Sleep Problems in Aging and their Relevance to Delirium

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Outline

- Age-related changes in sleep and related topics
- Common sleep problems in older adults and relevance to delirium
  - Insomnia
  - Sleep-related breathing disorders
  - Circadian rhythm disorders
  - Parasomnias (e.g., restless legs syndrome, REM sleep behavior disorder)
- Sleep and delirium in hospitalized older adults
## Age-related changes in sleep: Meta-analysis of sleep parameters

<table>
<thead>
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<th>From young adulthood (18-40) to elderly (60 – 70)</th>
<th>From elderly to ‘old elderly’ (≥70)</th>
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<td>Total sleep time</td>
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<td>Stages 1 and 2</td>
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<td>Slow wave sleep</td>
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<td>REM %</td>
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<td>Wake after sleep onset</td>
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*Ohayon et al, Sleep, 27:1255-1273, 2004*
Sleep and mortality
(Cappuccio et al. Sleep;33:585-92, 2010)

- Meta-analysis, 16 studies, >1.3 million people
- Short sleep duration (< 5 – 7 hours) is associated with a greater risk of death
  - RR: 1.12; 95% CI 1.06 to 1.18; P < 0.01
- Long sleep duration (> 8 – 9 hours) is associated with a greater risk of death
  - RR: 1.30; 95% CI 1.22 to 1.38; P < 0.0001
Sleep complaints in older adults as a geriatric syndrome

Possible common pathways between delirium and sleep disruption

Common sleep problems in older adults and relevance to delirium
Insomnia

- Definition of insomnia (ICSD-2):
  1) Difficulty initiating sleep, difficulty maintaining sleep, or waking up too early, or sleep that is chronically nonrestorative or poor in quality
  2) Occurs despite adequate opportunity and circumstances for sleep
  3) Daytime impairment related to the nighttime sleep difficulty (e.g., fatigue or malaise; attention, concentration or memory impairment)

ICSD-2: International Classification of Sleep Disorders, 2nd Ed., 2006
Insomnia in older adults is commonly comorbid with other conditions

- **Psychiatric conditions**
  - Depression
  - Bereavement
  - Anxiety and stress
- **Medical and other conditions**
  - Neurodegenerative disorders
  - Chronic pain
  - Paresthesias
  - Cough, dyspnea
  - Gastroesophageal reflux
  - Nocturia
Medications and other agents that interfere with sleep

- **Drugs associated with insomnia:**
  - alcohol
  - caffeine
  - nicotine
  - antidepressants (e.g., MAOIs, occasionally SSRIs)
  - asthma/COPD medications (e.g., theophylline)
  - corticosteroids (e.g., oral prednisone and dexamethasone, IV hydrocortisone)
  - decongestants (e.g., pseudoephedrine)
  - H2 blockers (e.g., cimetidine)
  - antihypertensives (e.g., B-blockers)
  - anticholinesterase inhibitors (e.g., donepezil)

- **Drugs associated with daytime sleepiness:**
  - analgesics (e.g., narcotics)
  - antidepressants (e.g., imipramine, trazodone)
  - antihypertensives (e.g., clonidine)
  - antihistamines
Cognitive behavioral therapy (CBT) is superior to zopiclone for chronic insomnia in older adults

(Sivertsen et al. JAMA 295:2851-2858, 2006)

- Randomized trial, Norway
- N = 46 adults with chronic primary insomnia
  - mean age 60.8 years, 48% women
- Treatment groups (6 weeks):
  - CBT (sleep hygiene, sleep restriction, stimulus control, cognitive therapy, relaxation)
  - 7.5 mg zopiclone
  - Placebo
- Results (6 week post treatment and 6 months follow-up):
  - Polysomnography: CBT improved sleep efficiency, decreased total wake time and increased slow wave sleep (compared to zopiclone and placebo)
  - Sleep diary: CBT decreased total wake time (compared to zopiclone) at 6 months
Obstructive sleep apnea (OSA)

- Typical patient = obese, sleepy, snorer with hypertension
  - physical exam: obesity, large neck circumference, big tongue, crowded oral pharynx
- OSA in older adults:
  - Prevalence increases with age
  - Less likely to be obese; little or no relationship with neck circumference
- Common signs/symptoms:
  - excessive daytime sleepiness, insomnia complaints, morning headache, personality changes
  - loud snoring, choking sounds
  - poor memory, nighttime confusion, irritability
  - difficult hypertension, cardiac arrhythmias
Treatment of sleep apnea

