Section 6
Arousal, Sleep & Dreaming
Sexual Development & Behavior

Sujin Park

COGS 17 A04

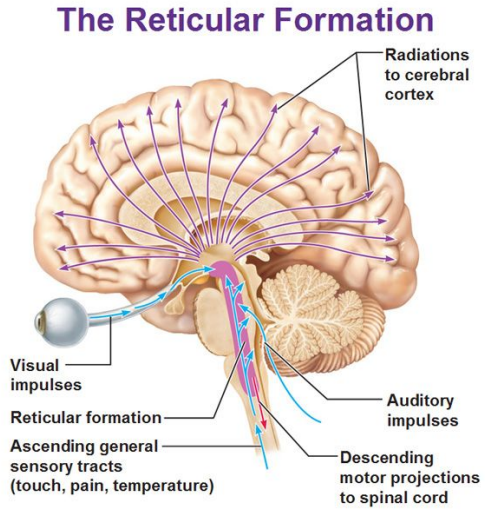
02/28/25

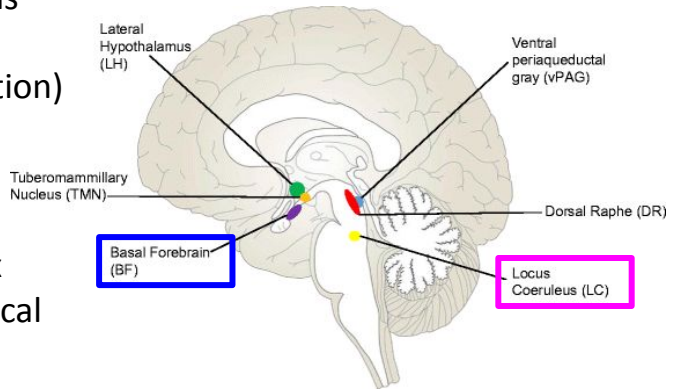
Arousal in the Brain

- **Reticular Formation**
  - A set of interconnected nuclei that are located throughout the brainstem, synapses to various regions of the cortex
  - Sensory information travels up through the Medulla & Pons and is distributed throughout the forebrain and cortex
  - receives from all sensory systems
  - Role: alerts brain, stimulates Thalamus and Basal Forebrain via ACh & Glutamate

- **Locus Coeruleus**
  - Part of the Reticular Formation in Pons
  - widespread connections including Thalamus, Cortex & Hippocampus
  - Releases bursts of Norepinephrine for vigilance and memory
  - Active when learning new tasks & during vigilance (sustained attention)

- **Basal Forebrain**
  - Anterior and dorsal to the Hypothalamus
  - Releases **ACh** thruout cortex for **arousal** and **GABA** to **inhibit** cortex
  - Damage: implicated in Alzheimer's Disease → arousal could be critical to memory activation





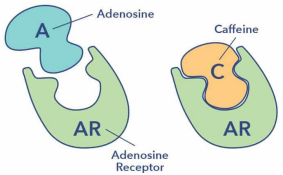
How does Caffeine help you wake up?

How does Caffeine help you wake up?

- Alertness/Sleepiness is controlled by an opponent system of ACh and GABA

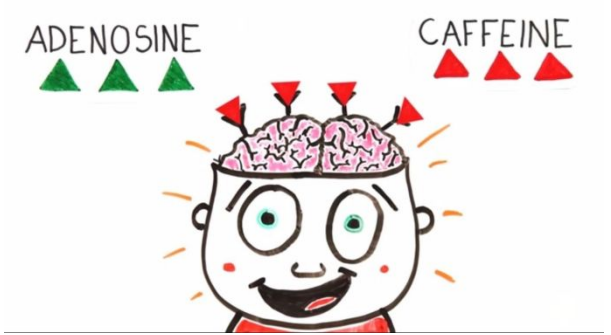
- Basal forebrain controls the balance of these NTs

- **Adenosine**
  - by-product of cell metabolism, builds up in cells during the day
  - Its release inhibits Basal Forebrain's release of Ach, allowing <u>GABA</u> system to dominate
    → cortical activity suppression, promotes sleep



- Caffeine
  - crosses blood brain barrier
  - allows Basal Forebrain to continue to arouse the brain by <u>blocking Adenosine Receptor sites</u> (x inhibit ACh cells)
    → awake

- Another contributor to alertness: Excitatory NT Orexin from the Lateral Hypothalamus



Caffeine only delays the onset of sleepiness, and only works before Adenosine binds to its receptor (i.e., when you're sleepy)

Stages of Wakefulness / Sleep

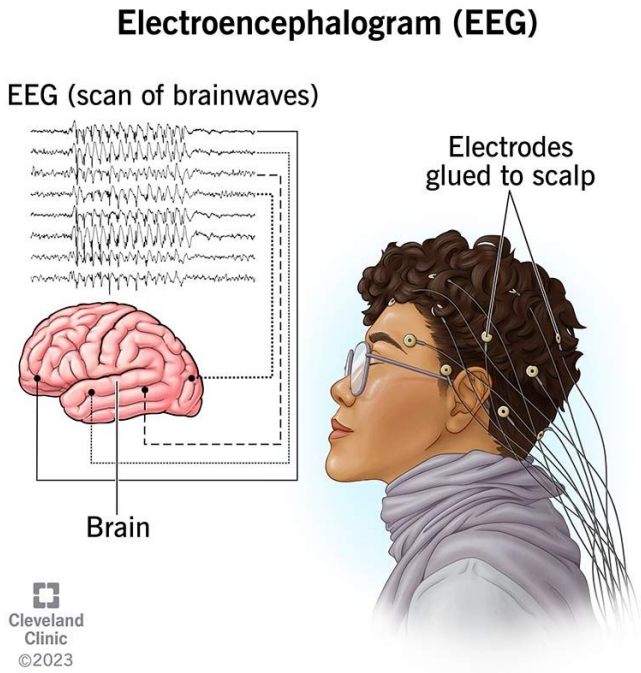
One way to measure brain activity during different states…

= Electro-Encephalogram (EEG): gross average of electrical potentials in an area under electrode

- Electrodes are attached to the scalp
- Records
  1) Amplitude = Voltage
  2) Frequency = # of changes in average potential/time (Hz)

- neural de-synchrony = high frequency, variable voltage waves (multiple sources of stimulation, “many pebbles”)

- neural synchrony = low frequency, high voltage waves (coherent source of stimulation, “one big rock”)



Stages of Wakefulness / Sleep

- Awake, active: **Beta** waves (18-24 Hz)
- Awake, relaxed: **Alpha** waves (8-12 Hz), “psychological clarity” after meditation, best performance (reaction time, memory…)

- Sleep Cycle: Multiple stages
  - Stage 1 Sleep: **Theta** waves (4-7 Hz)
  - Stage 2 Sleep: Theta waves + **Spindles** (rapid changes) and **K Complexes (slow wave)**
  - Stages 3 & 4: **Delta** waves (<4 Hz), Slow Wave Sleep (SWS)
    - Stage 3 if “Slow wave sleep (=< 4Hz)” =< 50%, very synchronized
    - Stage 4 if = > 50%, hardest to wake
    - As more sleep cycles progress, Stage 3 and 4 durations decrease
  - Rapid Eye Movement (REM) Sleep: Variable EEG (12-28 Hz)

