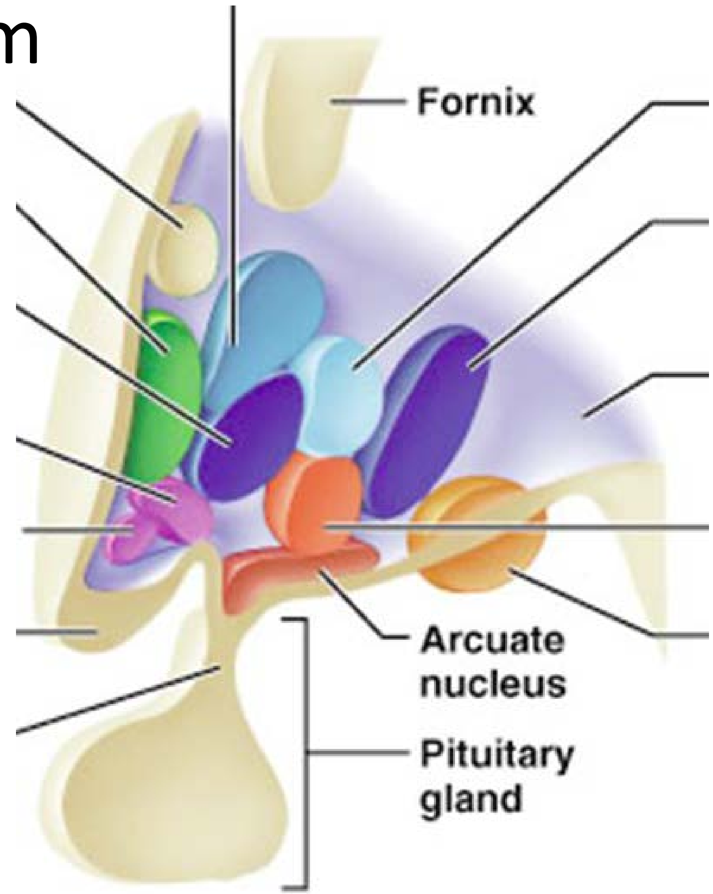
Limbic system

Lecture 29, November 10, 2017

Circadian rhythms
(Latin, “approximately a day”)

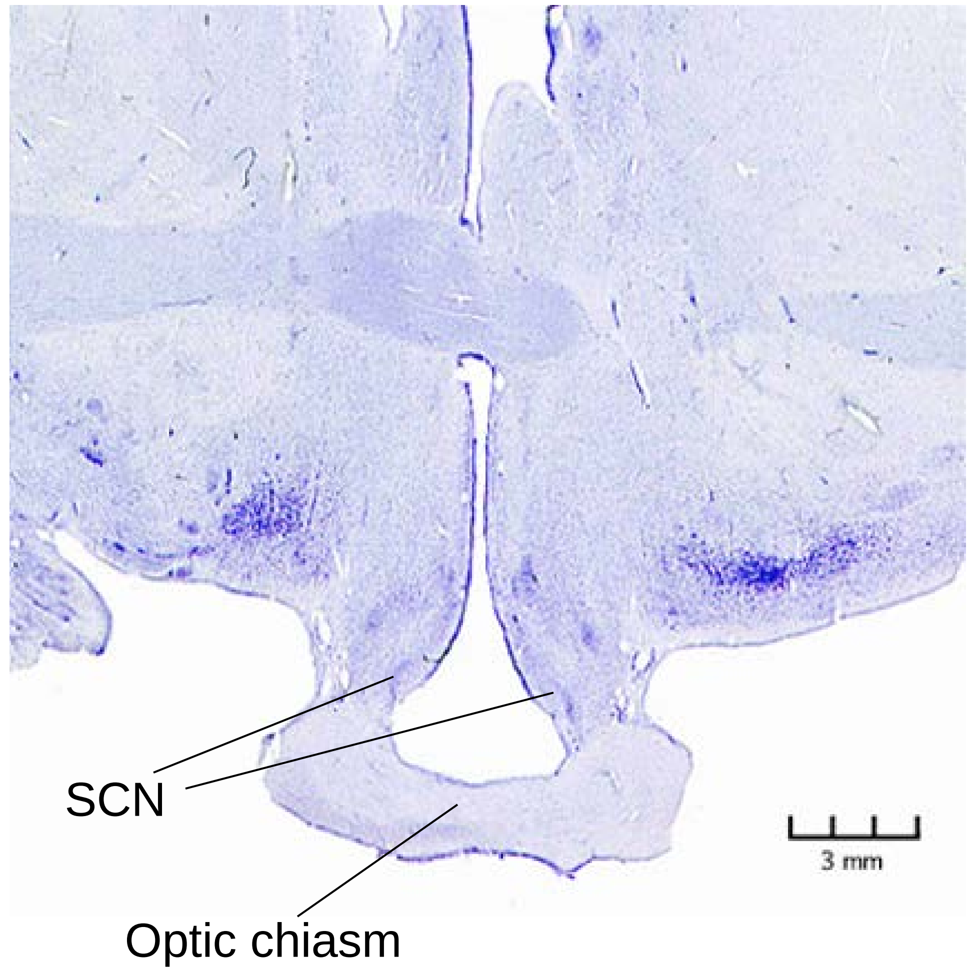
- Regulation of our daily rhythm
  - Eating
  - Sleeping
  - Defecating
  - Periods of activity
- Suprachiasmatic n.



http://slideplayer.com/slide/6351731/

Circadian pattern generation

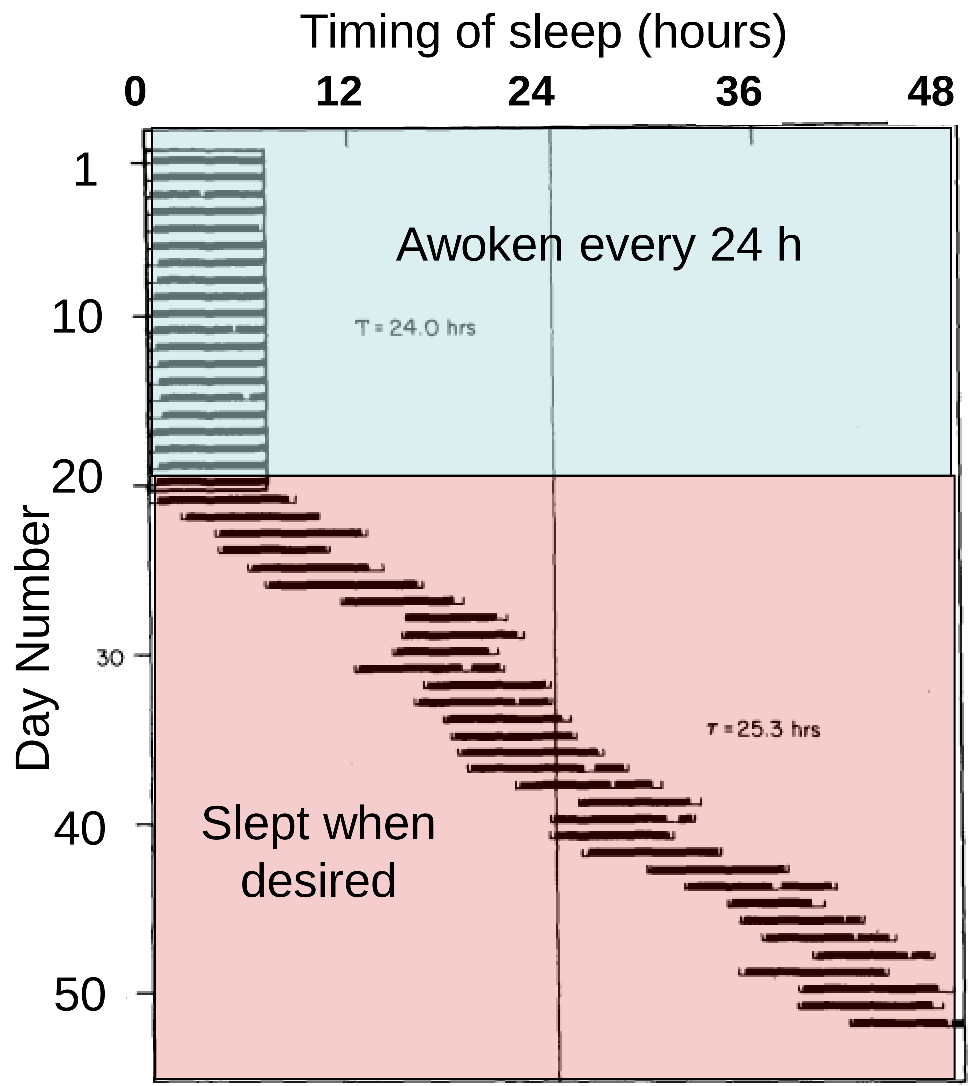
- Suprachiasmatic nucleus (SCN)
- SMALL: only 10,000 neurons
- “master clock”



https://msu.edu/~brains/brains/human/hypothalamus/1c.html

Intrinsic circadian rhythm runs slow

- Laboratory experiment; 20- y.o. male
- With no light cues, 25.3 hr sleep cycle
- Similar intrinsic rhythm also seen in SCN tissue slices



