Limbic System Neural Basis of Depression (CN I) Lab 6

March 20, 2024 - Dr. Krebs (claudia.krebs@ubc.ca)

Objectives:

1. Identify the major structures of the limbic system and the hypothalamus on brain specimens and micrographs.
2. Describe the main functions of the limbic system and associated brain structures in emotional processing, learning and memory.
3. Explain the basic mechanisms and neural substrates of memory.
4. Describe the anatomy of the olfactory system and relate its function to the limbic system (memory and wellbeing).

Resources

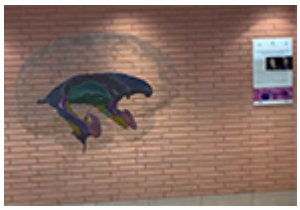
Here are the e-tutorials, videos and web resources for this lab - click the green buttons to access them.

Web Syllabus & Links

Videos:

Hypothalamus & Limbic System (Video)

Limbic Structures in 3D (Video)



Modules:

Limbic System (Module)

Hypothalamus (Module)

Antidepressants (Module)

3D Models:

Limbic System (3D)

Half Brain (3D)

Limbic System Model (3D)

There are two podcasts recommended in this lab handout - they are really engaging radio productions on damage to the hippocampus and damage to the amygdala.

*This icon located throughout the lab manual indicates **checklist items**!*

** NOTE: Interactive PDFs are best viewed on desktop/laptop computers - functionality is not reliable on mobile devices **

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Limbic System

Identify:

- ◯ Cingulate gyrus
- ◯ Parahippocampal gyrus
- ◯ Uncus
- ◯ Fornix
- ◯ Anterior commissure
- ◯ Hippocampus
- ◯ Amygdala

- Note relationship to columns of fornix -

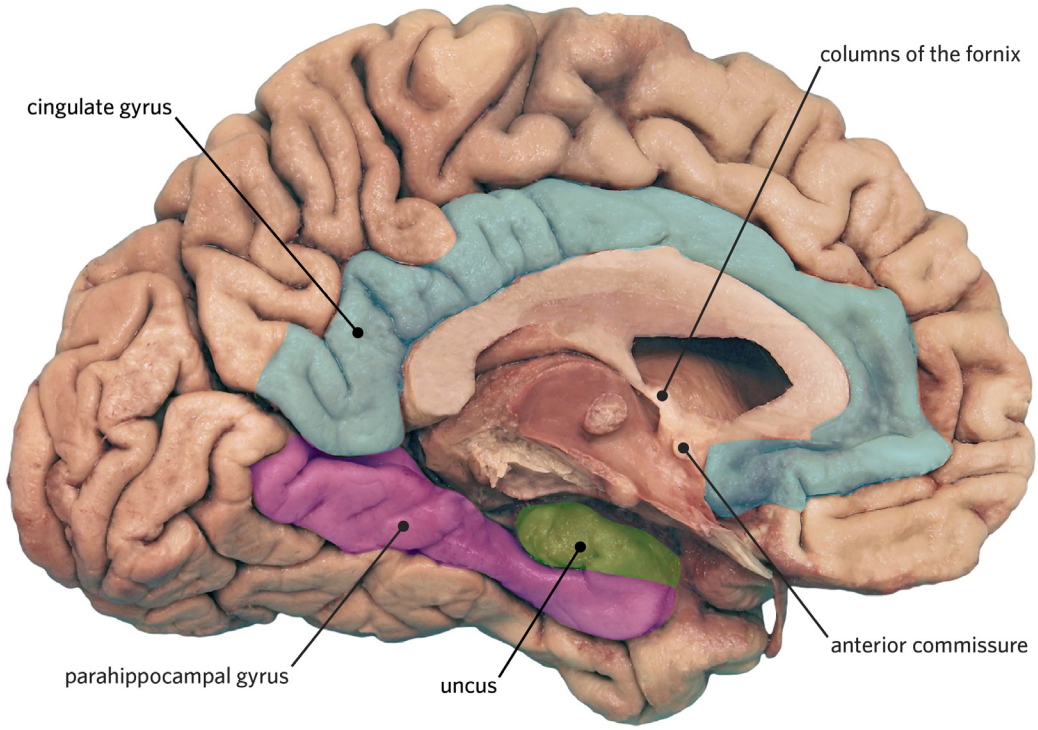
Follow fornix superiorly and anteriorly (from crus to body to columns) as it curves up from temporal lobe.