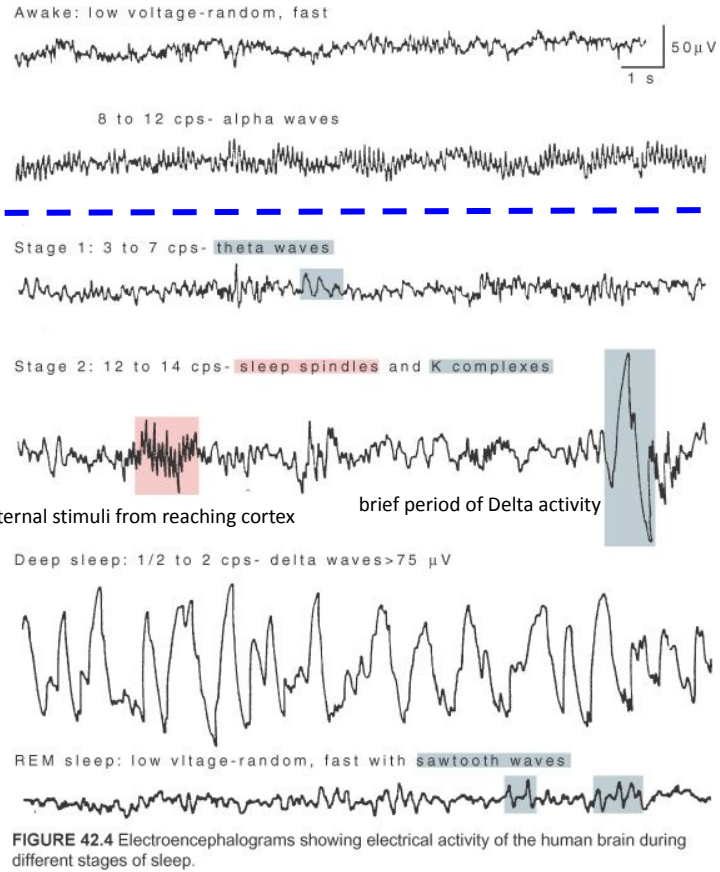


FIGURE 42.4 Electroencephalograms showing electrical activity of the human brain during different stages of sleep.

Stages of Wakefulness / Sleep

desynchronized
(lob many stones into a pond)

so as move into deeper sleep…

frequency decreases,
voltage increases
as brain activity becomes synchronized

synchronized
(lob one stone into a pond)

most desynchronized
(lob imaginary stones into a pond)

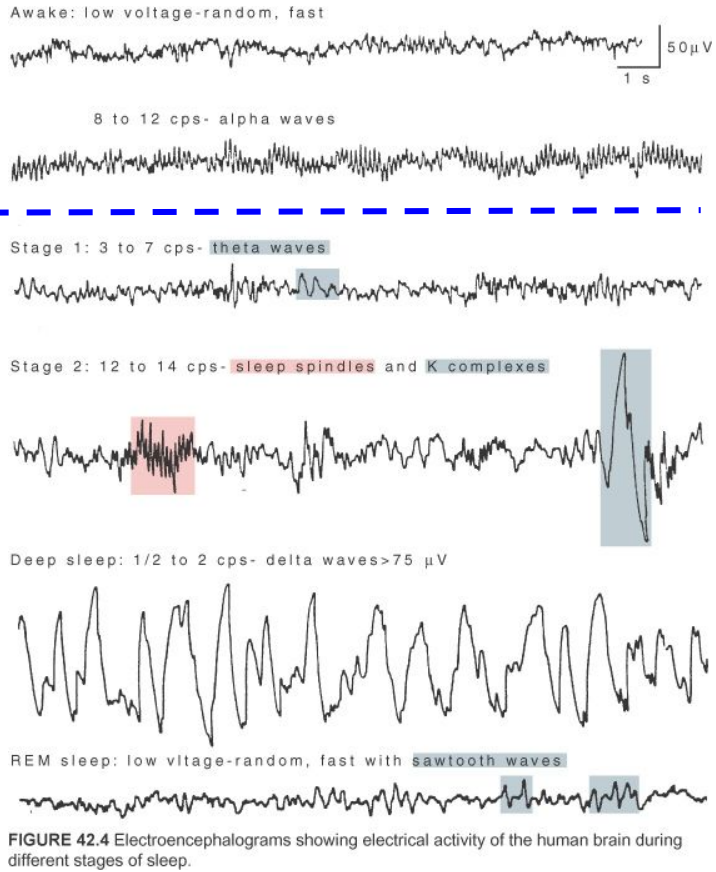


FIGURE 42.4 Electroencephalograms showing electrical activity of the human brain during different stages of sleep.

Rapid Eye Movement (REM)

- a.k.a Paradoxical Sleep, because of contradictory set of conditions that occur:

1. EEG is desynchronized: high frequency (like Sleep 1 or even Awake), low voltage (only Sleep 1 is lower) waves

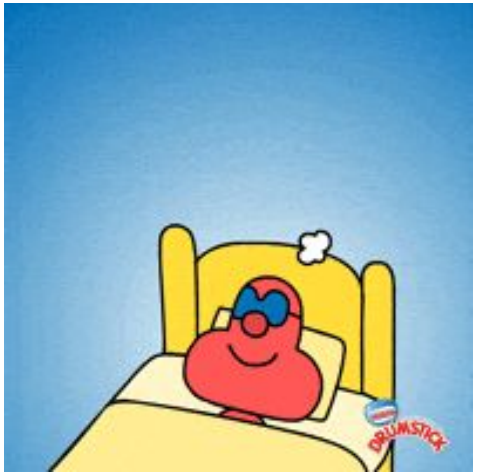
2. heart/breathing rate, blood pressure is more variable than in other sleep stages

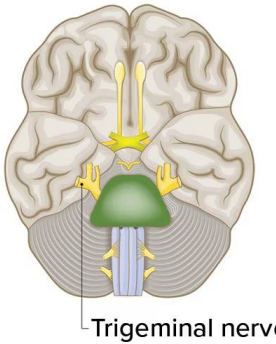
3. eyes move, genitalia active, but postural muscles are paralyzed, (=**Atonia**: Pons signals Medulla, which actively inhibits Motor Neurons in Spinal Cord & Cranial Nerves)

4. highly correlated with dreaming (but not 100%)

5. external stimuli detected, will awaken if meaningful (e.g., name) but otherwise may incorporate into dreams instead

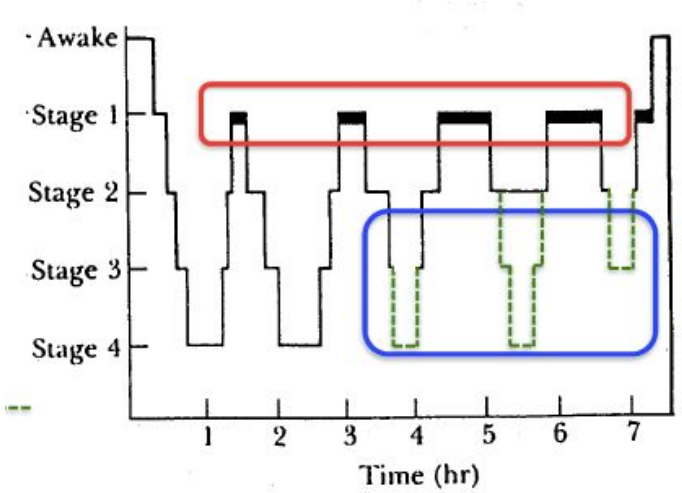
6. higher sensory areas of cortex often active during REM (also includes activation of Cranial Nerves from Tegmentum)





Changes in Sleep Cycles

- 90 minutes from stage 1 to REM
  - Stage 1,2,3,4,3,2,REM,2,3,4,3,2,REM…
- As night progress, duration of Stage 3&4 decreases, when REM durations increases (dreaming)
- Sleep Deprivation → Lethargy, Poor Concentration, Irritability, Memory impairment, Decreased resistance to infection
  - when allowed sleep, will show more Stage 4 as well as REM to make up what's lost
- REM Deprivation
  - System attempts to enter REM more frequently and bypasses early stages of sleep (REM rebound)
  - Continued → psychosis, hallucinations, death
- Functions of Sleep & Dreaming are still largely not well defined
  - but… maybe Sleep is restorative; Dreaming warms sleeping brain and REM might help consolidate memories and resolve psychological conflict



