Reticular Formation and Sleep/Wakefulness

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• The reticular formation is the oldest part of our nervous system phylogenetically.

• It is present throughout the midbrain, pons and medulla.

• Typically, the reticular formation is regions of the brainstem between clearly defined nuclei and tracts.

• It is groups of neurons embedded in a seeming disorganized mesh of axons and dendrites.
• Although seemingly disorganized, over 100 groups of neurons related by function and connections have been identified in the reticular formation.
Reticular Formation

- Locus Coeruleus
- Cortex
- Spinal Cord
- Motor Nuclei
- Hypothalamus
- Thalamus
- Periaqueductal Gray
- Hippocampus
- Cerebellum
- Superior Colliculus
- Amygdala
• The reticular formation receives input from all parts of the nervous system... every sensory system, all parts of the motor system, thalamus, hypothalamus, cortex, etc.

• The output of the reticular formation is as diverse as its input.

• Many of the neurons in the reticular formation have large, highly branched dendrites that receive diverse information.
The reticular formation has a major role in regulation of:

- Motor control
- Sensory attention
- Autonomic nervous system
- Eye movements
- Sleep and wakefulness
• Reticular formation (RF) in the lower pons and medulla receives motor information from premotor cortex, motor cortex and cerebellum as well as proprioceptive and vestibular sensory information.

• RF sends axons to cranial nerve motor nuclei and to ventral horn of the spinal cord via the reticulospinal tracts.
Reticular formation (RF) initiates ‘accompanying’ movements.

Accompanying movements are subconscious and are needed in support of a consciously initiated movement. These movements are often needed to maintain balance.

Accompanying movements may precede the conscious movement.

RF is required for this type of movement.
Reticular formation (RF) integrates visceral sensory information to influence somatic motor neuron activity.

Breathing, for example, is regulated by axons from RF to cervical spinal cord. Motor neurons in cervical spinal cord control the diaphragm.

RF also has essential roles in regulating blood pressure and heart rate largely through connections with brainstem and spinal cord autonomic preganglionic neurons.
• Connections of the reticular formation are bilateral.

• RF influences motor neuron activity through interneurons.
• The reticular formation has a major role in regulation of:
  
  • Motor control
  • Sensory attention
  • Autonomic nervous system
  • Eye movements
  • Sleep and wakefulness
Sensory Attention

- Helps in filtering sensory information via reticulo-thalamic neurons
- Touch, temperature, pain, auditory, and visual stimuli
- Can help to reduce irrelevant stimuli
The reticular formation has a major role in regulation of:

- Motor control
- Sensory attention
- Autonomic nervous system (S. McLoon)
- Eye movements
- Sleep and wakefulness
• The reticular formation affects autonomic functions like
  • Breathing
  • Heart rate and blood pressure
  • Vomiting, gagging, and coughing
• The glossopharyngeal (CN IX) and vagus (CN X) nerves are important efferents
The reticular formation has a major role in regulation of:

- Motor control
- Sensory attention
- Autonomic nervous system
- Eye movements (L. McLoon)
- Sleep and wakefulness
Horizontal Eye Movements
Reticular Formation

• The reticular formation has a major role in regulation of:
  • Motor control
  • Sensory attention
  • Autonomic nervous system
  • Eye movements
  • Sleep and wakefulness
Sleep & Wakefulness

- Sleep and wakefulness are **both** active processes.
• The reticular activating system from midbrain and pons is required for wakefulness.

• Noradrenergic neurons in the locus coeruleus and serotonergic neurons in the raphe nucleus of the reticular formation project to cortex and are required for wakefulness.
Sleep & Wakefulness

Circadian Rhythm
- Cyclical event with periodicity of about 24 hours
- Interplay between levels of cortisol and melatonin
  - Melatonin peaks in dark
  - Cortisol peaks in light

Melatonin

Cortisol
Sleep & Wakefulness

Even in total darkness, this *approximately* 24 hour periodicity is maintained, but it is shifted.

