



# 沒有放在心裡？ 生物學基礎？



Fragrance:  
Fried chicken  
Perfume

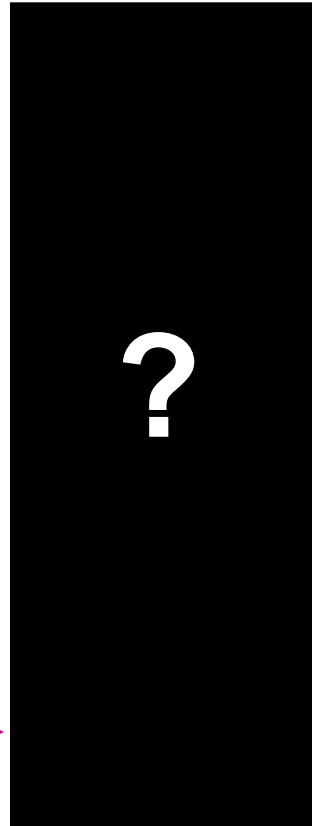
Olfactory  
nerve



Optic nerve



Cochlear  
nerve



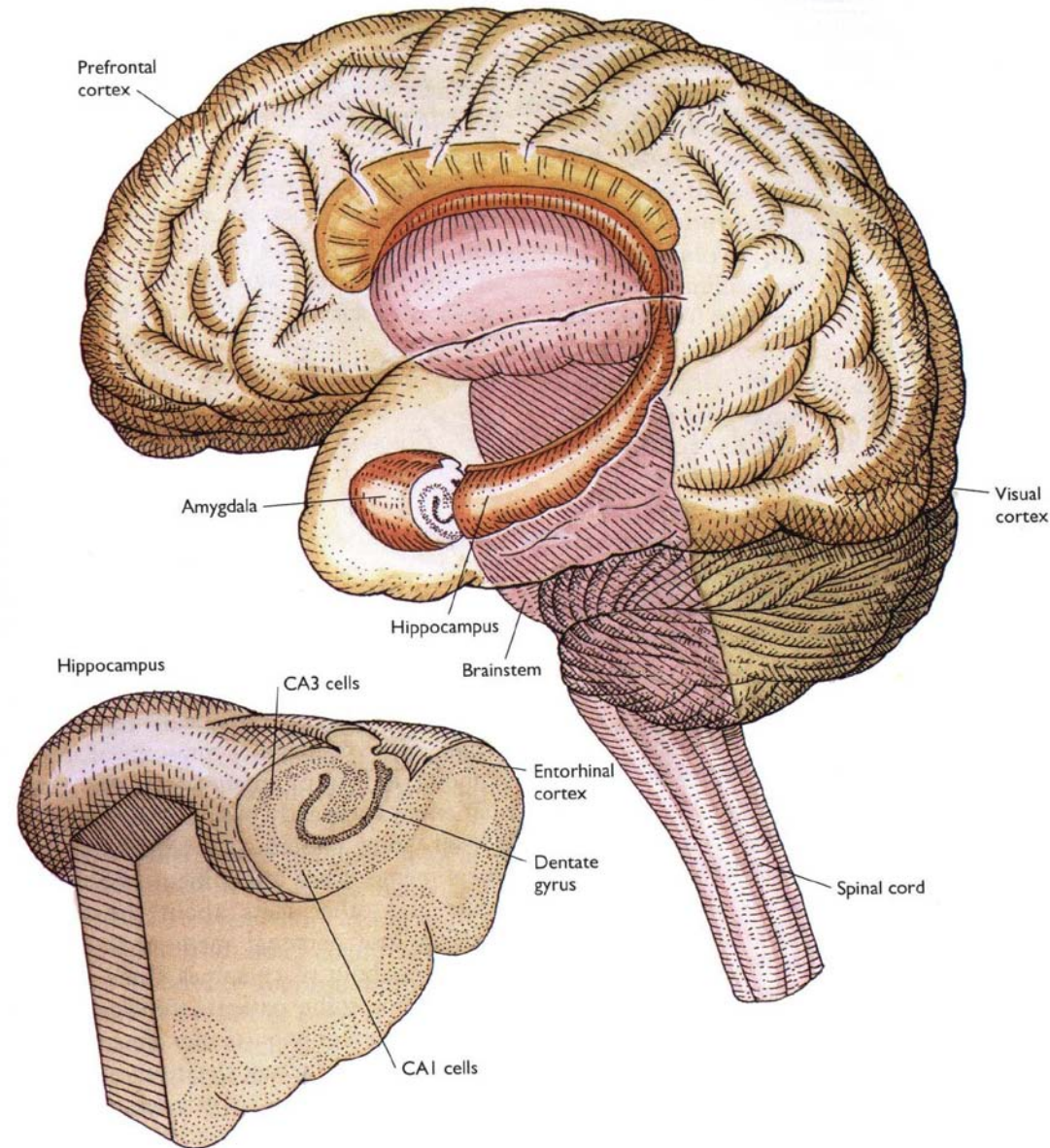
Motor pathways

Emotional  
responses



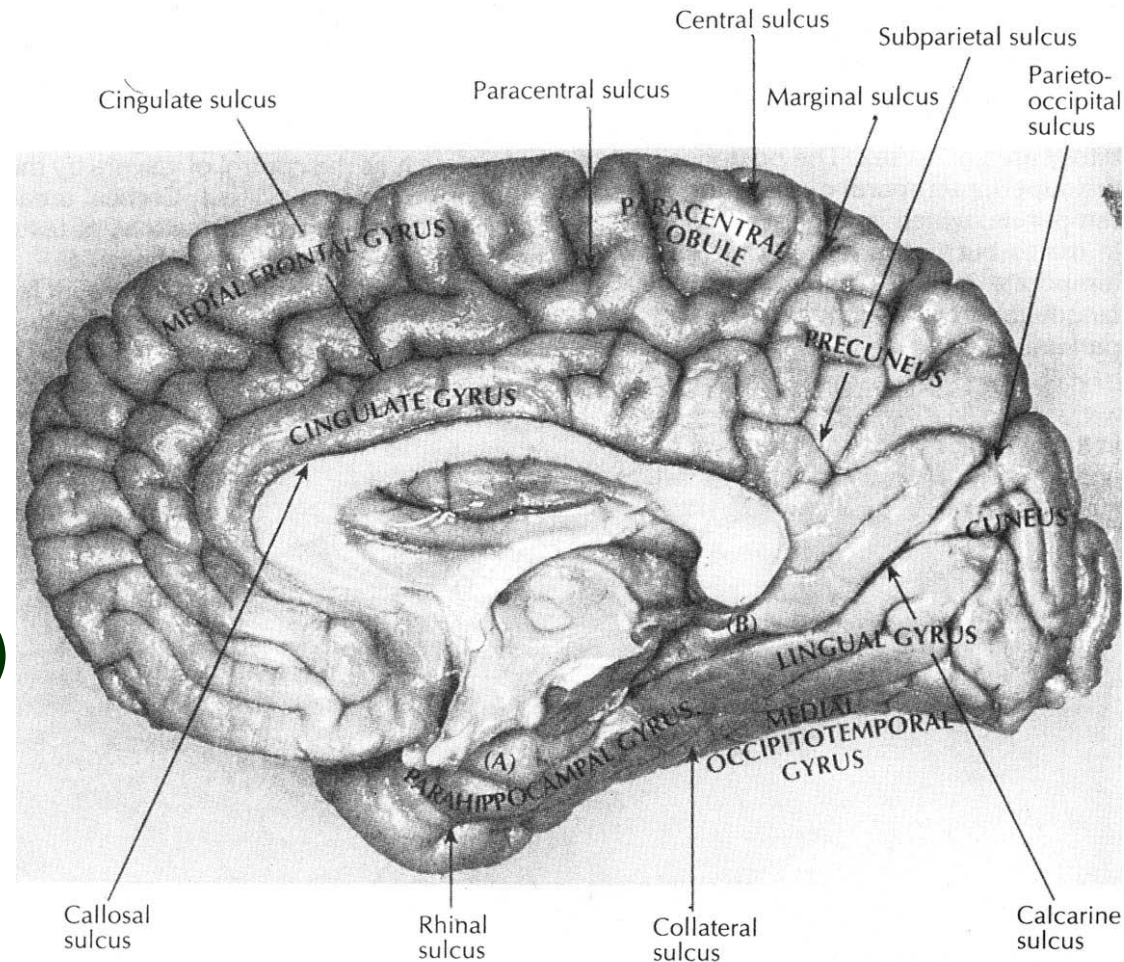
# Functions of Limbic system

- **Memory**
- **Emotions-related responses**



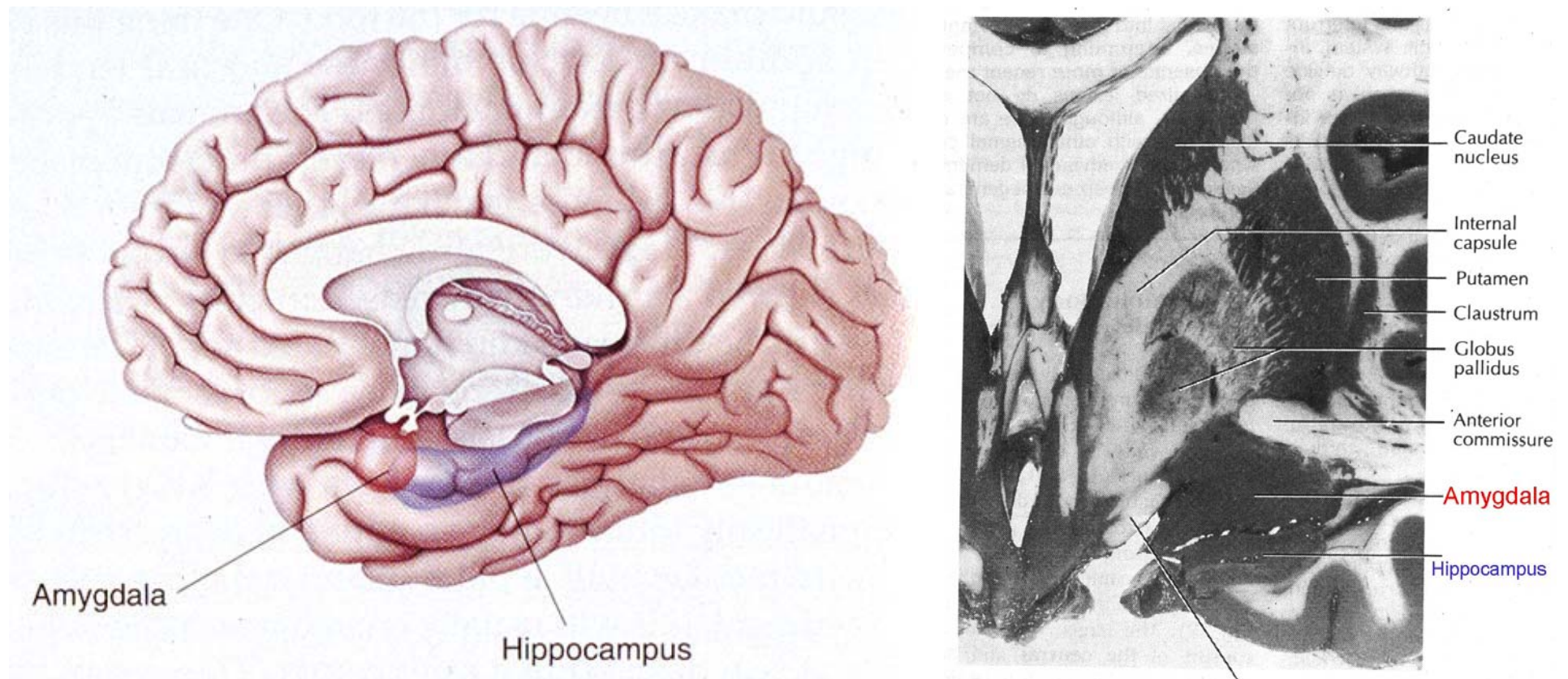
# Limbic system

- Amygdaloid body (amygdala)
- Hippocampal
  - Hippocampus
  - Parahippocampal gyrus
  - Dentate gyrus
- Septal area / Basal forebrain
- Hypothalamus
- (Limbic) cortex: Cingulate gyrus, Orbital (Orbitalfrontal) cortex, Prefrontal cortex, Insula
- Anterior thalamus

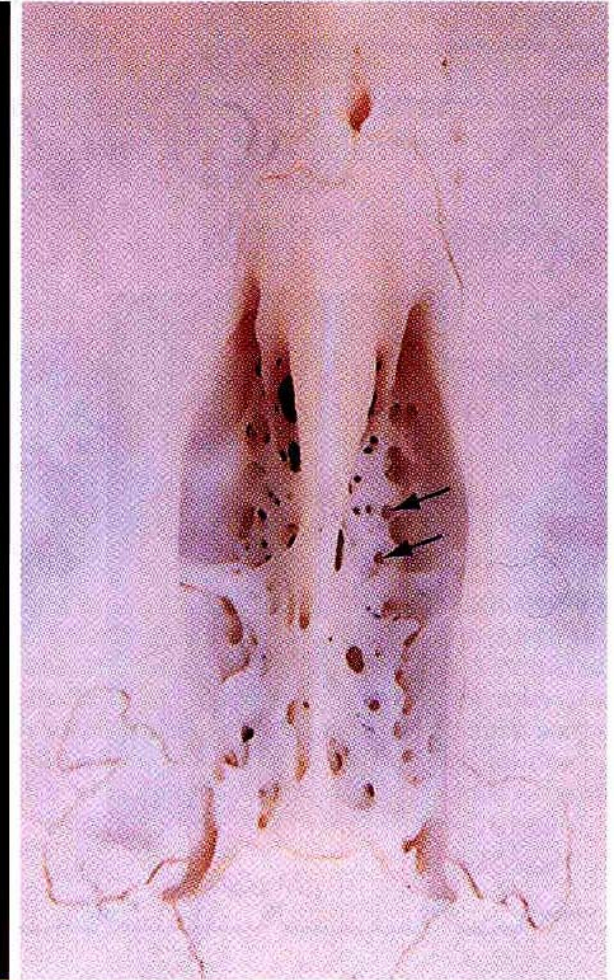
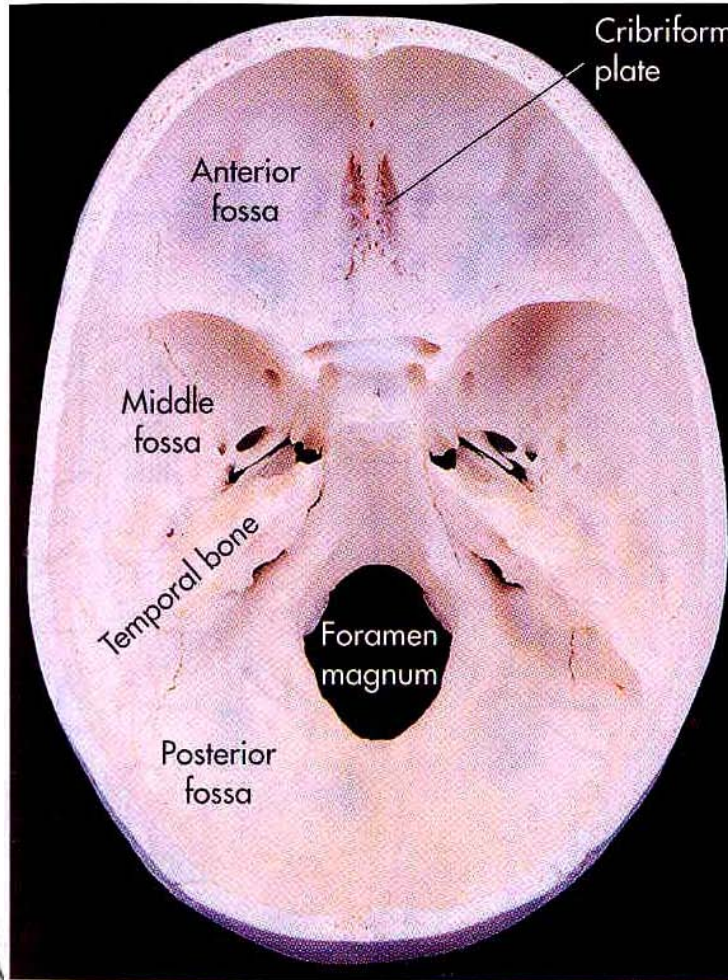
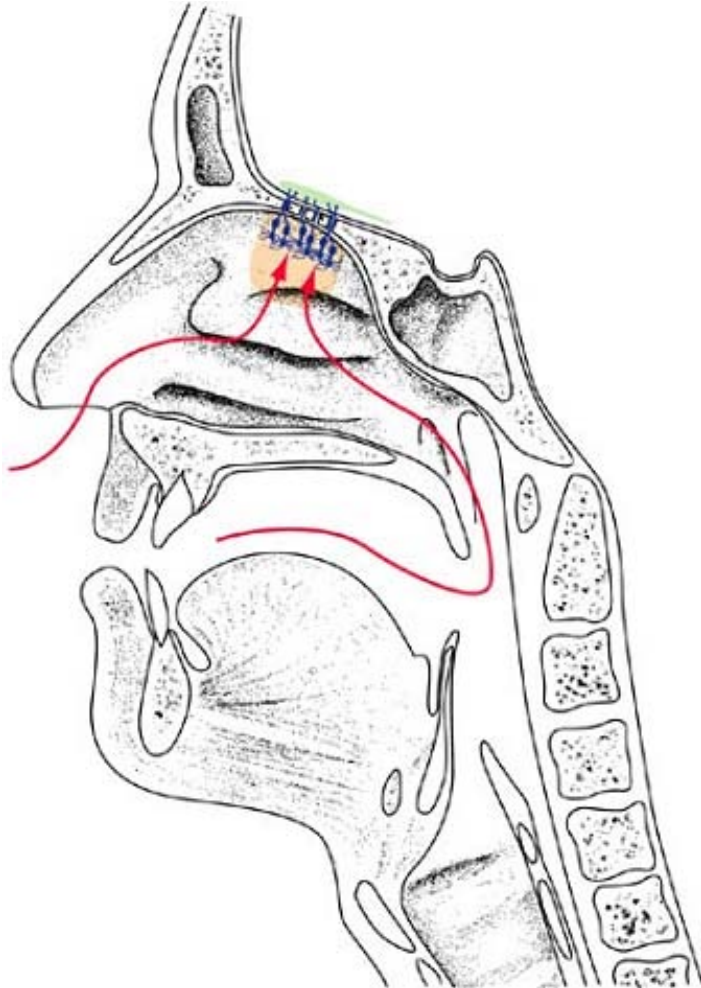


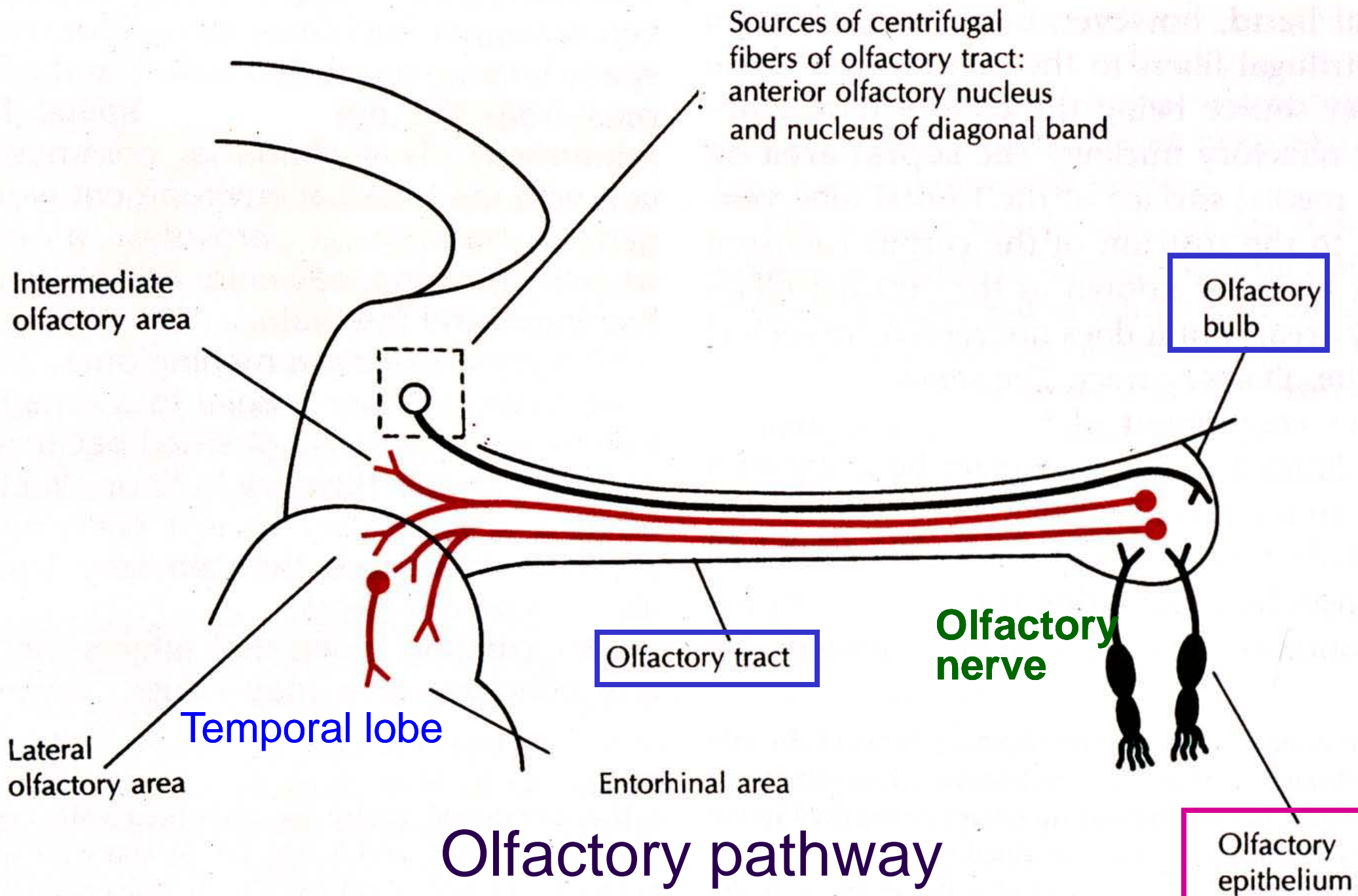
# Amygdaloid Body (Amygdala, AMG)

- Position: between anterior end of temporal horn of the lateral ventricle and the ventral surface of lentiform nucleus



# Olfactory nerve





Sources of centrifugal fibers of olfactory tract: anterior olfactory nucleus and nucleus of diagonal band

Intermediate olfactory area

Olfactory bulb

Olfactory tract

Olfactory nerve

Temporal lobe

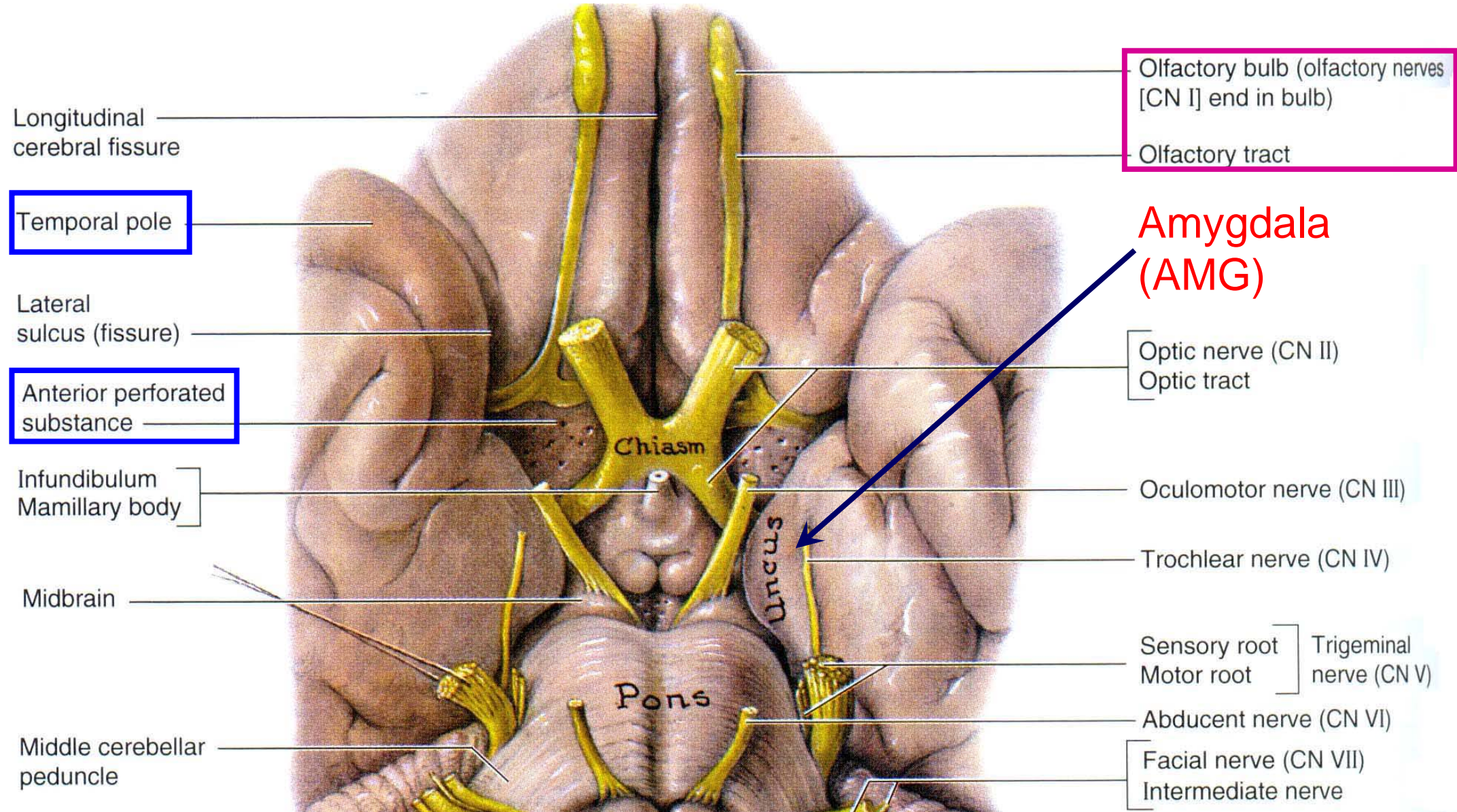
Lateral olfactory area

Entorhinal area

Olfactory epithelium

# Olfactory pathway

# Olfactory pathway and AMG

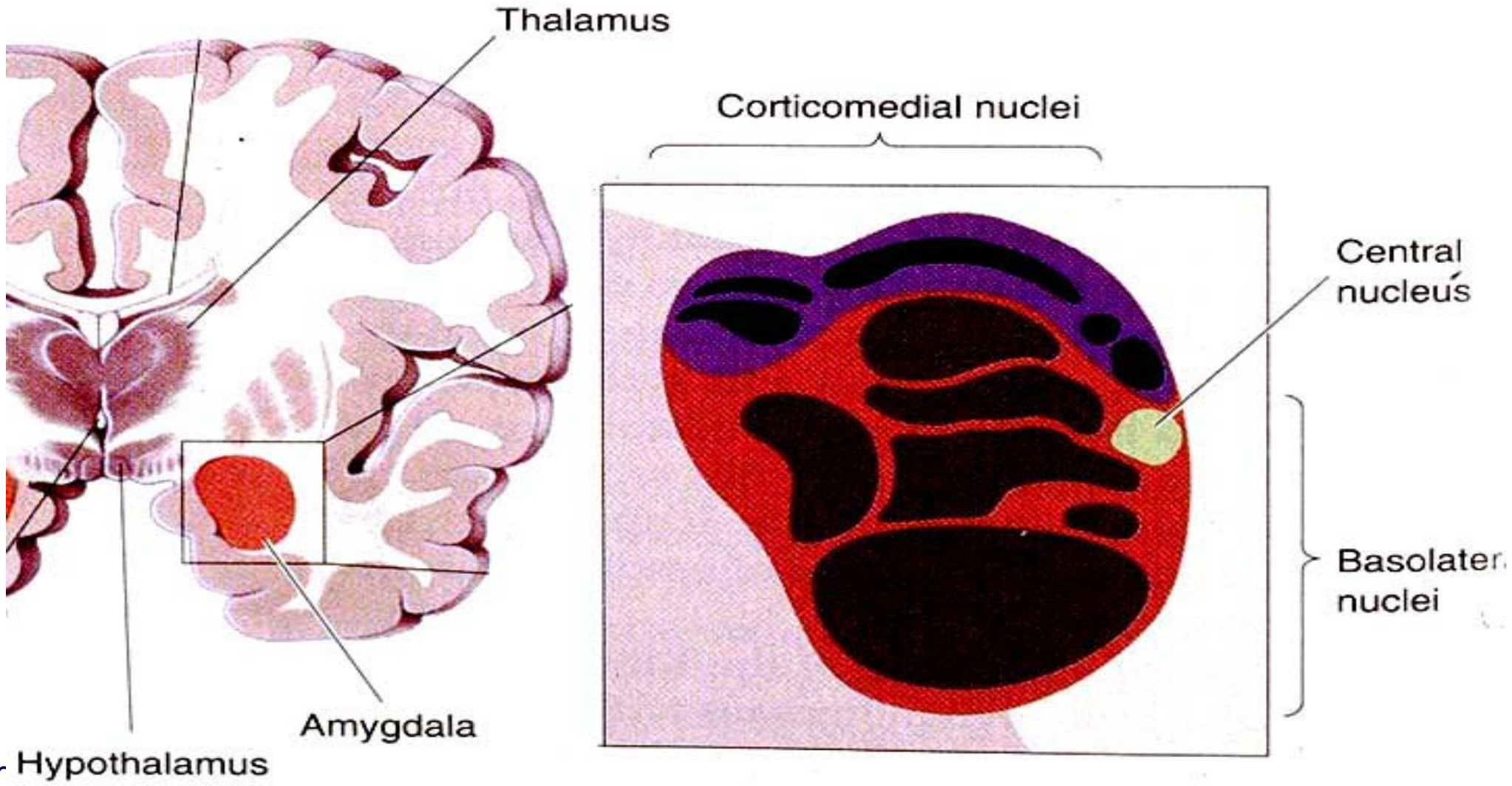




# AMYGDALA: division / nuclei

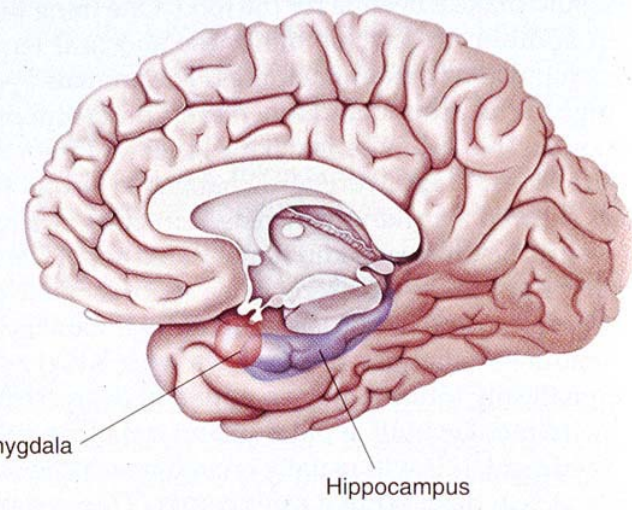
Dorsal (corticomedial nuclei)

