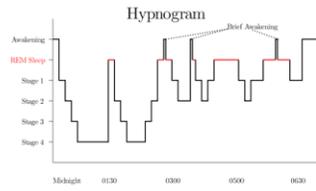




Introduction to Sleep Disorders for the Primary Care Provider

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May 13, 2016

Sleep Architecture



Disclosure

- I have no personal conflicts of interest or relevant financial relationships to disclose
- Views expressed in this presentation are those of the author and do not necessarily reflect the official policy or position of the Department of the Navy, Defense, nor the U.S. Government
- Some non-FDA approved treatments will be discussed

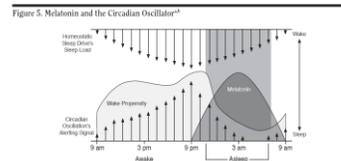
How much sleep is normal?

- No exact number
- Range is 6-9 hours with significant individual variability
- >10 hours seen in long sleeper
- <5 hours probably abnormal with symptoms of sleep deprivation

Objectives

- Normal Sleep Physiology
- Insomnia
- Obstructive Sleep Apnea
- Restless Legs Syndrome
- Narcolepsy
- Somnambulism

Sleep Regulation



*Adapted with permission from Kikuchi and Kawahara,²⁰ Edgar et al.,²¹ and Dijk et al.²²
Melatonin and the SCN circadian oscillator sharpen each other's wave form. The midline drop in circadian alerting signal between 10 and 11 p.m. is caused in part by the increase in melatonin secretion that is taking place at that time, inhibiting SCN neuronal firing. Without the release of melatonin, the decrease in SCN activity at nighttime would happen more gradually, making the transition to sleep and sleep onset a much longer and less predictable process.

Case 1

27 year old female PO2 with BMI=24 reports trouble staying asleep for the past 3 years since returning from IA deployment. She has been going to bed earlier every night at 2100 and falls asleep within 30 minutes. She awakens at 0500 but feels unrefreshed. She estimates she gets 4-5 hours sleep per night. She does not nap and wakes 3-4 times per night tossing turning. Sometimes she awakens gasping and anxious. She thinks she snores softly sometimes. She does not use caffeine, tobacco or alcohol. Her Epworth is 7/24.

Chronic Insomnia Disorder icd-3

- Difficulty initiating or maintaining sleep or waking up earlier than desired
- Adequate opportunity for sleep,
- Associated with daytime impairments such as fatigue, irritability, school/work impairments
- Present for over 3 months
- Symptoms at least 3 times per week
- No other disorder to explain symptoms
- Co-morbid with other conditions (depression)

What is the best diagnostic test for this patient?

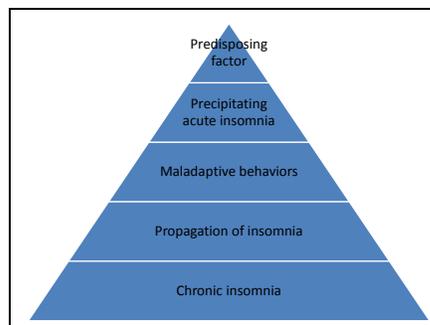
- A. Multiple sleep latency testing
- B. Sleep diary
- C. Psychomotor vigilance test
- D. Facility-based polysomnogram
- E. Unattended Sleep Study (Home Sleep Test)

Epidemiology

- 50 percent of primary care patients have occasional insomnia
- 10-30 percent of primary care patients have chronic insomnia
- More prevalent in women than men
- Increases with age and medical co-morbidities
- Disorder of increased arousal

What treatment would be most beneficial?

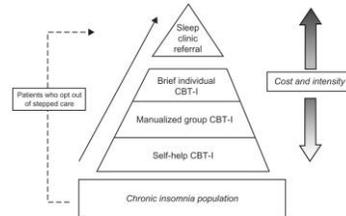
- A. Wake-promoting agent such as modafinil 100 mg twice daily
- B. Sleep-promoting agent such as zolpidem 5 mg at bedtime
- C. Sleep restriction by having the patient go to bed later than 2300
- D. Melatonin agonist such as ramelteon 8 mg at 1800
- E. Sleep hygiene instructions



