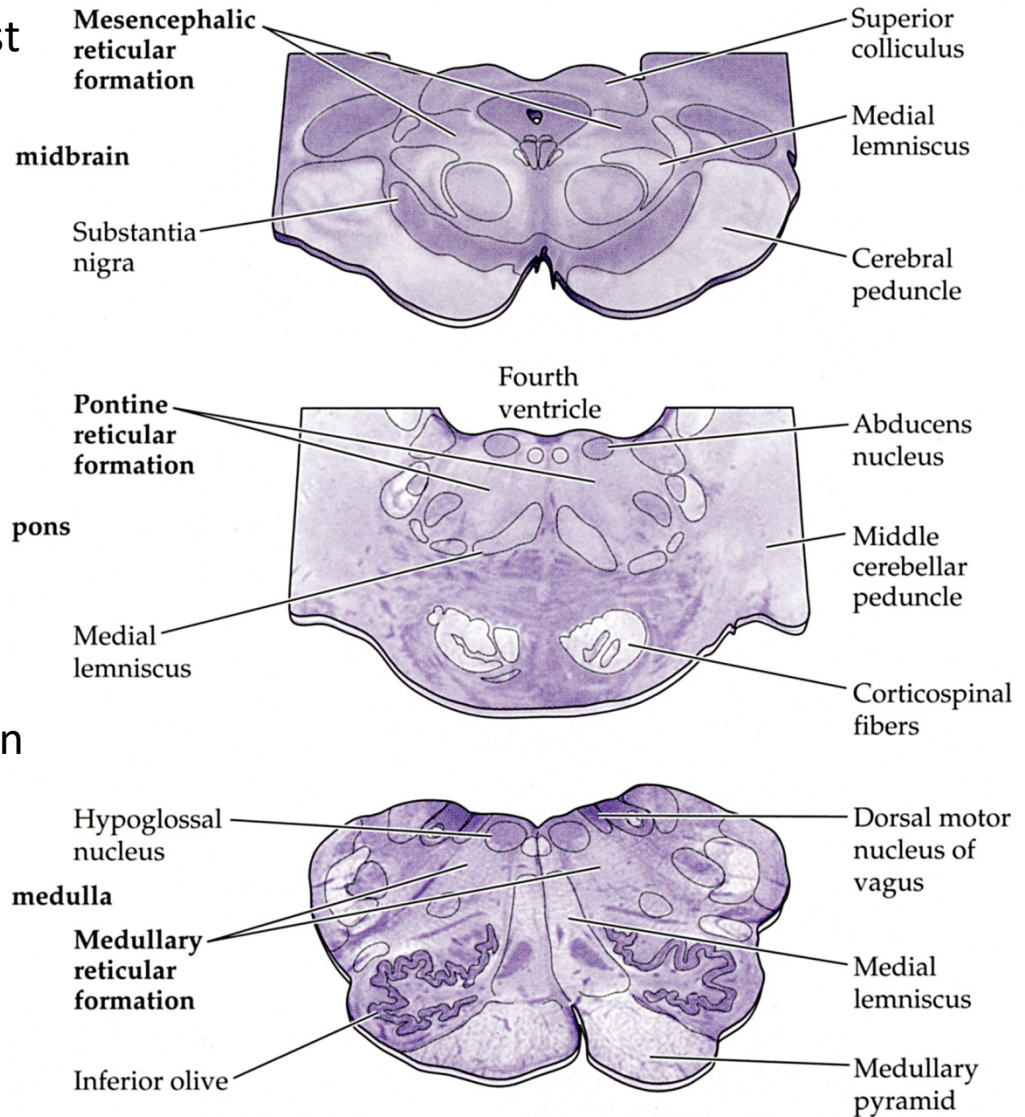


Reticular Formation and Sleep/Wakefulness

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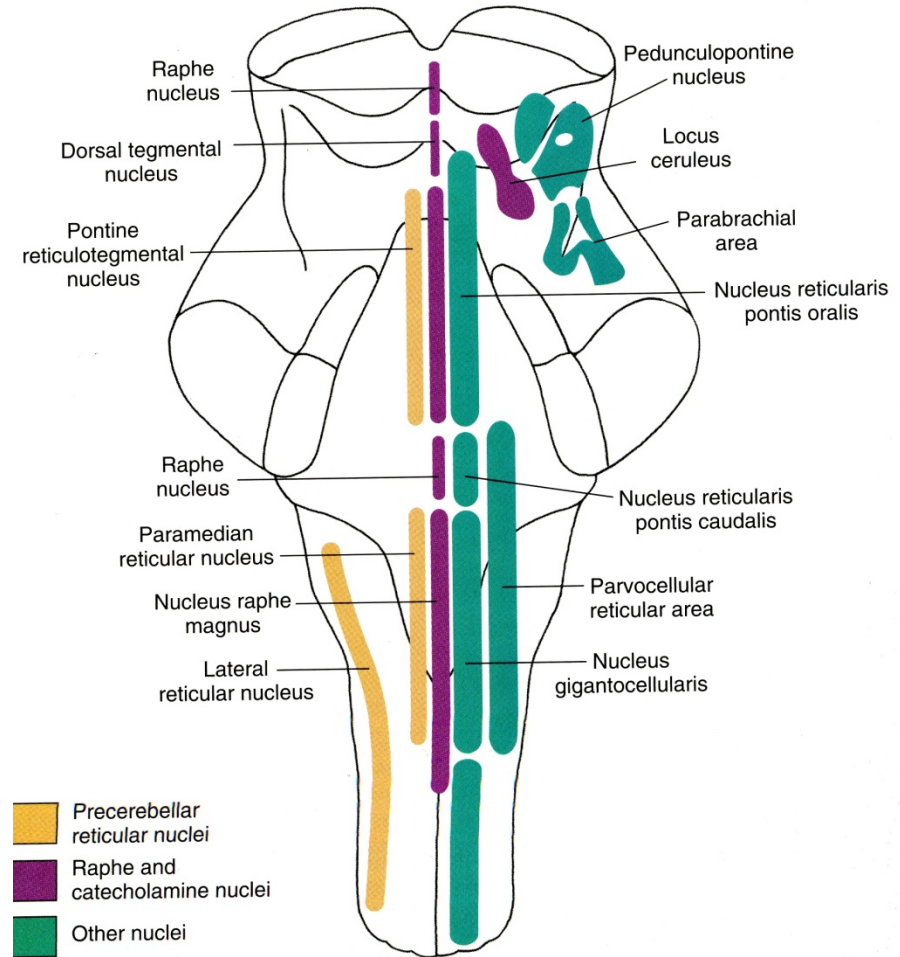
Reticular Formation

- 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 in 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.