Ventrolateral (central nuclei / basolateral nuclei)

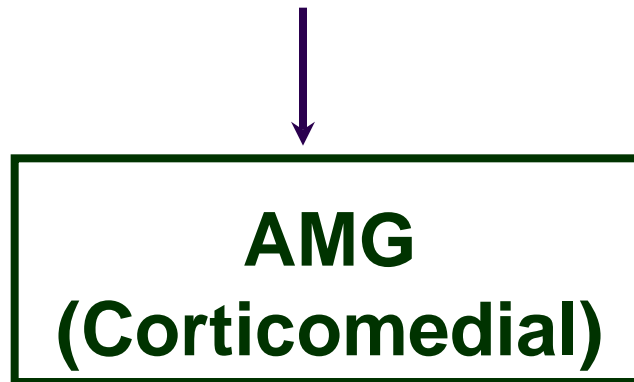


# Dorsal (Corticomedial, Cortical) nuclei of AMG

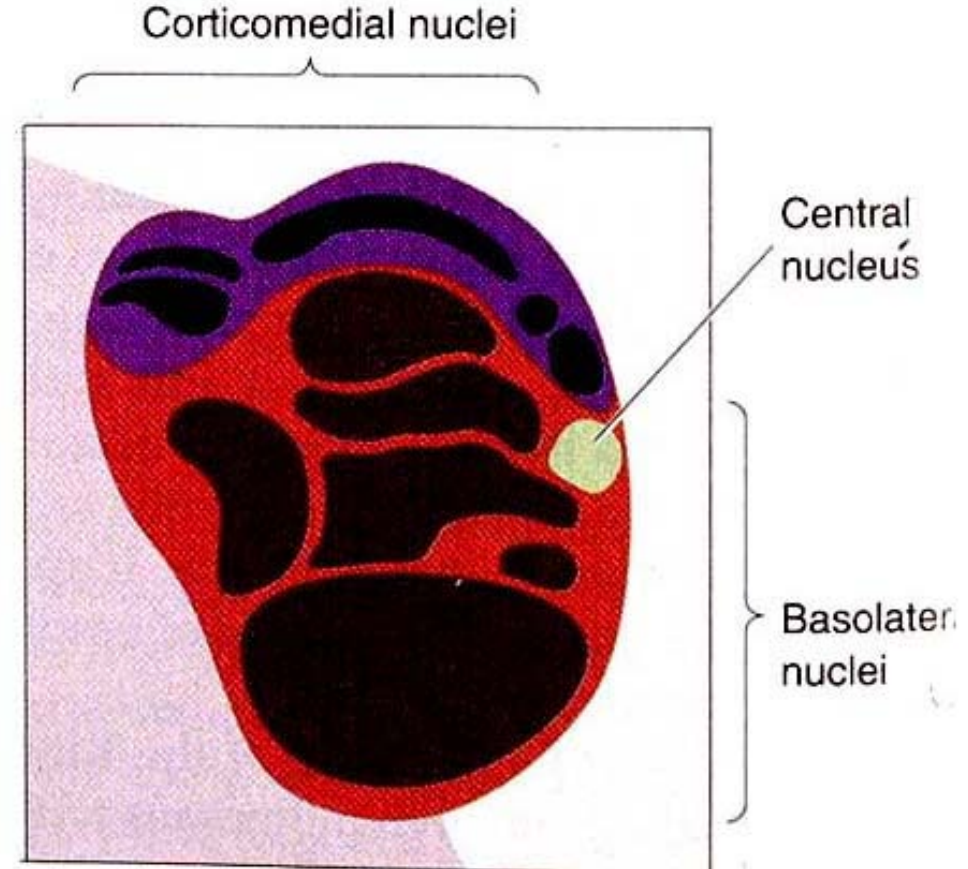
- blending with uncus
- with afferents from olfactory bulb (lateral olfactory area)



## Olfactory bulb and cortex

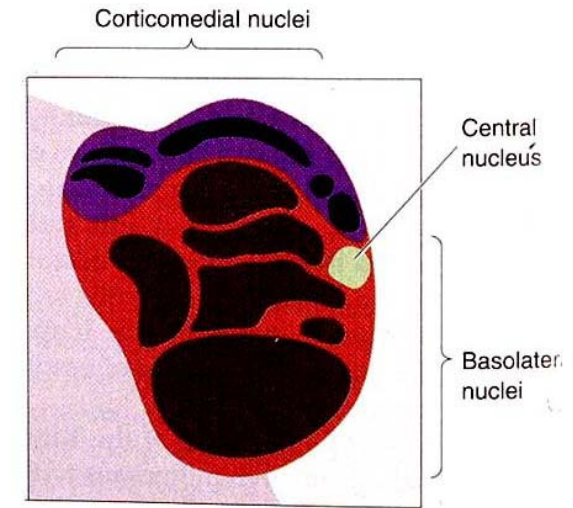


Hypothalamus

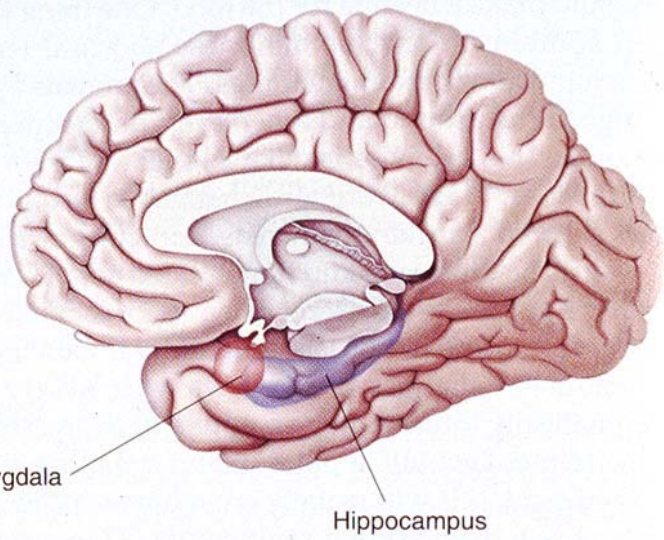


# Ventrolateral (central and basolateral nuclei) of AMG

- Both nuclei are a part of limbic system.
- **Central nuclei:** with corticomedial nu
- **Basolateral nuclei:** reciprocal connections with
  - limbic cortex (prefrontal, temporal lobes and cingulate gyrus);
  - thalamus and brainstem: medio-dorsal (dorsomedial) nuclei of thalamus, catecholamine nu, raphe nu, parabrachial nu of reticular formation;
  - septal area and anterior hypothalamus (stria terminalis)



# Interconnections of AMG



**Cortex**  
*temporal, insular,  
prefrontal, occipital*

Co-AMG

AMG-Co

**Sensory: somatic,  
visceral, auditory etc**

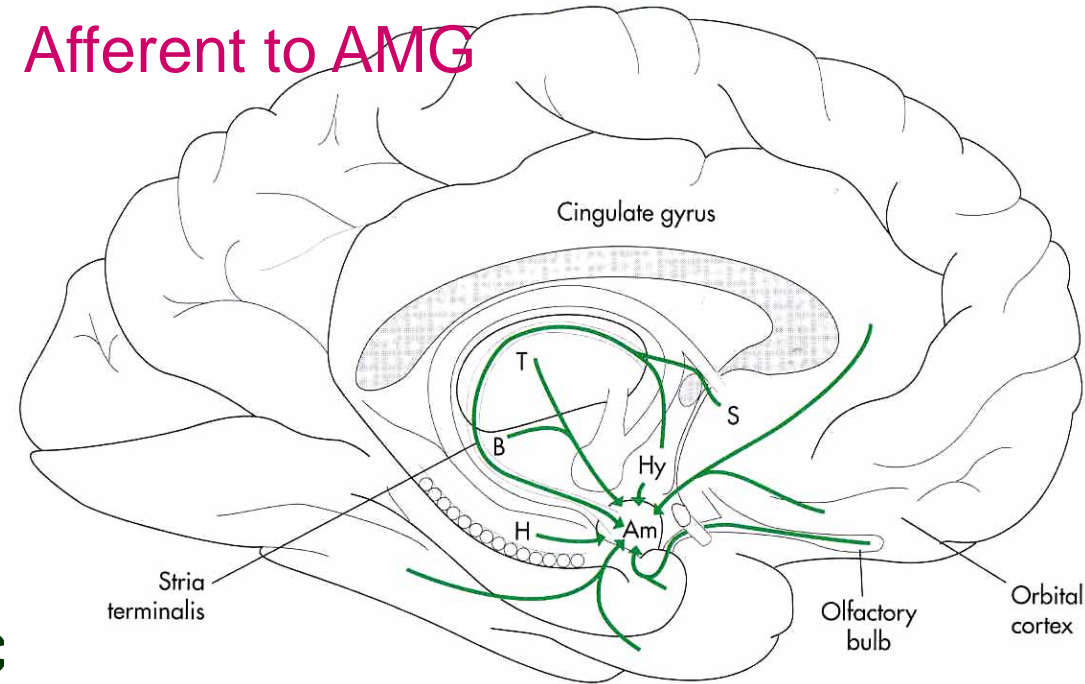
**VentroLat-AMG ↔ CM-AMG**

**Thalamus (Medio-dorsal)  
Hypothalamus  
Brainstem**

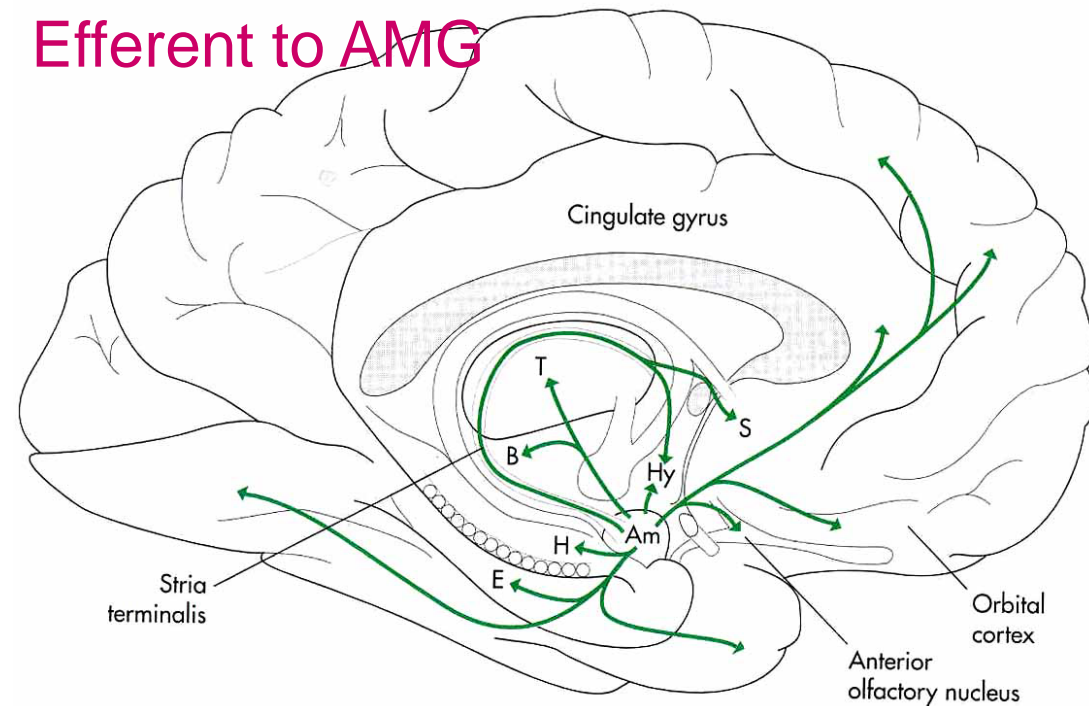
# Major pathways for amygdala

- Stria terminalis
  - To and from brainstem for regulations of autonomic responses etc
- Ventral amygdalofugal pathways via Diagonal band of Broca
- Medial forebrain bundle

## Afferent to AMG



## Efferent to AMG



# Stria terminalis: septal area --- AMG

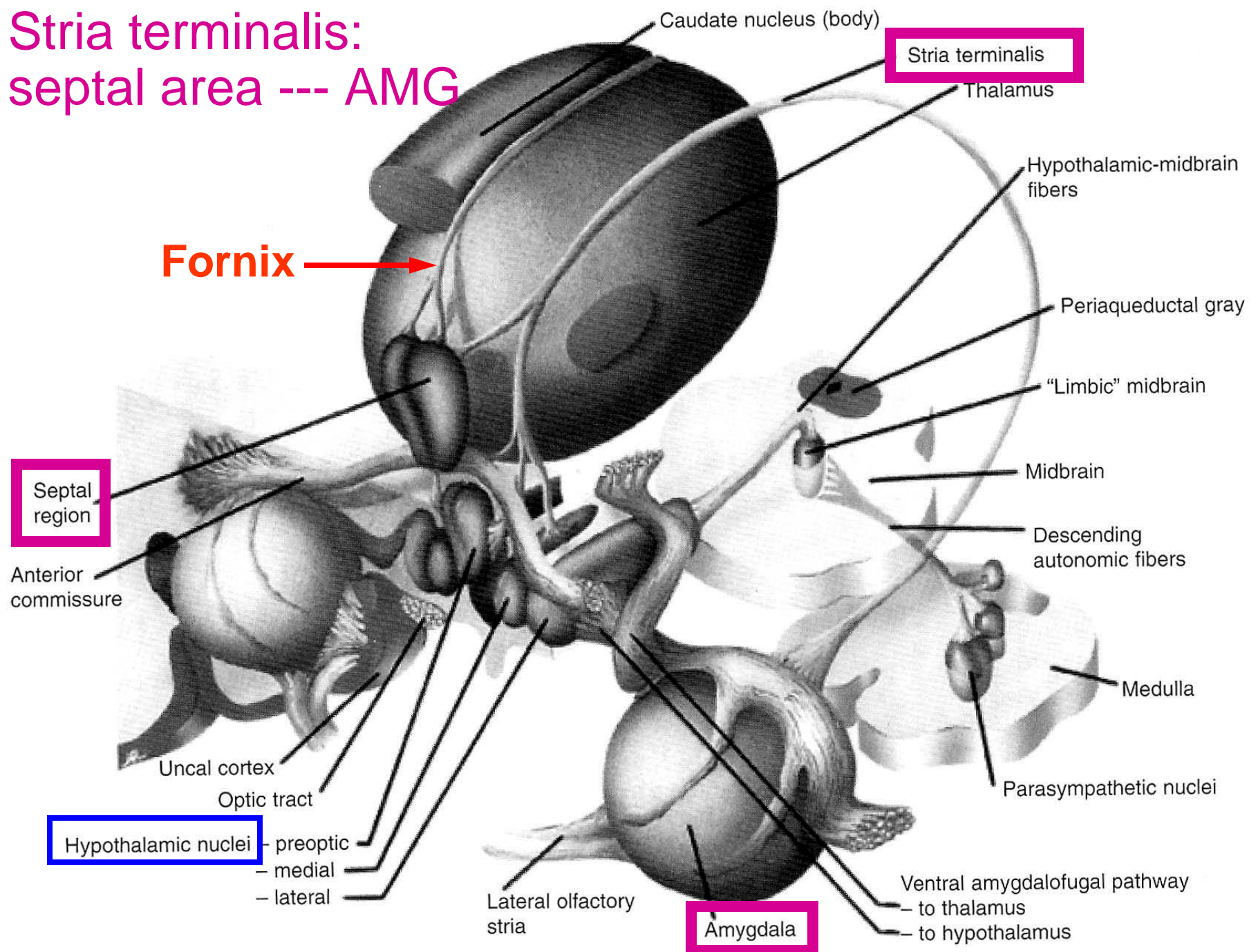
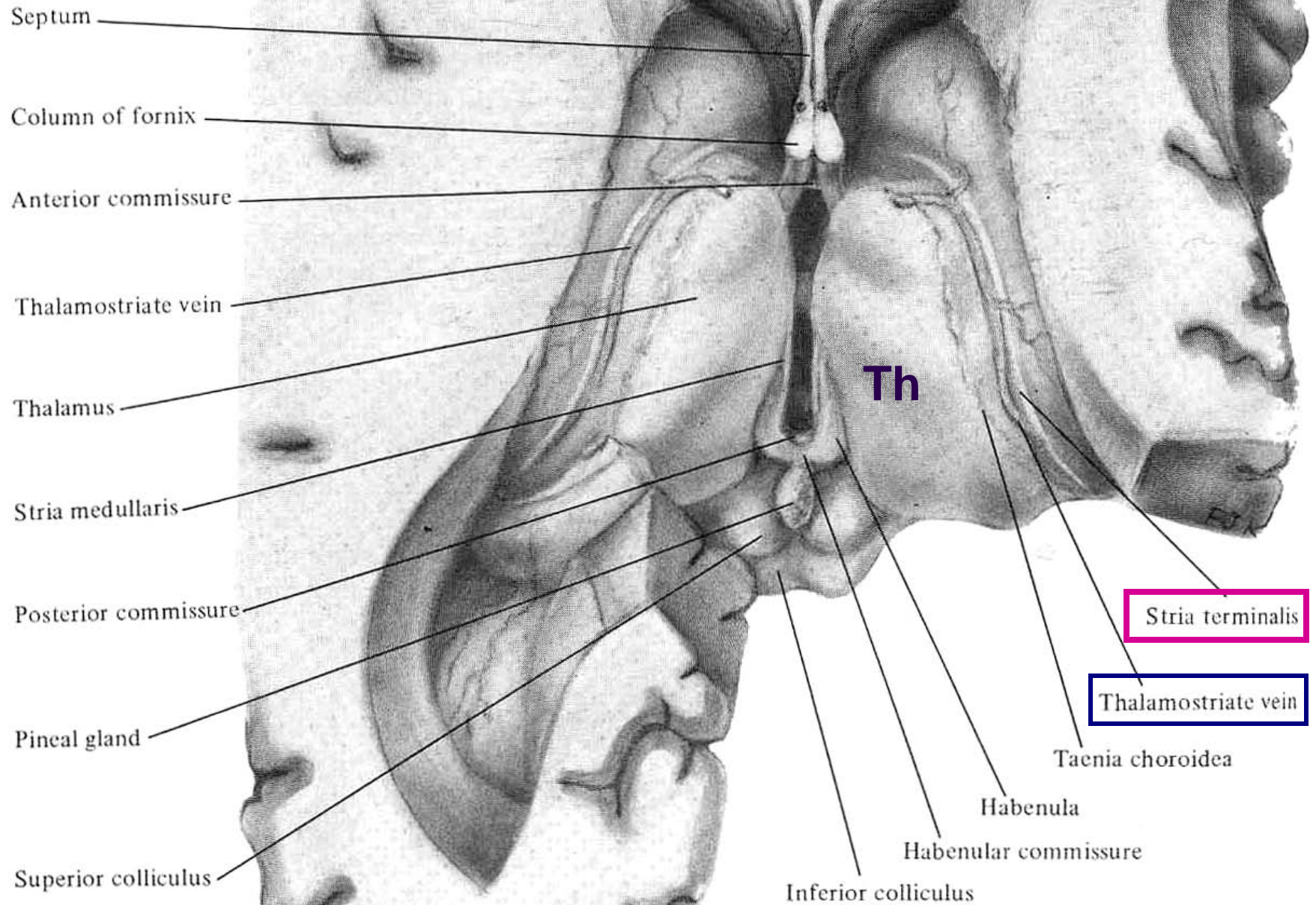
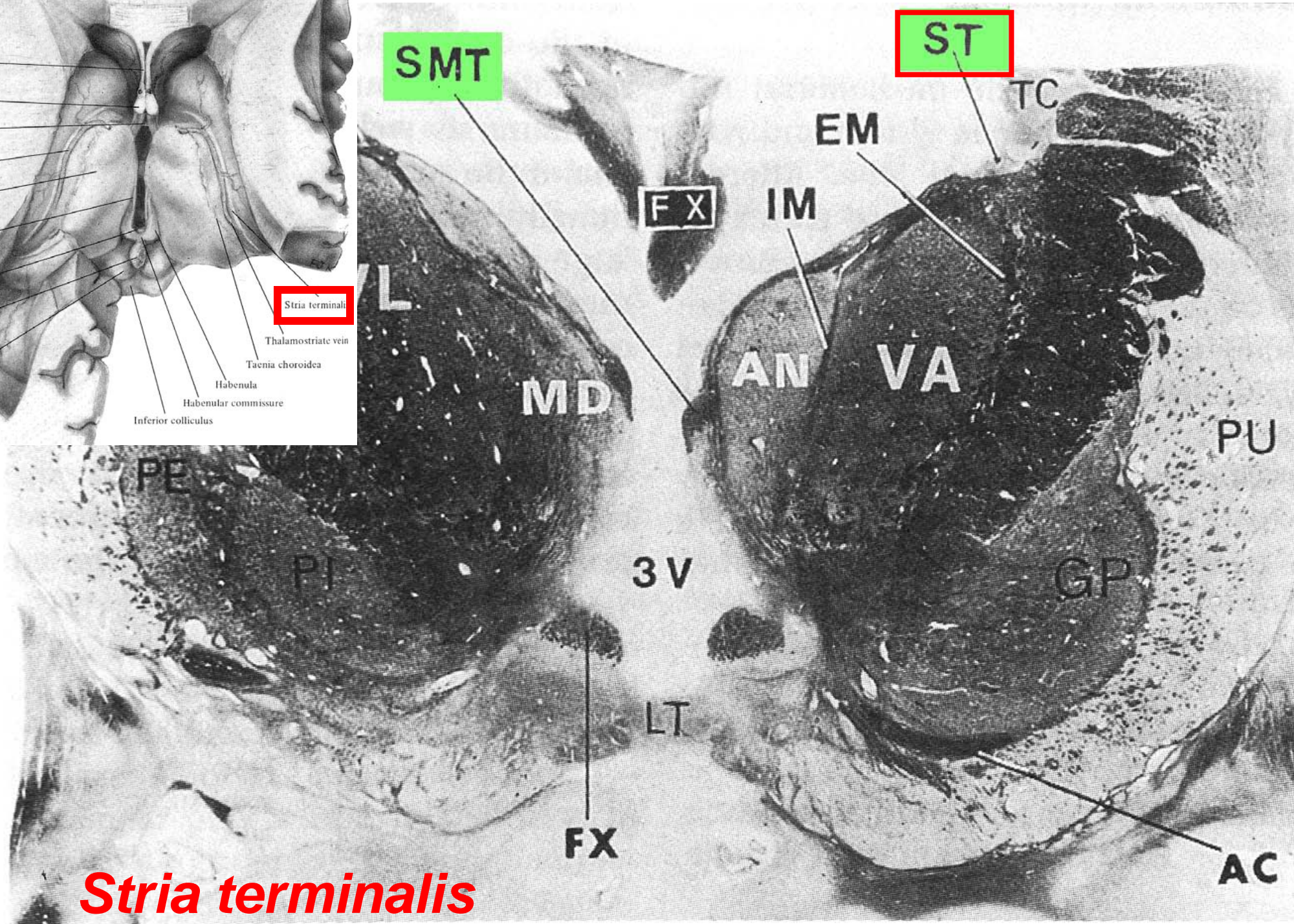
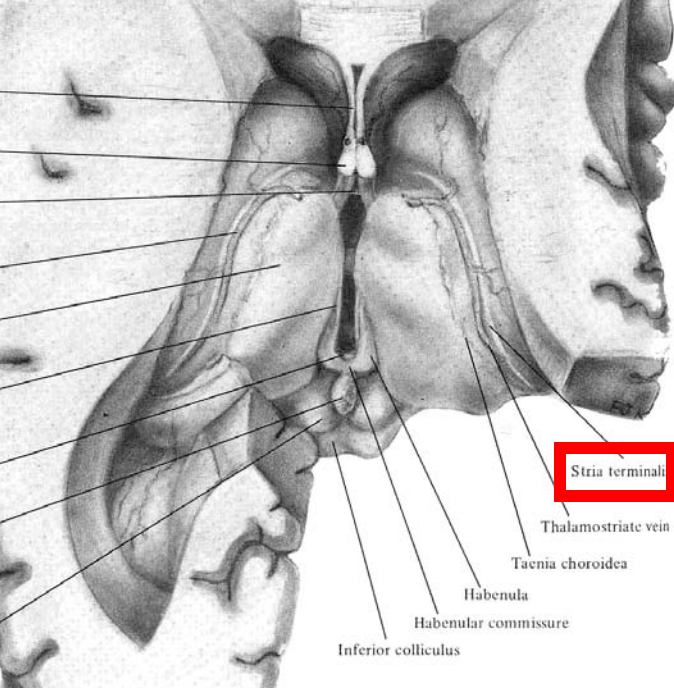


FIGURE 79B: Amygdala — Connections

# Stria terminalis

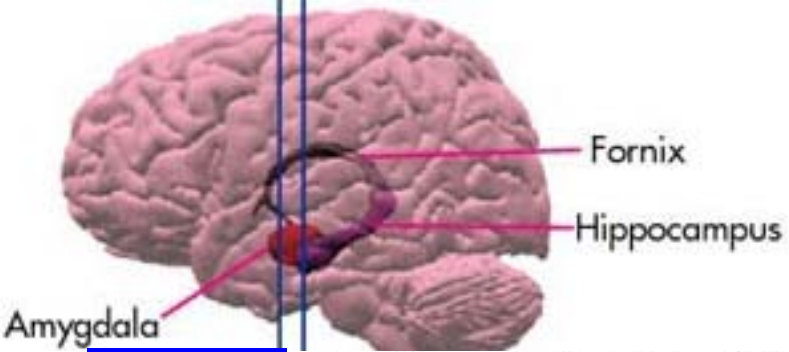




**Stria terminalis**



# Ventral amygdalofugal pathway (1)



Stria terminalis

Fornix (body)

Transverse fissure

Anterior nucleus

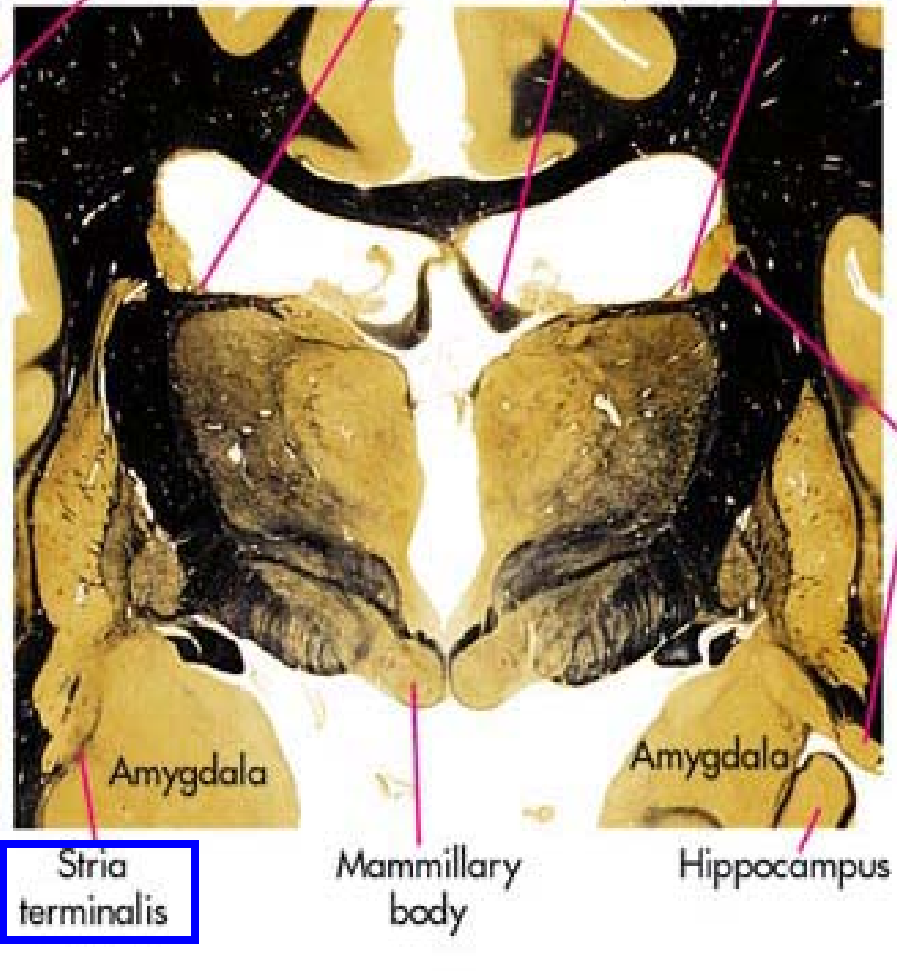
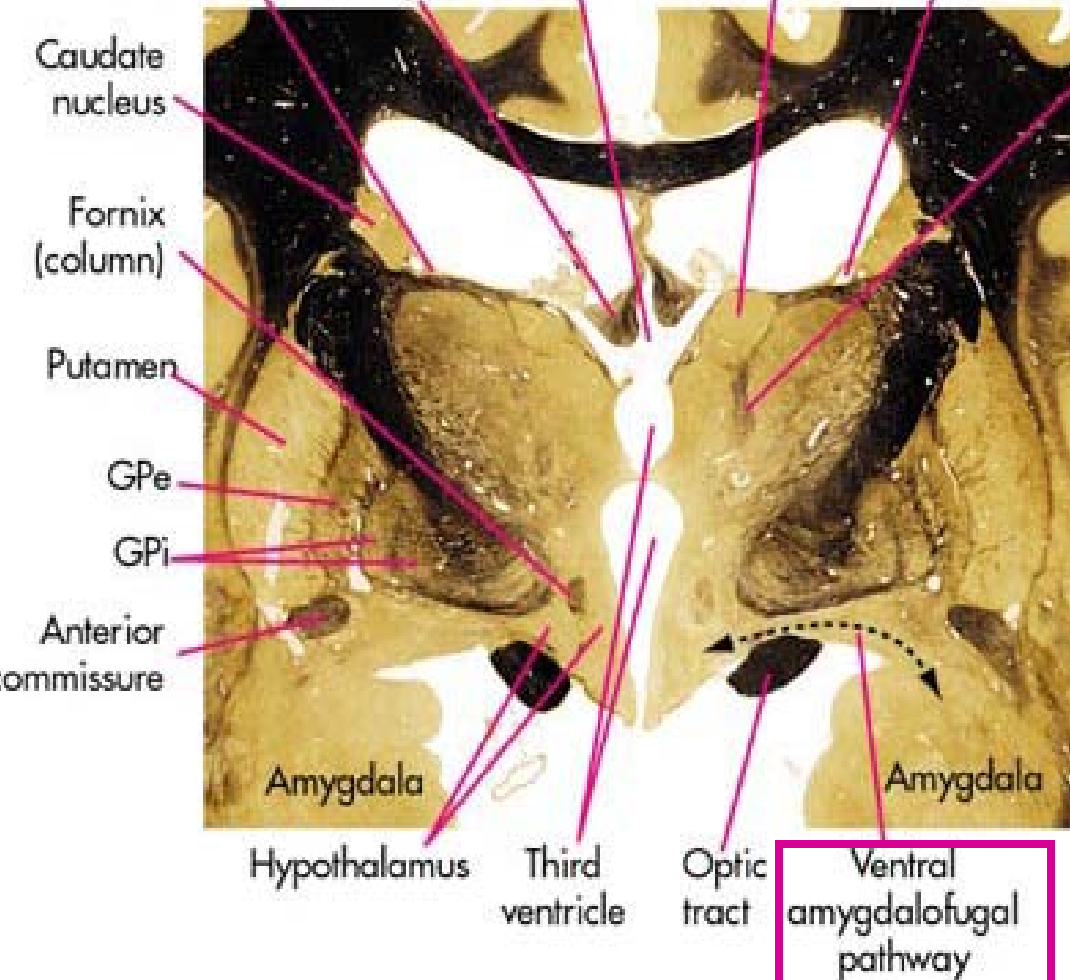
Terminal vein

