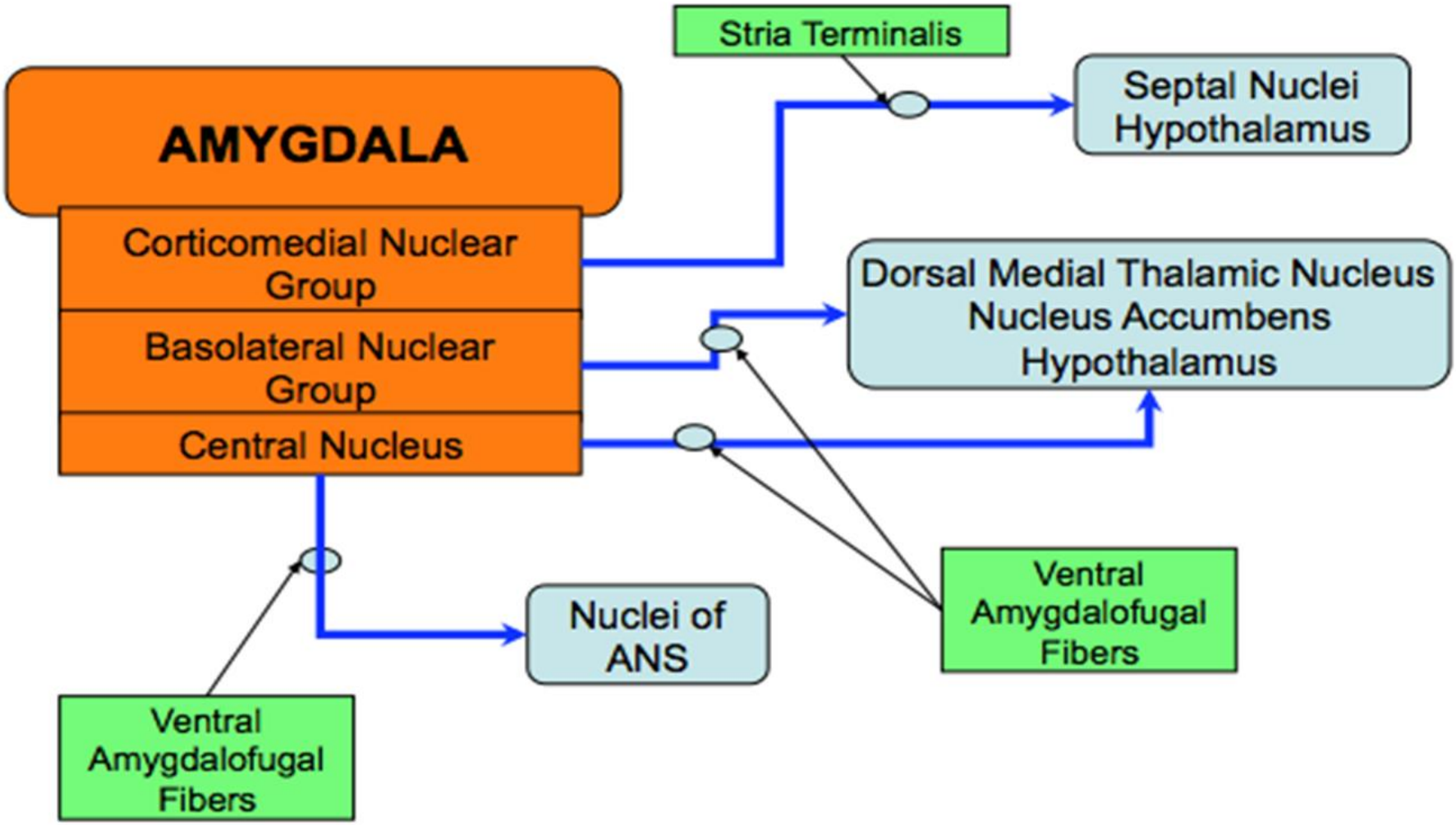
Basal ganglia loop
Codes for "rewards" & contributes to affective dimension of emotion

Feedback Output To:

- ✓ **accumbens nucleus**
- ✓ **dorsomedial thalamus**
- ✓ **orbitofrontal cortex**