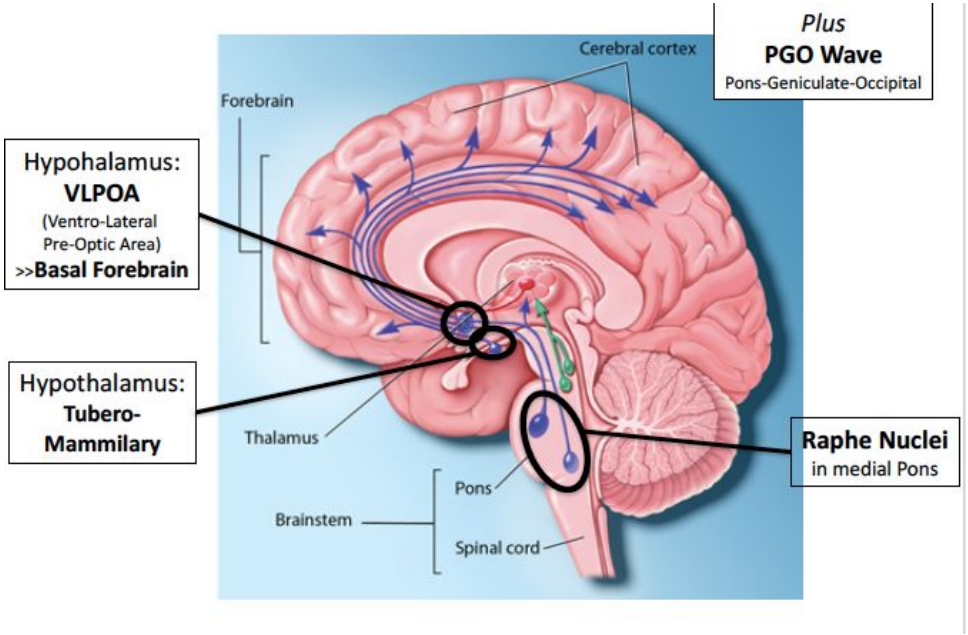
Dream is a Mystery

Neural Control of Sleep

- **Hypothalamus** nuclei are critical in initiating and regulating sleep!

1. **Ventrolateral Preoptic Area (VLPOA)** releases **GABA** to inhibit the brainstem via the basal forebrain and the cortex

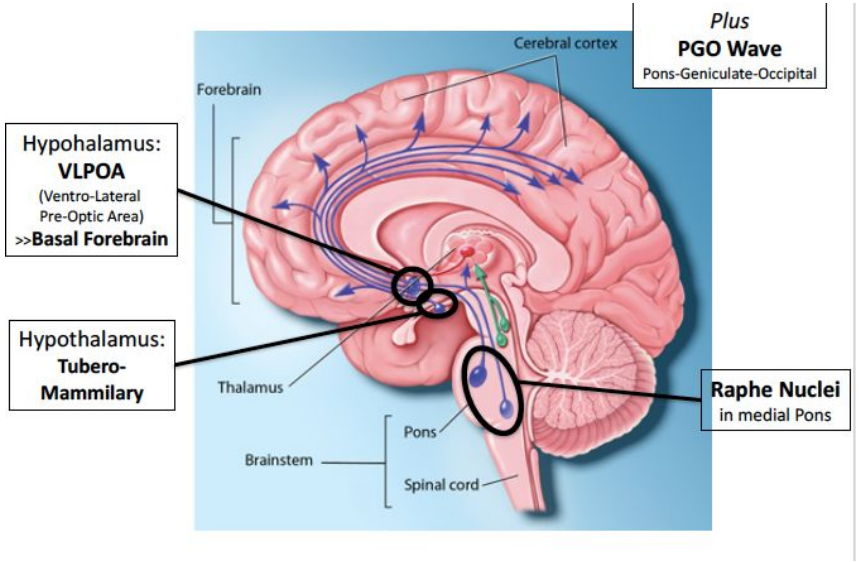
2. **Tubero-Mammillary body** releases excitatory Histamine 1 after periods of slow wave sleep, indirectly enables initiation of ACh release from Pons >> initiates PGO wave



Neural Control of Sleep

- **Pons, Geniculate, Occipital (PGO) Wave**
  - A sequence of activity in Pons → Lateral Geniculate Nucleus of Thalamus → Occipital Cortex - **initiates REM**
  - excitatory ACh arouses and desynchronizes visual & other sensory/motor pathways
  - ACh builds up just before REM, holds steady, then falls back to lower levels

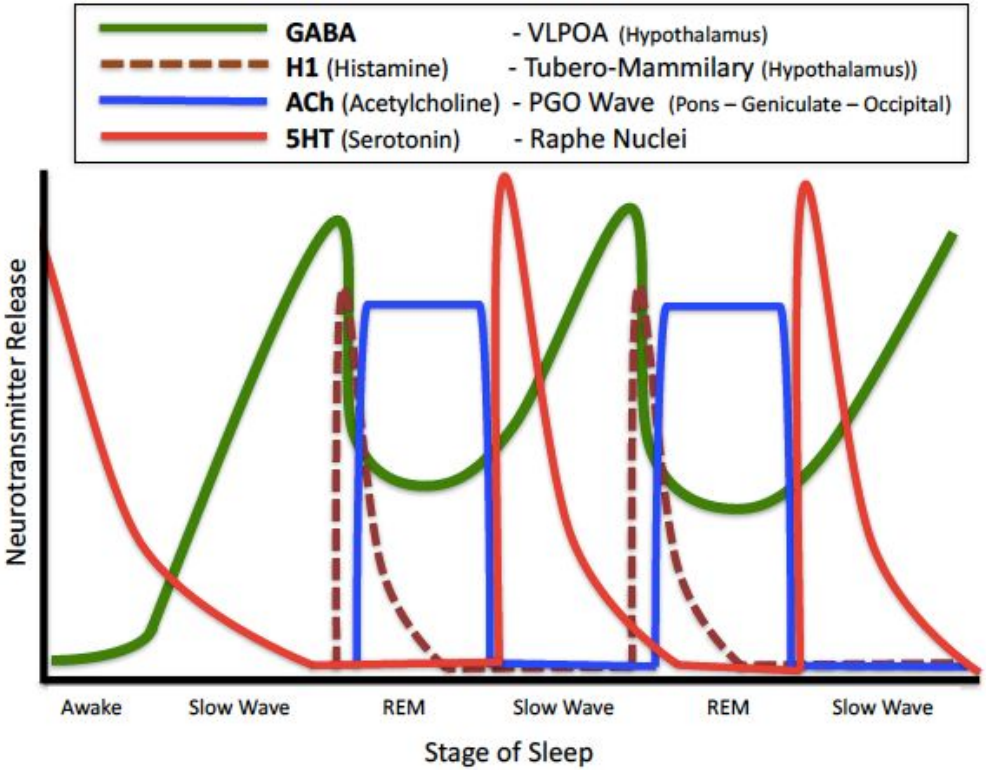
- **Raphe Nuclei in medial Pons**
  - Produces serotonin (5HT)
  - Decreasing serotonin output → sleepiness
  - Very low serotonin during sleep, none during REM, but sudden burst that shuts REM off
  - 5HT gradually falls, shifting system back to slow wave sleep
  - when 5HT flat, PGO wave is initiated again by Pons via ACh



>> Stages of sleep are controlled by an interaction of different types & sources of neural activity

