Stages of Sleep and Brain Mechanisms

WEEK 8, LECTURE 2

Instructor: Erin Horowitz

In this lecture, we'll talk about… well, what the title says: the stages of sleep and the brain mechanisms involved. Let's get started.

Stages of Sleep and Brain Mechanisms

Sleep is a specialized state evolved to serve particular functions

Research Question: What are the mechanisms for producing sleep?

Sleep appears to have evolved to serve specific functions. We'll talk about what some of those functions may be in our next lecture, but for now we can ask a different question – and this is a question you can ask about any mechanism (biological or otherwise) that serves a specific function – mainly, what mechanisms regulate it?

Sleep

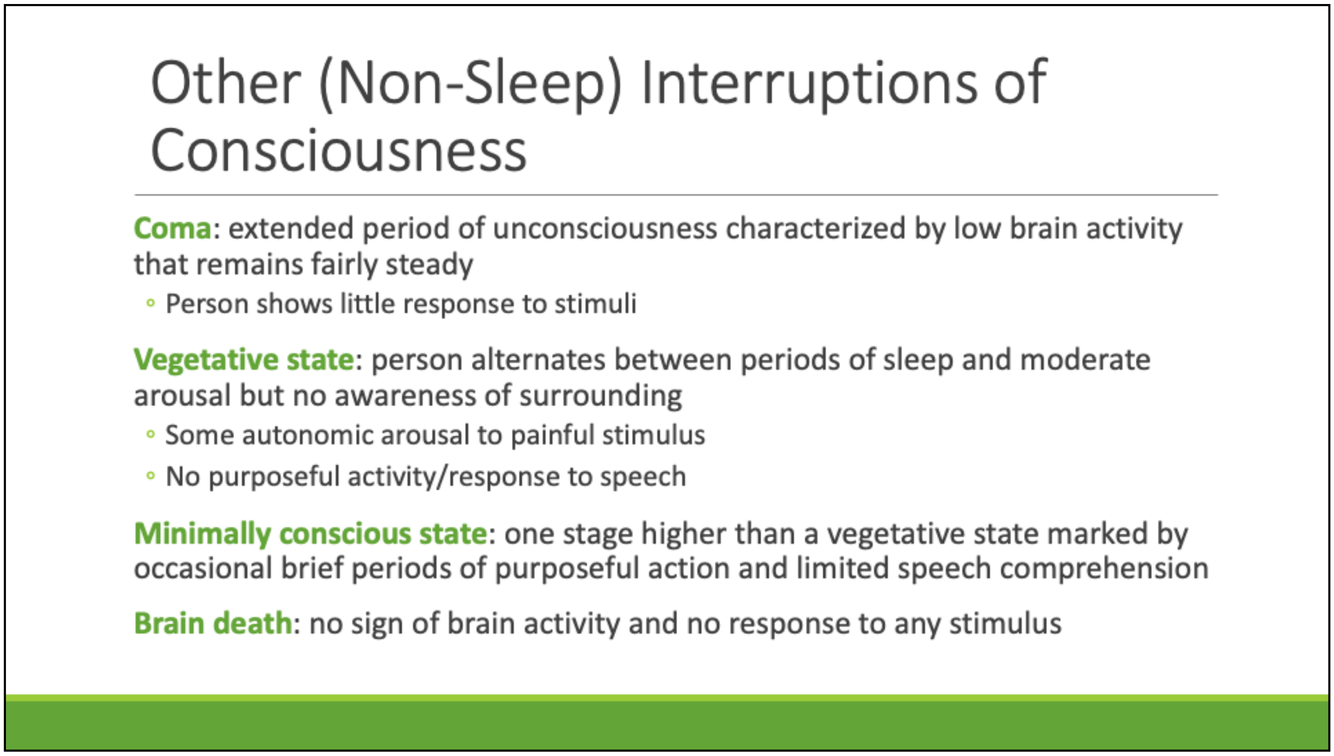
Sleep is a state that the brain actively produces

- Characterized by a moderate decrease in brain activity and decreased response to stimuli

Sleep differs from…

- Coma, vegetative state, minimally conscious state, and brain death

For a more technical definition of sleep, read the slide above. Note that sleep is different from other non-conscious states, in terms of behavior, response to outside stimuli, and brain activity.



