Cogs17 Neurobiology of Cognition

Lecture 8: Arousal & Sleep

Arousal Systems

- **Reticular Formation** = "Net" from Medulla & Pons > throughout Forebrain; Also receives from all sensory systems
  - Alerts brain, stimulating Thalamus and Basal Forebrain (and from there, cortex) via **ACh** and **Glutamate**

- **Locus Coeruleus** (="Dark Blue Place") Part of Reticular Formation in Pons,
  - Especially active during **new task** & during vigilance (sustained attention) Can also be inactive while awake
    - Widespread connections, including Thalamus, Cortex, & Hippocampus - plays a role in establishing **memory**
    - Releases bursts of **Norepinepherine** (**NE**) - Amphetamines (NE-agonists) likewise increase alertness, activity

- **Basal Forebrain** (just anterior and dorsal to Hypothalamus) releases **ACh** thruout cortex for arousal & **GABA** to inhibit cortex
    - Damage to Basal Forebrain implicated in **Alzheimer's Disease**; arousal critical to memory activation
  - **Adenosine** a by-product of cell metabolism, builds up thru day, released in brain, inhibits Basal Forebrain's release of ACh
    - Allows GABA connections to dominate, suppressing cortical activity, promotes sleep
      - NOTE: **Caffeine** blocks Adenosine receptors, allowing Basal Forebrain to continue to arouse brain

NOTE: Excitatory NT **Orexin** from **Lateral Hypothalamus** helps maintain arousal in above systems

- Takes into consideration homeostatic conditions (hunger, thirst, temperature, sleep needs etc.)

STAGES OF WAKEFULLNESS / SLEEP

Electro-Encephalogram (**EEG**) used to characterize brain activity during different states of wakefulness/sleep
- Gross average of the electrical potentials of the neurons in a general area of the brain (mostly Neocortex)
- Electrodes attached to scalp record Frequency (# changes in average potential/time) & Voltage (average amplitude)
- Simultaneous changes in potential (negative graphed above zero axis, positive below) summate such that...
  - Neural de-synchrony => High Frequency (w/variable Voltage) waves = Multiple sources of stimulation: "many pebbles"
  - Neural synchrony => Low Frequency, High Voltage waves = Coherent source of stimulation: "one big rock"

Awake, active => **Beta** Activity = 18-24 Hz, Very high frequency - very desynchronized
Awake, relaxed => **Alpha** Activity = 8-12 Hz, Like above, but somewhat lower frequency, somewhat desynchronized
Sleep 1 => **Theta** Activity = 4-7 Hz, Lower freq, still quite irregular, significantly more synchronized
Sleep 2 => Mostly **Theta** Activity, but with many interspersed **Spindles** and **K Complexes**
- Spindle and K Complex = intermittent bursts of high freq and/or voltage, as brain settles into deeper sleep
  - K Complex = Brief period of Delta activity Spindles = Help gate external stimuli from reaching cortex

Sleep 3 => **Delta** Activity = **<** 4 Hz observed in less than 50% of this stage, Very low freq, higher voltage, **very** synchronized
Sleep 4 => **Delta** Activity, in more than 50% of this stage, hardest to wake Stages 3 and 4 = **Slow Wave Sleep (SWS)**
- SO, as move into deeper sleep, freq decreases & voltage increases as brain activity becomes **synchronized**
- Heart rate and breathing rate also decrease, and brain is less responsive to external stimuli

REM (**Rapid Eye Movement**) or "**Paradoxical Sleep"** because of contradictory set of conditions that occur:
- EEG is desynchronized, High freq (like Sleep 1 or even Awake), Low voltage (only Sleep 1 is lower): "Imaginary pebbles?!"
- Heart rate, breathing rate, blood pressure more variable than in other sleep stages
- Eyes move, genitalia active, but postural muscles paralyzed, loss of muscle tonus thru most of body (=**Atonia**)
  - Atonia: Pons signals Medulla, which actively inhibits Motor Neurons in Spinal Cord & Cranial Nerves (e.g. Trigeminal)
- In REM, external stimuli detected, will awaken if meaningful (e.g. name) but otherwise may incorporate into dreams instead
- Highly correlated (tho not 100%) with dreaming – i.e. with "story" dreams
  - Some dream imagery in other stages: e.g. Night Terrors (scream awake, but w/out narrative nightmare) occur during Stage 4
- NOTE: Higher sensory areas of cortex often active during REM
  - Also includes activation of Cranial Nerves from Tegmentum for Rapid Eye Movement

