Limbic System Objectives

1. Describe the functions of the limbic system.

2. Identify on images the hippocampal formation, amygdala, fornix, nucleus basalis of Meynert, nucleus accumbens.

3. List the pathways and nuclei that make up Papez circuit. What is the significance of this circuit?

4. Describe the signs/symptoms seen in patients with hippocampal lesions.

5. What brain areas are lesioned in Alzeheimer's patients?

6. Describe the signs/symptoms associated with Korsakoff's syndrome. What brain areas are lesioned?

7. Describe the signs/symptoms of a bilateral lesion to the anterior aspect of the cingulate gyrus.

8. Describe the signs/symptoms of Kluver-Bucy syndrome. Where is this lesion?

9. Describe the signs/symptoms of a septal nuclei lesion.

10. What is the importance of the nucleus accumbens?.

Limbic System Outline

Limbic System

I. General Information

- A. Hippocampal formation
  1. Papez circuit
  2. Lesions
- B. Amygdala
  1. Lesions
- C. Septal Nuclei
  1. Lesions
- D. Nucleus Accumbens

I. General Information

The Limbic System is made up of several structures along the neuraxis that are interconnected in order to participate in complex activities such as learning, memory emotions, behaviors, and social interactions.

There are 2 levels of structural and functional organization to the limbic system. The first level involves cortical structures on the the medial edge of the hemisphere (limbus)/ limbic lobe
These structures include:
Subcallosal area
Cingulate gyrus
Parahippocampal gyrus (from the temporal lobe)
Uncus (from the temporal lobe)
Hippocampus (structure deep within the parahippocampal gyrus)

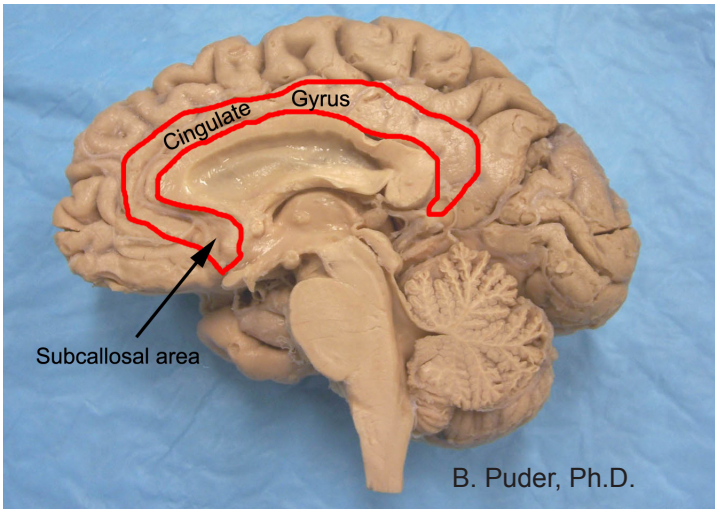
The second level of organization for the limbic system includes several nuclei that are anatomically located outside the limbus border.

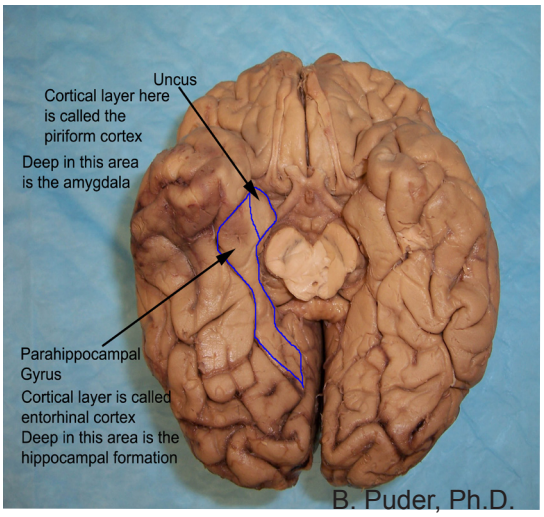
II. The First Level to the Limbic System = Limbic Lobe

Limbus = ring, border, or edge. The structures in this lobe make a ring around the medial rim of the hemisphere.
This lobe consists of:

- Cingulate gyrus
- Parahippocampal gyrus
- Uncus
- Subcallosal area

The Limbic system is a complex entity that involves the above named structures and several afferents and efferents making connections from other telencephalic areas, the diencephalon, and brainstem areas.





