Sleep Physiology and Disorders

28th Annual Family Medicine Review
Austin, TX
April 26, 2012
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Scott & White Sleep Institute
Pre-Test
Sleep-wake cycles are controlled in the:

- A. Thalamus
- B. Hypothalamus
- C. Pons
- D. Medulla
- E. I’m not sure
How many physiologic states do we have?

• A. 2
• B. 3
• C. 4
• D. 5
• E. I’m not sure
Which of the following is most often seen with obstructive sleep apnea?

- A. Congestive heart failure
- B. Cor pulmonale
- C. Pulmonary hypertension
- D. Systemic hypertension
- E. I’m not sure
Obstructive sleep apnea is a risk factor for:

- A. Cataplexy
- B. Sleep paralysis
- C. Right ventricular hypertrophy
- D. The metabolic syndrome
- E. I’m not sure
Restless legs syndrome is associated with:

• A. Fibromyalgia
• B. Chronic fatigue syndrome
• C. Iron deficiency
• D. Hypothyroidism
• E. I’m not sure
The diagnosis of restless legs syndrome should be made by:

• A. History and physical exam
• B. Overnight sleep study (polysomnography)
• C. Electromyogram (EMG)
• D. Nerve conduction velocities
• E. I’m not sure
End of Pre-Test
Objectives

- Identify basic concepts of primary care sleep medicine
- Formulate a differential diagnosis in patients with sleep complaints
- Determine appropriate management of common sleep disorders
Introduction to Sleep

• Describe normal sleep physiology
• Discuss adverse effects of sleep deprivation on daytime functioning
• Discuss the importance of taking a sleep history
• List the principles of good sleep hygiene
Definitions of Sleep

One can define sleep as:

• A *reversible* behavioral state of perceptual disengagement from, and unresponsiveness to, the environment.

• A very complex amalgam of physiological and behavioral processes.

• A process, unlike coma, that is physiologic, recurrent, and reversible.
Sleep & Wake Determinants
Determinants of Sleepiness

Homeostatic and Circadian Factors

Sleep Drive

• Medications
• Central Factors

Sleep Tendency

Level of Arousal

CNS and Physiological Arousal and Circadian Factors

• Medications
• Environment
Biologic Clock Activity

- The body’s master “clock” is located in the suprachiasmatic nucleus (SCN) of the hypothalamus.
- Light-dark signals reach the SCN via a retinohypothalamic track.
- SCN cells are circadian oscillators, exhibiting a stable, bi-phasic firing cycle.

Architecture and Physiology of Sleep
Principles of Sleep Hygiene

Keep Circadian Clock on Time:
  – Awaken at approximately the same time each day.
  – Obtain bright light during desired daytime hours.

Maximize Homeostatic Sleep Drive:
  – Limit napping in case of insomnia.
  – Go to bed only when sleepy.

Reduce Physiological and Psychological Arousal:
  – Limit or eliminate caffeine, nicotine, alcohol.
  – Exercise well before bedtime.
  – Shut your day down at least 1 hour before bedtime.
  – Sleep in a comfortable bedroom.
During non-REM and REM sleep, the physiology of all organs is changed from wakefulness.
EEG: Sleep Patterns

Awake: low voltage – random, fast

Drowsy: 8 to 12 cps – alpha waves

Stage 1: 3 to 7 cps – theta waves

Stage 2: 12 to 14 cps – sleep spindles and K complexes

Delta sleep: (stages 3 and 4) 1/2 to 2 cps – delta waves >75 µV

REM sleep: low voltage – random, fast with sawtooth waves
Adult Sleep Architecture

Non-REM: 75% of total sleep time
- Stage 1: 5-10%
- Stage 2: 45-50%
- Stage 3: 25%
- Delta sleep = stages 3 + 4 = Stage N3 = SWS

REM: 25% of total sleep time
Sleep Across Life

As a child develops, its sleep gradually becomes restricted to the night.
Hypnograms Across Life

- **Children**
- **Young Adults**
- **Elderly**
## Comparison of REM and NREM Sleep