Mammillothalamic tract

Stria terminalis

Fornix (body)

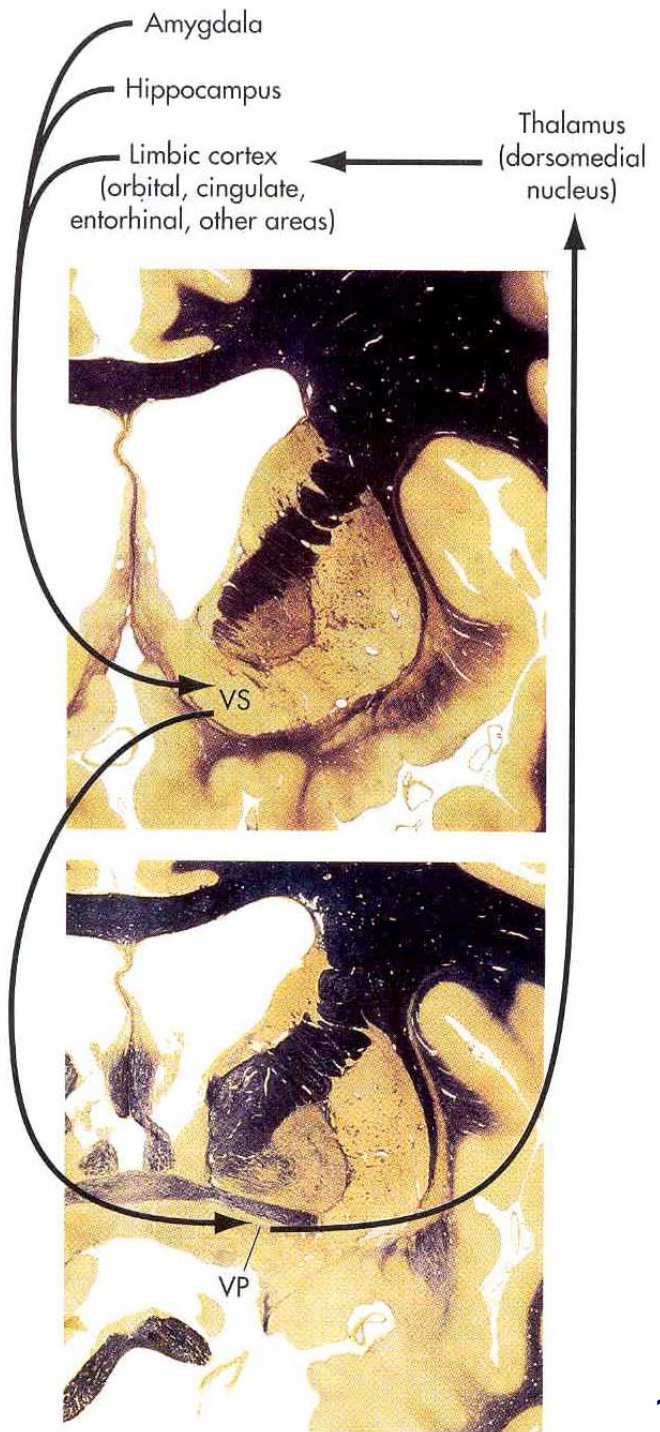
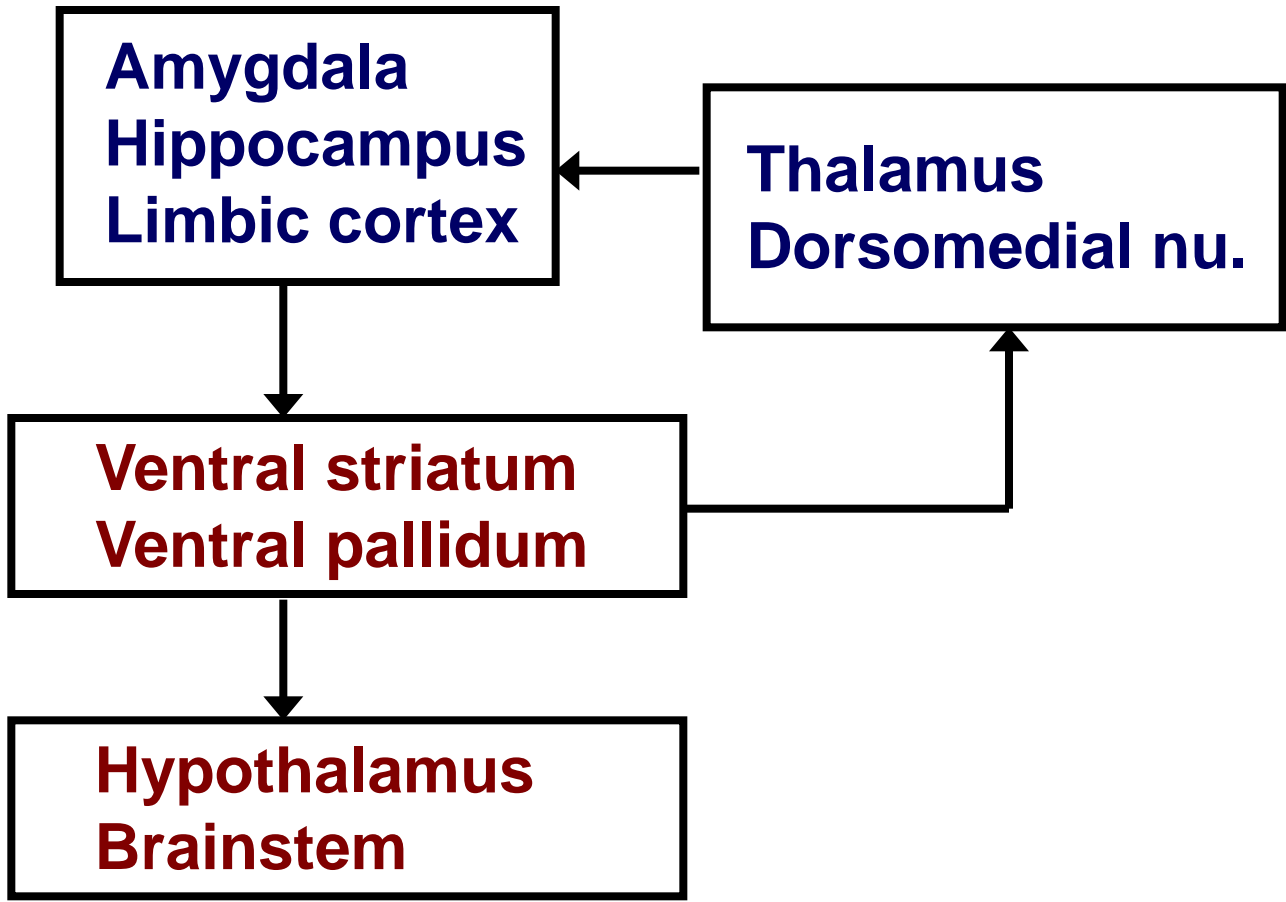
Terminal vein



Caudate nucleus

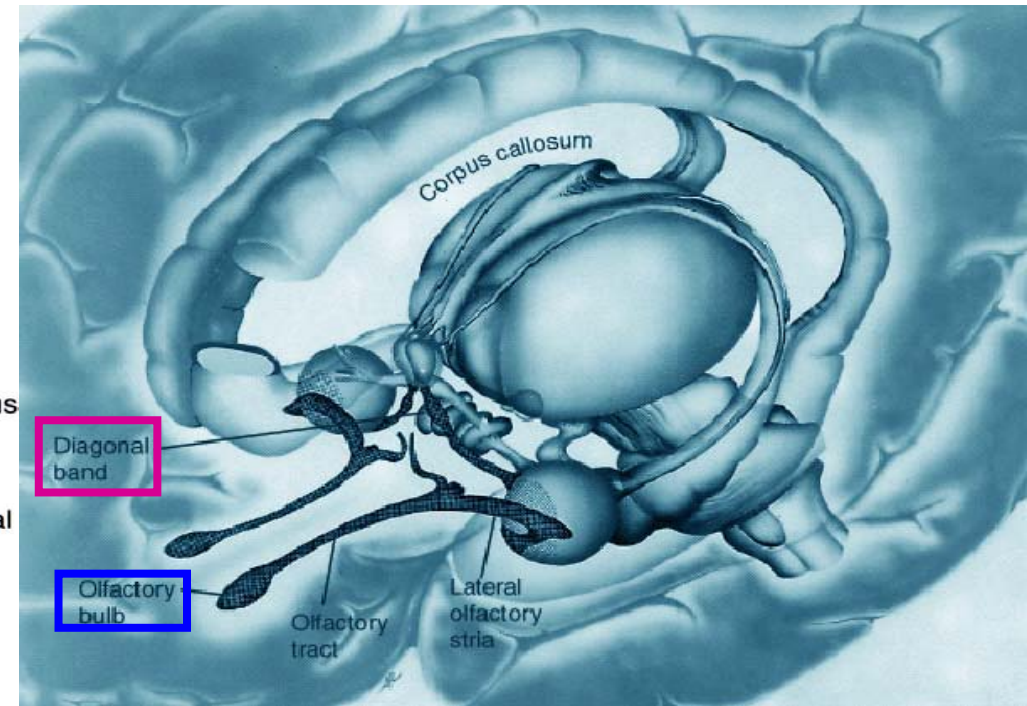
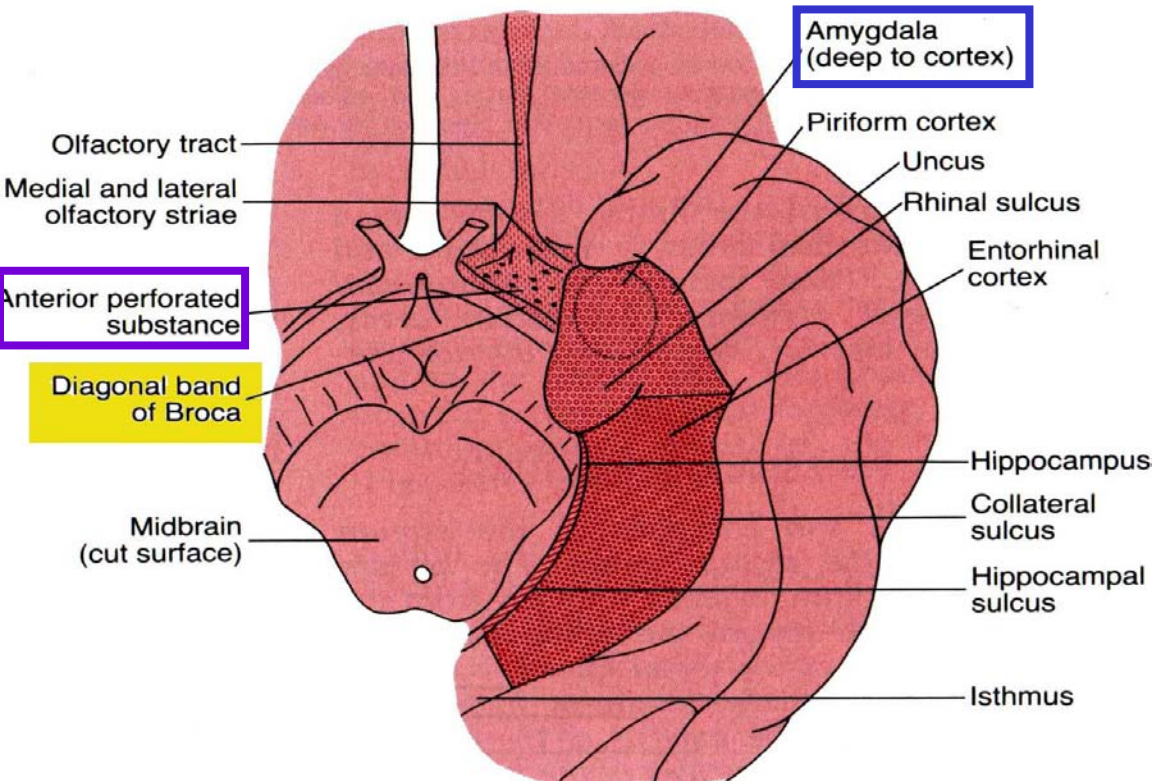
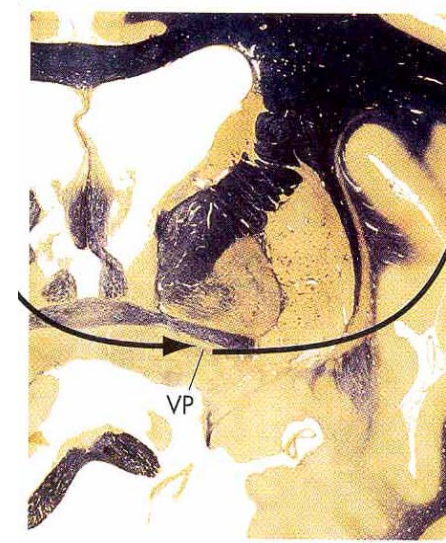
# Ventral amygdalofugal pathway (2)

- Emotionally driven activities
- also with some afferents



# Diagonal band of Broca

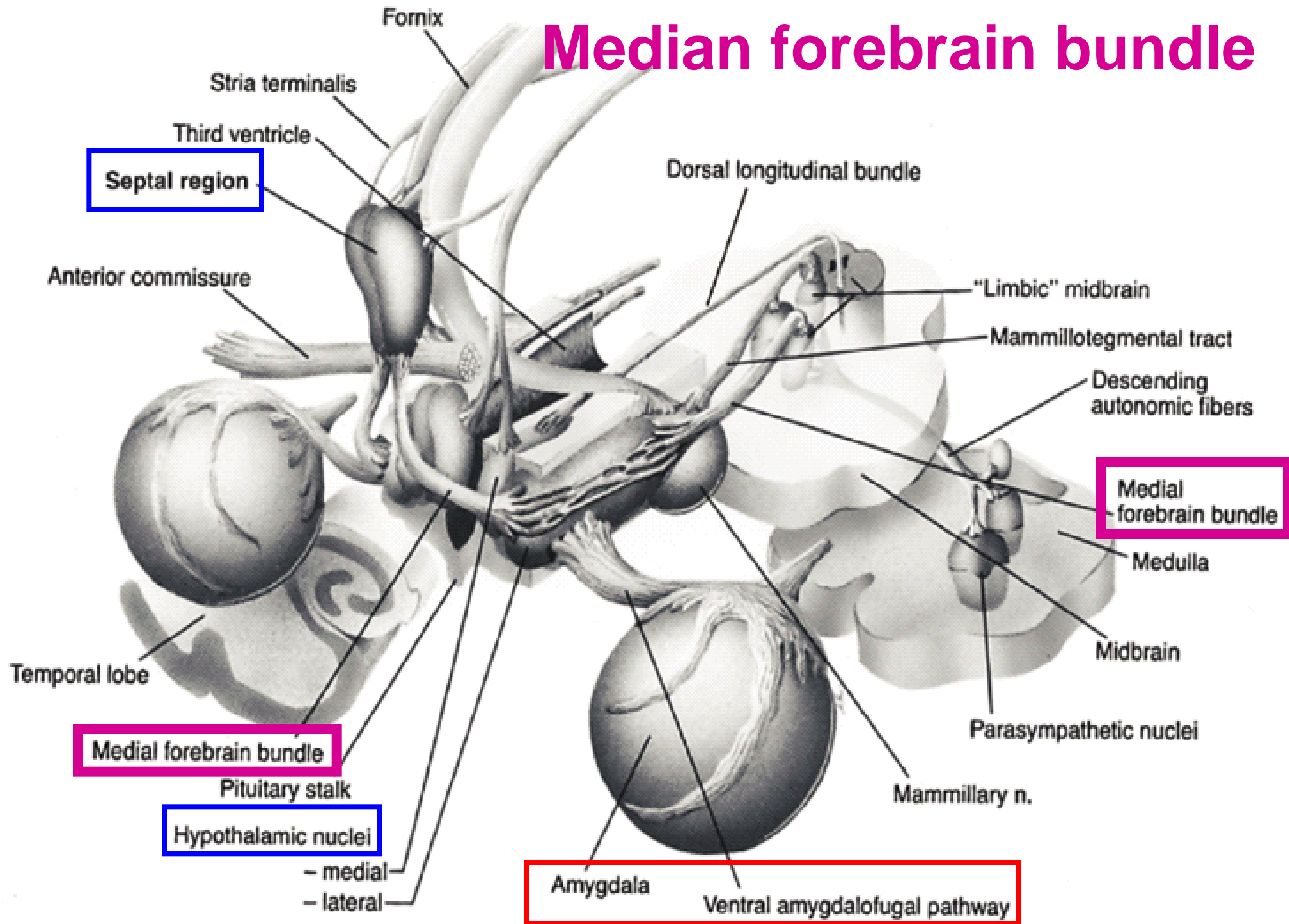
- in anterior perforated substance (orbital cortex, behind olfactory tract, with passage of vessels)
- connections between amygdala and septal area



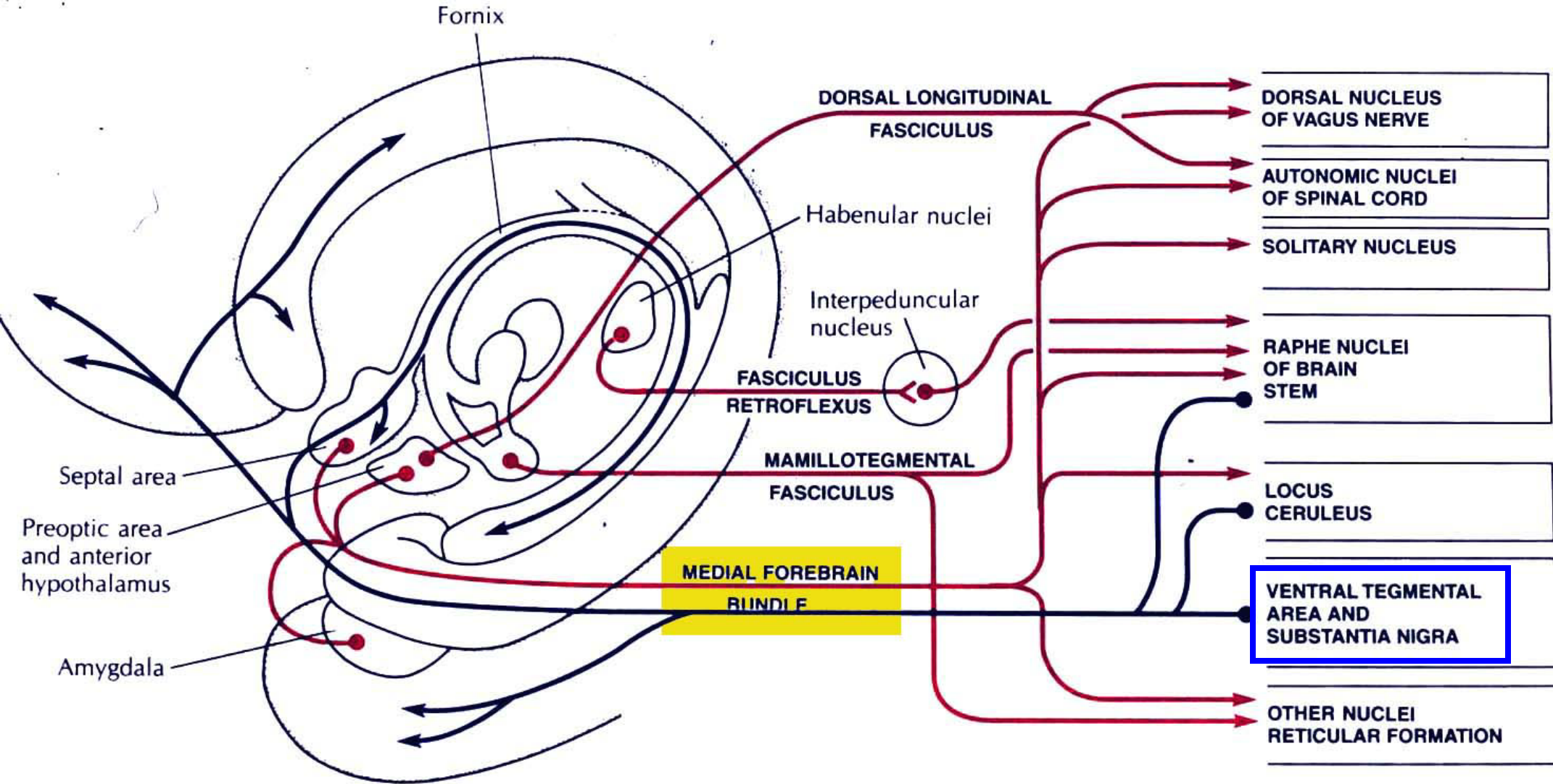
# Medial forebrain bundle

- a collective term for fibers passing the ventral (basal) surface of the brain
  - contains heterogeneous fiber tracts for different destinations
- important tracts for ascending and descending interconnections between septal area, hypothalamus and brainstem

# Median forebrain bundle



# Medial forebrain bundle



# AMG and autonomic nervous system

**AMG**

↓ **Stria terminalis**

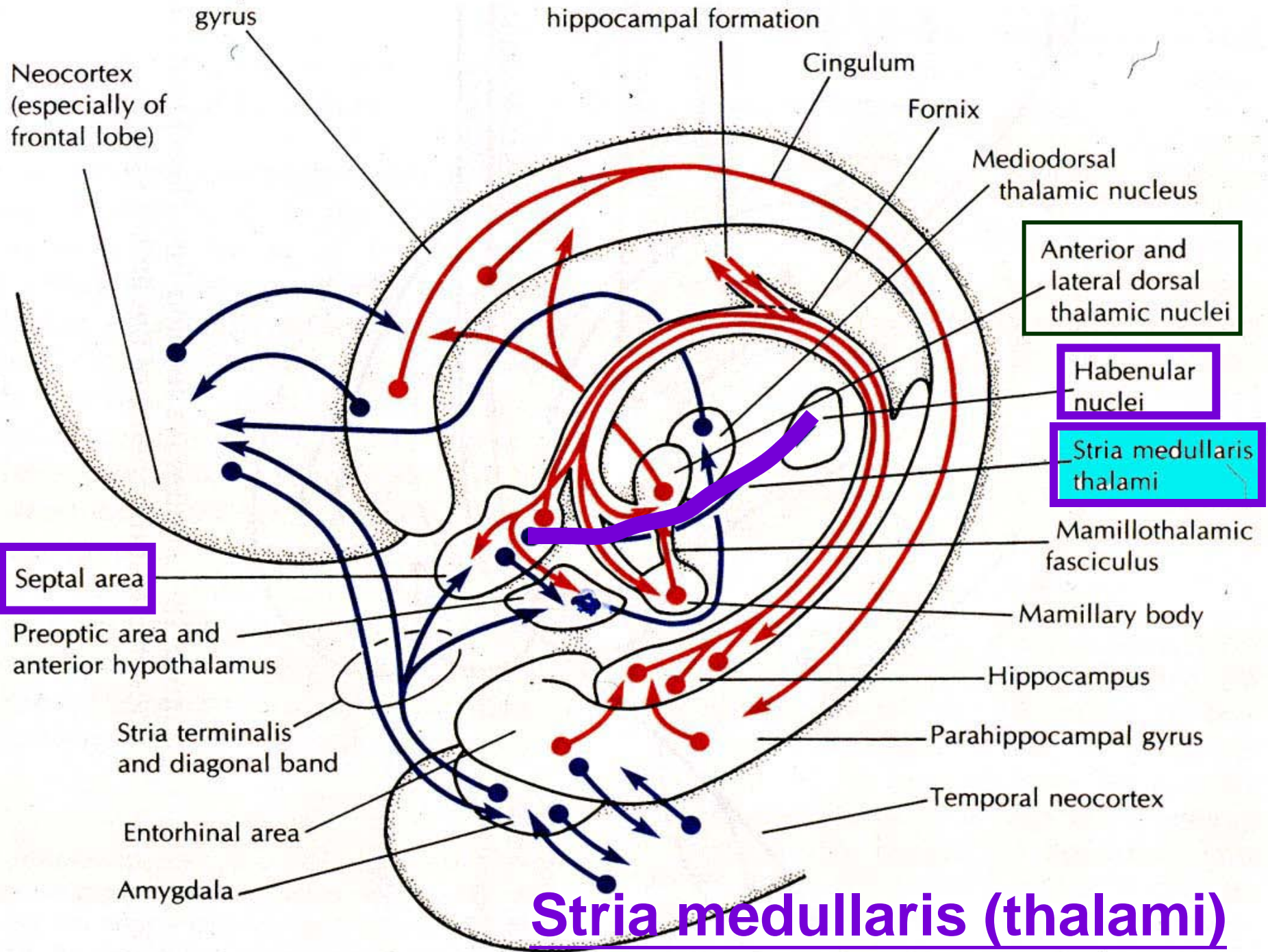
**Septal area / Anterior hypothalamus**

↓ **Stria medullaris (thalami)**

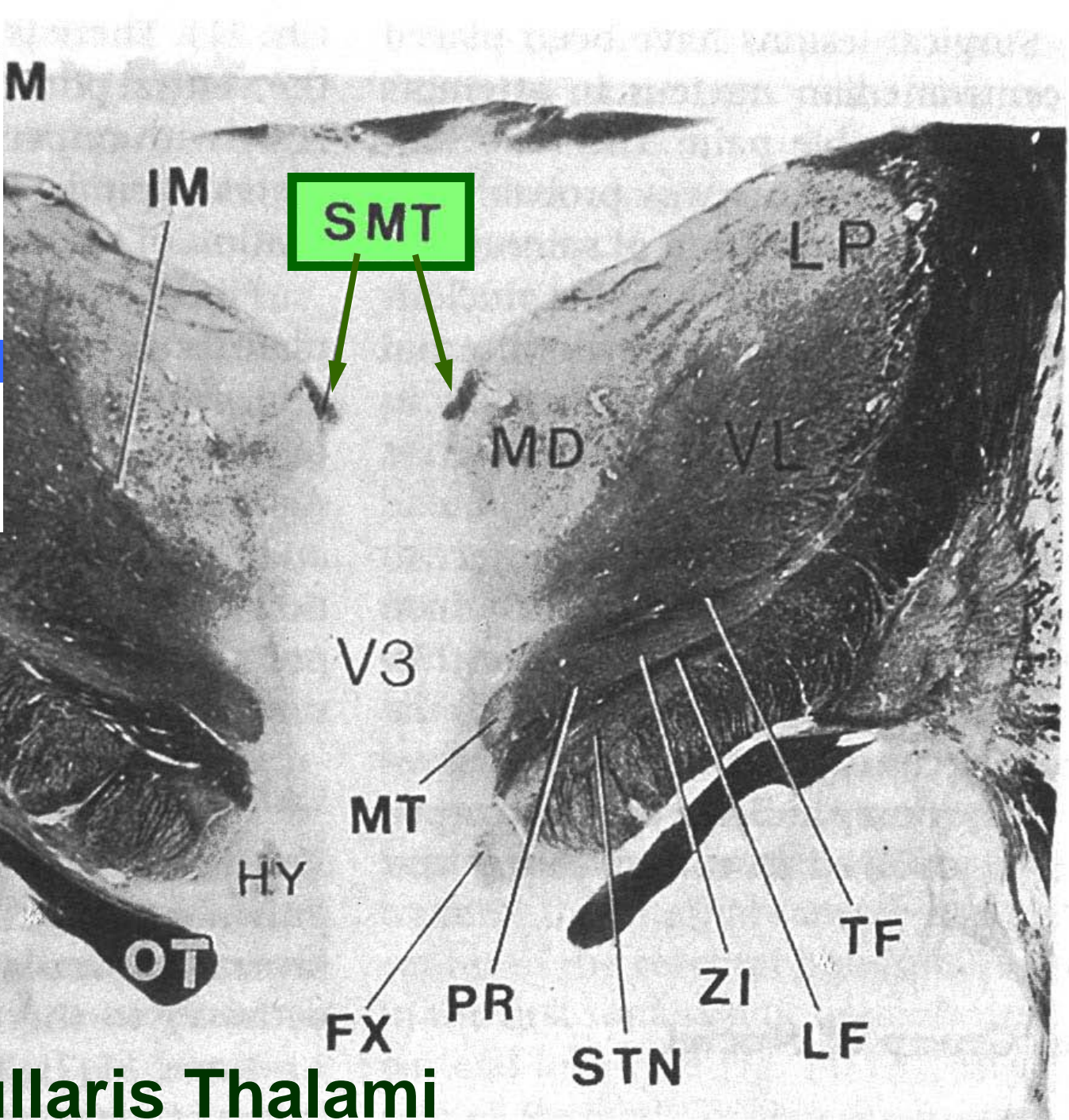
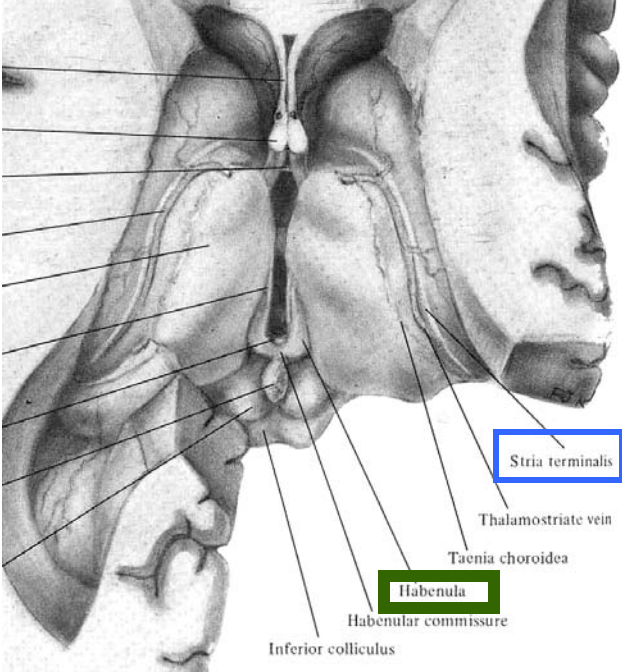
**Habenular nu. of dorsal thalamus**