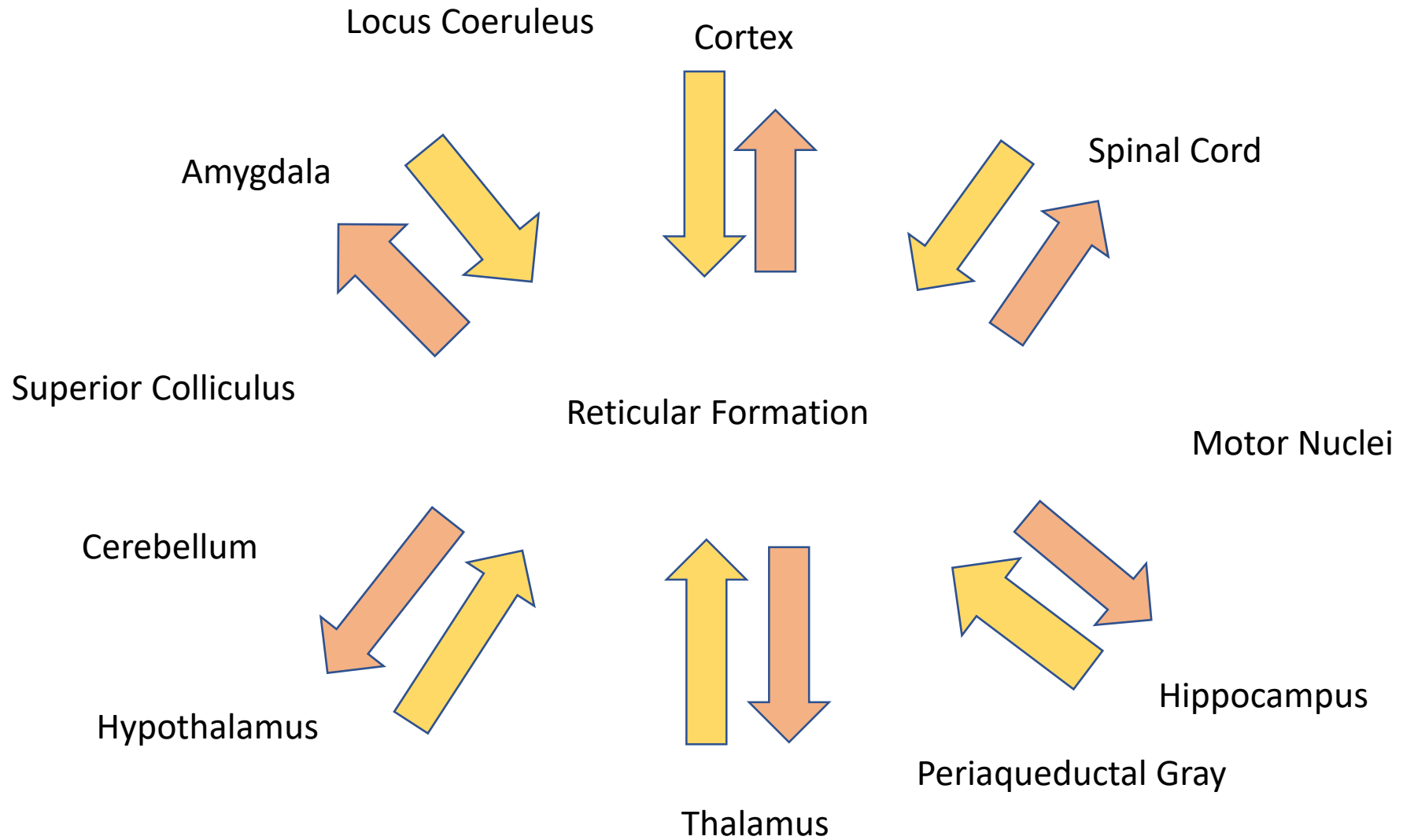


Reticular Formation

- Although seemingly disorganized, over 100 groups of neurons related by function and connections have been identified in the reticular formation.

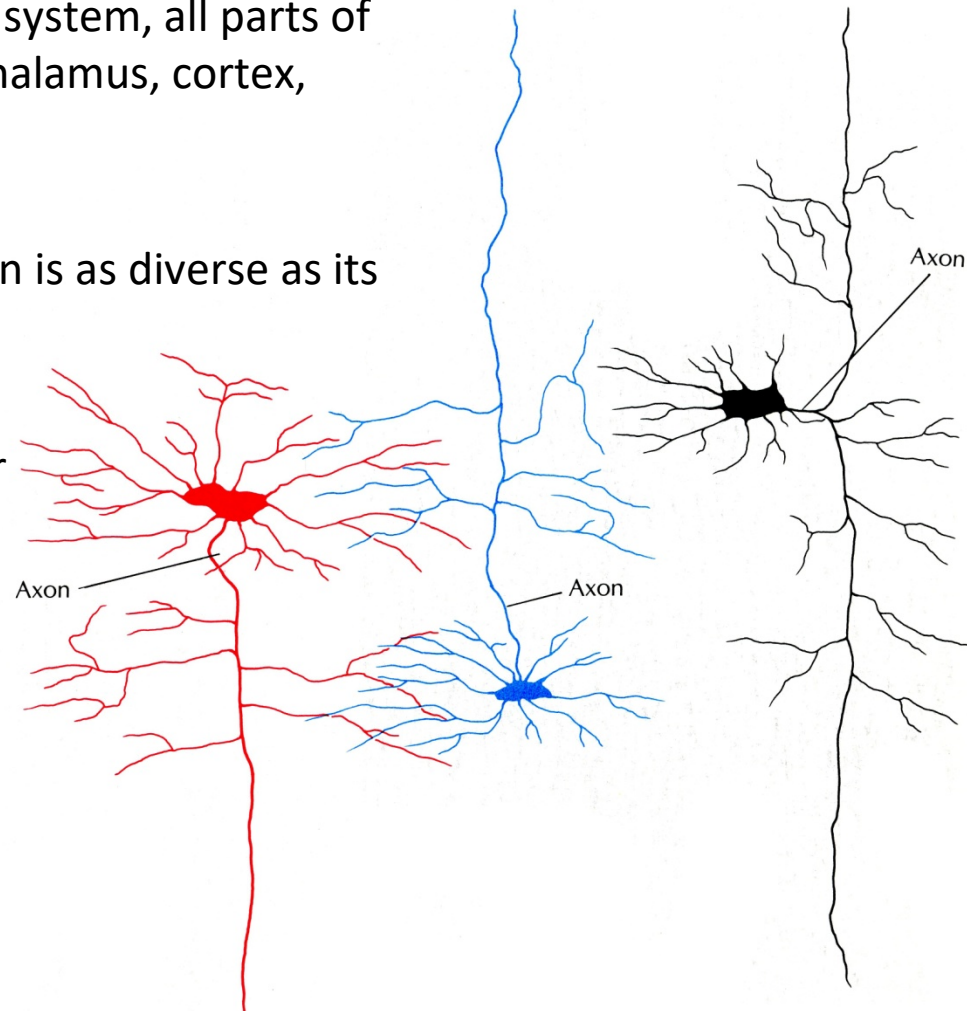


Reticular Formation



Reticular Formation

- 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.