<table>
<thead>
<tr>
<th>Physiologic Variable</th>
<th>NREM</th>
<th>REM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart Rate</td>
<td>Regular</td>
<td>Irregular</td>
</tr>
<tr>
<td>Resp Rate</td>
<td>Regular</td>
<td>Irregular</td>
</tr>
<tr>
<td>Blood Pressure</td>
<td>Normal</td>
<td>Variable</td>
</tr>
<tr>
<td>Muscle tone</td>
<td>Preserved</td>
<td>Absent</td>
</tr>
<tr>
<td>Brain O2 consumption</td>
<td>Reduced</td>
<td>Increased</td>
</tr>
<tr>
<td>Temperature</td>
<td>Normal</td>
<td>Decreased</td>
</tr>
<tr>
<td>Sexual changes</td>
<td>Rare</td>
<td>Frequent</td>
</tr>
</tbody>
</table>
Non-REM Sleep
Non-REM Disorders

- Parasomnias
  - Sleep Walking
  - Sleep Talking
  - Exploding Head Syndrome
  - Enuresis
- Seizure Disorder
- Periodic Limb Movement Disorder
REM Sleep
REM Sleep Disorders

- REM Sleep Behavior Disorder
- Nightmare Disorder
- Recurrent Sleep Paralysis
Mixed REM and NonREM disorders

• Sleep Related Breathing Disorders
  – Obstructive Sleep Apnea
  – Central Sleep Apnea
  – Sleep Related Non-obstructive Alveolar Hypoventilation

• Narcolepsy
Function of Sleep

• Grand Unified Theory for Sleep is unknown

• Approaches to understanding:
  – Compare to wake physiology
  – Effects of sleep deprivation
  – Effects of sleep enhancement
Function of Sleep

• Restoration and Somatic Growth Theory
  – Anabolic processes
  – Secretion of Growth Hormone in Stage N3

• Metabolic Theory
  – Energy Conservation
  – Temperature drops during sleep
  – Removal of Toxins generated during wake
Function of Sleep

• Survival Theory
  – Ecological hypothesis of foraging and predator avoidance
  – Human is only mammal that sleeps only at night
  – Immune defense function (IL-1β, TNF-α)

• Neural growth and processing theory
  – Neuronal synaptic plasticity
  – Brain development
  – Learning and memory consolidation
Taking a Sleep History and Sleep Testing
Sleep Review of Systems

General Screening

Ask the patients the following questions during their yearly well visit or initial new patient intake:

- Do you wake up feeling rested and refreshed?
- How long does it take you to fall asleep?
- Do you snore, or has your bed partner complained about you snoring?
- Do you have any leg discomfort at night?
Taking a Sleep History

Uncovering Daytime Sleepiness

– Attempt to get a history from bed partners, family members, or friends when possible.
– Patients may be unaware of events occurring during sleep.
  • Many people will deny daytime sleepiness.
    – Fear loss of job, loss of driving license, “lazy” label
– Perform thorough neuro, ENT, neck exams.
When is a Sleep Study Useful?

– Suspected sleep apnea
– Unexplained daytime somnolence
  • Exclude insufficient sleep
    – Normal = 7-8 adults, 9+ children
  • Correct endocrine/metabolic abnormalities
  • Exclude medication effects
– Abnormal movement activity in sleep
– Suspected Sleep Apnea
– Unexplained chronic insomnia > 2 months when organic cause suspected
  • After correcting sleep hygiene, etc.
  • When organic cause suspected (OSA, etc.)
Types of Sleep Studies

– Polysomnography (PSG)
  • Records multiple parameters (EEG, EKG, EMG, breathing, $O_2$, $CO_2$, limb movements, rarely esophageal pH or pressure) at normal sleep time

– Multiple Sleep Latency Test (MSLT)
  • 5 daytime naps, 20 minutes each
  • Objective measure of daytime sleepiness

– Maintenance of Wakefulness Test (MWT)
  • Similar to MSLT, but patient tries to stay awake
  • Documents ability to stay awake (FAA, DOT)
Sleep Laboratory Services: Polysomnography
Common Issues in Polysomnography

– Laboratory accreditation
– Physician certification
– Attended lab vs. unattended home studies
– Review of raw data by interpreting physician
– Use of medications on PSG night (e.g. caffeine, alcohol)
– Importance of the sleep medicine consultation
– Who will follow the patient?
Common Sleep Diagnoses

- Obstructive Sleep Apnea
- Restless Legs Syndrome
- Insomnia
- Narcolepsy
- Circadian Rhythm Disorders
- Parasomnia
Obstructive Sleep Apnea

• Characterized by *partial* or *complete* cessation of Airflow during sleep ended by an *arousal* from sleep and often associated with *oxygen desaturation*
  
