Sleep and Aging

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Disclosures

- Dr. Kauta does not have financial conflicts of interest with this activity.

Learning Objectives

- Identify two ways sleep differs between childhood and adulthood
- Identify two sleep disorders that there is increased risk for with age
- Identify two concerns related to treatment of insomnia with sleep medications

Outline

- About sleep
  - Patterns and Stages
  - How much sleep do we need?
- Sleep and Aging
- Sleep and Dementia
  - Tau protein and sleep
- Sleep Disorders
- Sleep testing

What do we know about sleep?

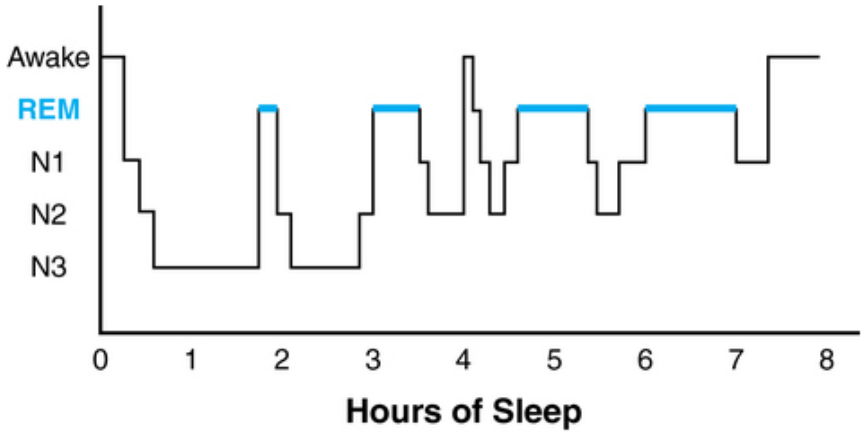
- **WE SPEND 1/3 OF OUR LIVES ASLEEP**
- **SLEEP IS AN ACTIVE PROCESS**
  - No organ or regulatory system "shuts down"
    - Slight decrease in metabolic rate
  - Many parts of the brain are as active as awake periods
  - Approximately 2-3 hours of dream state per night
- **SPECIFIC HORMONES INCREASE DURING SLEEP**
  - Growth hormone
  - Melatonin
  - Leptin (released by adipose tissue to give a sensation of satiety/fullness

https://www.sleepfoundation.org/stages-of-sleep

How much sleep do we need?

• Infants	16-20
• Toddlers	12-14
• Pre School	11-13
• School Age	10-11
• Teens	9.5-10

- Most adults need 7 ½ -8 hours to function well
  - About 10% require more or less sleep
  - Pregnant women need more sleep



Normal adult hypnogram: Slow wave sleep (N3) is more prominent during the first portion of the night. REM episodes increase as the night progresses with the longest episode before awakening.

