Round 10:
The Limbic System
Amygdala & Hypothalamus

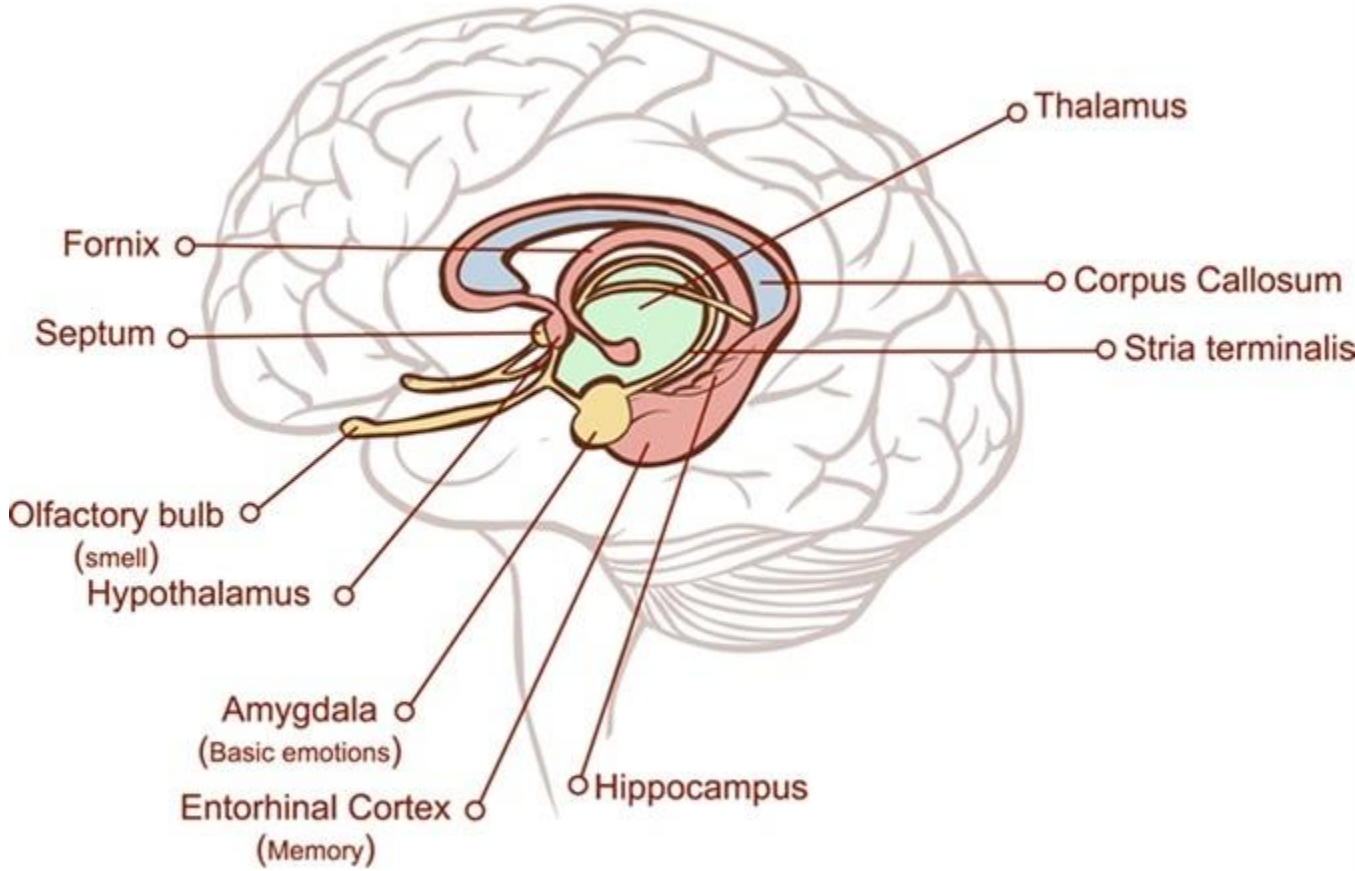
Kristy Snyder Colling, PhD

02/12/2021

The Limbic System

Functions:

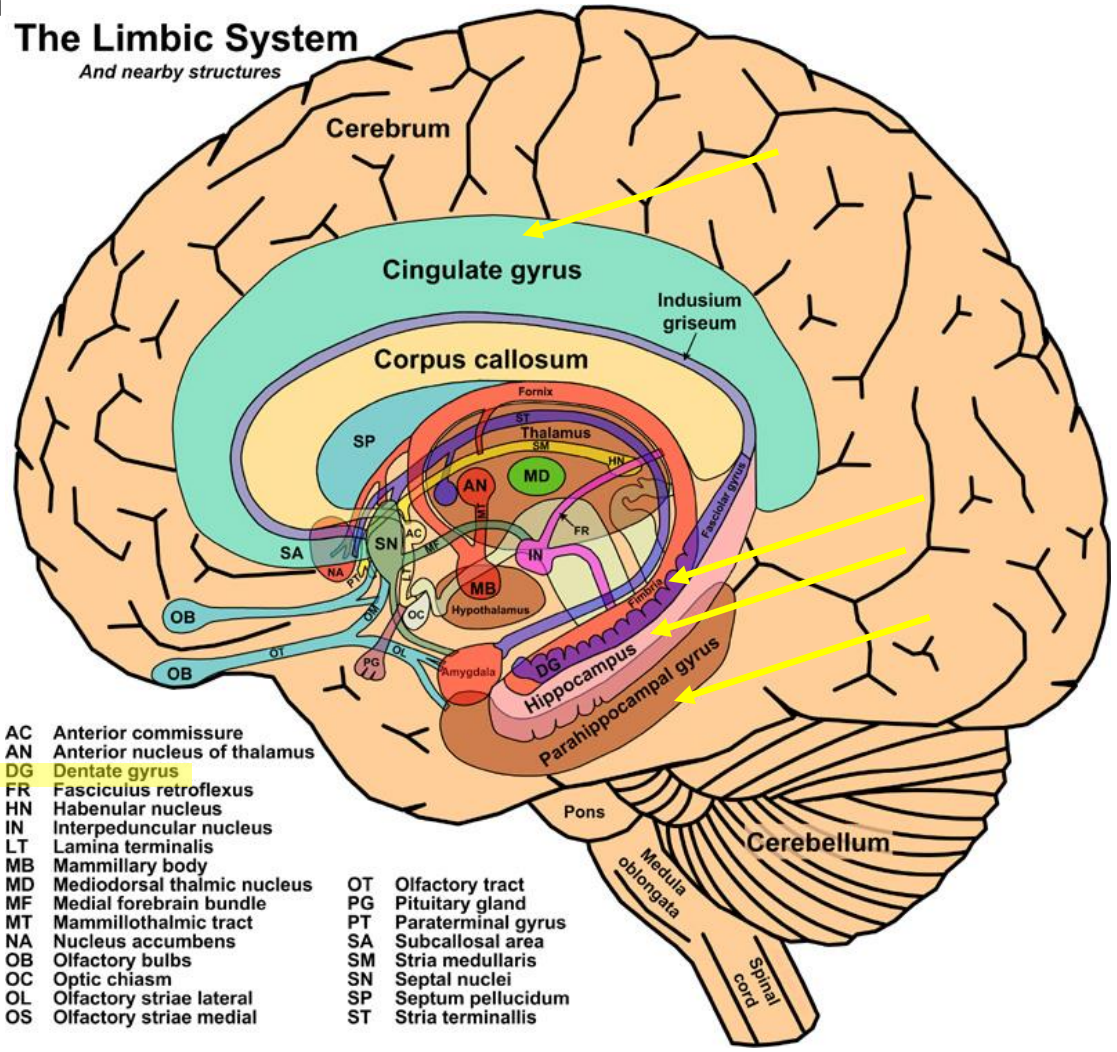
- Smell
- Learning & Memory
- Emotion (e.g., fear, aggression, anger)
- Sexual Behaviors
- Feeding