  • Apnea= no flow for 10 sec or more
  • Hypopnea=Decrease in flow by 30% with an O2 desaturation of at least 4%
  • Physiologically Hypopnea≈Apnea
Anatomy of the Upper Airway

Displayed:
- Genioglossus (protrudes tongue)
- Sternohyoid (displaces hyoid arch anteriorly)
- Pharyngeal constrictors (form lateral pharyngeal walls)

Not Shown:
- Alae nasi (widens nares)
- Levator palatini (elevates palate)
- Tensor palatini (stiffens palate)
- Geniohyoid (displaces hyoid arch anteriorly)
Maintains Upper Airway Patency

Arousal↑
GG Tone

Sleep Onset

Loss of Negative Pressure Reflex

Pharyngeal Dilator Activity

Airway Collapse

Resp Effort↑

Sympathetic Activation

Cardiovascular Sequelae

Inadequate Anatomy

Compensatory Negative Pressure Reflex

Neurocognitive Sequelae

Hypoxia & Hypercapnia

Adapted from Malhotra Lancet 2002
Visual Representation of an Apnea: Cessation of Airflow

Arousal from sleep

Apnea
Visual Representation of Hypopneas: Reduction of Airflow
Common Terms

- **AHI** = Apnea Hypopnea Index
  - Apneas + Hypopneas/Total sleep time (in hours)
- **RDI** = Respiratory Disturbance Index
  - AHI, more or less
  - May include Respiratory Effort-Related Arousal RERA
- **ODI** = Oximetry Desaturation Index
  - Number of 4% desats/hr
- **SDB** = Sleep-Disordered Breathing
  - May include snoring, RERAs, oxygen desaturation, etc.
- **UARS** = Upper Airway Resistance Syndrome
  - > 5 RERAs per hour of sleep
CMS’s Definition of Obstructive Sleep Apnea (OSA)

CPAP for adults with sleep-disordered breathing is covered if:

– AHI ≥ 15, or
– AHI ≥ 5 with:
  • Hypertension
  • Stroke
  • Sleepiness
  • Ischemic heart disease
  • Insomnia
  • Mood disorders
Obstructive Sleep Apnea

• Prevalence in US):
  • AHI ≥5------9% of Women and 24% of Men\(^1\)
  • AHI ≥5------2% of Women and 4% of Men
  +daytime sleepiness
• Most serious common sleep disorder
• Insomnia is most common sleep disorder
  – 40% of Americans affected by Insomnia

\(^1\) Young, NEJM 1993
Epidemiology

• Sleep in America Poll 2005
  – 32% of Americans Snore at least 3X per week
  – 26% of Americans “at Risk” of OSA based on Berlin Questionaire
    • Measures 3 sections
      » Snoring (5 questions)
      » Daytime tiredness (4 questions)
      » Height and Weight (BMI > 30) and self-reported Hypertension
    • People with 2 or more positive sections are considered high risk for OSA

• More Prevalent than Stroke or Cancer in the US
America is growing

- Calories are CHEAP
- Food Preparation is EASY
- TV is America’s main form of entertainment
- Farming and factory work have decreased
- More time spent indoors
- 1/3 of Americans are Obese
- 1/3 are overweight
Obesity and OSA

Courtesy Richard Schwab, M.D. UPENN
Obesity and OSA

Pre-Weight Loss

Post-Weight Loss

Lateral Fat Pads

Courtesy Richard Schwab, M.D. UPENN
Signs and Symptoms of OSA: History

Symptoms include:

- Snoring
- Un-refreshing sleep/daytime sleepiness
- Witnessed apneas
- Insomnia
- Restless sleep
- Nocturnal heartburn
- Morning headaches
- Nocturia
- Dry mouth, sore throat, sinus and nasal congestion
- Mood, memory, and learning problems
- None at all!
Is Subjective Daytime Sleepiness helpful in screening for OSA?
Epworth Sleepiness Scale

• How likely are you to doze off or fall asleep in the following situations (0-3 scale)
  – Sitting and reading
  – Watching TV
  – Sitting inactive in a public place
  – As a passenger in a car for an hour
  – Lying down in the afternoon
  – Sitting and talking to someone
  – Sitting quietly after a lunch without alcohol
  – In a car, while stopped for a few minutes in traffic
The following sleepiness scale can be helpful in determining how much sleeping disorder you have. How likely are you to doze 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. Use the following scale to choose the most appropriate number for each situation.