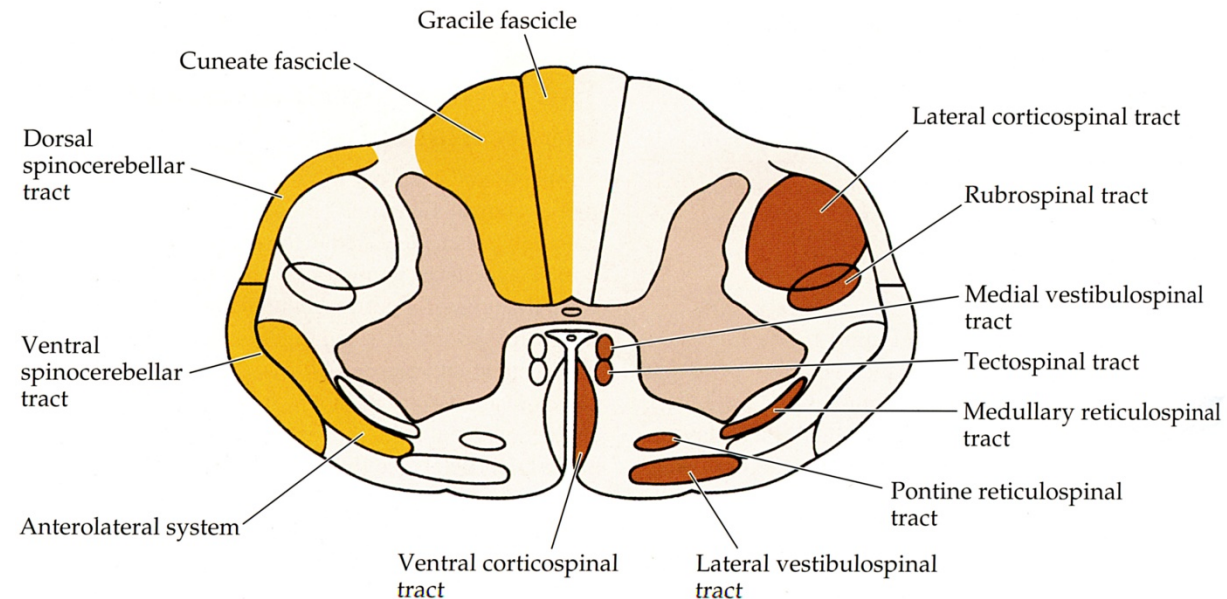


Reticular Formation

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

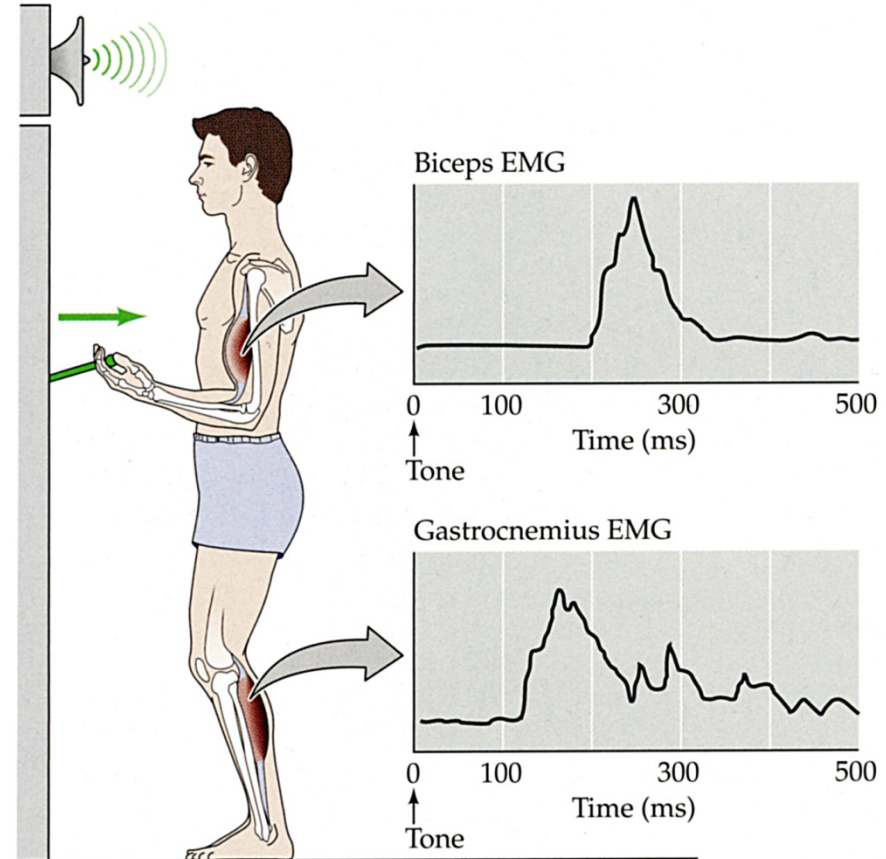
Reticulospinal & Reticulbulbar Projections

- 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.



Reticulospinal & Reticulobulbar Projections

- 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.

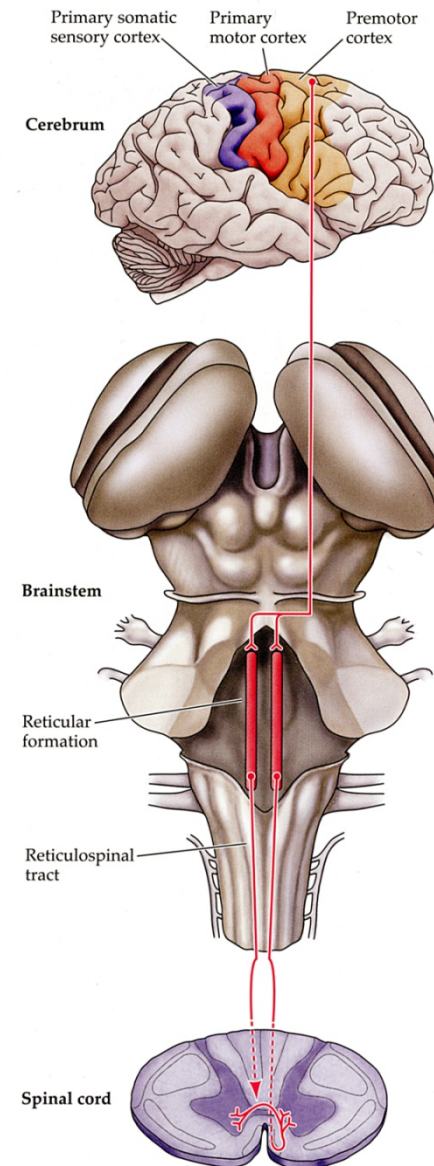


Reticulospinal & Reticulobulbar Projections

- 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.

Reticulospinal & Reticulobulbar Projections

- Connections of the reticular formation are bilateral.
- RF influences motor neuron activity through interneurons.