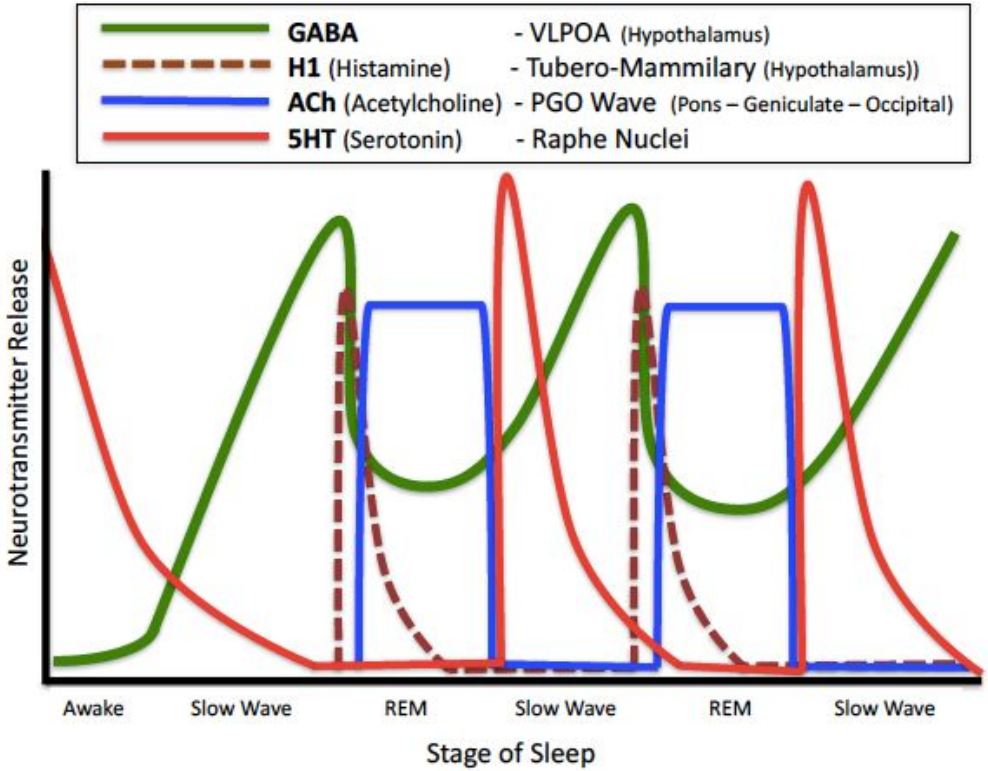
Neurotransmitters in Sleep

- **GABA**
  - Initiated by Ventrolateral Preoptic Area
  - Climbs during slow wave, low in REM
- **Histamine (H1)**
  - possibly related to hypothalamus's assessment of fall in brain temperature?
  - Spikes for the brain to warm up and initiate REM
- **ACh (Acetylcholine)**
  - High during REM
- **5HT (Serotonin)**
  - Activates to "turn off" REM



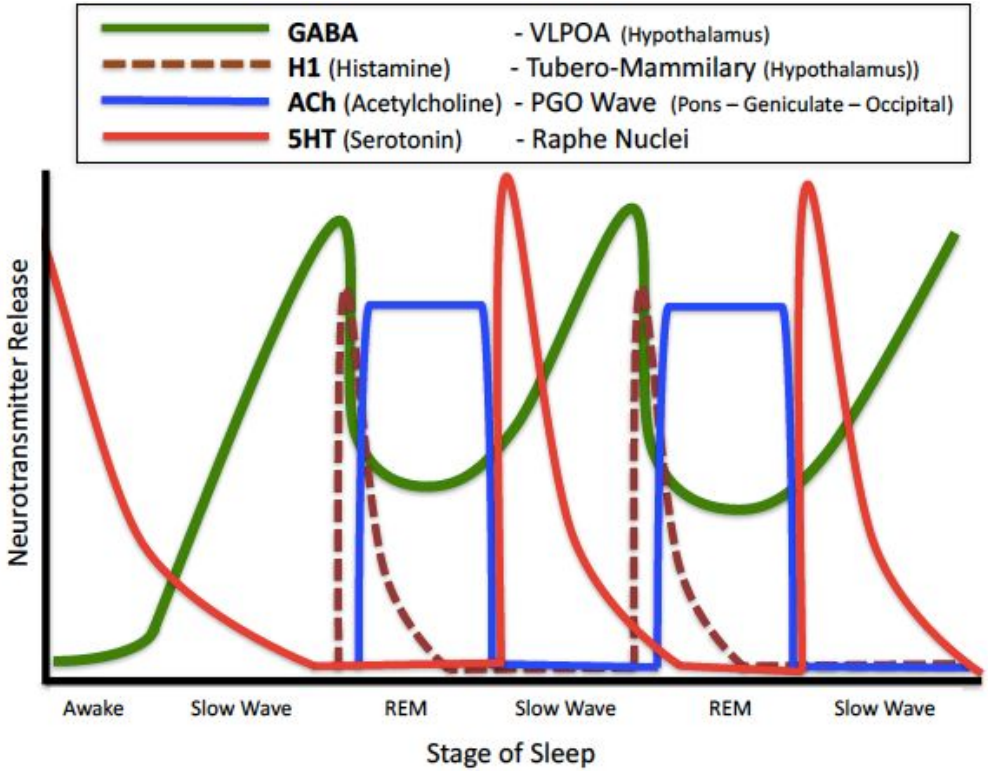
Neurotransmitters in Sleep

1. _____ arouses cortex during dreams
2. _____ promotes sleep
3. Burst of _____ shuts off REM
4. _____ is released when brain cools



Neurotransmitters in Sleep

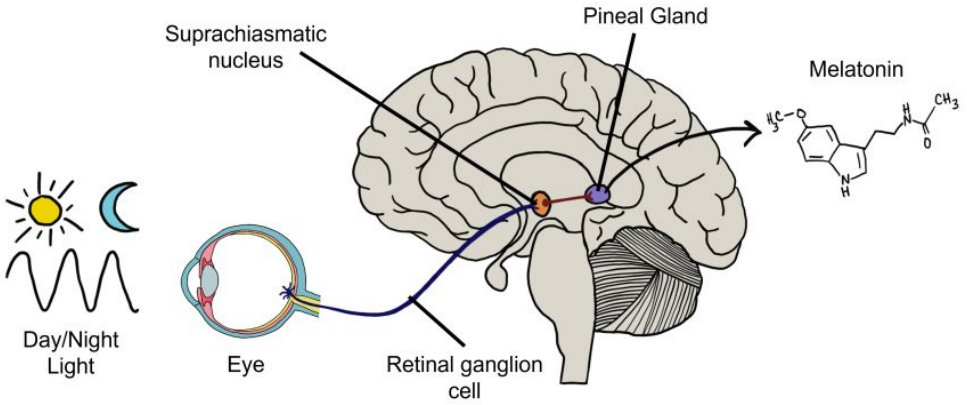
1. **ACh arouses cortex during dreams**
2. **GABA promotes sleep**
3. **Burst of 5HT shuts off REM**
4. **Histamine is released when brain cools**

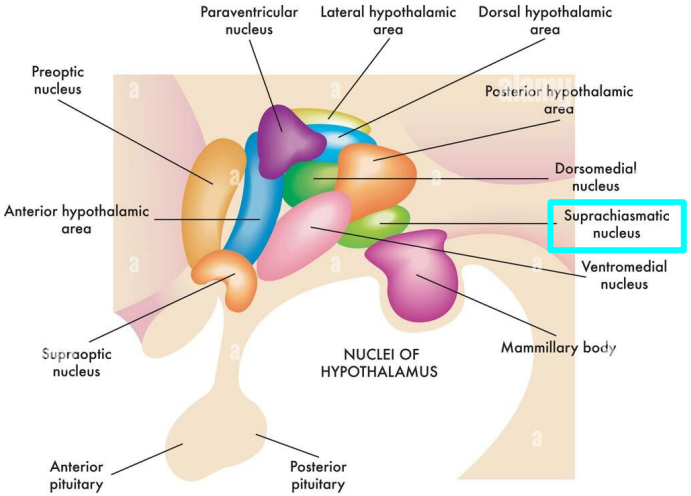


Biological Rhythms

: what regulates sleep and arousal sys, mediated by interaction b/w Suprachiasmatic Nucleus & Pineal Gland