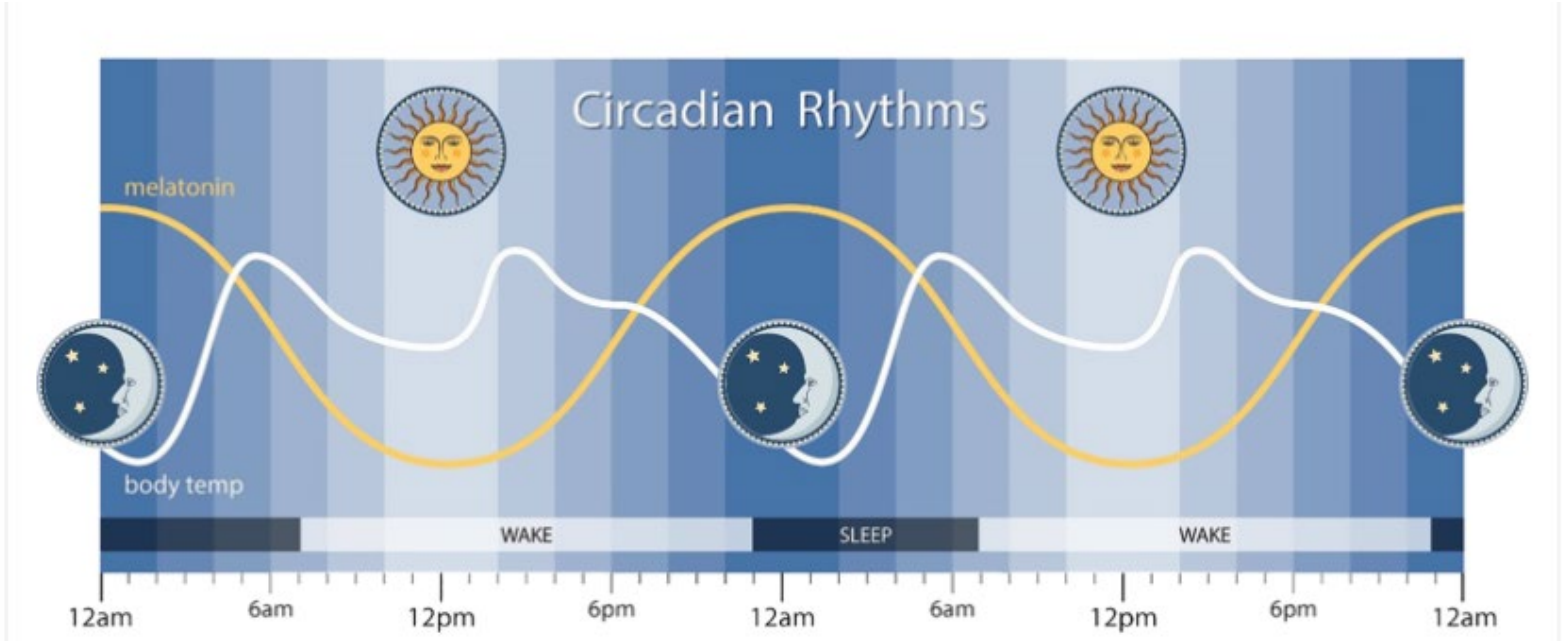
FIG 19-2 Hypnogram depicting the progression of the sleep stages of an adult. (From David N. Neubauer, MD, Johns Hopkins Sleep Disorders Center, Baltimore, MD [*American Family Physician*, 59(9):2551-2558, May 1, 1999].)

Stages of Sleep Cycle

NI	N2	N3	REM
Less than 10 minutes	30-60 minutes	20-40 minutes	Most of the dreaming
Light Sleep	Muscles are relaxed	Deep Sleep	Eyes and eyelids flutter
Awakened easily	Slow wave brain activity	Some body movement; Hard to wake up	Occurs after N1,N2,N3

Note : Cycle is repeated 3-4 times each night

David Neubauer, MD, Johns Hopkins Sleep Disorders Center, Baltimore (American Family Physician) 1999



National Institute of Neurological Disorders and Stroke
https://www.ninds.nih.gov/health-information/public-education/brain-basics/brain-basics-understanding-sleep