Left image: right medial brain view depicting the cingulate gyrus and subcallosal area. Right image: inferior view depicting the uncus and parahippocampal gyrus. These structures are part of the limbic lobe.

III. Second level of Limbic System

The second level includes all structures of the first level plus some subcortical nuclei.

These second level structures include:

- Nucleus accumbens
- Nucleus basalis of Meynert (substantia innominata)
- Amygdala
- Septal nuclei
- Some hypothalamic nuclei (ESPECIALLY the Mammillary bodies)
- Anterior and dorsomedial nuclei of the thalamus
- Habenular nuclei
- Ventral tegmental area (from the midbrain)
- Periaquaductal gray (from the midbrain)

Some of the main efferents from the limbic system include:

- Fornix
- Mammillothalamic tract
- Stria terminalis
- Ventral amygdalofugal pathway

As noted earlier, most of the cortex has 6 layers, however, the structures in the limbic system have less than 6 layers.

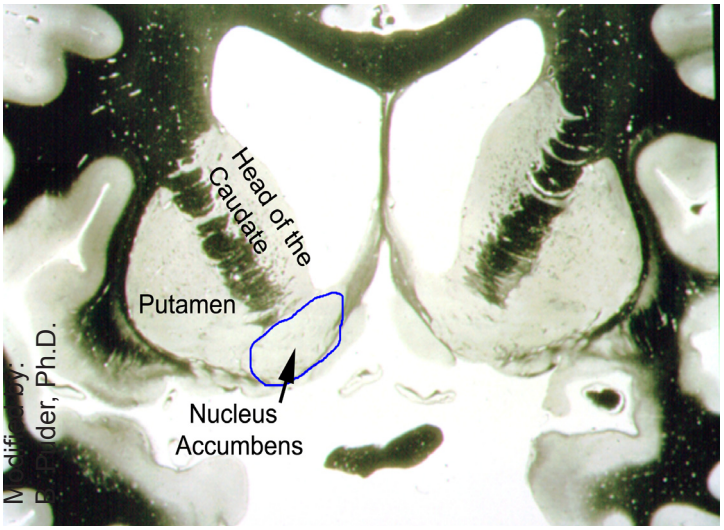
3-5 layers (paleocortex) found in the cortex of the parahippocampus and uncus

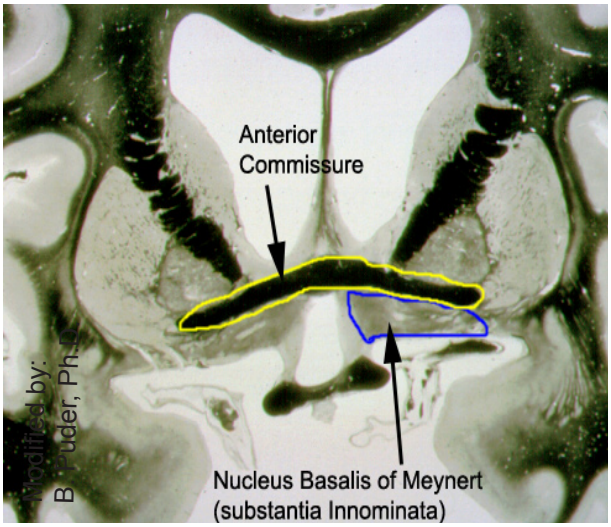
3 layers (archicortex) found in the hippocampus and the dentate gyrus
(remember that there is a dentate nucleus in the deep cerebellar nuclei of the cerebellum - this is different - it is a gyrus)

IV. Second level Limbic System - nuclear groups

1. Nucleus Accumbens - located anteriorly and inferiorly where at the junction between the head of the caudate and the putamen.
This area is the “pleasure” center and is part of the limbic system as well.