The Limbic System: Grey Matter Structures

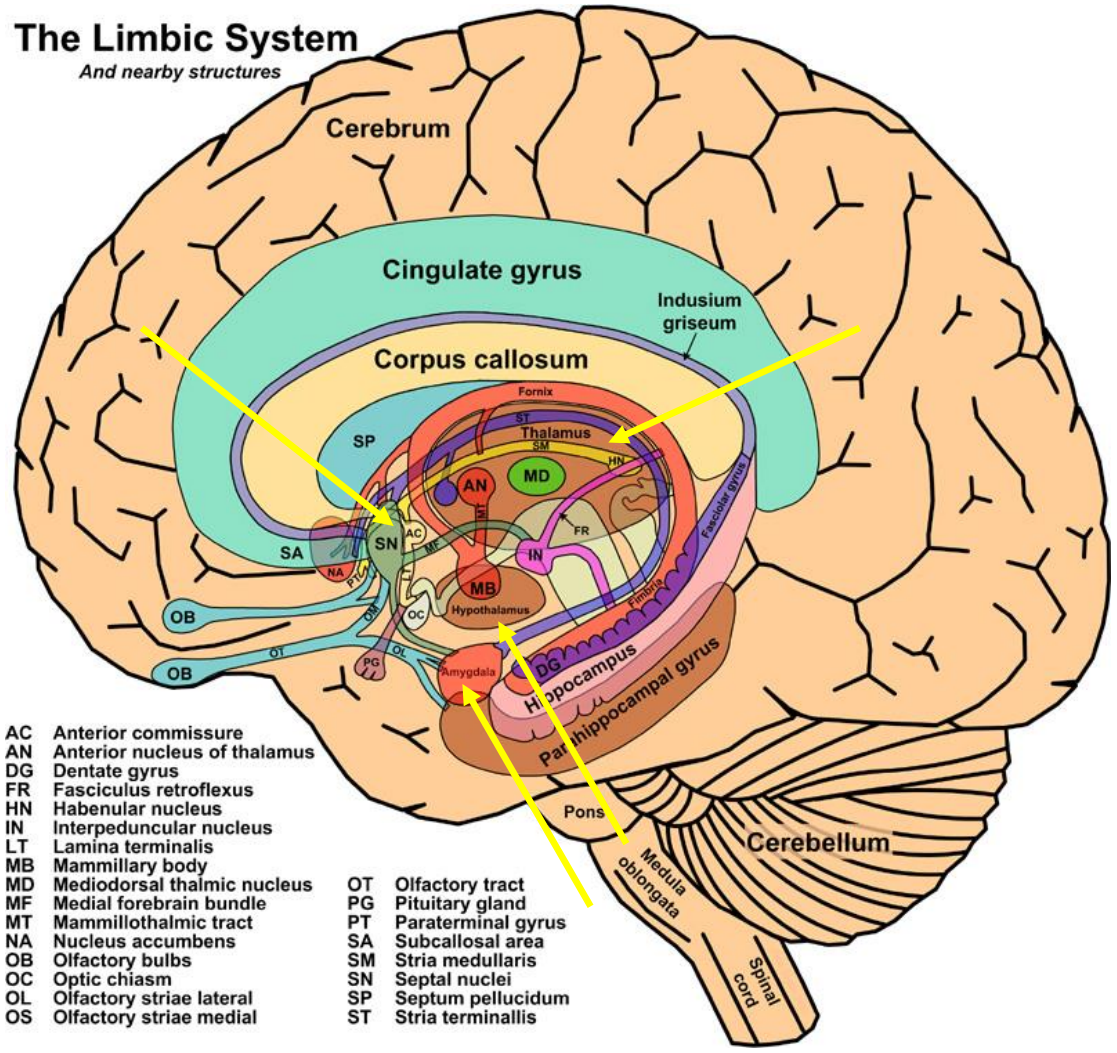
- Limbic lobe
  - Cingulate gyrus – memory, emotion, autonomic nervous system
  - Parahippocamal gyrus in the temporal lobe – memory

- Hippocampal formation - memory
  - Dentate gyrus – receives afferent information
  - Subiculum – efferent component
  - Hippocampus proper –efferent component



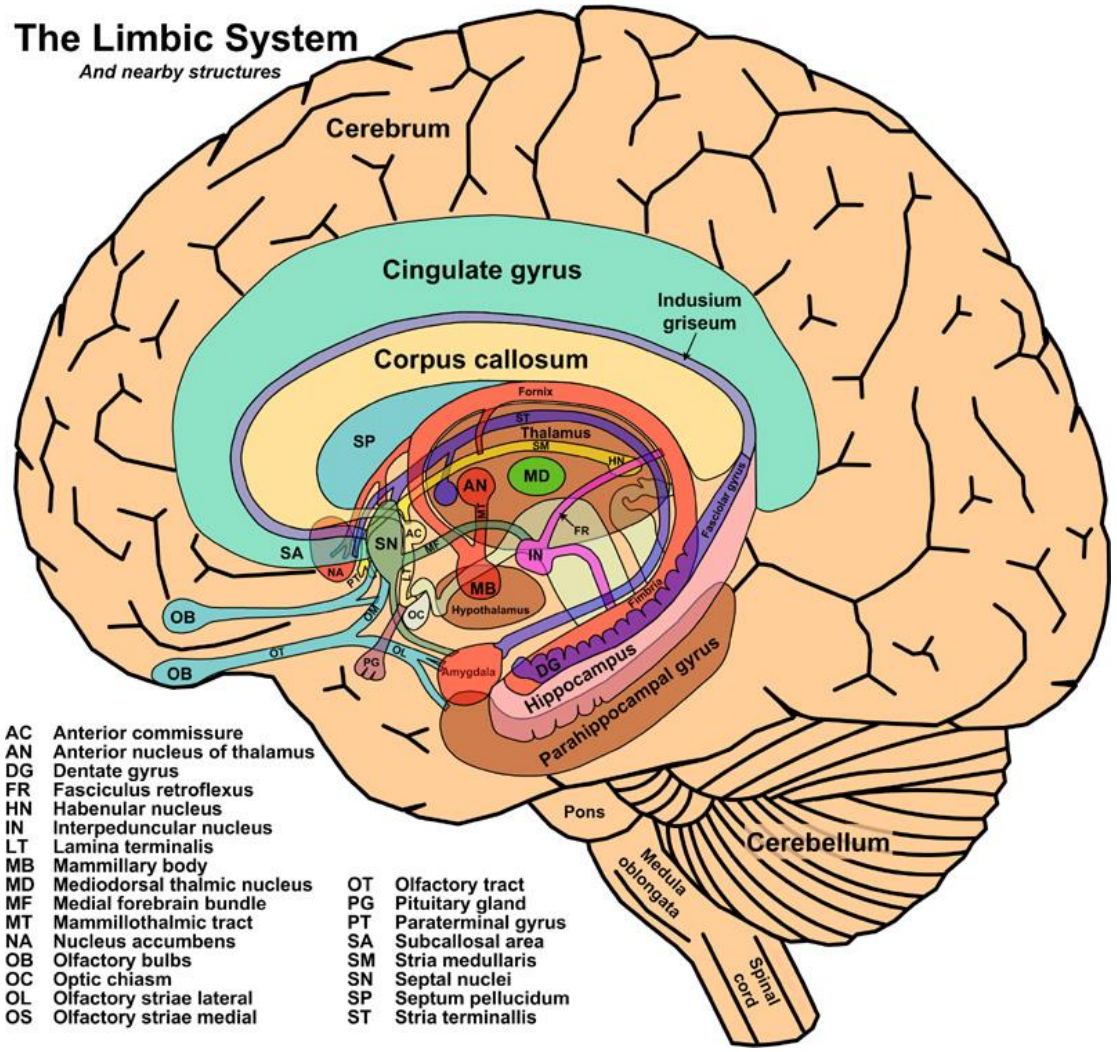
The Limbic System: Grey Matter Structures

- Amygdala
  - Emotions & behavior.
  - Smell – emotional responses to smell
- Hypothalamus
- Thalamus
  - Anterior nucleus – Memory
  - Mediodorsal nucleus – Emotion & Behavior
- Septal area - reward pathway
- Habenula - reward pathway