1. **Suprachiasmatic Nucleus (SCN)** of Hypothalamus (just anterior to Optic Chiasm) = Circadian clock
   - Establishes rhythm of ~ 24 +/-1 hours
   - very robust: even if blinded, food/water/oxygen-deprived
   - Releases hormones into bloodstream & projects to other Hypothalamic Nuclei, Brainstem, Pituitary glands
   - Cycle regulated through projections to and from Pineal Gland

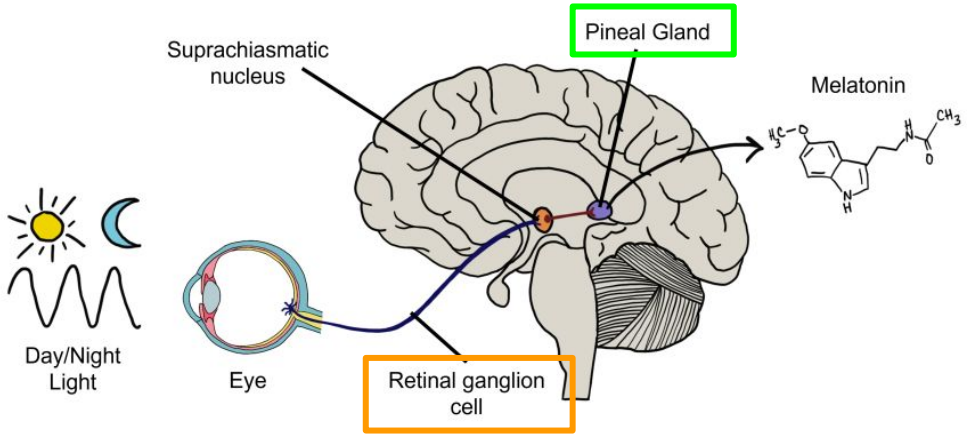


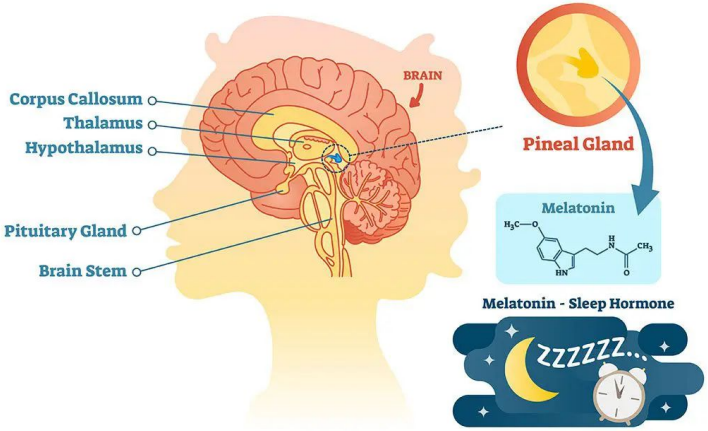


Biological Rhythms

: what regulates sleep and arousal sys, mediated by interaction b/w Suprachiasmatic Nucleus & Pineal Gland

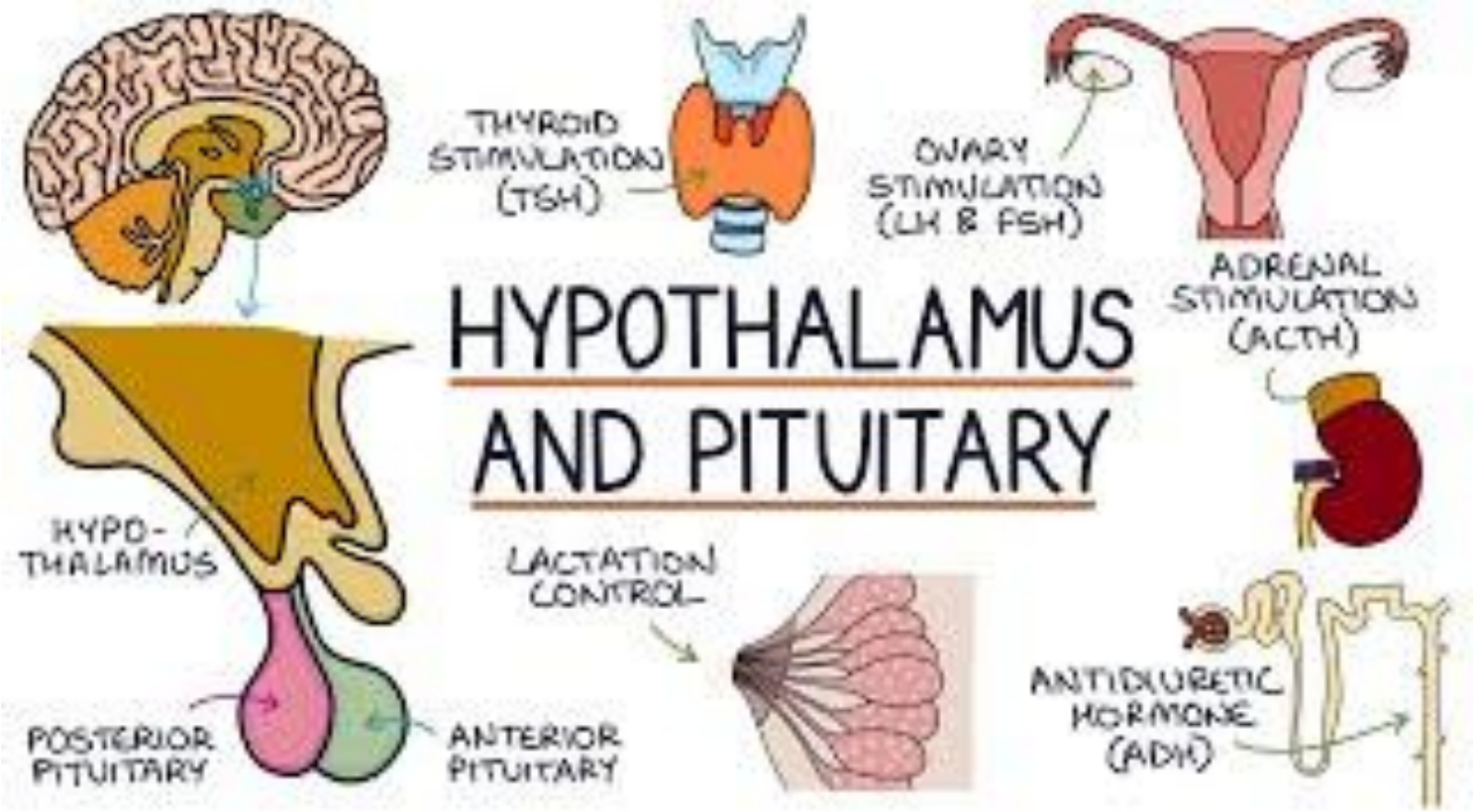
2. **Pineal Gland** (just superior to midbrain, posterior to Thalamus)
   - decide "whether to produce hormone **Melatonin** or not?" which increases sleepiness
   - SCN has receptor sites for Melatonin, so when Pineal increases Melatonin output at end of day → helps regulate cycle
   - When light comes up in the morning, the light goes to SCN via Retino-Hypothalmic Path produces inhibitory output to Pineal → decreases Melatonin production, allows wakefulness