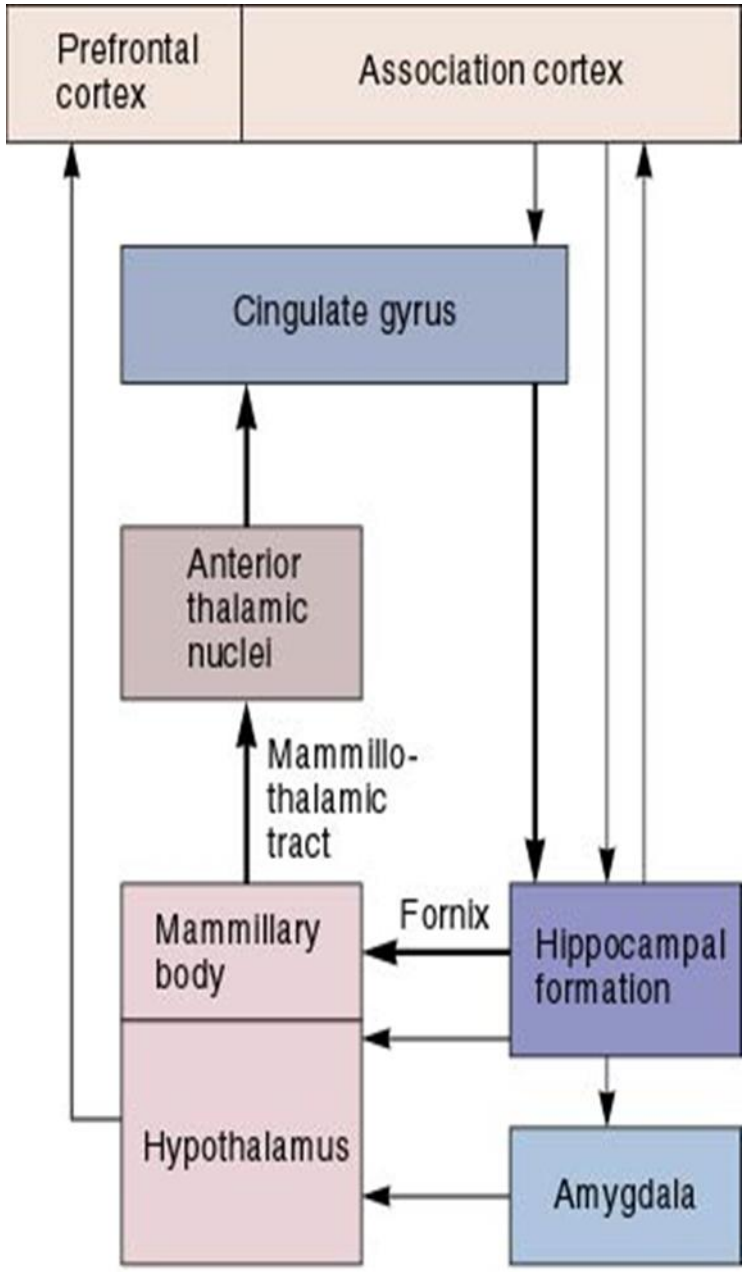


Amygdala Outputs

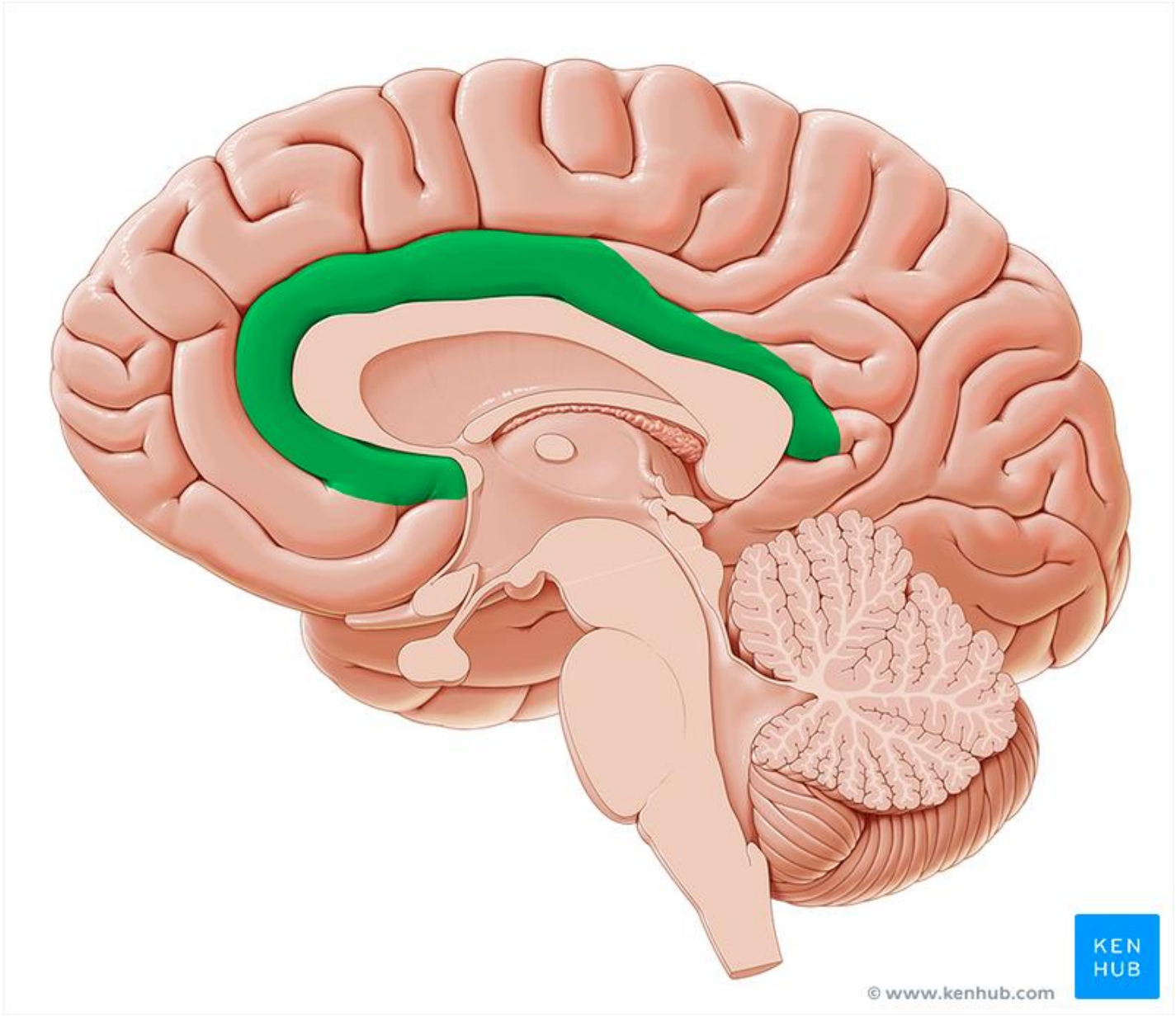


Amygdala Function

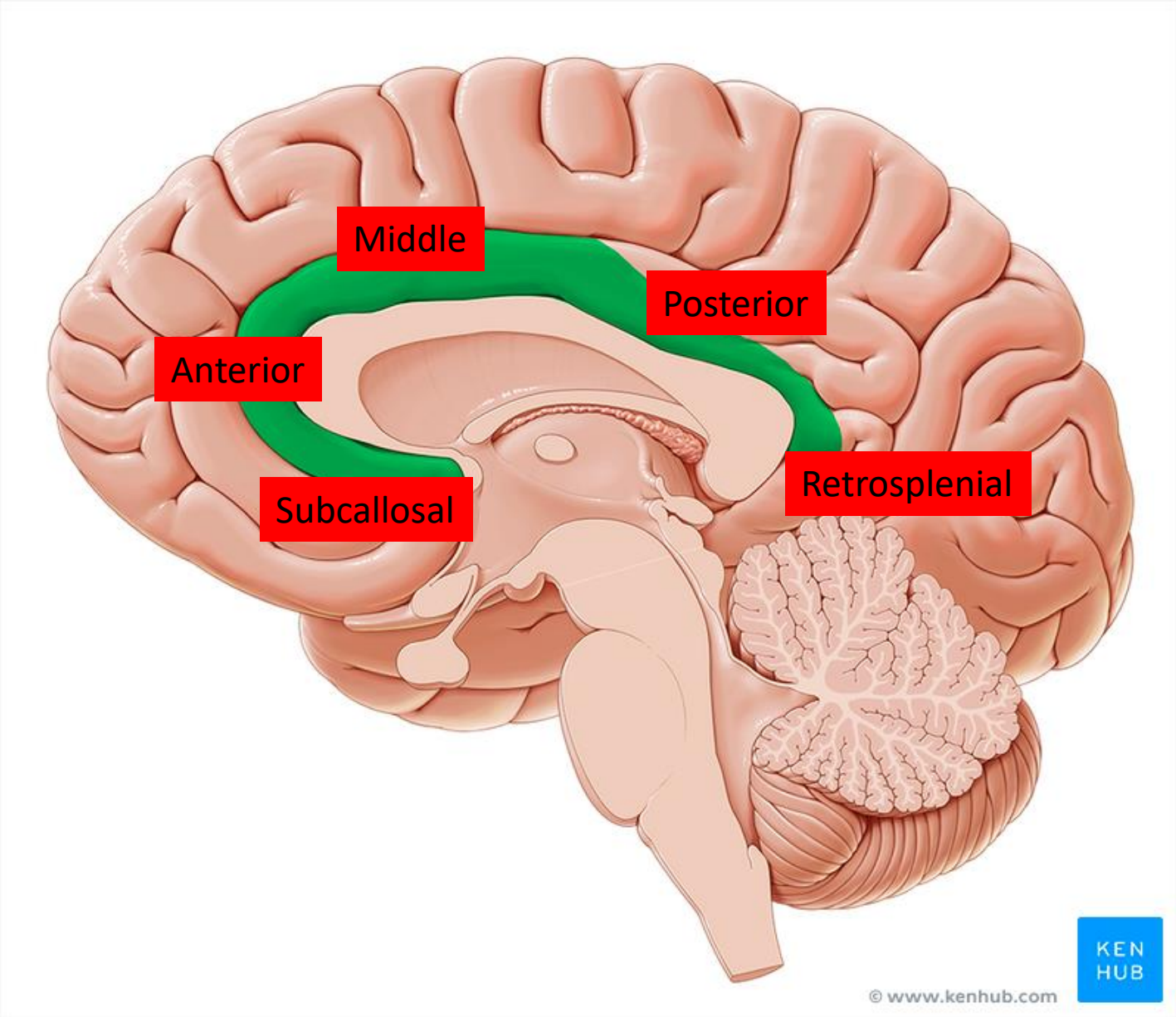
- ✓ **Limbic neural circuit are involved in emotion processing**
- ✓ **Amygdala now recognized as key coordinator**
- ✓ **It links cortical processing to hypothalamus & other subcortical brain structures important for emotional behavior**



