Sleep disorders in older persons

Daniel J. Buysse, MD
UPMC Professor of Sleep Medicine
Professor of Psychiatry and Clinical and Translational Science
University of Pittsburgh School of Medicine
buyssedj@upmc.edu

25th Annual Clinical Update in Geriatric Medicine
Pittsburgh, PA
April, 2017
Disclosures

- Current funding: NIA, NHLBI, NIA, NCATS, AHRQ, NIGMS
- Other financial relationships and potential conflicts of interest

<table>
<thead>
<tr>
<th>Type of Potential Conflict</th>
<th>Details of Potential Conflict</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grant/Research Support</td>
<td>None</td>
</tr>
<tr>
<td>Consultant</td>
<td>Bayer, BeHealth Solutions, Cereve, Emmi Solutions, Merck,</td>
</tr>
<tr>
<td>Speakers’ Bureaus</td>
<td>None</td>
</tr>
<tr>
<td>Financial support</td>
<td>None</td>
</tr>
<tr>
<td>Other</td>
<td></td>
</tr>
</tbody>
</table>

- This talk does not present material that is related to these potential conflicts. References are provided throughout this lecture as support.
Sleep quality and quantity influence age effects on telomere length

Self-reported sleep quality, age, and telomere length

Age effect on telomere length is greater among those with poor (p<0.0001) vs. good (p=0.24) sleep quality

Self-reported sleep duration, age, and telomere length

Age moderates the effect of sleep duration on telomere length p<0.001)

n = 154 adults, 45-77 y.o.

Cribbet, 2014; SLEEP 37:65-70
Sleep and the glymphatic system

- Natural sleep and anesthesia result in increased exchange of CSF with interstitial fluid
- Result: Increased β-amyloid clearance during sleep
- Glymphatic system (CSF, interstitial fluid) function mainly during sleep, and are disengaged during wakefulness

Sleep disorders in older persons

- Normative characteristics of sleep in the elderly
  - Self-reports
  - Polysomnographic recordings of sleep
- Sources of age-related sleep changes
- Recognition and treatment of sleep disorders
  - Insomnia
  - Sleep apnea
  - Restless legs syndrome/ Periodic limb movements
  - REM Behavior Disorder
  - Advanced Sleep Phase Disorder
Age-related changes in self-reports of sleep

- Earlier
- Lighter
- Shorter
- More fragmented
- More insomnia
- More daytime sleepiness
Age-related changes in sleep and circadian rhythms

Age effects on sleep

Meta-Analysis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Direction</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>TST</td>
<td>↓</td>
<td>-0.60</td>
</tr>
<tr>
<td>Latency</td>
<td>↔</td>
<td>+0.27</td>
</tr>
<tr>
<td>Efficiency</td>
<td>↓</td>
<td>-0.71</td>
</tr>
<tr>
<td>Stage 1</td>
<td>↑</td>
<td>+0.38</td>
</tr>
<tr>
<td>Stage 2</td>
<td>↑</td>
<td>+0.28</td>
</tr>
<tr>
<td>Stage 3-4</td>
<td>↓</td>
<td>-0.85</td>
</tr>
<tr>
<td>REM</td>
<td>↓</td>
<td>-0.46</td>
</tr>
<tr>
<td>WASO</td>
<td>↑</td>
<td>+0.89</td>
</tr>
</tbody>
</table>

All effect size p values <.001

TST=Total Sleep Time. WASO = Wakefulness After Sleep Onset

Williams, EEG of Human Sleep, 1974

Ohayon et al., SLEEP 2004; 27: 1255-73
Contributors to sleep problems

- Acute Stressors
- Medications, Substances
- Primary Sleep Pathology
- Circadian Factors
- Behavioral and Conditioning Factors
- Medical and Neurological Disorders
- Psychiatric Disorders

Factors:
- Age
- Arousal

Buysse, Diagnosis and classification of insomnia disorders. From *Insomnia: Principles and Management*. Dinges, Kloss, Szuba (eds), 2003
Prevalence of insomnia comorbid with medical disorders