- **Gold standard:** Positive airway pressure (PAP)
  - PAP adherence is determined early in therapy (e.g., within the first week)
  - Adjustments to PAP therapy can make it more tolerable

- **Other treatments:**
  - weight loss
  - avoid nighttime alcohol, sedatives
  - oral devices (if mild OSA or do not tolerate PAP)
Treatment of sleep apnea in patients with Alzheimer’s disease

- **Sleep apnea improves with CPAP in Alzheimer’s patients** *(Chong et al. JAGS; 54:777-781, 2006)*
  - Randomized controlled trial (CPAP versus sham CPAP); MMSE > 17
  - Results: CPAP adherence = 5.2 hours per night; daytime sleepiness improved with CPAP

- **Unclear if cognition improves with CPAP in Alzheimer’s patients** *(Ancoli-Israel et al. JAGS 56:2076-2081, 2008)*
  - Randomized controlled trial (CPAP versus sham CPAP); MMSE>17
  - Results: Neuropsychological testing improved in the CPAP group; but results were not statistically different between groups

- **Sleep apnea may improve with donepezil in Alzheimer’s patients** *(Morales et al. Chest 133:677-683, 2008)*
  - Randomized controlled trial (donepezil versus placebo); mild-moderate Alzheimer’s disease
  - Results: Apnea-hypopnea index and oxygen saturation improved with donepezil
Central sleep apnea: Cheynes Stokes respiration

- Sleep disordered breathing with:
  - Absence of airflow and respiratory effort
  - Hyperventilation in a crescendo-decrescendo pattern
  - Most often occurs with congestive heart failure; may predict higher morbidity/mortality

- Treatment*
  - Optimize therapy for heart failure
  - Other treatment options for CSA in CHF:
    - CPAP therapy to normalize AHI (Standard)
    - Nocturnal oxygen therapy (Standard)
    - Adaptive Servo-Ventilation to normalize AHI (Standard)

*Aurora et al. Treatment of Central Sleep Apnea Syndromes in Adults. Sleep. 35(1)17-40, 2011
Possible mechanisms of an association between sleep apnea and delirium

- Sleep stage abnormalities (as may occur with OSA) may increase the risk of delirium
- Hypoxia in OSA may lead to:
  - Vascular injury
  - Low grade systemic inflammation and oxidative stress
  - Decrease in insulin growth factor-1 (IGF-1)
  - These changes may be associated with neuronal injury and apoptosis, which may lead to cognitive dysfunction and delirium

*Mirrakhimov, Brebaker, Krystal and Kwatra. Sleep Breath. Springer Epub 2013 Apr 14*
OSA increases postoperative delirium after elective knee replacement

- Prospective, observational study in two hospitals (Duke University Medical Center and Durham VA)
- Enrolled $N = 106$ nondemented patients (aged $\geq 65$ years) undergoing elective knee replacement
- Delirium assessed using the Confusion Assessment Method (CAM) and the Delirium Rating Scale-Revised-98 (DRS-R98) at baseline and post-op days 2 and 3
- OSA diagnosis based on medication records (verified by prior PSG or PAP use)
- Results:
  - 53.3% (8/15) OSA patients developed post-op delirium, compared with 20.9% (19/91) of controls (exact $p=0.0123$, odds ratio $= 4.3$, 95% CI 1.2 to 15.8)
  - OSA remained a significant independent predictor of delirium in adjusted multiple logistic regression (largest $p=0.0237$)

Flink et al. Anesthesiology. 2012 April; 116(4): 788–796
Selected circadian rhythm abnormalities in older adults

- **Advanced sleep phase syndrome**
  - Treatment = prescribed sleep/wake scheduling, evening light exposure (Option, some uncertainty in evidence)*

- **Delayed sleep phase syndrome**
  - Treatment = morning bright light therapy (Guideline), and/or evening melatonin (Guideline)
  - Chronotherapy (progressive delay in sleep schedule; Option; some uncertainty in evidence).