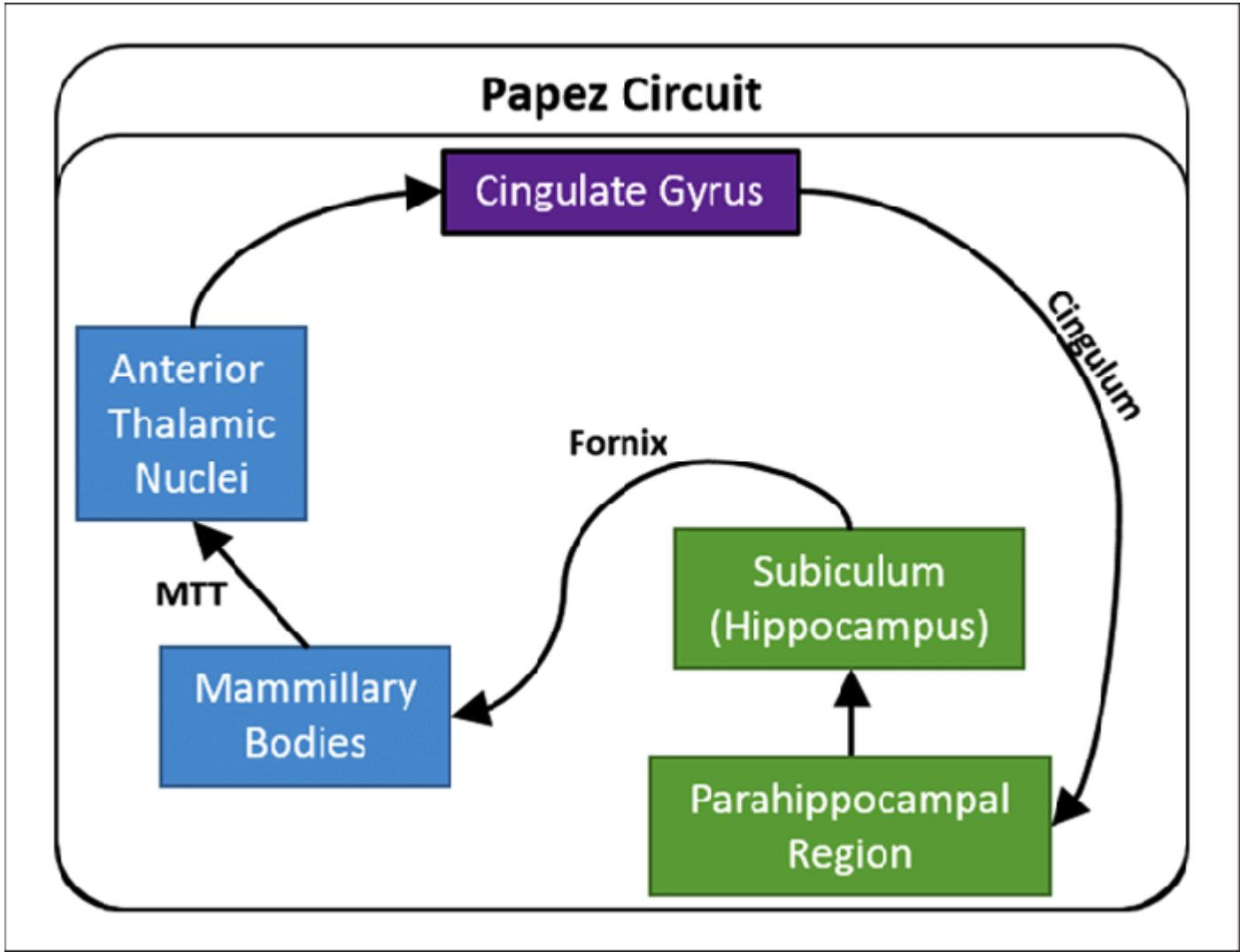
The Limbic System: Olfaction

- Olfaction
  - Smell -> olfactory bulb -> olfactory tract -> lateral olfactory striae ->
    - Parahippocampul gyrus (memory of smells)
    - Amygdala (emotions related to smell)

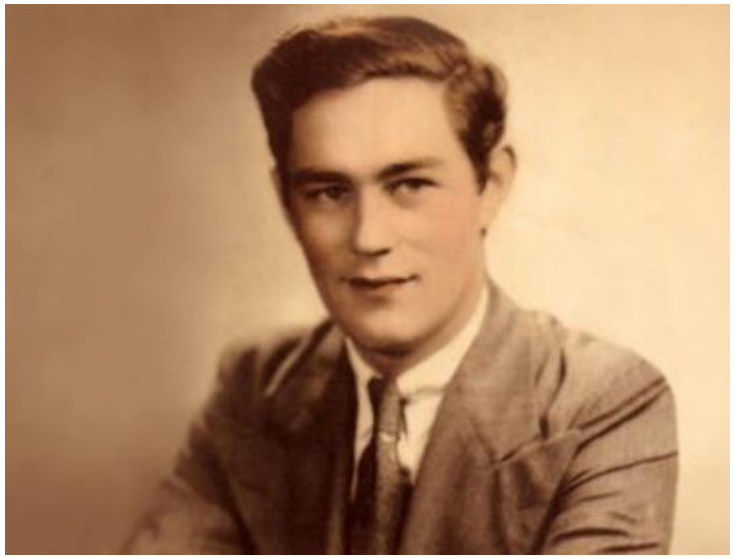


The Limbic System: Memory & Learning

- Memory & Learning
  - Papez Circuit
    - Subiculum -> fornix -> mamillary bodies -> thalamus -> cingulate gyrus
      - Paraphypocampal gyrus -> entorhinal cortex -> hippocampus dentate gyrus -> subiculum
      - Prefrontal cortex – involve memory with thoughts & decision making



Hippocampus: HM & Memory

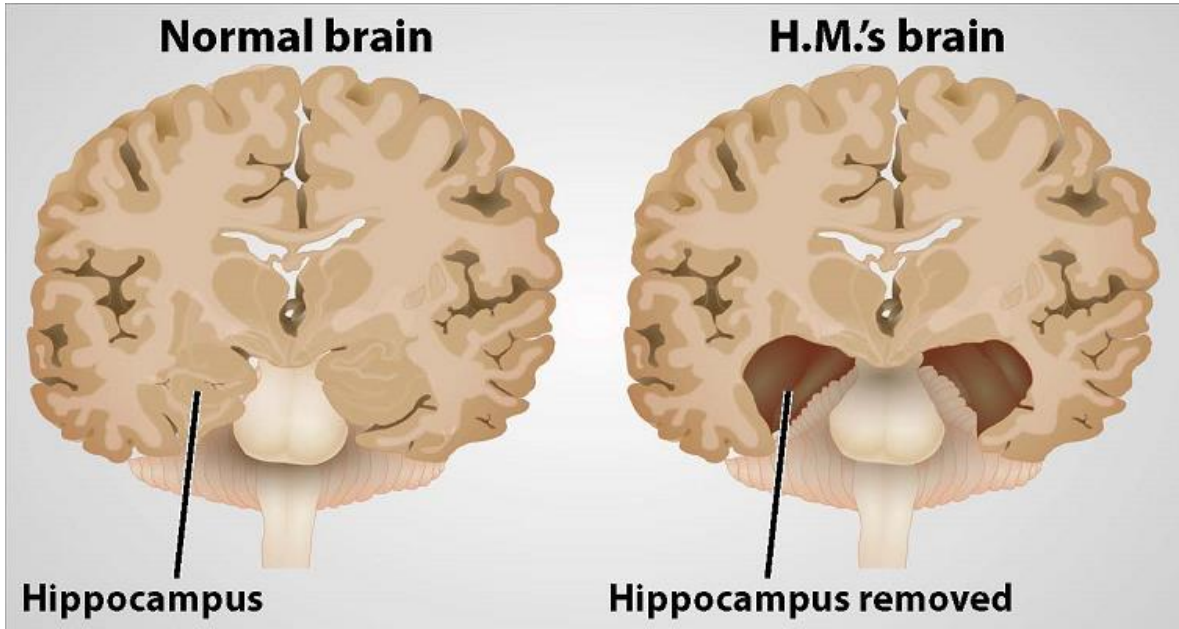


- HM – head trauma -> seizures
- 1953 – William Scoville neurosurgeon removed HM's Hippocampus
- At the time, thought to be involved in emotions as part of limbic system

- Seizures disappeared, no change in personality, even increase in IQ
- Lost memory of preceding decade & unable to form new memories
- Could remember things in short-term or working memory for about 15 mins by repeating information to himself