<table>
<thead>
<tr>
<th>Condition</th>
<th>Adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ulcer</td>
<td>2.1 (1.6-2.7)</td>
</tr>
<tr>
<td>Neurological problem</td>
<td>2.0 (1.5-2.7)</td>
</tr>
<tr>
<td>COPD</td>
<td>1.9 (1.5-2.5)</td>
</tr>
<tr>
<td>Migraine</td>
<td>1.8 (1.5-2.1)</td>
</tr>
<tr>
<td>Arthritis</td>
<td>1.8 (1.5-2.2)</td>
</tr>
<tr>
<td>Menstrual</td>
<td>1.7 (1.3-2.1)</td>
</tr>
<tr>
<td>Asthma</td>
<td>1.6 (1.3-2.0)</td>
</tr>
<tr>
<td>Heart disease</td>
<td>1.6 (1.2-2.3)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.5 (1.2-1.8)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.4 (1.05-2.0)</td>
</tr>
<tr>
<td>Colitis</td>
<td>1.4 (0.9-2.3)</td>
</tr>
<tr>
<td>Cancer</td>
<td>1.2 (0.8-1.8)</td>
</tr>
<tr>
<td>Thyroid disorders</td>
<td>1.1 (0.8-1.6)</td>
</tr>
</tbody>
</table>

Assessment of sleep disorders in the elderly

- **Sleep timing**: What time do you normally go to bed/wake up?
- **Sleep quantity**: How much sleep do you need to feel alert and function well?
- **Sleep continuity**: Do you often have trouble falling asleep? How many times do you wake up? Do you have trouble falling back to sleep?
- **Key sleep symptoms**:
  - Are you or your partner aware of snoring, gasping for air, or not breathing? (Obstructive sleep apnea)
  - Do you walk, eat, kick, punch, or scream during sleep? (Parasomnias)
  - Do you have an urge to move your legs/ uncomfortable feelings in your legs during rest or at night? (Restless Legs Syndrome)
- **Daytime sleepiness**: Are you sleepy or tired during much of the day? Do you usually take one or more naps? Do you usually doze off without planning to during the day?
- **Sleep medications**: Are you currently taking medication or other preparations to help you sleep?

Bloom et al., JAGS 2009; 57:761-89.
### Types of sleep disorders

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insomnia</td>
<td>Difficulty with falling or staying asleep</td>
</tr>
<tr>
<td>Sleep-related breathing disorders</td>
<td>Obstructive and central sleep apnea; sleep-related hypoventilation, hypoxemia</td>
</tr>
<tr>
<td>Central disorders of hypersomnolence</td>
<td>Conditions causing severe daytime sleepiness (e.g., narcolepsy, idiopathic hypersomnia)</td>
</tr>
<tr>
<td>Circadian rhythm sleep-wake disorders</td>
<td>Sleep disturbances resulting from problems with the biological clock (e.g., shift work problems)</td>
</tr>
<tr>
<td>Parasomnias (NREM, REM related)</td>
<td>Unusual behaviors or experiences during sleep (e.g., sleep terrors, sleepwalking, nightmares)</td>
</tr>
<tr>
<td>Sleep-related movement disorders</td>
<td>Periodic leg movements, body rocking</td>
</tr>
</tbody>
</table>

American Academy of Sleep Medicine, International Classification of Sleep Disorders, 3rd Edition, 2014
Chronic insomnia disorder: International Classification of Sleep Disorders, 3rd Edition

A. The patient reports, or the patient’s parent or caregiver observes, one or more of the following:
   1. Difficulty initiating sleep
   2. Difficulty maintaining sleep
   3. Waking up earlier than desired
   4. Resistance to going to bed on appropriate schedule
   5. Difficulty sleeping without parent/caregiver intervention

B. One or more of the following related to the nighttime sleep difficulty: (e.g., fatigue, cognitive, functional, mood, alertness problems; sleep dissatisfaction)

C. Reported sleep/wake complaints not explained by inadequate opportunity or circumstances for sleep

D. Frequency: 3X/week

E. Duration: 3 Months

F. Not explained by another sleep disorder

American Academy of Sleep Medicine, 2014
How to treat insomnia: Practice guideline from the American College of Physicians

Recommendation 1

- ACP recommends that all adult patients receive cognitive behavioral therapy for insomnia (CBT-I) as the initial treatment for chronic insomnia disorder.

- Grade: strong recommendation, moderate-quality evidence

Recommendation 2

- ACP recommends that clinicians use a shared decision-making approach, including a discussion of the benefits, harms, and costs of short-term use of medications, to decide whether to add pharmacological therapy in adults with chronic insomnia disorder in whom cognitive behavioral therapy for insomnia (CBT-I) alone was unsuccessful.