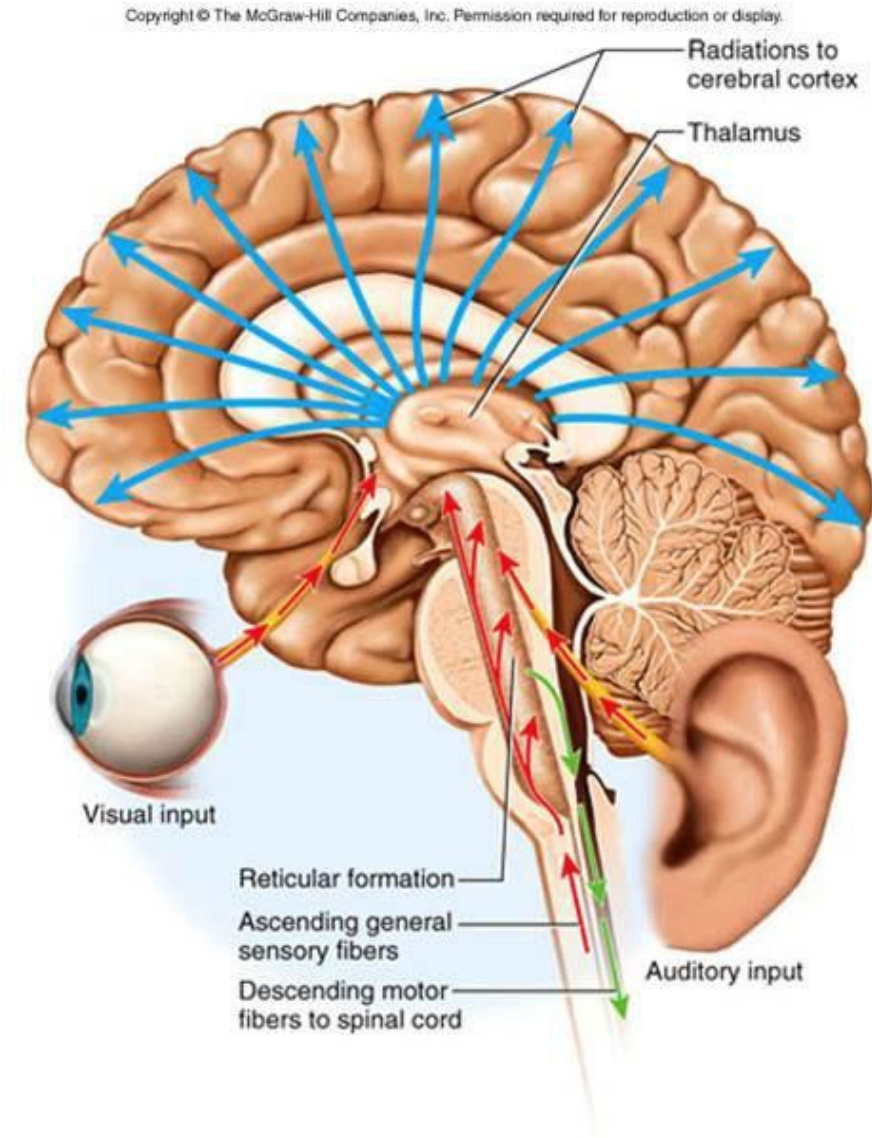


Reticular Formation

- 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

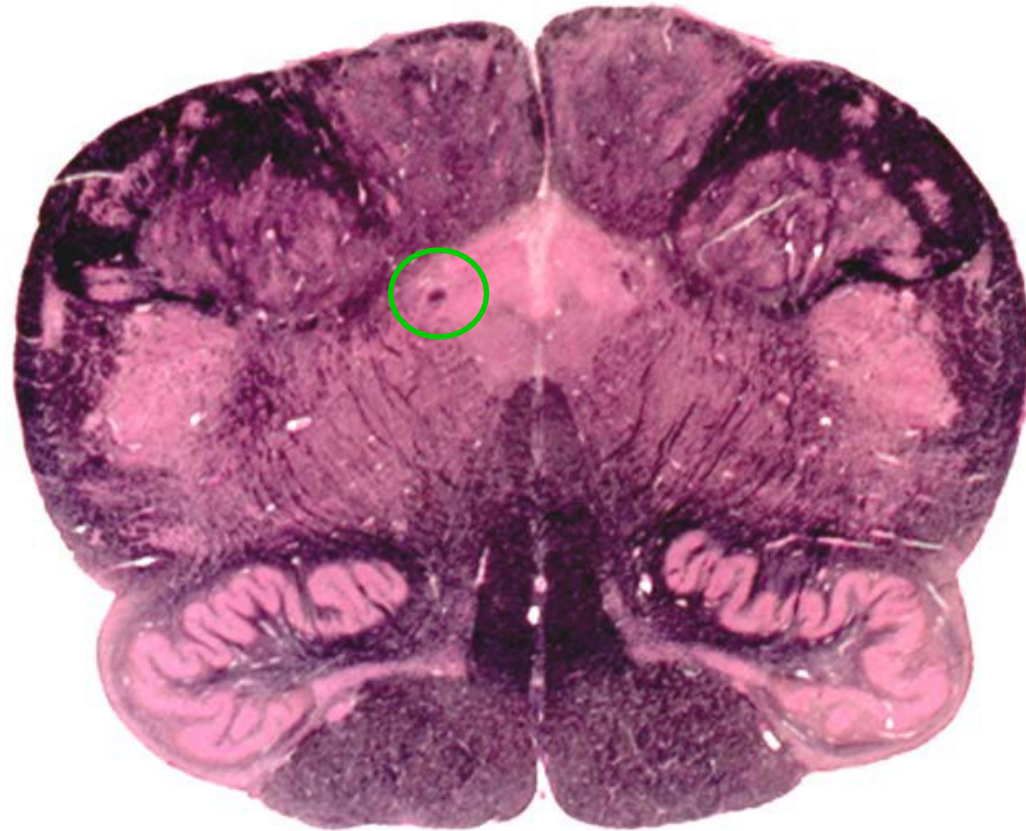


Reticular Formation

- The reticular formation has a major role in regulation of:
 - Motor control
 - Sensory attention
 - [Autonomic nervous system \(S. McLoon\)](#)
 - Eye movements
 - Sleep and wakefulness

Autonomic Nervous System

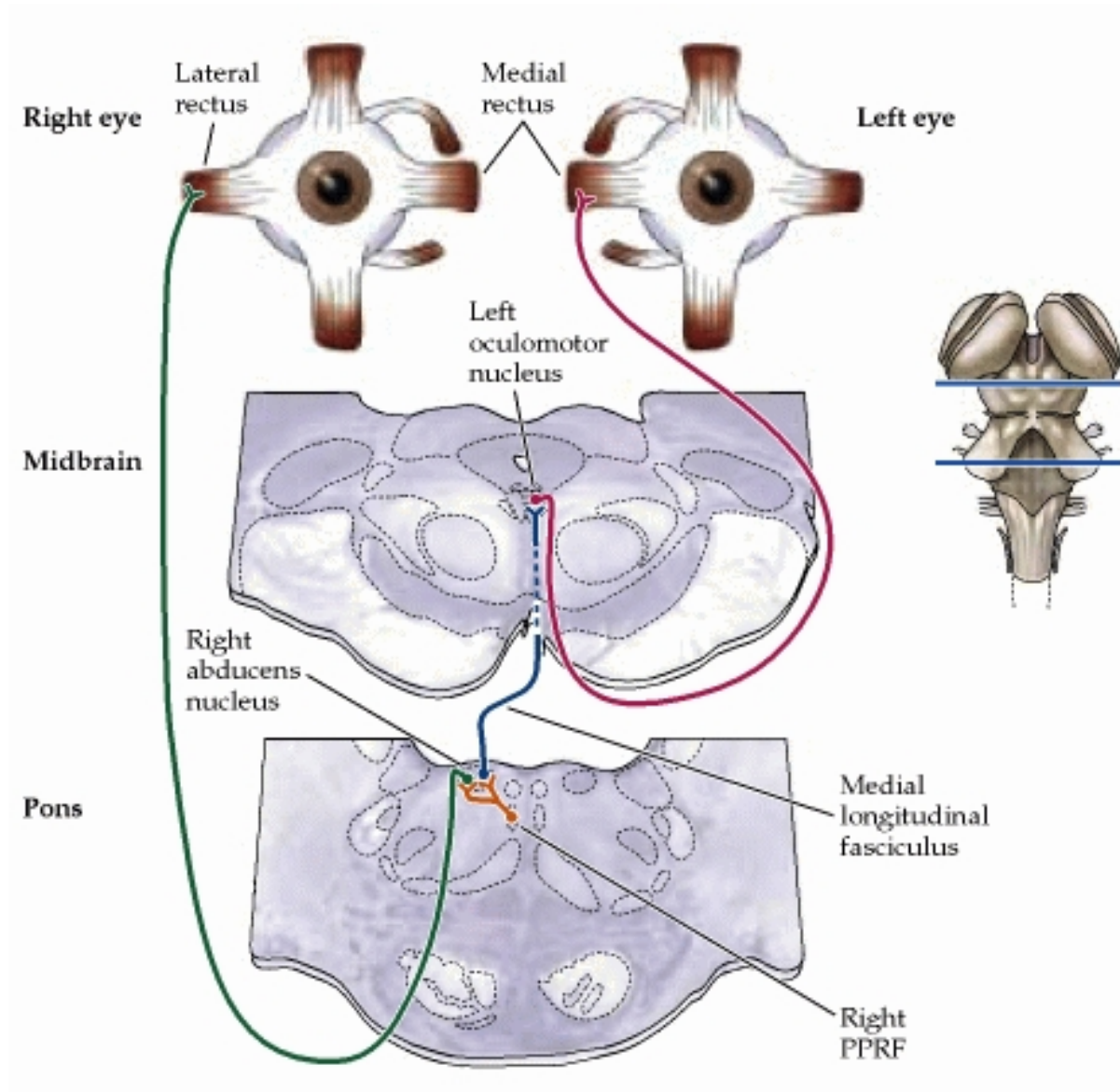
- The reticular formation affects autonomic functions like
 - Breathing
 - Heart rate and blood pressure
 - Vomiting, gagging, and coughing
- The glossopharyngeal (CN IX) and vagus (CN X) nerves are important efferents



Reticular Formation

- The reticular formation has a major role in regulation of:
 - Motor control
 - Sensory attention
 - Autonomic nervous system
 - [Eye movements \(L. McLoon\)](#)
 - Sleep and wakefulness