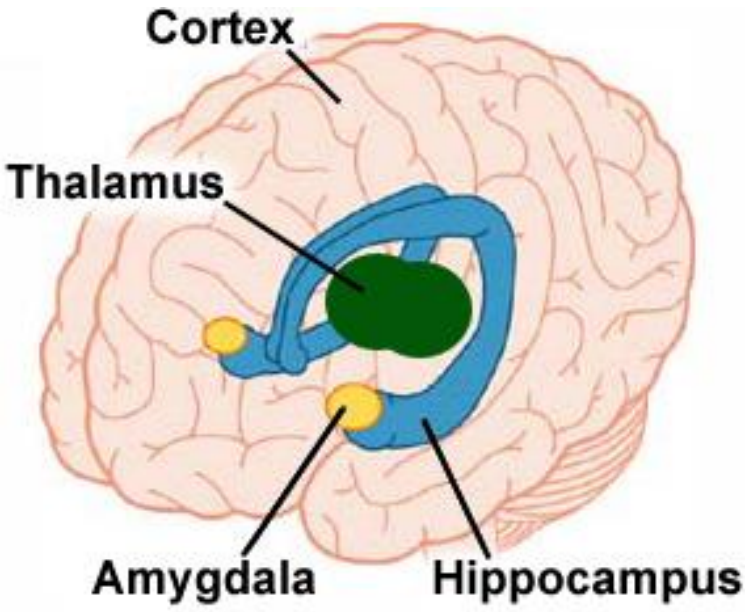
- Hippocampus necessary for memory consolidation

- Procedural motor knowledge relies on different mechanisms
  - Trace a star in a mirror - performance got better over time even though he could not declaratively remember having done the task before.
  - Procedural memory relies more on basal ganglia and cerebellum
  - Distinction between "knowing that" & "knowing how"



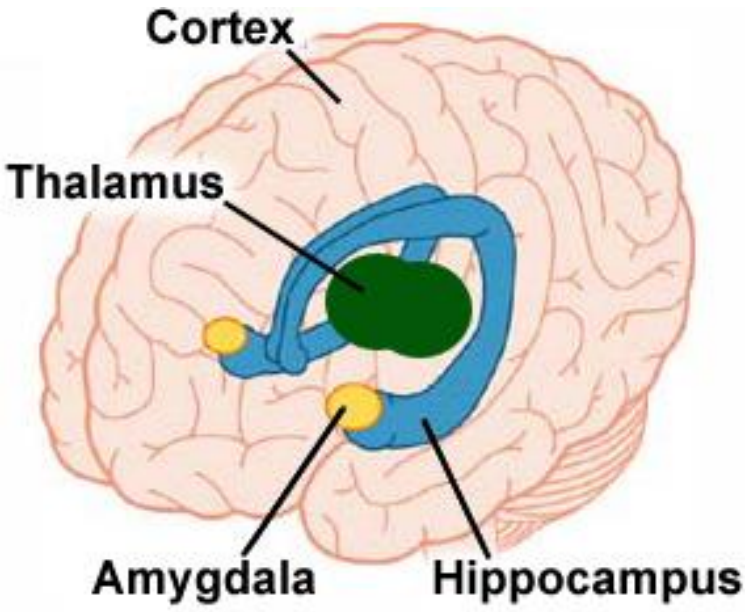
The Amygdala

- Functions
  - Fear, anger, rage, sadness
  - Feeding
  - Autonomic functions
  - Learning, specifically tasks that require integrating information from different sensory modalities or the linking of a stimulus to an emotional response



The Amygdala

- Emotions/emotional responses
  - Amygdala receives information from
    - Prefrontal cortex – reasoning, judgement, personality
    - Temporal lobe - smell, taste
    - Insula - visceral sensation
    - Auditory association
    - Posterior association area - somatosensory, vision, auditory
  - Amygdala sends info to septal area & hypothalamus (autonomic nervous system)
    - Hypothalamospinal tract -> sympathetic organs autonomic response to fear
      - Liver - increase glucose production -> more energy for muscles
      - Heart - increase heart rate/blood flow
      - Increase blood pressure
      - Lungs - increase respiratory rate
      - Stimulate pituitary to release cortisol



The Amygdala

- Charles Whitman
  - Texas Tower Sniper (August 1, 1966)
    - Killed wife & mother with knives
    - Just under two hour rampage
      - Killed 3 people in the tower
      - Sniper killed 11, wounded 31
      - +1 died 35 years later from injuries
  - 1965 complained of headaches and violent impulses
  - Suicide note asked for a brain autopsy because he thought something was wrong with him
    - tumor pressing on the amygdala

The Amygdala

- Innate Fear - evolutionarily beneficial
  - Rats are afraid of cat urine even if they have never seen a cat

- Learned Fear
  - Tone elicits no amygdala response
  - Pair that with a shock and eventually the tone will elicit an amygdala response (conditioning)

- Social Justice
  - Lesion – naive trusting
  - Otherwise more vigilant and can better determine if you are being treated fairly -> aggression

The Amygdala & Autism

- Emotion plays a large role in social function
- Damage to amygdala in dominate monkey -> falling off social hierarchy
- People with damaged amygdala have social behaviors that look like autism (e.g., avoid eye contact, difficulty judging facial expressions
- Autistic individuals:
  - amygdala grows usually fast in children making it larger than usual but then it stops growing or even shrinks in adults
  - Studies shows less amygdala activation when evaluating facial expressions but more activation when evaluating the eye area
  - Weak connections between amygdala and hippocampus correlated with most sever autistic traits
  - Connections between amygdala and prefrontal cortex weaker in autistic individuals – less able to regulate emotions

The Amygdala & Developmental Trauma

- Trauma - sudden intense surge of anxiety secondary to some external event that exceeds the subject's ability to cope with and to defend against
- Traumatic experiences -> significant structural and functional changes in brain regions implicated in emotional and cognitive processing (i.e., medial prefrontal cortex, anterior cingulate cortex, hippocampus, and amygdala)

- Amygdala mediates the acquisition and expression of conditioned fear and the enhancement of emotional memory

- Childhood trauma -> increased amygdala volume.
- Adulthood trauma -> decreased amygdala volume
  - PTSD, MDD, BPD associated with reductions in amygdala volume (adult)

- Excessive amygdala activity to emotionally negative stimuli -> associated with trait anxiety, PTSD, and MDD
- Positive correlation between physical abuse & right amygdala activity
- Excessive amygdala activity -> mediator between childhood trauma and the development of trauma-related psychiatric (e.g., PTSD and MDD).

The Amygdala & Developmental Trauma

- Functional connectivity between the amygdala and the prefrontal cortex -> emotion regulation.
  - conditioning
  - extinction of memories of traumatic fear.
- Prefrontal cortex regulates stress-induced fear and anxiety via inhibitory effects on amygdala activity
- Strength of the anatomical amygdala–prefrontal pathway predicts lower levels of normal trait anxiety

- Trauma-related psychiatric disorders -> structural and functional disconnection between the amygdala and the prefrontal cortex
  - Effective interactions between these two brain areas are needed for healthy outcomes of traumatic experiences.