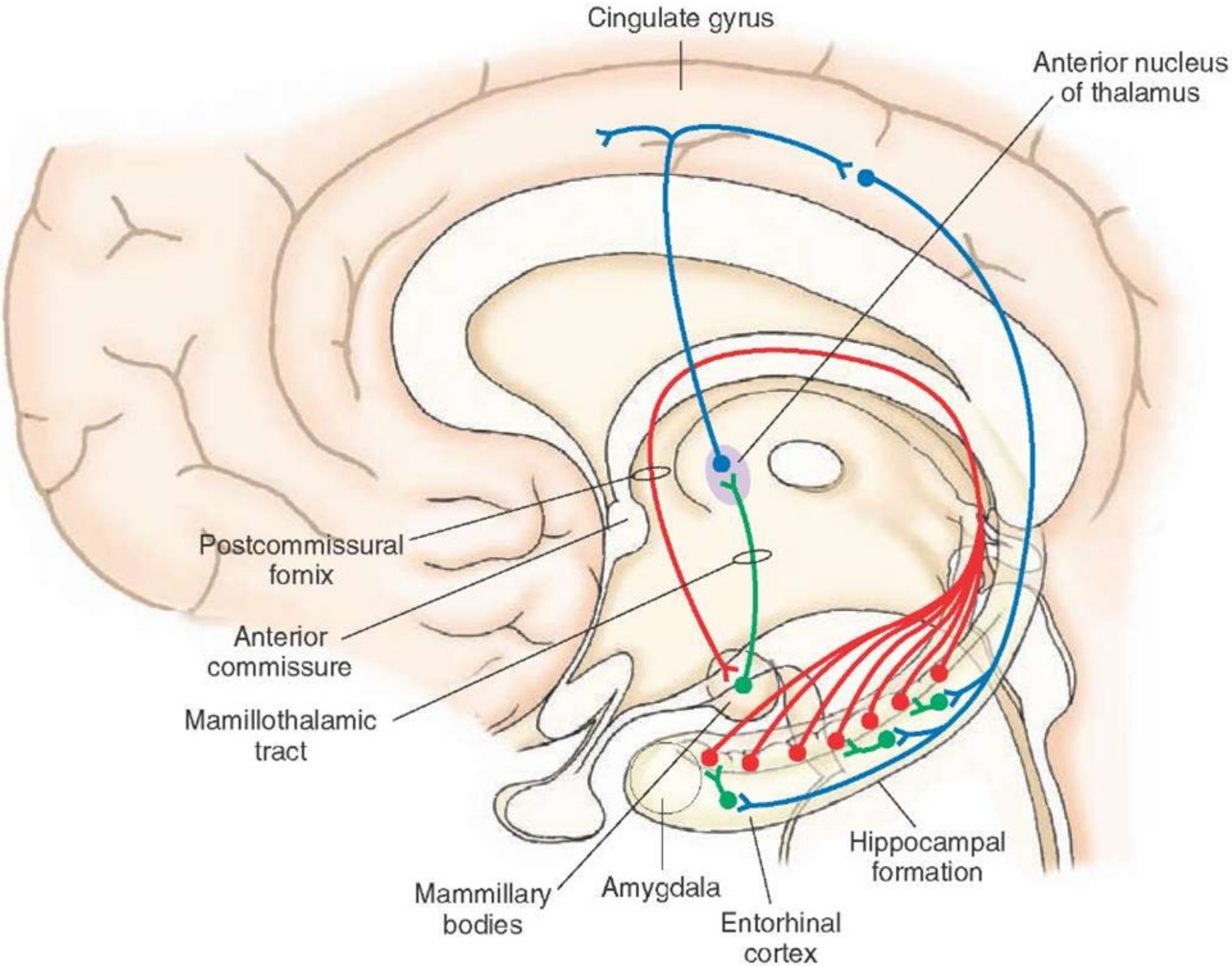
Czeisler CA; Sleep. 4(1):1-21, 1981.

Setting the circadian beat

- Light sets the circadian clock
  - Input from eyes: retino-hypothalamic pathway
  - Light-sensitive retinal ganglion neurons
- SCN expresses melatonin receptors
  - Melatonin is secreted by pineal
  - Secretion increases at night

Limbic system

“limbus”: a border (around the diencephalon)



A definition of limbic system

- A set of interconnected brain regions that are involved in **autonomic control**, **behavior, memory, emotion**, and the **integration of these functions**

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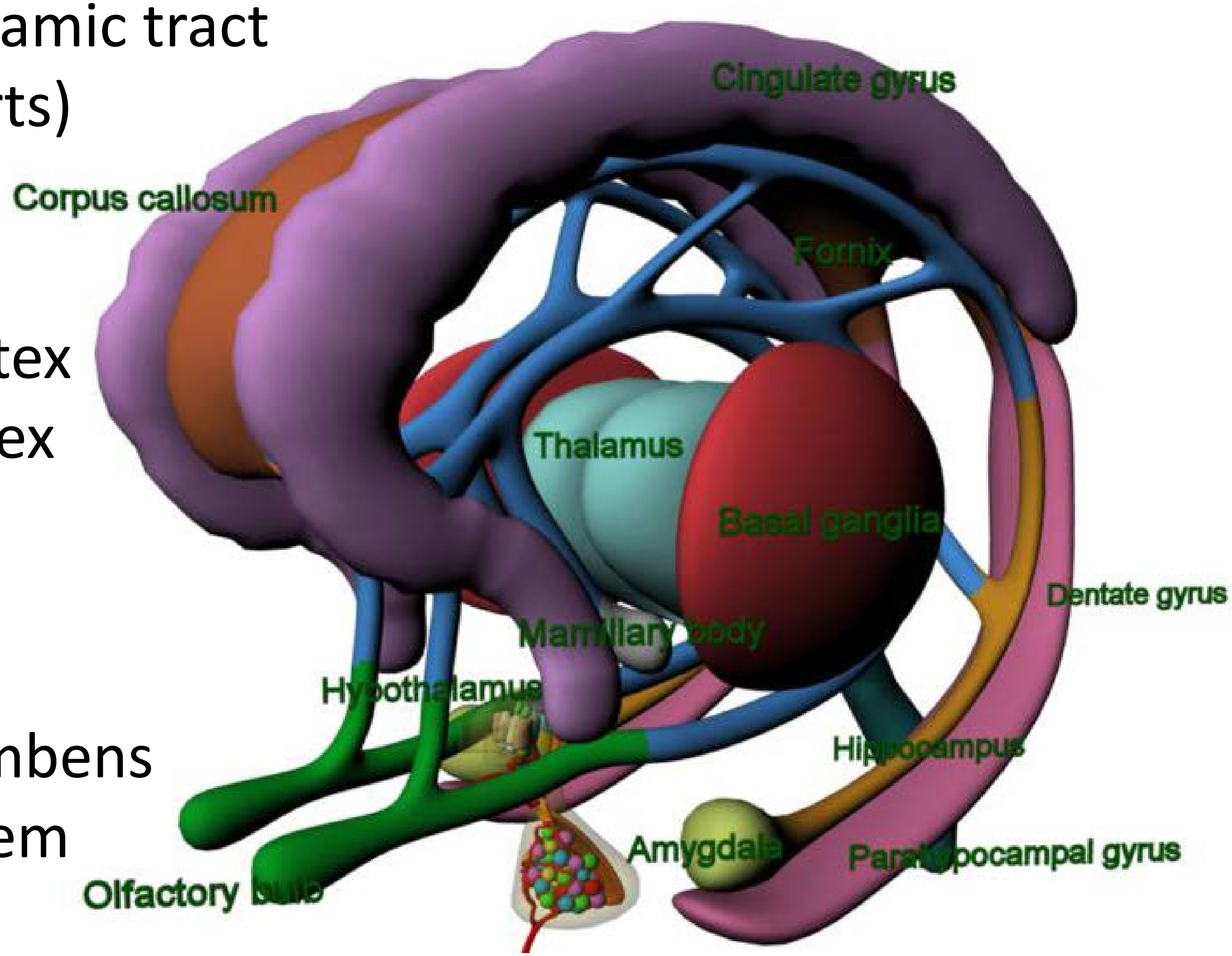
- A set of interconnected brain regions that are involved in **autonomic control**, **behavior, emotion**, and the **integration of these functions**
- Limbic structures are interposed between neocortex and the hypothalamus
- Limbic system links **motivation with behavior & autonomic control**