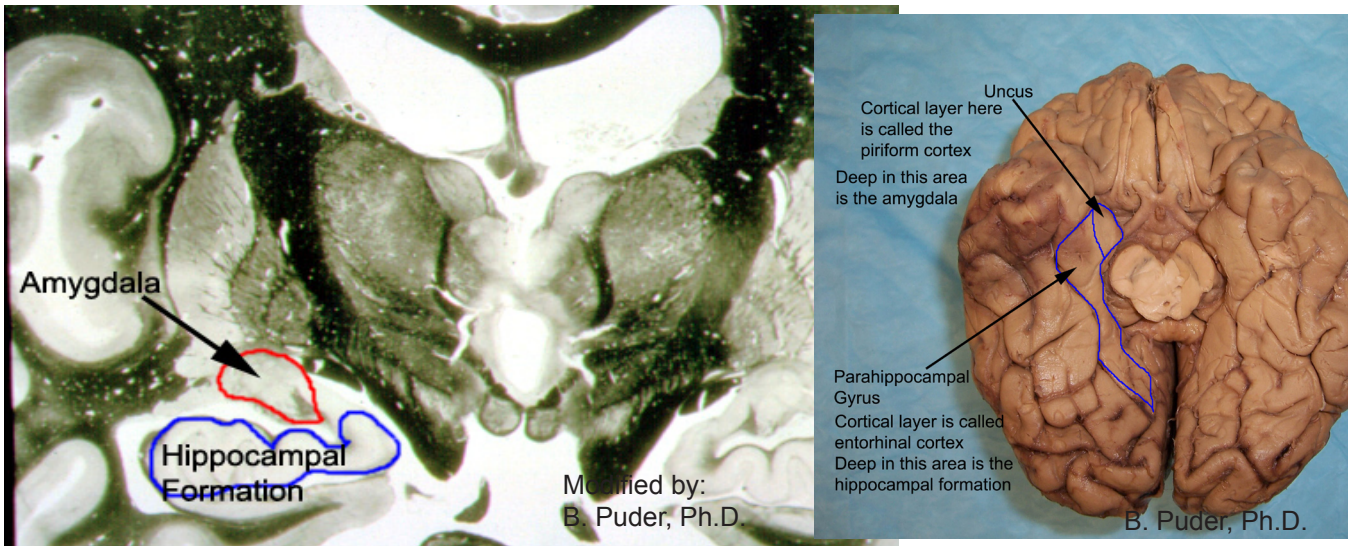
2. Nucleus Basalis of Meynert (substantia innominata) - located inferior to the anterior commissure. This nucleus is part of the Limbic system and has significant neuronal cell death in Alzeheimer’s patients.





Left: Coronal section anterior to the anterior commissure the depicts the Nucleus accumbens
Right: Coronal section at the anterior commissure that depicts the Nucleus Basalis of Meynert

3. Hippocampal formation
    located in the temporal lobe, deep in the parahippocampal gyrus
    consists of:
        subiciulum
        hippocampus
        dentate gyrus
    Is part of the Limbic system
    Major efferents are called the fornix
    Involved in learning, memory
4. Amygdala
    located in the temporal lobe, deep in the uncus
    Is part of the Limbic system
    Major efferents are the stria terminalis and the ventral amygdalofugal pathway
    Involved in behavioral aspects, lesion here causes Kluver-Bucy syndrome (we'll talk about later)



Left: Coronal section depicting amygdala and hippocampal formation Right: Inferior brain image depicting parahippocampal gyrus and the uncus.

V. Functional Aspects of Limbic System Structures
1. Hippocampal formation
    The function of the hippocampal formation is to consolidate long term memories from immediate and short term memories.

Note: Remember that the above 2 structures are located in the parahippocampal gyrus and instead of calling the cortex of the parahippocampal gyrus "the parahippocampal cortex" it is called the entorhinal cortex.

