Sleep disorders in older adults

Early treatment of these complex disorders can greatly improve patients’ quality of life

As humans live longer, a renewed focus on quality of life has made the prompt diagnosis and treatment of sleep-related disorders in older adults increasingly necessary. Normative aging results in multiple changes in sleep architecture, including decreased total sleep time, decreased sleep efficiency, decreased slow-wave sleep (SWS), and increased awakenings after sleep onset. Sleep disturbances in older adults are increasingly recognized as multifactorial health conditions requiring comprehensive modification of risk factors, diagnosis, and treatment.

In this article, we discuss the effects of aging on sleep architecture and provide an overview of primary sleep disorders in older adults. We also summarize strategies for diagnosing and treating sleep disorders in these patients.

Elements of the sleep cycle

The human sleep cycle begins with light sleep (sleep stages 1 and 2), progresses into SWS (sleep stage 3), and culminates in rapid eye movement (REM) sleep. The first 3 stages are referred to as non-rapid-eye movement sleep (NREM). Throughout the night, this coupling of NREM and REM cycles occurs 4 to 6 times, with each successive cycle decreasing in length until awakening.

Two complex neurologic pathways intersect to regulate the timing of sleep and wakefulness on arousal. The first pathway, the circadian system, is located within the suprachiasmatic nucleus of the hypothalamus and is highly dependent on external stimuli (light, food, etc.) to synchronize sleep/wake cycles. The suprachiasmatic nucleus regulates melatonin...
The effects of aging on sleep architecture

It has long been known that sleep architecture changes significantly with age. One of the largest meta-analyses of sleep changes in healthy individuals throughout childhood into old age found that total sleep time, sleep efficiency, percentage of slow-wave sleep, percentage of rapid eye movement sleep (REM), and REM latency all decreased with normative aging. Other studies have also found a decreased ability to maintain sleep (increased frequency of awakenings and prolonged nocturnal awakenings).\(^2\) Based on several meta-analyses, the average total sleep time at night in the adult population decreases by approximately 10 minutes per decade in both men and women.\(^7,9,11\) However, this pattern is not observed after age 60, when the total sleep time plateaus.\(^2\) Similarly, the duration of wake after sleep onset increases by approximately 10 minutes every decade for adults age 30 to 60, and plateaus after that.\(^1,2\)

Epidemiologic studies have suggested that the prevalence of daytime napping increases with age.\(^9\) This trend continues into older age without a noticeable plateau. A study of a nationally representative sample of \(>7,000\) Japanese participants found that a significantly higher proportion of older adults take daytime naps (27.4\%) compared with middle-age adults (14.4\%).\(^12\) Older adults nap more frequently because of both lifestyle and biologic changes that accompany normative aging. Polls in the United States have shown a correlation between frequent napping and an increase in excessive daytime sleepiness, depression, pain, and nocturia.\(^13\)

While sleep latency steadily increases after age 50, recent studies have shown that in healthy individuals, these changes are modest at best,\(^7,9,14\) which suggests that other pathologic factors may be contributing to this problem. Although healthy older people were found to have more frequent arousals throughout the night, they retained the ability to reinitiate sleep as rapidly as younger adults.\(^19\)

Obstructive sleep apnea (OSA) is one of the most common, yet frequently underdiagnosed reversible causes of sleep disturbances. It is characterized by partial or complete airway obstruction culminating in periods of involuntary cessation of respirations during sleep. The resultant fragmentation in sleep leads to significant downstream effects over time, including excessive daytime sleepiness and fatigue, poor occupational and social performance, and substantial cognitive impairment.\(^3\) While it is well known that OSA increases in prevalence throughout middle age, this relationship plateaus after age 60.\(^16\) An estimated 40\% to 60\% of Americans age >60 are affected by OSA.\(^17\) The hypoxemia and fragmented sleep caused by unrecognized OSA are associated with a significant decline in activities of daily living (ADL).\(^18\) Untreated OSA is strongly linked to the development and progression of several major health conditions, including cardiovascular disease, diabetes mellitus, hypertension, stroke, and depression.\(^19\) In studies of long-term care facility residents—many of whom...
may have comorbid cognitive decline—researchers found that unrecognized OSA often mimics the progressive cognitive decline seen in major neurocognitive disorders.\textsuperscript{20} However, classic symptoms of OSA may not always be present in these patients, and their daytime sleepiness is often attributed to old age rather than to a pathological etiology.\textsuperscript{19} Screening for OSA and prompt initiation of the appropriate treatment may reverse OSA-induced cognitive changes in these patients.\textsuperscript{21}

