



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

	From young adulthood (18-40) to elderly (60 – 70)	From elderly to 'old elderly' (≥ 70)
Total sleep time	↓	↔
Sleep latency	↔	↔
Sleep efficiency	↓	↓
Stages 1 and 2	↑	↔
Slow wave sleep	↓	↔
REM %	↓	↔
Wake after sleep onset	↑	↔

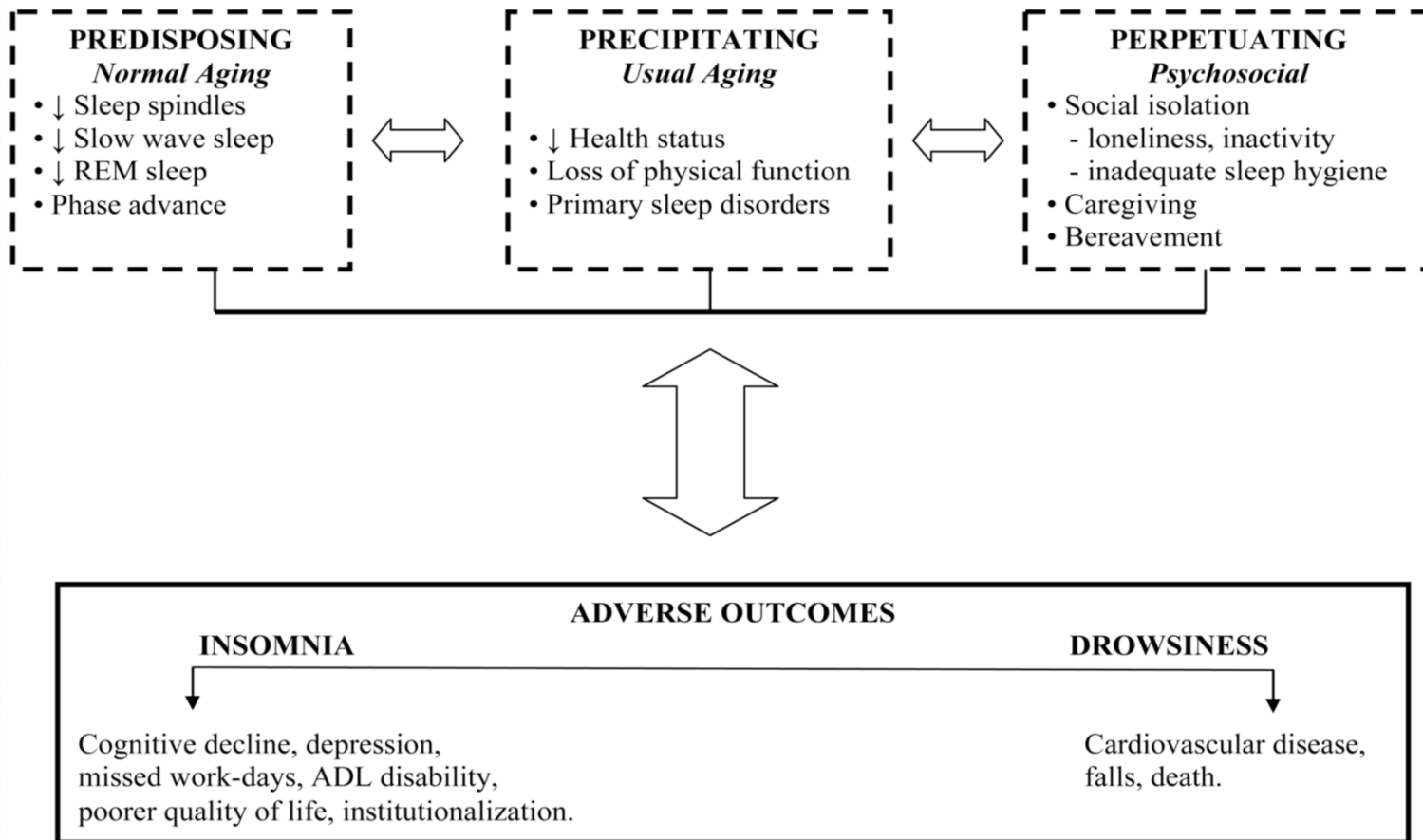


Sleep and mortality

(Cappuccio et al. Sleep;33:585-92, 2010)