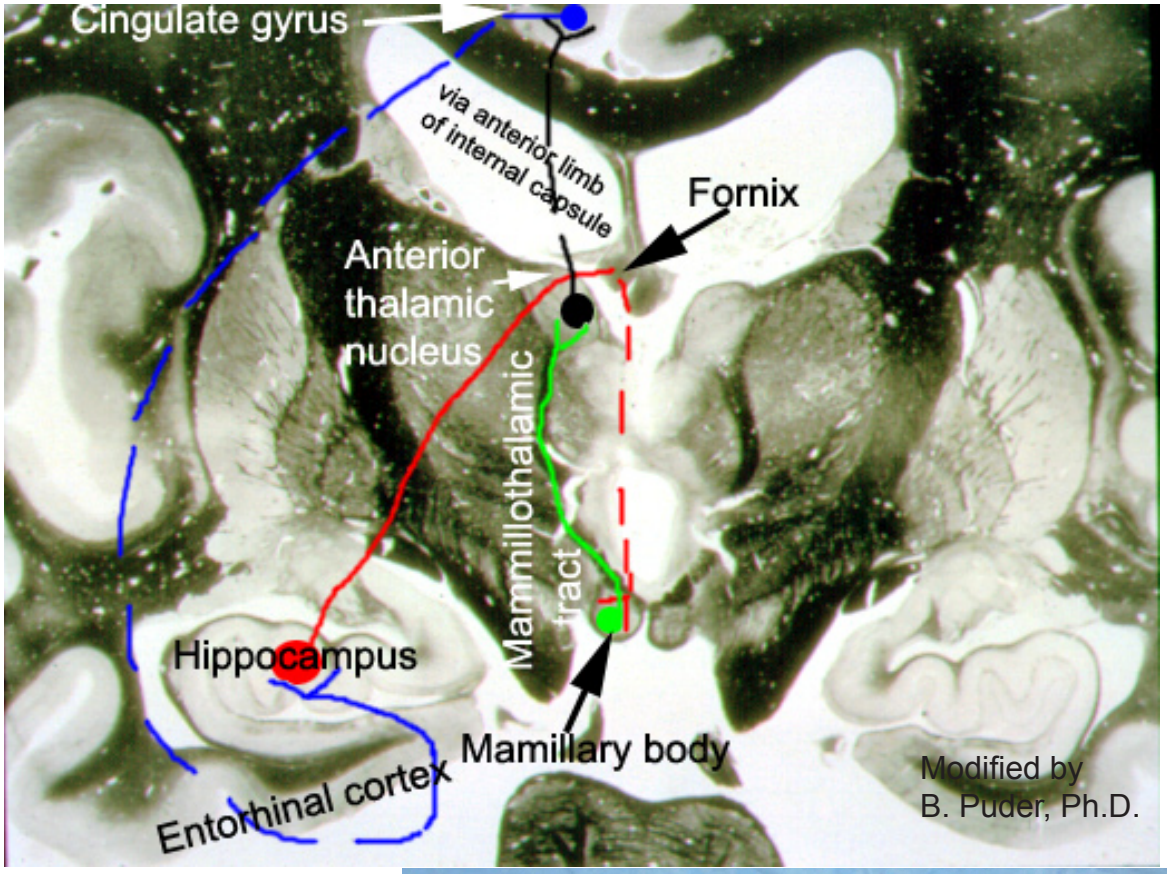
Afferents to the hippocampal formation
    Fibers from the entorhinal cortex synapse on the dentate gyrus and hippocampus.

Efferents leaving the hippocampal formation
    The fornix is the major efferent fibers from the hippocampus.
    (The fornix fibers will make a backwards "C" shaped path from inferiolateral to anterior/medial. When the fornix is superior to the anterior commissure it splits and some of the fornix fibers will synapse on the mammillary bodies, while some will synapse on the nucleus accumbens and the septal nuclei.

A. Papez circuit

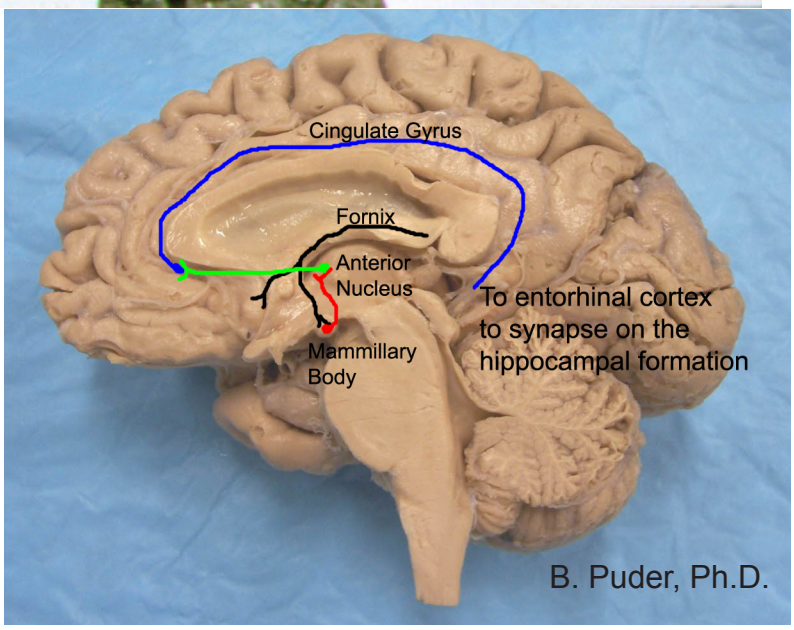
Hippocampal fornix fibers synapse on the mammillary bodies of the hypothalamus. The mammillothalamic tract are the axons of the cell bodies of the mammillary bodies and this pathway will synapse on the anterior nucleus of the thalamus. The cell bodies of the anterior nucleus of the thalamus send their axons via the anterior limb of the internal capsule to the cingulate gyrus. The axons of the cingulate gyrus projects to the entorhinal cortex, which projects its axons to the hippocampal formation.