There are many other types of non-conscious states, and you can read about them in more detail above.

Stages of Sleep: EEG

The electroencephalograph (EEG) allowed researchers to discover that there are various stages of sleep

- Allows researchers to compare brain activity at different times during sleep

A **polysomnograph** is a combination of EEG and eye-movement records

There are four (or five, if you consider REM) stages of sleep…

One of the best ways to study sleep is by doing something called a sleep study, in which you essentially hook someone up to an EEG and record their brain activity through a whole night's sleep. Often participants are also hooked up to a device called a polysomnograph, which records both brain activity and eye movements. It produces a readout that looks something like the image here – each row represents the readout from a different electrode, so you can not only tell when different wavelengths are occurring, but also *where* they're occurring.

In any case, using this methodology, researchers have identified four (or five) primary stages of sleep. We'll review them over the next few slides.

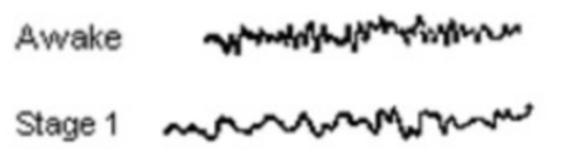
Relaxation and Stage 1 Sleep

Beta waves are present when one is awake and alert

Alpha waves are present when one begins a state of relaxation

Stage 1 sleep is when sleep has just begun

- The EEG is dominated by irregular, jagged, and low-voltage waves
- Brain activity begins to decline (lower than alpha waves, but higher than other sleep stages)

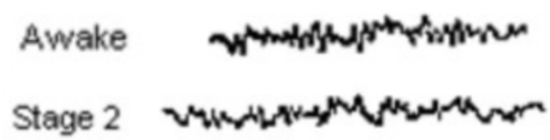


You can read about each stage in the slides above…

Stage 2 Sleep

Stage 2 sleep is characterized by the presence of:

- **Sleep spindles**: 12- to 14-Hz waves during a burst that lasts at least half a second
- **K-complex**: a sharp wave associated with temporary inhibition of neuronal firing



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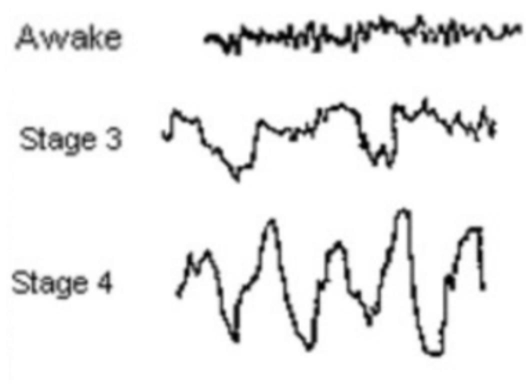
Sleep spindles appear to results from interactions between the thalamus and the cortex, and increase in number after learning a new skill or knowledge set – they appear to be related to the consolidation of new memories. K-complexes are associated with a temporary inhibition of neural firing, which might play a role in downregulating the body's response to external stimuli during sleep. K-complexes have also been implicated in memory consolidation.

Slow Wave Sleep: Stage 3 and Stage 4

Stage 3 and stage 4 together constitute slow wave sleep (SWS) and is characterized by:

- EEG recording of slow, large amplitude wave
- Slowing of heart rate, breathing rate, and brain activity
- Highly synchronized neuronal activity



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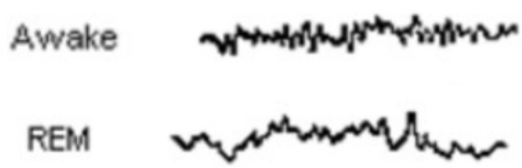
Nowadays these two stages are often referred to as “slow wave sleep” together, rather than as two separate stages. The general difference between the two (and you can see this in the image above) is that waves become slower as one moves from stage 3 to stage 4.