Coronal Sections

Coronal Sections (Web)

- ◯ Amygdala
- ◯ Hippocampus
- ◯ Fornix
- ◯ Mammillothalamic tracts
- ◯ Mammillary bodies
- ◯ Anterior nucleus of thalamus
- ◯ Anterior nucleus of hypothalamus (general location)

Note: these 3 structures are not necessarily visible on coronal sections



Medial Cortex

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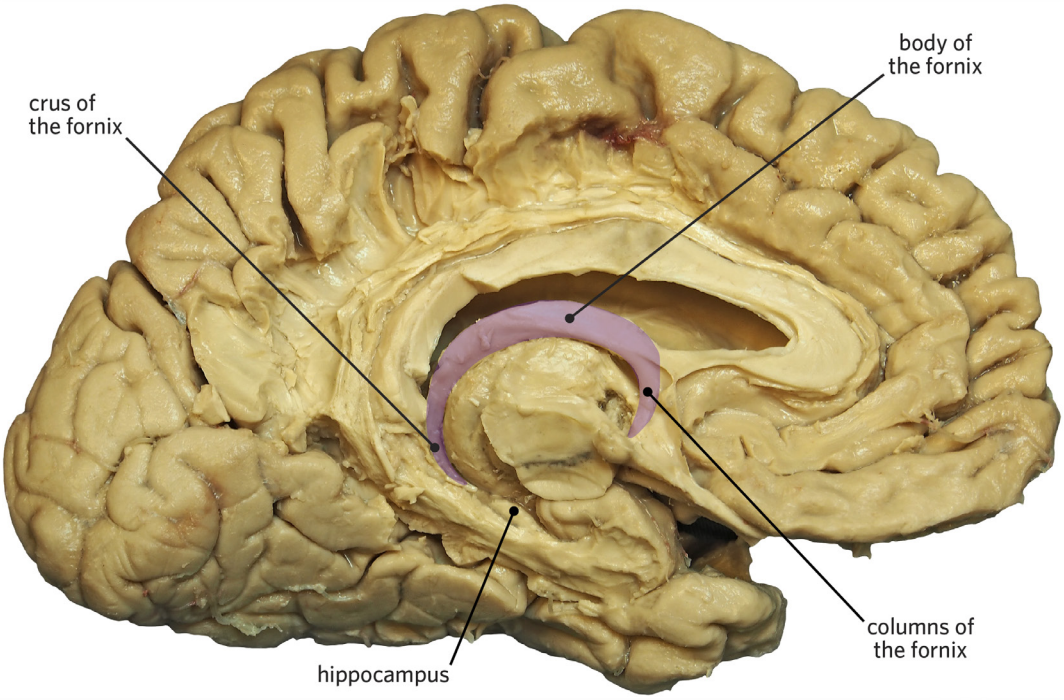

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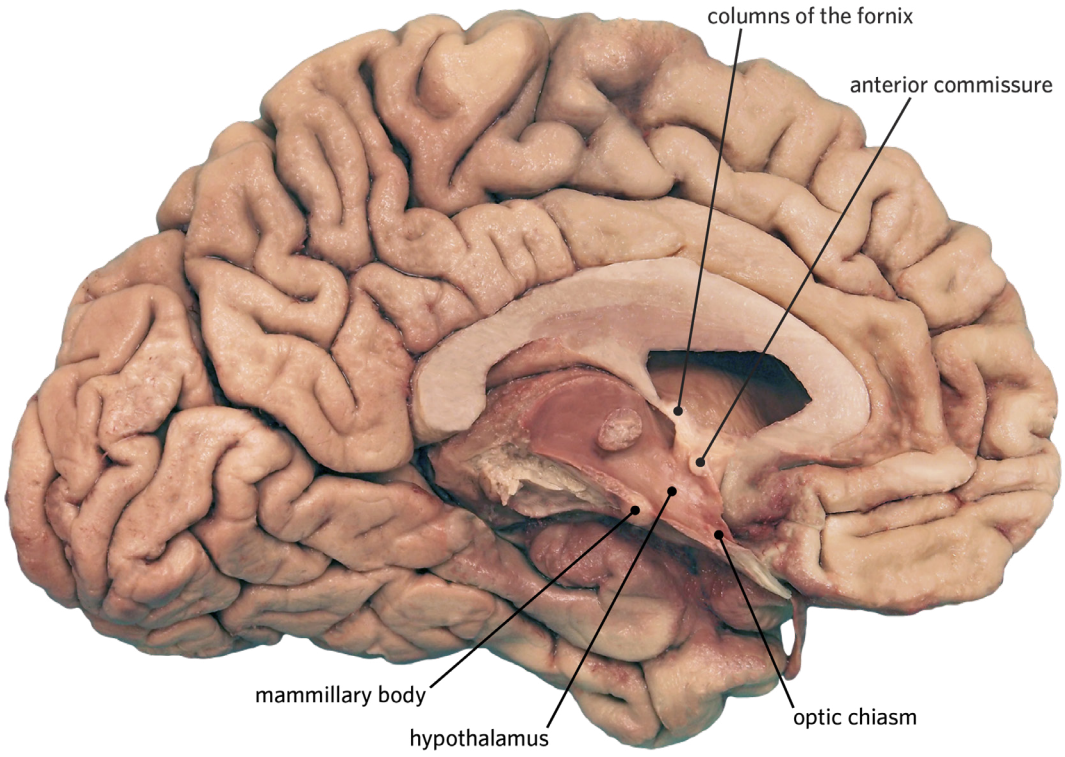
Fornix in Medial Cortex



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Hypothalamus in Medial Cortex

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Hypothalamus

- Anatomical location is inferior to thalamus, below hypothalamic sulcus. Surrounds the third ventricle.
- The hypothalamus has 2-way communication with limbic system structures → Limbic structures have 2-way communication with cortex, basal ganglia and cerebellum.