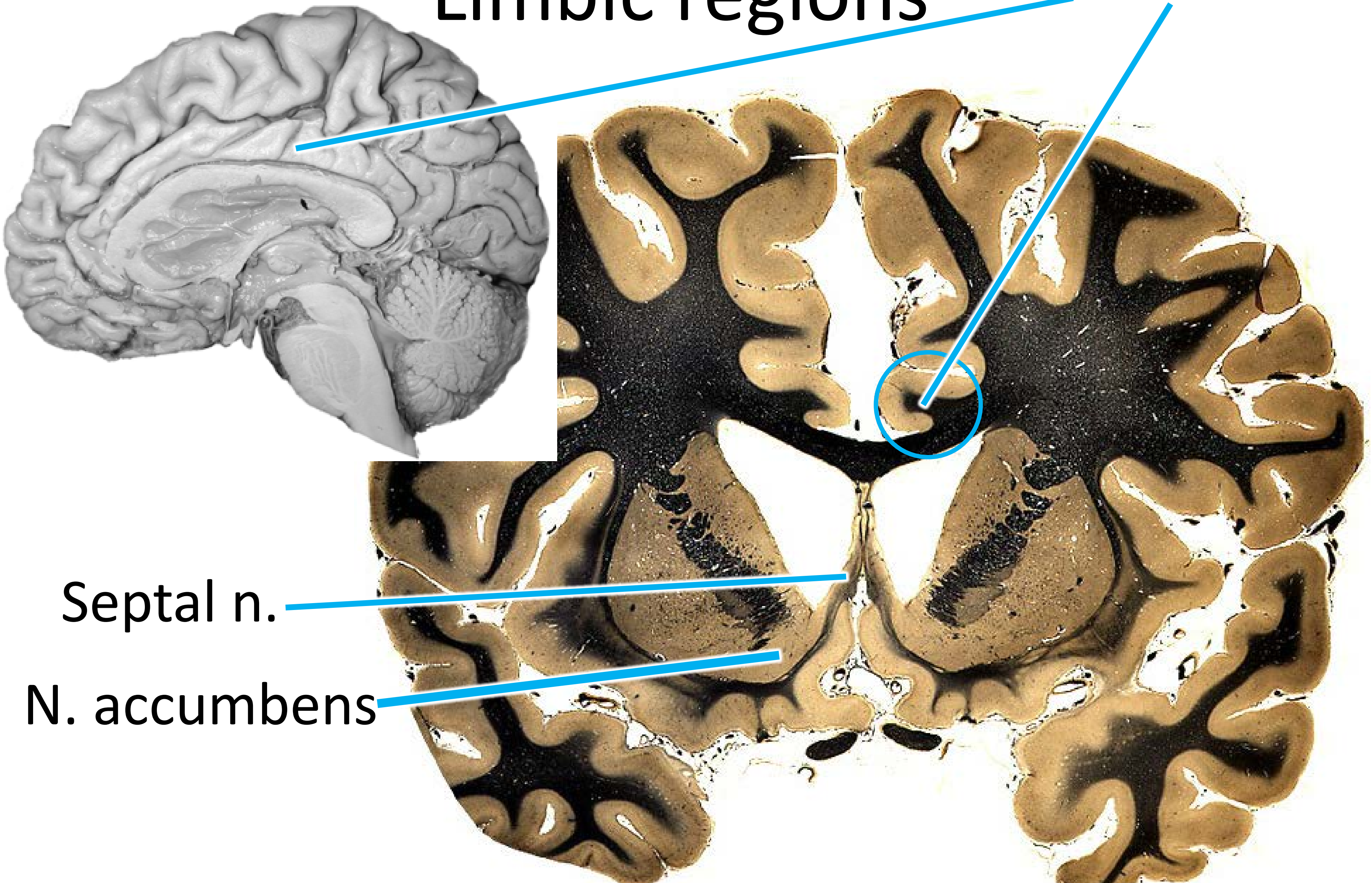
Limbic regions

- Diencephalon
  - Hypothalamus (parts)
  - Mammillothalamic tract
  - Thalamus (parts)
  - Fornix (tract)
- Telencephalon
  - Prefrontal cortex
  - Cingulate cortex
  - Hippocampus
  - Septal nuclei
  - Amygdala
  - Nucleus accumbens
  - Olfactory system