↘ **Fasciculus retroflexus**  
**Interpeduncular nu. of midbrain**

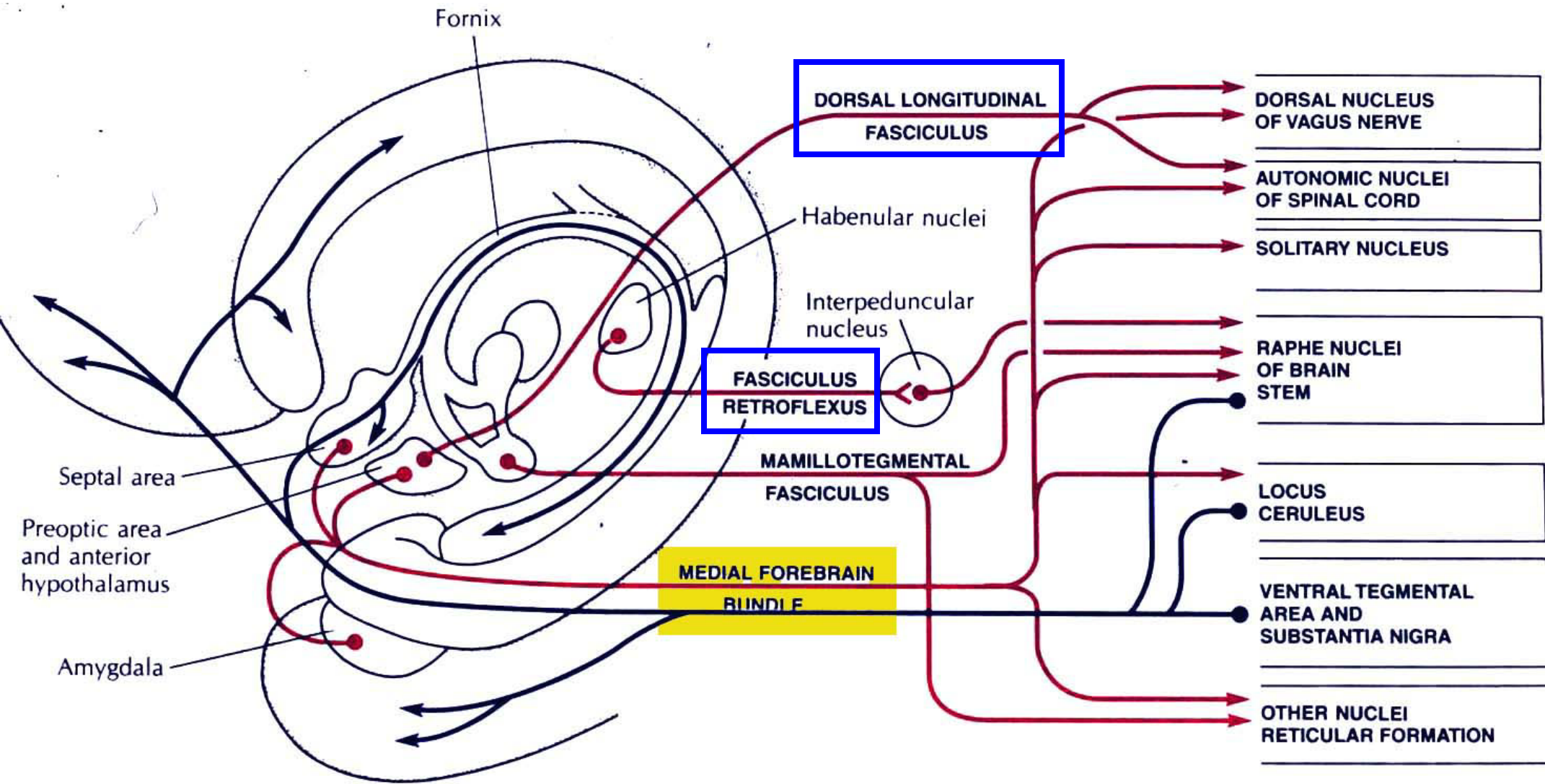
↓ **Dorsal longitudinal fasciculus**  
**Hypothalamospinal fibers**





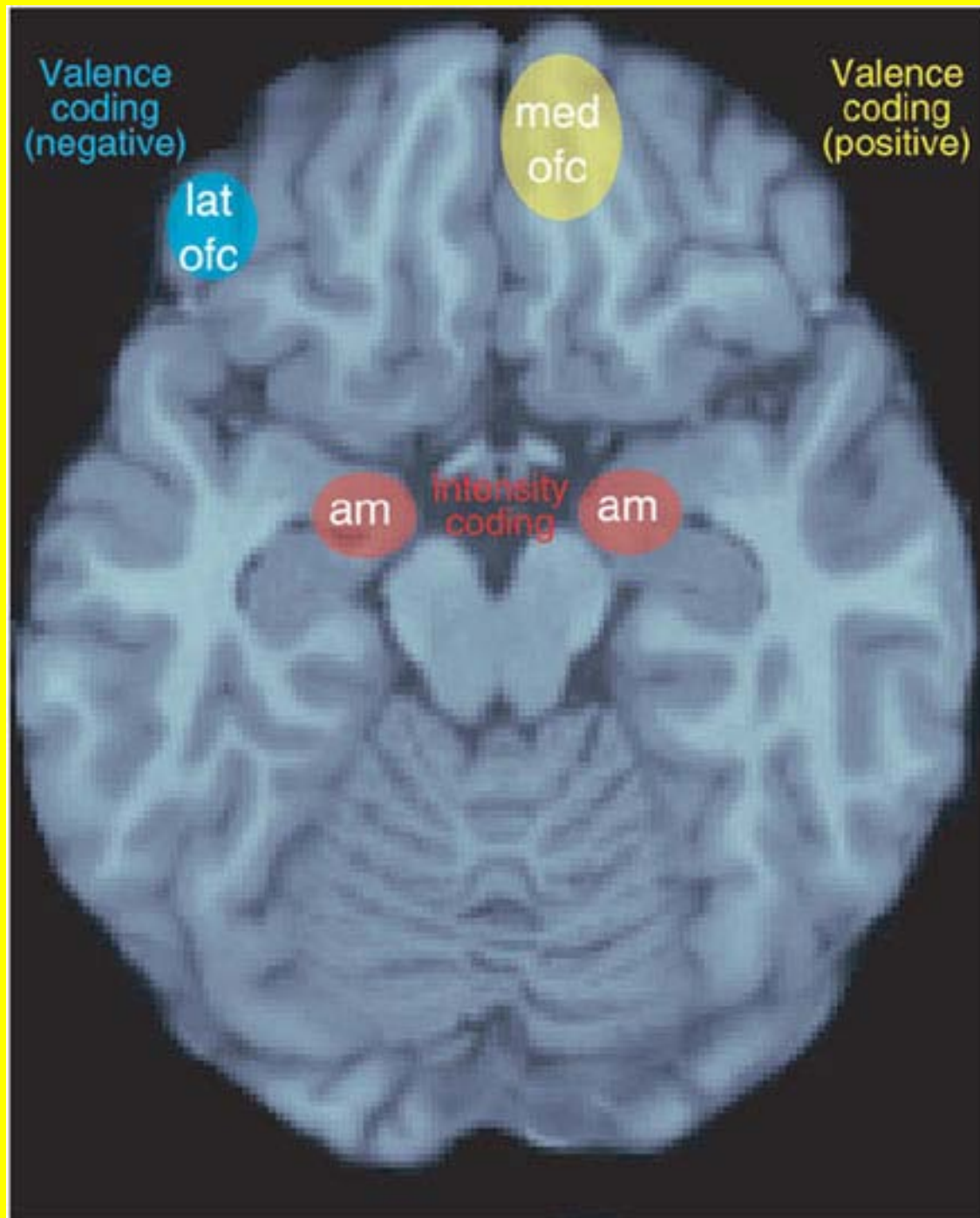


Limbic **Stria Medullaris Thalami**



# Functions of Amygdala

- Related to emotional feelings
  - Fear
  - Anger
- Methods of study
  - Electrical stimulation
  - Functional magnetic resonance imaging (fMRI)
  - Destructive lesions in temporal lobes
    - **Kliver-Bucy Syndrome**: docility, loss of ability to learn, and abnormal sexual activity

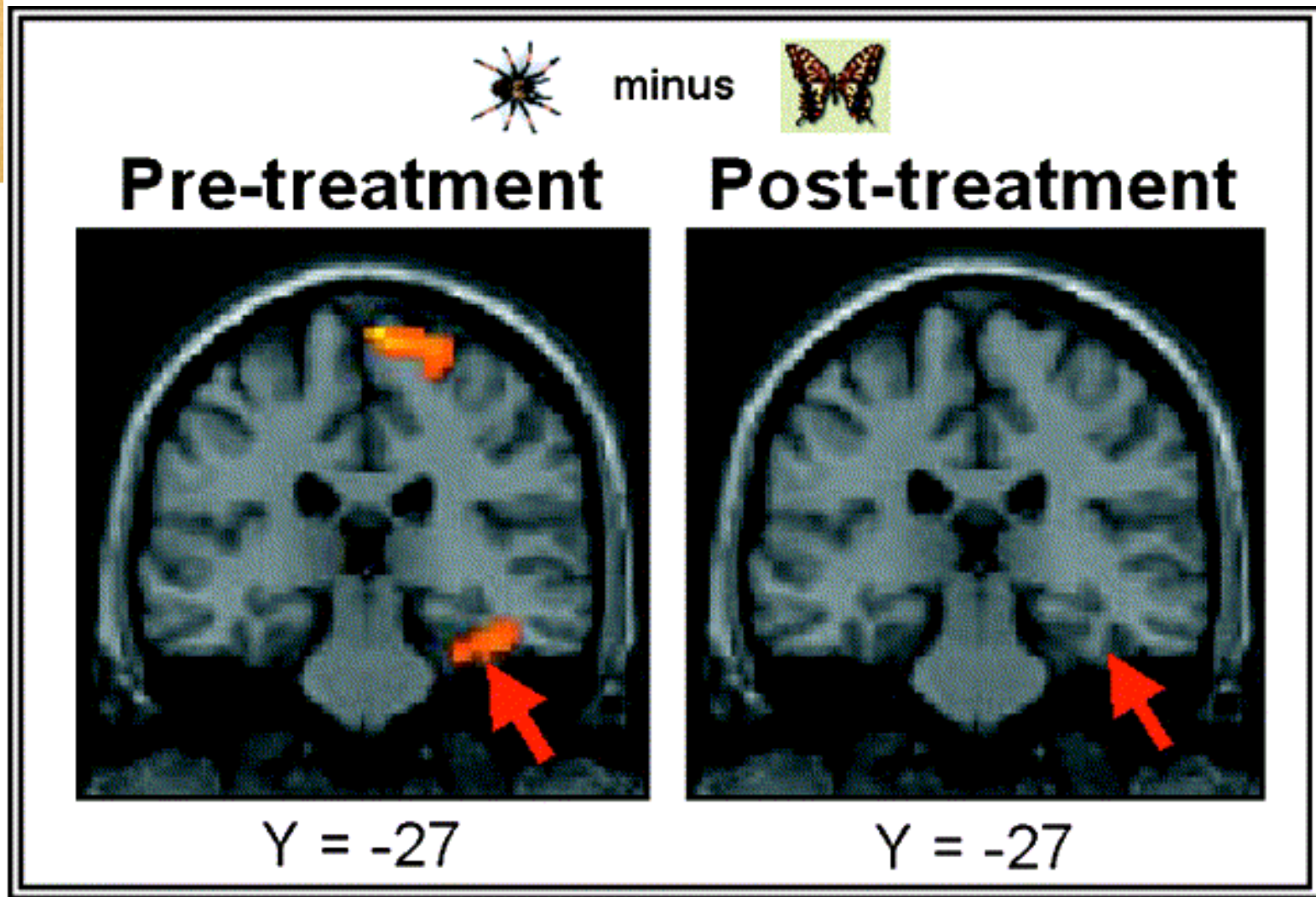


# Olfactory system and Amygdala

# Fear perception and response



- Visual perception
- Amygdala
  - Neocortex: fear sensations / recognition
  - Autonomic system: (unconscious) responses
  - Conditional reflex, Memory

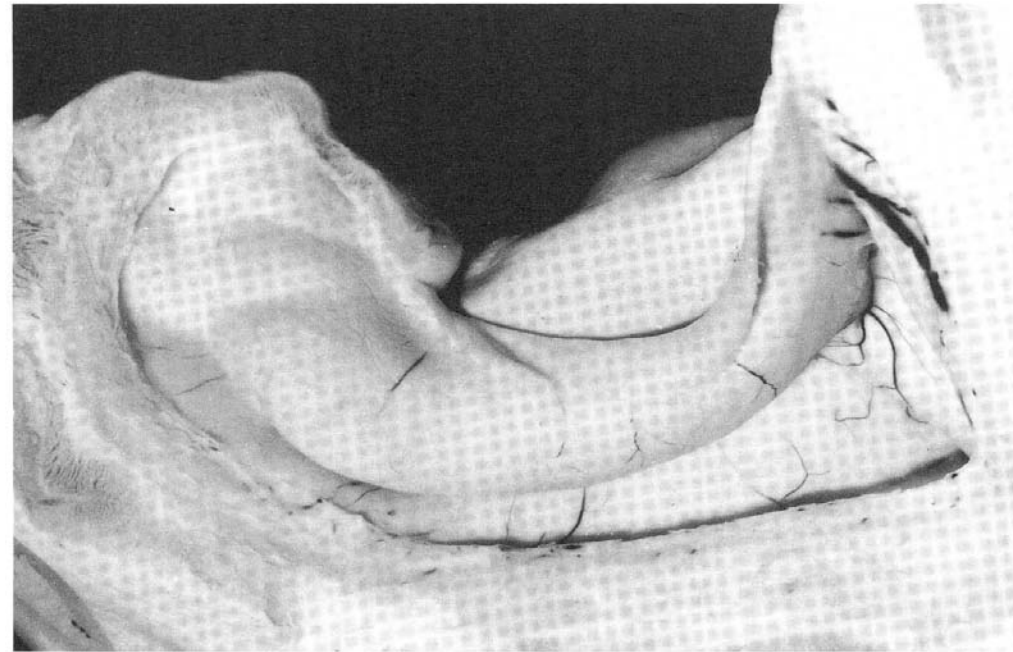
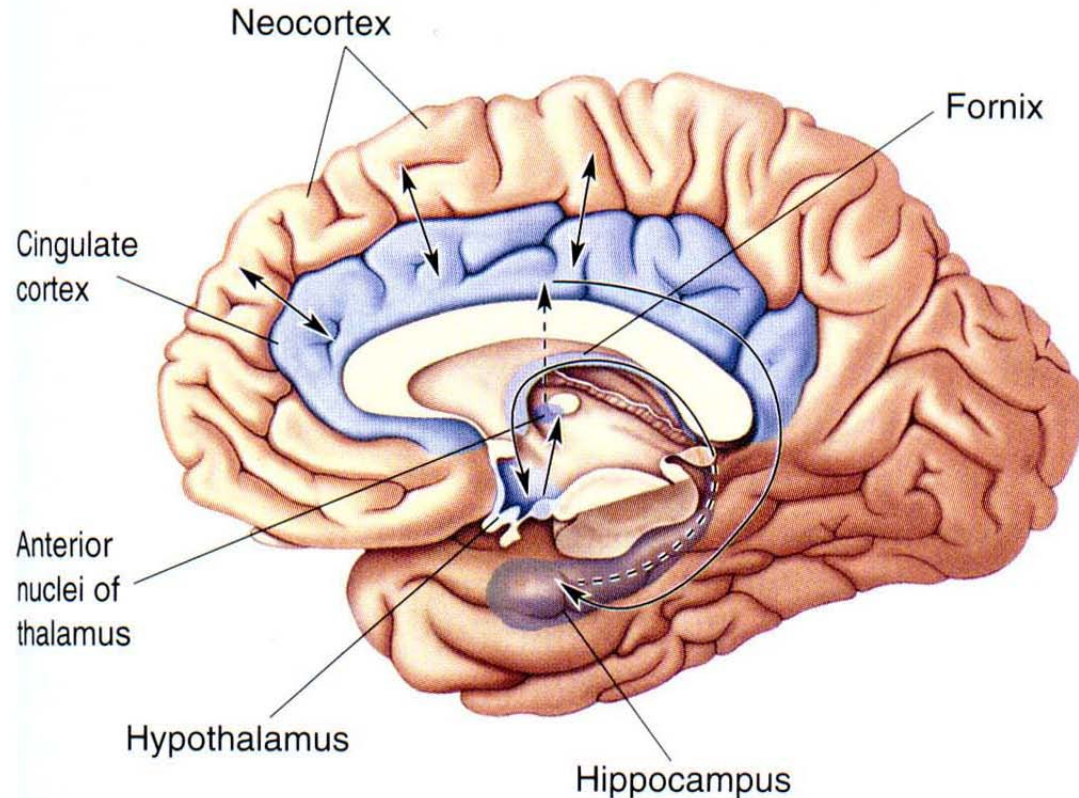


# Summary: amygdala

- **Organization**
  - **corticomedial (olfactory)**
  - **ventrolateral (limbic)**
- **Connections**
  - **cortex (limbic: prefrontal, temporal, cingulate)**
  - **thalamus (medio-dorsal)/brainstem (catechoaminergic)**
  - **other limbic structures: septal area, hypothalamus**
- **Pathways**
  - **Stria terminalis**
  - **Medial forebrain bundle**
  - **Ventral amygdalofugal pathway**

# Hippocampus

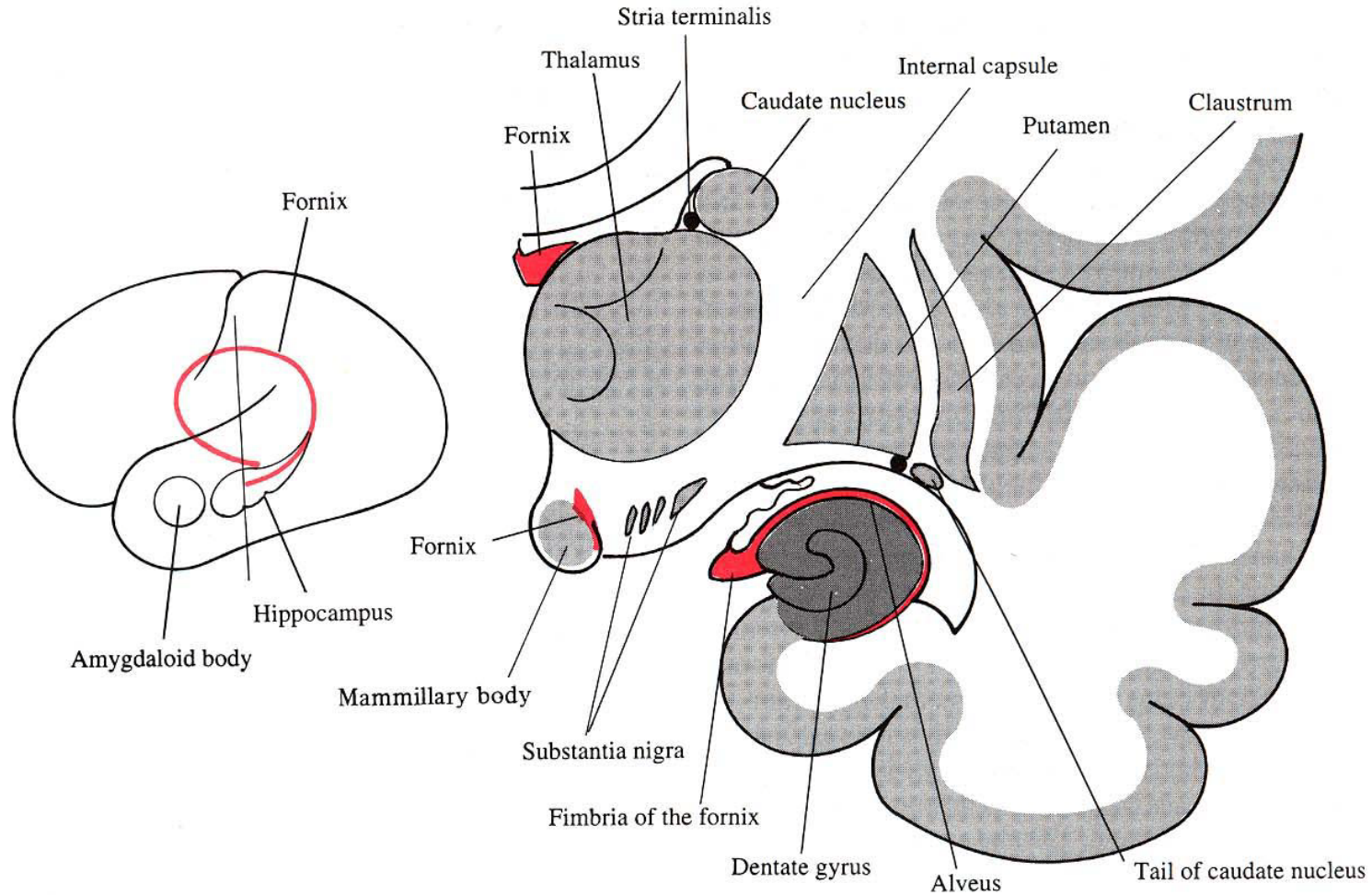
- **Medial (mesial) surface of temporal lobe**
- **Anterior-posterior extension**





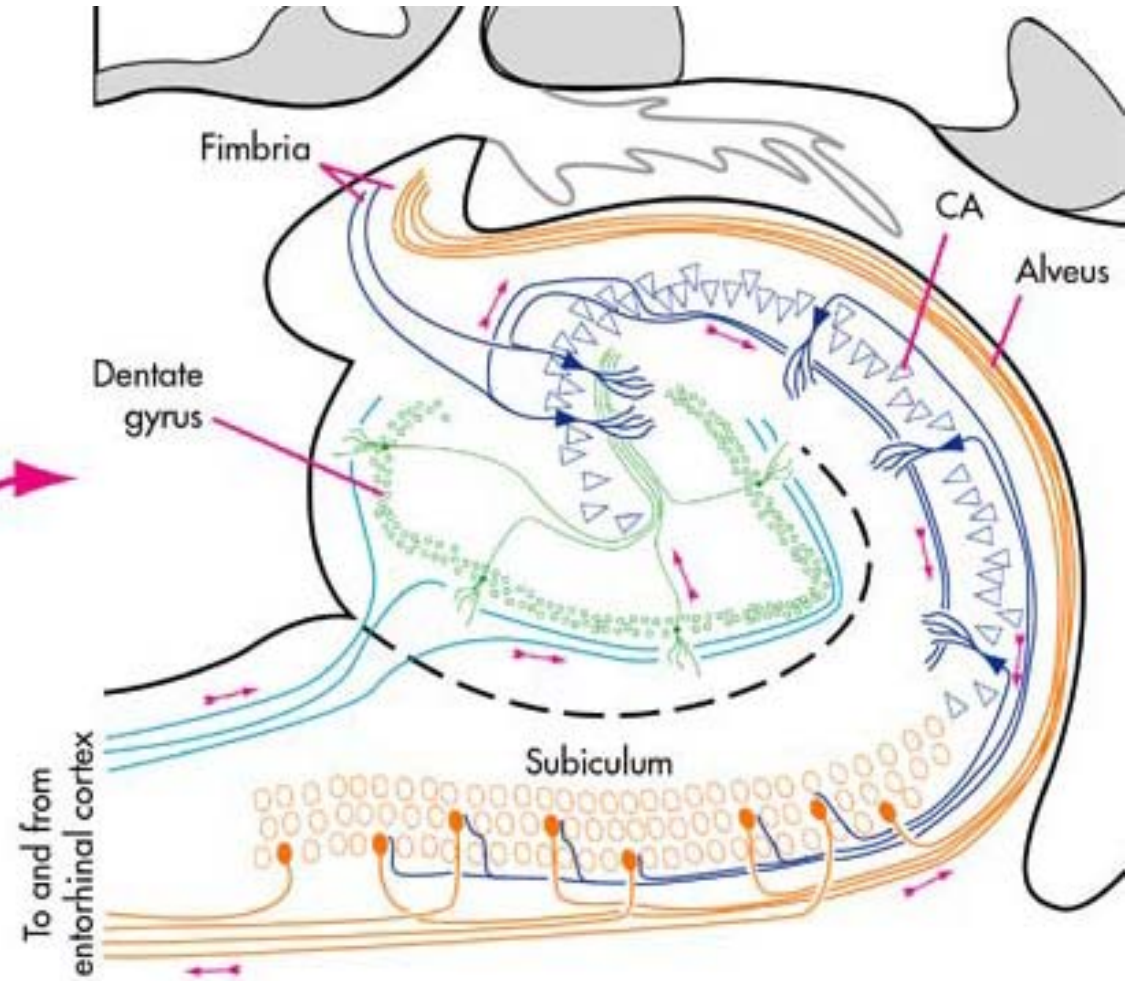
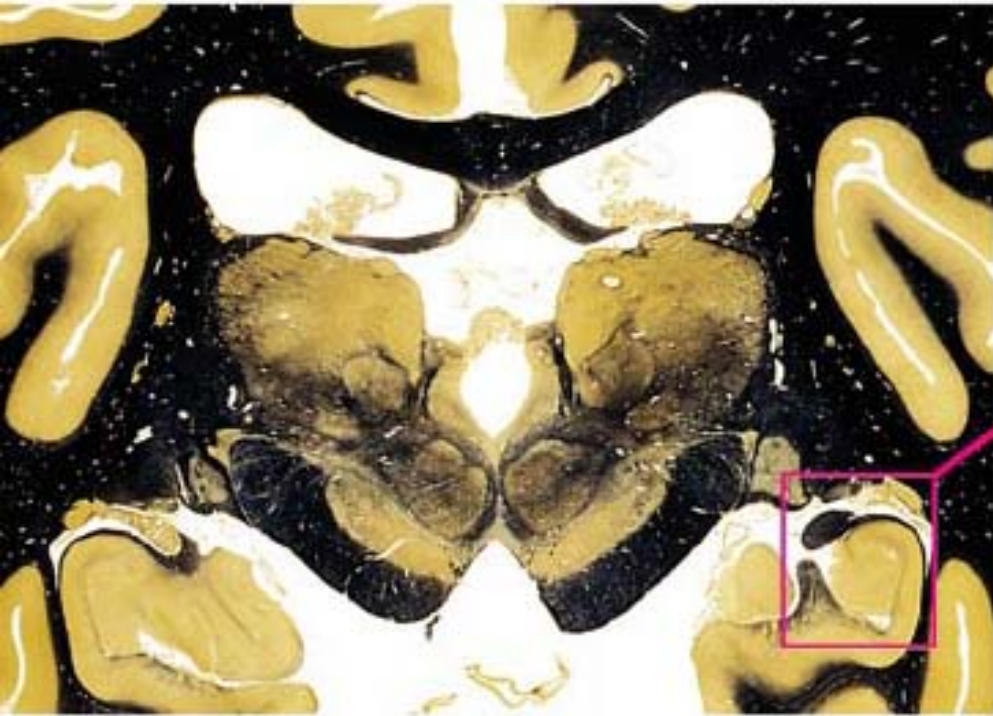
# Hippocampus

- **Medial surface of temporal lobe**
- **Beneath lateral ventricle**



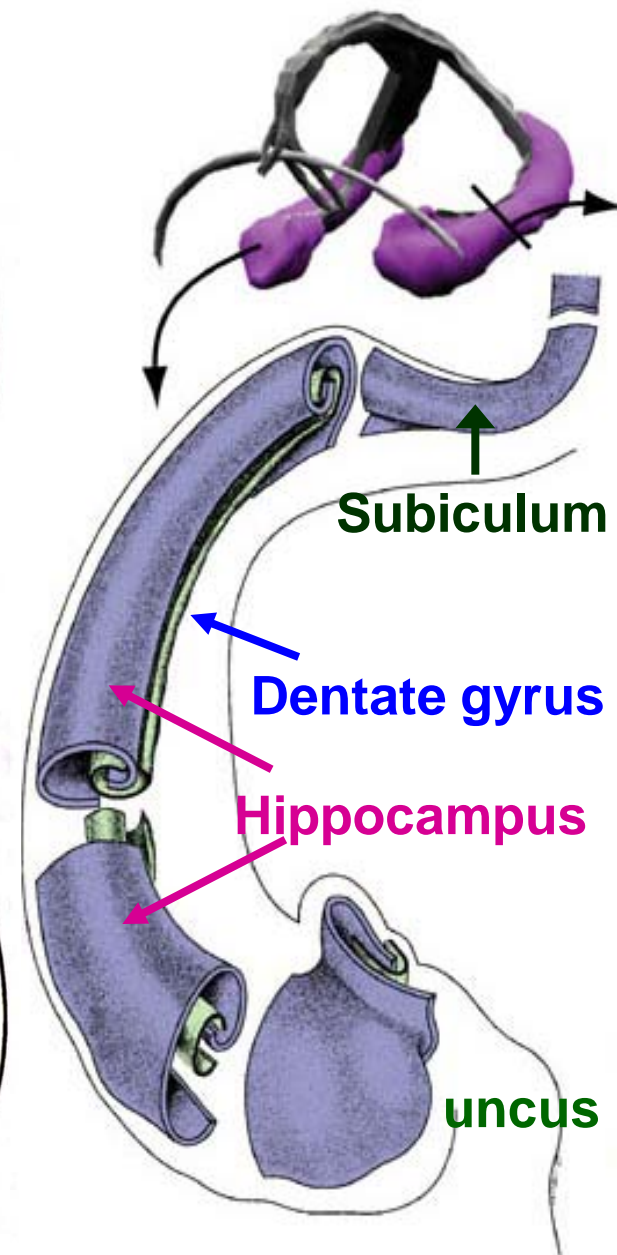
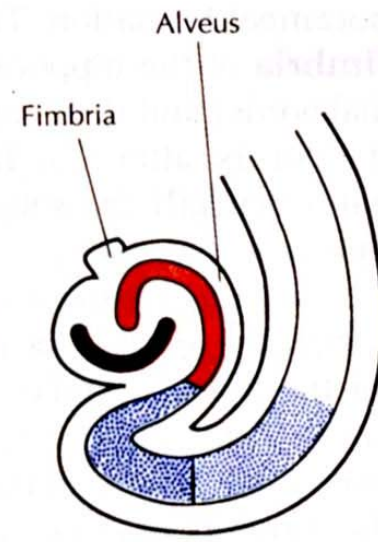
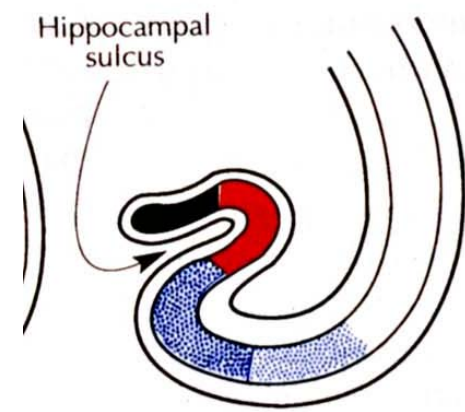
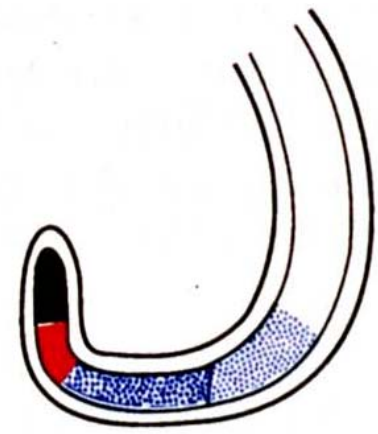
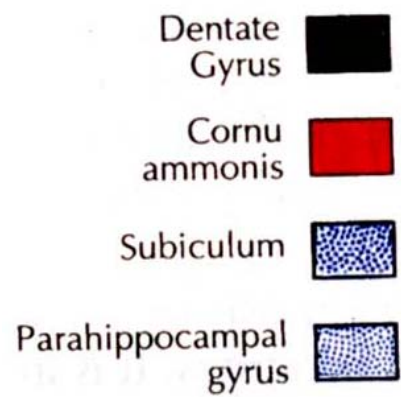