Identify:

- ◯ Mammillary bodies
- ◯ Infundibular (pituitary) stalk
- ◯ Hypothalamic sulcus (separates hypothalamus from thalamus)
- ◯ Columns of fornix
- ◯ Mammillothalamic tracts
- ◯ Attachment of infundibular stalk

Observe relationship of hypothamus to:

- ◯ Thalamus
- ◯ Fornix
- ◯ Third ventricle
- ◯ Position of optic chiasm and optic tracts

Micrographs

Micrographs (Web)

- ◯ Locus ceruleus (noradrenergic neurons)
- ◯ Raphe nuclei (serotonergic neurons)
- ◯ Ventral tegmental area (dopaminergic neurons)

Connections of the Hypothalamus *(for your information only)*

- Hypothalamic - hypophysial tract (and portal system), interconnecting hypothalamus and pituitary.
- Fornix and mammillothalamic tract, interconnecting hippocampus, hypothalamus and thalamus.
- Stria terminalis and ventral amygdalofugal fibers, interconnecting amygdala and hypothalamus.
- Medial forebrain bundle and dorsal longitudinal fasciculus, the primary hypothalamic efferents.

Amygdala

Can you speculate on the consequences of bilateral amygdala damage?

What would be the consequences for fear processing, memory formation and saliency filtering?

Fearless http://www.npr.org/programs/invisibilia/377515477/fearless

Based on the experiences described in this podcast, what are some of the clinical symptoms of bilateral amygdala damage?

This is an excellent paper on the function of the amygdala:

The Human Amygdala and the Induction and Experience of Fear

Justin S. Feinstein[1], Ralph Adolphs[2], Antonio Damasio[3], and Daniel Tranel[1]

1University of Iowa, Iowa City, IA 52242, USA
2California Institute of Technology, Pasadena, CA 91125, USA
3University of Southern California, Los Angeles, CA 90089, USA

Summary:

Although clinical observations suggest that humans with amygdala damage have abnormal fear reactions and a reduced experience of fear, these impressions have not been systematically investigated. To address this gap, we conducted a new study in a rare human patient, SM, who has focal bilateral amygdala lesions. To provoke fear in SM, we exposed her to live snakes and spiders, took her on a tour of a haunted house, and showed her emotionally evocative films. On no occasion did SM exhibit fear, and she never endorsed feeling more than minimal levels of fear. Likewise, across a large battery of self-report questionnaires, 3 months of real-life experience sampling, and a life history replete with traumatic events, SM repeatedly demonstrated an absence of overt fear manifestations and an overall impoverished experience of fear. Despite her lack of fear, SM is able to exhibit other basic emotions and experience the respective feelings. ***The findings support the conclusion that the human amygdala plays a pivotal role*** in triggering a state of fear and that the absence of such a state precludes the experience of fear itself.

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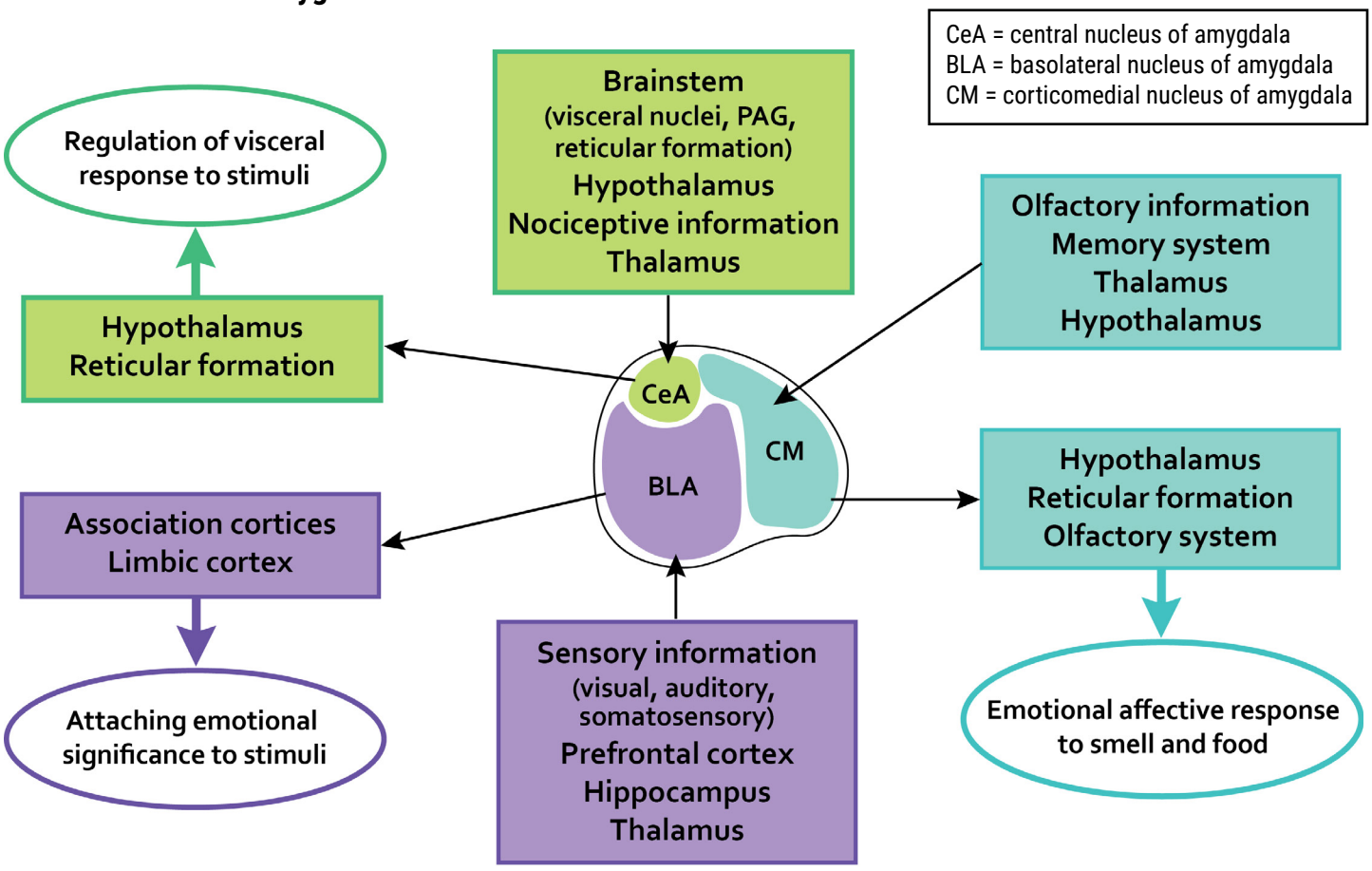
Amygdala and Emotion