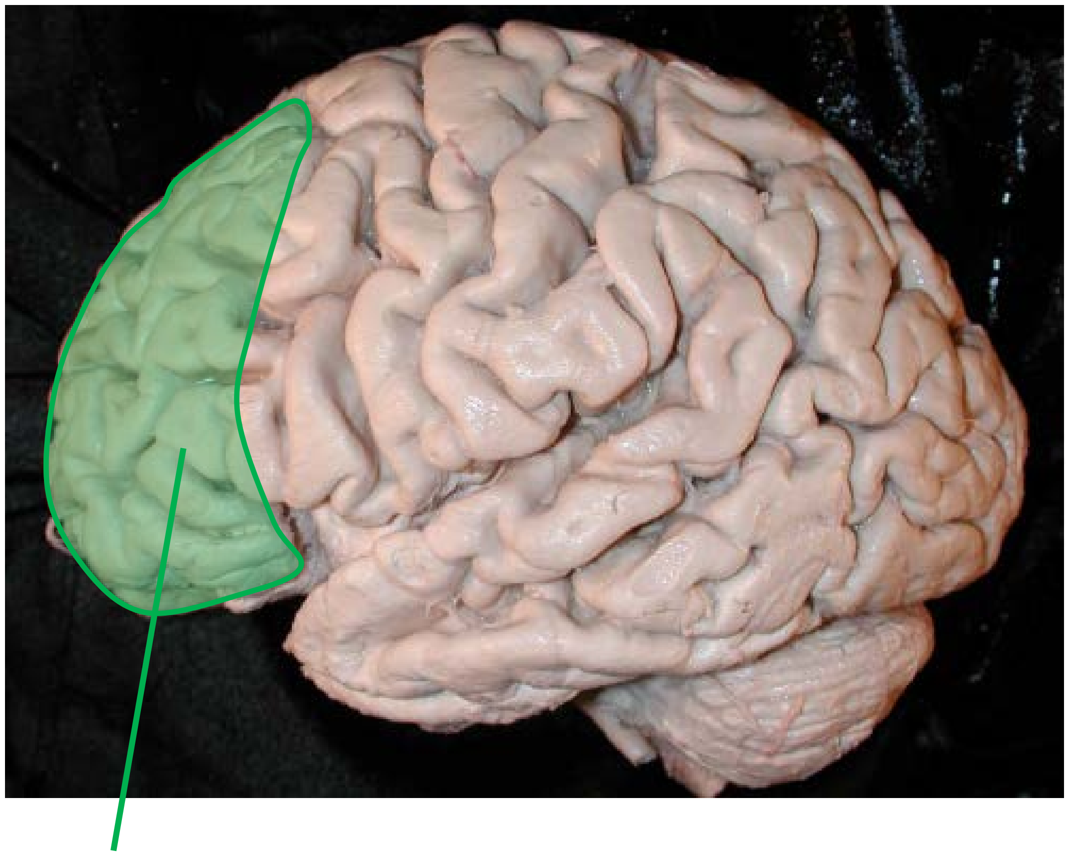
http://people.upei.ca/bate/limbic.jpg

Limbic regions



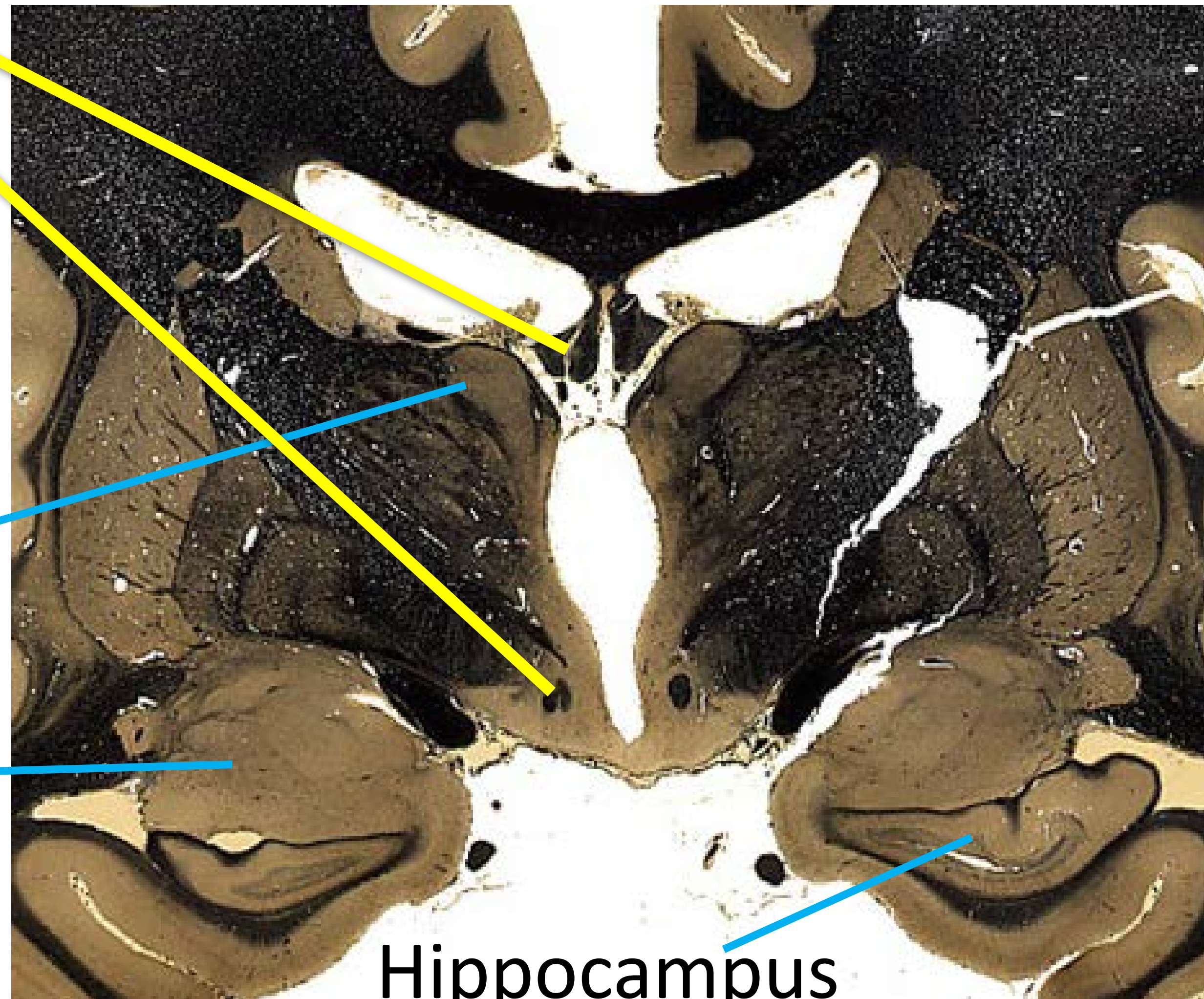
https://msu.edu/~brains/brains/human/index.html