Since this pathway includes the hippocampus, it plays a role in learning and memory. Papez himself proposed that this pathway played a role in expression of emotion and allowed scientists the first clue as to the role of the limbic system.



Above: Coronal section with the Papez circuit schematically drawn in.

Right: Right medial view with Papez circiut schematically drawn in.



B. Lesions to the Hippocampus

A lesion to the hippocampal formation causes patients not to be able to form long term memories. Less severe lesions cause the patient to have more difficulty learning new things, and they may have trouble remembering to return to a previously started task if interupted.

The case about H.M.

H.M. was a patient with severve epilepsy in his hippocampal area, so physicians decided in 1954 to remove his hippocampus. It stopped the seizure activity, but now H.M. was unable to from long term memories, thus he had anterograde amnesia. And this helped verify that the hippocampus is an important structure for learning and memory.

Since the hippocampus is the key structure for learning and memory, let's talk a minute about memory.

Declarative (explicit) memory = conscious recollection of facts/experiences. Occurs in the temporal lobe/hippocampus.

Nondeclarative memory (implicit) memory = nonconscious learning of skills, habits, acquired behavior. Occurs in the basal nuclei, cerebellum, amygdala, brainstem, spinal cord.

Anterograde amnesia - inability to form new memories

Retrograde amnesia - inability to recall events from the past

Korsakoff syndrome

Caused by a thiamine deficiency and seen in chronic alcoholics. Degeneration is seen in the mamillary bodies, fornix, hippocampus and dorsomedial thalamic nucleus.

Signs/symptoms include:

- Dementia
- Confabulation
- Memory loss
- Confusion
- Cerebellar damage (ataxia)

Wernicke-Korsakoff syndrome

When the patient has the above stated signs/symptoms and learning difficulties, it is called Wernicke-Korsakoff syndrome (thus involving Wernicke's area as well).

Bilateral lesions to the anterior part of the cingulate gyrus can cause:

the patient may be alert, but have no idea who they are, or unable to recall the order of past events

2. Amygdala

The amygdala is part of the limbic system.
It is an almond shaped structure located deep in the uncus of the temporal lobe.
There are 2 major nuclei groups located within the amygdala.