- The amygdala **associates experiences with consequences** and then programs the appropriate behavioral response to the experience. Specifically, the amygdala plays a role in **emotional learning** and **emotional processing**, with a particular role in the expression of fear and anger.
- Input to the amygdala comes mainly from the **cerebral cortex**.
- After assessing the nature of the input, i.e. friendly, unfriendly, frightening, dangerous, etc., the amygdala sends signals to centers in the **hypothalamus** that elicit the appropriate autonomic and motor responses. Signals are also sent from the basolateral amygdala via the **dorsomedial nucleus of the thalamus** to the **orbitofrontal cortex**.
  - The orbitofrontal cortex provides the perception of emotions, whereas the hypothalamus provides the expression of emotions.

Connections of the Amygdala



Modified from Lippincott's Illustrated Reviews: Neuroscience by C. Krebs, J. Weinberg, E.J. Akesson, and E. Dilli.

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Hippocampus

HM, the man with no memory http://www.abc.net.au/radionational/programs/allinthemind/hm---the-man-with-no-memory/5067570

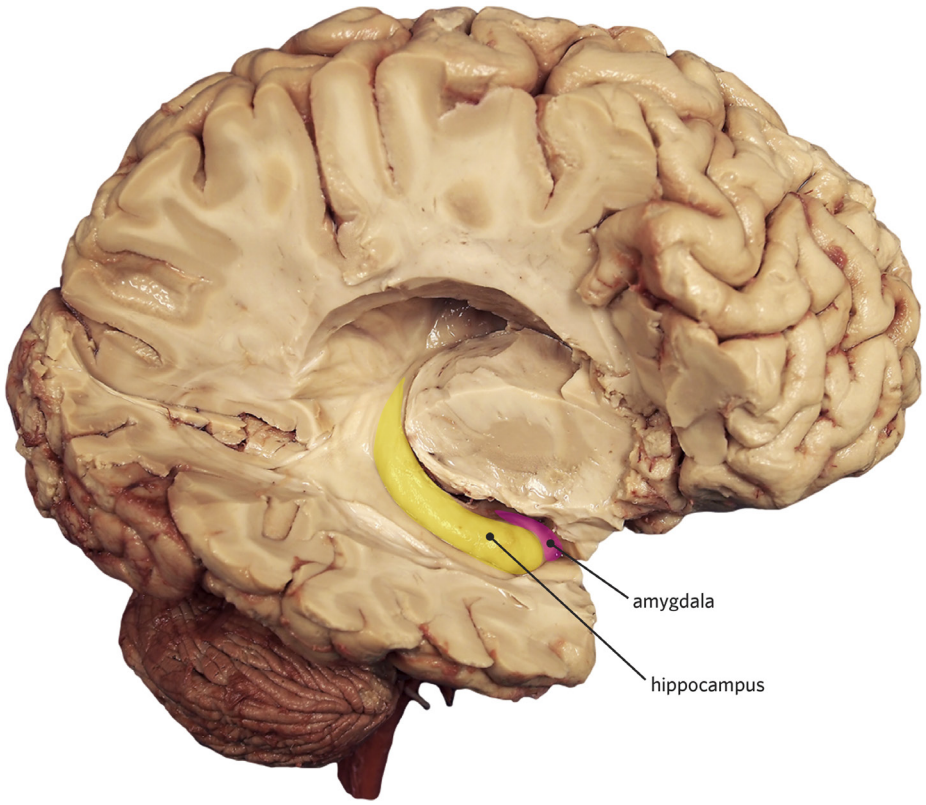
Based on this podcast, can you list and explain his symptoms based on your anatomical knowledge?