Reticular Formation



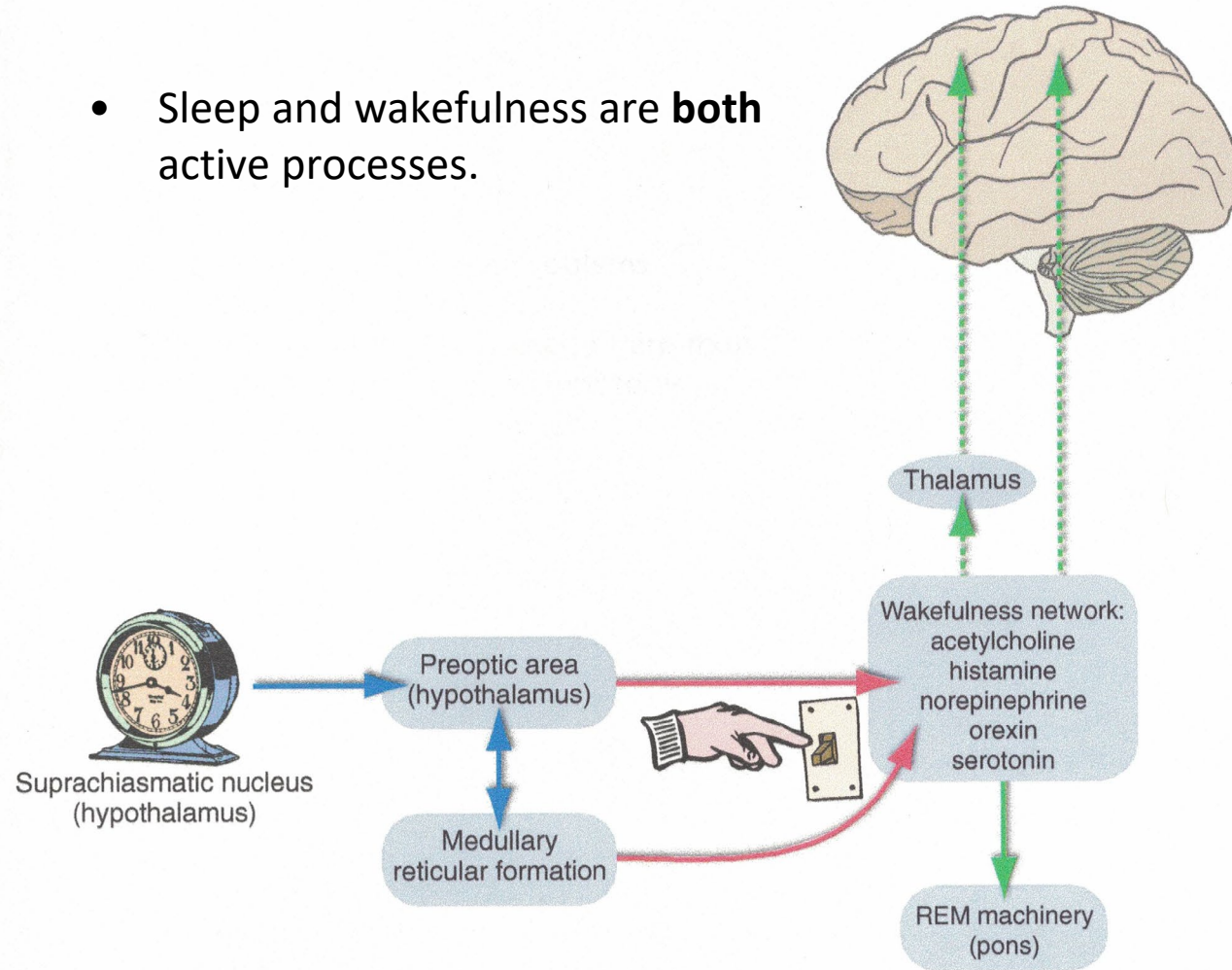
Horizontal Eye Movements

Reticular Formation

- The reticular formation has a major role in regulation of:
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 - Sleep and wakefulness

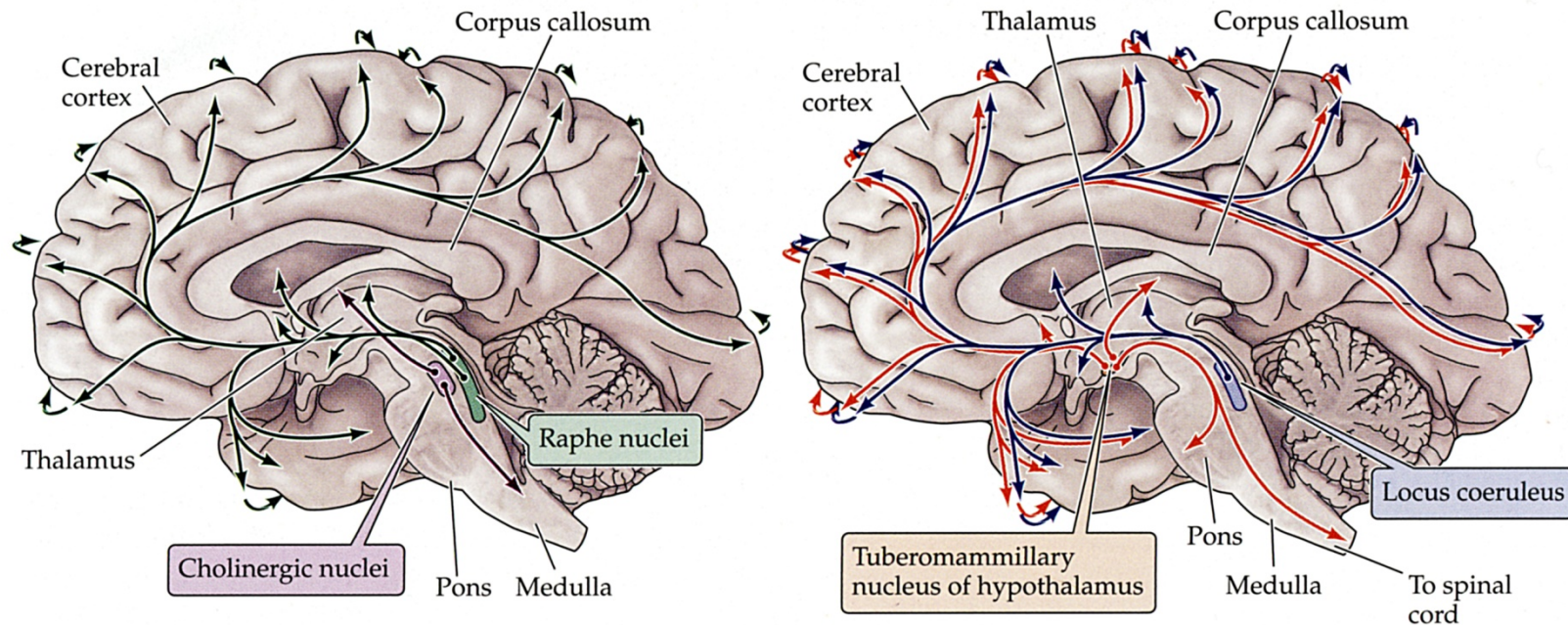
Sleep & Wakefulness

- Sleep and wakefulness are **both** active processes.



Sleep & Wakefulness

- 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.