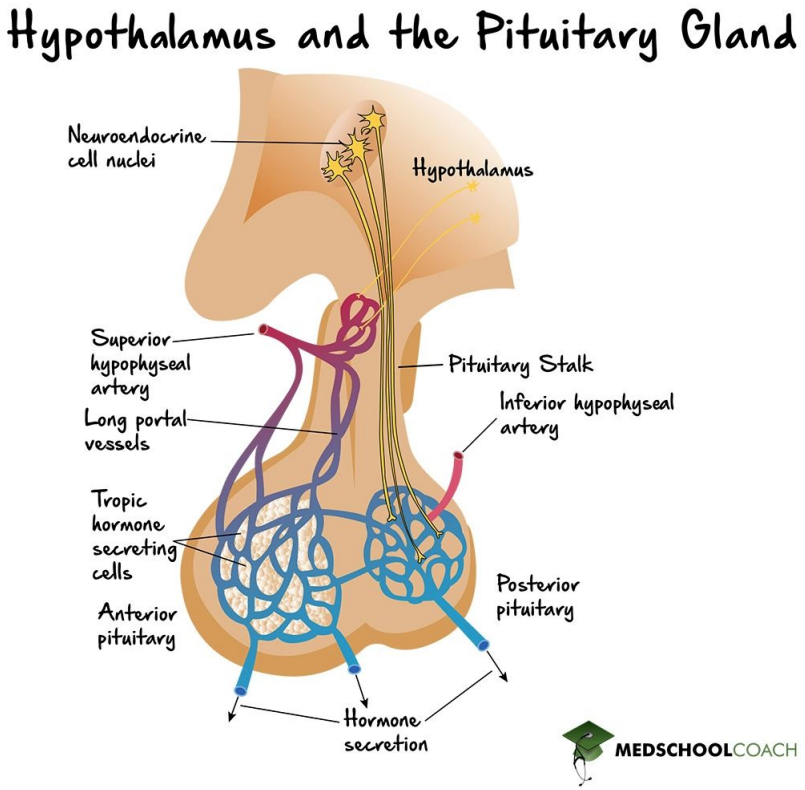
Sexual Development & Behavior

Hypothalamus



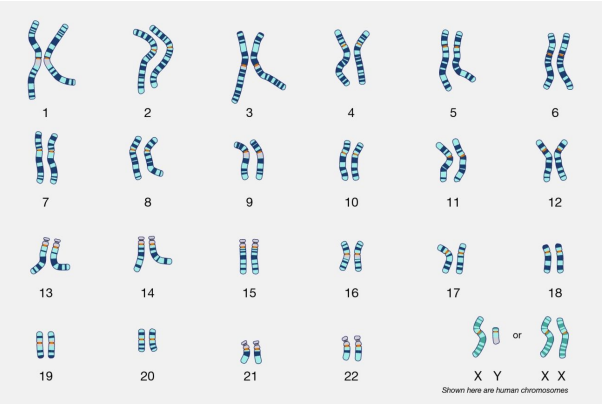
Hypothalamus

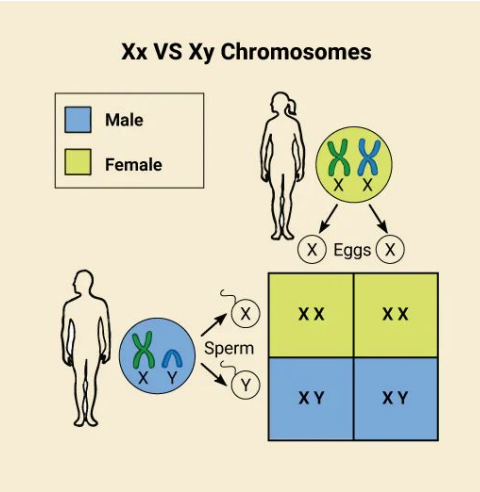
- Anatomically and functionally related to the **pituitary gland**
- controls endocrine systems via commanding Pituitary Gland
- produces **Releasing Hormones** that flow via blood vessels to Anterior Pituitary > “Hey Pituitary, RELEASE hormones”
- Releases other hormones as NTs via axons to posterior pituitary
- Reproductive Hormones have Organizing effects (on anatomy in fetal development & puberty) & Activating effects (influence behavior)
- Communicates to adrenal gland, and gonads (ovaries/testis)



Chromosomes

- 23 pairs inherited from your parents
- Chromosomes are necessary but insufficient for determining gender
- Female: XX, Male XY, but hormone activity is required to determine gender!
- **Steroid hormones**
  - **Androgens**: General term to describe **male** hormones (e.g., testosterone)
  - **Estrogens**: General term to describe **female** hormones (e.g., estradiol)
- But we all have both! (mix of Androgens and Estrogens in varying proportions)
  - Males have more androgens than estrogens
  - Females have more estrogens than androgens