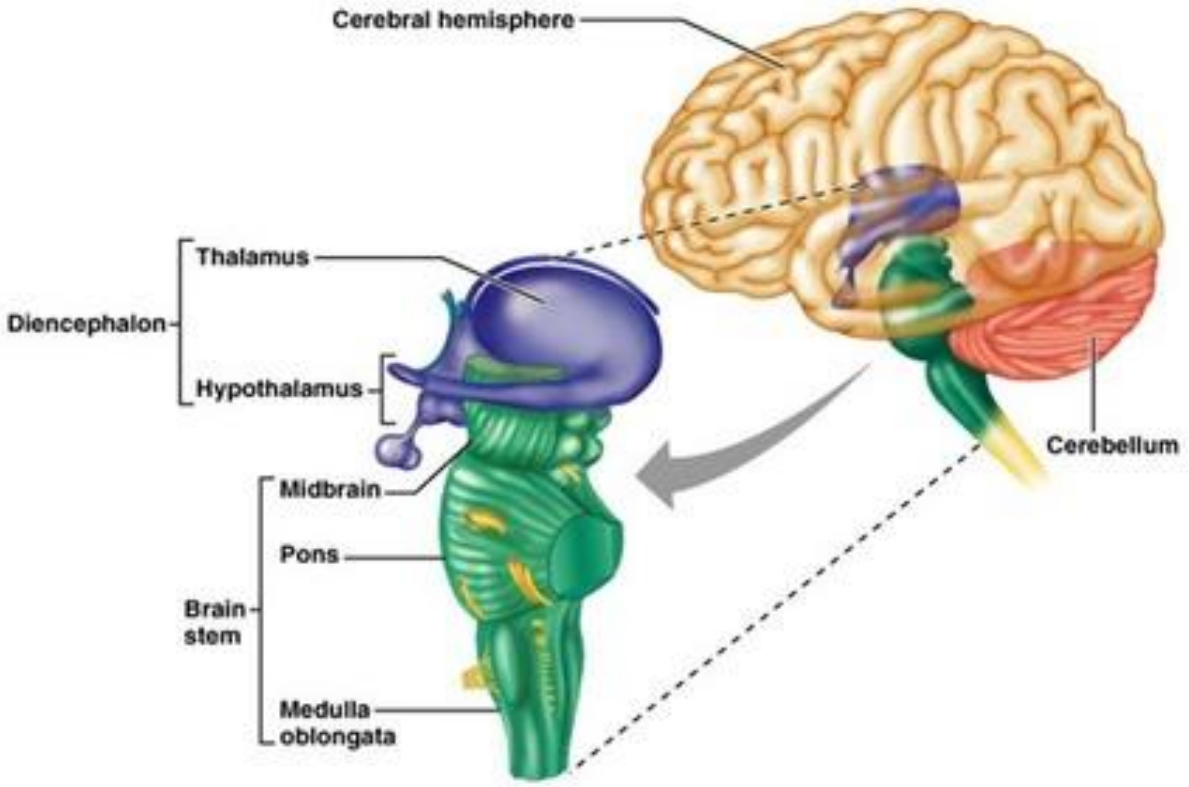
The Hypothalamus

- Part of diencephalon

- Function: Control internal environment (i.e., homeostasis)

  - Endocrine system (Hormones)
    - converts neural information to hormonal information
    - Also acts on CNS
      - Hormonal effects can be fairly slow -> long-term regulation of synaptic effectiveness that modify mood & behavioral states

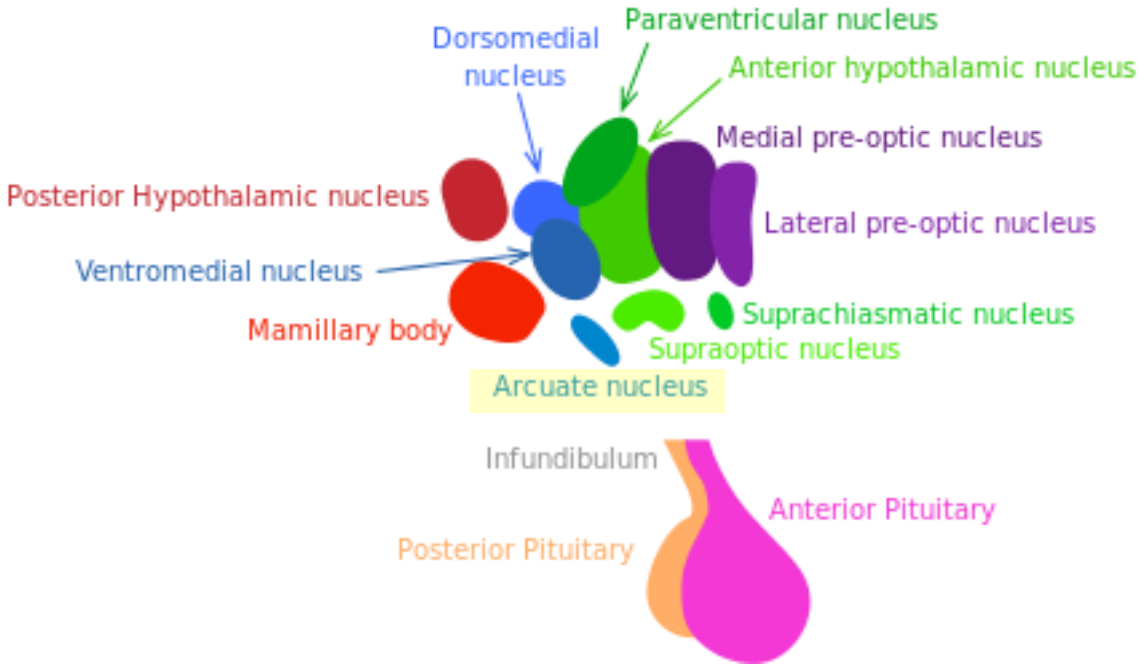
  - Autonomic nervous system
    - Sympathetic (i.e., Fight/flight)
    - Parasympathetic (i.e., Rest/Digest)
  - Neural system concerned with motivation – stimuli result in different responses based on internal state



- Direct Route -> endocrine system & autonomic nervous system
  - Example: cold room -> peripheral vasoconstriction
- Indirect Route -> motivate to act on environments
  - Example: cold room -> Close a window, turn up the heat

Hypothalamus: The Endocrine System

- Arcuate Nucleus
  - Releasing & Inhibiting factors into pituitary
    - Growth hormone
    - Cortisol precurser
    - Prolactin
    - Thyroid hormone