In humans in total darkness, circadian rhythm is closer to 25 hours
Sleep & Wakefulness

Suprachiasmatic nucleus

- Intrinsic pacemaker

- Synchronizes rhythms to the light/dark cycle

- Receives input from the retinal ganglion cells

- Sends output to many brain regions
  - Including pineal
Sleep & Wakefulness

Suprachiasmatic Nucleus

- Green – input from retina
- Red – output to other brain areas
Sleep & Wakefulness

- SCN sends projections to preoptic area and to reticular formation
• Ideally, spend 1/3 of every day sleeping
• Sleep has five stages:
  • The first four stages (non-REM sleep) are characterized by progressively decreasing frequency and increasing amplitude of EEG cortical activity.
  • The fifth, rapid eye movement (REM) sleep, is characterized by high frequency and low amplitude EEG cortical activity, similar to the awake state.
Sleep & Wakefulness

- Stages I through IV take about 1 hour; REM sleep lasts about 10 minutes, and then the cycle repeats.

- Many physiological processes that are slowed during non-REM sleep increase during REM sleep.

- Somatic muscle activity is reduced during REM sleep.

- Most dreaming takes place during REM sleep.
## Sleep & Wakefulness

<table>
<thead>
<tr>
<th>Non REM or Slow Wave Sleep (SWS)</th>
<th>Rapid Eye Movement (REM) Sleep</th>
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<tbody>
<tr>
<td>Muscle Activity</td>
<td>Reduced muscle activity</td>
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<tr>
<td>Little dreaming</td>
<td>Frequent dreaming</td>
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<tr>
<td>Few eye movements</td>
<td>Increased eye movements</td>
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<tr>
<td>Slowing of breathing</td>
<td>Enhanced breathing</td>
</tr>
<tr>
<td>Reduced BP</td>
<td>Increased BP</td>
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</tbody>
</table>
Sleep & Wakefulness

- Non-REM sleep is characterized by an inactive brain in an active body.
- REM sleep is characterized by an active brain in an inactive body.
The amount of REM sleep a person gets per night decreases with age:

- ~8 hours at birth
- ~2 hours at 20 years of age
- ~45 minutes at 70 years of age
• Cholinergic axons from the reticular formation to thalamus activate GABAergic neurons in thalamus, which inhibit thalmo-cortical axons during REM sleep.

• Pontine reticulospinal axons inhibit the activity of spinal motor neurons during REM sleep.

• Pontine RF projection to the superior colliculus is required for the rapid eye movements during REM sleep.
• The lack of sleep results in mental and physical fatigue, poor decision-making, impaired learning, emotional irritability, and an increased risk of migraine and epileptic seizures.

• Chronic insomnia results in death.

• We have little understanding of how sleep ‘restores’ the brain
In a paper published in 2013, it was shown that:

• The extracellular space in the brain of an awake mouse accounts for 14% of the brain volume; during sleep this increases to 23%.

• CSF flows through the extracellular space, and this flow increases 95% during sleep.

• Noradrenaline is responsible for the loss of extracellular space when awake.

• β-amyloid, a peptide linked to Alzheimer’s disease, is cleared from the extracellular space during sleep.

Xie et al. (2013)
Science 342:373-377
Sleep Disorders

• Narcolepsy
  – Disabling form of sleepiness
  • Sleep occurs in abnormal situations, e.g., driving
  • May also involve loss of muscle tone with ↑ emotion
  – Orexin/hypocretin: ~30 amino-acid peptide that promotes wakefulness
  – Orexin/hypocretin is decreased in some forms of narcolepsy
  – Appears to be autoimmune
Sleep Disorders

• Sleep-walking (somnambulism)
  – More common in children than adults
  – Occurs early in non-REM sleep
• Night terrors
  – More common in children than adults
  – Person appears to awaken & to be terrified, but remembers nothing in morning
  – Non-REM sleep
Sleep Disorders

- Restless Leg Syndrome
  - Pain or tingling in legs that is relieved by movement
  - Occurs during non REM sleep
  - Cause is unknown, but may be related to anemia
  - Variety of drugs have been tried, mostly anti-depressants
Sleep Disorders

• Sleep Apnea
  - Interruption of breathing
  - Decline in oxygen
  - Can be central or obstructive
  - More common in people who snore or who are obese
  - Causes awakening from sleep – sleep is less restful and restorative
Sleep Disorders

• Parkinson’s disease
  - Typically thought of as disease of motor systems
  - Characterized by tremor, rigidity, and problems with gait
  - Degenerative disease
  - Now recognized that other symptoms can appear long before motor symptoms
    - Very vivid dreams
    - REM behavioral disorder and acting out dreams
      - Inhibition of spinal motor neurons during REM sleep doesn’t occur