The primary presenting symptom of OSA is snoring, which is correlated with pauses in breathing. Risk factors include increased body mass index (BMI), thick neck circumference, male sex, and advanced age. In older adults, BMI has a lower impact on the Apnea-Hypopnea Index, an indicator of the number of pauses in breathing per hour, when compared with young and middle-age adults.\textsuperscript{16} Validated screening questionnaires for OSA include the STOP-Bang Questionnaire (Table 1), OSA50, Berlin Questionnaire, and Epworth Sleepiness Scale, each of which is used in different subpopulations. The current diagnostic standard for OSA is nocturnal polysomnography in a sleep laboratory, but recent advances in home sleep apnea testing have made it a viable, low-cost alternative for patients who do not have significant medical comorbidities.\textsuperscript{23} Standard utilized cutoffs for diagnosis are ≥5 events/hour (hypopneas associated with at least 4% oxygen desaturations) in conjunction with clinical symptoms of OSA.\textsuperscript{24}

\textbf{Treatment.} First-line treatment for OSA is continuous positive airway pressure therapy, but adherence rates vary widely with patient education and regular follow-up.\textsuperscript{25} Adjunctive therapy includes weight loss, oral appliances, and uvulopalatopharyngoplasty, a procedure in which tissue in the throat is remodeled or removed.

Central sleep apnea (CSA) is a pause in breathing without evidence of associated respiratory effort. In adults, the development of CSA is indicative of underlying lower brainstem dysfunction, due to intermittent failures in the pontomedullary centers responsible for regulation of rhythmic breathing.\textsuperscript{26} This can occur as a consequence of multiple diseases, including congestive heart failure, stroke, renal failure, chronic medication use (opioids), and brain tumors.

The Sleep Heart Health Study—the largest community-based cohort study to date examining CSA—estimated that the prevalence of CSA among adults age >65 was 1.1% (compared with 0.4% in those age <65).\textsuperscript{27} Subgroup analysis revealed that men had significantly higher rates of CSA compared with women (2.7% vs 0.2%, respectively).

CSA may present similarly to OSA (excessive daytime somnolence, insomnia, poor sleep quality, difficulties with attention and concentration). Symptoms may also mimic those of coexisting medical conditions in older adults, such as nocturnal angina or paroxysmal nocturnal dyspnea.\textsuperscript{28} Any older patient with daytime sleepiness and risk factors for CSA should be referred for in-laboratory nocturnal polysomnography.

\begin{table}[h]
\centering
\caption{Screening for obstructive sleep apnea: The STOP-Bang Questionnaire\textsuperscript{a}}
\begin{tabular}{|l|l|}
\hline
\textbf{Snoring} & Do you snore loudly? \\
\textbf{Tiredness} & Do you often feel tired during the daytime? \\
\textbf{Observed apnea} & Has anyone observed you stop breathing during sleep? \\
\textbf{Pressure} & Do you have high blood pressure? \\
\textbf{Body mass index} & Body mass index >40 kg/m\textsuperscript{2} \\
\textbf{Age} & >50 years \\
\textbf{Neck circumference} & >40 cm \\
\textbf{Gender} & Male \\
\hline
\end{tabular}
\textsuperscript{a}Add 1 point for each positive response. Low risk = 0 to 2; intermediate risk = 3 to 4; high risk = ≥5
\textsuperscript{Source: Reference 22}
\end{table}
Sleep disorders in older adults

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The gold standard diagnostic test. Unlike in OSA, ambulatory diagnostic measures (home sleep apnea testing) have not been validated for this disorder.