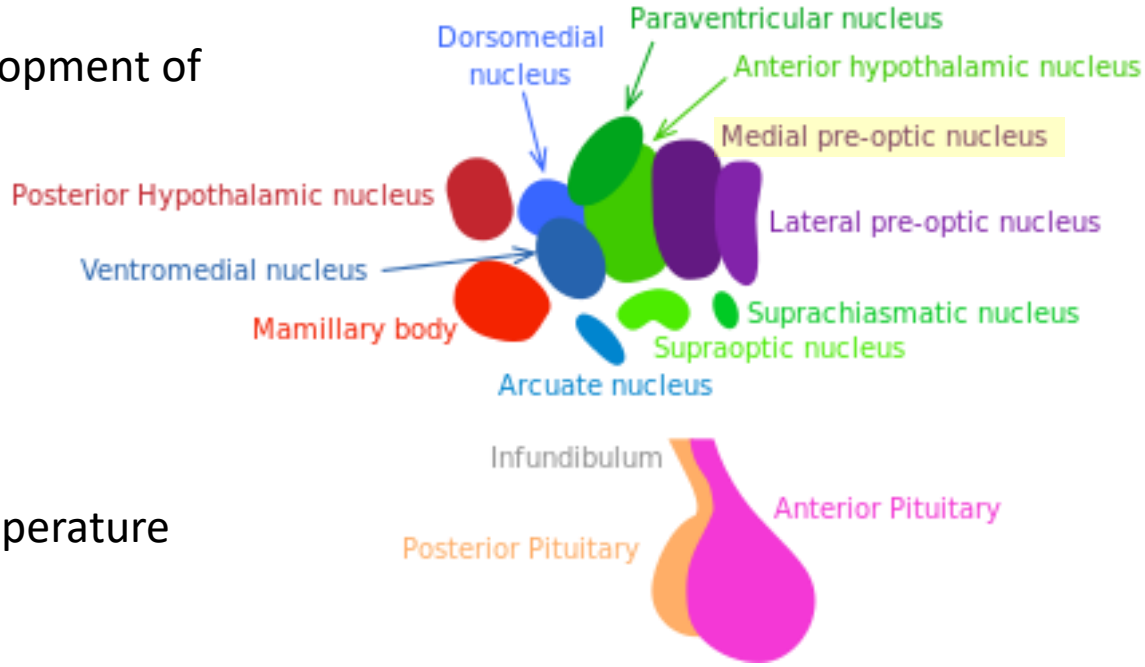
Hypothalamus: The Endocrine System

- Medial Preoptic Nucleus

  - Gonadotropin -> Follicle stimulating hormone /Luteinizing hormone

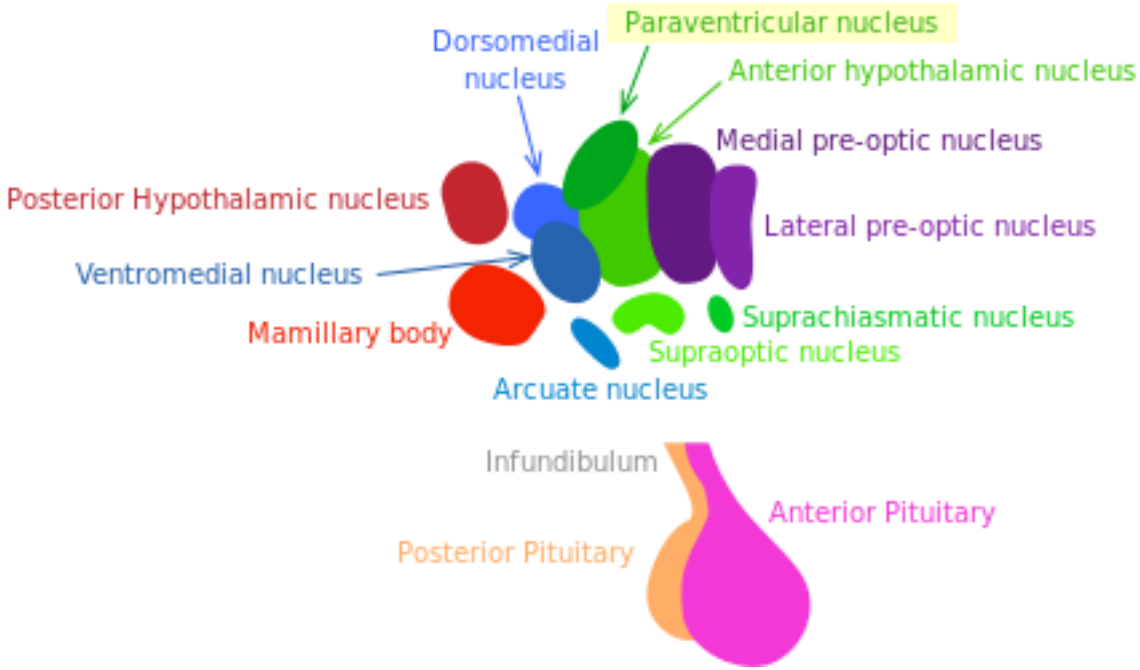
    - Female
      - FSH - Estrogen production
      - LH - Progesterone production
        - prepare the uterus for implantation & development of placenta
    - Male
      - FSH - Sperm production
      - LH - Testosterone

    - Role in Temperature regulation
      - Panting vs shivering
      - May play a role in fevers – setting a different temperature "setpoint" to regulate



Hypothalamus: The Endocrine System

- Paraventricular Nucleus
  - Release oxytocin
    - Women
      - Suckling –> milk ejection
        - Also communications with higher centers -> sight or sound of baby crying also induces milk release
        - Stress inhibits milk release
      - Uterine stretch -> uterine contraction (labor)
    - Men
      - Sexual drive, orgasm & increase blood flow to penis

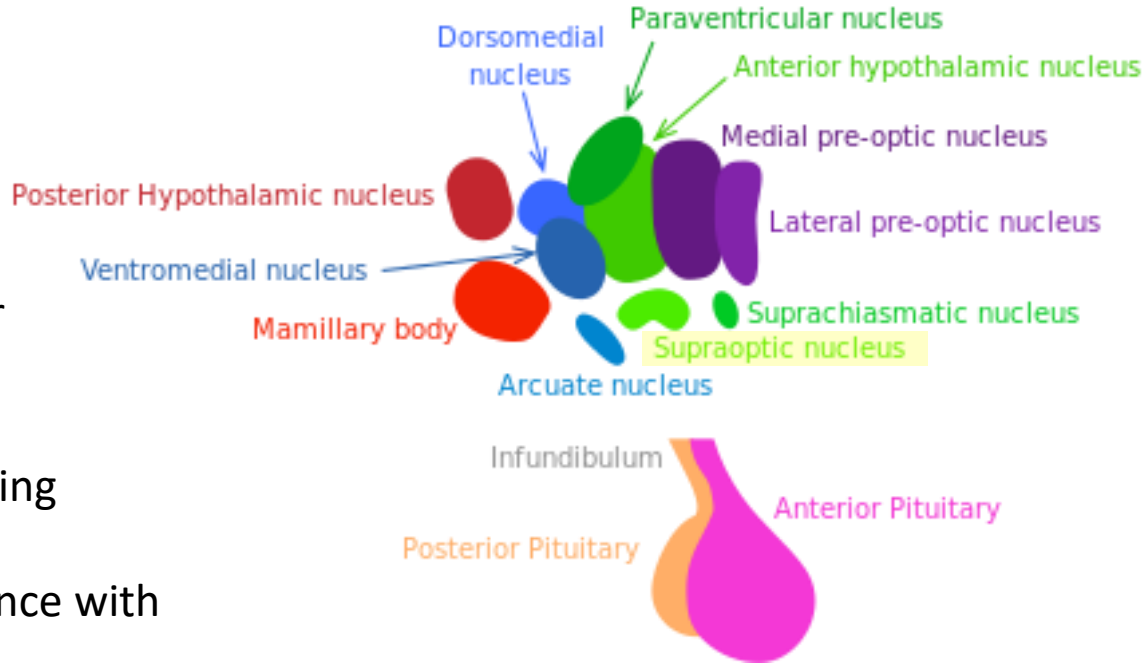


Hypothalamus: The Endocrine System

- Supraoptic Nucleus

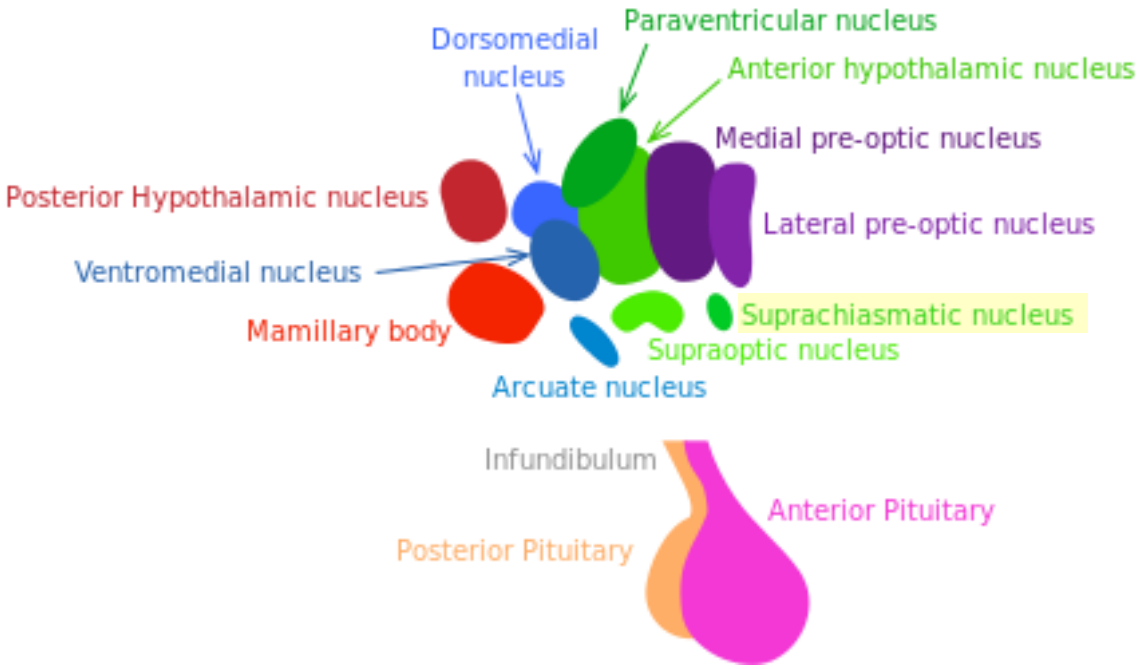
  - Response to water balance –> decreased water & increased solutes stimulate
  - Release Vassopressin
    - acts on blood vessels ->
      - vasoconstriction increase blood pressure
      - kidneys increase water reabsorption
    - Cold inhibits vasopressin (urinate more)
    - Heat stimulates – conserve water more used for sweating

    - Release of vasopressin also linked to counteracting fevers
      - May also play a role in convulsions experience with very high fevers