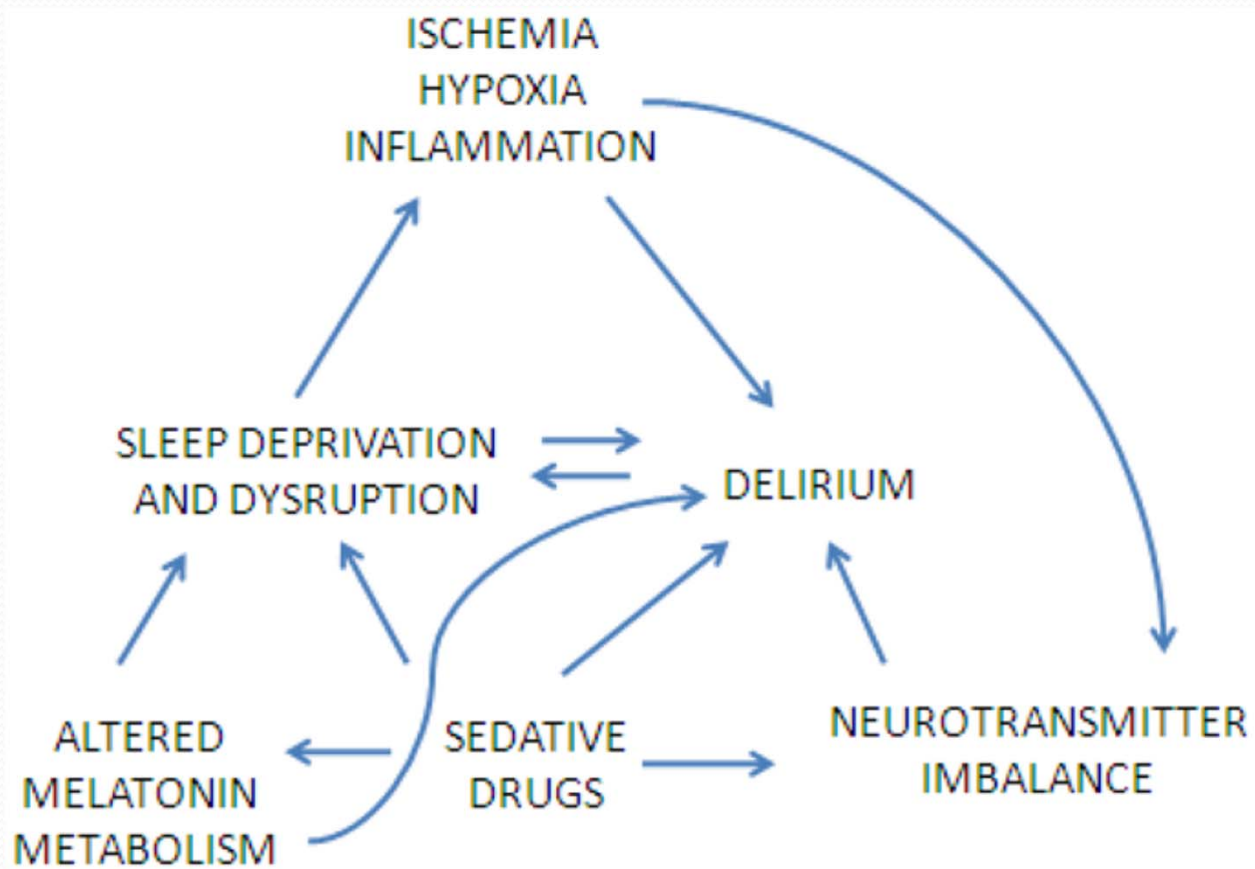
- Meta-analysis, 16 studies, >1.3 million people
- Short sleep duration (< 5 – 7 hours) is associated with a greater risk of death
 - RR: 1.12; 95% CI 1.06 to 1.18; P < 0.01
- Long sleep duration (> 8 – 9 hours) is associated with a greater risk of death
 - RR: 1.30; 95% CI 1.22 to 1.38; P < 0.0001

Sleep complaints in older adults as a geriatric syndrome



From: *Fragoso and Gill (Adapted from insomnia model from Spielman and colleagues). J Am Geriatr Soc 55:1853-1866, 2007*