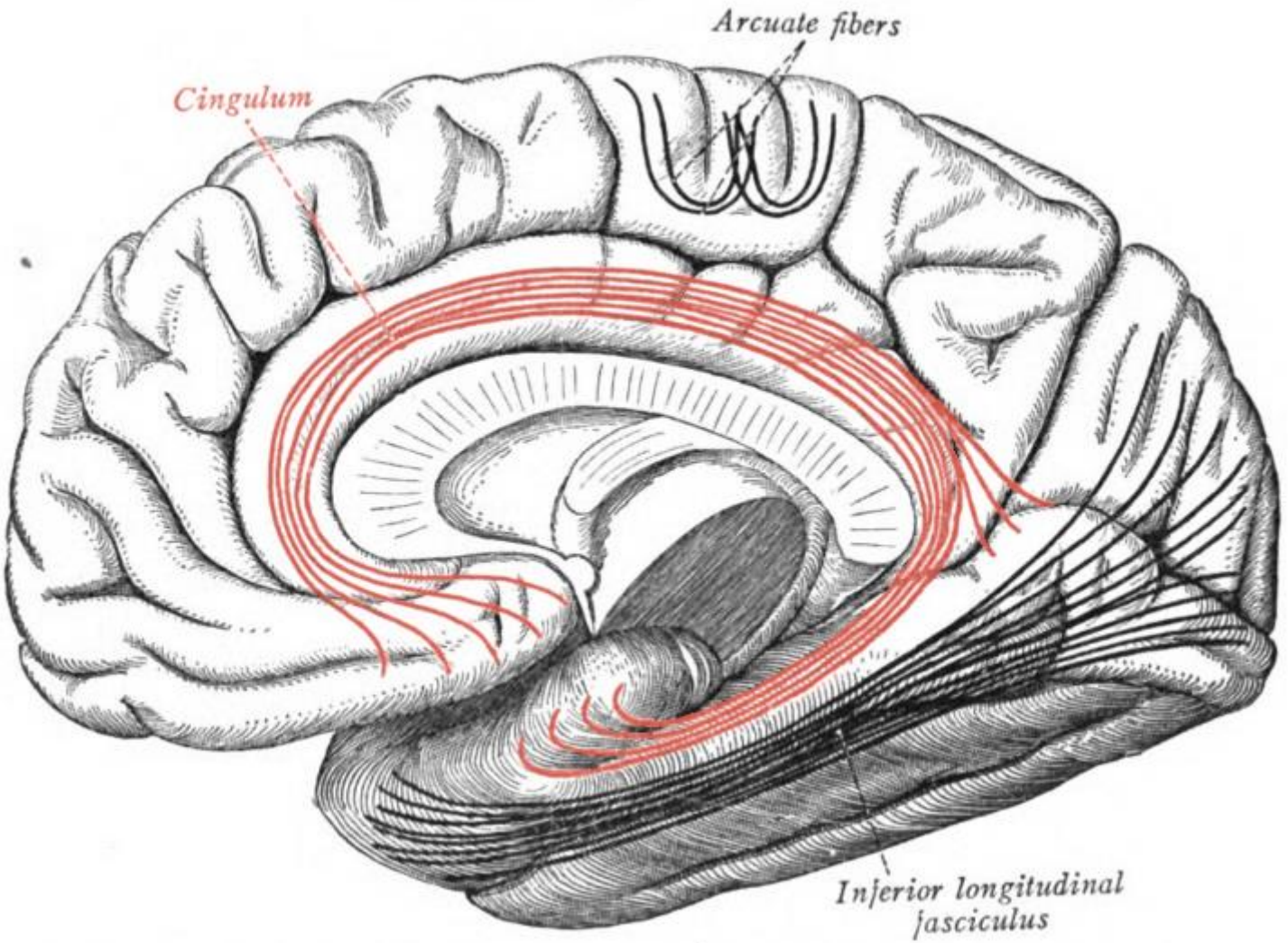
Cingulate Gyrus



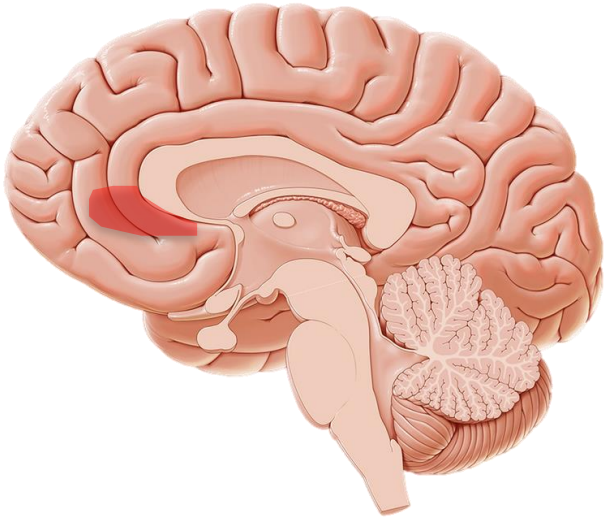
Cingulate Gyrus



Cingulate Gyrus

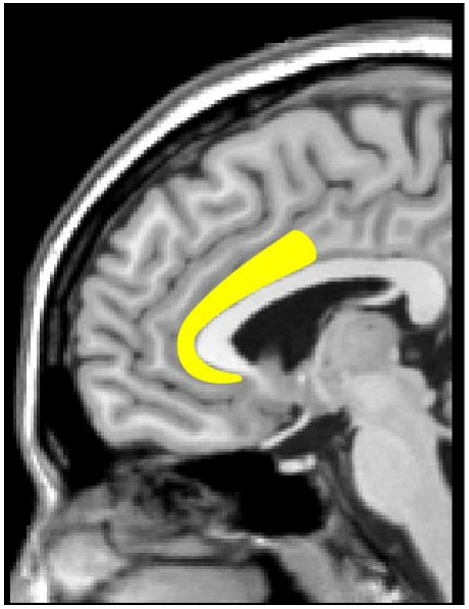


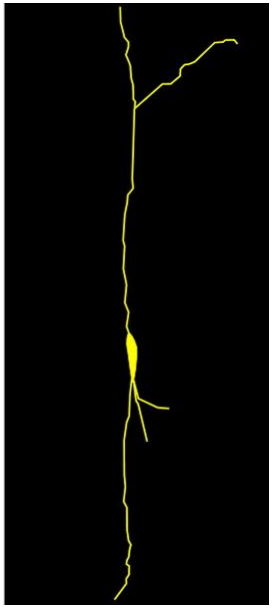
Anterior Cingulate Gyrus



- von Economo neurons
- Detection of errors or shortfalls
- Preparation for an action
- Handling of emotions