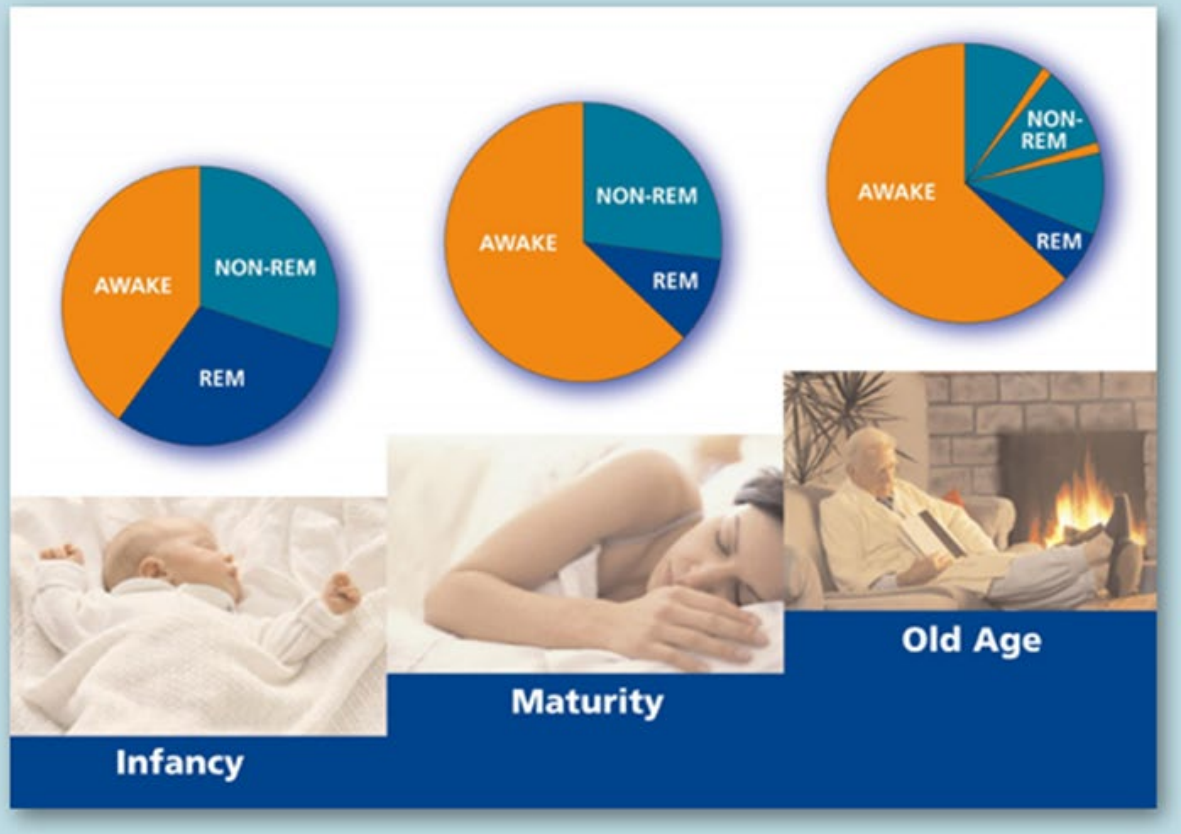
Sleep Characteristics Vary for Each Person

- Larks- Early to bed and early to rise- 10% of the population
- Night Owls- Late to bed and late to rise- 20% of the population
- The rest of us are somewhere in between and can vary based on lifestyle/job/school

Sleep and Aging

- Sleep changes with age just like physical ability, weight/metabolism, and memory
- The first step to optimal sleep as we age is understanding it is natural that sleep can become more difficult with age
- It requires time and commitment to certain habits to maintain at an optimal state

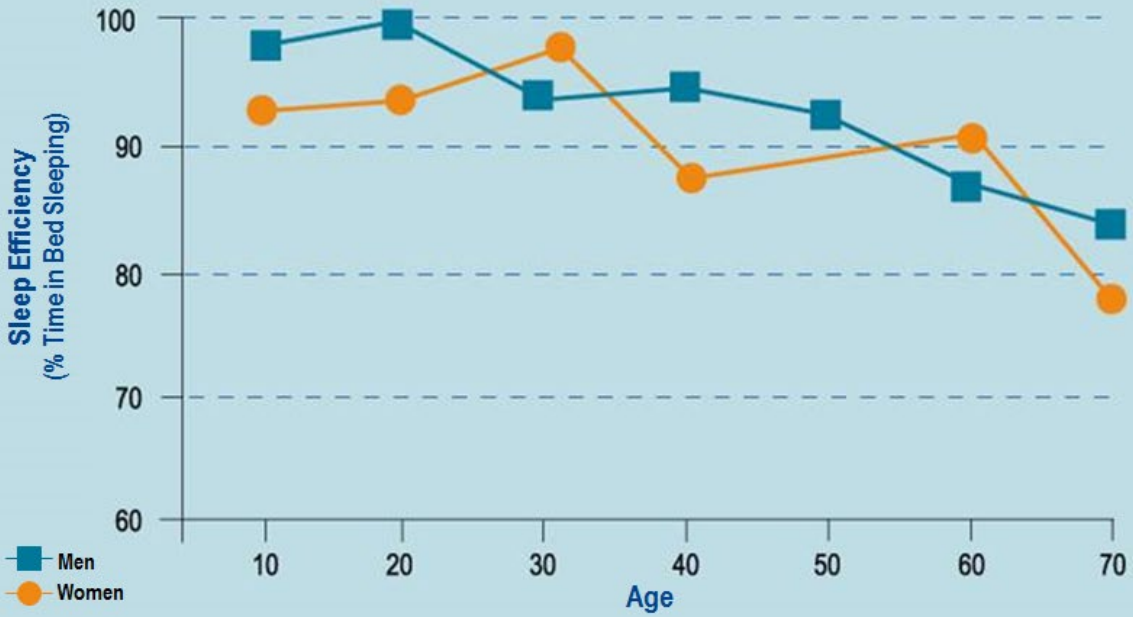
Normal Sleep and Normal Aging: Less Deep Sleep