Note:
HM had a long history of major seizure disorder. A radical bilateral temporal lobe resection, involving both hippocampi, was performed.

Hippocampus and Memory

Important role in learning & formation of new memories:

- Hippocampus acts as "encoding area" for translating short-term memories into long-term memories. Important for declarative memory.
- May be the initial storage site for memory. As process of consolidation occurs, more permanent memories laid down (probably diffusely) in cortex.
- Overlying cortex (uncus, entorhinal cortex) also plays important role in memory.
- Bilateral removal of hippocampi results in inability to form new memories of facts and events. Deficits less severe if overlying cortex not involved.
- The hippocampus and amygdala are linked to two independent memory systems. They act in concert when 'emotion meets memory'.



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Amygdala and Hippocampus

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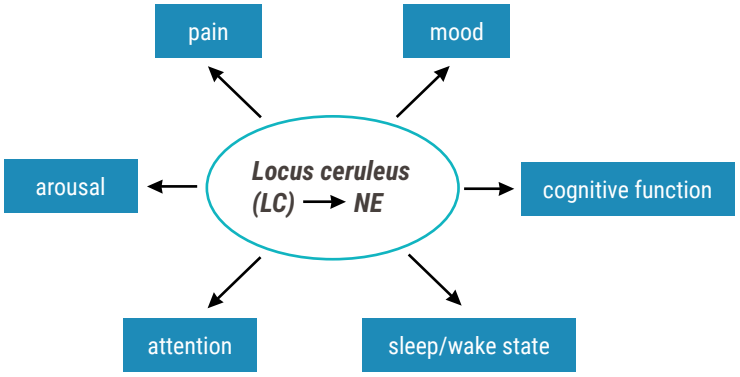
Monoaminergic Nuclei of the Reticular Formation

Micrographs (Web)

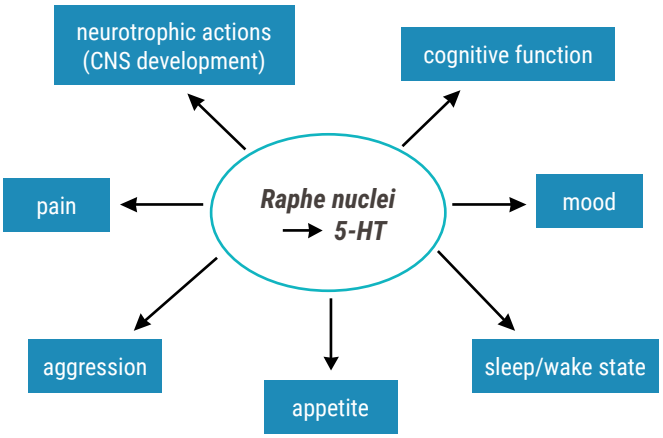
These nuclei have widespread projections to the entire brain.
Drugs that influence these systems will have widespread effects.

NE = norepinephrine
5-HT = serotonin
DA = dopamine



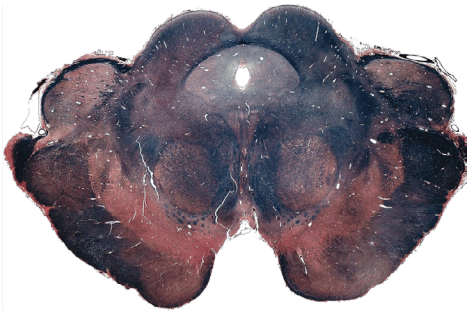
Locus Ceruleus (#9)

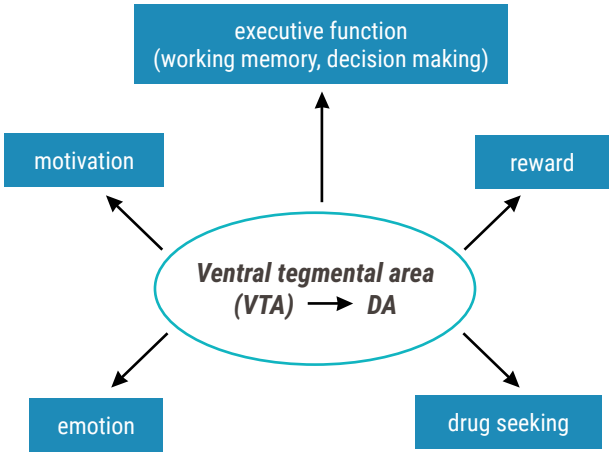
◯ noradrenergic neurons



Raphe Nuclei (#10)

◯ serotonergic neurons





Ventral Tegmental Area (#11)

◯ dopaminergic neurons

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Memory

What is explicit memory?

What are the neural substrates of explicit memory?

What is implicit memory?

What are some of the neural substrates of implicit memory?