Limbic regions

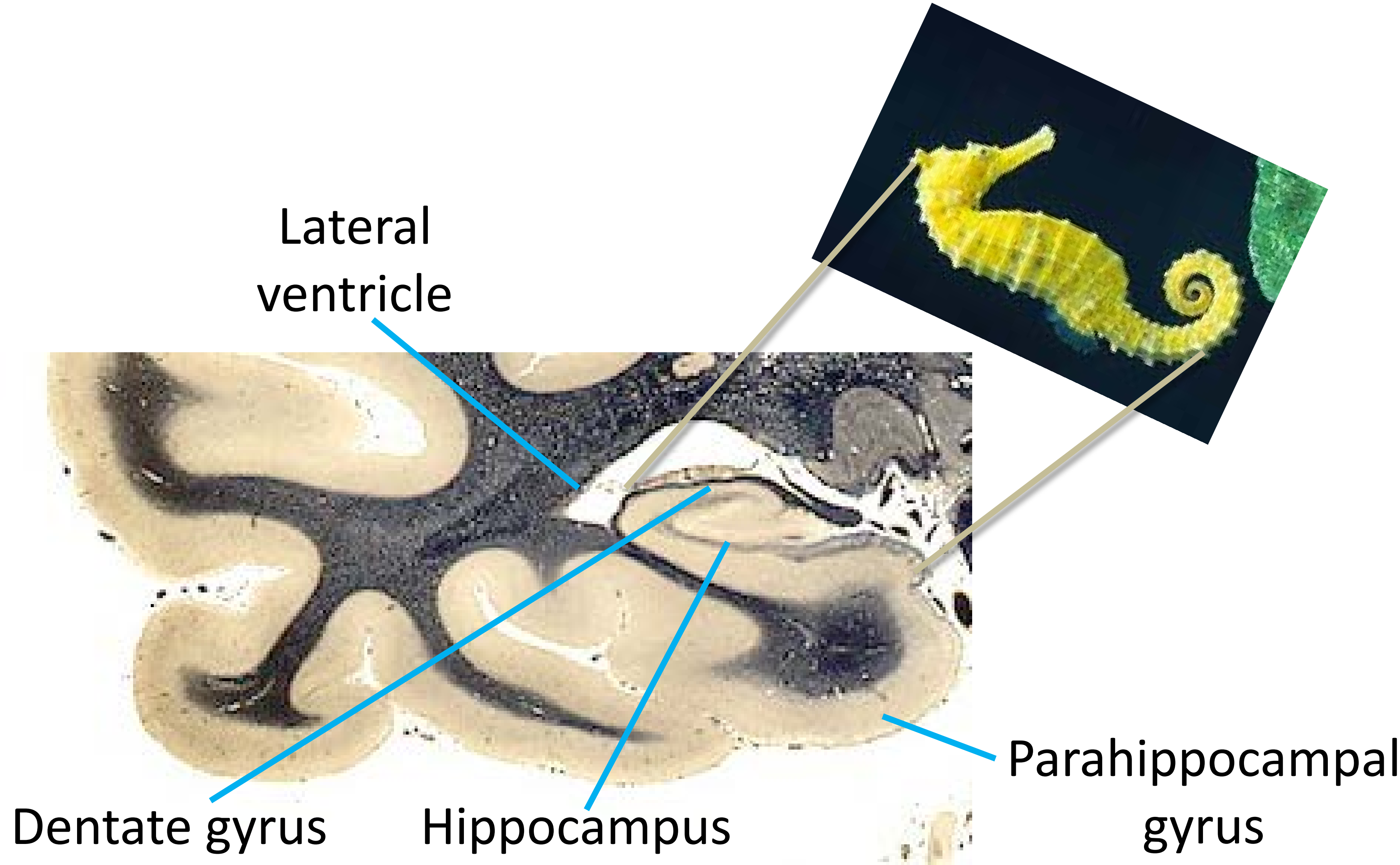


Prefrontal cortex

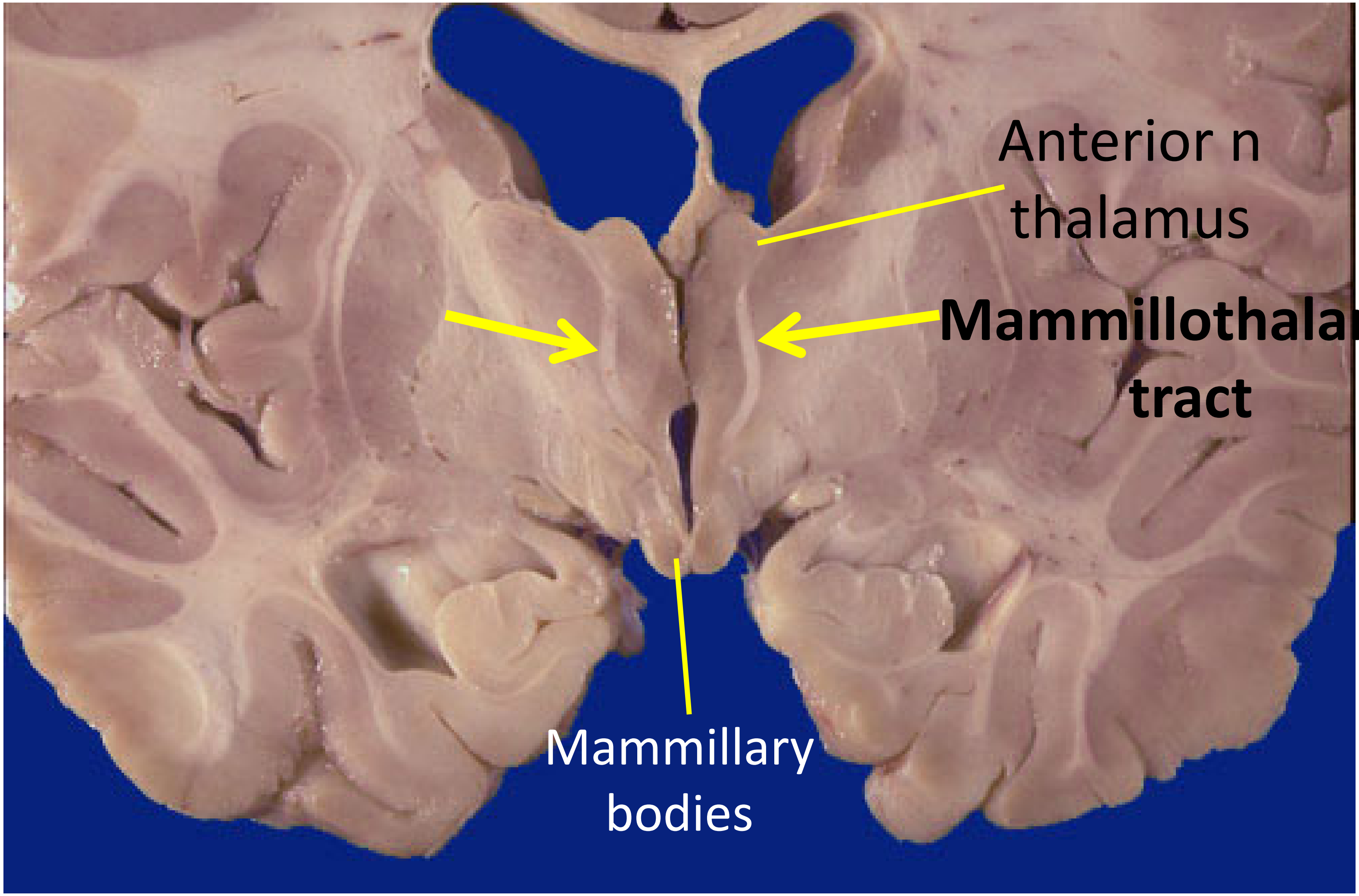
More limbic regions



Hippocampus: “sea horse”

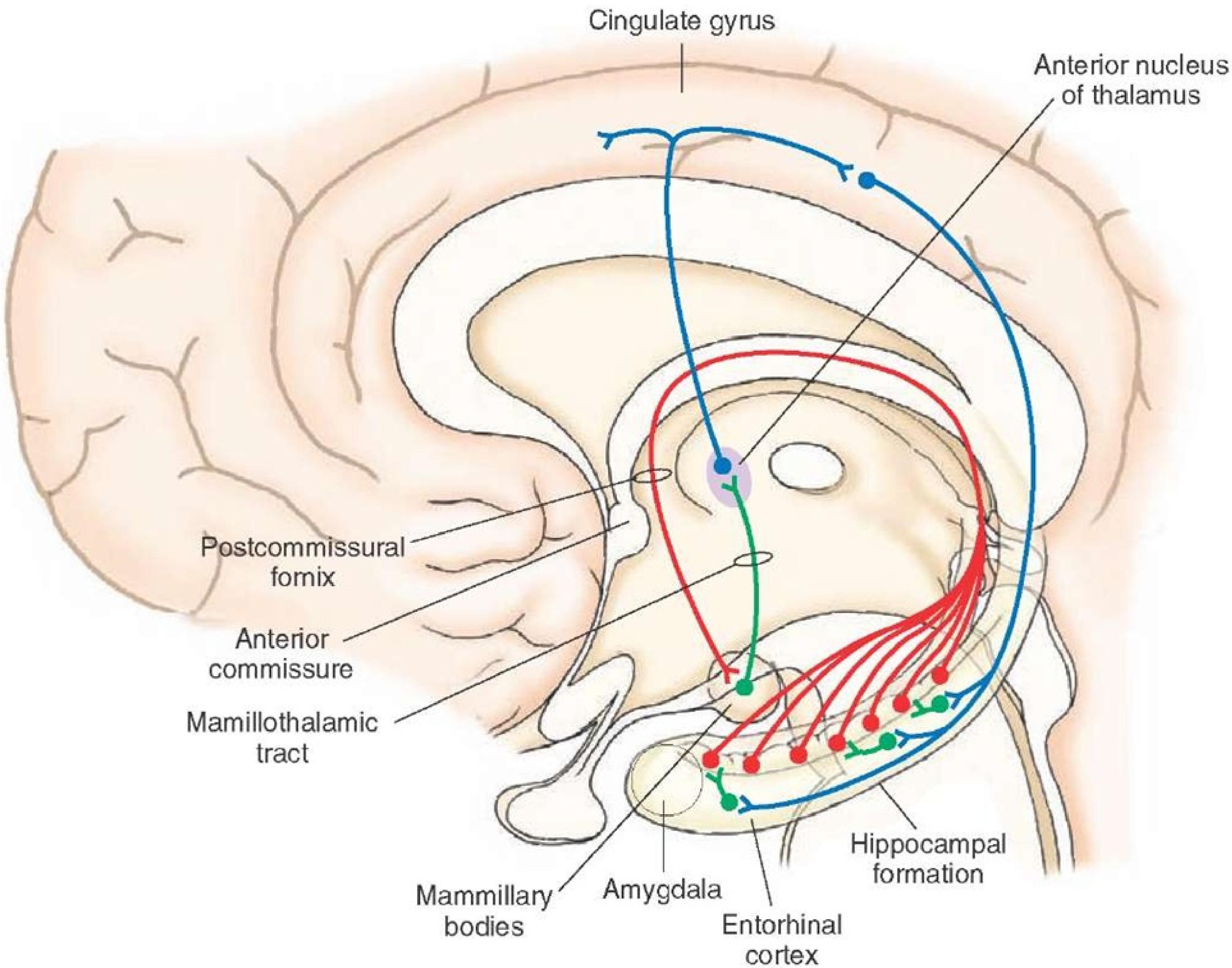


Mammillothalamic tract: from mammillary bodies to anterior n thalamus



http://library.med.utah.edu/WebPath/HISTHTML/NEURANAT/CNS262A.html

Papez circuit: basis of emotion?



http://66.media.tumblr.com/a52a7f7df71de425d803ab05a4fbc739/tumblr_mngxc1RAQD1s2ybeco1_1280.jpg

Phenomena associated with limbic system

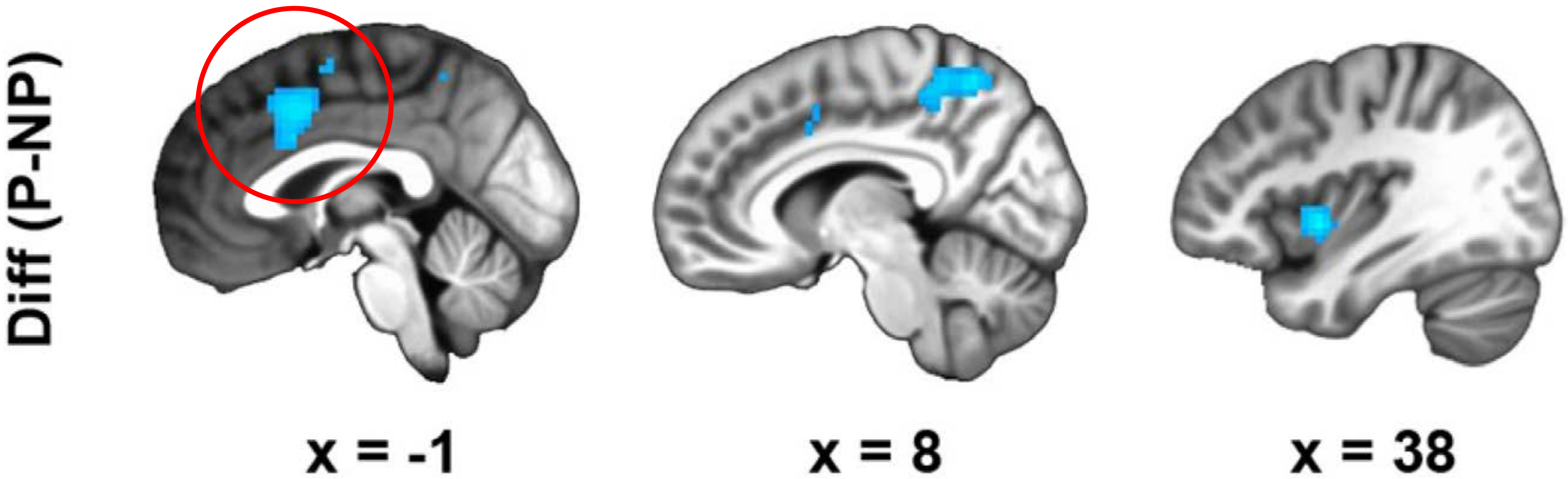
- Self-control, rage, & aggression
- Learning/memory
- Fear/emotion
- Addiction