- **Irregular sleep-wake rhythm**
  - In nursing home residents, nonpharmacological interventions decrease daytime sleeping; not much effect on nighttime sleep

*Morgenthaler et al. Sleep. 30(11):1445-1459, 2007*
Potential role of impaired circadian rhythms and reduced melatonin in ICU delirium

Restless legs syndrome (RLS)

- An urge to move the legs, with an unpleasant sensation of the legs
- Other key features:
  - begins or worsens with rest
  - worse in the evening or night
  - partially or totally relieved with movement
- Prevalence may be 10% in older people
  - (women > men)
- May have PLMS on polysomnography
- **Diagnosis**: history and physical exam
REM Sleep Behavior Disorder

- **Major features:**
  - vigorous motor behaviors, vivid dreams
  - lack of muscle atonia during REM
  - may result in injury; > 85% of cases are men

- **Etiology:**
  - **acute:** drug-induced (e.g., SSRIs, TCAs) and drug withdrawal
  - **chronic:** idiopathic, synucleinopathies (e.g., Parkinson’s disease, Lewy body dementia, multi-system atrophy), psychiatric illness

- **Diagnosis:**
  - polysomnography
Sleep and dementia

- Changes in sleep in dementia patients:
  - ↑ sleep latency, nighttime awakenings
  - ↓ sleep efficiency, total sleep time and delta sleep
  - Nighttime wandering, sundowning
- Two-thirds of adult caregivers have sleep disturbance (McCurry 2007).
- Restless legs syndrome may present as agitation/wandering behavior.
  - Periodic limb movements are associated with decreased nighttime sleep in cognitively impaired older people (Richards 2008).
Sleep and delirium in hospitalized older adults
Bright light therapy in delirious older hospitalized patients

- Prospective, uncontrolled
- N = 228 delirious patients admitted to a geriatric monitoring unit in one hospital in Singapore
- Intervention included:
  - Core interventions from the Hospital Elder Life Program (HELP), including standardized protocols for managing cognitive impairment, sleep deprivation, immobility, visual and hearing impairment and dehydration
  - Bright light therapy (2000 – 3000 lux in ceiling lights) and sleep hygiene
- Results:
  - Sleep measures (from nurse completed hourly patient sleep logs) improved between admission and discharge, regardless of delirium subtype (hyperactive, hypoactive, mixed)

Ear plugs in critically ill adults: effects on sleep and delirium

- Randomized controlled trial (N= 136 patients in an intensive care unit in one hospital in Belgium)
- Nighttime use of ear plugs versus ‘dummy canister’ at the bedside without ear plugs, for up to 5 nights while in ICU (average length of time in study was < 2 days)
- Blinded researcher assessed delirium (using NEECHAM scale) and perception of sleep (5 questions) each morning
- Results:
  - 60% of controls versus 35% of earplug group had delirium or mild confusion while in ICU (biggest effect was on mild confusion)
  - Earplugs decreased the risk of delirium or mild confusion by 53% (HR .0.47, CI 0.27 to 0.82)
  - Earplugs were associated with significantly better sleep perception after the first night (P = 0.042), no difference on subsequent nights

Van Rompaey et al. Critical Care 2012 16:R73
A multifaceted sleep-promoting intervention in the ICU: Results of a quality improvement project

- Observational, pre-post design, N = 300 medical ICU patients (122 at baseline, 178 with intervention)
- Intervention implemented in 3 stages:
  - Stage 1: Environmental changes to decrease nighttime sleep disruption and promote daytime wakefulness
  - Stage 2: Ear plugs, eye masks and soothing music added
  - Stage 3: Pharmacological guideline added for patients unable to sleep despite Stage 1 and Stage 2 interventions
- Results:
  - Significant decrease in ratings of nighttime noise.
  - No difference in ratings of sleep.
  - Decreased incidence of delirium (OR 0.46; 95% ci 0.23 -0.89; p=.03)

Conclusions

- Sleep disturbance in older adults is associated with age-related changes in sleep, comorbid conditions, medications, primary sleep disorders, and other factors.
- Sleep complaints in older adults may be considered as a geriatric syndrome.
- Increasing evidence suggests a link between sleep disturbance and delirium, particularly in hospitalized older adults. Further research is needed to understand the pathophysiological basis of this relationship.
- Although a variety of interventions have been developed, further research is needed to develop and test interventions to address sleep and delirium in older adults.