Anterior Cingulate Cortex (ACC)

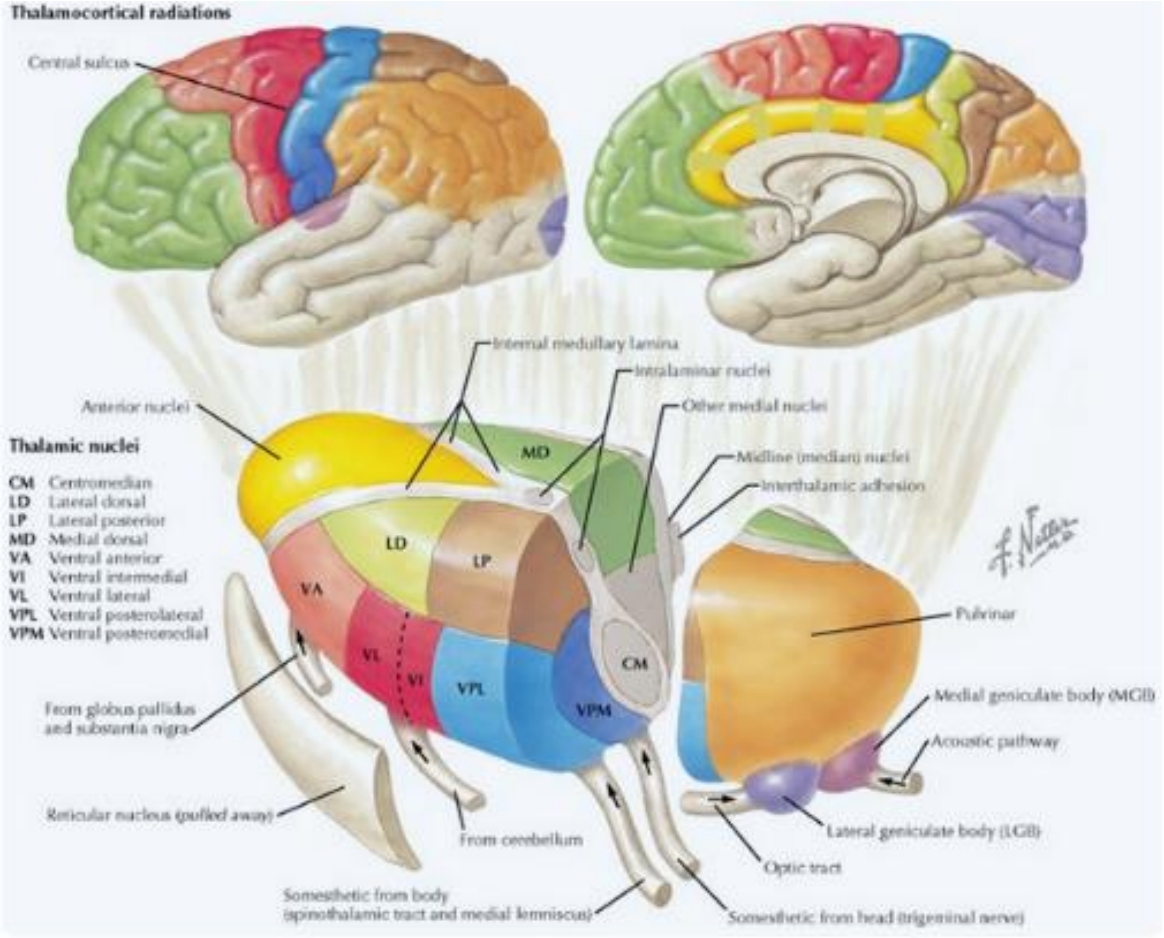




Anterior Thalamic Nucleus

Afferents: Mammillary bodies, hippocampus