# Hippocampus



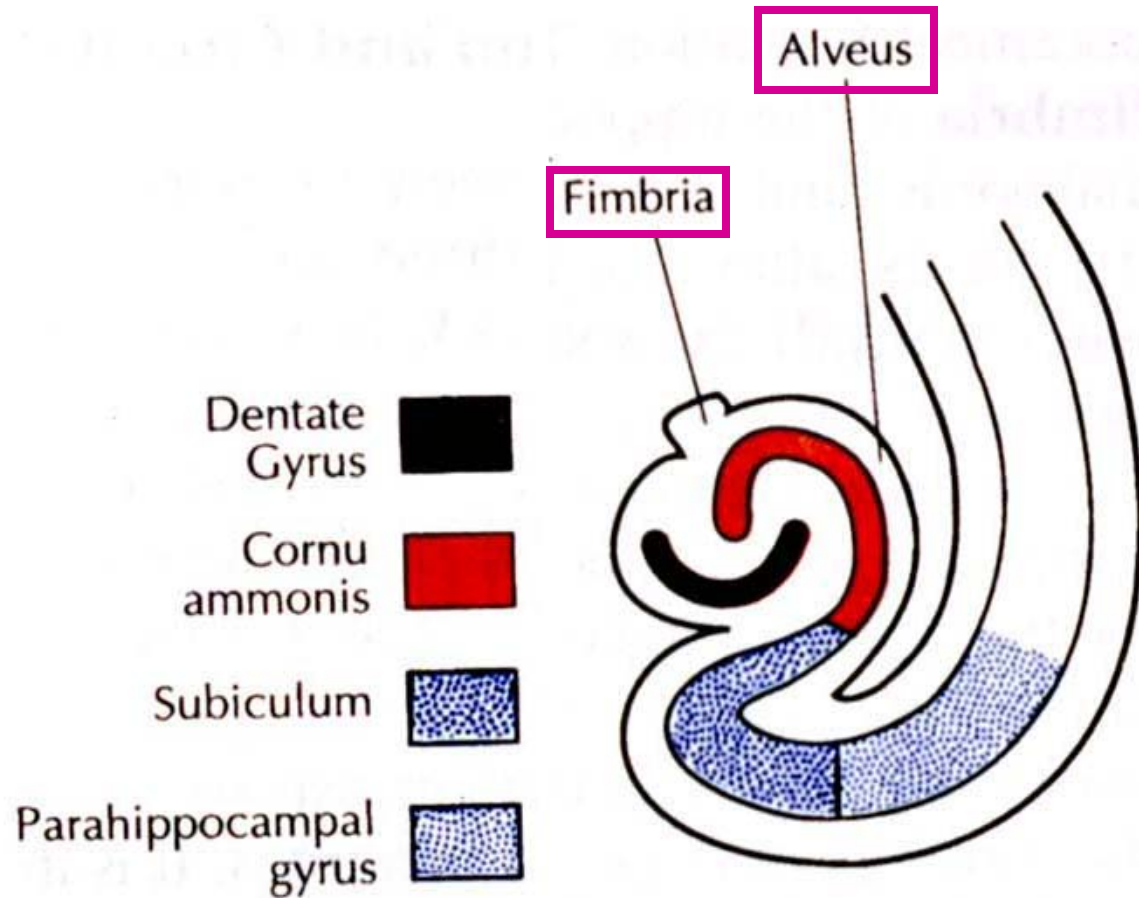
# Structure of hippocampus

- Dentate gyrus
- Hippocampus (proper), cornu ammonis
- Parahippocampal gyrus
  - Subiculum

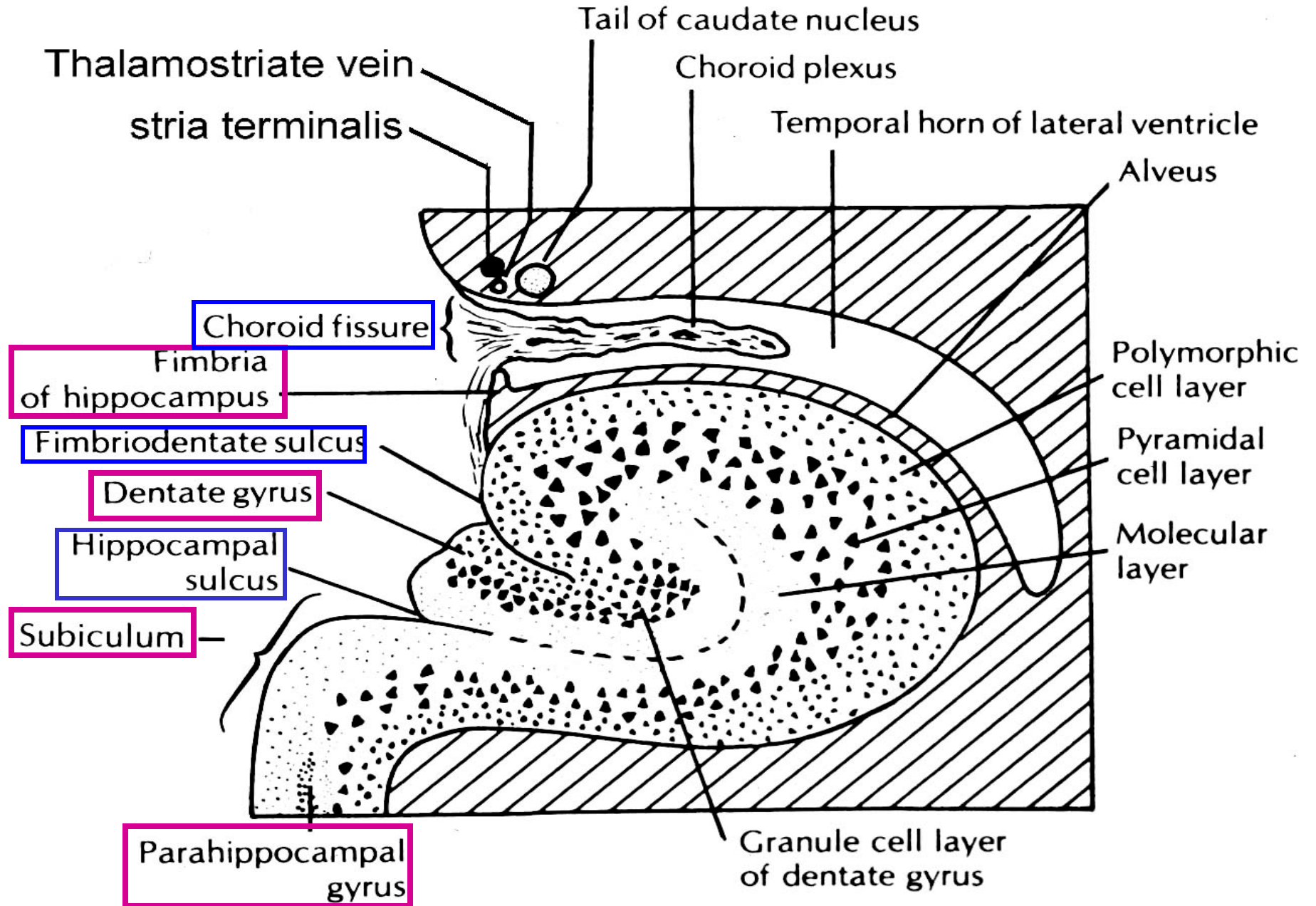


# Hippocampus: Alveus

- Myelinated axons (leaving & entering hippocampus) on ventricular surfaces of hippocampus;
- Forming the fimbria of hippocampus continuous with crus of fornix

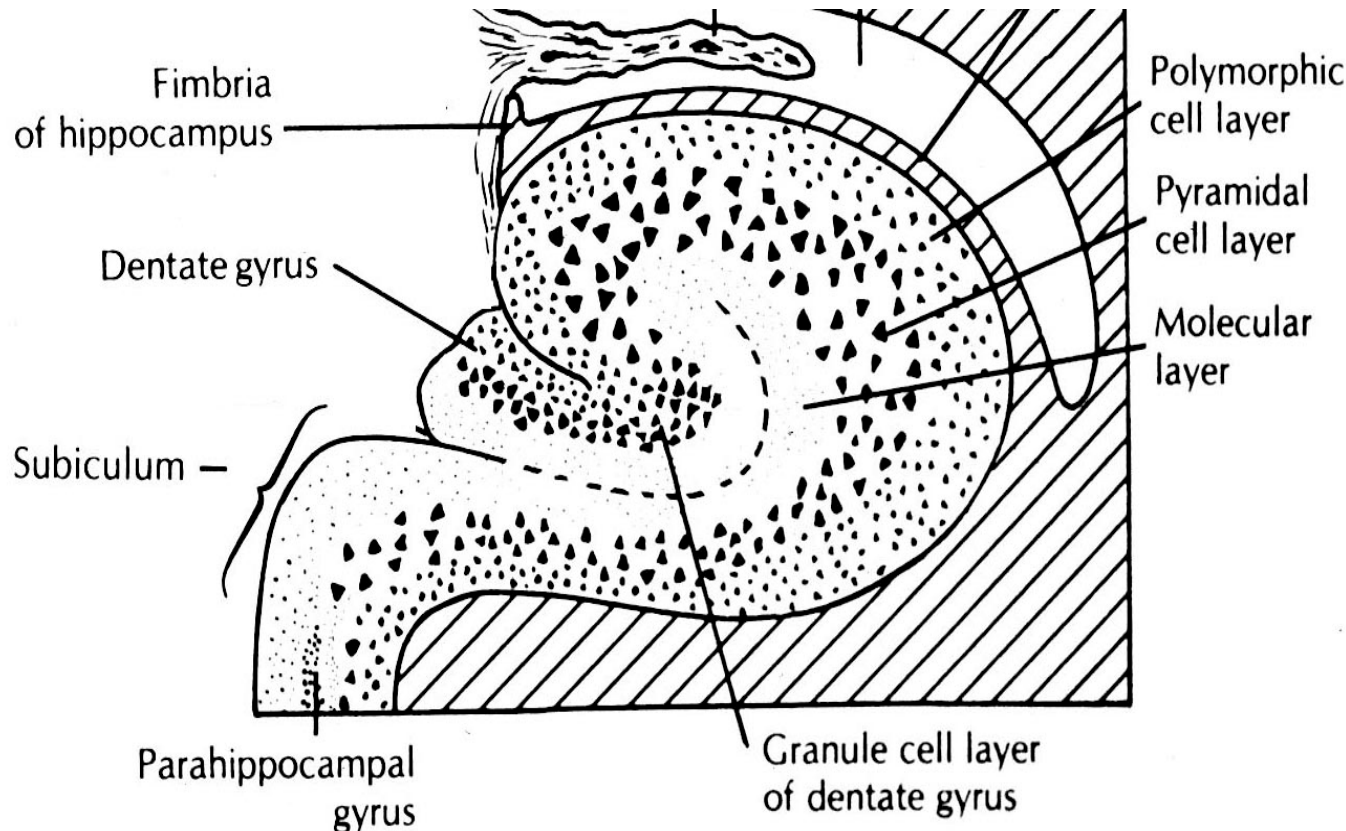


# Hippocampus



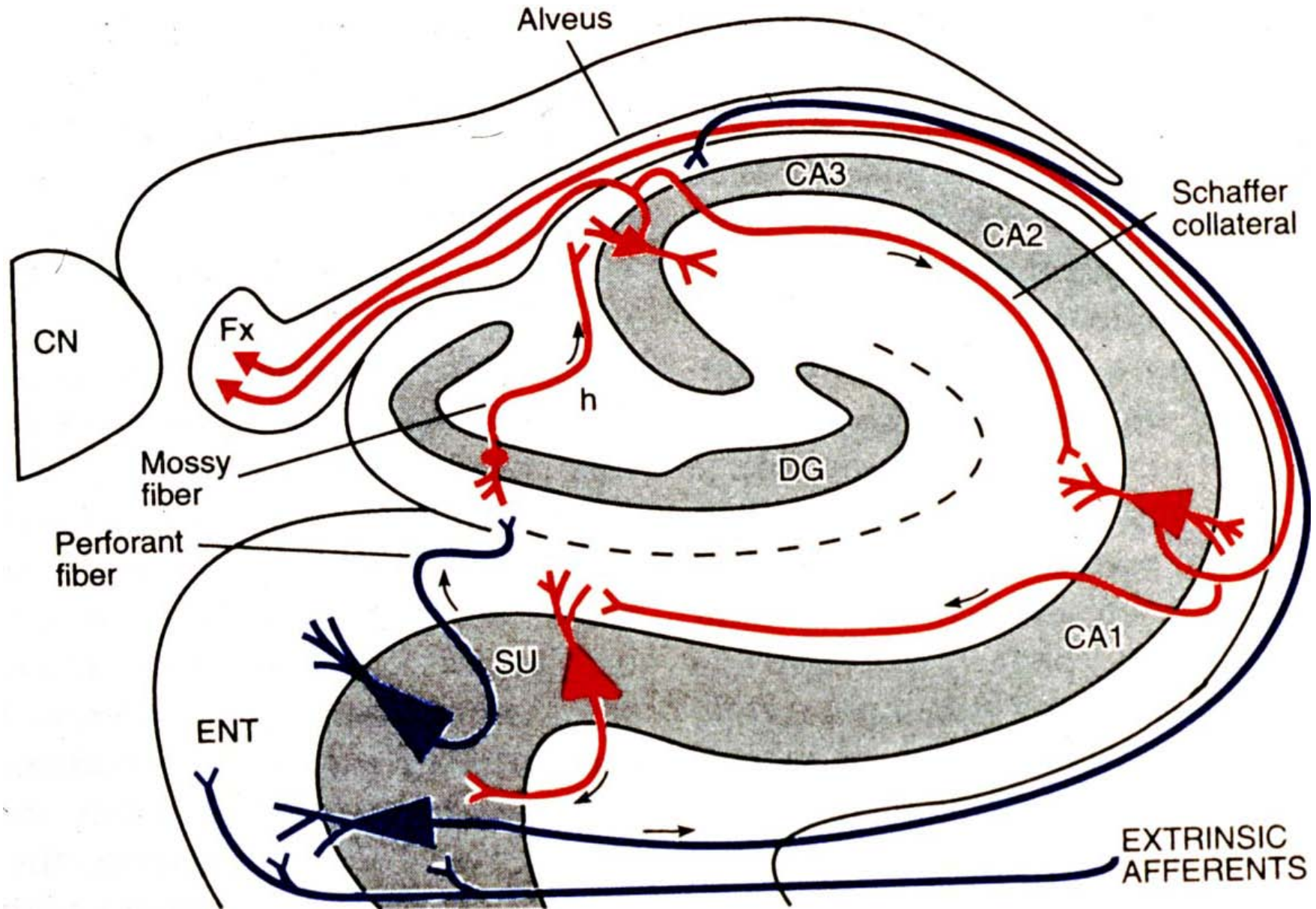
# Organization of Hippocampus: 3 layers

- **Molecular layer**
- **Pyramidal cell layer**
- **Polymorphic layer**
  - parahippocampal gyrus: neocortex, with 6 layers

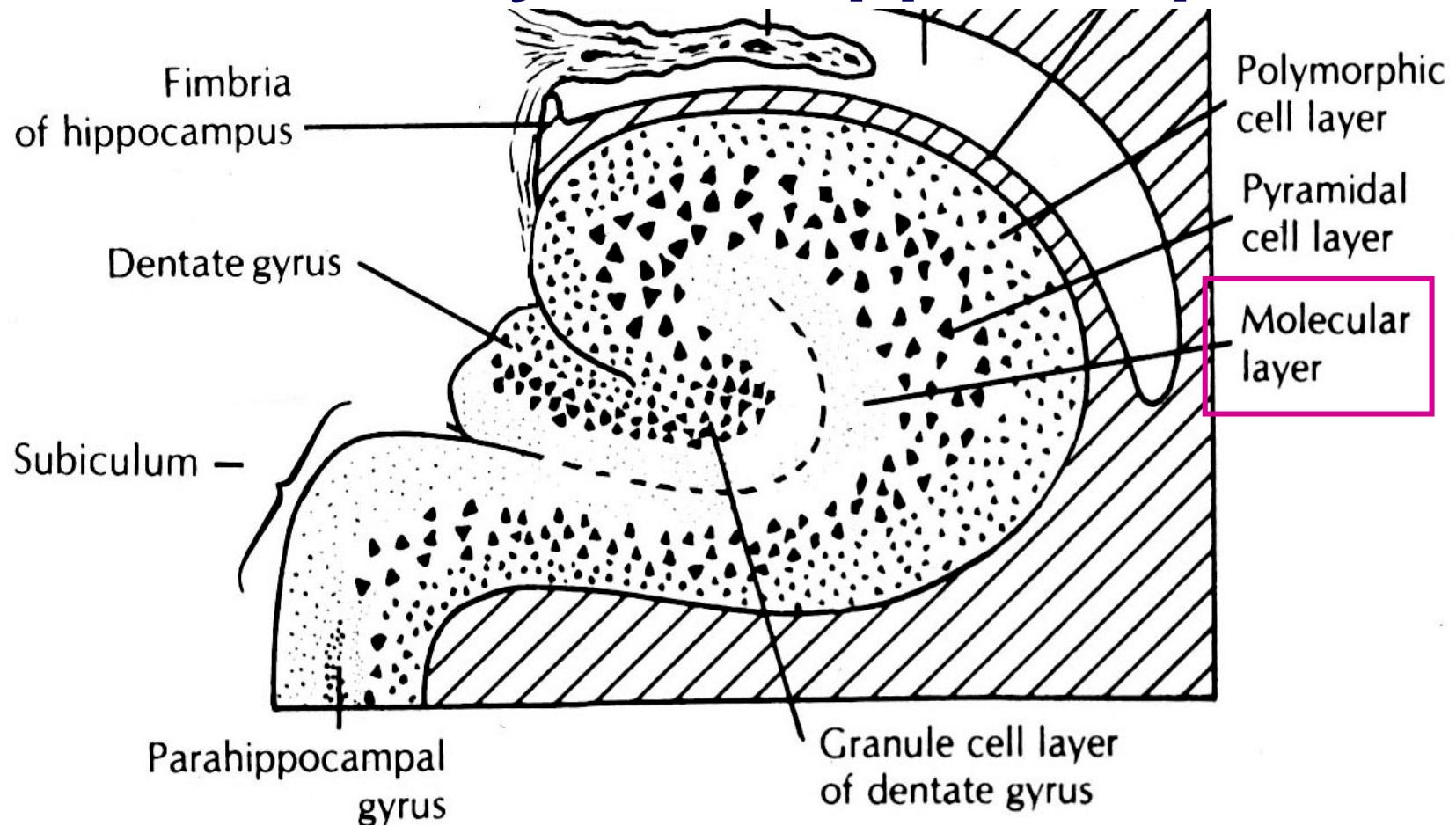


# Organization of Hippocampus: CA 1-3

- CA (Cornus ammonis); CA1: Sommer's sector



# Molecular layer of Hippocampus

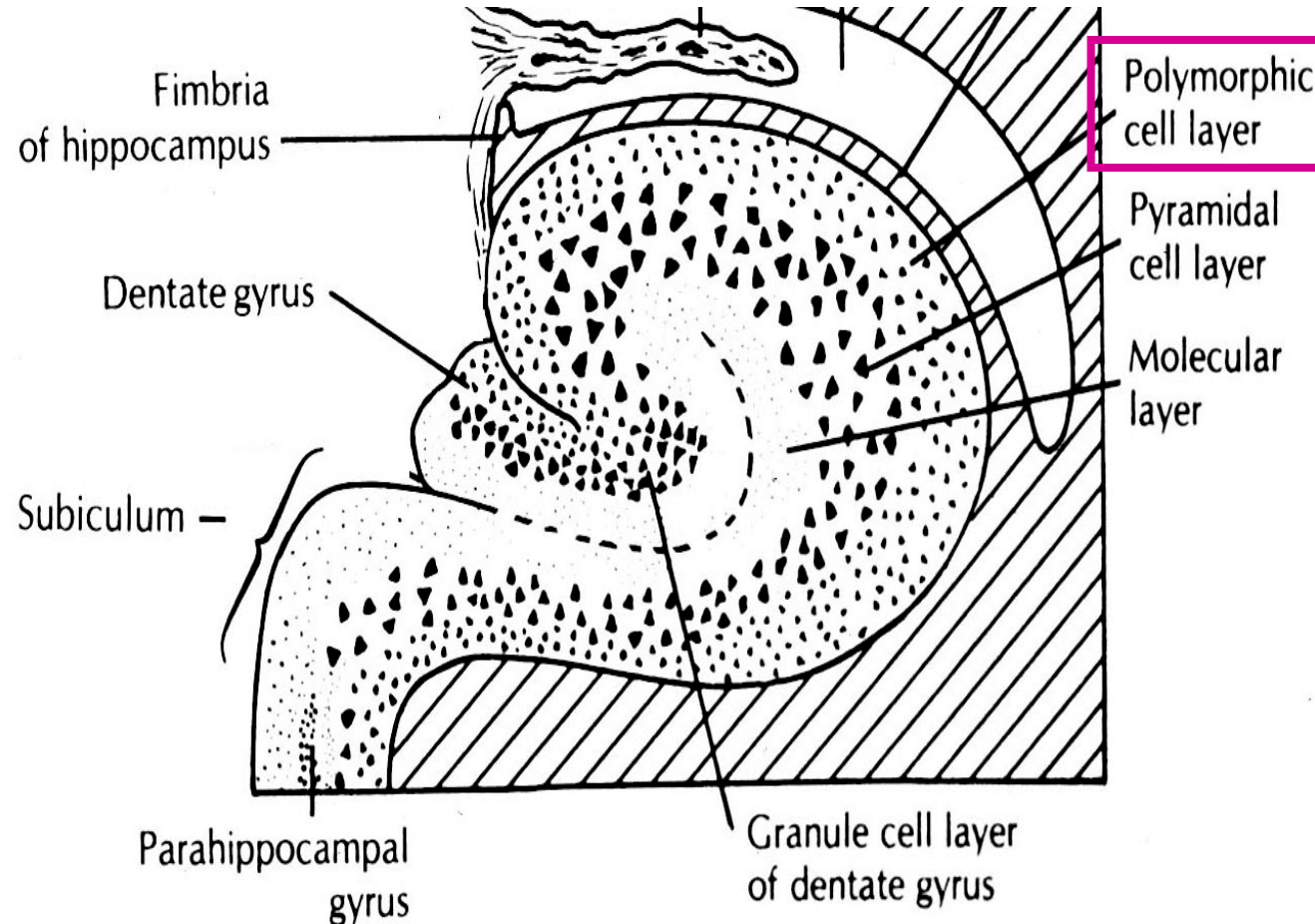


- with axons and dendrites
- continuous with molecular layers of dentate gyrus and neocortex



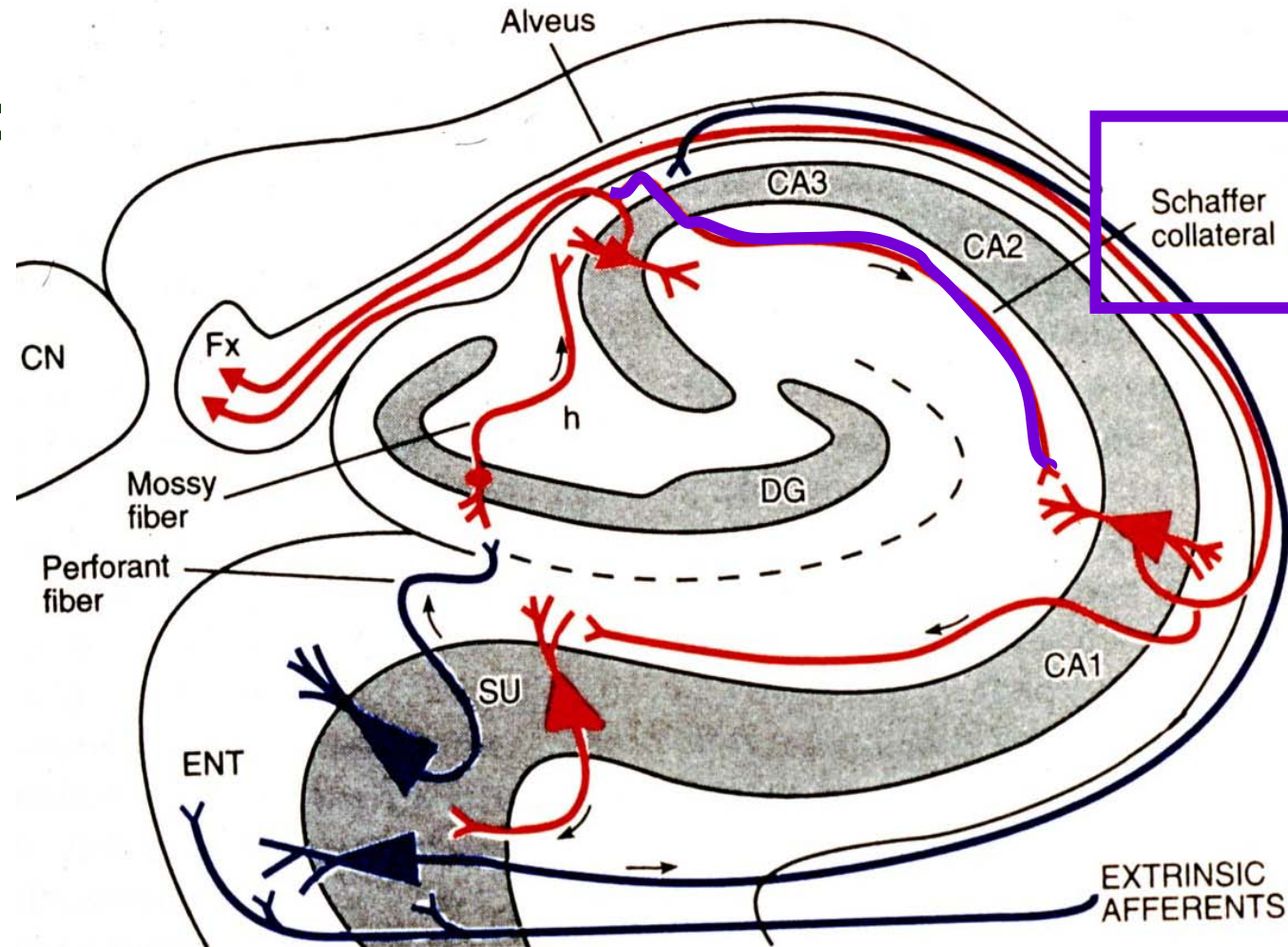
# Pyramidal cell layer of Hippocampus

- **Large neurons: pyramidal cells**
- **Principal cells of hippocampus;**
- **With dendrites into Molecular layer;**
- **Axons through alveus & fimbria to fornix**