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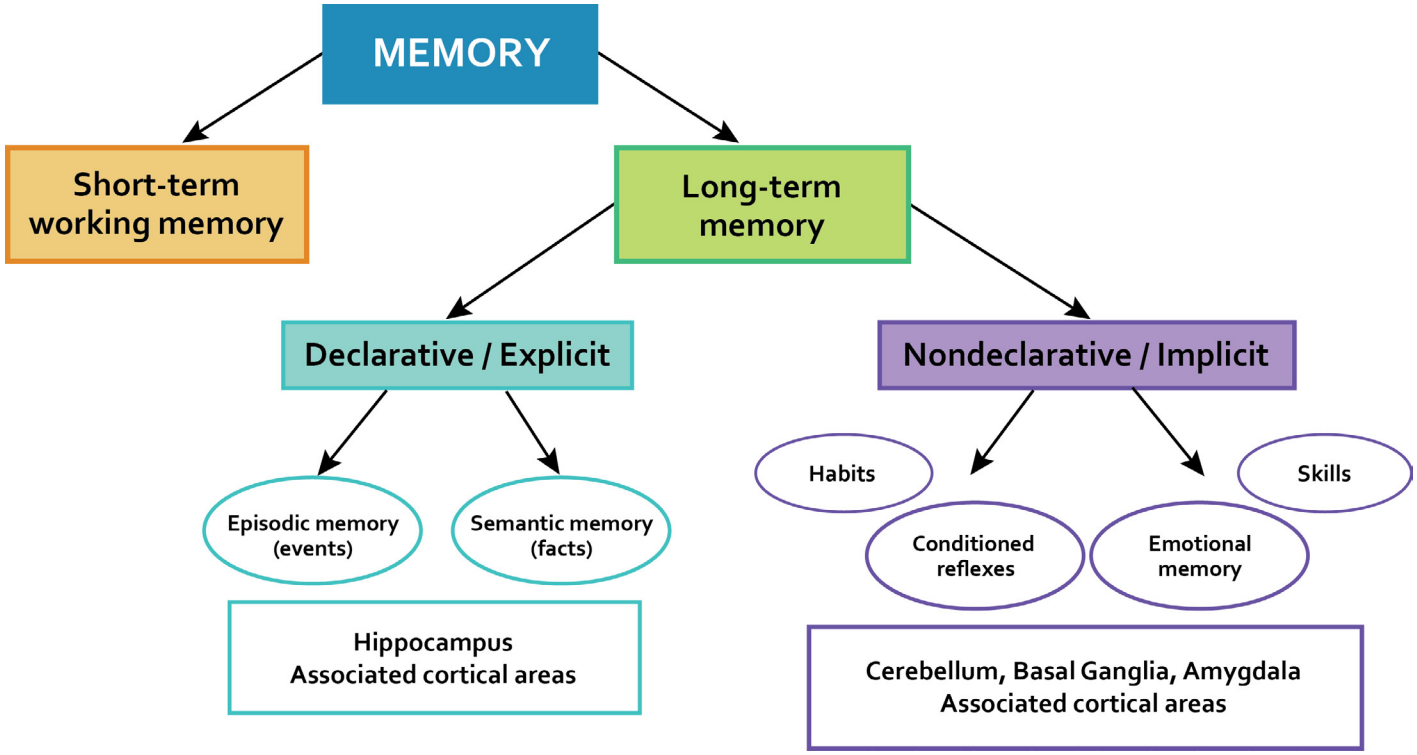
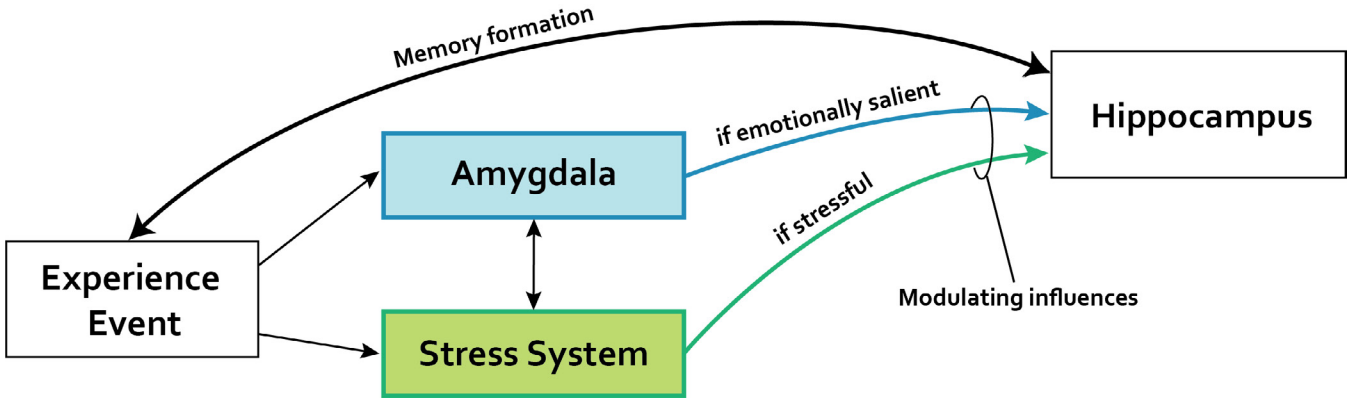
Types of Memory and Their Neural Correlates