Self-control, aggression & rage

- Septum
  - Lesion → "septal rage" in rats
- Pre-frontal cortex
  - Stimulation in animals
    - Suppresses predatory aggression & defensive rage
  - Lesions (e.g., pre-frontal lobotomy)
    - Decreased aggressiveness in some psychotic patients
    - Increased feeding
    - Decreased intellectual function in some tests

Altered cingulate connections in psychopaths

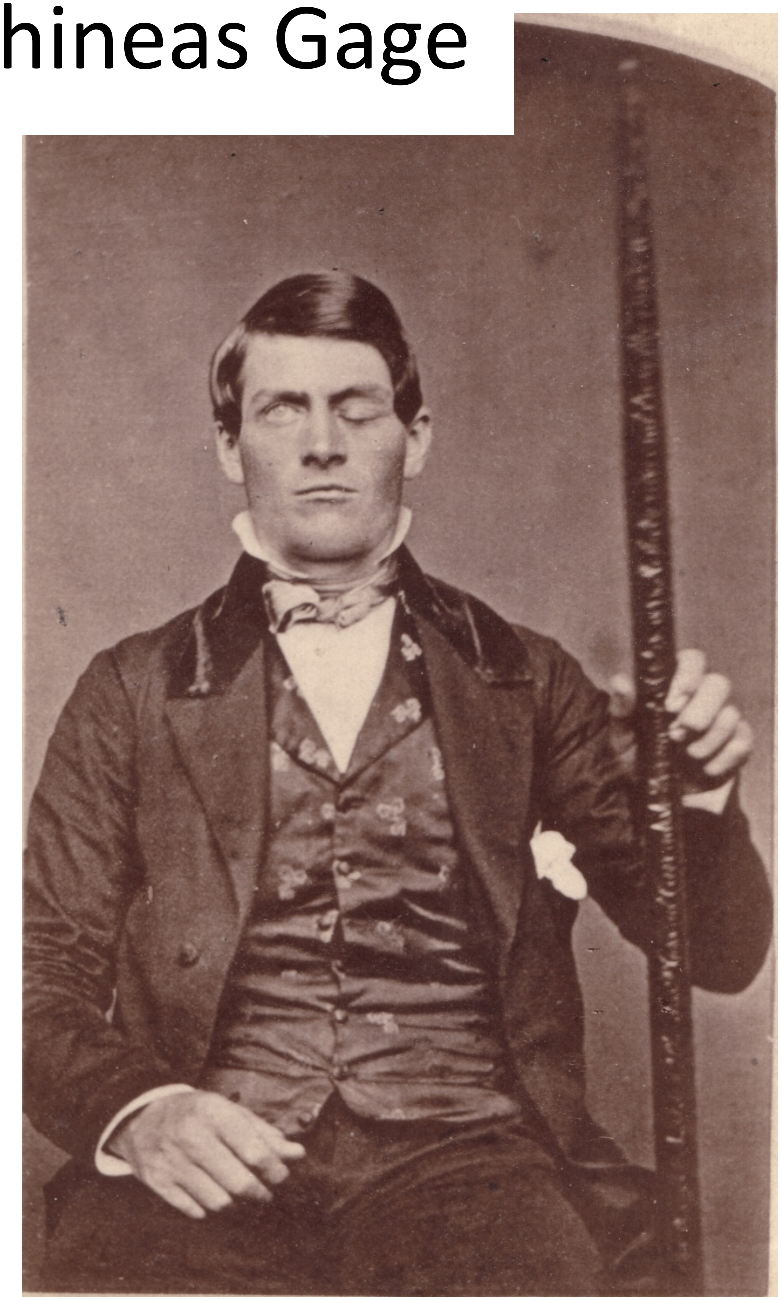
Altered Resting-State Functional Connectivity in Cortical Networks in Psychopathy Philippi et al. J Neuroscience **35(15)**:6068, 2015



- Antisocial traits in psychopathic prison inmates correlated with decreased connectivity between cingulate & other brain regions

Self-control: the case of Phineas Gage

- Foreman on railroad crew in 1848, supervising blasting with black powder
- 1.05 meter-long tamping rod blown through left cheek & out top of head. He survived.
- Damage to prefrontal cortex and anterior cingulate gyrus



Gage's injury: current estimate

Polygon data is generated by Database Center for Life Science(DBCLS)[3]. - Ratiu P, Talos IF, Haker S, Lieberman D, Everett P. The tale of Phineas Gage, digitally remastered. J Neurotrauma. 2004 May;21(5):637-43. PMID: 15165371 [1]Polygon data is from BodyParts3D[2]., https://commons.wikimedia.org/w/index.php?curid=44466338

Results of Gage’s injury

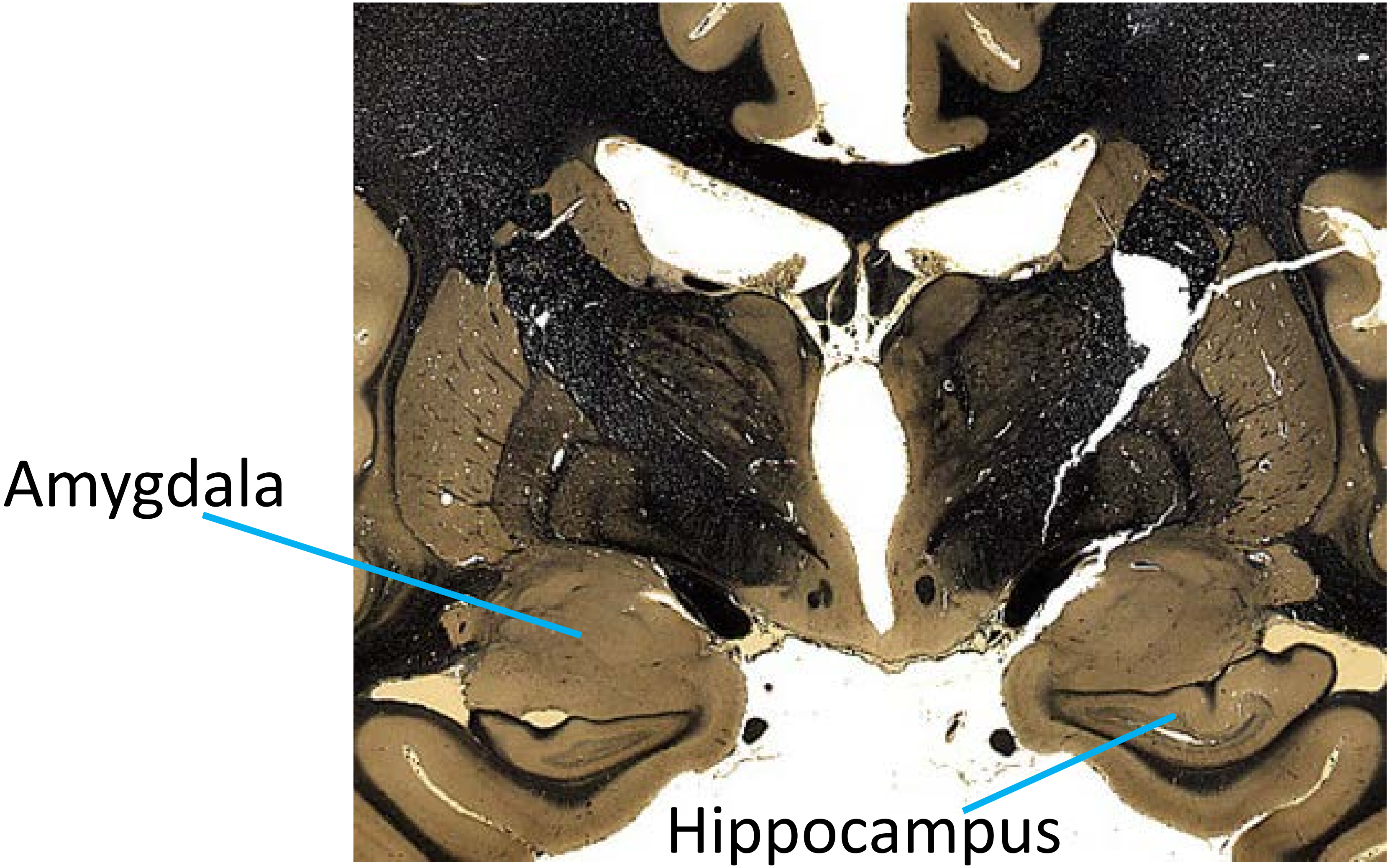
- Profound personality changes
  - Before
    - Hardworking
    - Responsible
    - Well thought-of
  - After
    - Little self-restraint
    - Irresponsible & short-sighted; moved from job to job
    - Tactless & profane
  - “[He] is no longer Gage”
  - Suggested a role for pre-frontal cortex in self-control

Phineas Gage: aftermath of injury

- Eventually appears to have recovered self-control
- Held steady job as stagecoach driver
- Died 12 years later of seizure disorder

- Any hypotheses for mechanism of recovery?
- What might this say about the anatomy underlying self-control?