1. Basolateral group
2. Corticomedial group

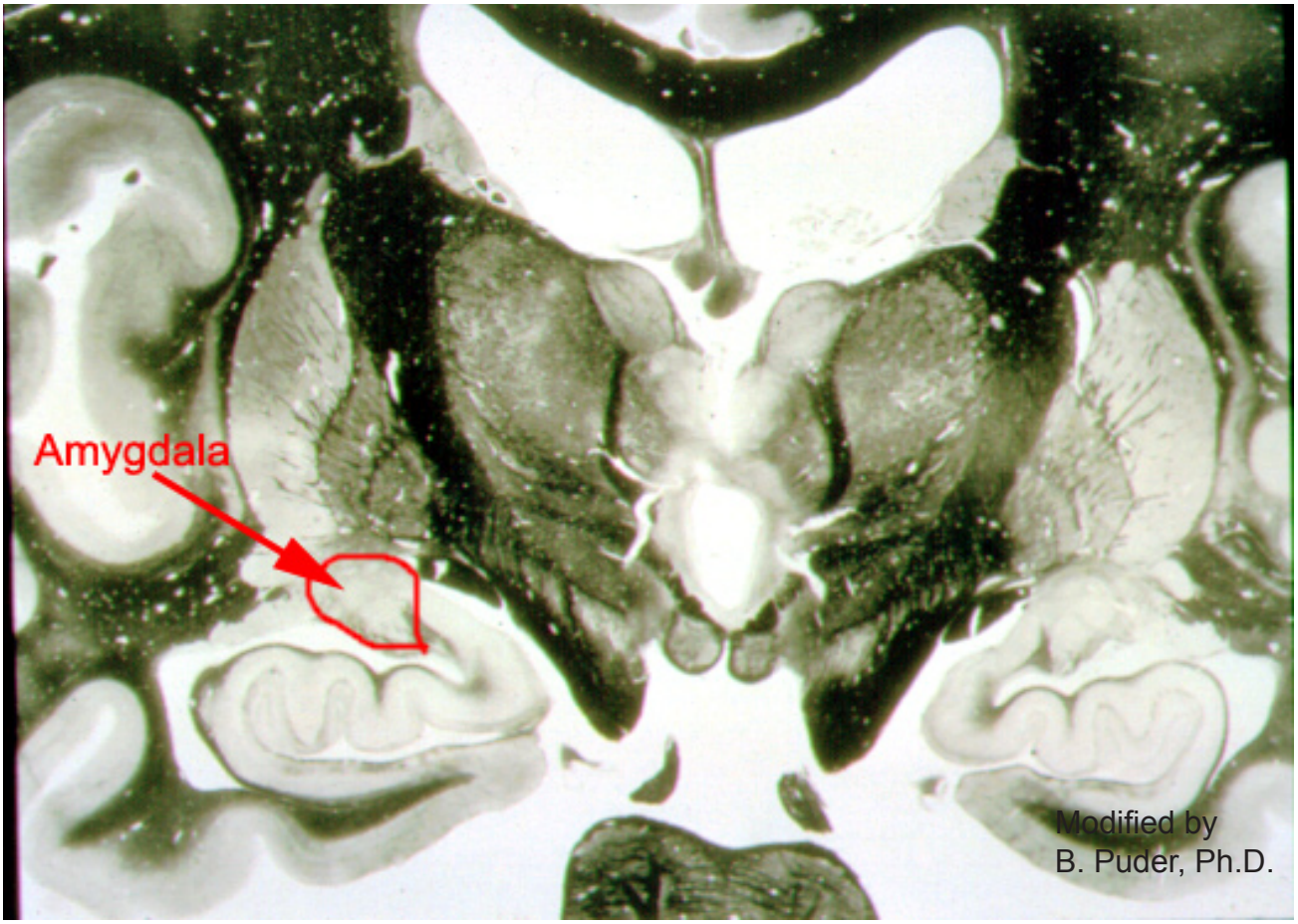
Afferents to the basolateral amygdala

thalamus
prefrontal areas
cingulate gyrus
parahippocampal gyrus
temporal lobe
insular cortex

→ Somatosensory
Visual
Visceral
Information

Afferents to the corticomedial amygdala

Olfactory
Ventral medial nucleus of the hypothalamus
Dorsomedial nucleus of the thalamus
brainstem - periaquaductal gray and solitary nucleus



Efferents of the amygdala (via the ventral amygdalofugal pathway)

- Nucleus basalis of Meynert
- Hypothalamus
- Septal nuclei
- Frontal, prefrontal, cingulate, insular, and inferior temporal cortices
- Brainstem (dorsal motor nucleus of the Vagus (parasympathetic)
- Locus ceruleus
- Periaquaductal gray

Efferents of the amygdala (via the stria terminalis)

- Hypothalamus
- Nucleus accumbens
- Septal nuclei
- Caudate
- Putamen

Lesions of the Amygdala and Hippocampus

Lesions to the temporal lobe damaging the amygdala and hippocampus are called Kluver-Bucy syndrome

A pair of scientists lesioned the amygdala in monkeys and here are the signs/symptoms that the monkeys exhibited. This is also seen in humans with temporal lobe damage.

1. Visual Agnosia - can't recognize objects by sight
   (May also have tactile and auditory agnosias as well).
2. Hyperorality - examine objects by mouth or by smelling them
3. Hypermetamorphisis - overly explore the environment and over react to visual stimuli
4. Hyperphagia - Eating excessive amounts of food - some not appropriate for the species
5. Placidity - No fear or anger
6. Hypersexuality - the monkeys tried to mount everything - other monkeys of the same sex, cats, non-living objects; in humans this is seen as suggestive behaviors and talk and sexual contact