Behavioral Therapy

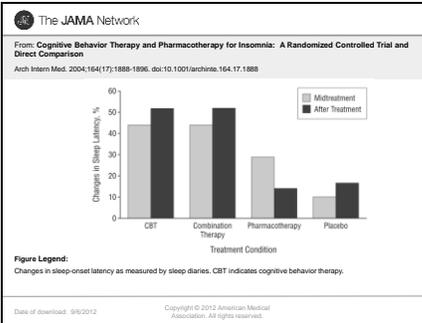
- Relaxation training
 - Progressive muscle relaxation
 - Guided imagery
 - Abdominal breathing

Stepped Care Model



Cognitive behavioral therapy for insomnia (CBT-I)

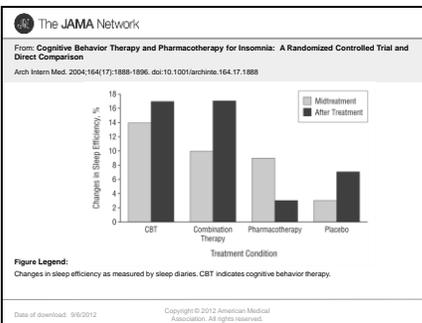
- Common cognitive distortions are identified and addressed in the course of treatment. These include:
 - “I can’t sleep without medication,”
 - “I have a chemical imbalance,”
 - “If I can’t sleep I should stay in bed and rest,”
 - “My life will be ruined if I can’t sleep.”
 - “I need medication for deeper sleep”



Non-Pharmacologic Treatments

Technique	Goal	Method
Stimulus Control Therapy*	Strengthen bed and bedroom as sleep stimuli	If unable to fall asleep within 20 min, get out of bed and repeat as needed
Relaxation Therapies*	Reduce arousal and decrease anxiety	Biofeedback, progressive muscle relaxation
Restriction of Time in Bed (Sleep Restriction)	Improve sleep continuity by limiting time spent in bed	Decrease time in bed to equal time actually asleep and increase as sleep efficiency improves
Cognitive Therapy	Dispel faulty beliefs that may perpetuate insomnia	Talk therapy to dispel unrealistic and exaggerated notions about sleep
Paradoxical Intention	Relieve performance anxiety	Try to stay awake
Sleep Hygiene Education	Promote habits that help sleep; eliminate habits that interfere with sleep	Promote habits that help sleep; eliminate habits that interfere with sleep
Cognitive Behavioral Therapy*	Combines sleep restriction, stimulus control, and sleep hygiene education with cognitive therapy	Combines sleep restriction, stimulus control, and sleep hygiene education with cognitive therapy

* Standard therapy (high clinical certainty).
Data from Mergenthaler T, Kraemer M, Alavi C, et al. Proven parameters for the psychological and behavioral treatment of insomnia are updated. An American Academy of Sleep Medicine report. Sleep. 2006;29(11):1475-78.



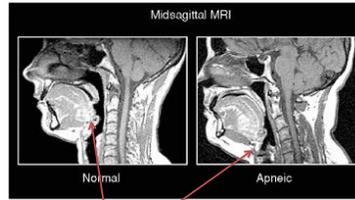
Pharmacologic Therapy

- Most efficacy studies are short-duration (2-5 weeks) Longer studies have looked at zaleplon¹ and ramelteon²
- FDA indications: all agents are for **short-term use** except Eszopiclone, zolpidem extended-release, and ramelteon

¹ Ancoli-Israel S, et. Al., Long-term use of sedative hypnotics in older patients with insomnia. *Sleep Med.* 2005;6:107-113

² DeMicco M, et. Al., Long-term therapeutic effects of ramelteon treatment in adults with chronic insomnia: a 1 year study. *Sleep.* 2006;29(suppl):A234

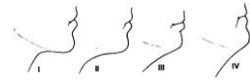
Difference in Static Airway Anatomy in Patients with OSA



Note: inferior hyoid location and angled orientation of the genioid

Sedating low-dose antidepressants trazodone, amitriptyline, nortriptyline

- **Not recommended** as first line therapy for insomnia (consider after CBTi and two BzRAs)
- Poor efficacy data
- High side-effect profile
 - Weight gain
 - Daytime sedation
- Tolerance, rebound insomnia
- Ineffective alone in depression and insomnia



Cervicomental angle predicts OSA as well as neck circumference >17"/43 cm in men

Insomnia Summary

- Chronic insomnia is a behavioral problem and generally responds well to behavioral treatment
- Pharmacotherapy alone is not as effective and benefits are not sustained long-term