Efferents: Hypothalamus, cingulate gyrus

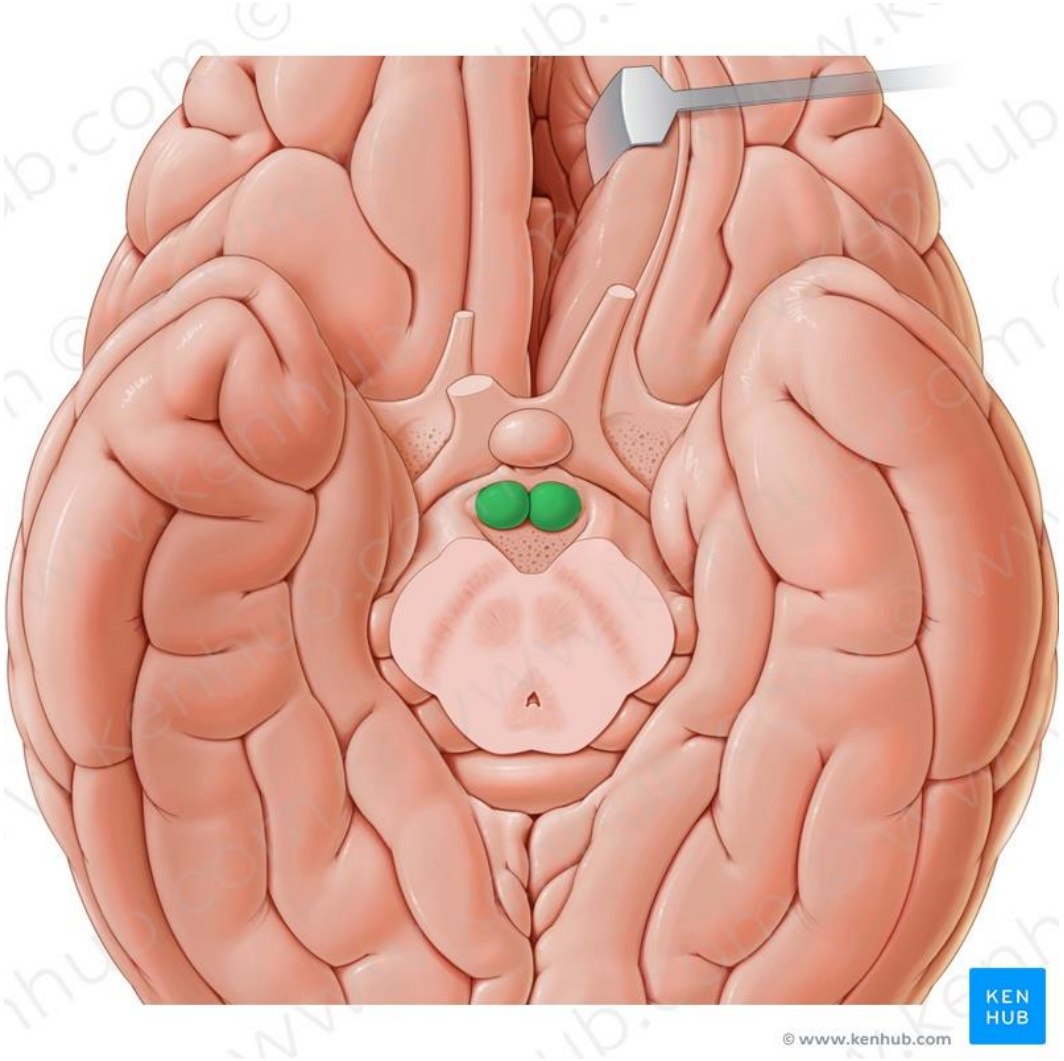


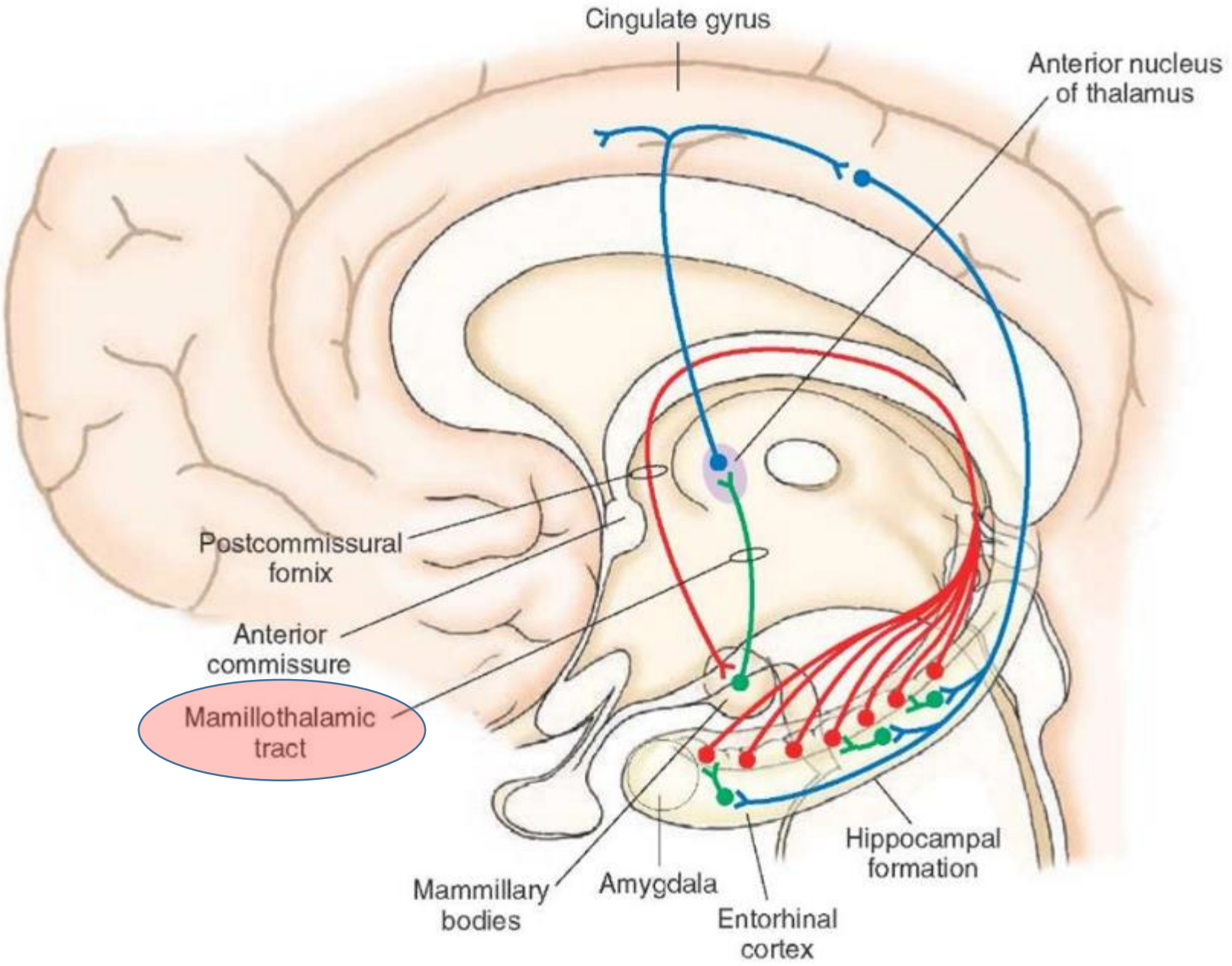
Mammillary Bodies