3. Nucleus Basalis of Meynert

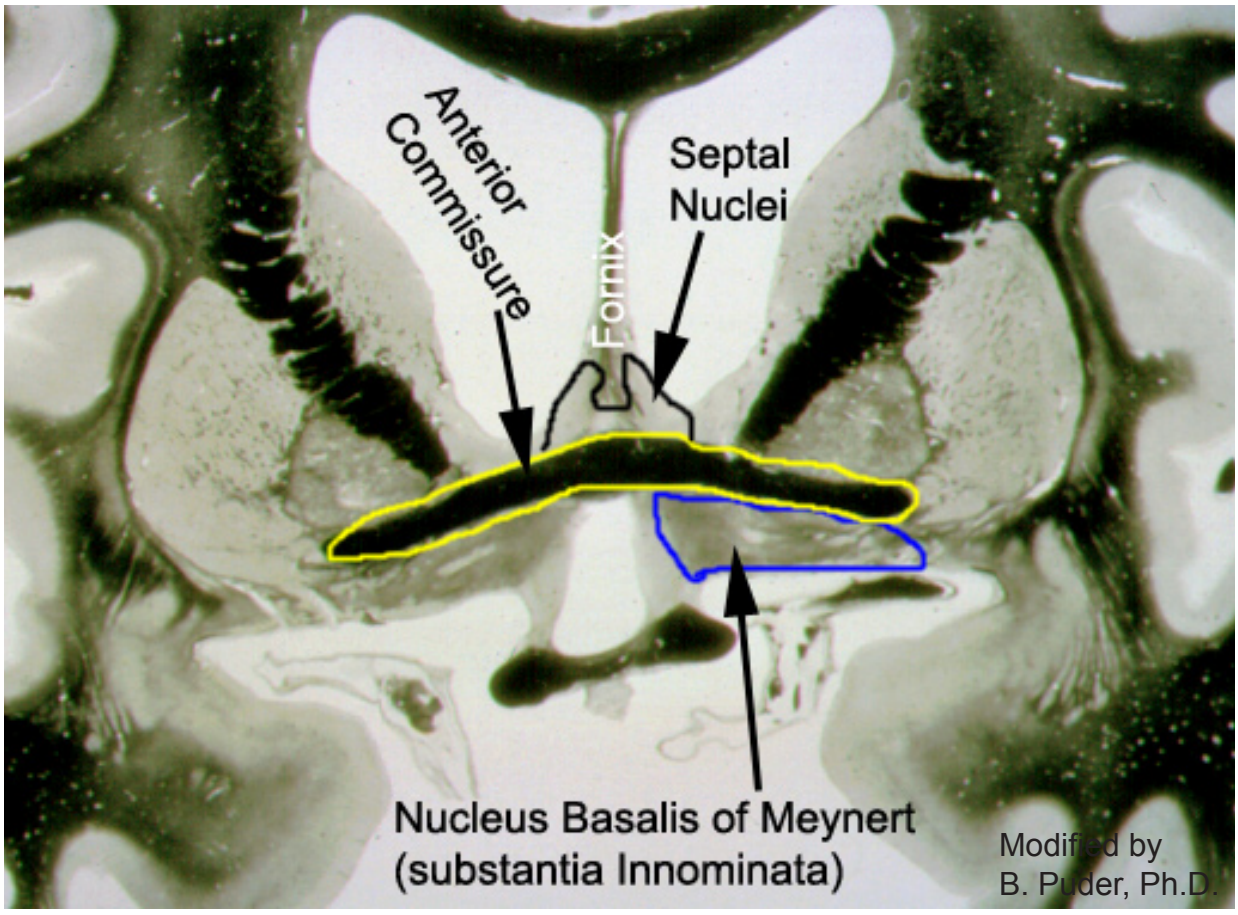
Alzeheimer's disease

Alzeheimer's disease is excessive neuronal cell death not attributed to normal aging and thus causing severe cognitive dysfunction and death. Patients with Alzeheimer's disease have neurofibrillary tangles and neuritic plaques which destroy the functionality of the neuron. The first area to show evidence of this disease is the entorhinal cortex and the nucleus basalis of Meynert.

4. Septal nuclei
    The septal nuclei are part of the limbic system.
    They are located inferior and anterior to the septum pellucidum.
    Afferents
        Fornix
        Amygdala
        Hypothalamus
        Midbrain
    Efferents
        Stria medullaris thalami to habenular nuclei and thalamus
        Fornix
        Median forebrain bundle to hypothalamus

Note about the median forebrain bundle. It is a diffuse group of fibers that connect the hypothalamus, septal areas, and brainstem. The dopamine released from the fibers is said to be related to perceptions of pleasure or drive reduction.