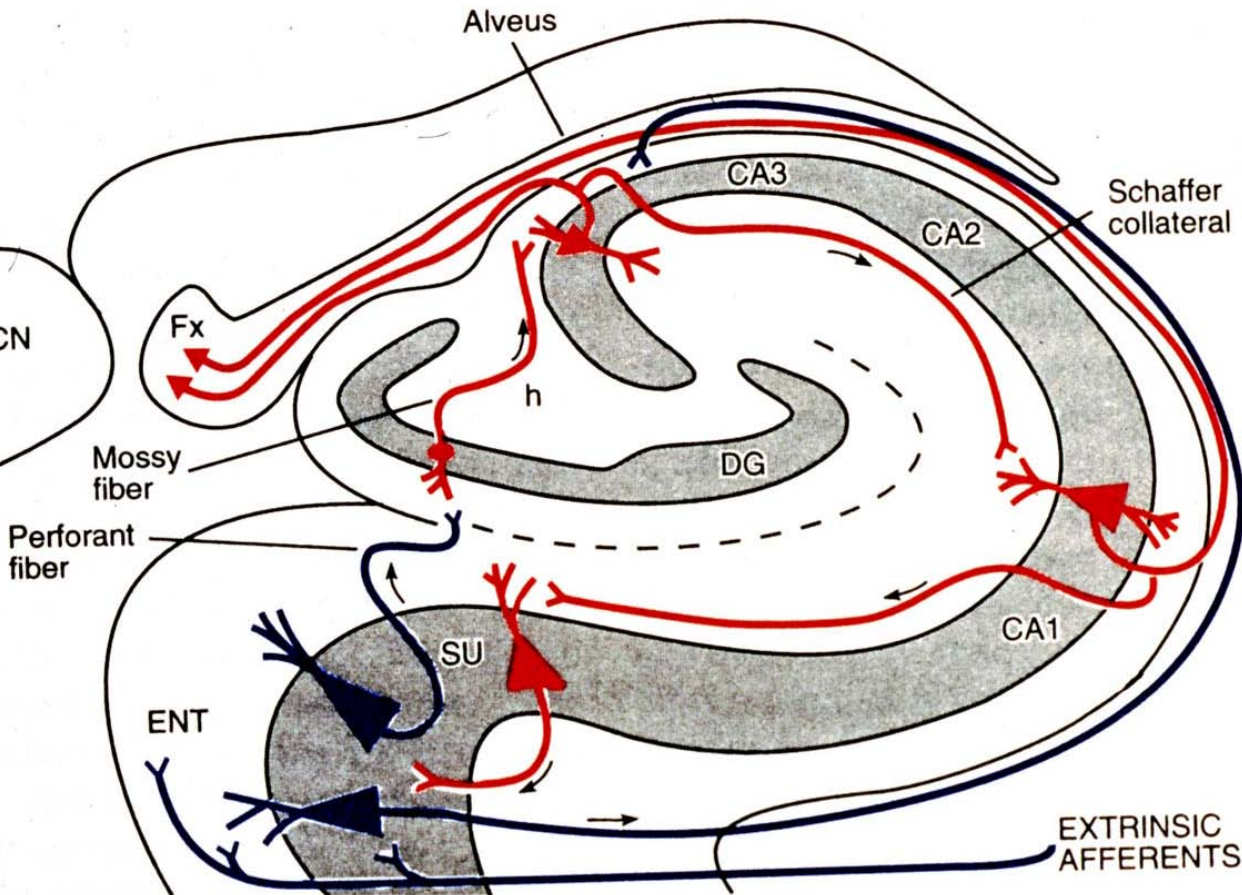


# Schaffer collateral

- **Schaffer collaterals:** branches of axons of pyramidal cells;
- passing polymorphic and pyramidal cell layers to synapse with dendrites of other pyramidal neurons



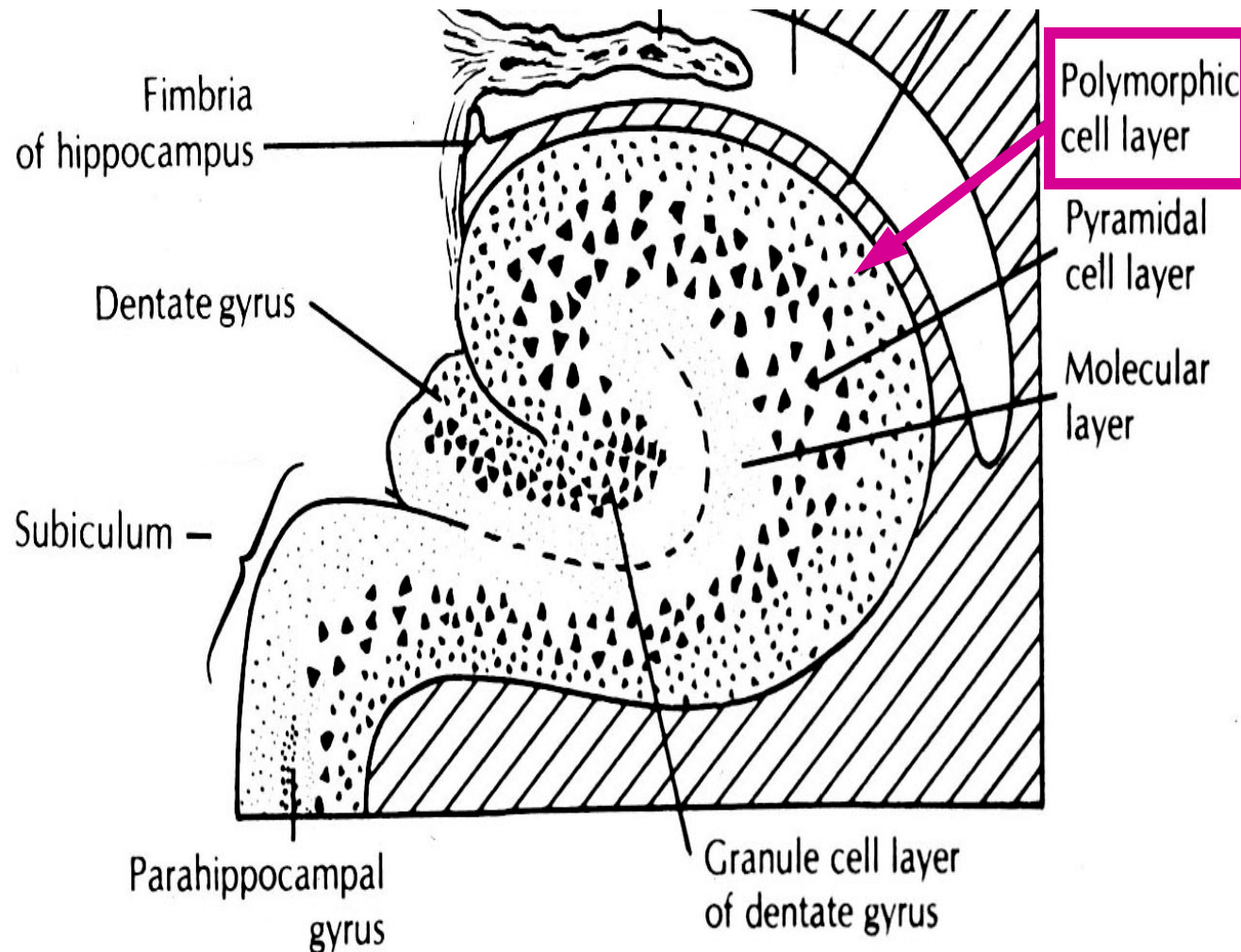
# Pyramidal cell layer of hippocampus



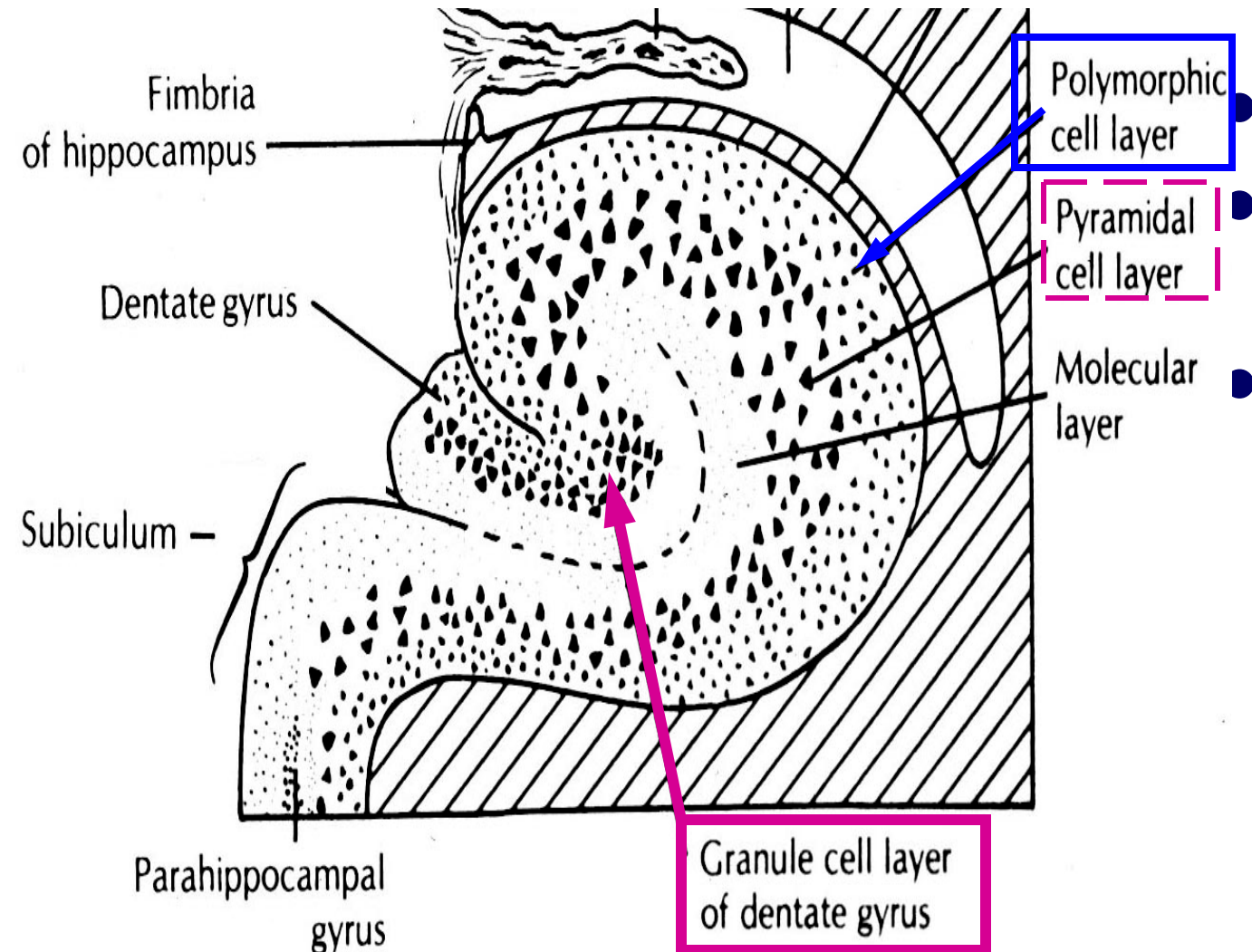
- pyramidal neurons of CA1: sensitive to oxygen deprivation
  - Temporal sclerosis
  - Alzheimer disease
- continuous with layer 5 (internal pyramidal) of neocortex

# Polymorphic cell layer of hippocampus

- **Beneath alveus,**
- **With axons, dendrites and interneurons;**
- **Equivalent to layer 6 of neocortex**



# Organization of Dentate gyrus: 3 layers



● Molecular layer

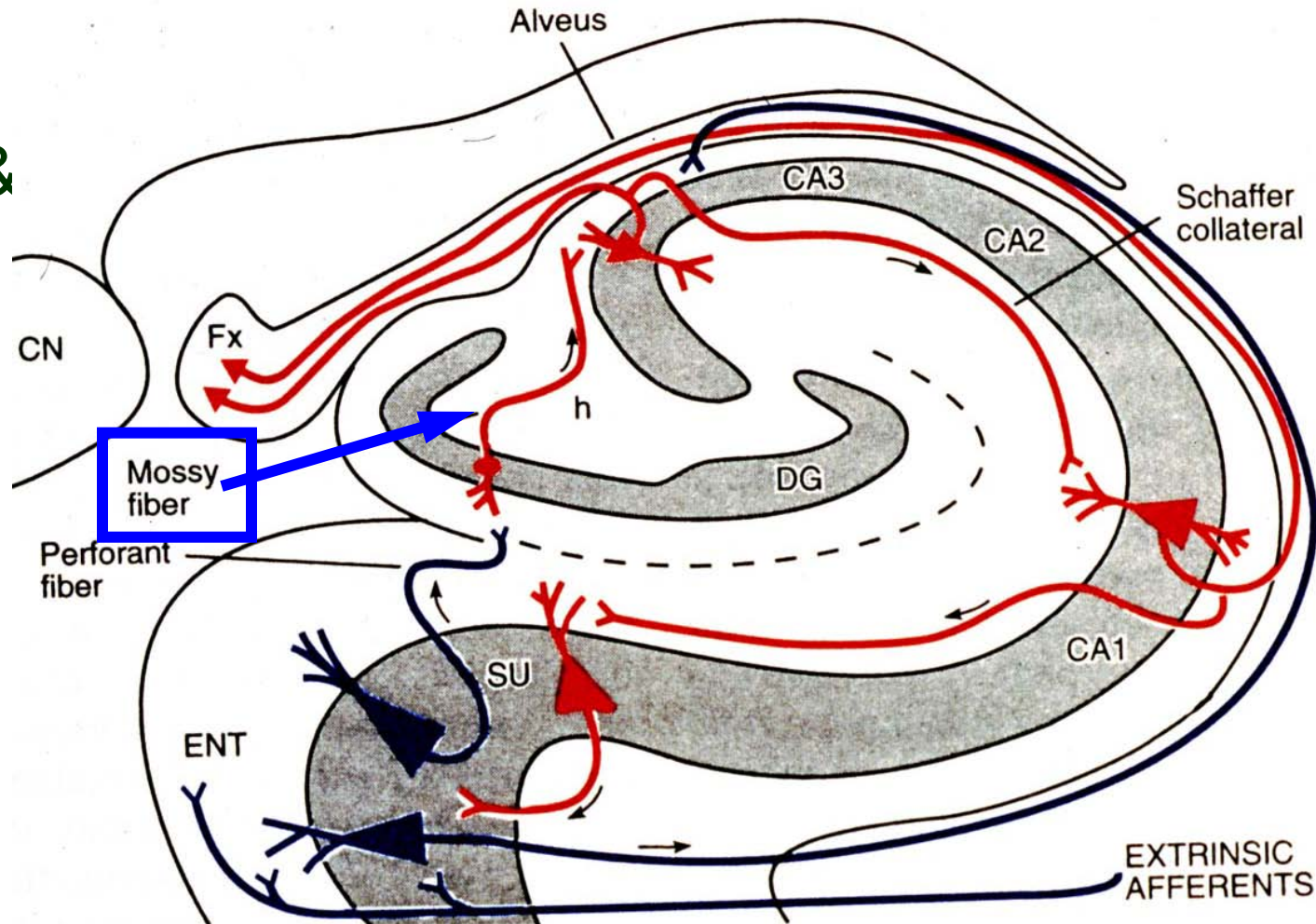
:  
● principal cells

● Polymorphic layer:

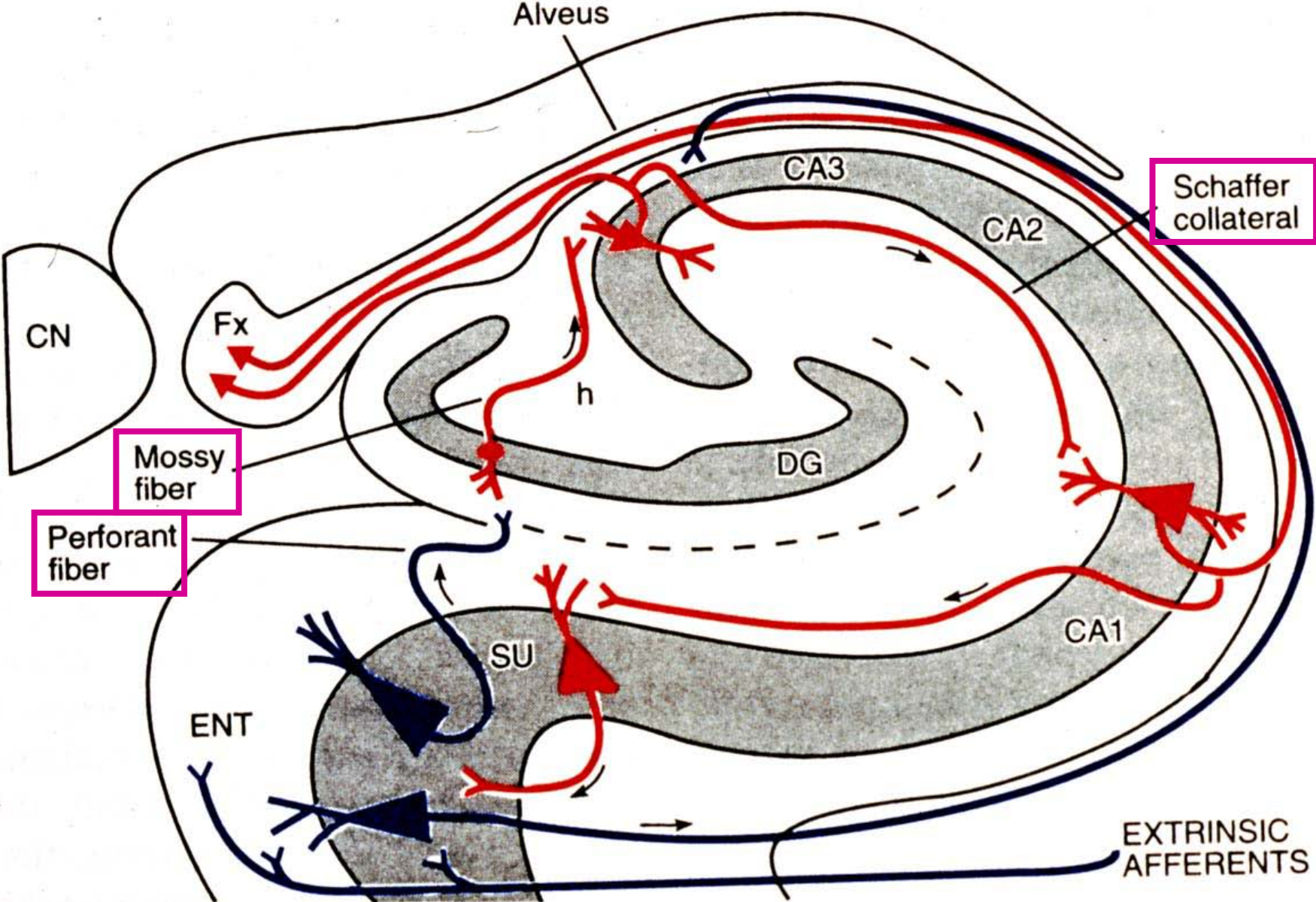
- Polymorphic layer of dentate gyrus: continuous with that of CA3

# Efferent fibers of Dentate gyrus

- Mossy fibers
- Traveling in hilus & polymorphic layer; giving branches to synapse with pyramidal cells of CA2 and CA3
- Roles for memory: long-term potentiation



# Hippocampus: Intrinsic connections

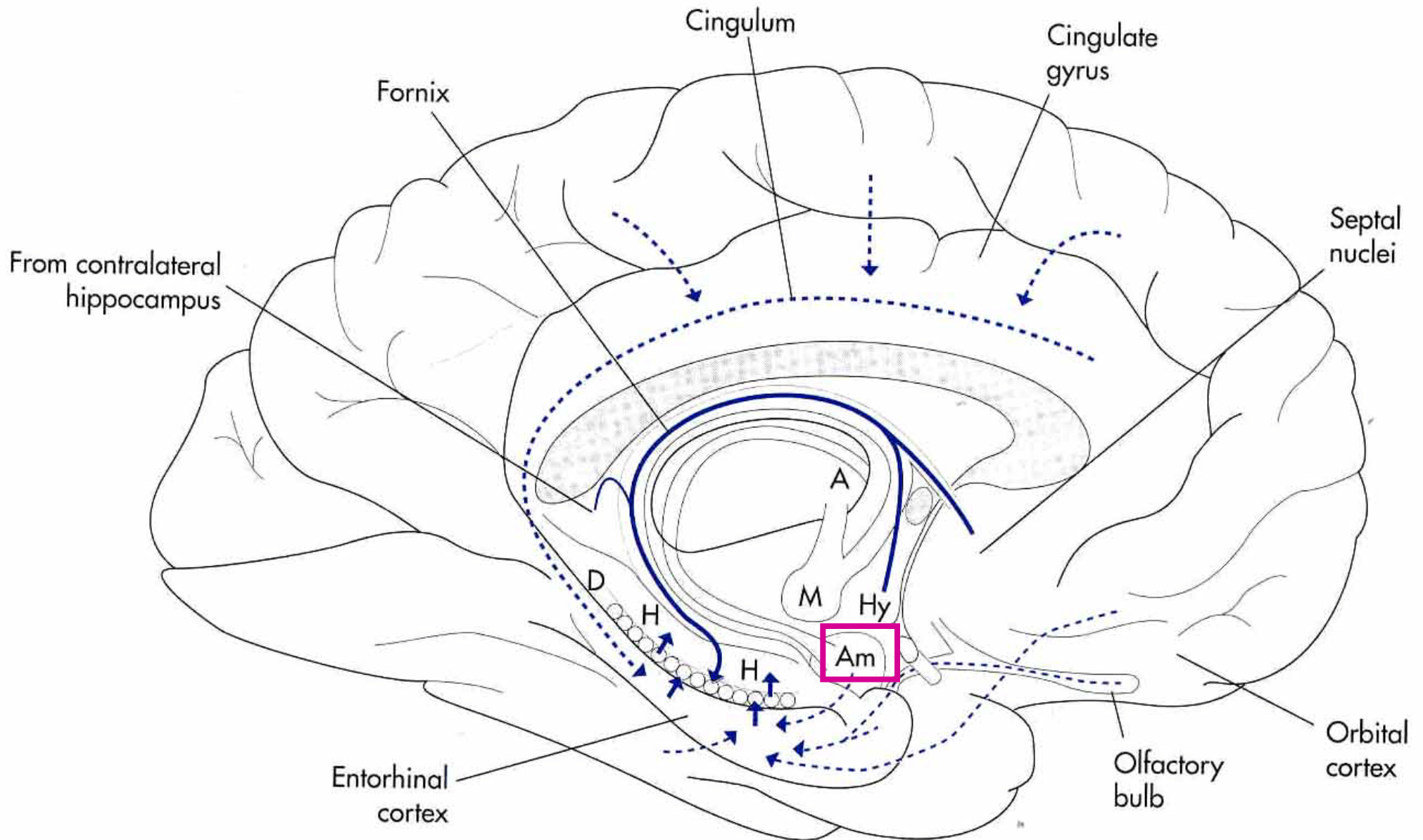


# Long-Term Potentiation (LTP)

- present in Schaffer collaterals and mossy fibers of hippocampus
- increase in synaptic efficiency following high-frequency activity of a pre-synaptic terminals
- as molecular and cellular mechanism underlying long-term memory

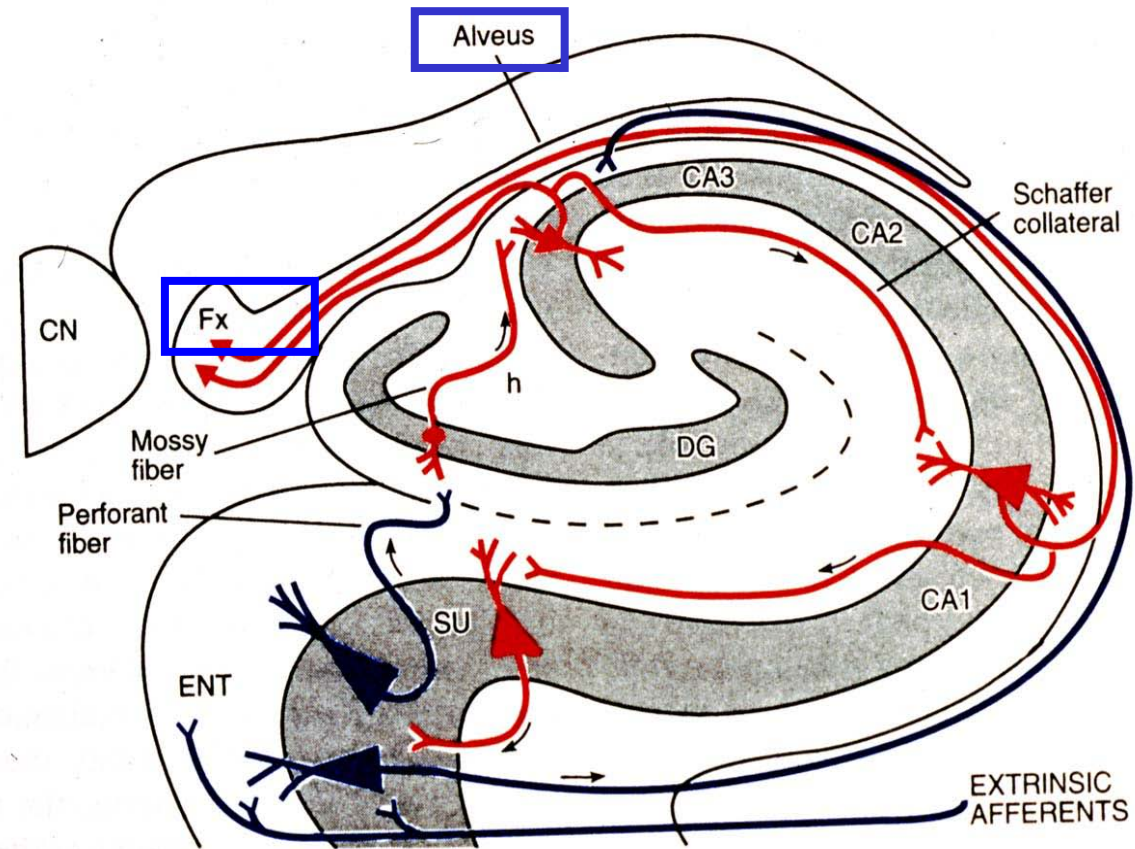


# Afferents to Hippocampus



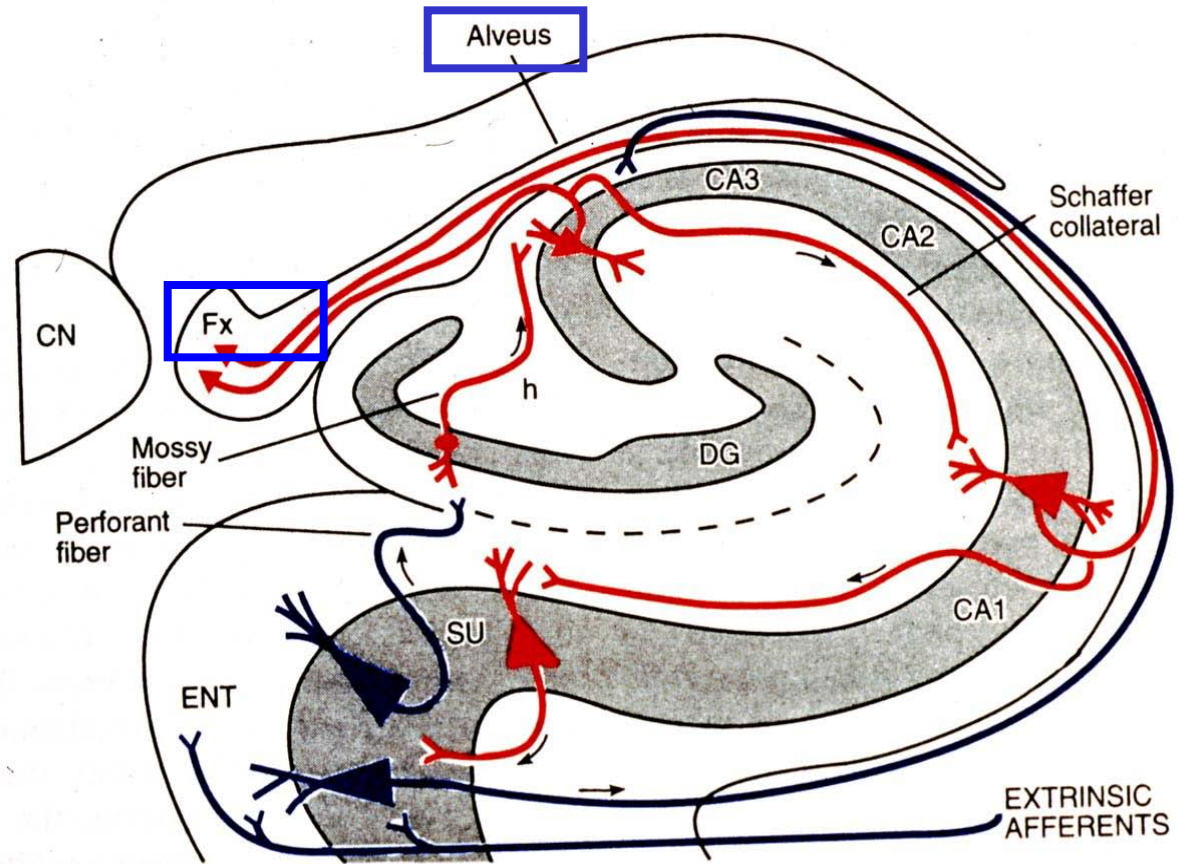
# Entorhinal afferents

- The largest afferents of hippocampal formation
  - ❖ Perforant path
  - ❖ Alvear path
- Entorhinal area: a part of lateral olfactory area and a gate for other cortical areas; receiving association fibers of temporal lobe and other neocortex



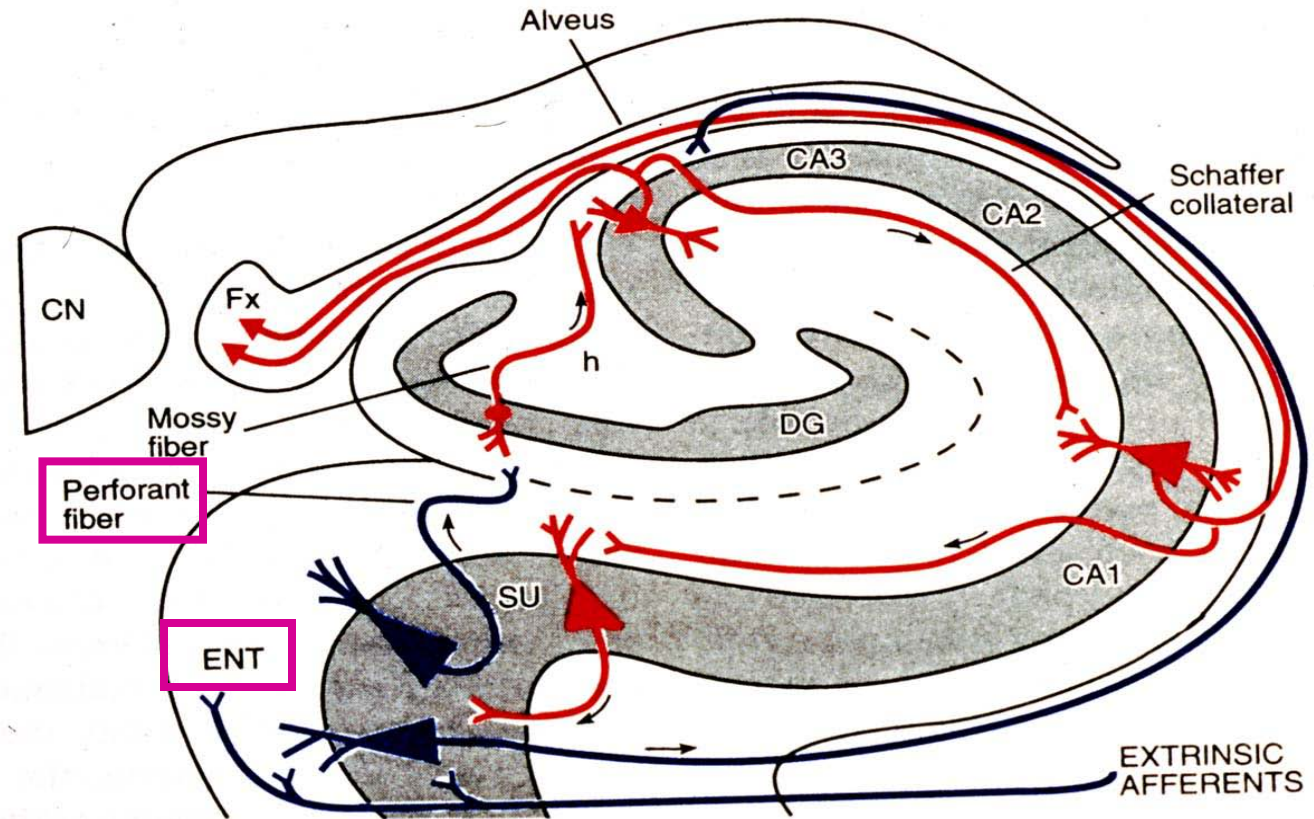
# Alvear path

- through subcortical white matter and alveus to end in hippocampus
- **Fornix and fimbria** afferents: from contralateral hippocampus, from septal areas, basal forebrain cholinergic neurons (substantia inominata)