REM or Paradoxical Sleep

Rapid eye movement sleep (REM) describes periods characterized by rapid eye movements during sleep
- Also know as paradoxical sleep: deep sleep in some ways, but light in other ways

EEG waves are irregular, low-voltage, and fast

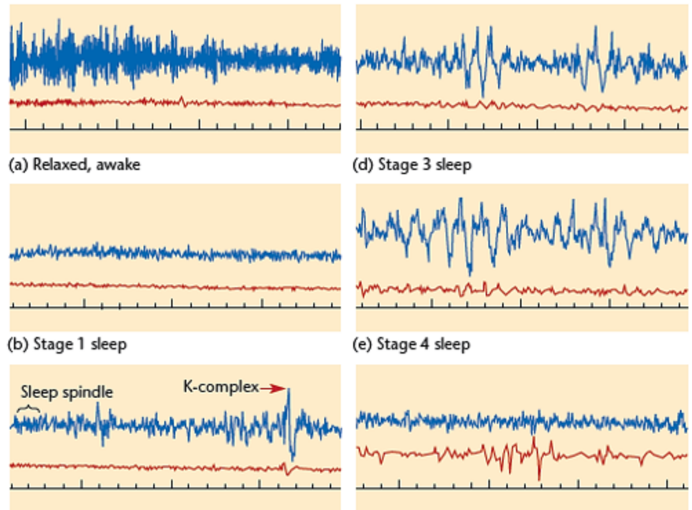
Postural muscles of the body are more relaxed than other stages, which prevents motor movement



Finally we have REM, or "paradoxical" sleep, which you can read about above.

The brain is also more active than stages 3 and 4 – this is the stage of sleep in which dreaming occurs.

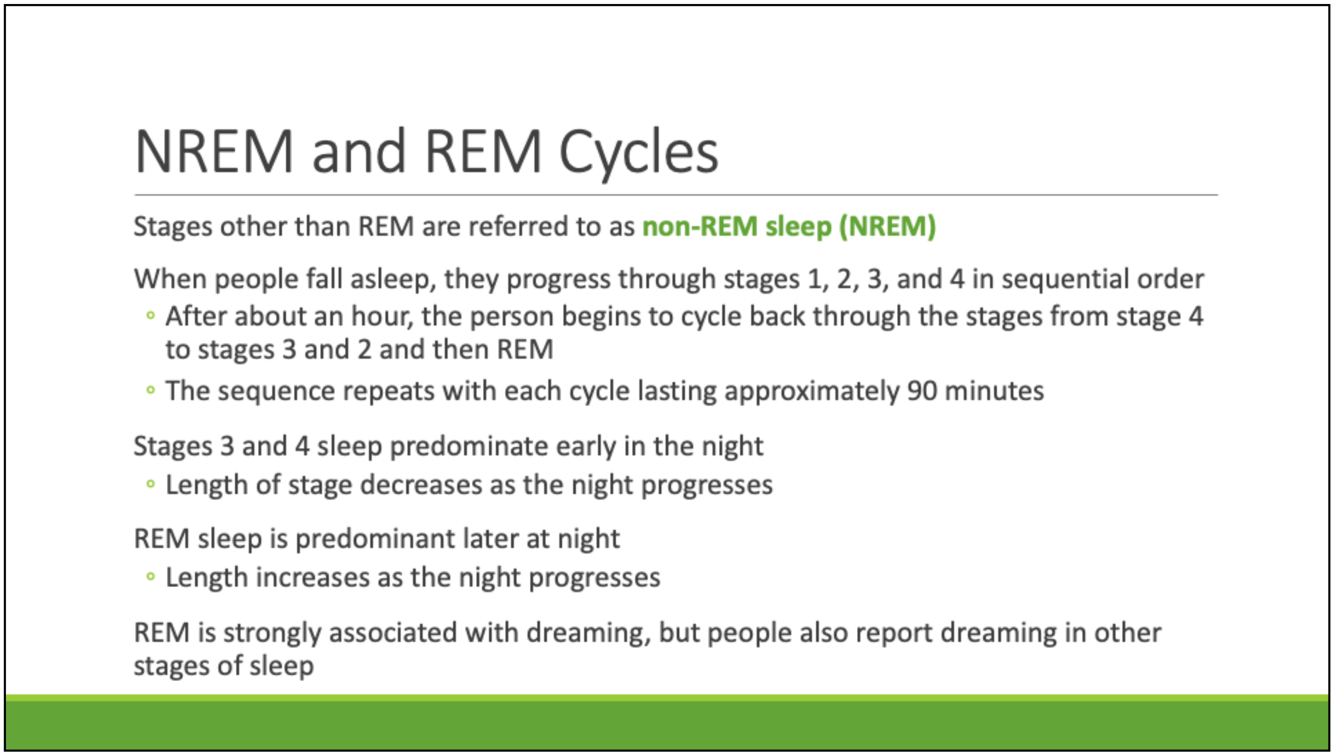
Polysomnograph Records of Different Sleep Stages…



