Neural Activity

- Lower metabolic and neural activity rate in the brain during sleep:
  - SWS < NREM stage 1 & 2 < awake

- Exception is REM sleep, where some areas actually more active (e.g., pons)

The brain and wakefulness: *The reticular formation and the ascending reticular activating system (ARAS).*

Reticular formation:
- One of the oldest parts of the brain.
- A poorly differentiated part of the brain stem (brain stem = pons, medulla oblongata, midbrain, reticular formation), centered roughly around the pons.
- Involved in routine action: waking/sleep, walking, lying down.
- Speculation that it may be involved in about 25 behaviors (e.g., eating, urination, sex, introversion/extroversion).
**Ascending Reticular Activating System (ARAS)**

- Part of the Reticular Formation.
- Critical for maintaining the waking state.
  - Projects to the thalamus, hypothalamus, and basal forebrain.
  - Excites widespread areas of cortex to produce arousal/alertness/wakefulness.
  - Deactivated during NREM sleep, but reactivated during REM sleep.
The brain and NREM sleep

• The basal forebrain and adjacent hypothalamus.
  – Both structures can dampen general forebrain activity, both directly and by dampening ARAS activity
  – In animals lesions in this area cause long-lasting insomnia
  – Alzheimer’s patients who suffer from insomnia present with damage to this area.
  – Electrical and chemical stimulation of basal forebrain induces NREM sleep.
  – Adenosine acts in this area

• Other brain areas appear to also be important in regulating NREM sleep.
  – Example: the solitary nucleus is a brain stem structure near the medulla that receives sensory input and sends it to the forebrain. Stimulation in that area produces SWS.

• Recent work shows that TMS at sensory-motor area can also induce slow waves.

• TMS and “Power naps” on demand?
The brain and REM sleep

- Work driven largely by transection studies on cat brain stem

13

The brain and REM sleep

- Transection at B separates the brain stem from the forebrain.
  - Animals can survive for weeks or months
  - Brain stem & body show signs of REM sleep (theta waves & atonia)
  - Forebrain EEG shows NREM stage cycling but no phasic REMS features.
  - Thus, REMS is governed by brain stem structures.

14

The brain and REM sleep

- With transection at C, between medulla and pons, REM sleep signs are observed only in rostral structures (including pons and forebrain).
  - If pons is destroyed, no REM signs at all occur.
  - With transection both caudal and rostral to the pons (C and B), isolating the pons intact, signs of REMS can be seen in the pons only (periodic theta onset; REM-on REM-off cell oscillation).
  - Thus REM sleep controlled by structures in the pons.

15

The brain and REM sleep
The Brain and REM sleep

• Cells in the pons that are closest to the cerebellum are referred to as REM-on cells.
  – These neurons excite neurons in the thalamus, which in turn excite neurons in the cortex.

• Cells in other parts of the pons mediate a REM-off system.
  – During wakefulness, activity of these cells is regular (tonic)
  – During REMS these cells have lowest activity and many are completely silent.

The Brain and REM sleep

• Specific REMS components have been traced to specific brain structures.
  • Example: atonia vs. other components
    – 1) Small medulla lesions block atonia while not affecting other aspects of REMS.
    – 2) Injection of a cholinergic agonist (carbachol) into the dorsal pons blocks all aspects of REMS except atonia.

Chemistry of Wake / Sleep

• In waking state, high levels of:
  – Norepinephrine
  – Dopamine
  – Acetylcholine (also high in REM sleep)
  – Histamine (blocking it causes drowsiness)
  – Glutamate (also high in NREM sleep)
  – Serotonin (high relative the REM, but even higher in NREM sleep than when awake)
    • Levels: REM < awake < NREM
  – Adenosine (gradually increasing levels while awake)
Chemistry of Sleep

- Orexin: neurotransmitter that regulates wakefulness and appetite.
  - Regulates levels of norepinephrine, dopamine, acetylcholine and histamine
  - Drugs that activate orexin (modafinil) can increase alertness with fewer side effects of amphetamine.

- Data on modafinil vs. dextroamphetamine vs. placebo
  - Tested using pilots in a helicopter flight simulator

Chemistry of Sleep

- In NREM sleep, high levels of:
  - Serotonin:
    - Maximum level during NREM: facilitates sleep onset by dampening the brain’s response to sensory input
    - Tryptophan is an ingredient in synthesizing serotonin, has mild sleep onset effect (warm milk)
    - Produced in raphe nuclei (locus of REM-off cells)
    - Selective serotonin uptake inhibitor (SSRI) anti-depressants limit REMs
  - GABA: inhibitory neurotransmitter
  - Glutamate: promotes slow waves and spindles

- In REM sleep, high levels of Acetylcholine (back to awake levels)
  - Histamine, norepinephrine/dopamine dramatically reduced