

Sleep Disturbances across Stages of Cognitive Decline

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Key highlights:

- Sleep disturbance is highly prevalent among older adults across different stages of cognitive decline.
- Sleep disturbance represent one of the earliest symptoms of Alzheimer's disease and can negatively impact cognitive function and neuropsychiatric symptoms.
- The most common aspects of sleep disturbance compromised are rapid eye movement (REM), sleep efficiency, sleep latency, and sleep duration in pathological older adults.
- EEG slowing in REM sleep shows the highest correlation with cognitive decline, which may be a sensitive marker of the neurodegenerative process in early stages.

Sleep disturbances are common among people with Alzheimer's disease (AD), other dementia and mild cognitive impairment. The prevalence of sleep disturbances varies significantly, depending on the dementia subtypes, the severity of people in the sample being studied, and the measures used to identify sleep problems. In a recent systematic review and meta-analysis, the prevalence of any sleep disturbance was 26% and 19% for clinically significant sleep disturbance in people with dementia living in the community [1]. Patients with Lewy body dementia, vascular dementia and frontotemporal dementia report higher prevalence of sleep disturbance than AD. The consequences of poor sleep quality in dementia patients may have negative consequences related to unwanted behaviors, agitation, delirium, increased fall risk, greater caregiver burden, and early nursing home placement. Identification of sleep disturbances may contribute to early detection of cognitive decline, which could provide an opportunity for appropriate management and modification of potential risk factors.

Previous studies have shown that poor sleep quality is associated with worsening cognitive function and contribute to AD. The candidate mechanisms linking sleep disturbances to the neuropathophysiology of AD may be hyperarousal features of insomnia. Miranda G Chappel-Farley et al.

hypothesized that different aspects of hyperarousal including physiological, cortical, and emotional-cognitive can dysregulate hypothalamic-pituitary-adrenal (HPA) axis activity, disrupt the balance of A β and tau protein production and clearance, and result in a heightened systemic and neuroinflammatory state, thereby facilitating AD neurodegeneration [2]. In addition, short sleep duration and circadian rhythm disruption compound AD pathogenesis by interacting with hyperarousal-associated effects and on AD biomarkers directly. Neuroinflammation is also considered a crucial mediating pathway of sleep disturbances in mild cognitive impairment (MCI) and AD [3]. The amyloid cascade hypothesis supposes that β -amyloid (A β) deposition may activate microglia and astrocytes and release inflammatory factors in response; it may also lead to pineal gland calcification, causing the reduction of melatonin, and this relationship is bidirectional, because melatonin has anti-inflammatory properties in itself. Although there are many possible mechanisms between sleep disturbances and cognitive decline, further studies are needed to clarify the pathophysiology.

Sleep disturbances can not only generate or accelerate cognitive decline, but also represent one of the earliest symptoms of AD. To clarify the relationship between sleep quality and pathological aging, there is greater interest in identifying the main characteristics of sleep and sleep disturbances in the continuum of cognitive decline. Despite the high prevalence of poor sleep and sleep disturbances in healthy older adults, pathological aging including MCI and AD still are associated with worse impoverishment of sleep [4]. The most common aspects compromised are rapid eye movement (REM), sleep efficiency, sleep latency, and sleep duration. MCI patients show intermediate sleep disorders between healthy subjects and AD patients. The main differences include reduced percentage of REM sleep and higher percentages of stage 1 and stage 2 sleep in AD compared to MCI and healthy subjects, and reduced REM sleep in MCI compared to healthy older adults. A secondary analysis in 2022 further showed insomnia symptoms increased risk of progression from cognitively normal status to MCI at 4-year follow-up but did not appear to be significant from MCI to dementia [5]. One possible explanation is that insomnia may arise in the preclinical phase of AD reflecting early stages of neurodegeneration.

In addition to clinical features, other objective examinations such as electroencephalographic (EEG) may provide further information across different stages of cognitive impairment. Previous studies have revealed that

patients with AD show increased low-frequency (0.5-7.0 Hz) activity and decreased high-frequency activity in awake EEG starting in prodromal stages [6]. Triphasic waves and lack of clear EEG distinction between wakefulness, drowsiness, and light sleep were noted as well. Different EEG features were also observed in AD, MCI and healthy subjects during sleep and pre-sleep/post-sleep wakefulness. A cohort study focusing on detailed topographic and frequency-specific alterations in EEG revealed that the primary EEG indices differentiating AD/MCI from healthy older adults were a decrease in alpha activity in temporo-parieto-occipital regions, a decrease in sigma activity during both NREM and REM sleep, and an increase in delta activity during REM sleep and wakefulness in temporo-frontal regions [7]. Among the alterations, EEG slowing in REM sleep shows the highest correlation with cognitive decline, which suggests that REM sleep may be a sensitive marker of the neurodegenerative process in early stages.

Sleep disturbance is not only an early symptom of cognitive decline, but also a predictor of poor outcomes in those with AD. It may worsen cognitive function and neuropsychiatric symptoms, and lead to reduced quality of life. Both subjective and objective evaluation can help identify sleep disturbance in those with cognitive decline earlier, and therefore offer timely management and prevention strategies.

[Image(s) or figure(s)] nil

For further reading:

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5. Virginia T. Gallagher, Shannon E. Reilly, et al. Patterns of sleep disturbances across stages of cognitive decline. *Int J Geriatr Psychiatry*. 2023;e5865. <https://doi.org/10.1002/gps.5865>
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