(a) Relaxed, awake
(b) Stage 1 sleep
(c) Stage 2 sleep
(d) Stage 3 sleep
(e) Stage 4 sleep
(f) REM, or "paradoxical" sleep

Putting it all together, this is a polysomnograph of all of the different stages of sleep.

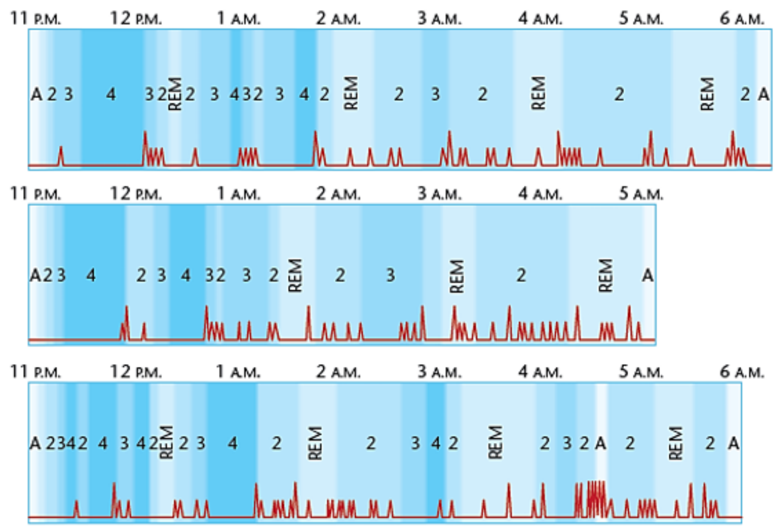
For each image, the top (blue) line is the EEG from one electrode on the scalp. The middle (red) line is a record of eye movements. The bottom (black) line is a time marker, indicating 1-second units. You can see, for example, that there is a lot more activity in stage 1 sleep, and this gradually decreases (and becomes more synchronized) as the brain progresses through stage 2 into stage 3 and 4 sleep. You can also note the sleep spindles and k-complexes in stage 2 sleep, and in increase in eye movements in REM sleep.



All stages besides REM sleep (i.e., stages 1-4) are collectively referred to as “non-REM (NREM)” sleep.

Above, you can read about how humans progress from stage 1 through REM sleep over the course of a sleep period. It is not a linear progression; rather, it fluctuates in a cycle that lasts approximately 90 minutes.

Typical Sequences of Sleep Stages

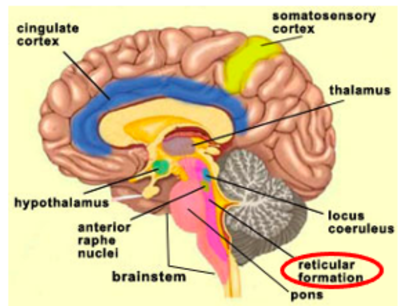


This is a polysomnograph readout from a single person, over the course of three separate nights, and you can see how long this person spent in each stage throughout the night. “A” here indicates that the person was awake, and each number corresponds to its respective sleep stage (hopefully “REM” is obvious here). The red line at the bottom shows the person’s body movements throughout each night; you can see that there are definite periods of little to no movement, and these occur mostly during slow-wave sleep. Also note that slow-wave sleep is more prevalent early on, while REM becomes more prevalent towards the end of the sleep cycle.