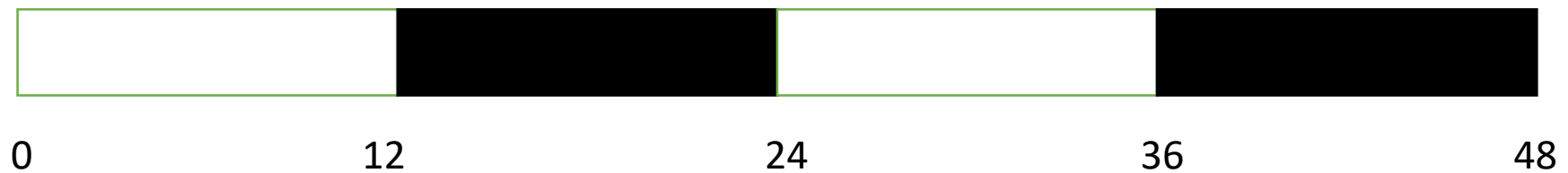


Sleep & Wakefulness

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

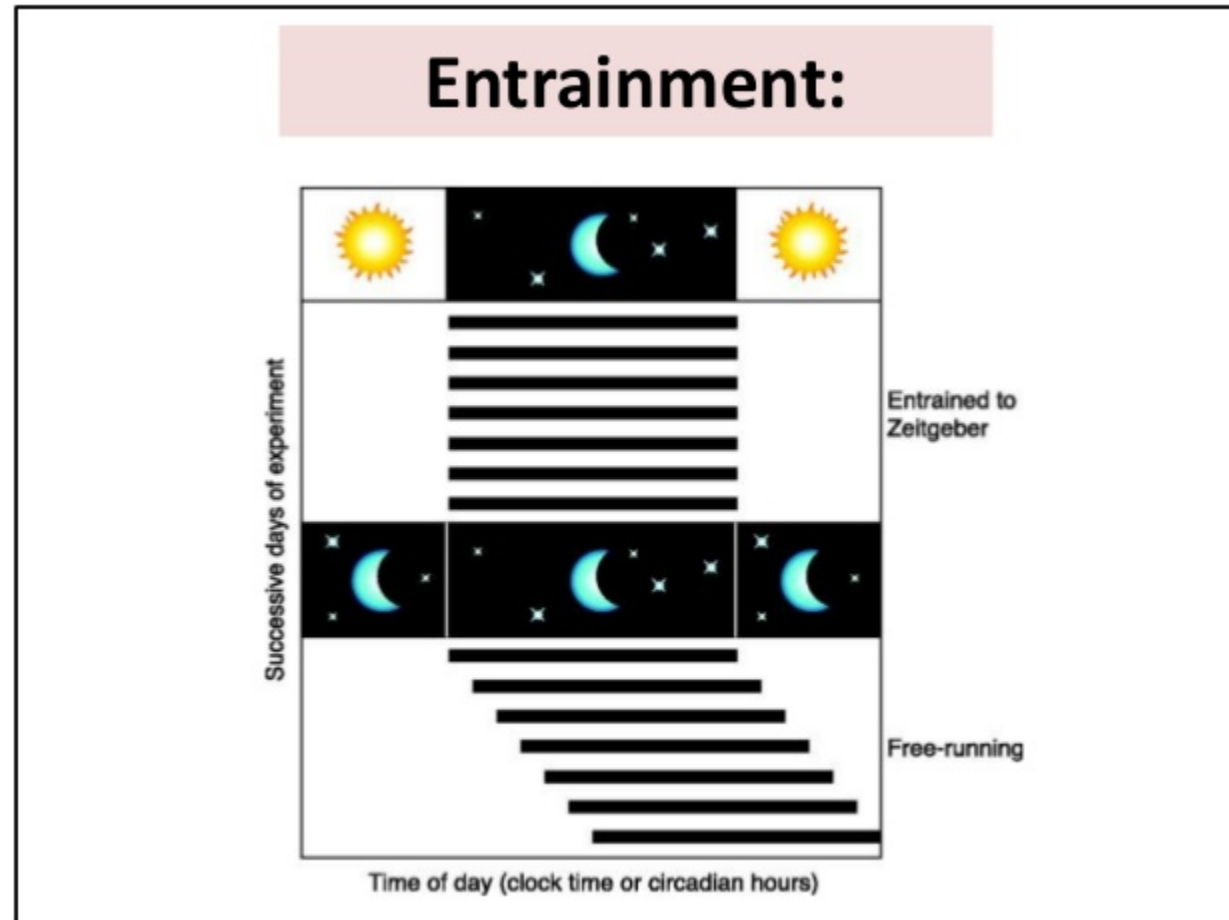


Cortisol

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

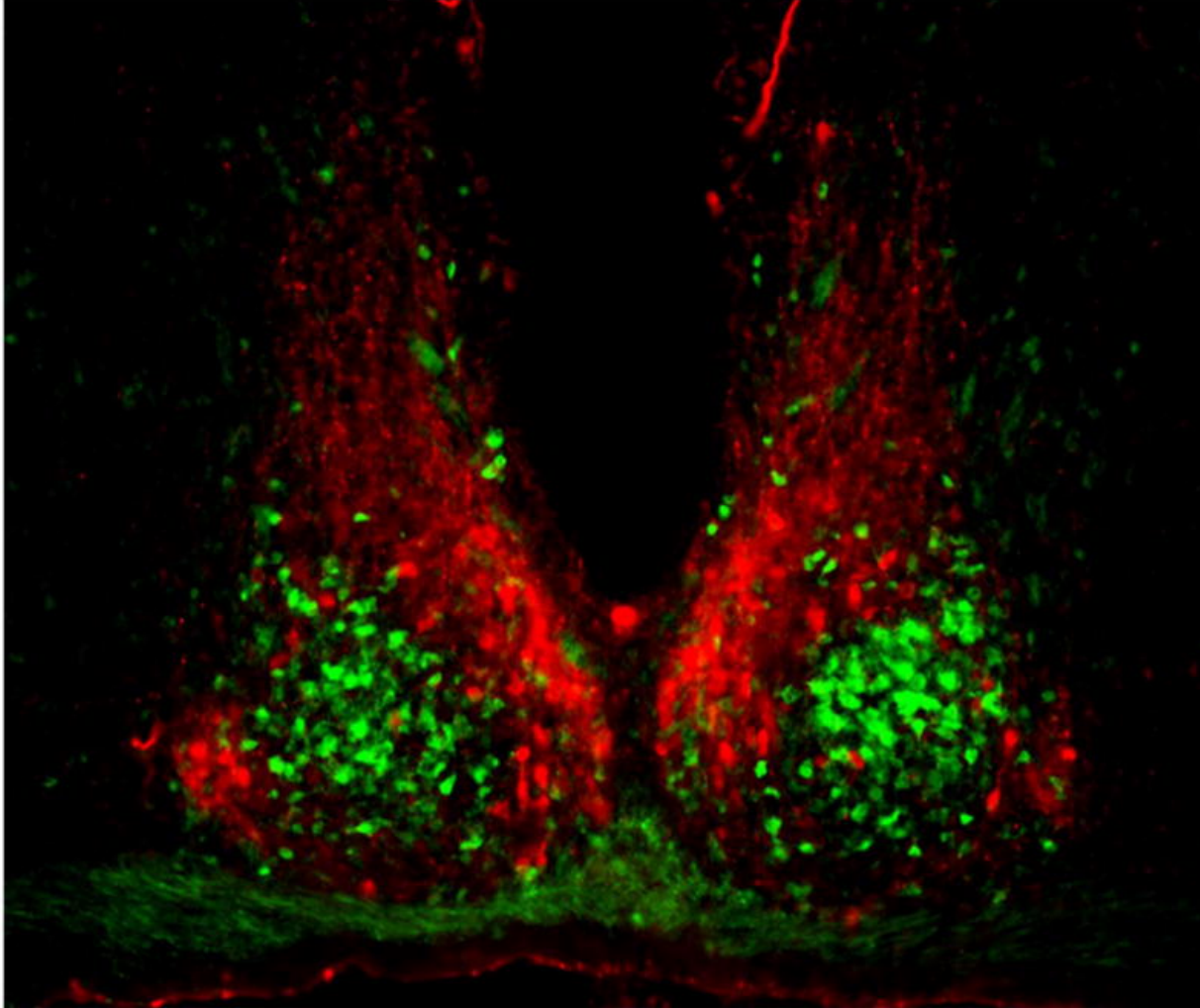


Sleep & Wakefulness

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

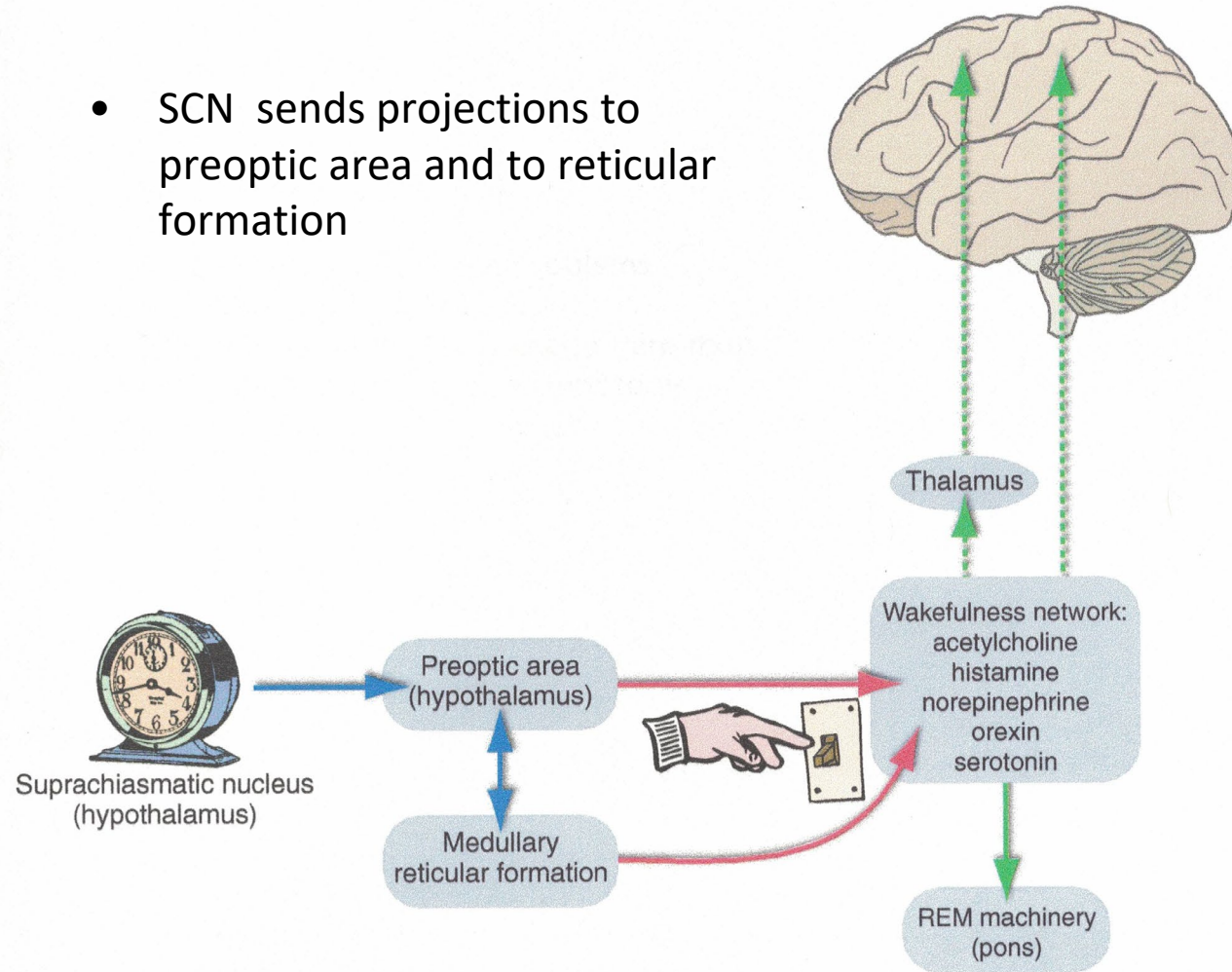


Suprachiasmatic Nucleus

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

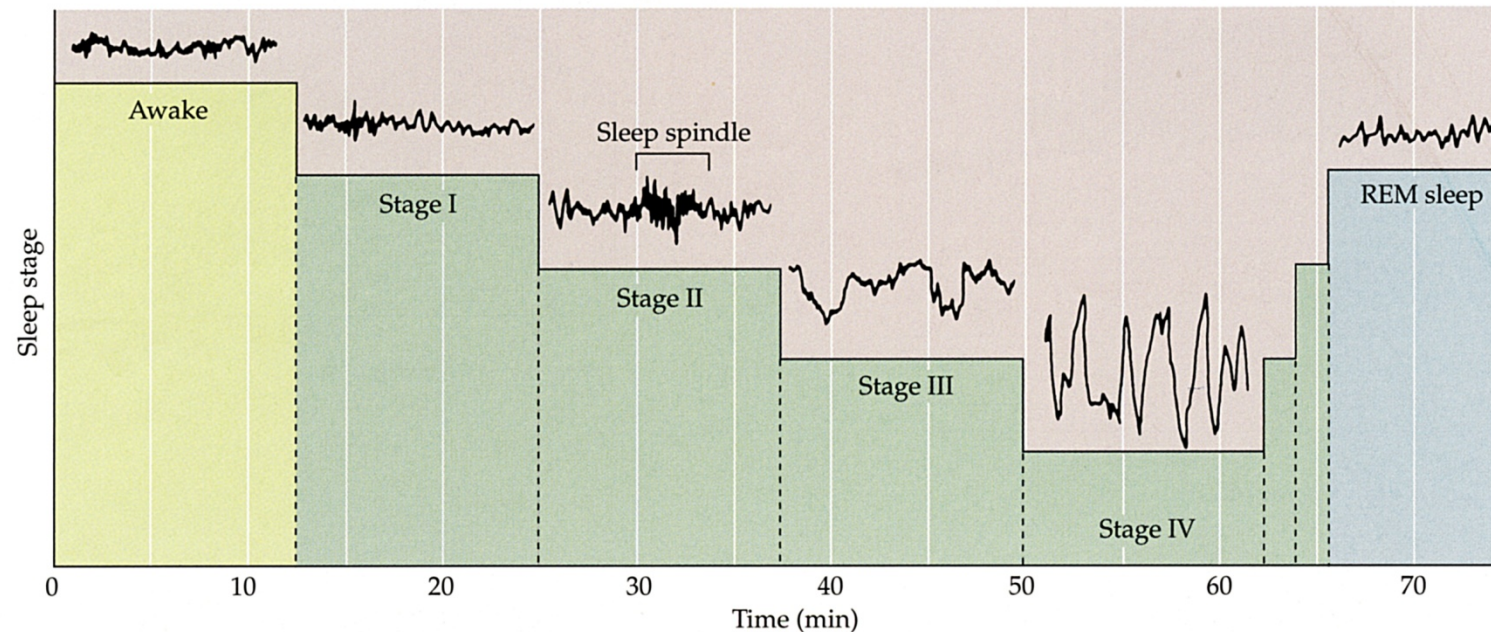
Sleep & Wakefulness