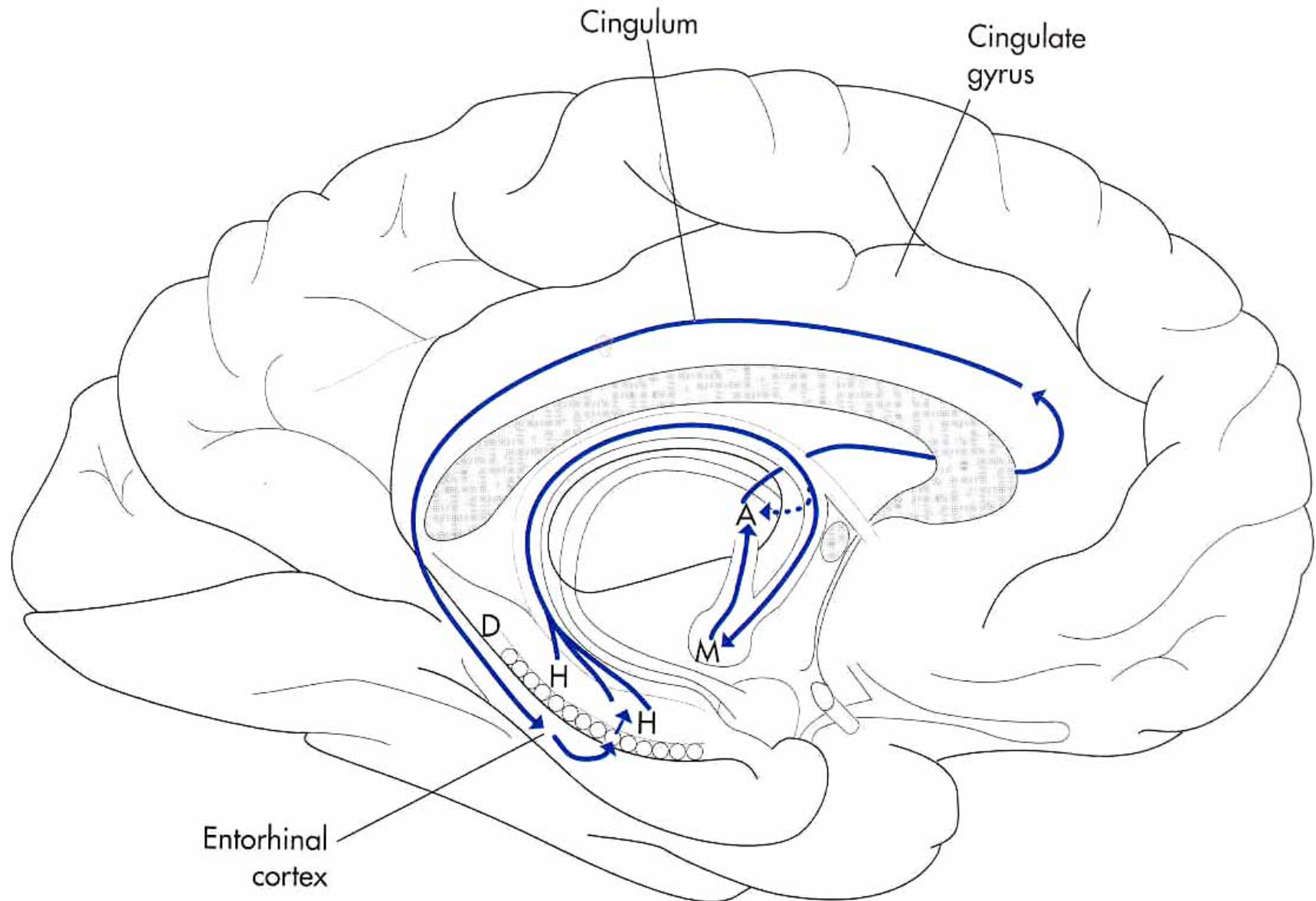


# Perforant path

- axons from entorhinal area through subiculum & base of hippocampus to end in dentate gyrus

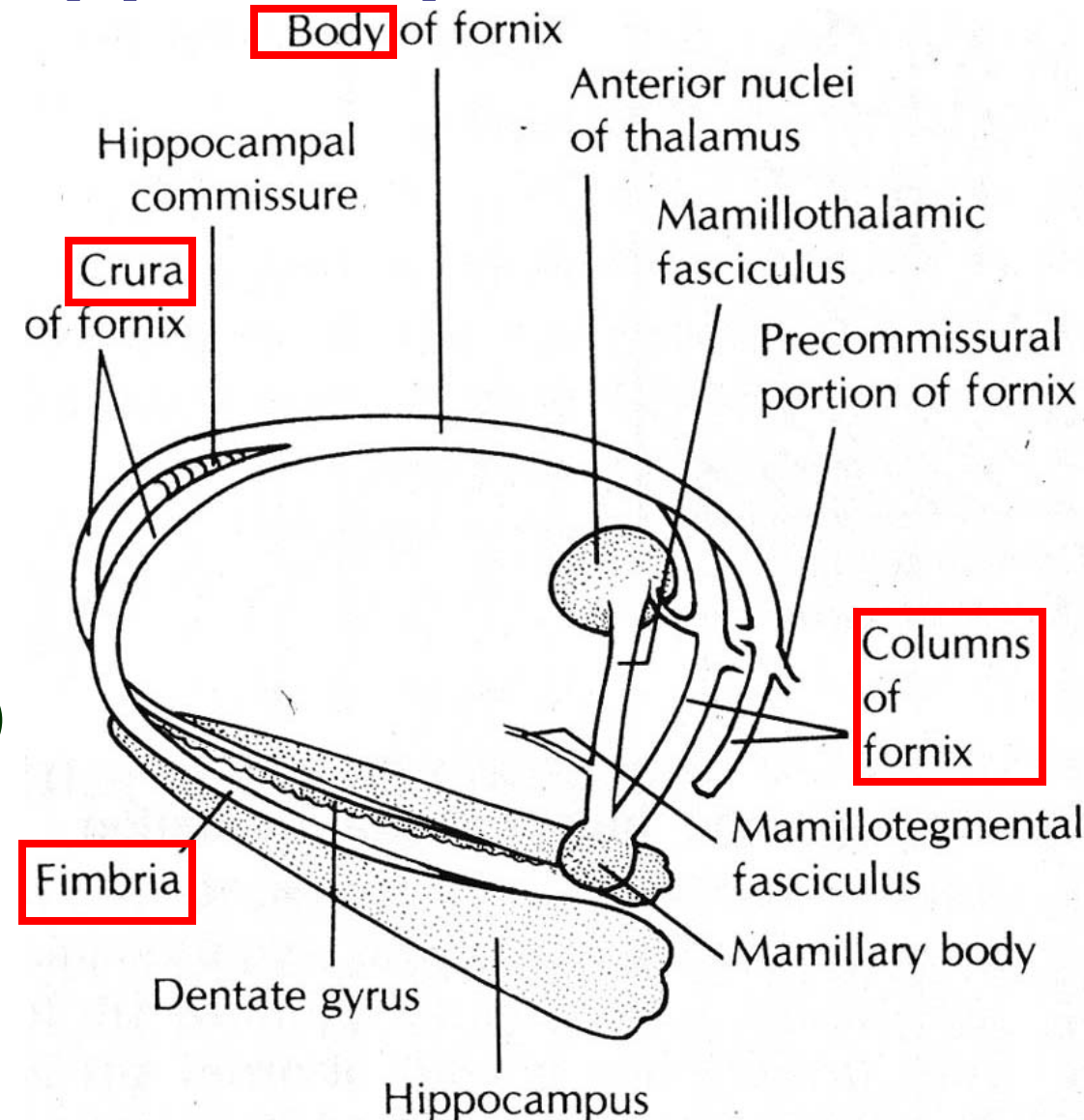


# Hippocampal efferents



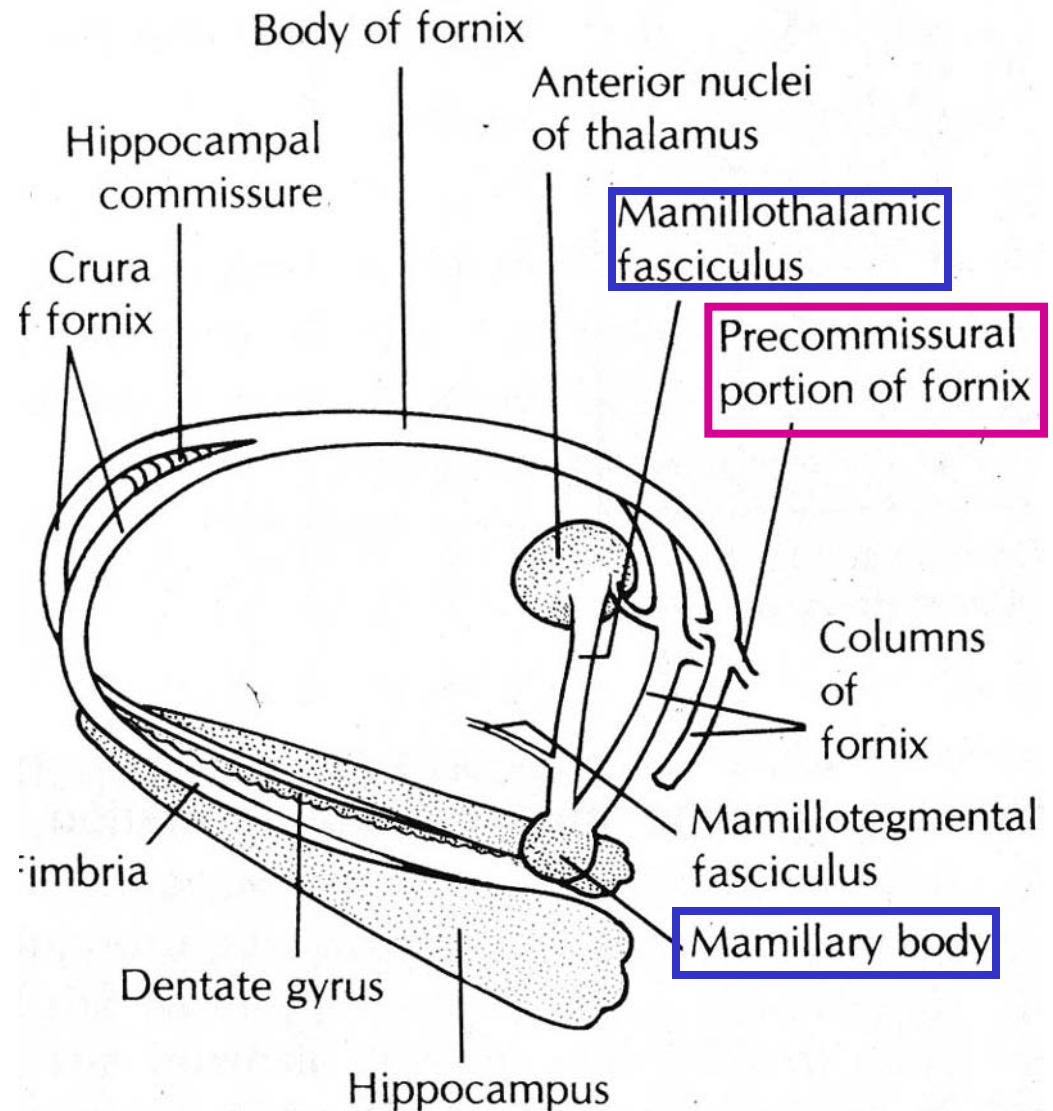
# Fornix: the largest hippocampal efferents

- ❖ **Origin:** hippocampus & parahippocampal gyrus
- ❖ **Fimbria**
- ❖ **Crus:** posterior limit of hippocampus
- ❖ **Body:** in contact of splenium (dorsal hippocampal commissure)
- ❖ **Column:** above the 3<sup>rd</sup> ventricle; in front of interventricular foramen

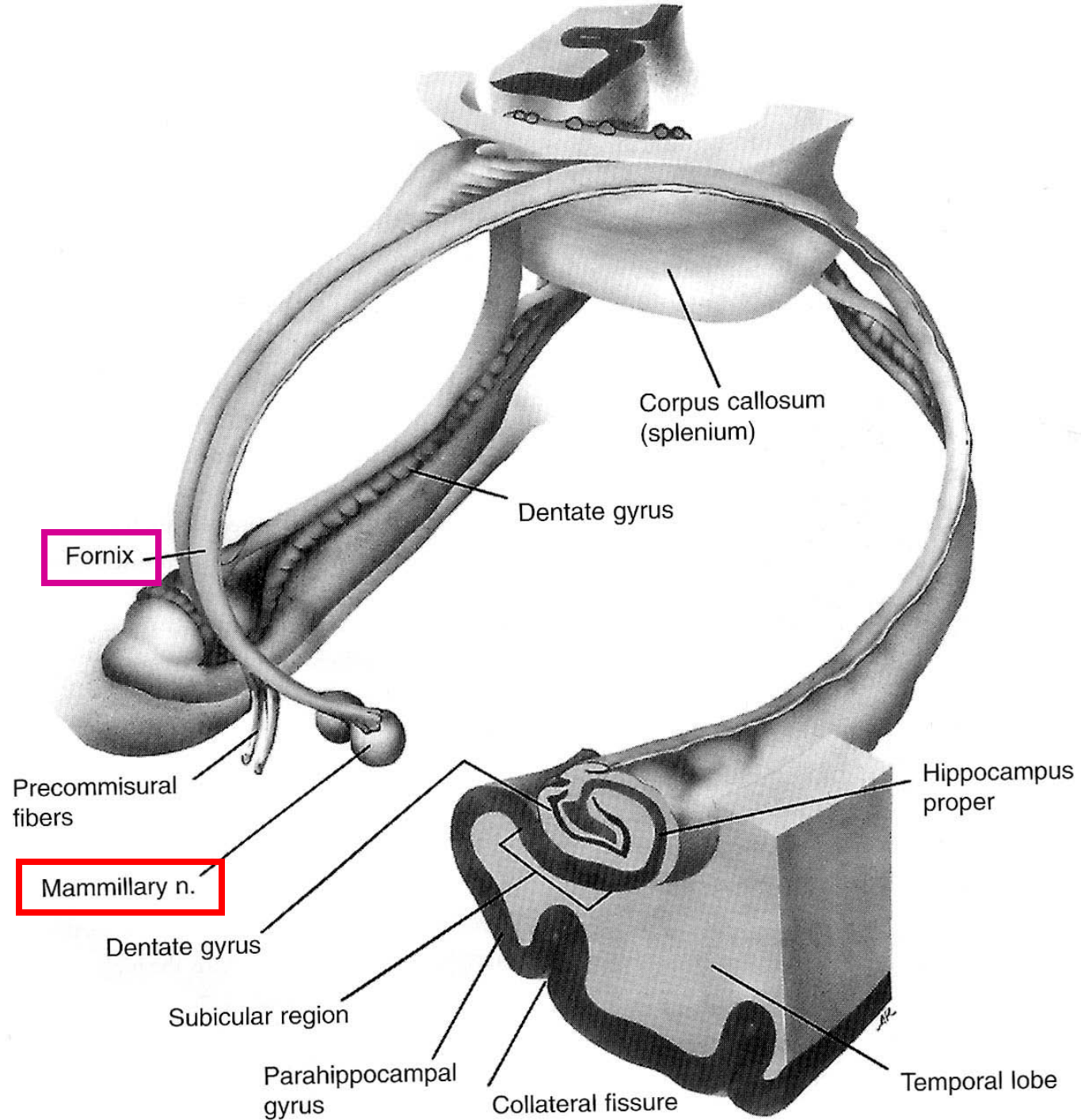


# Column of Fornix

- pre-commissural portion of fornix: above anterior commissure; giving fibers to septal area, anterior hypothalamus, substantia inominata
- post-commissural portion of fornix: fibers to lateral dorsal thalamic nuclei, hypothalamus (mamillary body via mamillothalamic fasciculus to ant. nu of Th, ventromedial nucleus)

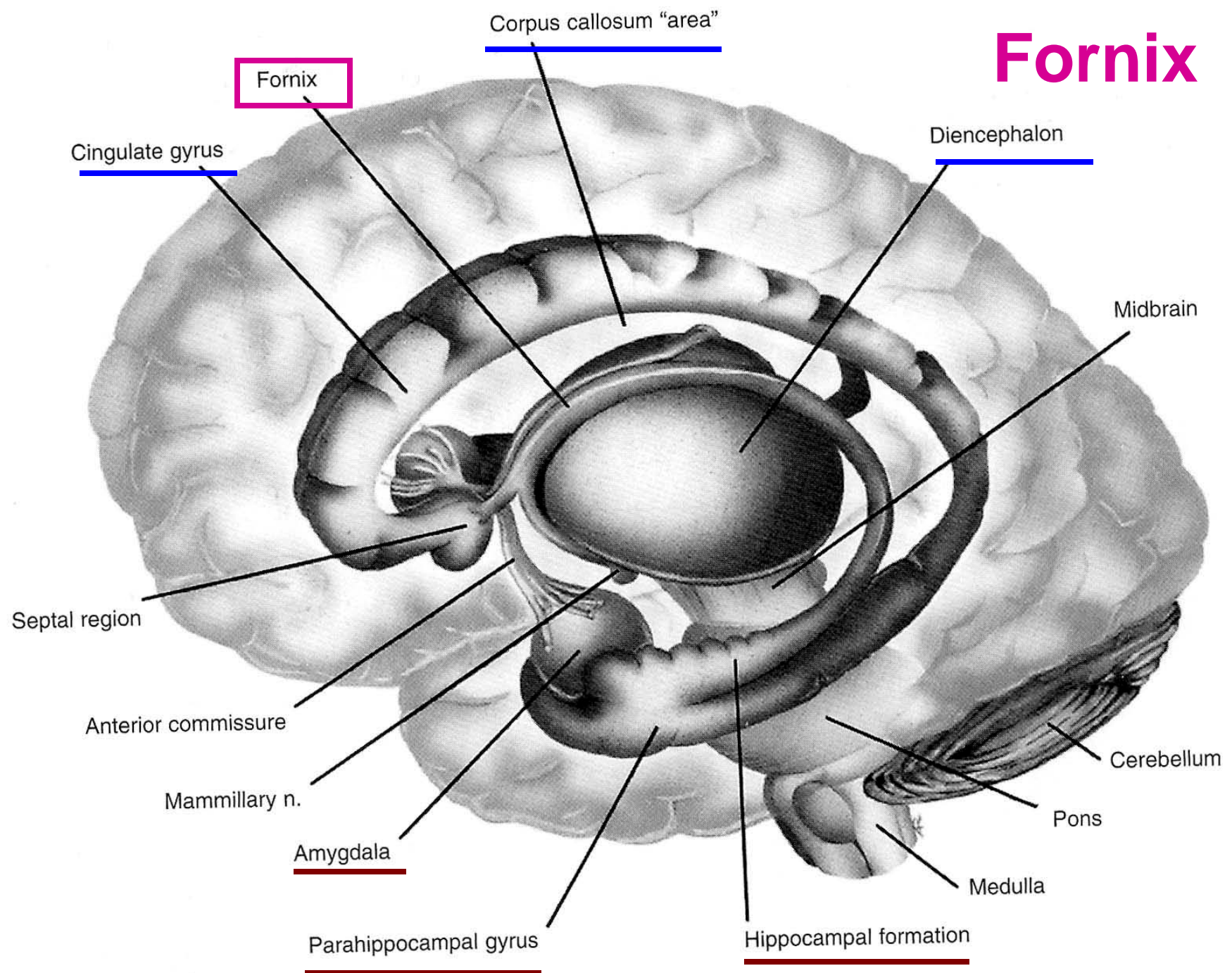


# Fornix





# Fornix



Stria terminalis

Choroid plexus

Reticular nucleus  
and external medullary lamina

Internal capsule (posterior limb)

Internal medullary lamina

Fornix (body)

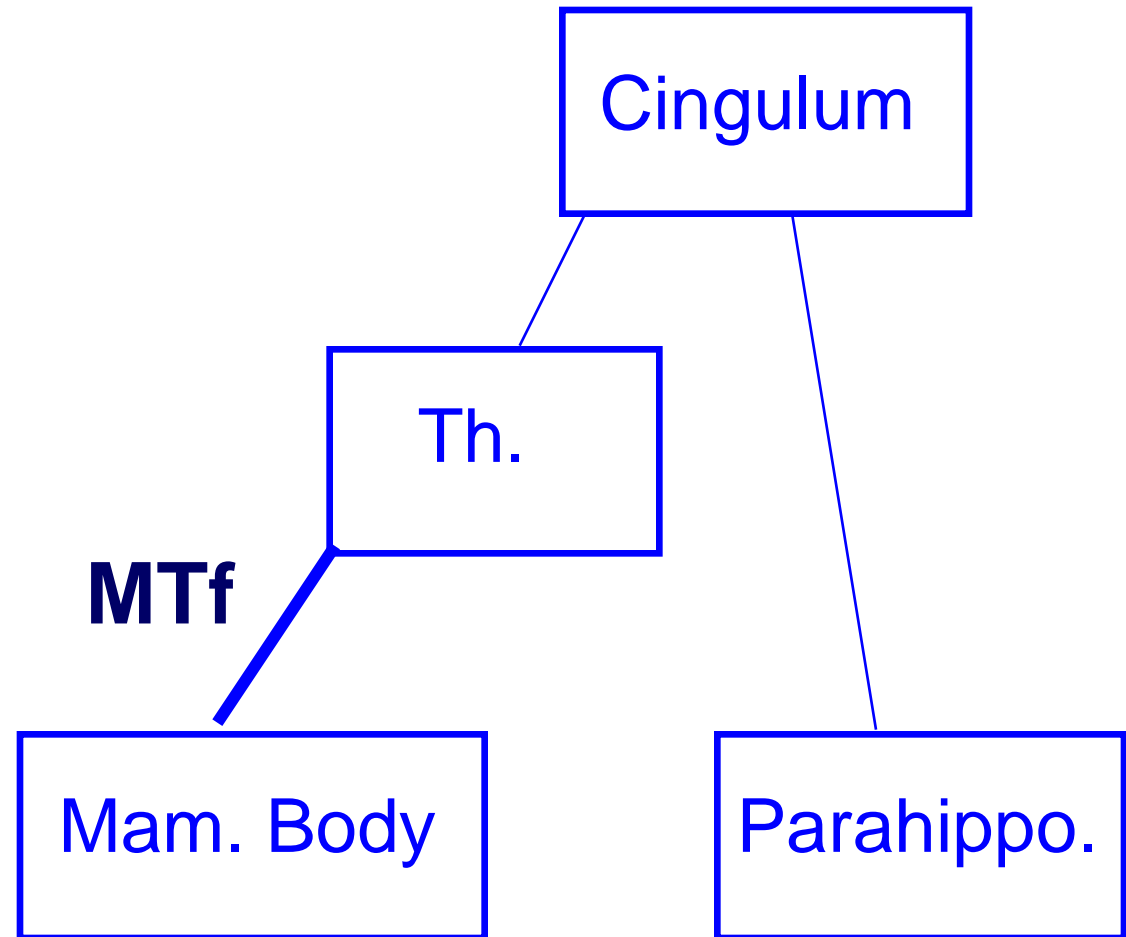
Internal capsule (genu)

Internal capsule (anterior limb)

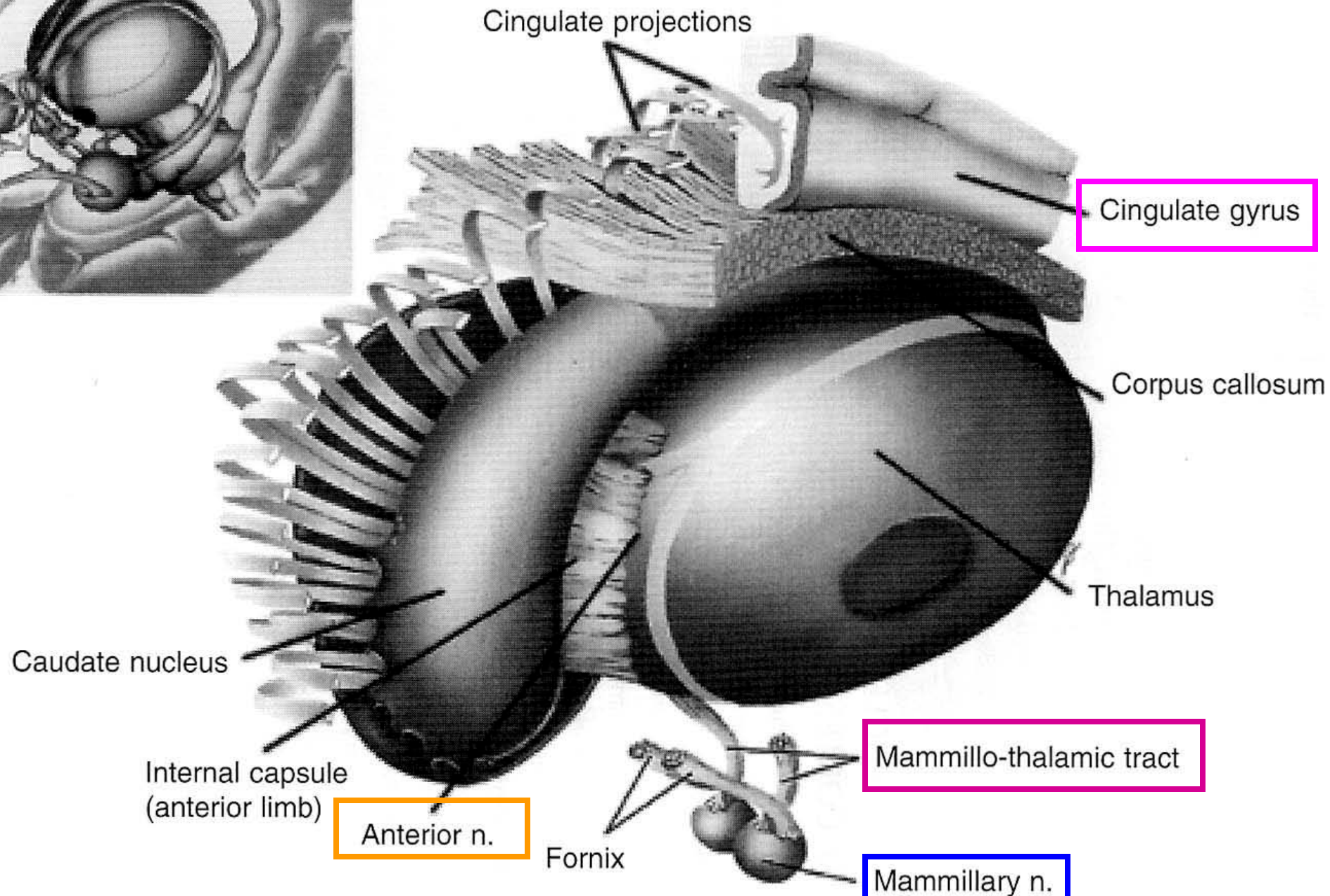
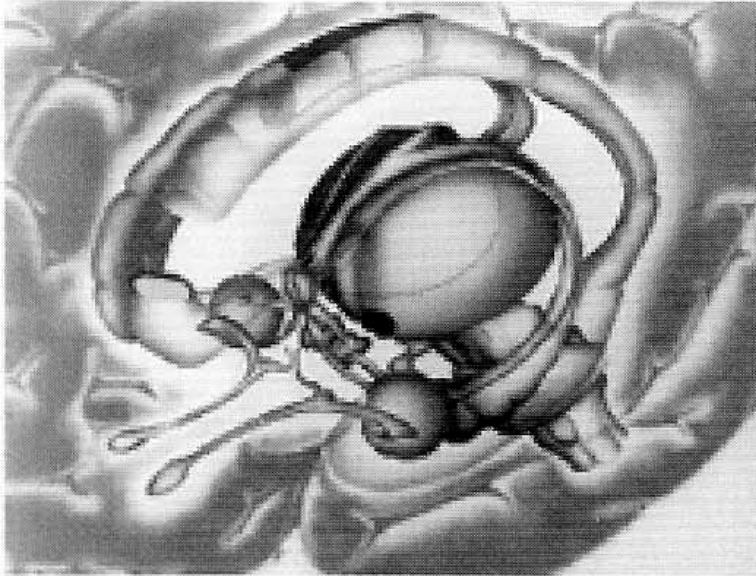