The Role of the Amygdala in Memory



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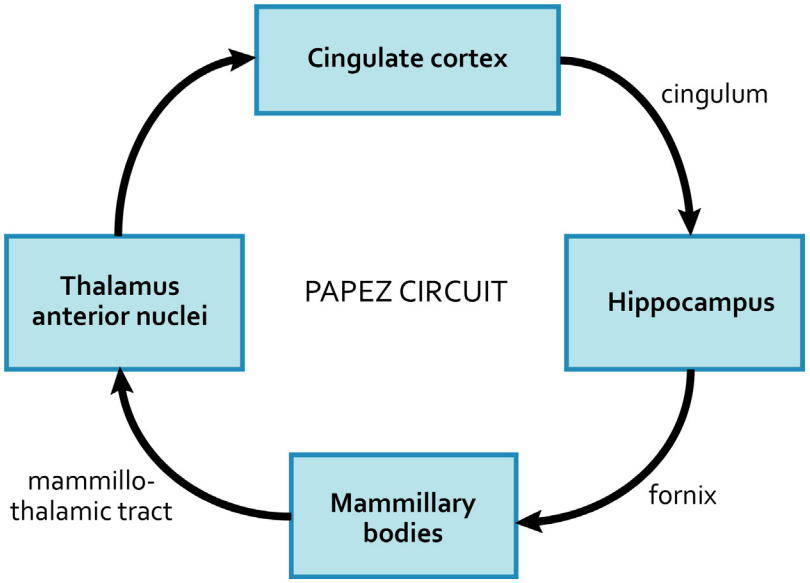
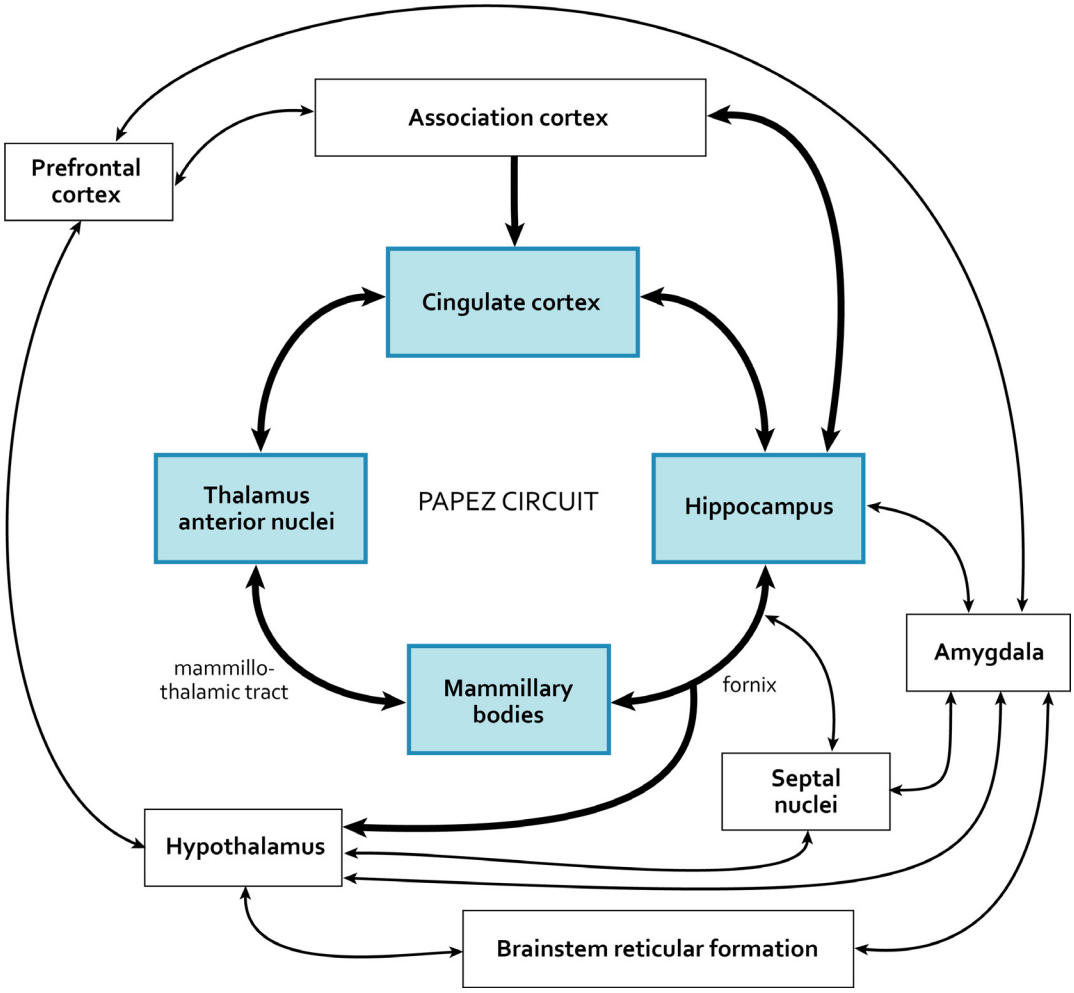
Classic Papez Circuit