National Sleep Foundation

Normal Sleep and Normal Aging: Sleep Efficiency

Changes with age



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Changes in Sleep with Aging

- Increased sensitivity to external factors- light/sound/temperature
- Increased napping during the day and sleep latency at night
- Decreased Stage 3 sleep/REM sleep and increased light sleep
- Phase advancement
- Decreased melatonin levels which contributes to sleep fragmentation
- Women tend to have more sleep difficulties with age than men
- Increased risk for sleep apnea and insomnia
  - Insomnia is present in approximately 50% of the elderly

Healthy Sleep Practices as you Age

- There is an increased opportunity to nap after you retire. It is important to avoid naps to increase your sleep drive
  - The more time you spend awake the more sleepy you are when you get closer to bedtime
- Write it down- as memory is affected, patients worry about forgetting things they need to do and focus on it as they are trying to fall asleep
  - Ask patient to write their worries/to do lists down before they get into bed to sleep so they don't have to worry about forgetting them
- A regular bedtime and wake time help solidify the natural circadian rhythm
- Exposure to bright light during the daytime hours helps strengthen sleep to follow the circadian rhythm
- Exercise improves mood and reduces boredom/need to nap. Avoiding naps helps sleep at night. Ask patients to incorporate 30 minutes of exercise daily

Sleep and Dementia

- SLEEP IS A COMMON COMPLAINT IN PATIENTS WITH DEMENTIA- TOO MUCH OR TOO LITTLE SLEEP
- SUNDOWNING IS COMMON IN THESE PATIENTS
- THE MAJORITY OF CAREGIVERS ALSO HAVE SLEEP ISSUES
- THE CAREGIVER'S SLEEP IS A COMMON REASON FOR MOVING A PATIENT TO A CARE FACILITY

Sleep-Wake Cycle regulates Tau in CSF

- Testing in mice found new findings related to sleep and tau, a protein which is present in normal brains but accumulates in tangles in the brain in patients with Alzheimer's disease
- Tau deposits can track closely with disease progression and cognitive decline
- Wake neurons release tau and during sleep it is cleared
- Sleep deprivation not only causes tau to accumulate because it is not cleared but it is released in higher amounts when neurons chronically activated
- This new data supported prior studies that showed healthy adults who were forced to stay up all night had a 50% increase in levels of tau in CSF

Holtzman DM. The sleep-wake cycle regulates brain interstitial fluid tau in mice and CSF tau in humans. Science. Jan. 24, 2019

Relevance of Sleep/Tau data

- Awareness that Alzheimer's disease and sleep loss are more intertwined than had been realized
- Good sleep habits and protecting sleep can potentially play a role in slowing AD
- Poor sleep may worsen AD
- It is clear there is a relationship so getting the best sleep possible can only help and definitely not hurt in managing dementia and cognitive impairment

Sleep Review for Dementia Patients

- Review all medications- prescribed and over the counter medications.
  - Diphenhydramine and high doses of melatonin are frequently under recognized important to review
- Review sleep environment
- Review any recent events or changes that may have been stressful for the patient
- Evaluate for depression
- Evaluate for sleep disorders: OSA, restless leg syndrome and insomnia

Common Sleep Disorders

SLEEP APNEA

INSOMNIA

RESTLESS LEG SYNDROME

PARASOMNIA

NARCOLEPSY

Obstructive Sleep Apnea

- Repetitive closure of the pharyngeal airway associated with oxygen desaturation and/or arousal from sleep
- Daytime symptoms
  - Sleepiness/Fatigue
  - Irritability
  - Difficulty focusing
  - Morning Headaches
- Sleep related symptoms
  - Snoring
  - Restless sleep
  - Interruption of breathing
  - Need to urinate in the middle of the night