Ann Intern Med. Published online 3 May 2016 doi:10.7326/M15-2175

STOP-BANG Sleep Apnea Questionnaire

Chang F et al. *Anesthesiology*. 2003 and BJA 2002

STOP		
Do you SNORE loudly (louder than talking or loud enough to be heard through closed doors)?	Yes	No
Do you often feel Tired, fatigued, or sleepy during daytime ?	Yes	No
Has anyone OBSERVED you stop breathing during your sleep?	Yes	No
Do you have or are you being treated for high blood PRESSURE ?	Yes	No
BANG		
BMI more than 35kg/m ² ?	Yes	No
AGE over 50 years old?	Yes	No
NECK circumference > 16 inches (40cm)?	Yes	No
GENDER, Male ?	Yes	No
TOTAL SCORE		

High risk of OSA: Yes 5 - 8

Intermediate risk of OSA: Yes 3 - 4

Low risk of OSA: Yes 0 - 2

The Epworth Sleepiness Scale (ESS)

How likely are you to do off or fall asleep in the following situations, in contrast to feeling just tired? This refers to your usual way of life in recent times. Even if you have not done some of these things recently try to think and how they would have affected you. Use the following scale to choose the most appropriate number for each situation:

0 = would never do so
 1 = slight chance of dozing
 2 = moderate chance of dozing
 3 = high chance of dozing

SITUATION	CHANCE OF DOZING (0-3)
Sitting and reading	
Watching television	
Sitting inactive in a public place (e.g. a theater or meeting)	
As a passenger in a car for an hour without a break	
Lying down to rest in the afternoon when circumstances permit	
Sitting and talking to someone	
Sitting quietly when a bench without alcohol	
In a car, while stopped for a few minutes in the traffic	
TOTAL SCORE	

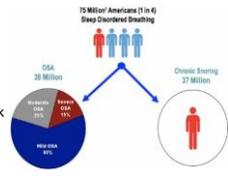
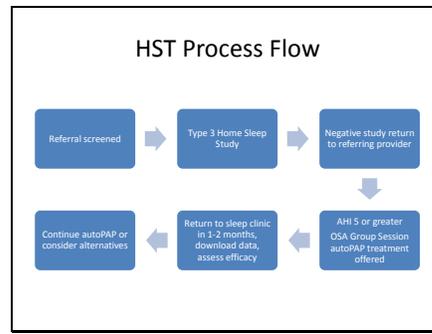
SCORE MEANS:
 1-4 Congratulations, you are getting enough sleep!
 5-8 Your score is average
 9 and up Very sleepy and should seek medical advice



- ### Mechanisms
- Anatomic factors
 - Loss of airway dilator muscle tone
 - Damage due to vibration
 - Fatigue due to increased tone during wake
 - Loss of lung volume (FRC) from obesity, supine position
 - Ventilatory control instability with cycling loss of airway tone and drive causing central apnea
 - Arousal threshold

Prevalence of OSA

- Overall prevalence of OSA **10-25%** (30+ million Americans)
- Males are affected more commonly (2x risk)**
- Obesity (body-mass index >30) increases risk **4-fold**
- Increases after menopause in women
- Runs in families

- ### Risk factors
- Male gender RR=2
 - Obesity RR=4
 - Age (highest increase from age 40-60)
 - Blacks tend to have higher risk of OSA than whites
 - Asians tend to have more OSA lower BMI than whites
 - Daytime sleepiness (Epworth) is not strongly correlated with OSA
 - No screening tool is available to exclude OSA

Home Sleep Testing

- ECG channel
- 2 nasal airflow channels
- 2 effort channels (chest and abdomen)
- Blood oxygen level
- Heart rate
- Snore
- Position