Afferents: Hippocampus

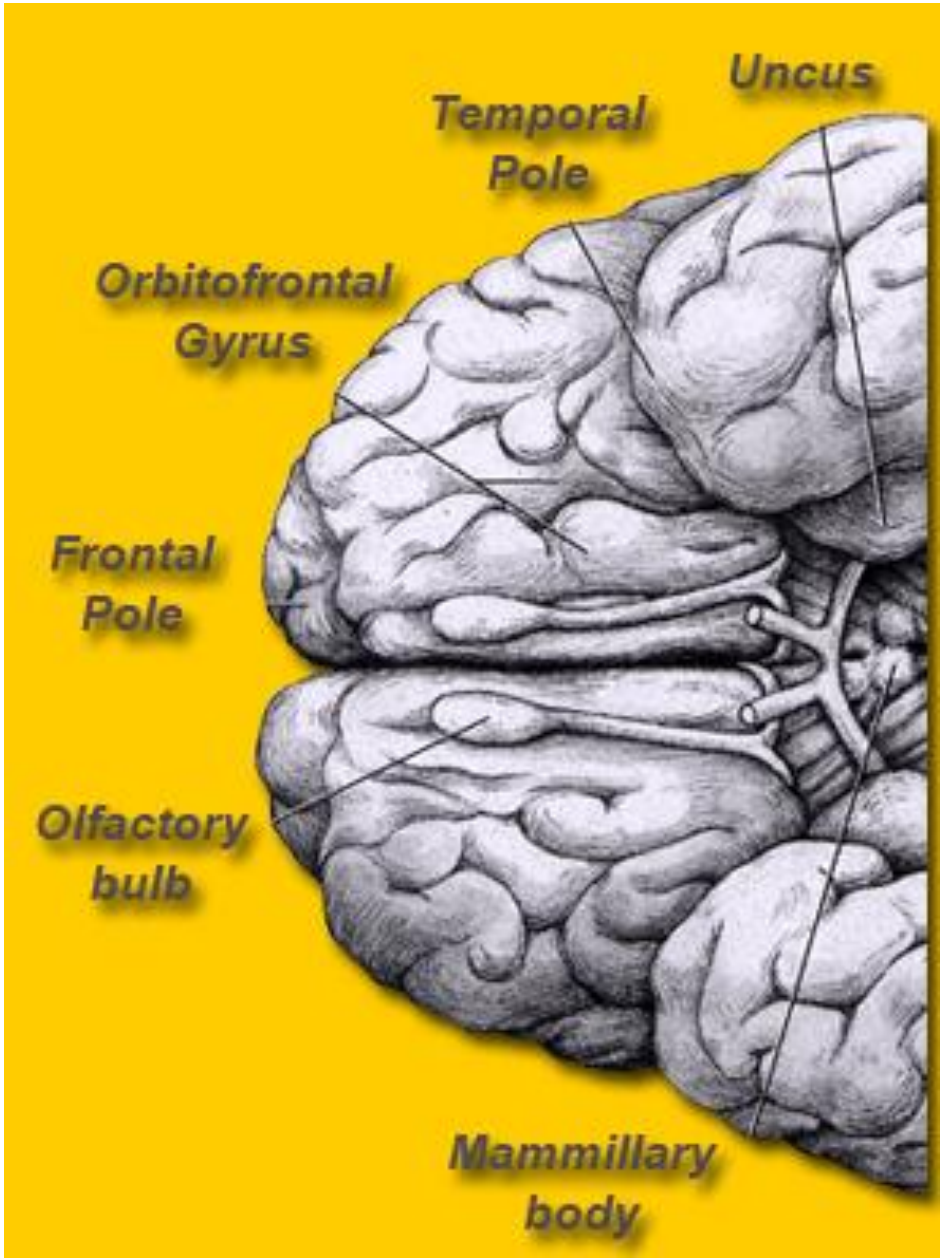
Efferents: Anterior Thalamic Nucleus

✓Mammillothalamic tract (Bundle of Vicq d'Azyr)