Physical features of OSA

- Obesity
- Large neck size
- Narrow airway
  - Look at the back of the throat and observer for a narrow opening between pharyngeal walls
- Macroglossia
  - Look for ridging of the tongue
- Retrognathia
  - Look at a patient from a profile position- observe is their chin sits further back than the bridge of their nose

Associated Conditions

- Sleepiness and motor vehicle accidents
- Memory and OSA
  - Hypoxemia and hypercarbia cause deficits in attention, memory, executive function and language ability
- Atrial fibrillation
  - More patients with a-fib resistant to ablation have OSA compared to patients with a-fib that are successfully treated with ablation
- Heart failure
  - Men with severe OSA are more likely to develop heart failure than those without OSA

Olaithe M, Bucks RS, Hillman DR, Eastwood PR. Cognitive deficits in obstructive sleep apnea: Insights from a meta-review and comparison with deficits observed in COPD, insomnia, and sleep deprivation. Sleep Med Rev. 2018 Apr;38:39-49. doi: 10.1016/j.smrv.2017.03.005. Epub 2017 Mar 30.

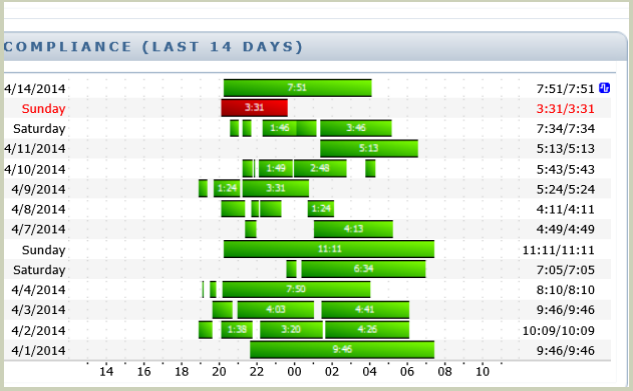
OSA treatments

- Positive Airway Pressure
- Oral appliances
- Positional therapy
- Weight loss
- Inspire- Upper airway stimulation
- Upper airway surgery

Currently in development- oral medications for OSA

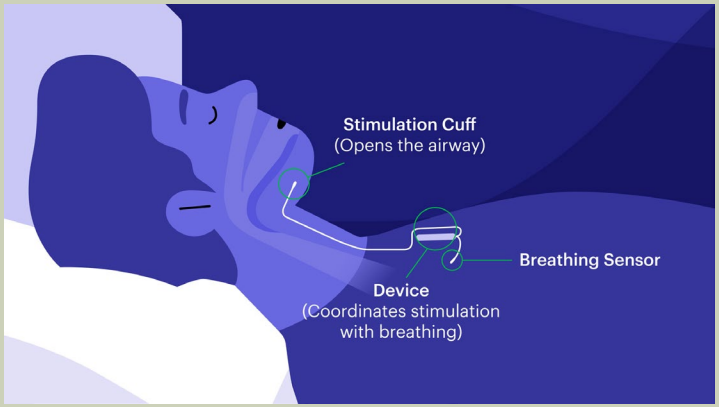
Updates in PAP therapy

- More comfortable masks and PAP delivery
- Auto therapy which can provide a range of pressures
- Travel CPAPs
- Compliance monitoring- viewable to the patient and provider
- Remote pressure adjustments by the provider



Inspire/Upper airway stimulation

- Stimulator that wraps around the hypoglossal nerve to push the tongue forward during sleep and open up the airway
- Requirements to be a candidate for therapy:
  - Moderate to severe OSA
  - Tried and failed PAP therapy
  - BMI < 32
  - Anterior-posterior airway collapse



Insomnia

- Difficulty falling asleep
- Difficulty staying asleep
- Waking up early and unable to fall asleep
- About 30 percent of American adults have symptoms of insomnia
- About 10 percent of adults have insomnia that is severe enough to cause daytime consequences
- Patient with insomnia have insufficient sleep but have opportunity to get enough sleep; this differs from sleep deprivation

Types of Insomnia

- Transient
  - < 4 weeks triggered by excitement, stress, grief, or occurs when away from home
- Short-term
  - 4 weeks to 6 months, ongoing stress at home or work, medical problems or psychiatric illness
- Chronic
  - Poor sleep every night or most nights for > 6 months, initial trigger or cause may have resolved
  - Can be closely related to psychologic factors- depression/anxiety