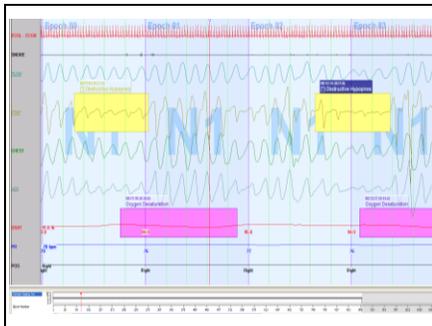
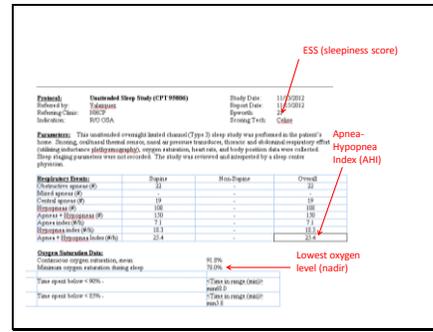
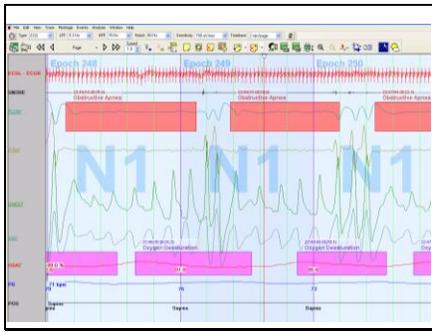
Definitions

- Apnea: cessation of breathing for >10 seconds
May be central, obstructive or mixed
- Hypopnea: decreased flow >30% for >10 seconds leading to a drop in SpO2 4% or an arousal
- Respiratory effort related arousals (RERA): arousals associated with decreased flow not meeting criteria for hypopnea
- AHI: (apnea hypopnea index) number of breathing problems divided by the hours of sleep or recording time (RDI)

Apnea-hypopnea index (AHI)

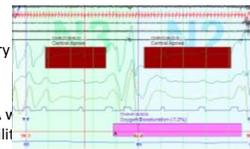
- AHI is all the apneas+hyponeas divided by the recording time
- For example: (17 apneas + 66 hypopneas)/7 hours recording = AHI of 11.8
- AHI<5 is considered **normal**

AHI	SEVERITY	TREATMENT
5-14	MILD	OPTIONAL
15-30	MODERATE	RECOMMENDED
>30	SEVERE	HIGHLY RECOMMENDED



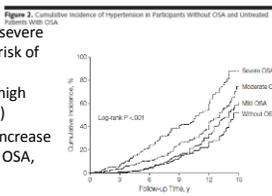
Central Apnea

- Apnea: stopped breathing for ten seconds or more without respiratory effort
- Can be seen after arousals or in OSA v respiratory instability



Moderate-Severe OSA

- Moderate and severe OSA increases risk of developing hypertension (high blood pressure)
- No significant increase seen with mild OSA, however



Marin, JAMA, May 2012; 307,20

Data download example

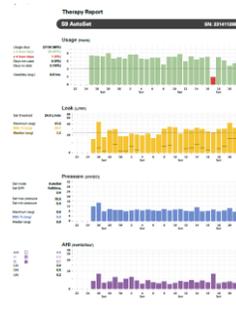


Moderate-Severe OSA in Women

- OSA with AHI>10 associated with 2.76x increased risk of stroke or heart disease (CI 1.35-5.62) after adjustment for age, BMI, HTN, diabetes, atrial fibrillation in women
- CPAP treatment seems to reduce this risk

Campos-Rodriguez, AJRCCM, June 15, 2014

Data download example



Continuous Positive Airway Pressure (CPAP)

- The most effective treatment for OSA is continuous positive airway pressure (CPAP)
- A machine is used to generate air pressure to maintain airway patency during sleep
- It usually takes some effort to acclimate to CPAP but it is generally well-tolerated
- Side effects include dry nose or mouth, gas or bloating, mask discomfort

Oral Appliance Therapy (OAT)

- Custom-fitted dental device
- Advances mandible during sleep to open airway
- Suitable for mild-moderate OSA
- Reduces snoring



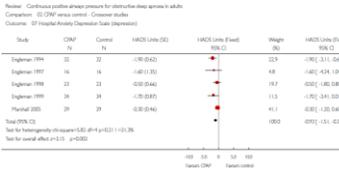
Oral appliances

- Fitted by sleep dentists
- Gradual adjustment increases advancement of jaw
- Takes 2-3 weeks to fabricate and a few weeks for adjustments



CPAP has a modest effect on anxiety and depression

Analysis 02.07 Comparison 02 CPAP versus control - Crossover studies, Outcome 07 Hospital Anxiety Depression Scale (Depression)



CPAP vs OAT

CPAP

- Slightly cumbersome
- Requires electricity
- Monitors and adjusts pressure depending on apneas and hypopneas
- Objective data
- Recommended for severe OSA
- Rapid issue