- SCN sends projections to preoptic area and to reticular formation



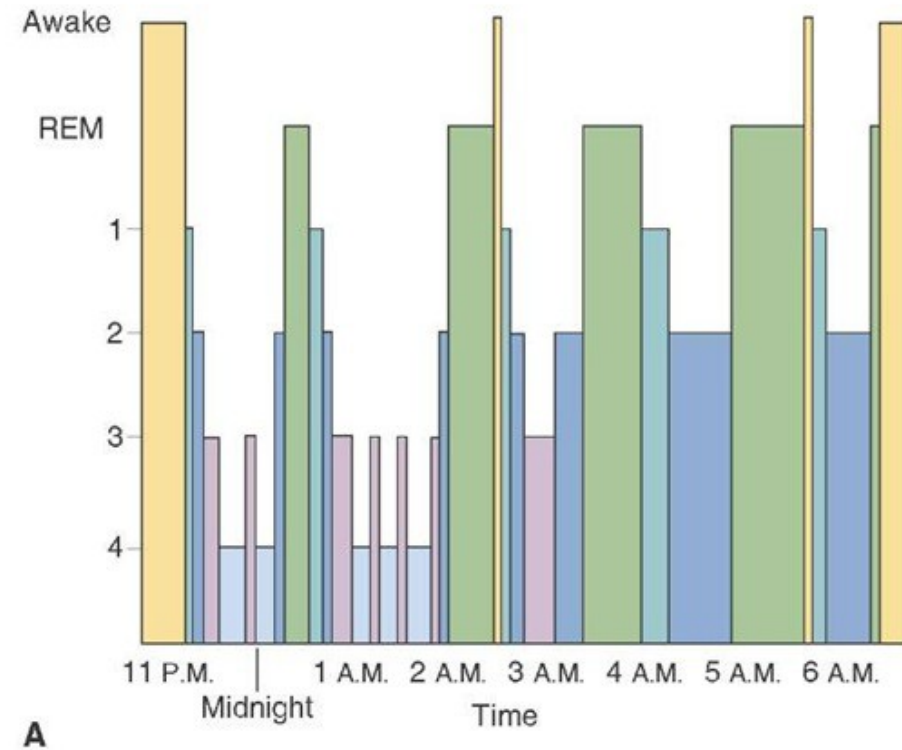
Sleep & Wakefulness

- 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

Non REM or Slow Wave Sleep (SWS)

- Muscle Activity
- Little dreaming
- Few eye movements
- Slowing of breathing
- Reduced BP

Rapid Eye Movement (**REM**) Sleep

- Reduced muscle activity
- Frequent dreaming
- Increased eye movements
- Enhanced breathing
- Increased BP

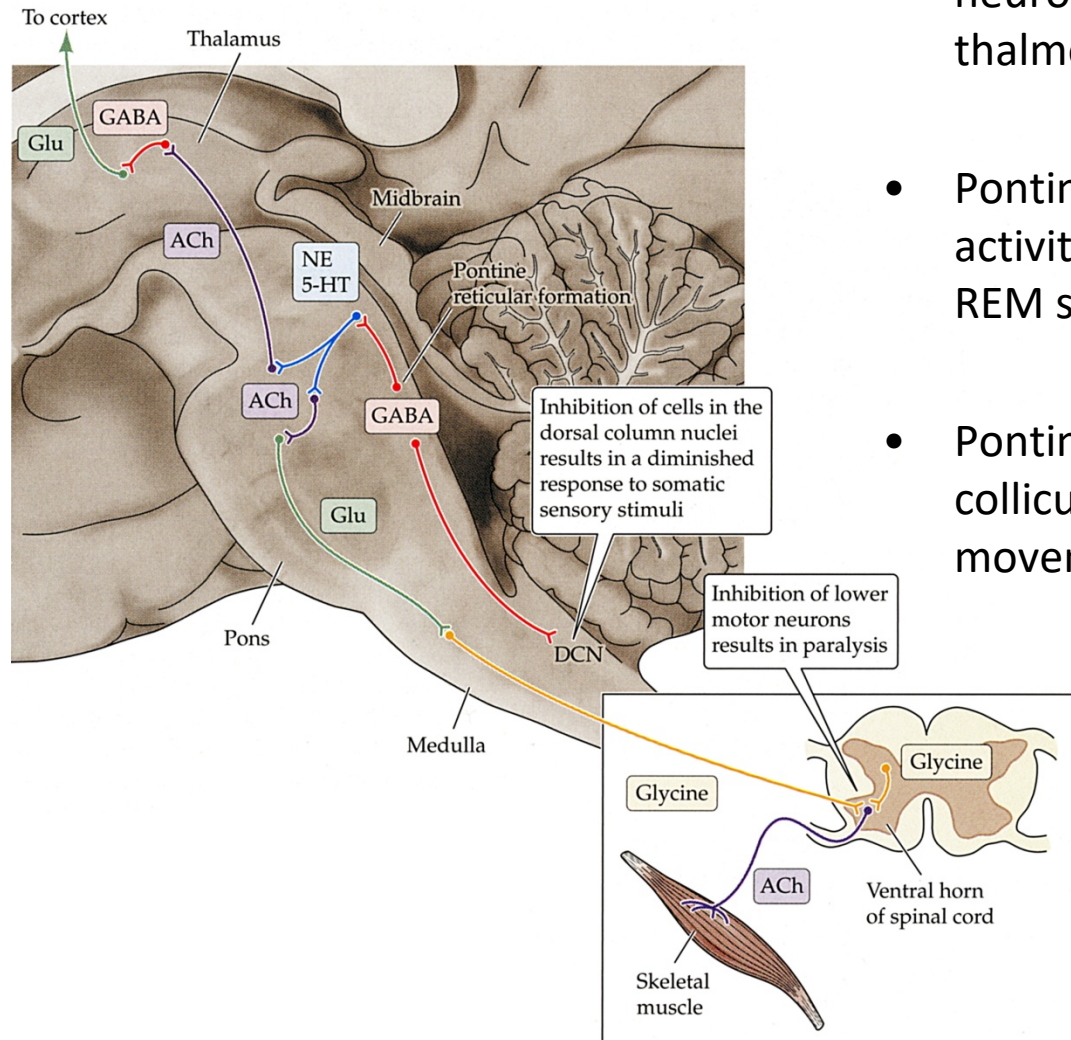
Sleep & Wakefulness

- 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.