Brain Mechanisms of Wakefulness and Arousal: The Reticular Formation

Various brain mechanisms are associated with wakefulness and arousal

The reticular formation is a part of the midbrain that extends from the medulla to the forebrain and is responsible for arousal



So those are the stages of sleep in a nutshell. Let's move on now and talk about the flipside of sleep: wakefulness and arousal. And we'll start by talking about the reticular formation, which is an area that lies between the medulla to the forebrain.

Brain Mechanisms of Wakefulness and Arousal: The Pontomesencephalon

The pontomesencephalon, a part of the reticular formation, also contributes to cortical arousal

- Axons extend to the hypothalamus, thalamus, and basal forebrain, which release acetylcholine, glutamate, or dopamine
  - Produces excitatory effects to widespread areas of the cortex
- Stimulation of the pontomesencephalon awakens sleeping individuals and increases alertness in those already awake
- Axons also release GABA, which inhibits behavior and helps promote slow wave sleep

The reticular formation generally contributes to arousal, and it has sub-components that appear to be specialized for this function as well. One of these is the pontomesencephalon, which you can read about above.

Brain Mechanisms of Wakefulness and Arousal: The Locus Coeruleus

The locus coeruleus is a small structure in the pons whose axons release norepinephrine to arouse various areas of the cortex and increase wakefulness

- Usually dormant while asleep, but releases powerful bursts of impulses in response to events (especially those that increase emotional arousal)
- Releases norepinephrine to many different areas of the cortex
- Increases "gain" → increases activity of most active neurons and decreases activity of least active neurons
    - Results in enhanced attention to important information and enhanced encoding of memories

Another area is the locus coeruleus, which again you can read about above…

Brain Mechanisms of Wakefulness and Arousal: The Hypothalamus

The hypothalamus contains neurons that release histamine to produce widespread excitatory effects throughout the brain

- Antihistamines produce sleepiness

The hypothalamus also contains pathways which promote wakefulness…

Finally there is the hypothalamus (which is *not* part of the reticular formation). As you know at this point, the hypothalamus controls a number of different behaviors – many of them are regulatory, and many involve the release of hormones. One of its many functions is to release histamine, which (among other functions) promotes arousal in different areas of the brain.

In addition to the production of histamine, the hypothalamus also contains pathways that are specialized to promote wakefulness.

Brain Mechanisms of Wakefulness and Arousal: Orexin

The lateral and posterior nuclei of the hypothalamus releases orexin

- Orexin is a peptide neurotransmitter and is sometimes also called hypocretin
- Orexin is needed to stay awake, rather than to wake up
- Released by cells into the **basal forebrain** to stimulate neurons responsible for wakefulness and arousal
  - Side note: The basal forebrain is an area just anterior and dorsal to the hypothalamus

One such pathway involves the release of a neurotransmitter called orexin (or hypocretin), which you can read about above (sorry for the lack of notes here – these areas and pathways are fairly straightforward).

One point I'd like to highlight, though, is that orexin does not initiate arousal – it maintains it.

Brain Mechanisms of Wakefulness and Arousal: GABA and Acetylcholine

Cells of the basal forebrain release the inhibitory neurotransmitter GABA
- Inhibition provided by GABA is essential for sleep

GABA is also important for…
- Decreasing temperature and metabolic rate
- Decreasing the stimulation of neurons

Other axons from the basal forebrain release acetylcholine, which is excitatory and increases arousal

There are two other neurotransmitters at play here: GABA and acetylcholine.