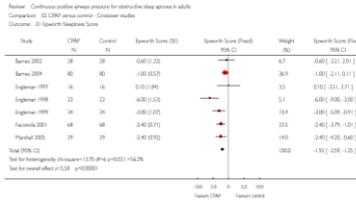
OAT

- Portable
- No need for electricity
- No need for supplies
- No monitoring of apneas during sleep
- Subjective data
- Not recommended for severe OSA
- May take a few weeks to fabricate



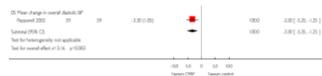
CPAP improves ESS 2-3 points Also improves MSLT and MWT

Analysis 02.01 Comparison 02 CPAP versus control - Crossover studies, Outcome 01 Epworth Sleepiness Score



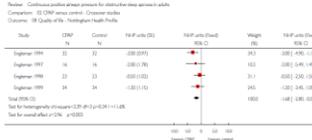
CPAP has modest impact on BP

- CPAP improves diastolic BP -3.3 mm Hg
- CPAP improves systolic BP -3.4 mm Hg
- CPAP improves nocturnal MAP -4.20 mm Hg

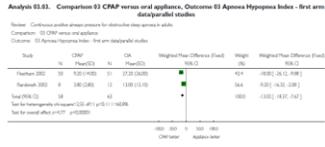


CPAP improves Quality of Life

Analysis 02.08 Comparison 02 CPAP versus control - Crossover studies, Outcome 08 Quality of Life - Nottingham Health Profile



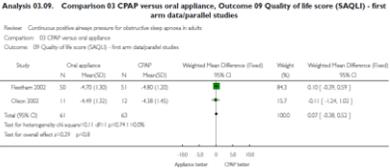
CPAP better at lowering AHI than Oral Appliance



Summary

- Home testing and Lab testing strategies have similar outcomes in managing OSA
- CPAP is the best tolerated, most effective therapy for OSA
- Oral appliance is a good alternative treatment for mild-moderate OSA
- Surgery is reserved for special cases

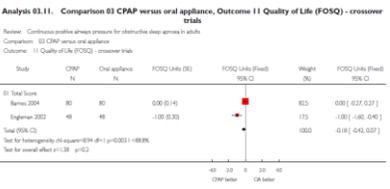
CPAP and Oral Appliance have similar impact on Quality of Life



Restless Legs Syndrome (RLS)

- Clinical diagnosis (PSG not required)
- Should cause sleep disturbances
- Associated with mood disorders
- Family history often positive (50%)
- Associated with periodic limb movements but not required for diagnosis
- Arms often affected as well as legs
- **RLS-WED is not diagnosed by a sleep study (PSG not required)**

CPAP and Oral Appliance have similar impact on Quality of Life



RLS Diagnostic Criteria

- Uncomfortable sensation in legs
- Urge to move legs
- Worse at rest, improves with movement
- Worse at night (circadian pattern)
- Causes significant impairment of sleep or other functioning
- Exclude other causes (neuropathy, nervous foot tapping, cramps, myalgias)
- **40% of people without RLS-WED will report some urge to move their legs at night**

RLS

- U – Uncomfortable feeling in extremities
- R – Rest makes symptoms worse
- G – Getting up and moving makes symptoms better
- E – Evening symptoms are worse

RLS-WED Treatment

- Iron replacement (ferritin >75 mcg/L, transferrin 20-50%)
- Dopaminergic agents
 - Pramipexole
 - Ropinirole
 - Rotigotine
 - Warn about **impulsivity** and nausea
- Gabapentin extended release
- Relaxation techniques, massage, warm baths, external counter pulsation
- Opioids

RLS-Risk Factors

- Family history (single nucleotide polymorphisms-SNPs)
- Iron deficiency (ferritin <50 mcg/L)
- Antidepressants (except bupropion)
- Antihistamines TCAs
- Dopamine antagonists (risperidone)
- Pregnancy (2-3x) increases with parity
- Chronic kidney disease (2-5x)
- Gastric bypass