Sleep Cycle = 90 Minutes from Stage 1 to REM: Stage 1, 2, 3, 4, 3, 2, REM, 2, 3, 4, 3, 2, REM, 2, 3, 2, REM, 2, REM . . .
- Stage 4 becomes increasingly shorter as night goes on, drops out altogether after 2-3 cycles, then Stage 3 drops out
- REM becomes increasingly longer as night goes on

Sleep deprivation=> Lethargy, poor conc, irritability; Inc temp, metabolism & appetite; Decreased resistance to infection
- When allowed sleep, will show more cycles of/longer in Stage 4 as well as REM (**REM Rebound** – see below)

REM deprivation: Wake subject when EEG = REM (or when atonia makes cat fall off platform into water)
- System attempts to enter REM more & more frequently; When allowed to REM, shows Rebound effect
- If continuously deprived =>Irritable, poor concentration, anxious => Psychosis, hallucination, death

Functions of Sleep & Dreaming - ?! Controversial
- Sleep is restorative. But not clear why some species (e.g. prey) can sleep so much less than others (e.g. predators)
- Dreaming warms sleeping brain; Some evidence REM esp helps consolidate memory; May help resolve psychol conflict

Neural control of sleep…

- **Hypothalamus** nuclei are critical in initiating & regulating sleep
  - **VLPOA** (Ventro-Lateral Preoptic Area) releases **GABA**, inhibiting Brainstem and (via **Basal Forebrain)** the Cortex
  - **Tubero-Mammillary Body** of Hypothalamus releases excitatory **Histamine 1** after periods of Slow Wave Sleep
    - Possibly based on Pre-Optic Hypothalamus's assessment of fall in brain temperature??
    - This indirectly enables initiation of ACh release from Pons >> initiates PGO Wave
- **PGO Wave** = Sequence of activation in Pons => (Lateral) Geniculate => Occipital Cortex - initiates **REM**
  - Excitatory **ACh** arouses (**desynchronizes**) visual (& other sensory/motor) pathways
    - ACh builds up just before REM, holds steady during, then drops off radically as REM ends
    - Note this arousal enters thru posterior cortex (where Basal Forebrain arousal/de-arousal enters thru anterior cortex)
  - **Raphe Nuclei** (medial Pons - Damage = no sleep) Decreasing Serotonin (**5HT**) output > sleepiness, irritability if not sleep
    - 5HT very low during sleep, none during REM, then Raphe produces sudden, strong burst of 5HT, **shuts REM off**
    - 5HT gradually falls, shifting system back into Slow Wave sleep. When 5HT flat, PGO again initiated by Pons via ACh

SO, stages of sleep are controlled by an **interaction** of different types & sources of neural activity

Biological Rhythms

The above sleep and arousal systems are regulated by biological rhythms, mediated by interaction between **SCN & Pineal Gland**

- **Suprachiasmatic Nucleus** (**SCN**) of Hypothalamus (just anterior to Optic Chiasm) = **Circadian Clock**
  - Establishes free-running rhythm in humans (and other land animals) of activity/rest of ~ 24 +/-1 hours
  - Very robust: even if blinded, food-, water-, oxygen-deprived, anesthetized, brain damaged; or isolated cells in tissue culture!
    - **Genetic**: Replace SCN in adult hamster with fetal SCN cells from 20-hour-cycle strain, hamster will adopt 20 hour cycle
    - Releases hormones into bloodstream & projects to other Hypothalamic Nuclei, Brainstem, Pituitary glands
  - Cycle regulated through projections to and from Pineal Gland (see below)

- **Pineal Gland** (just superior to midbrain, posterior to Thalamus)
  - Shows daily cycle of production of hormone **Melatonin** which increases sleepiness
  - SCN has receptor sites for Melatonin, so when Pineal increases Melatonin output at end of day, helps regulate cycle
    - Melatonin can be taken as sleep aid a few hours before bed, helps reset clock (e.g. anti-Jet Lag)
    - Seasonal Affective Disorder (SAD) = less light in winter, some people over-produce Melatonin; Light therapy can help
  - First light of day to SCN via Retino-Hypothalmic Path produces inhibitory output to Pineal
    - Decreases Melatonin production, allows wakefulness

-Together, above interaction becomes your **Zeitgeber** = "Time Giver"

- Possible to reset clock, via exposure to bright light, strenuous exercise, seasonal or travel-based changes etc.
- e.g. Receptors in Retina (not Rods or Cones but specialized Ganglions!) w/photopigment **Melanopsin** react to light
  - These Receptor's axons synapse in SCN (not in retina or thalamus!) via collateral of Optic Nerve

= **Retino-Hypothalamic-Path**