Limbic system, learning and memory



Patient H.M.

- Lesions of medial temporal lobe disrupt consolidation of memory
  - Patient H.M.: temporal lobe epilepsy
  - Treated by bilateral lesion of medial temporal lobe, affecting amygdala & part of the hippocampus
  - Unable to lay down new long-term “declarative memory” (e.g., names; dates) after surgery
  - No loss of long-term memory from pre-surgery
  - Motor memory (“procedural memory”) unimpaired
  - Intellectual ability unimpaired

Limbic system, learning & memory

- Other limbic-system lesions also disrupt consolidation of long-term memory
  - Korsakoff syndrome: damage from alcoholism to mammillary bodies & thalamus
    - Inability to form new declarative memory
    - “Confabulation”: will create a plausible story if they don’t remember the answer to a question
    - Damage may be due to alcoholic malnutrition

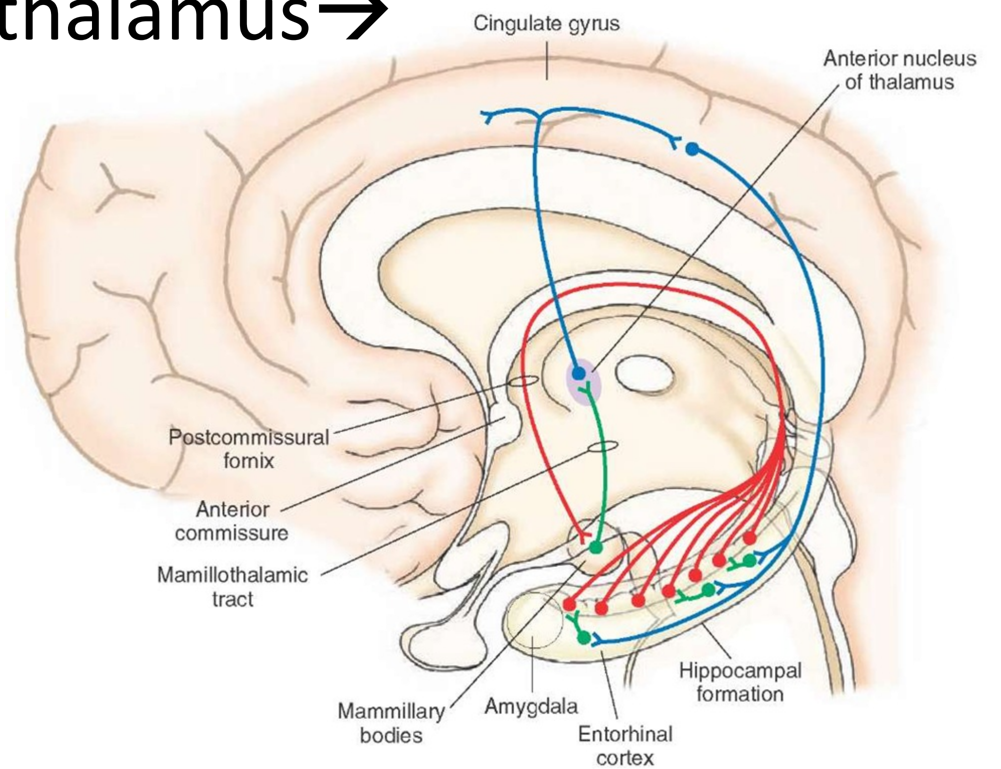
Papez circuit and memory

Hippocampus (via fornix)→

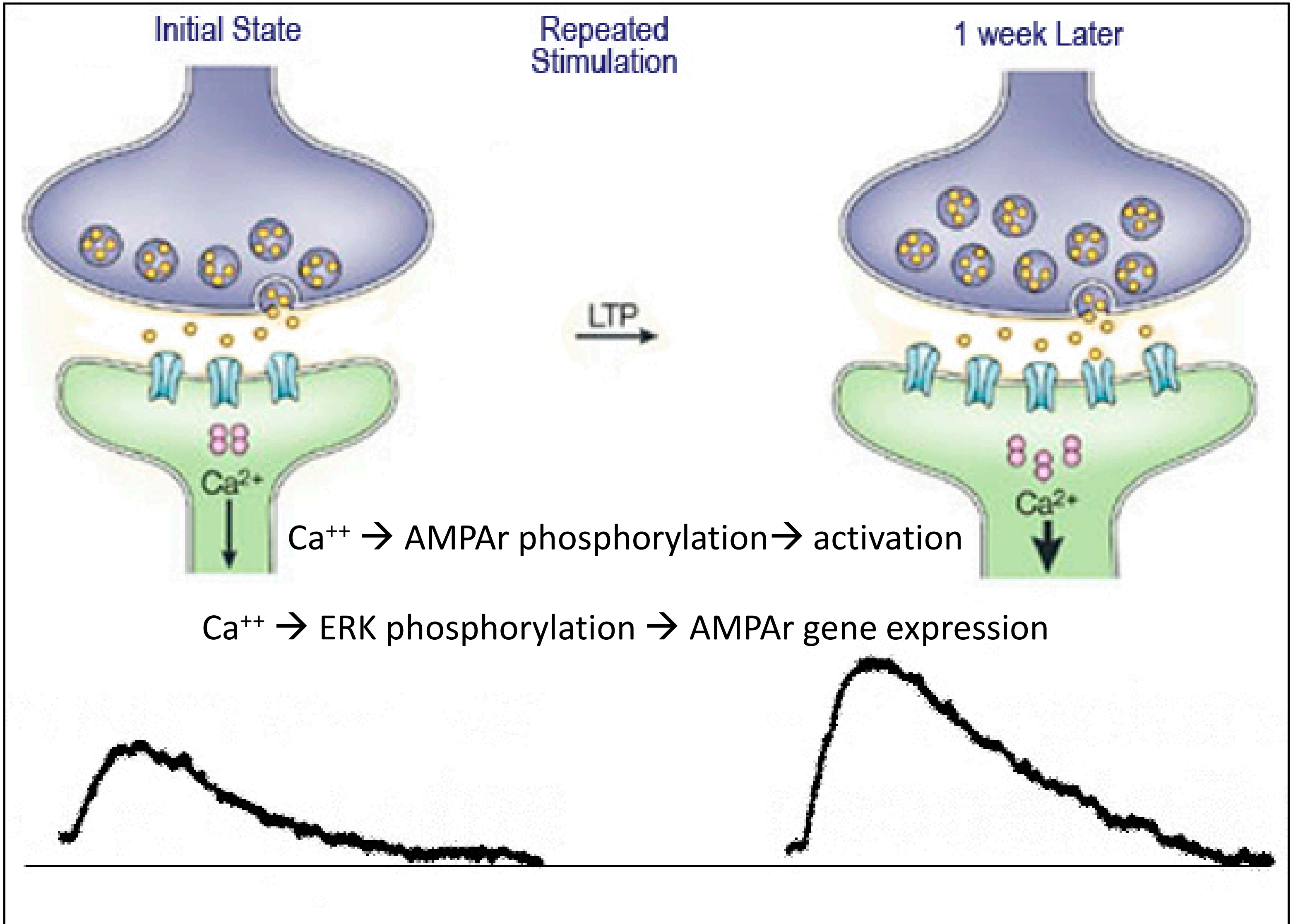
Mammillary bodies (via mammillothalamic tract) →