Question 2

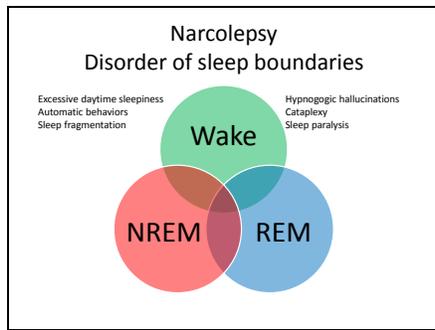
- A 26 year-old man BMI=28 with excessive daytime sleepiness for six years is referred for snoring. He undergoes a home sleep test which shows AHI=6 per hour, nadir O2 saturation 86% and is diagnosed with mild OSA. He is treated with auto-titrating CPAP and feels better initially but hyper-somnolence returns. His adherence with CPAP is good and residual AHI is 0.9 on CPAP. He reports taking naps in parking lot after driving to work and consumes 600 mg caffeine daily to stay awake. He has no cataplexy. He reports kicking and restless sleep and awakens 3-5 times per night.

Pathophysiology

- Decreased CNS iron levels in substantia nigra
- Decreased dopaminergic activity
- Increased glutamate activity or imbalance
- Genetic factors (BTBD9, MEIS1, MAP2K5/LBXCOR may alter iron homeostasis)

What is the next step?

- Polysomnogram with 4 limb leads to assess for periodic limb movement disorder
- Add modafinil for excessive daytime somnolence refractory to CPAP
- Perform in-lab PSG and CPAP titration
- 1-2 week sleep diary followed by CPAP titration and MSLT
- Maintenance of wakefulness test after overnight use of CPAP to document hyper-somnolence



- ### Cataplexy
- Duration seconds to minutes with subsequent full recovery
 - Complete collapse uncommon
 - Not always reproducible, may be worse after sleep deprivation
 - Partial weakness (jaw dropping, knees giving out) common
 - May present 3-5 years after onset of daytime sleepiness
 - Almost always HLA DQB1-0602 positive

- ### Hypersomnolence in Narcolepsy
- Epworth scores typically range 18-24/24
 - Often predates cataplexy
 - Transient improvement with sleep and naps
 - **Naps are often required before noon**
 - Urge to sleep occurs without warning or prodrome (sleep attacks)

- ### Narcolepsy Type 2
- Daily irrepresible need for sleep for at least 3 months
 - No cataplexy
 - Mean sleep latency <8 minutes and 2+ sleep onset REM periods, one which may be on PSG
 - Hypersomnolence not explained by another disorder
 - **Note: Anyone who is sleep-deprived can meet the sleep test criteria above**

- ### Cataplexy
- Suggestive of narcolepsy (Type 1)
 - Loss of bilateral muscle tone
 - Fully conscious
 - Triggered by strong emotion, most commonly laughter but also anger, excitement and surprise
 - Spares eye and respiratory muscles
 - Reflexes absent

- ### Narcolepsy treatment
- Strategic naps
 - Modafinil 200-400 mg daily in split doses
 - Armodafinil 150-250 mg daily (R-enantiomer, slightly longer effect)
 - Sodium oxybate for cataplexy (69-85% reduction) and EDS (Standard)
 - TCA, SSRI, SNRI (venlafaxine) for cataplexy (Guideline)
 - Methylphenidate (Concerta) 18-54 mg (Guideline)

Slide 76

Sleepwalking (Somnambulism)

- 4% Adults, 22% lifetime prevalence
- Leaving the bed during N3 sleep (first half of the night)
- May have multiple episodes per night
- More complex and goal-directed behavior than in confusional arousals but similar in nature
- Typical duration <10 minutes
- Little or no recall

Military Service and Hypersomnia

- “To constitute a physical disability, the medical impairment or physical defect must be of such a nature and degree of severity as to interfere with the member’s ability to adequately perform his or her duties.”
- Narcolepsy generally mandates a PEB
- Sleep apnea and idiopathic hypersomnolence may mandate a PEB depending on severity, response to treatment ,and patient’s occupation
- Sleepwalking does not merit PEB and is disqualifying for military service (ADSEP)

Slide 77

Sleepwalking (Somnambulism)

- Increase seen with z-drugs (zolpidem), stimulants, antihistamines, SSRIs.
- Increase seen with N3 sleep rebound after sleep deprivation
- Increase with stress, illness, anxiety, alcohol use, bladder distension
- Increase with sleep fragmentation from other sleep disorders (OSA)

Questions

Somnambulism Treatment

- Reassurance and address contributing factors
- Safety (lock keys, firearms, windows)
- Gently guide patient back to bed
- Scheduled awakenings
- Adequate sleep duration
- Avoid antihistamines
- Medications generally not used but can consider TCAs.