- Grade: weak recommendation, low-quality evidence

Brief Behavioral Treatment of Insomnia (BBTI)

- Reduce your time in bed
- Get up at the same time every day of the week, no matter how much you slept the night before
- Don’t go to bed unless you’re sleepy
- Don’t stay in bed unless you’re asleep

Buysse, Arch Int Med, 2011; 171:887-895
# Medications used to treat insomnia

<table>
<thead>
<tr>
<th>Medication Class</th>
<th>Examples</th>
<th>Potential Advantages</th>
<th>Potential Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzodiazepine receptor agonists (BzRA)</td>
<td>Zolpidem, zaleplon, eszopiclone, temazepam</td>
<td>• Efficacious&lt;br&gt;• Variety of half-lives</td>
<td>• Cognitive effects&lt;br&gt;• Falls&lt;br&gt;• Dependence</td>
</tr>
<tr>
<td>Sedating antidepressants</td>
<td>Doxepin, amitriptyline, nortriptyline</td>
<td>• No abuse&lt;br&gt;• Effective for WASO</td>
<td>• Anticholinergic&lt;br&gt;• Cardiac effects&lt;br&gt;• Falls</td>
</tr>
<tr>
<td>Antihistamines</td>
<td>Diphenhydramine, doxylamine</td>
<td>• Widely available</td>
<td>• Cognitive effects&lt;br&gt;• Limited efficacy data</td>
</tr>
<tr>
<td>Melatonin, receptor agonist</td>
<td>Melatonin, ramelteon</td>
<td>• “Natural” mechanism&lt;br&gt;• Some efficacy data</td>
<td>• Limited efficacy on WASO</td>
</tr>
<tr>
<td>Orexin antagonist</td>
<td>Suvorexant</td>
<td>• Novel mechanism, blocks wake signal</td>
<td>• Limited efficacy, effectiveness data</td>
</tr>
<tr>
<td>Sedating antipsychotics</td>
<td>Quetiapine, olanzapine</td>
<td>• Not BzRA&lt;br&gt;• Efficacy for psychosis, depression</td>
<td>• Metabolic, neurological, cardiovascular effects</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>Gabapentin, pregabalin</td>
<td>• Not BzRA&lt;br&gt;• Efficacy for pain</td>
<td>• Limited sleep efficacy data</td>
</tr>
</tbody>
</table>

WASO = Wakefulness After Sleep Onset. *Italicics* = Not FDA-approved for insomnia
Meta-analyses of benzodiazepine receptor agonist effects in insomnia

- Statistically significant effect for self-report and/or PSG outcomes (sleep quality, sleep latency, WASO, TST)
- Most studies short-term
- Older adults
  - Reduced efficacy
    - Sleep quality effect size: 0.14
    - Number Needed to Treat: 13
  - Side effects significant
    - Adverse effects odds ratios: 2.25-4.78
    - Number Needed to Harm: 6

Insomnia, insomnia treatment, and nocturia

- Improvement in nocturia with BBTI\(^1\)
  - 30 older adults with insomnia and nocturia
  - Randomly assigned to BBTI (n=14) or control (n=16)
  - BBTI associated with significant reduction in nocturia compared to control (p=.04, \(d=0.82\))

- Smaller magnitude of BBTI response among insomnia patients with nocturia\(^2\)
  - True for sleep diary, actigraphy, and categorical outcomes
  - No differences by nocturia in polysomnography

\(\chi^2 = 9.05,\ p=0.006\)
\(\chi^2 = 4.99,\ p=0.04\)

BBTI = Brief Behavioral Treatment of Insomnia. \(^1\)Tyagi, JAGS, 2014; 62: 54-60. \(^2\)Tyagi, SLEEP, 2014; 37:681-687.
Obstructive sleep apnea syndrome (OSA)

- Sleep disruption related to repeated airway closures during sleep
- Key symptoms and signs
  - Excessive daytime sleepiness
  - Loud snoring, rescucitative snort/gasp
  - Witnessed breathing pauses
  - Obesity
  - Hypertension
  - Upper airway “crowding”
- PSG findings
  - Repeated episodes of airflow cessation (apnea) or limitation (hypopnea) lasting >10 seconds
  - Oxygen desaturation
  - Repeated arousals

American Academy of Sleep Medicine, 2005
Obstructive sleep apnea in younger and older adults