0 = would never doze  
2 = moderate chance of dozing  
1 = slight chance of dozing  
3 = high chance of dozing  
4 = Always

SITUATION  CHANCE OF DOZING

Sitting and reading  4

Watching Television  4

Sitting, inactive in a public place (theater or movie)  4

As a passenger in a car for an hour without a break  4

Lying down to rest in the afternoon  4

Sitting and talking to someone  4

Sitting quietly after a lunch without alcohol  4

In a car, while stopped for a few minutes in traffic  4

Driving down interstate  4

For each of the beverages listed, write in the average number that you drink each day.
Sequelae in OSA

The effects of sleep-disordered breathing include:

– Neuro-cognitive impairment (memory loss)
– Daytime sleepiness
– Impaired quality of life
– Metabolic effects
– Cardiovascular effects
OSA and Metabolic Dysfunction

– OSA is associated with glucose intolerance and insulin resistance, independent of potential confounders.
– OSA is an independent risk factor for the metabolic syndrome.
  • Hypoxemia may be the predisposing factor to the metabolic alterations associated with OSA.
– CPAP improves insulin sensitivity in some patients with OSA.

Cardiovascular Effects of OSA

These include:

– Systemic hypertension
– Pulmonary hypertension (only with sustained hypoxemia)
– Nocturnal arrhythmias
– Coronary artery disease
– Congestive heart failure
– TIA/stroke
– Death
Treatment for OSA

- CPAP
- Oral Appliance
- Medical/Behavioral
- Surgical

OSA Treatment Options
CPAP

- Positive Pressure Ventilation
- Mask covers Nose or Mouth and Nose (Full Face)
- Forces air into the pharynx
- Splints the Airway open
- Reduces Upper Airway edema
- Reduces Afterload on the heart
Benefits of CPAP therapy on OSA

• Stops the sleep fragmentation
• Improves cognitive function
• Improves quality of life
• Reduces daytime sleepiness
• Reduces health care costs
• Reduces blood pressure
• Reduces glucose intolerance
• Improves cardiac function in heart failure
• Reduces risk of vehicle crashes
Restless Legs Syndrome

- Definition: A neurological movement disorder characterized by an irresistible urge to move the legs accompanied by uncomfortable sensations in the legs that often occur at night or at rest which can temporarily be improved by movement.
Physiology of Dopamine Synthesis and Metabolism

Tyrosine → Tyrosine hydroxylase* → DOPA → DOPA decarboxylase → Dopa → Dopamine → Storage vesicle → Synaptic gap → Release → Dopamine receptor → Postsynaptic terminal

Presynaptic terminal

DOPAC → Dopamine breakdown → Monamine oxidase B → uptake

* Rate-limiting step; iron required

Key Diagnostic Criteria

• Urge to move legs
• Temporary relief with movement
• Onset of symptoms with rest or inactivity
• Worsening of symptoms at night

• Developed by International RLS Study Group in collaboration with NIH
Primary vs Secondary RLS

- Primary-Directly due to CNS dysfunction
  - Familial/genetic disorder
  - Autosomal Dominant inheritance
  - Presents at early age
  - Usually symptoms before age 30
Primary vs Secondary

• Secondary
  – Association with another condition or disease
  – Treat the underlying disease $\rightarrow$ RLS symptoms improve
  – Low iron stores is commonly the cause
  – CSF ferritin usually is low
Secondary Causes

- Pregnancy
- Low Serum Ferritin or Iron deficiency
  - Ferritin <50ng/mL in symptomatic patients
- Renal Failure
  - Seen commonly in ESRD
- Peripheral Neuropathy
Use of Dopaminergic Agents

• Medication    Starting dose
• Carbidopa/Levodopa    25/100mg
• Pramipexole*    .125mg
• Ropinirole*    .25mg
• Pergolide    .05mg

*FDA approved for treatment of moderate to severe RLS
Other meds for RLS

- **Anticonvulsants**
  - Gabapentin Extended Release* 300-600mg

- **Opiates**
  - Hydrocodone 5-10mg
  - Methadone 10-20mg

- **Benzodiazepines**
  - Clonazepam .5-1mg
  - Temazepam 15-30mg

- **Non-Benzodiazepines**
  - Zolpidem 5-15mg
  - Ezopiclone 1-3mg
  - Zalphelon 5-10mg
Questions