Treatment. The primary treatment for CSA is to address the underlying medical problem. Positive pressure ventilation has been attempted with mixed results. Supplemental oxygen and medical management (acetazolamide or theophylline) can help stimulate breathing. Newer studies have shown favorable outcomes with transvenous neurostimulation or adaptive servoventilation.

Insomnia. For a primary diagnosis of insomnia, DSM-5 requires at least 3 nights per week of sleep disturbances that induce distress or functional impairment for at least 3 months. The International Classification of Disease, 10th Edition requires at least 1 month of symptoms (lying awake for a long time before falling asleep, sleeping for short periods, being awake for most of the night, feeling lack of sleep, waking up early) after ruling out other sleep disorders, substance use, or other medical conditions. Clinically, insomnia tends to present in older adults as a subjective complaint of dissatisfaction with the quality and/or quantity of their sleep. Insomnia has been consistently shown to be a significant risk factor for both the development or exacerbation of depression in older adults.

While the diagnosis of insomnia is mainly clinical via a thorough sleep and medication history, assistive ancillary testing can include wrist actigraphy and screening questionnaires (the Insomnia Severity Index and the Pittsburgh Sleep Quality Index). Because population studies of older adults have found discrepancies between objective and subjective methods of assessing sleep quality, relying on the accuracy of self-reported symptoms alone is questionable.

Treatment. Given that drug elimination half-life increases with age, and the risks of adverse effects are increased in older adults, the preferred treatment modalities for insomnia are nonpharmacologic. Sleep hygiene education (Table 2) and cognitive-behavioral therapy (CBT) for insomnia are often the first-line therapies. It is crucial to manage comorbidities such as heart disease and obesity, as well as sources of discomfort from conditions such as arthritic pain. If nonpharmacologic therapies are not effective, pharmacologic options can be considered. Although benzodiazepines are helpful for their sedative effects, they are not recommended for older adults because of an increased risk of falls, rebound insomnia, potential tolerance, and associated cognitive impairment. Benzodiazepine receptor agonists (eg, zolpidem, eszopiclone, zaleplon) were initially developed as a first-line treatment for insomnia to replace the reliance on benzodiazepines, but these medications have a “black-box” warning of a serious risk of complex sleep behaviors, including life-threatening parasomnias. As a result, guidelines suggest a shorter duration of treatment with a benzodiazepine receptor agonist may still provide benefit while limiting the risk of adverse effects.

Doxepin is the only antidepressant FDA-approved for insomnia; it improves sleep latency (time taken to initiate sleep after lying down), duration, and quality in adults age >65. Melatonin receptor agonists such as ramelteon and melatonin have shown positive results in older patients with insomnia. In clinical trials of patients age ≥65, ramelteon, which is FDA-approved for insomnia, produced no rebound insomnia, withdrawal effects, memory impairment,
Suvorexant, an orexin receptor antagonist, decreases sleep latency and increases total sleep time equally in both young and older adults.

Parasomnias are undesirable behaviors that occur during sleep, commonly associated with the sleep-wake transition period. These behaviors can occur during REM sleep (nightmare disorder, sleep paralysis, REM sleep behavior disorder [see page 36]) or NREM sleep (somnambulism [sleepwalking], confusional arousals, sleep terrors). According to a cross-sectional Norwegian study of parasomnias, the estimated lifetime prevalence of sleep walking is 22.4%; sleep talking, 66.8%; confusional arousal, 18.5%; and sleep terror, 10.4%.