Insomnia Treatments

- Avoid sleeping medications if possible
  - High risk for tolerance and side effects
  - In many cases it becomes ineffective when you take it nightly
- **In elderly, sleeping medications can increase risk for falls and negatively effect cognitive function**
- If you need to use sleeping medications, use as a temporary treatment in the setting of an acute stressor like grief or job change or as an as needed medication.
- Favored treatment approach is Cognitive Behavioral Therapy for insomnia

What is Cognitive Behavioral Therapy for Insomnia?

- Comprehensive approach targeting factors that maintain insomnia
- Rooted in the science of sleep/wake regulation and principles of behavior change
  - Sleep restriction and getting out of bed for prolonged sleep wake ups
- Skill based and brief (4-8 sessions)
- Paid and free online options are available
  - CBT-i Coach is a free app option that was developed by the VA

Treating Insomnia with Other Disorders

- Insomnia with headaches/pain: amitriptyline or nortriptyline 10-30mg, gabapentin 100-300mg, pregabalin 50-100mg
- Insomnia with anxiety and depression: trazodone 25-75 mg and mirtazapine 7.5-15 mg (can be stimulating as dose increases) **watch out for weight gain**
- Insomnia with delusions, hallucinations, paranoia- quetiapine 25-50mg (more sedating properties at lower dosages) **watch out for metabolic syndrome**

Antidepressants and quetiapine can worsen RLS and parasomnias

Restless Leg Syndrome

- Uncontrollable urge to move legs at rest
  - **Sensations that begin after rest.** The sensation typically begins after you've been lying down or sitting for an extended time, such as in a car, airplane or movie theater.
  - **Relief with movement.** The sensation of RLS lessens with movement, such as stretching, jiggling your legs, pacing or walking.
  - **Worsening of symptoms in the evening.** Symptoms occur mainly at night.
  - **Nighttime leg twitching.** Periodic limb movement of sleep. This causes your legs to twitch and kick, possibly throughout the night, while you sleep.
- This condition can be associated to low iron stores, medications, caffeine, stimulants, kidney disease, other sleep disorders and stress

Restless Leg Syndrome

- Occurs in 5 to 15 percent of adults
- More common in Caucasians, Female Populations and Northern European Populations
- Family history of RLS is present in 40 to 60 percent of cases
- No diagnostic test available, diagnosis is purely clinical
  - An elevated PLM index on a sleep study is supportive

RLS Treatment

- Important to rule out and address contributing factors
  - OSA
  - Caffeine
  - Medications- antidepressants and other psych medications can worsen RLS
  - Low ferritin levels- goal ferritin is > 75
  - Thyroid abnormalities

RLS Treatment

- First line treatment is now gabapentin-100-900mg hs
- Pregabalin 50-150mg hs
- Gabapentin Encarbil (Horizant)- 300-600 mg hs
- First line of treatment used to be dopamine agonists like ropinirole and pramipexole but no longer is due to augmentation
  - Augmentation- increase in symptom severity in the evening, symptoms occur earlier in the day, and symptoms spread to other areas of the body
- If using dopamine agonists- use lowest dose possible
  - Ropinirole daily max 4mg and pramipexole max 0.75mg
  - If using this medication class monitor for compulsive behaviors- eating/shopping/gambling
- Opiates- therapy for severe drug resistant RLS

Parasomnia

- Non REM parasomnia- more common in childhood
  - Sleep walking/talking eating
  - Occur in stage 2 and stage 3 of sleep
  - More commonly in the first half of the night
  - Rarely violent but patient can be scared
- REM behavior disorder- more common in elderly
  - Occurs during REM sleep
  - Patient is partially paralyzed so rarely walking out of the room
  - Usually fighting someone or something
  - Can fall out of bed or hurt bed partner
  - Has an association to Parkinson's Disease- 45%

RBD Treatment

- Treat OSA if present
- Avoid medications that worsen RBD- SSRIs primarily. Bupropion is the favored antidepressant
- Start with melatonin 1mg, increase as high as 20mg
  - 60-70% effective in treated RBD
- Clonazepam- 0.25-2mg- watch out of side effects of sleepiness, grogginess, imbalance
- Rivastigmine (cholinesterase inhibitor) can be used for refractory RBD