Anterior nucleus of thalamus→

Cingulate cortex

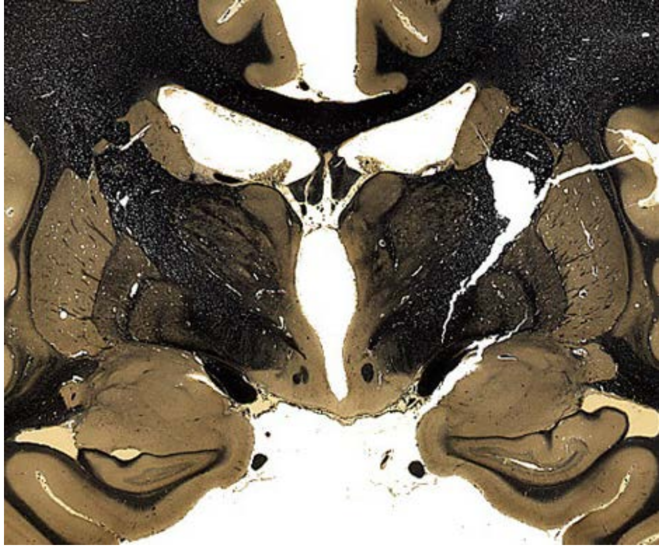


Long-term potentiation (LTP)& memory: increase in synaptic efficacy from use



https://sites.google.com/site/mcauliffeneur493/home/synaptic-plasticity

Amygdala, fear & emotion



- Stimulation of amygdala → attention (animals) or fear (humans)
- Increased activity of amygdala in humans with anxiety
- Bilateral amygdala damage
  - **No conditioning to aversive stimuli**
  - No recognition of fearful faces
- Kluver-Bucy syndrome: lesions to entire temporal lobe other than auditory cortex
  - Animals are unresponsive to possible & actual threats

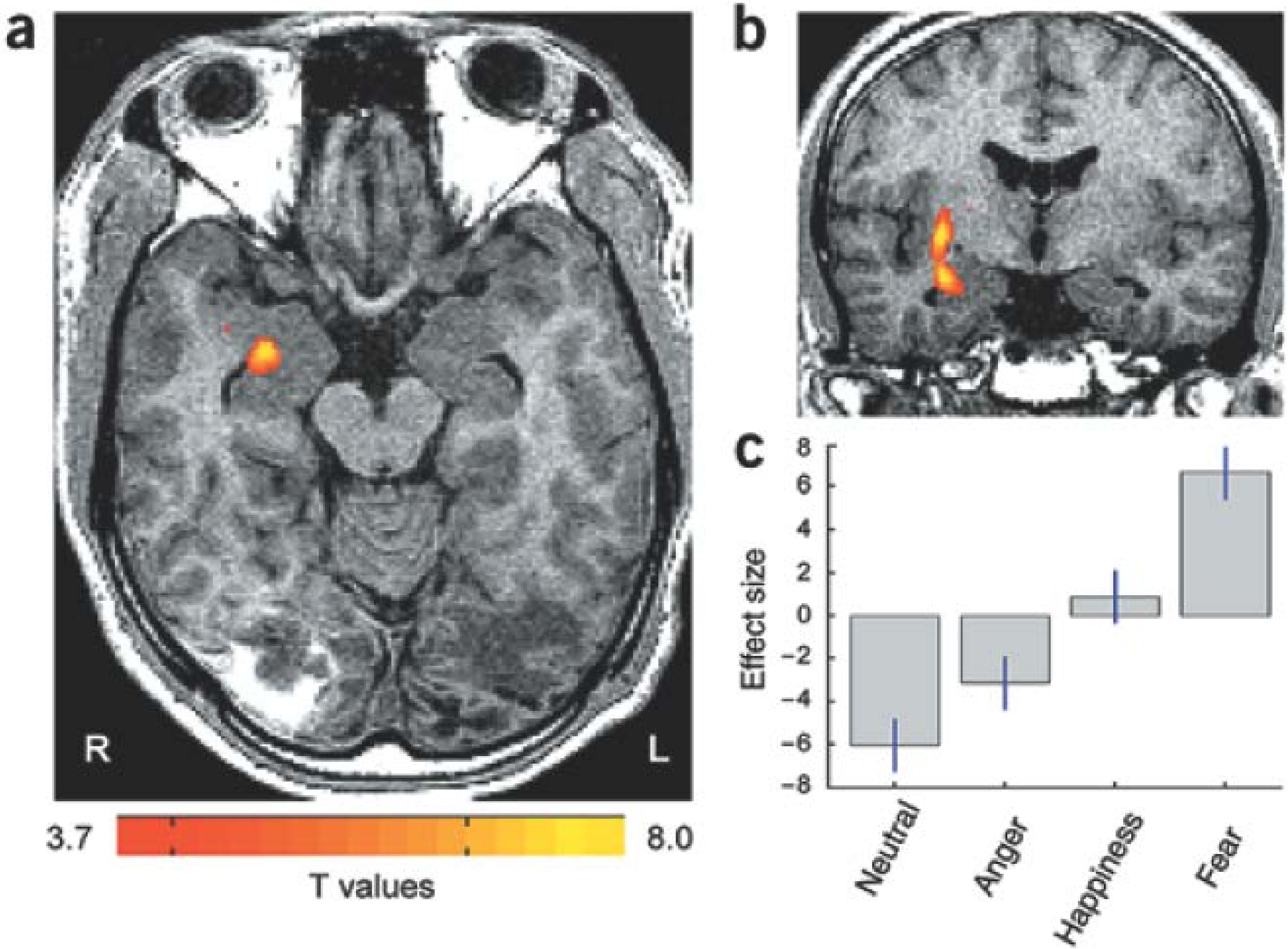
Fear and panic in humans with bilateral amygdala damage

Justin S Feinstein[1,2,11], Colin Buzza[3,11], Rene Hurlemann[3,4,11], Robin L Follmer[3], Nader S Dahdaleh[5], William H Coryell[3], Michael J Welsh[5–9], Daniel Tranel[1,2,8] & John A Wemmie[3,5,7,8,10]

Nature Neuroscience 2013 **16**(3): 270

- Humans: Urbach-Wiethe disease (U-W) → bilateral loss of amygdala → loss of fear
  - – However, breathing $C0_2$ → fear/panic in U-W patients
  - – Sensation of fear/panic not necessarily localized to amygdala

Amygdala & recognition of emotion without awareness



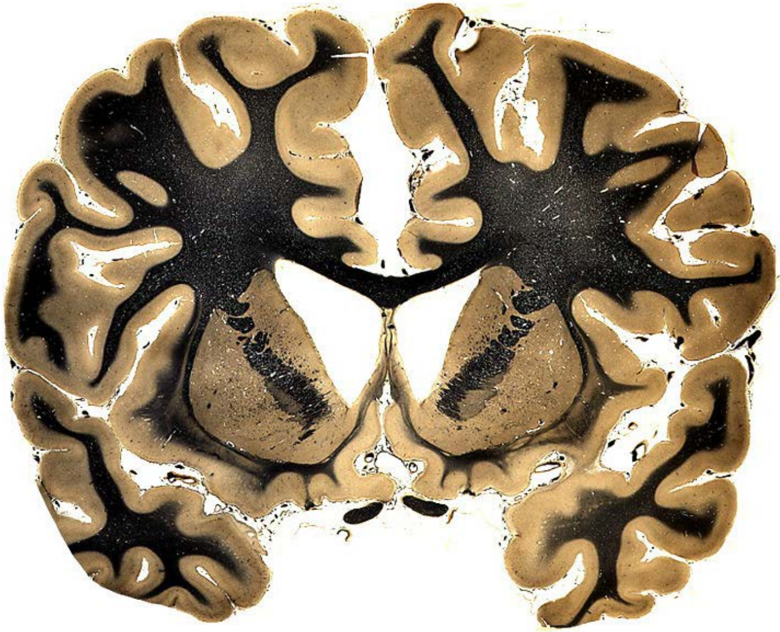
Pegna et al, Nature Neuroscience 8: 24-25, 2005

Addiction & nucleus accumbens

Beer self-administration provokes lateralized nucleus accumbens dopamine release in male heavy drinkers

Oberlin et al., Psychopharmacology. 232(5):861-70, 2015

- Addictive drugs produce dopamine release in n. accumbens
  - Ethanol
  - Cocaine
  - Heroin
  - Methamphetamine



https://msu.edu/~brains/brains/human/index.html

Addiction & nucleus accumbens

- Naturally pleasant activities also cause dopamine release in n. accumbens
  - Eating
  - Sex
  - Exercise
  - etc.

Addiction & nucleus accumbens

- Nucleus accumbens appears to be a structure underlying natural reward
- Addictive drugs appear to hijack the reward system
  - Positive reward from drug use
  - Negative reward from drug abstinence.