When evaluating a patient with parasomnias, it is important to review their drug and substance use as well as coexisting medical conditions. Drugs and substances that can
Sleep disorders in older adults

Clinical Point
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Affect sleep include prescription medications (second-generation antidepressants, stimulants, dopamine agonists), excessive caffeine, alcohol, certain foods (coffee, chocolate milk, black tea, caffeinated soft drinks), environmental exposures (smoking, pesticides), and recreational drugs (amphetamines)\textsuperscript{33,36}.

Certain medical conditions are correlated with specific parasomnias (eg, sleep paralysis and narcolepsy, REM sleep behavior disorder and Parkinson’s disease [PD], etc.).\textsuperscript{54} Diagnosis of parasomnias is mainly clinical but supporting evidence can be obtained through in-lab polysomnography.

Treatment. For parasomnias, treatment is primarily supportive and includes creating a safe sleeping environment to reduce the risk of self-harm. Recommendations include sleeping in a room on the ground floor, minimizing furniture in the bedroom, padding any bedside furniture, child-proofing door-knobs, and locking up weapons and other dangerous household items.\textsuperscript{54}

REM sleep behavior disorder (RBD). This disorder is characterized by a loss of the typical REM sleep-associated atonia and the presence of motor activity during dreaming (dream-enacted behaviors). While the estimated incidence of RBD in the general adult population is approximately 0.5%, it increases to 7.7% among those age \geq 60.\textsuperscript{57} RBD occurs most commonly in the setting of the alpha-synucleinopathies (PD, Lewy body dementia, multisystem atrophy), but can also be found in patients with cerebral ischemia, demyelinating disorders, or alcohol misuse, or can be medication-induced (primarily antidepressants and antipsychotics).\textsuperscript{58} In patients with PD, the presence of RBD is associated with a more impaired cognitive profile, suggestive of widespread neurodegeneration.\textsuperscript{59} Recent studies revealed that RBD may also be a prodromal state of neurodegenerative diseases such as PD, which should prompt close monitoring and long-term follow up.\textsuperscript{60} Similar to other parasomnias, the diagnosis of RBD is primarily clinical, but polysomnography plays an important role in demonstrating loss of REM-related atonia.\textsuperscript{54}

Treatment. Clonazepam and melatonin have been shown to be effective in treating the symptoms of RBD.\textsuperscript{54}

Depression, anxiety, and sleep disturbances

Major depressive disorder (MDD) and generalized anxiety disorder (GAD) affect sleep in patients of all ages, but are underreported in older adults. According to national epidemiologic surveys, the estimated prevalence of MDD and GAD among older adults is 13% and 11.4%, respectively.\textsuperscript{61,62} Rates as high as 42% and 39% have been reported in meta-regression analyses among patients with Alzheimer’s dementia.\textsuperscript{63} Depression and anxiety may have additive effects and manifest as poor sleep satisfaction, increased sleep latency, insomnia, and daytime sleepiness.\textsuperscript{64} However, they

Bottom Line
Sleep disorders in older adults are common but often underdiagnosed. Timely recognition of obstructive sleep apnea, central sleep apnea, insomnia, parasomnias, and other sleep disturbances can facilitate effective treatment and greatly improve older adults’ quality of life.
may also have independent effects. Studies showed that patients with depression alone reported overall poor sleep satisfaction, whereas patients with anxiety alone reported problems with sleep latency, daytime drowsiness, and waking up at night in addition to their overall poor sleep satisfaction.65-67 Both depression and anxiety are risk factors for developing cognitive decline, and may be an early sign/prodrome of neurodegenerative diseases (dementias).68 The bidirectional relationship between depression/anxiety and sleep is complex and needs further investigation.

Treatment. Pharmacologic treatments for patients with depression/anxiety and sleep disturbances include selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors, tricyclic antidepressants, and other serotonin receptor agonists.69-72 Nonpharmacologic treatments include CBT for both depression and anxiety, and problem-solving therapy for patients with mild cognitive impairment and depression.73,74 For severe depression and/or anxiety, electroconvulsive therapy is effective.75

References

Sleep disorders in older adults

Clinical Point

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