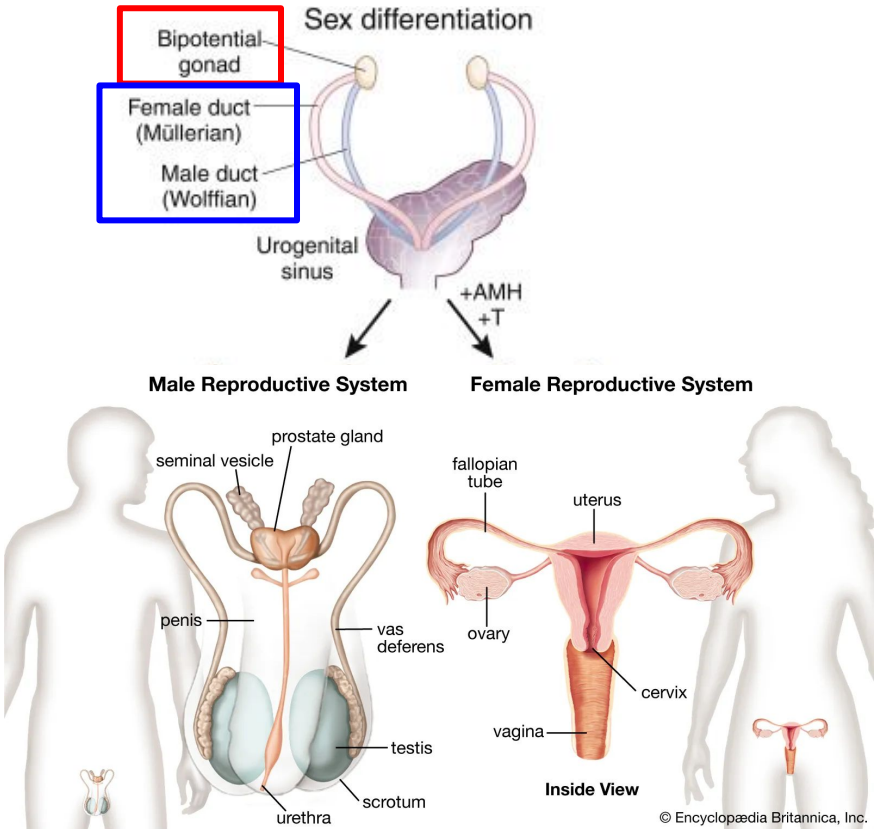
Organizing Effects

Fetal Development of Sexual Anatomy

- every mammalian fetus has the anatomical <u>precursors</u> for both sexes

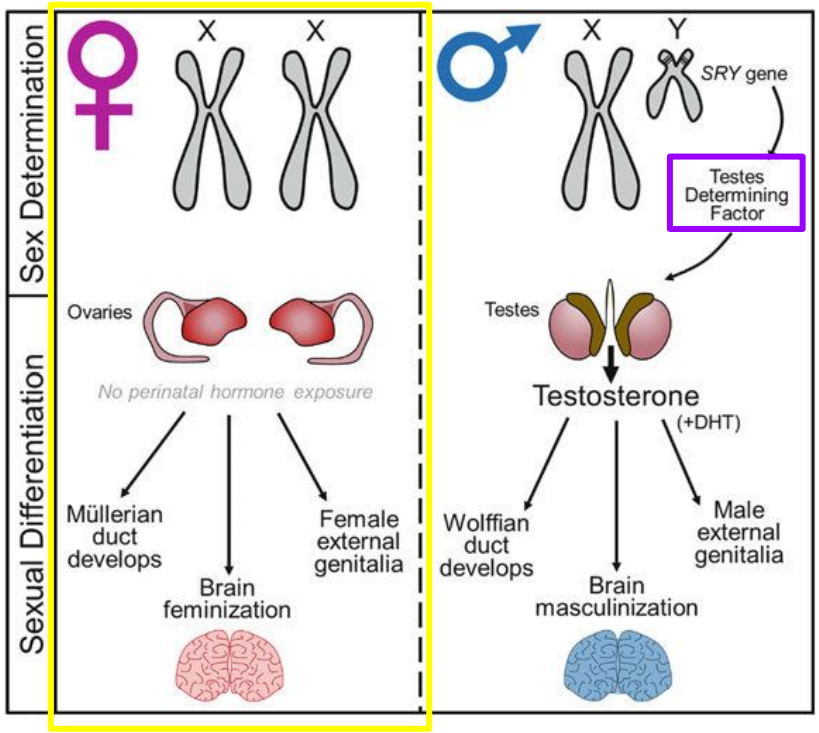
e.g., same initial structure…

1. **Gonads** (later become either Testes or Ovaries)
2. **Gentalia** (later become M/F anatomy, depending on Androgens/Not)
3. Each fetus has both
   a. (M) Wolffian duct → Vas Defrens & Prostate
   b. (F) Muellerian duct → Fallopian Tubes & Uterus
   c. other system degenerates and these ducts development also depends on Androgens/Not



Organizing Effects

- The genes controlling M/F body & brain development are also present in both sexes, except…



the "SWITCH"

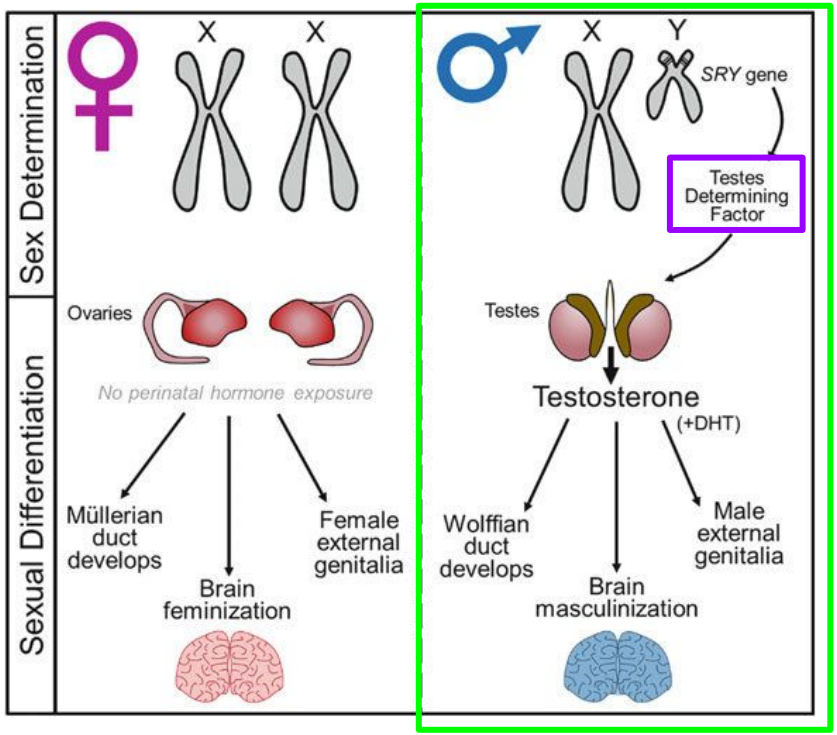
- found only on Y chromosome
- signals production of the **Testis-Determining Factor (TDF) Enzyme**
- occurs during Critical Period of fetal development (TDF appears 6-8th week, genitals developed by 4th month)

If TDF is **NOT** present → Female

- ovaries differentiate, Mullerian sys develops, Wolffian regresses, female genitalia develop
- But what if…
  1) fetus is XY, but lacks specific gene for TDF
  2) fetus is XO (Turner's Syndrome, no Y chromosome)
  : both will develop internally & externally as female, but will be infertile, since two Xs are required to produce ova (eggs)

Organizing Effects

- The genes controlling M/F body & brain development are also present in both sexes, except…



If TDF **is** present → Male

- testes differentiate, producing Androgens, Wolffian ducts and male genitalia develop
  - testes also produce Anti-Mullerian Hormone (AMH -inhibits Mullerian sys development)

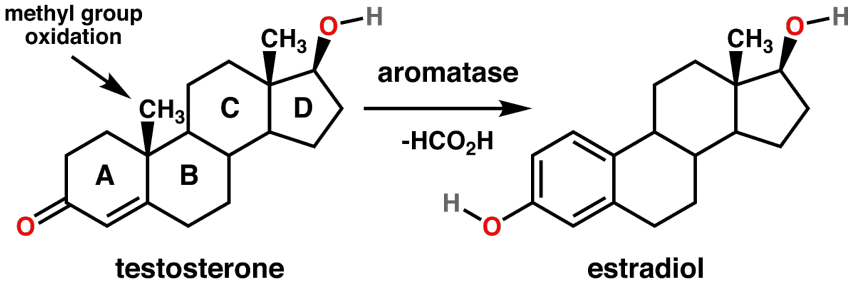
- If XY fetus is Androgen-insensitive, testes still produce Androgens and AMH
  - but the lack of androgen receptors inhibits Wolffian system development
  - while AMH is still functioning → inhibit the Mullerian system

  → no internal sex organs and so will be infertile

- If XX fetus is exposed to Testosterone during critical period, develops (semi-)male form, sometimes infertile
  - some tendency for these individuals to be homosexual (+ body, brain, societal influences)?

Estrogen and its Masculinizing Effect

- When testosterone enters a fetal cell, it is “aromatized” or converted into Estrogen, which leads to male development
- One can ask… if the Mother has Estradiol present, why aren’t all offspring masculinized?
  - If there is exposure to estradiol from the mother, **Alpha-Fetoprotein** (AFP) binds to it, preventing it from influencing the fetus’s sexual development
    - AFP: produced by the fetal liver, allows the fetus’s own hormones to determine its gender
  - But… when excessive estrogens administered (e.g., DES, synthetic estrogen that was prescribed to pregnant women between 1938 and 1971 to prevent miscarriage), this safeguarding protective sys can be overwhelmed → potential masculinization in the fetus



Testosterone can be converted into estrogen through an enzyme called **aromatase**