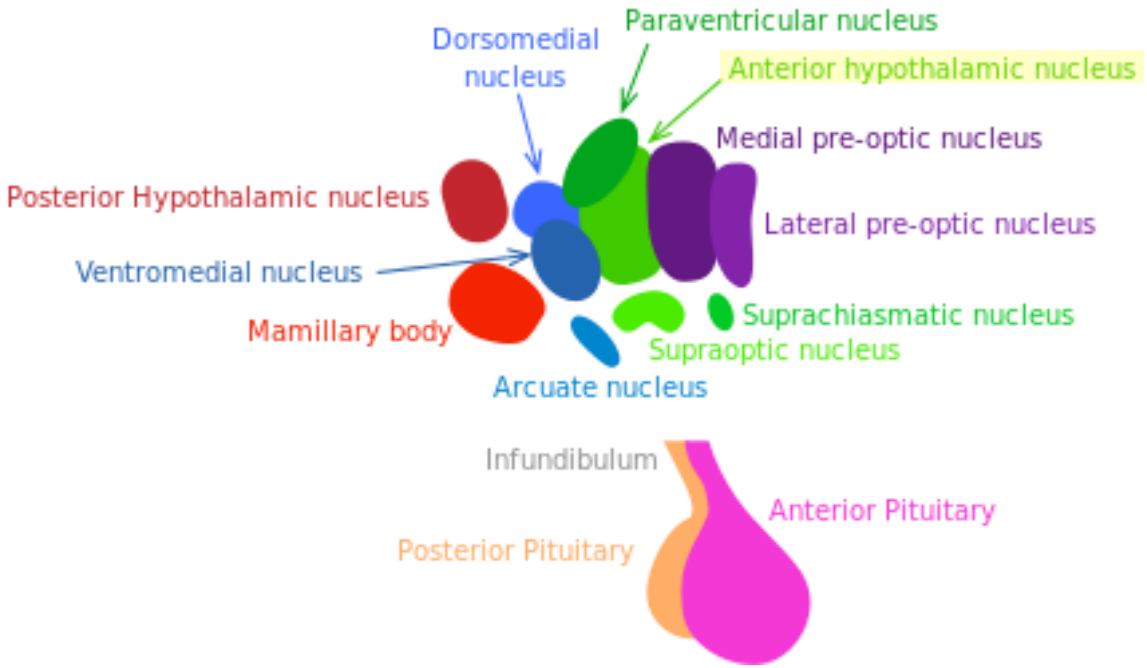
Hypothalamus: The Endocrine System

- Superchiasmatic Nucleus
  - Circadian rhythm - sleep/wake cycle
    - Light hits retina -> optic nerve -> retinohypothalamic tract -> pineal gland -> [darkness] release melatonin



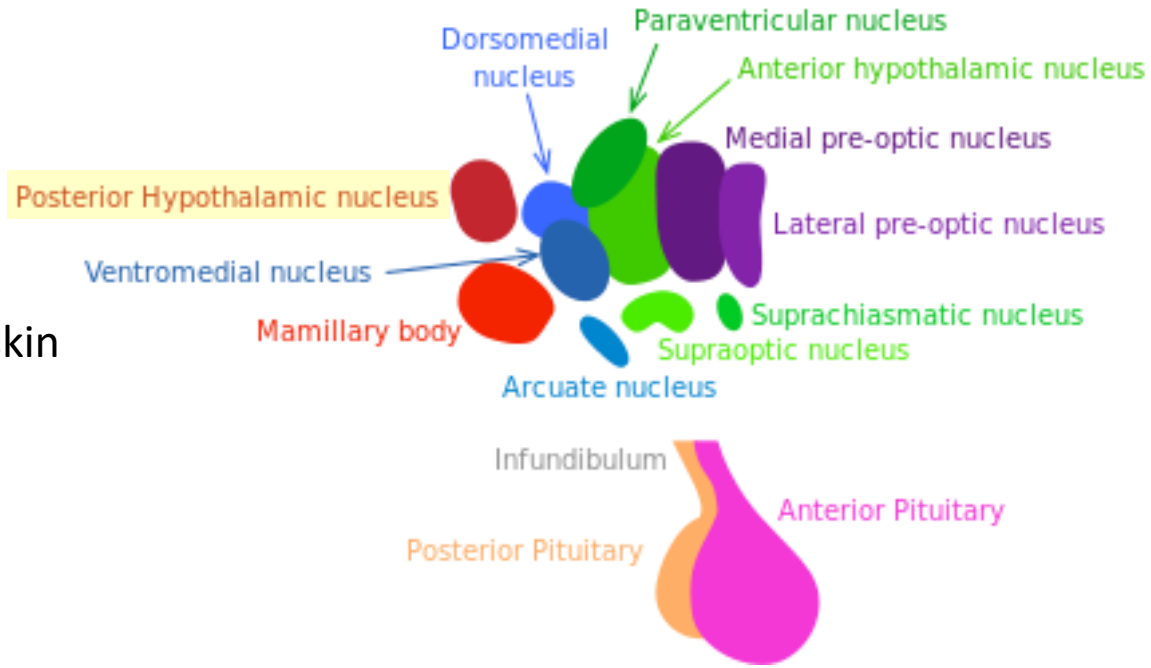
Hypothalamus: Autonomic Nervous System

- Anterior Hypothalamic Nucleus
  - Parasympathetic Nervous - Rest & Digest
    - Descends to
      - brain stem
        - CN III – Pupillary constriction
        - CN VII & IX- Salivatory glands
        - CN X – Vagus
      - spinal cord - S2-S4
      - Reticular formation – Arousal
    - Thermoregulation
      - Cool down -> decrease body temp
        - Vasodilation - bring blood close to the surface to radiate heat out the skin
        - Stimulate sweat glands – evaporative cooling



Hypothalamus: Autonomic Nervous System

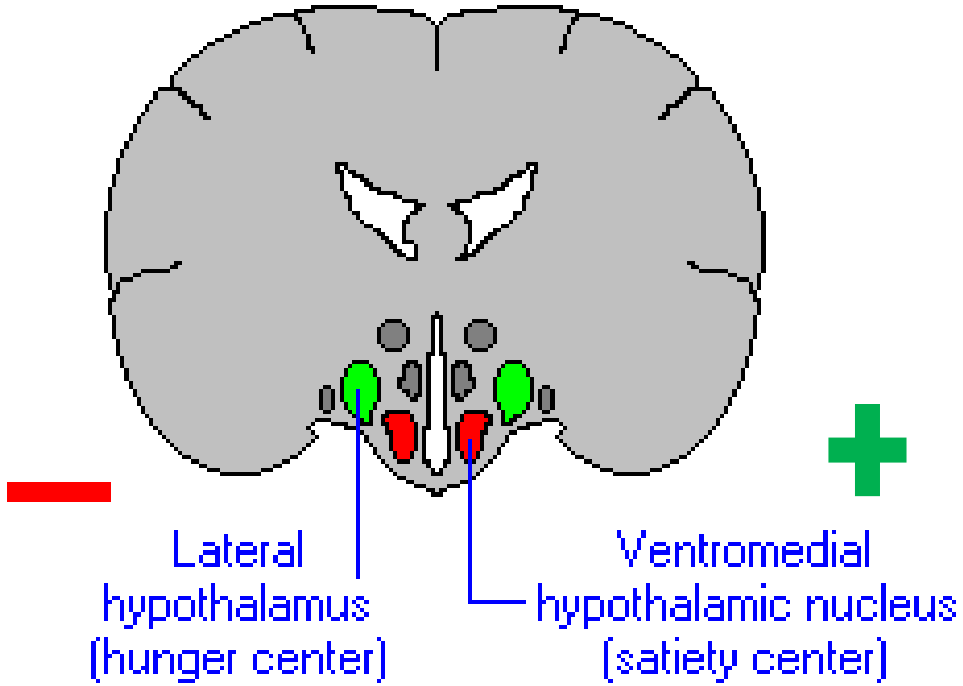
- Posterior Hypothalamic Nucleus
  - Sympathetic Fibers – Fight/Flight
    - T1 – L2
  - Thermoregulation
    - Warm up -> increase body temp
      - Vasoconstriction – bring blood away from skin & to internal organs
      - Shivering - generate heat



Hypothalamus: Feeding Behavior

- VentroMedial Nucleus (VMN) – satiety
  - damage leads to obesity
- Lateral Hypothalamic Nucleus (LHN) – hunger
  - damage in infants -> failure to thrive
  - adults -> anorexia ?