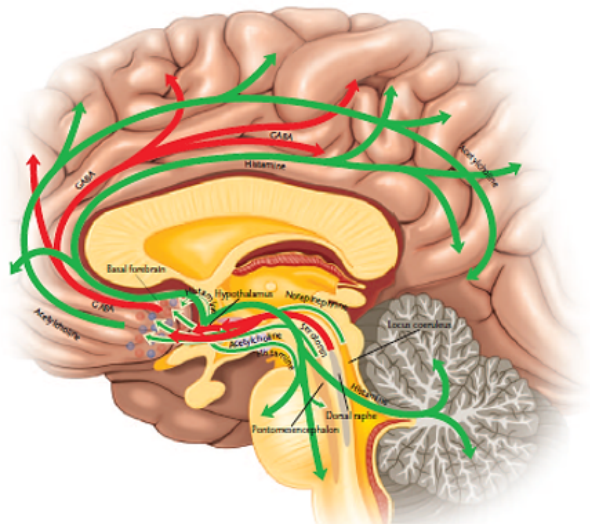
GABA is generally inhibitory, and so its main function is to strategically inhibit certain brain areas according to one's circadian rhythms (and other external factors), which promotes sleepiness. GABA helps downregulate metabolic rate and temperature, and generally decreases the stimulation of both nerves and neurons. It also decreases one's ability to respond to outside stimuli by hyperpolarizing neurons in the thalamus. The general effect of GABA is to decrease communications between different brain areas.

On the flipside is the neurotransmitter acetylcholine, which is generally excitatory and increases arousal in areas it's released to.

Brain Mechanisms of Wakefulness and Arousal

Green arrows = excitatory connections

Red arrows = inhibitory connections



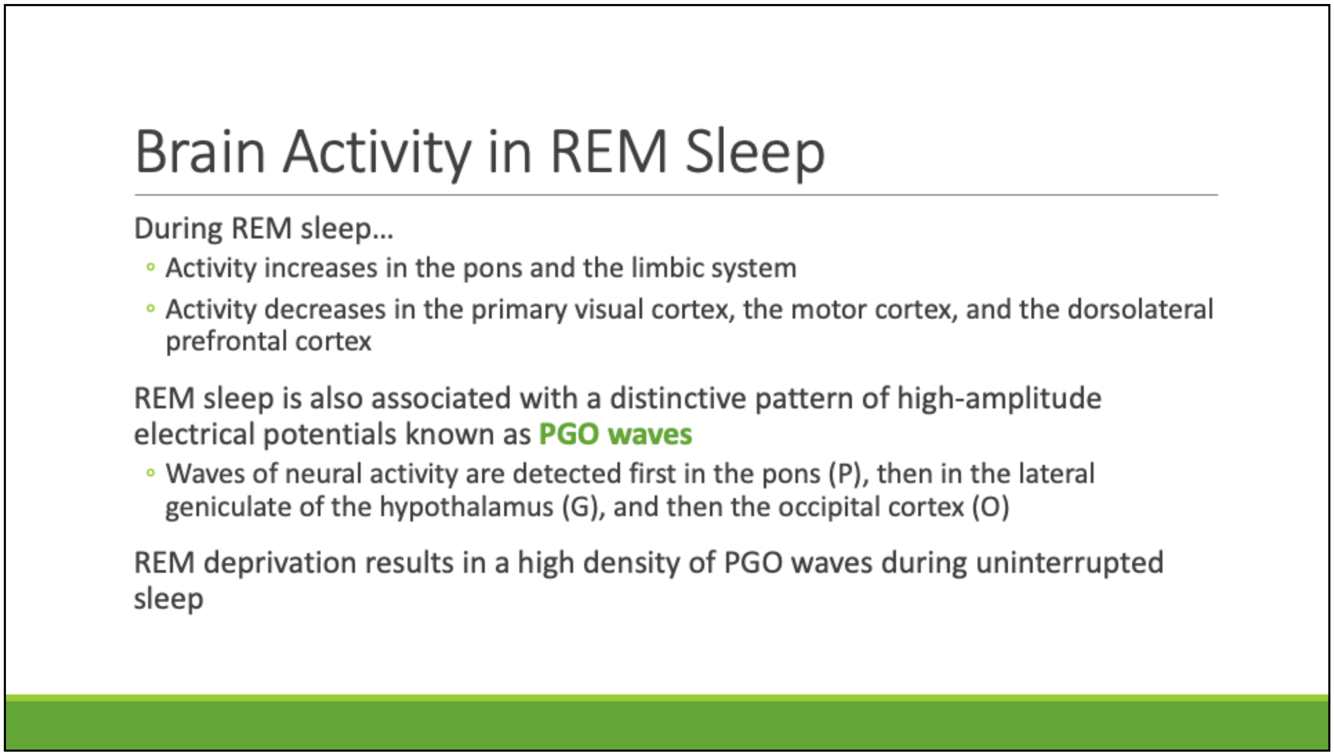
This is a diagram of the different pathways involved in wakefulness and sleepiness. As the slide says, green indicates excitatory pathways (mainly acetylcholinergic) while red indicates inhibitory (mainly GABAergic) ones. You can see that the excitatory pathway passes through the reticular formation (via the pontomesencephalon) and the locus coeruleus, and both pathways pass through the hypothalamus on their way to the rest of the cerebral cortex.