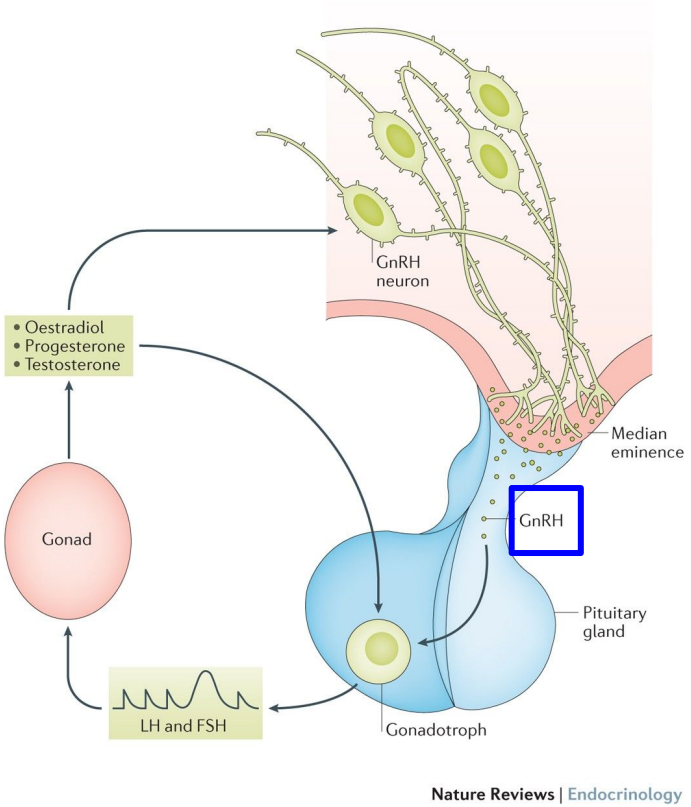
Secondary Sexual Characteristics

During Adolescence

- In both sexes, hypothalamus releases **Gonadotrophin-Releasing Hormones (GnRH)**
    - causing Anterior Pituitary to release Gonadotropic Hormones, Lutenizing (**LH**) & Follicle Stimulating Hormone (**FSH**)
        - Present in both males and females

- LH and FSH stimulates the testes in **males** to produce sperm and testosterone (and other androgens, and low levels of estrogens) → adult male form

- LH and FSH stimulates the ovaries in **females** to release ova and estradiol (and other estrogens, and low levels of androgens) → adult female form
    - In females, Androstenedione (androgen) is released by adrenal glands to stimulate secondary hair growth



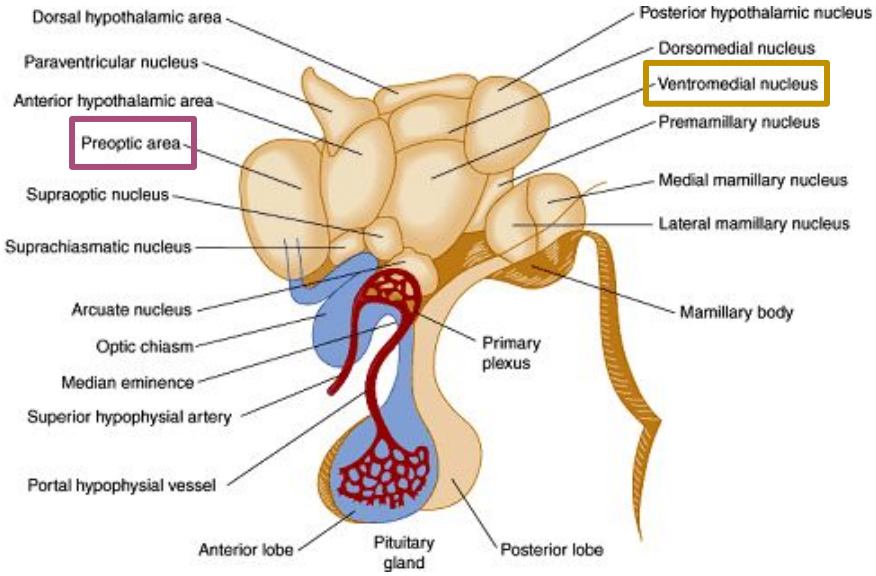
Sexual Differences in Brain Development

- Presence/absence of testosterone during prenatal period and early infancy → differences in brain

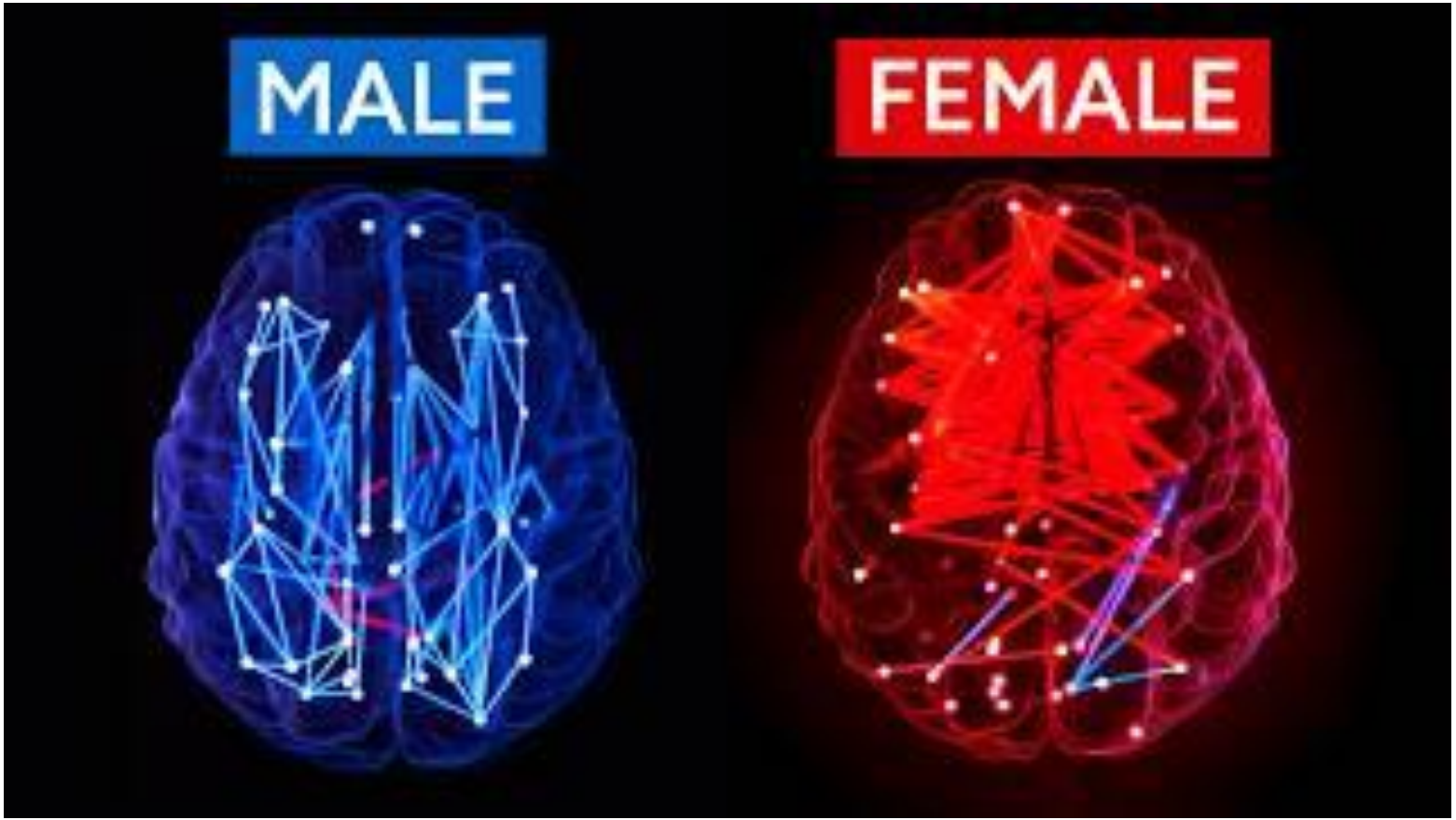
Hypothalamus

- **Medial Preoptic Area (MPOA)**
  - Has androgen receptor sites, esp. active during Male sexual behavior
  - Includes the **Sexually Dimorphic Nucleus (SDN),** 2.5X larger in males (vs. females)
  - Early testosterone is required for SDN development and without it, males will not respond to androgen activity

- **Ventromedial Nucleus (VMH)** is larger in females than males
  - Has estrogen receptor sites, esp. active during Female sexual behavior
  - Develops in absence of early Testosterone
  - Also regulates feeding behavior or control of eating



Gender differences in Brains



Happy Friday!