Lesions of the septal nuclei cause rage behavior



Coronal brain section at the anterior commissure which depicts the septal nuclei

5. Nucleus Accumbens

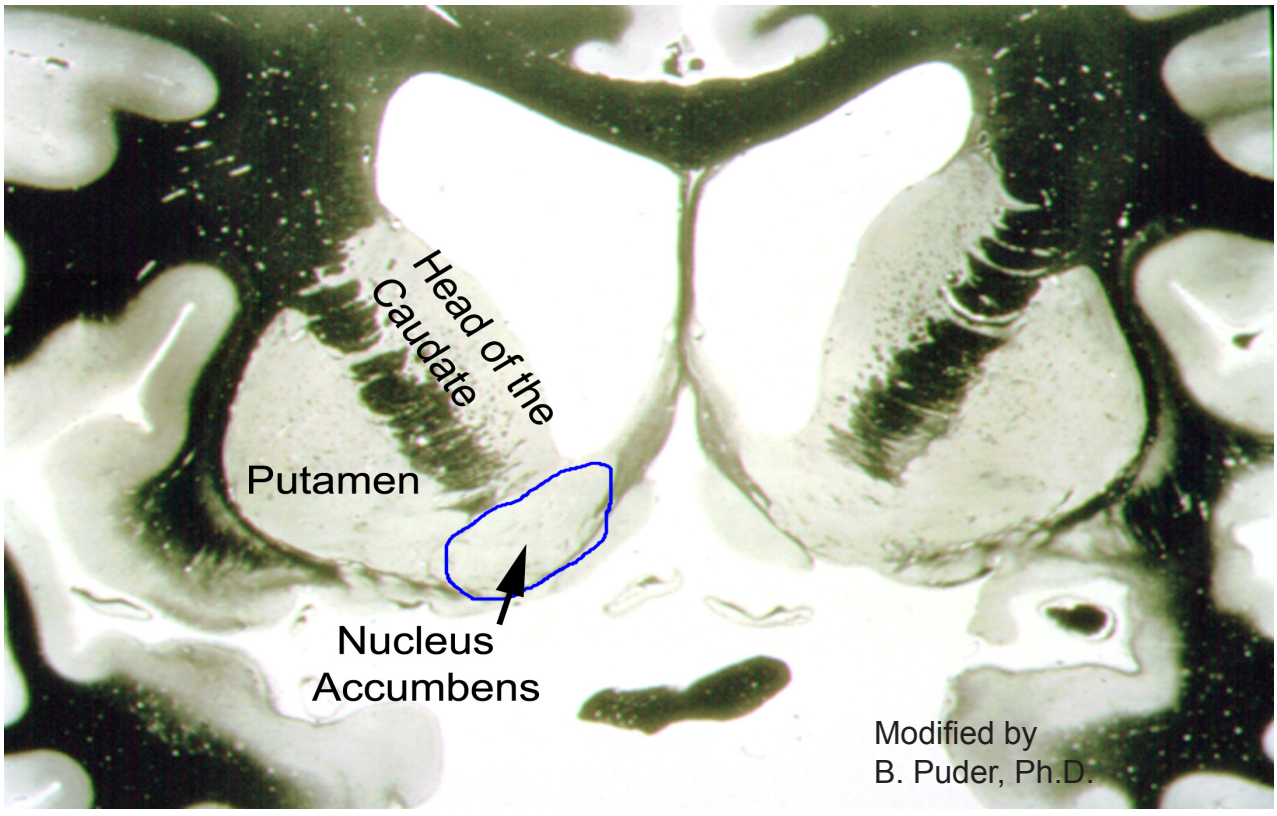
Part of the limbic system
Located between the head of the caudate and the putamen
Is the “pleasure center “of the brain, or is considered to play a role in addictive behaviors
In addicts, studies have shown increased binding of substances to nucleus accumbens cells.

Afferents

- Fornix
- Ventral amygdalofugal pathway
- Stria terminalis
- Median forebrain bundle

Efferents

- Hypothalamus
- Brainstem
- Globus pallidus



Coronal section anterior to the anterior commissure that depicts the nucleus accumbens.

Limbic System and emotions

There are aversion and gratification centers in the limbic system.
The hippocampus and amygdala have been shown to have alot of aversion centers.
The nucleus accumbens has been shown to have alot of gratification centers.