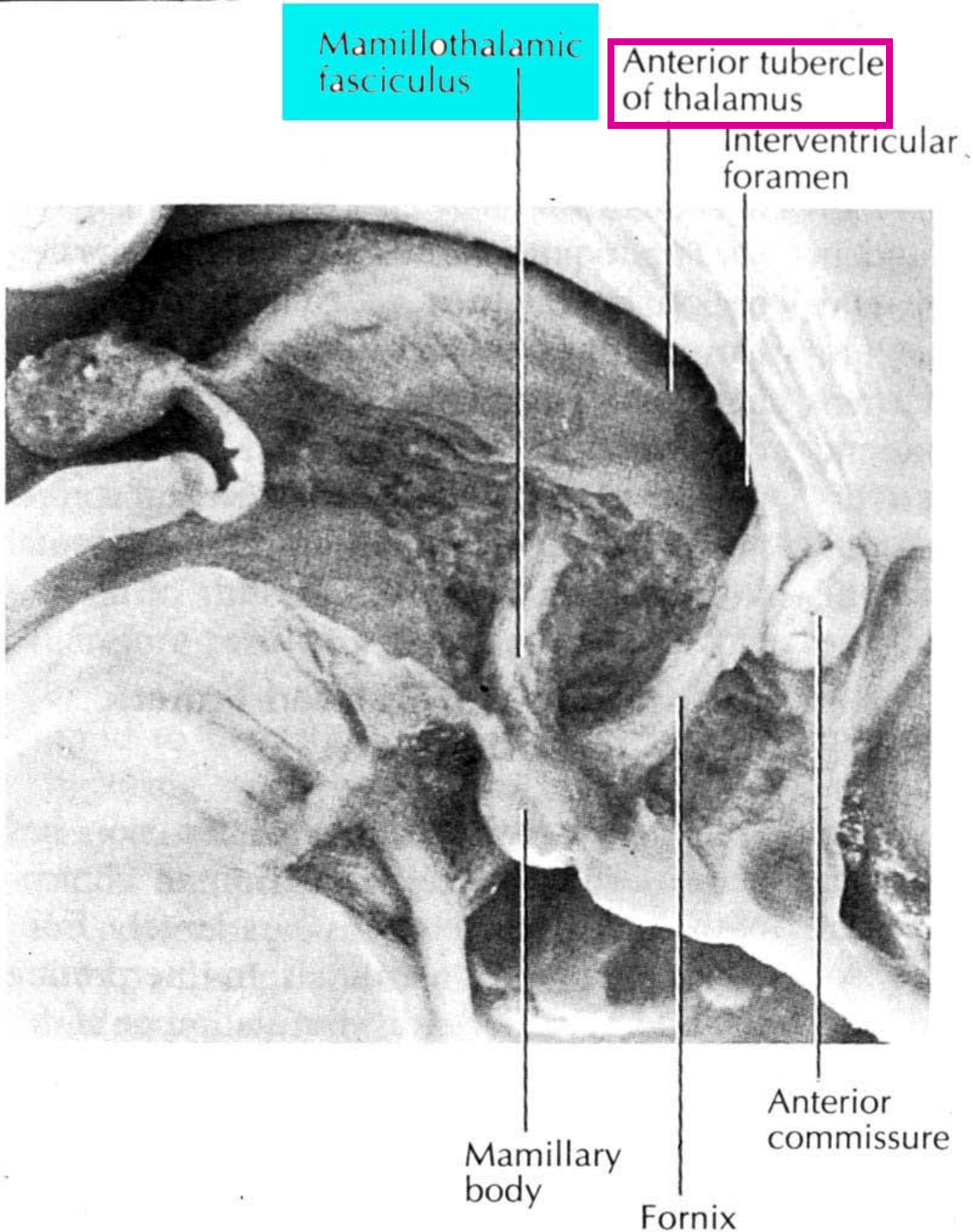
# Mammillothalamic fasciculus (MTf)

- Origin: mamillary body
- Terminals: anterior nuclei of thalamus
- Anterior and lateral dorsal thalamic nucleus having reciprocal communications with cingulate gyrus, which also has reciprocal communication with parahippocampus gyrus



# Mamillo-thalamic fasciculus





## Mamillo-thalamic (Mamillothalamic) fasciculus / tract

- Damaged in Korsakoff syndrome (alcoholic dementia)
  - Amnesia
  - Confabulation
  - Apathy
  - Lack of insight

<http://www.youtube.com/watch?v=wDcyBXJAZNM>  
<http://www.youtube.com/watch?v=UbSILtsJfUY>

# Hippocampal function & dysfunction: memory and memory disorders

- **Types of memory**
  - **Explicit (Declarative)** memory: knowledge
    - mainly verbal, language, mathematic contents etc
  - **Implicit** memory: learned skills, procedures, emotions
    - associated structures: cerebellum, basal ganglia etc

# Declarative Memory

- Steps of memory
  - Immediate recall; Recent memory
  - Memory consolidation; Long-term memory
  - Information retrieving
  - Factors: enhancing, interfering, emotional etc
- Role of hippocampus in memory
  - Retention of short-term memory and its Transfer to long-term declarative memory

# Hippocampus and Memory: Cellular mechanism

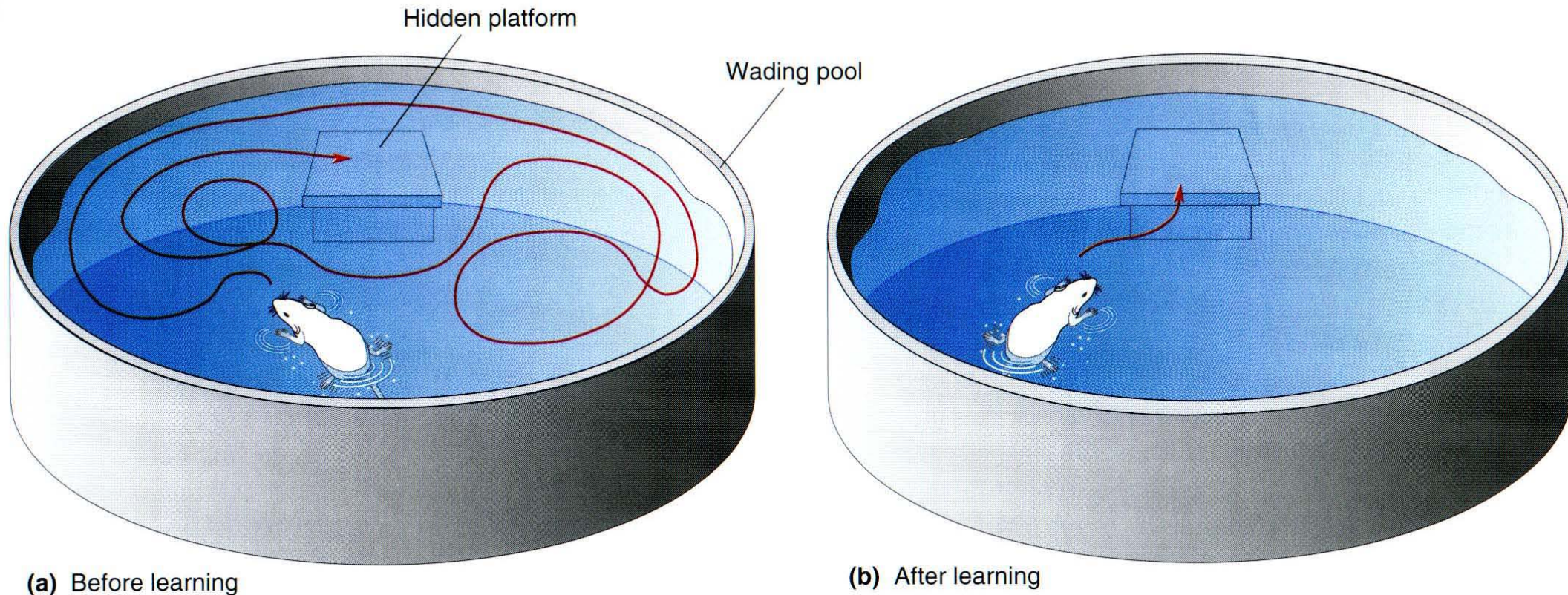
- Long-term potentiation (LTP)
- a postulated mechanism for storage of recent memory
- requiring for permanent memory
  - new protein synthesis
  - new synapse formation





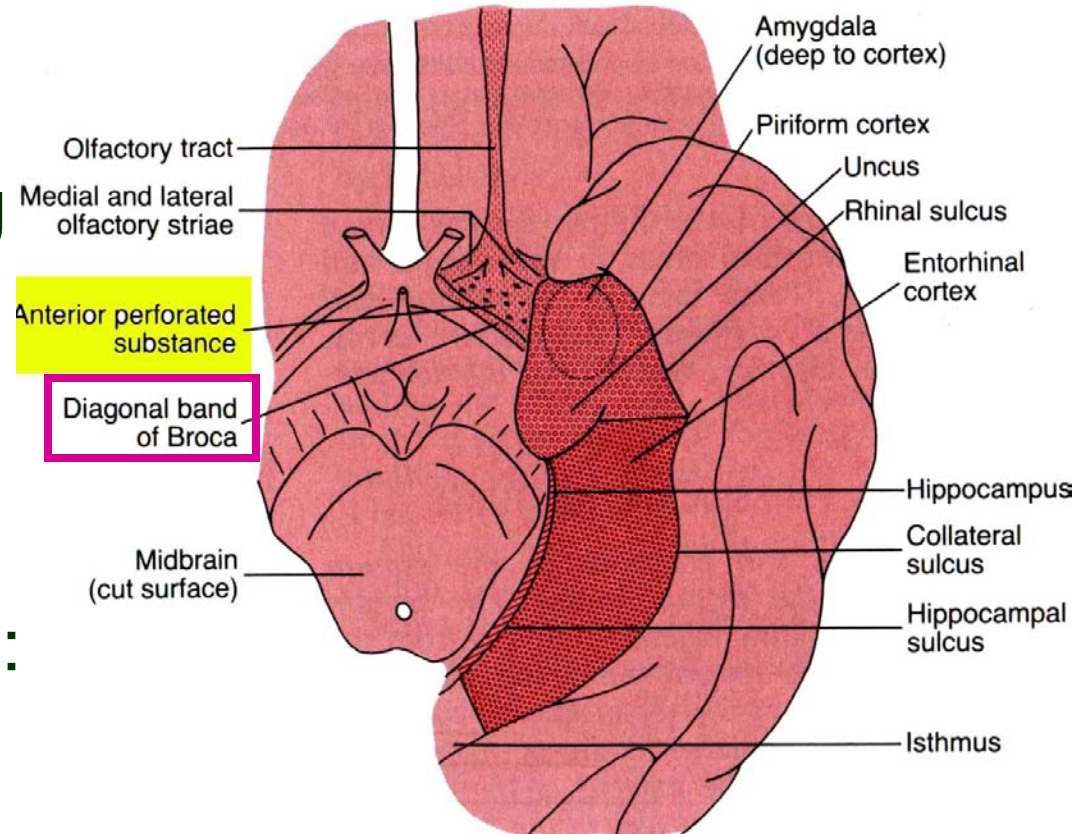
# Role of hippocampus in learning

- “learning and memory”: impaired in mice with defective functions of neurotransmitters in hippocampus



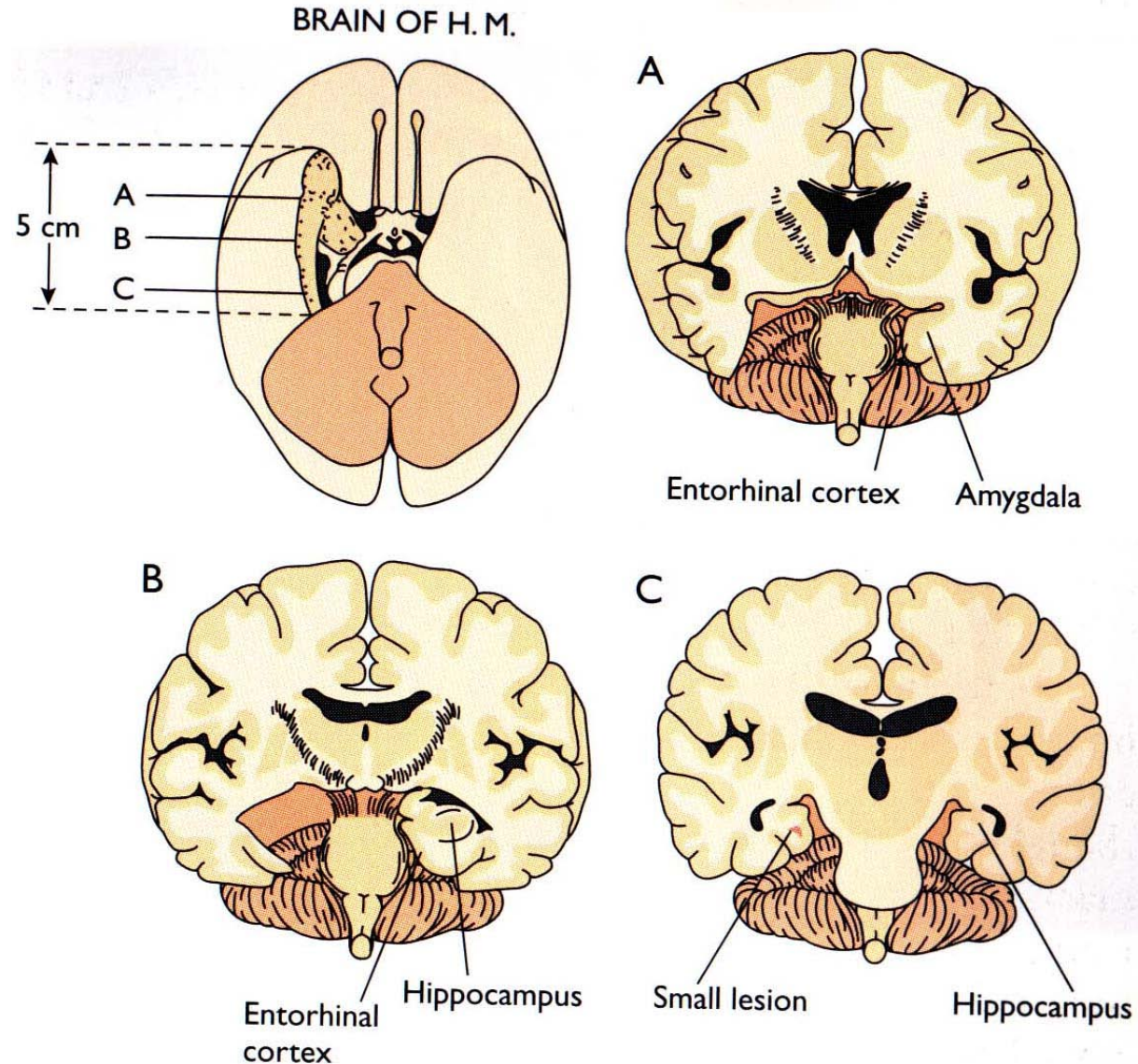
# Clinical Note of Hippocampus: Alzheimer disease

- Pathophysiology: cholinergic hypothesis
  - loss of cholinergic neurons in basal forebrain projecting to limbic system (particularly hippocampus)
  - degeneration in entorhinal cortex, and hippocampus
- Essential role of hippocampus: bilateral hippocampal lesions lead to memory loss, particularly recent memory



# The story of H.M.

- Intractable seizure
- Temporal lobectomy, partial
- Consequences
  - Seizure: under control
  - Blunt emotions
  - Loss of memory



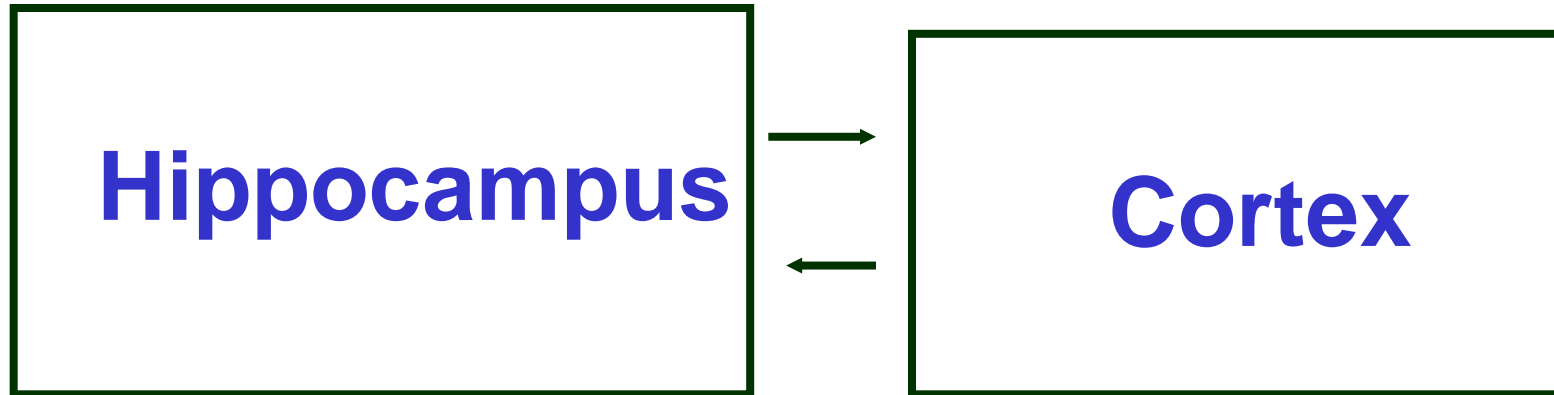
H.M.

On the Wechsler Memory Scale (Wechsler, 1945) his immediate recall of stories and drawings fell far below the average level and on the "associate learning" subtest of this scale he obtained zero scores for the hard word associations, low scores for the easy associations, and failed to improve with repeated practice. These findings are reflected in the low memory quotient of 67. Moreover, on all tests we found that once he had turned to a new task the nature of the preceding one could no longer be recalled, nor the test recognized if repeated.

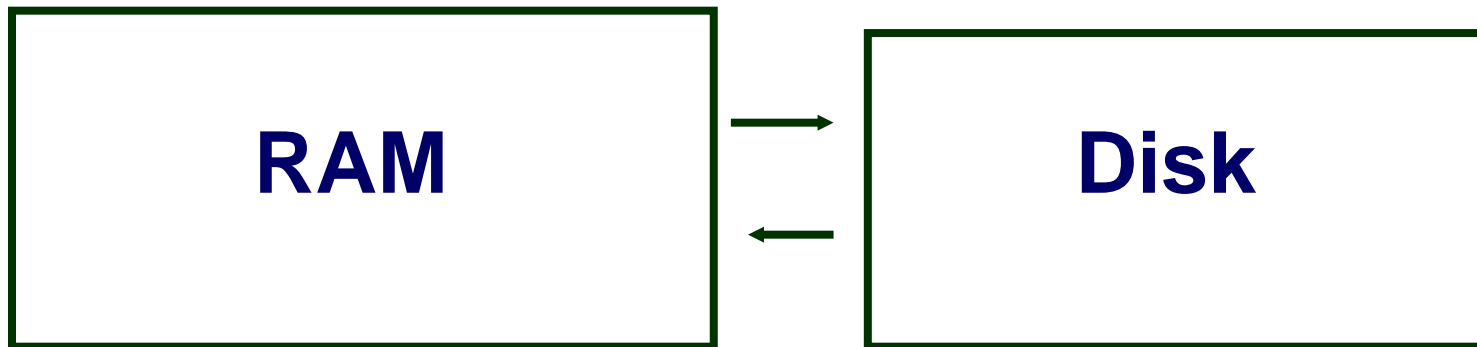
In summary, this patient appears to have a complete loss of memory for events subsequent to bilateral medial temporal-lobe resection 19 months before, together with a partial retrograde amnesia for the three years leading up to his operation; but early memories are seemingly normal and there is no impairment of personality or general intelligence.

# What happens to H.M.?

(How to improve memory for exam? 臨陣磨槍!)



**Memory consolidation / Information retrieval**



**(macro)**

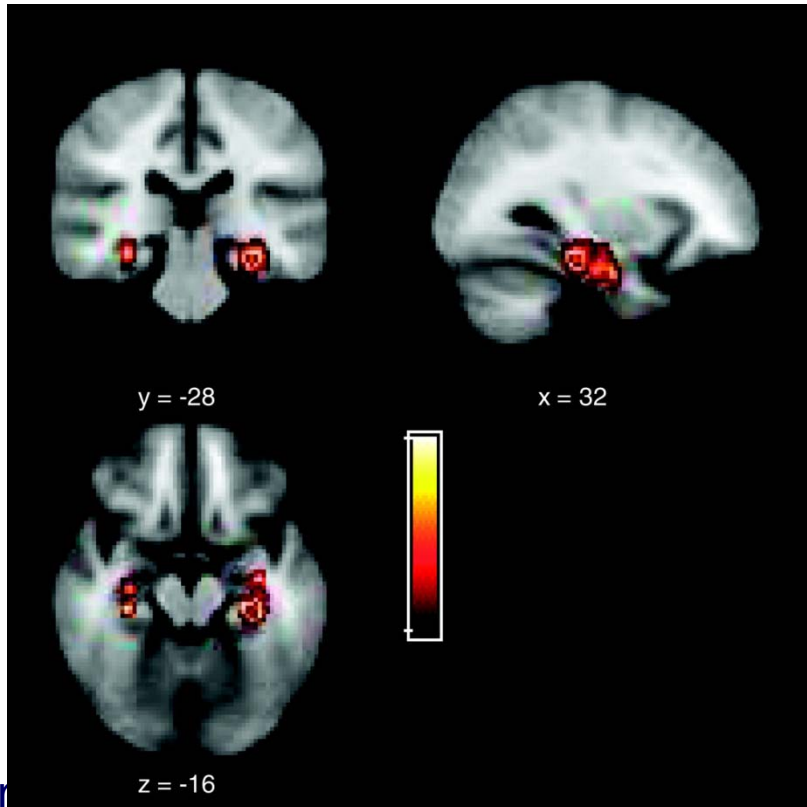
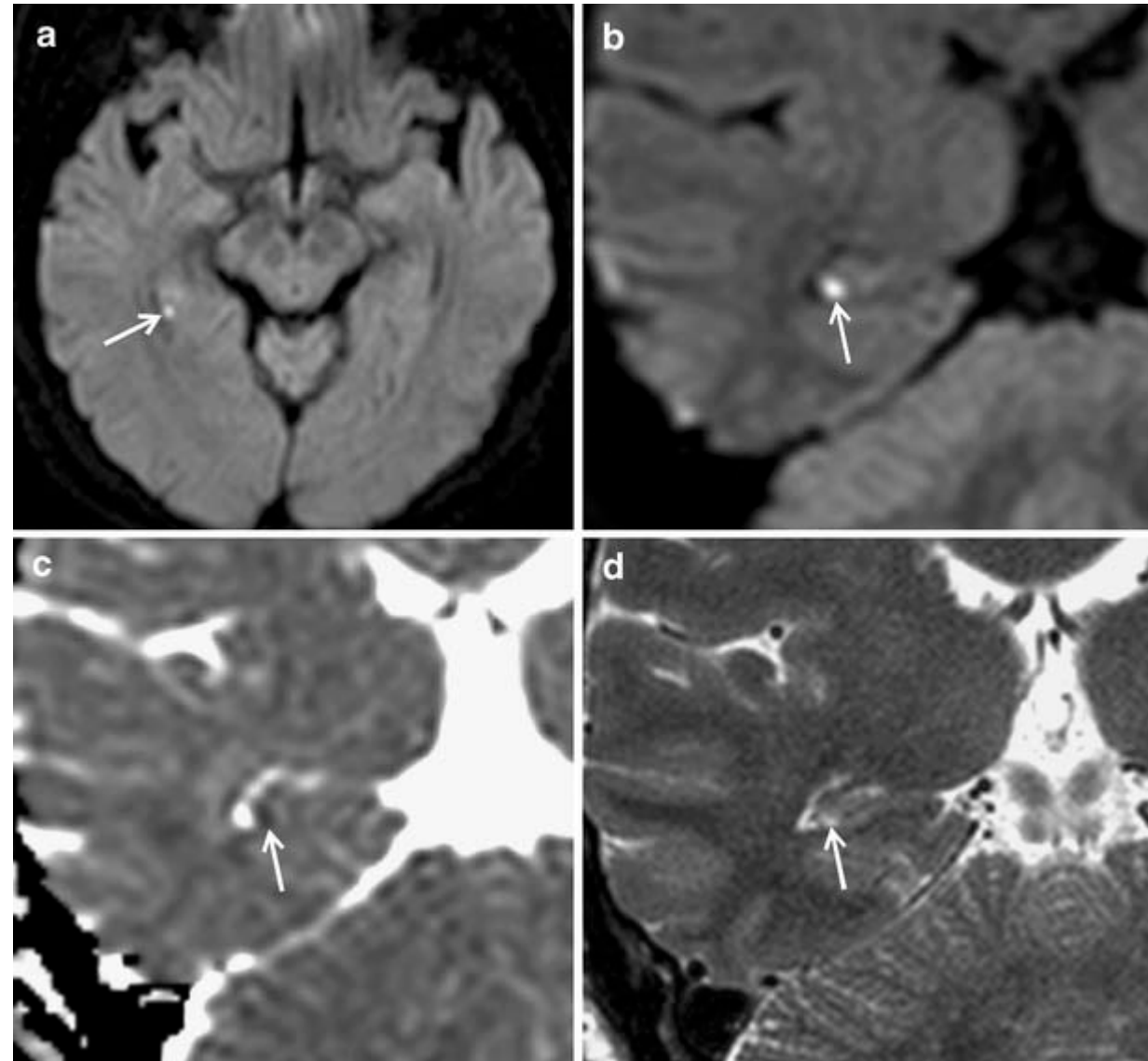
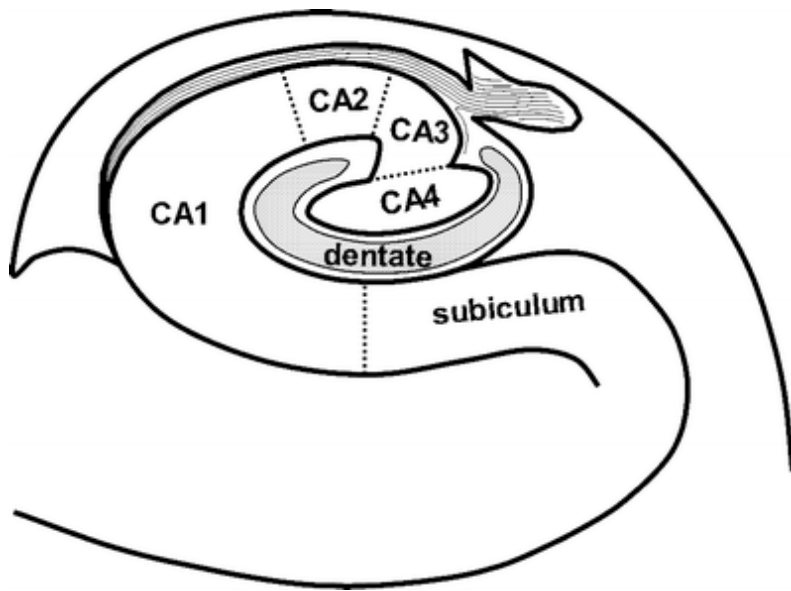
# Case history

- 住台北的一位退休公務員
- 3/13：上午與太太搭高鐵南下高雄，中午參加一位老朋友的喪禮，晚上到台南，夜宿嫁到台南的女兒家。
- 3/14：清晨醒來，問：為什麼在這裡？對於昨天 (3/13) 參加喪禮的事，一概否認，不記得有到高雄參加喪禮的事。一整天，一直“ㄈㄨㄥ”個不停。
- 3/15：早上離開台南，中午回到台北，一切恢復正常，但對於 3/12 晚間開始到 3/14 之間的事，完全沒有記憶。
- What is your diagnosis ?
- 中邪？

# Transient Global Amnesia (TGA)

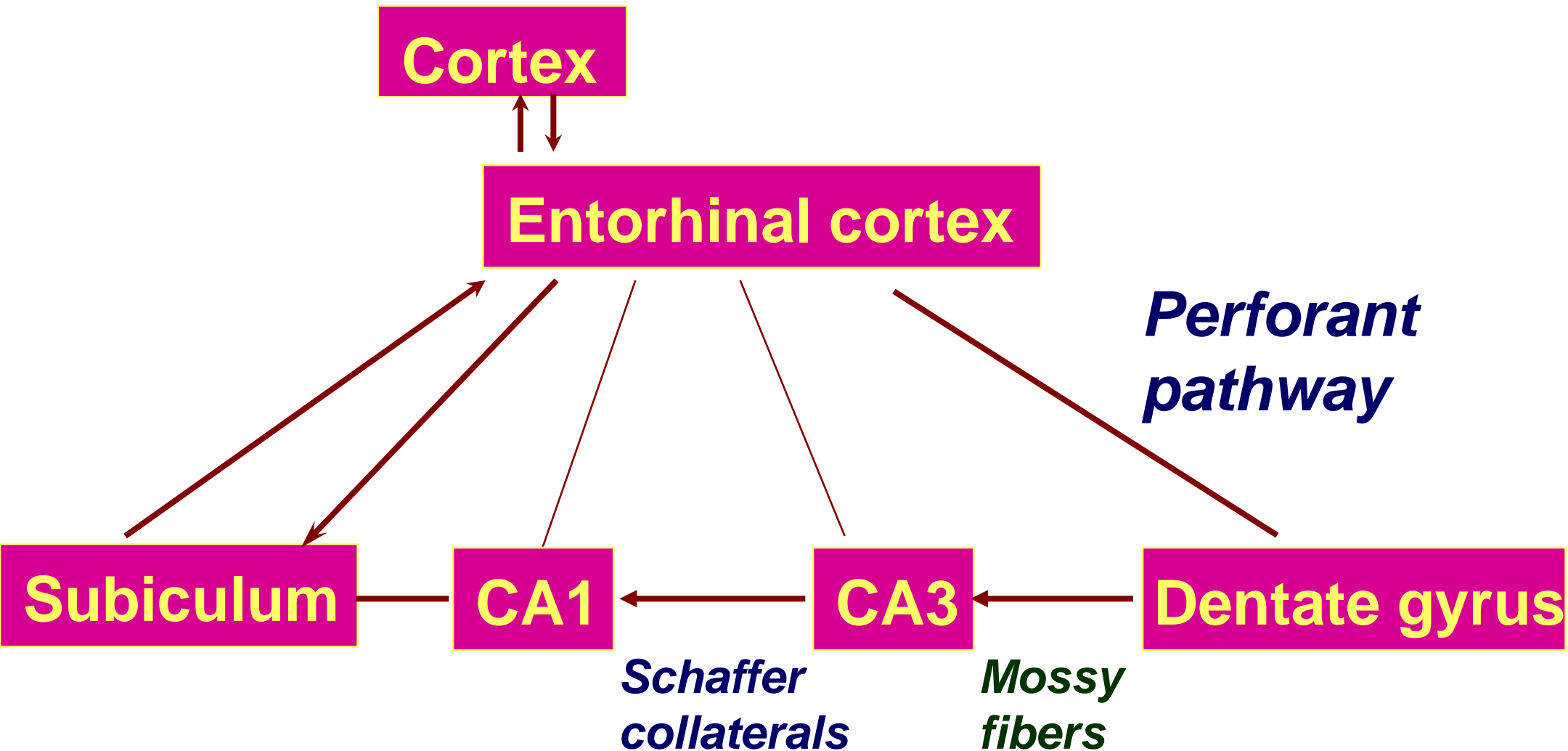
- a transient loss of memory, mainly recent events with
  - Normal intellectual functions
  - Intact (1) immediate recall and (2) remote memory
- Duration: usually resolve within 24 h
- Etiology and mechanisms: unknown, with transient lesions (mainly vascular insufficiency) in the hippocampus

# Transient global amnesia





# Hippocampus and Cerebral cortex



# Review: Hippocampus

- **Organization**
  - **Hippocampus**
  - **Dentate gyrus**
- **Synaptic pathways**
  - **Schaffer collaterals**
  - **Mossy fibers**
- **Major afferents and efferents**
  - **Alvear path**
  - **Perforant path**
  - **Fornix**