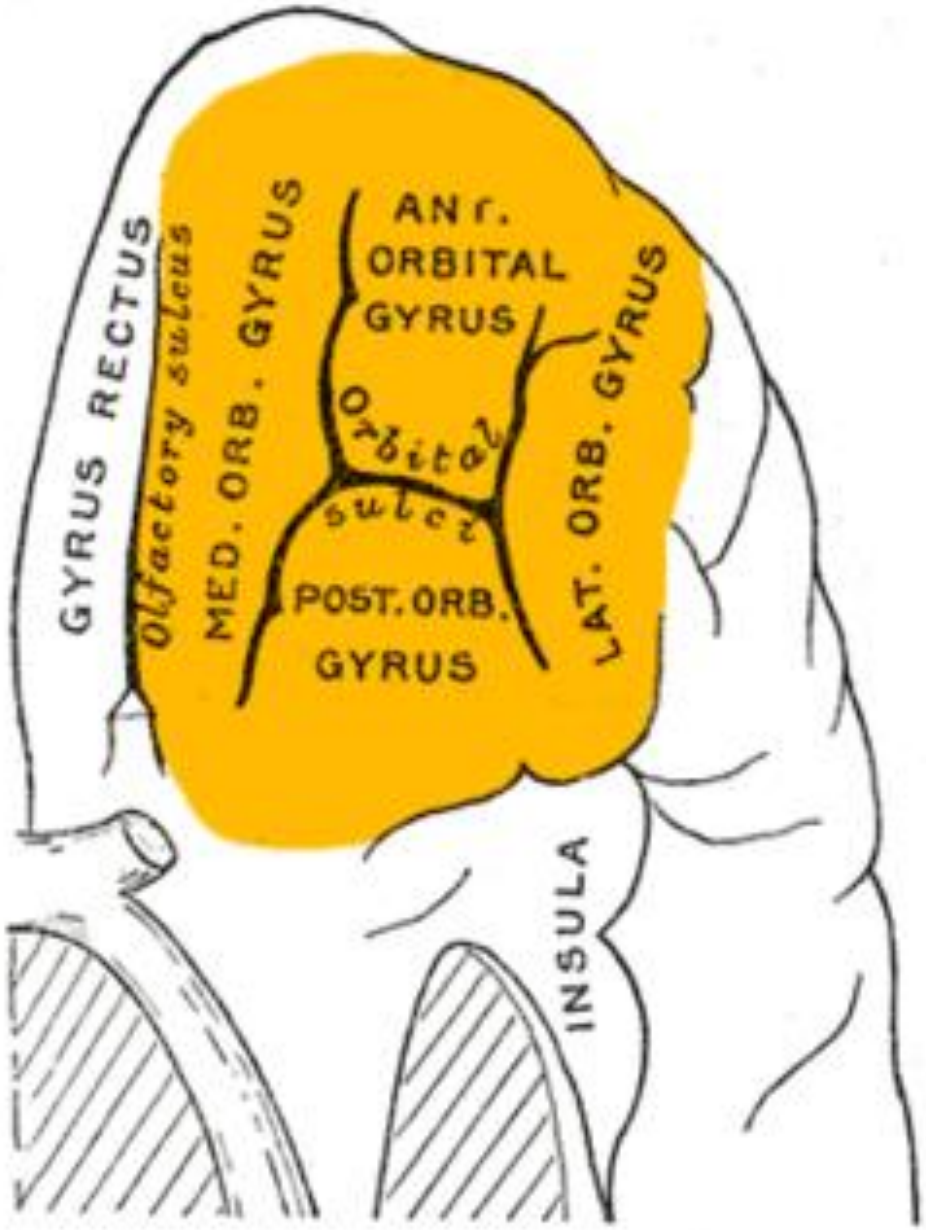



Cingulate gyrus
Anterior nucleus of thalamus
Postcommissural fornix
Anterior commissure
Mamillothalamic tract
Mammillary bodies
Amygdala
Entorhinal cortex
Hippocampal formation

Orbitofrontal Cortex



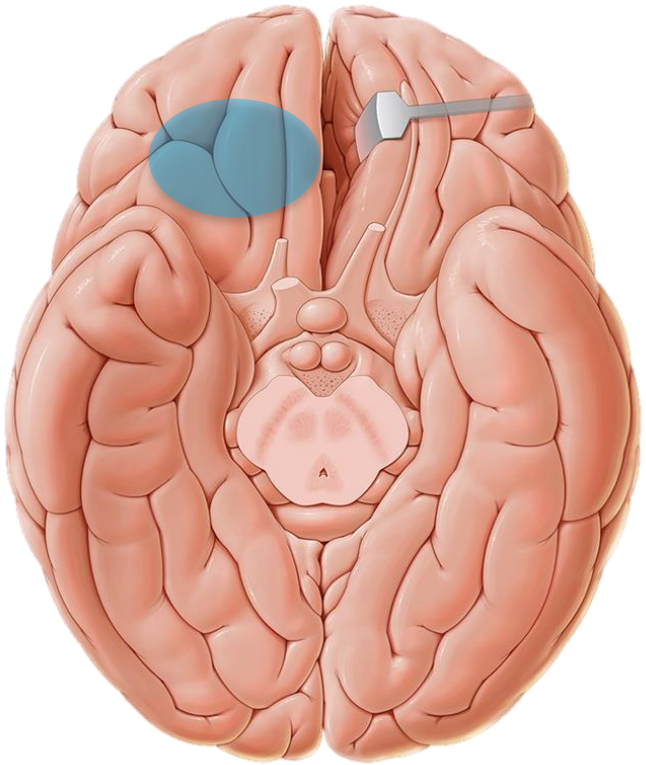
Orbitofrontal Cortex



Orbitofrontal Cortex

- Sensory integration
- Punishment
- Reward

"The what system"



Orbitofrontal PFC (OFC)

Model for decision-making