Possible common pathways between delirium and sleep disruption




From: Watson, Ceriana and Fanfulla. Best Prac and Res Clin Anaesthesiology. 26:355-366, 2012



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)



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)



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

OSA increases postoperative delirium after elective knee replacement

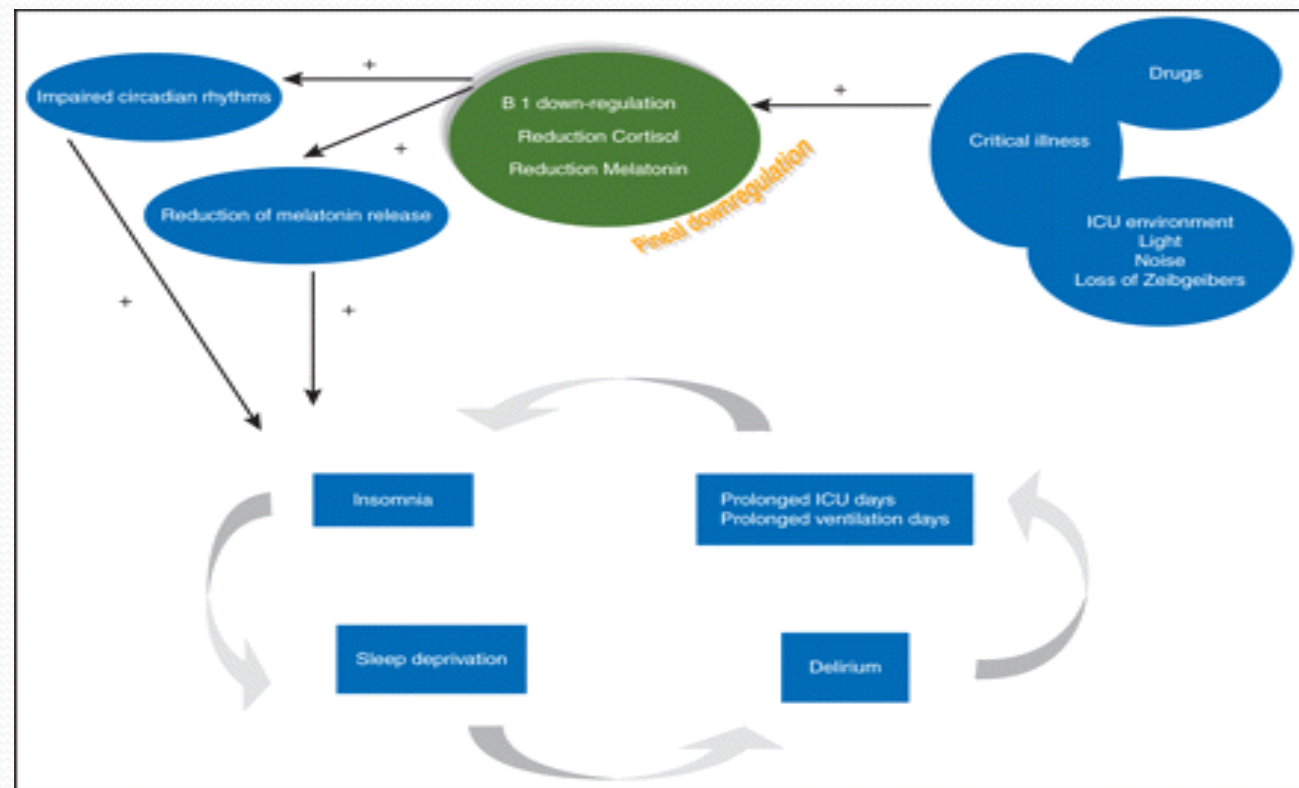
- Prospective, observational study in two hospitals (Duke University Medical Center and Durham VA)
- Enrolled N = 106 nondemented patients (aged ≥ 65 years) undergoing elective knee replacement
- Delirium assessed using the Confusion Assessment Method (CAM) and the Delirium Rating Scale-Revised-98 (DRS-R98) 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 $p=0.0237$)

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



From: Bellapart and Boots. *Brit J Anaesthesia* 108:572-580, 2012



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

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.