Sleep & Wakefulness

- 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

Sleep & Wakefulness



- Cholinergic axons from the reticular formation to thalamus activate GABAergic neurons in thalamus, which inhibit thalamocortical 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.

Sleep & Wakefulness

- 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

Sleep & Wakefulness

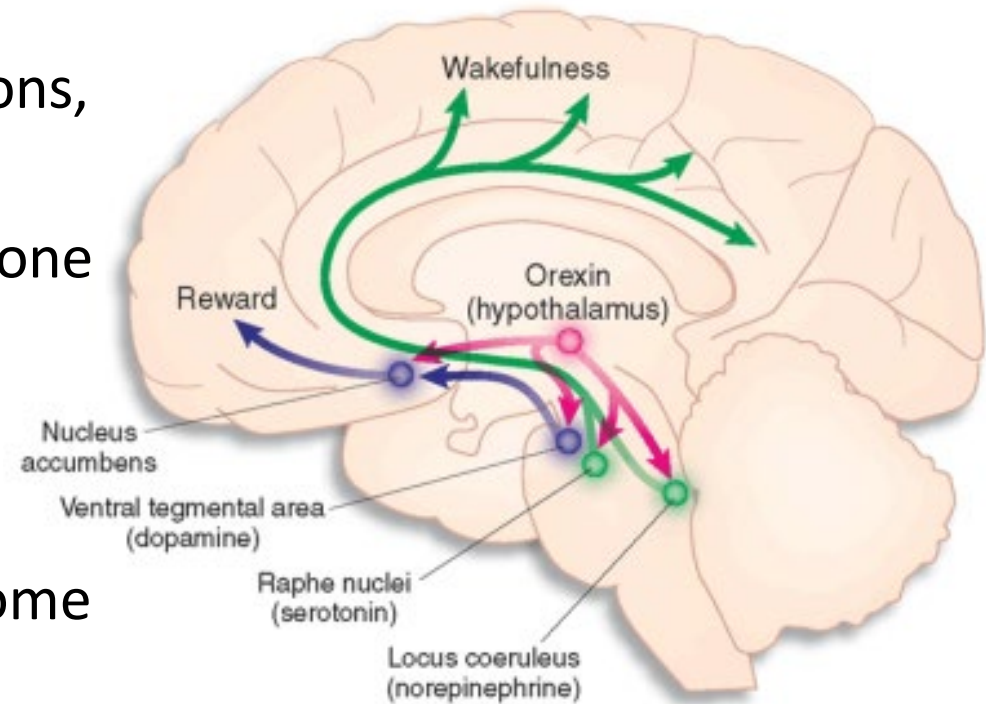
In a paper published in 2013, it was shown that:

- 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