<table>
<thead>
<tr>
<th>Feature</th>
<th>Older Adults &gt;60 yo</th>
<th>Younger Adults &lt;60 yo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>M = F (1:1)</td>
<td>M &gt; F (2:1)</td>
</tr>
<tr>
<td>Obesity</td>
<td>Not important</td>
<td>Very important</td>
</tr>
<tr>
<td>Witnesses apneas</td>
<td>Rarely reported</td>
<td>Strongly predictive</td>
</tr>
<tr>
<td>Snoring</td>
<td>Infrequently reported</td>
<td>Frequently reported</td>
</tr>
<tr>
<td>Prevalence AHI &gt; 5</td>
<td>30 – 40%</td>
<td>9% Men, 4% Women</td>
</tr>
<tr>
<td>Prevalence RDI &gt; 10</td>
<td>62%</td>
<td>10%</td>
</tr>
<tr>
<td>Morbidity, mortality</td>
<td>Nocturia, impaired cognition, atrial fibrillation, mortality</td>
<td>Death, coronary heart disease, depression, heart disease, metabolic disorders</td>
</tr>
<tr>
<td>Pathophysiology</td>
<td>↑ Airway collapsibility ↓ Chemosensitivity</td>
<td>↓ Airway collapsibility ↑ Chemosensitivity</td>
</tr>
<tr>
<td>CPAP pressure</td>
<td>Lower</td>
<td>Higher</td>
</tr>
</tbody>
</table>

Obstructive Sleep Apnea: Treatment options

- **Lifestyle**
  - Fitness, exercise, weight loss
  - Lateral sleep position
  - Elevate head of bed

- **Positive pressure via nasal/oronasal mask**
  - Continuous positive airway pressure (CPAP)
  - Bilevel pressure
  - Auto PAP

- **Oral appliance**

- **Surgical**
  - Nasal surgery
  - Upper airway bypass (tracheostomy)
  - Upper airway reconstruction
  - Upper airway stimulation (Inspire)

\(^\text{1Dobrosielski, 2015; Med Sci Sports Exerc 47; 20-26}\)
Restless legs syndrome

- **Symptoms**
  - Urge to move the legs
  - Unpleasant feelings
  - Worse at rest
  - Worse at night
  - Relieved by movement

- **Pharmacologic Treatment**
  - Dopamine receptor agonists (pramipexole, ropinirole, rotigotine)
  - Gabapentin, pregabalin
  - Opioids
  - Benzodiazepines

- **Other**
  - Relaxis (counter-stimulation pad)
  - Iron supplementation (if ferritin <50)
Circadian rhythm sleep wake disorders

Normal

Advanced Sleep Phase Type

Delayed Sleep Phase Type

Shift Work Type

Time of Day

4:00 pm  Midnight  8:00 am  4:00 pm
Treatment of circadian rhythm sleep wake disorders

- Evening light delays sleep and temperature rhythms
- Morning light advances sleep and temperature rhythms
- Late afternoon/early evening melatonin advances sleep and temperature rhythms
- Morning melatonin delays sleep and temperature rhythms (in theory)
REM sleep behavior disorder (RBD)

- **Key symptoms**
  - Violent dreams with good recall
  - Violent, injurious behavior consistent with dream
  - Onset in mid-late life, M > F

- **Polysomnographic findings**
  - Increased muscle tone during REM sleep
REM sleep behavior disorder (RBD)

- **Pathophysiology**
  - Release from brainstem-initiated atonia during REM
  - Association with alpha-synucleinopathies (Lewy Body dementia, Parkinson’s, Progressive Supranuclear Palsy, related disorders)

- **Treatment**
  - Benzodiazepine (e.g., clonazepam)
  - Melatonin in high dose (12 mg)
  - Avoid SSRI, SSNRI antidepressants
Sleep in nursing homes

Sleep Problems
- Night awakenings, agitation
- Daytime sleep, napping
- Reduced circadian rhythm of sleep-wakefulness

Sources of Sleep Problems
- Brain changes (dementia, circadian rhythms)
- Medical and psychiatric illness
- Medication
- Environmental
  - Reduced light
  - Reduced activity
- Care routines
  - Continence and medical care
  - Long time in bed

Sleep in nursing homes: Interventions

- **Behavioral sleep measures**
  - Regular sleep-wake schedule
  - Minimize daytime napping
  - Increase daytime physical activity
  - Reduce time in bed

- **Nighttime environment**
  - Dark
  - Quiet
  - Comfortable temperature
  - Match roommates on nighttime care routine

- **Daytime environment**
  - Increase light; encourage outdoor activities
  - Encourage physical activity, especially in afternoon
  - Consistent meal and activity schedule

- **Medications**
  - Avoid sedatives, hypnotics when possible

Sleep disorders in the elderly: Take-home points

- Sleep in older adults is subjectively lighter, more fragmented, and earlier.
- Objective methods confirm subjective reports.
- Sleep changes in the elderly are related to changes in physiological regulation as well as the effects of neuropsychiatric and medical illness.
- Age-related increases are observed in specific sleep disorders: insomnia, sleep apnea, restless legs syndrome, circadian rhythm disorders, insomnia/hypersomnia related to medical illness.
- Treatment involves behavioral, pharmacologic, and other treatments, combined with optimal medical care.