RBD and Parkinson Syndromes

- RBD is recognized as a manifestation of α-synucleinopathies
  - Parkinson's Disease
  - Multiple System Atrophy
  - Dementia with Lewy Body
- RBD conversion to α-synucleinopathies is 34 % at the 4 year mark and 73% at the 12 year mark
  - Faster if there are associated features- loss of smell, rigidity, hypomimia, hypophonia
- Patients with PD and RBD are more likely to develop dementia than PD patients without RBD
- There is an association of RBD to PTSD, these patients do not have the same risk to develop α-synucleinopathies

Narcolepsy

- Profound sleepiness (“sleep attack”) during the day despite getting enough total sleep during the day
- Patients can have fragmented sleep at night
- Disorder affecting the brain’s ability to control sleep-wake cycles- related to a deficiency in hypocretin.
  - This is a neurotransmitter that regulates arousal , wakefulness , and appetite
- Associated symptoms- cataplexy, sleep paralysis, sleep related hallucinations, and parasomnia
- Testing- over night and daytime sleep study- PSG/MSLT (polysomnogram and multiple sleep latency test)
- Treatments- wake promoting medications, traditional stimulants, SSRIs, and night medications that can help consolidate sleep at night

Sleep deprivation was declared as a public health problem in 2006

- An estimated 50% of Americans are sleep deprived
  - 30% average less than 6 hours per night
- Many people do not have trouble sleeping or a sleep disorder but chose to stay up late. This leads to sleep deprivation with daytime consequences
- The cumulative effects of sleep loss and sleep disorder represent an under recognized public health problem

Sleep Studies
Who needs one and who does not?

THE PRIMARY REASON TO GET A SLEEP STUDY IS TO LOOK FOR SLEEP APNEA OR NARCOLEPSY/HYPERSOMNIA

IT IS IMPORTANT TO RECOGNIZE THAT YOU ALTHOUGH SLEEP STUDIES DO NOT ALWAYS HELP DIAGNOSE RLS, RBD, INSOMNIA, AND PARASOMNIA, YOU MAY STILL GET A STUDY BECAUSE OSA MAY BE WORSENING THESE CONDITIONS FOR THE PATIENT.

Screening Questionnaires for OSA

- Screening questionnaires:
- Epworth Sleepiness Scale
  - 8 questions that assess sleepiness during sedentary activities.
  - A score of >10 is consistent with excessive daytime sleepiness
- STOP-BANG
  - 8 questions reviewing risk factors for OSA- snoring, apneas, sleepiness, HTN, BMI, age, gender, neck circumference
  - A score >5 is high risk for OSA

Types of Studies

- Home sleep study
  - Easiest study that that the patient can complete at home with no EEG wires
  - Sometimes misses sleep apnea due to inability to differentiate sleep and wake time
- Polysomnogram
  - In lab sleep study
  - Monitors brain waves/EEG, movements, and breathing
- PAP titration study
  - Most patients do well on autoCPAP but some need further testing to see if they need oxygen or a higher level of PAP therapy.
- Multiple Sleep Latency test
  - This study is necessary to diagnose narcolepsy or hypersomnia
  - 4-5 daytime nap opportunities to see how fast someone falls asleep and if they go into REM sleep

Someone you do not want to get a sleep study in due to minimal clinical benefit

- 28 yo F with a BMI of 20, no snoring or nocturia, and normal airway exam presenting with sleep onset insomnia.
- She unlikely to have OSA and testing would not help in her management as her insomnia occurs before falling asleep

Home sleep study vs In-Lab Study

Home sleep study

- High clinical probability for OSA
- Patient preference
- Insurance requirement
- Generally can get scheduled sooner

In-lab study

- Patient with complex medical conditions
- Cognitive limitations
- Failed/negative home sleep study
- Need for MSLT (in lab PSG needs to be done the night prior

- Sleep is an important physiologic process we should protect and support with a healthy lifestyle.
- Screening for sleep disorders is key for patients with cognitive symptoms.
- As we age, it is important to reduce medications that may cause daytime sleepiness.

THANK YOU!

QUESTIONS ?

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