Extended Papez Circuit



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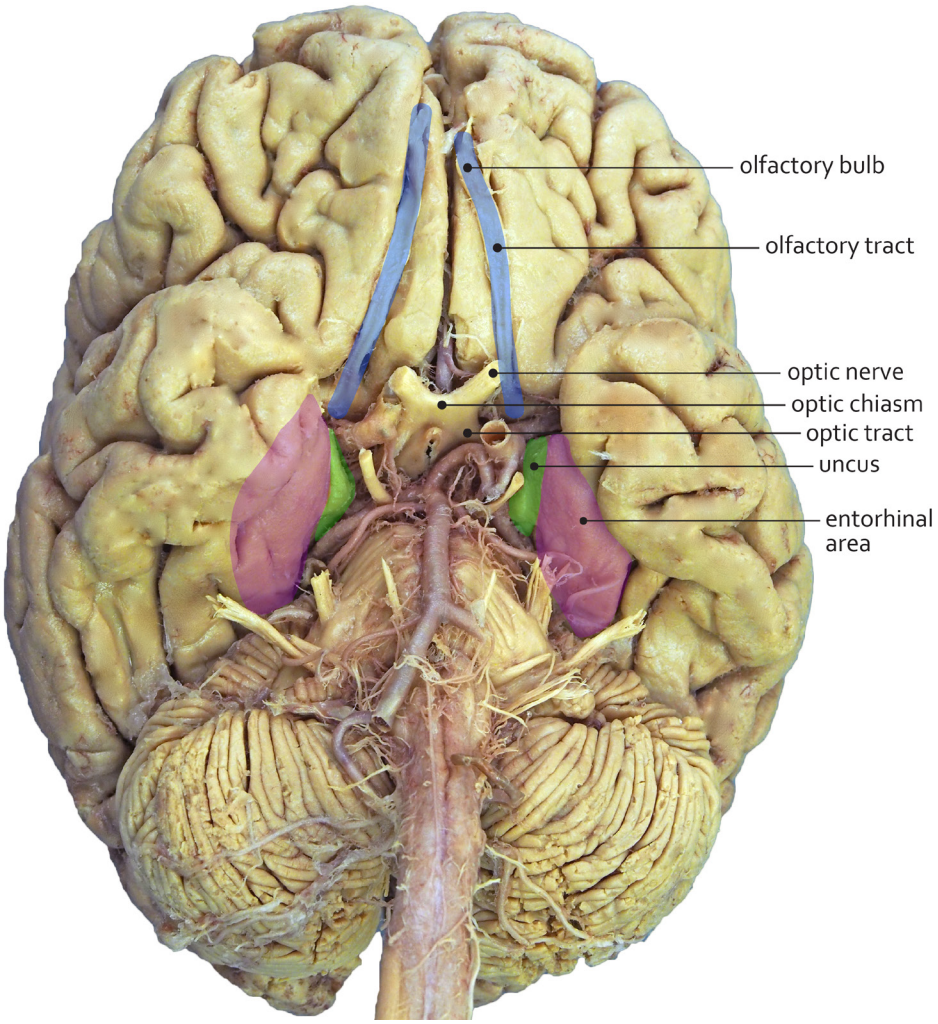
Olfactory System (CN I)

Identify:

- ◯ Olfactory bulbs
- ◯ Olfactory tracts
- ◯ Olfactory stria (medial and lateral)

- **Medial olfactory striae** - information (mostly inhibitory) to opposite **olfactory bulb** via anterior commissure.
- **Lateral olfactory striae** - information to **primary olfactory cortex**: consists of the **uncus, entorhinal area** (anterior part of parahippocampal gyrus), **amygdala,** and the **limen insulae** (junction point between the cortex of the insula and cortex of the frontal lobe).
- Projections are then sent to **olfactory association cortex** (area 28 - **entorhinal cortex**).
- Projections from primary and association areas to **orbitofrontal cortex** (conscious appreciation of smell), hypothalamus, DM thalamus, and **structures of limbic system** (amygdala, hippocampus and striatum), cranial nerve nuclei (salivatory nuclei and DMN X). Influence visceral functions, social and reproductive behavior.



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Inferior Cortex

RESOURCES

Websites:

Neuroanatomy | Entrada

Recommended Textbooks:

Lippincott Illustrated Reviews: Neuroscience
By: Claudia Krebs, Joanne Weinberg, Elizabeth J. Akesson, Esma Dilli
Lippincott Williams & Wilkins
ISBN 978-1-4963-6789-1

Neuroanatomy Through Clinical Cases
By: Hal Blumenfeld
Sinauer
ISBN 978-0-8789-3613-7

Neuroanatomy in Clinical Context: An Atlas of Structures, Sections, Systems, and Syndromes
By: Duane E. Haines
Wolters kluwer Health
ISBN 978-1-4511-8625-3

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Instructional Design: Monika Fejtek
Medical Illustration Lead: Paige Blumer
Academic Lead: Claudia Krebs

Prosector: Lien Vo

Content Review: Esma Dilli