- Adipose tissue – increase in fat storage -> release leptin
  - stimulates VMN, inhibits LHN
- Pancreas – high glucose levels -> produce insulin
  - stimulates VMN, inhibits LHN
- GI tract – food distends/stretch -> Vagus nerve (CN X) -> hypothalamus
  - stimulates VMN, inhibits LHN
- Stomach – fasting -> Ghrelin
  - inhibits VMN, stimulates LHN

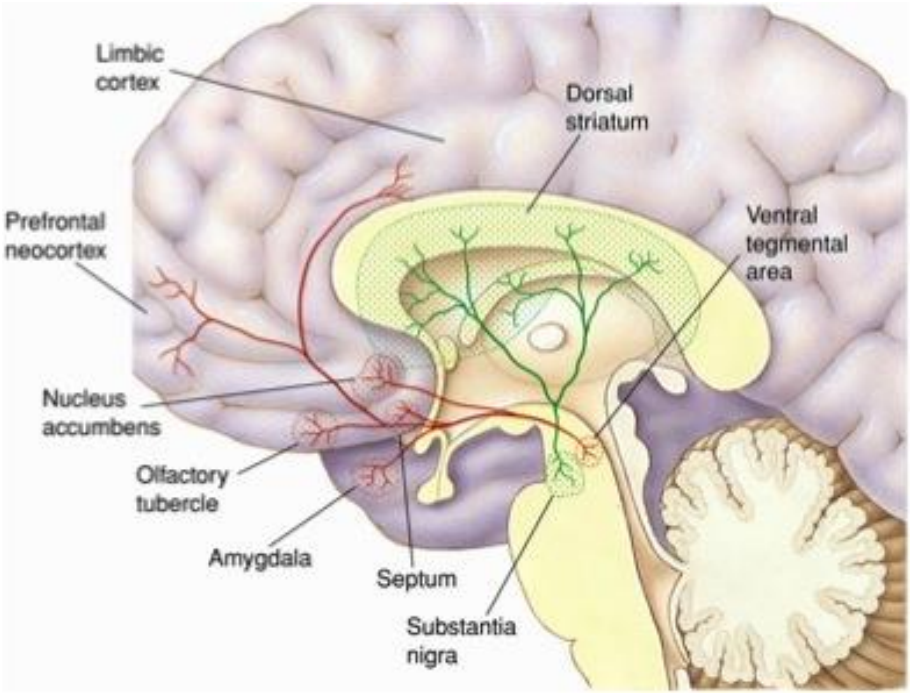


Addiction Cycle

- 3 stage cycle
  - Binge/Intoxication
    - Consume substance, experience reward/pleasurable effects

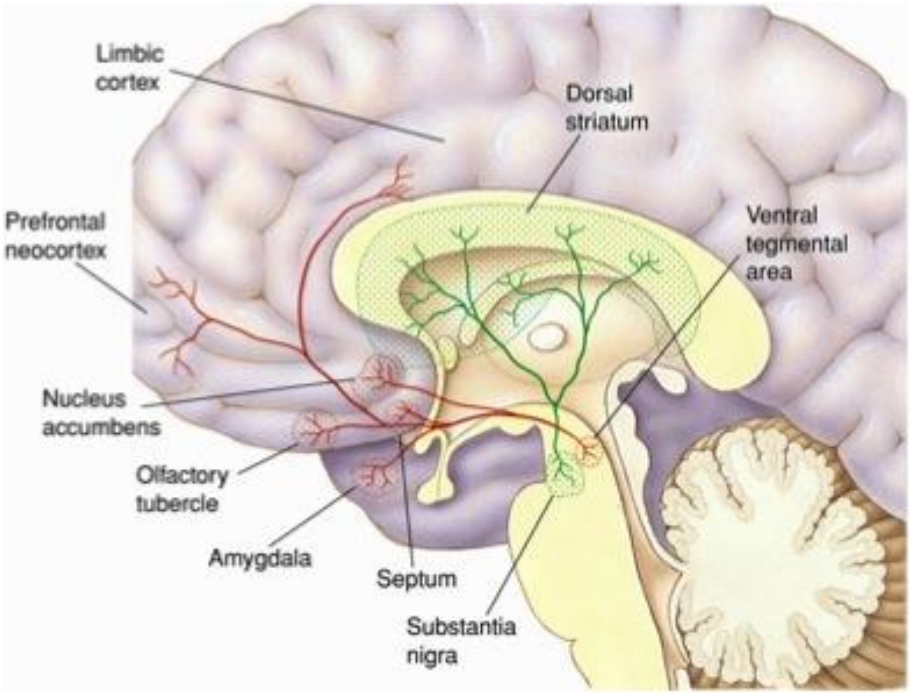
  - Basal Ganglia
    - Reward/pleasure, dopamine, & habit formation
    - Enable substance-associated cues to trigger substance seeking (i.e., increase incentive salience)
      - Nucleus Accumbens – Links stimulus with response
        - motivation, experience of reward
        - Release glutamate – excitatory neurotransmitter
        - Release of dopamine & Brain's natural opioids
        - Associate people, places, drug paraphernalia, moods with rewards -> triggers

      - Dorsal Striatum – habit formation, routine behaviors



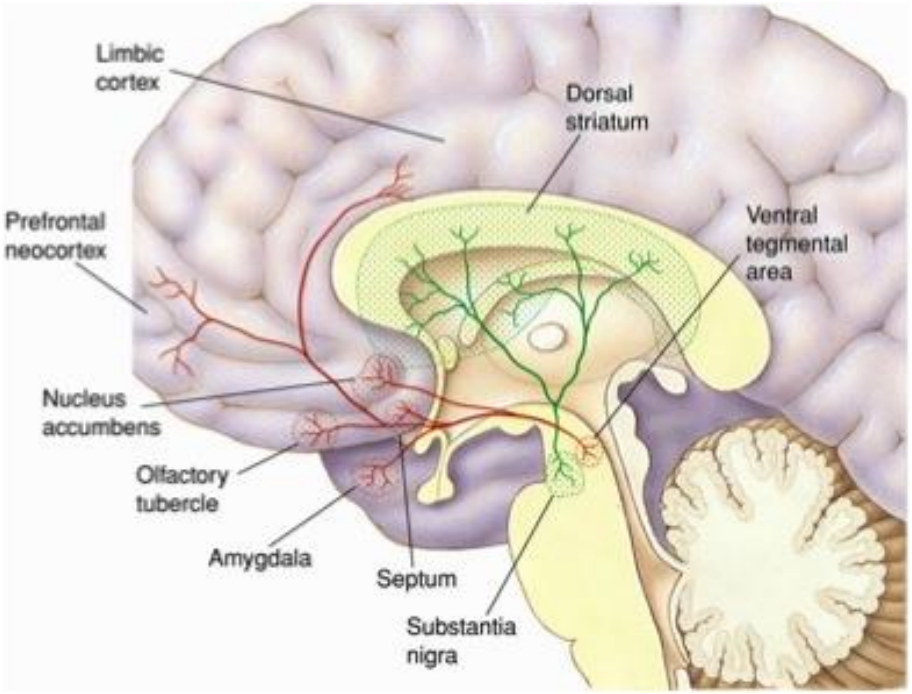
Addiction Cycle

- 3 stage cycle
  - Withdrawal/Negative Affect
    - negative emotions in response to substance absence
      - As sensitivity to the reward system reduces with continued use -> increases stress
        - Release of Corticotropin-releasing factor (cortisol) & norepinephrine
        - Blocking stress receptors reduces seeking behaviors
  - Amygdala - Stress & emotions related to withdrawal
    - Reduce sensitivity of pleasure/reward
  - Hypothalamus – hormone production response to stress
    - Heighten activation of stress systems



Addiction Cycle

- 3 stage cycle
  - Preoccupation/Anticipation “Craving”
    - Substance seeking after period of abstinence (may be short as hours)
  - Prefrontal Cortex
    - Reduce executive control function responsible for regulating one’s actions, emotions, and impulses
    - Smaller volume in abstinent, previously addicted individuals predicts shorter relapse time
    - Reduced prefrontal control over amygdala in PTSD



Limbic System Syndromes

- Kluver-Bucy Syndrome – bilateral damage to amygdala
  - Placidity – no reaction to fear or anger
  - Hyperphagia – over-eating
  - Hypersexual
  - Amnesia

- Wernickes Encephalopy - B1 deficiency
  - Damages mamillary bodies (memory pathway)
  - Confabulation – fill memory blanks with made up things
  - Ataxia
  - Ophthalmoplegia

Thank You

The Amygdala & Developmental Trauma

https://www.intechopen.com/books/the-amygdala-a-discrete-multitasking-manager/traumatic-experiences-disrupt-amygdala-prefrontal-connectivity