Brain Structures for Arousal and Sleep

Structure	Neurotransmitter(s) It Releases	Effects on Behavior
Pontomesencephalon	Acetylcholine, glutamate	Increases cortical arousal
Locus Coeruleus	Norepinephrine	Increases information storage during wakefulness; suppresses REM sleep
Basal Forebrain (Excitatory Cells)	Acetylcholine	Excites thalamus and cortex; increases learning, attention; shifts sleep from NREM to REM
Basal Forebrain (Inhibitory Cells)	GABA	Inhibits thalamus and cortex
Hypothalamus (parts)	Histamine	Increases arousal
Hypothalamus (parts)	Orexin	Maintains wakefulness
Dorsal Raphe and Pons	Serotonin	Interrupts REM sleep

You only need to know the structures we discussed in the slides…

We've talked about most of the areas involved in sleep and arousal, and this is just a handy chart for you to use as a study aid. There are some areas we haven't discussed (I'm looking at you, dorsal raphae and pons), and so you'll only be responsible for the areas we've discussed here. This does include the basal forebrain, so please be mindful of that.



Let's finish up by talking about brain activity in REM sleep – not just different brain waves, but what is happening in other areas of the brain. REM sleep is associated with increases in some areas and decreases in others, as well as a distinctive pattern of activity called "PGO waves" – you can read more about all of this above.

PGO waves themselves are associated with dreaming – and specifically with the more "visual" aspects of it (hence the activation of the occipital cortex). Their function may be to help consolidate memories, which is one of the proposed functions of sleep.

Brain Activity in REM Sleep

Cells in the pons send messages to the spinal cord, which inhibits motor neurons that control the body's large muscles

- Prevents motor movement during REM sleep

REM is also regulated by serotonin and acetylcholine

- Drugs that stimulate acetylcholine receptors quickly move people to REM
- Serotonin interrupts REM

You're actually paralyzed during REM sleep, and this is because of a specific pathway that leads from the pons to the spinal cord. The result is an inhibition of motor neurons in the periphery, which prevents you from moving during sleep. This has a lot of functional utility, as it prevents you from harming yourself (at the very least, falling out of bed) while you're in arguably the most active stage of sleep (i.e., dreaming).

Lastly, other neurotransmitters can affect the quality and duration of REM sleep. Acetylcholine, for example, can move a person into REM sleep faster, while serotonin and norepinephrine can interrupt REM sleep.

Questions for your discussion groups…

1. Pick one brain structure or chemical involved in arousal. How does it contribute to states of arousal?
2. Name three factors that differentiate REM sleep from nREM sleep

Okay, that does it for this lecture! Apologies that there was less commentary for this one – I've found that the information on sleep cycles is incredibly straightforward. If you don't feel the same way – if you have lingering questions – please feel free to reach out to me or Sierra, either via lecture chat, the class forum, or e-mail. I'll see you in the next lecture, which is on the function of sleep!