

Sleep Structure Alterations in Early Alzheimer's Disease and Their Predictive Value

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Abstract. Alzheimer's disease (AD), the leading cause of dementia, poses a significant challenge in early detection. Research indicates that sleep disturbances may precede noticeable cognitive decline. Normal ageing makes sleep lighter and shorter, but the changes are much more substantial in AD. Patients usually have less slow-wave sleep (SWS), reduced rapid eye movement (REM) sleep, more awakenings at night, and a longer time to fall asleep. Electroencephalography (EEG) reveals slower rhythms, fewer spindles, and abnormal spindle-slow wave coupling. Some suggest impaired sleep accelerates AD by hindering amyloid clearance. Recent work shows that sleep measures, especially EEG features, might help predict who will decline and can be added to models with magnetic resonance imaging (MRI) or cerebrospinal fluid (CSF) markers. There are also studies using machine learning with polysomnography (PSG) and EEG, which look promising. But there are problems too, since sleep varies a lot between people, and not every sleep problem means AD. Ethical considerations arise, such as the appropriateness of informing individuals of potential health risks based solely on sleep data. This paper will go over what is known about sleep in early AD, the brain mechanisms behind it, and how sleep might be used to predict disease.

Keywords: Alzheimer's disease, Sleep architecture, Slow-wave sleep, REM sleep, EEG biomarkers

1. Introduction

Alzheimer's disease (AD) is a brain disorder that slowly damages memory and thinking. Changes like amyloid- β ($A\beta$) plaques and tau tangles start many years before doctors can diagnose them. Therefore, researchers are focusing on identifying early biomarkers that can predict the onset of AD prior to the manifestation of clinical symptoms. One area that is getting a lot of attention is sleep. Sleep is essential for learning, memory, and cleaning the brain. In particular, slow-wave sleep (SWS) can help wash out waste like $A\beta$. However, prolonged sleep deprivation could exacerbate inflammation and accelerate disease progression [1].

Some studies have found that people with sleep problems are more likely to get dementia. For instance, sleeplessness may nearly double the probability [2]. Sleep apnea is also connected with faster decline and more amyloid [3]. Extensive research, including meta-analyses, indicates that

sleep disturbances elevate the risk of Alzheimer's disease by approximately 50% [3]. This shows that sleep is not just something that changes with age but could be part of the disease itself.

Still, normal aging also makes sleep worse. Healthy older adults often sleep less, with less REM and SWS, and their nights are more broken [1]. The real question is when these normal changes become signs of disease. Researchers can try to see which changes are abnormal by comparing normal ageing with early AD. This paper will review (1) sleep structure in normal aging vs. AD, (2) the neurophysiological mechanisms behind these changes, and (3) the predictive value of sleep for AD. Understanding how sleep changes in Alzheimer's disease compared with normal aging is important since it may provide non-invasive, early-warning markers and open new directions for prevention and treatment.

2. Sleep structure in Alzheimer's disease

2.1. Sleep in normal aging

Age-related changes in sleep patterns are common. Older individuals typically experience an earlier bedtime and wake time, as well as increased nocturnal awakenings [1]. Their sleep is lighter, too. Polysomnography (PSG) studies have shown more stage N1 light sleep, less SWS and REM, and lower sleep efficiency [1]. EEG studies also report that older adults have weaker delta activity and fewer spindles than young adults. Due to these physiological shifts, a significant portion of the elderly demographic report experiencing non-restorative sleep, irrespective of time spent in bed.

2.2. Abnormal sleep features in early AD

AD patients usually have much bigger sleep problems compared with normal aging. Recent polysomnographic investigations and meta-analyses reveal that individuals exhibit diminished total sleep time (TST), reduced sleep efficiency, and prolonged sleep latency. They wake up more often during the night (WASO); the most clear difference is that they lose a lot of deep sleep [4].

Table 1. PSG measures in Alzheimer's disease vs. healthy controls [4]

PSG Parameter	AD Patients (mean)	Controls (mean)	Effect / Difference
Total Sleep Time (TST)	~331 min	~370 min	↓ AD significantly
Sleep Efficiency (SE)	~71%	~81%	↓ AD significantly
Slow-Wave Sleep (N3/SWS %)	~4.7%	~10%	↓ AD significantly
REM Sleep %	~14%	~18%	↓ AD significantly
Sleep Latency (SL)	~34 min	~19 min	↑ AD significantly
Wake After Sleep Onset (WASO)	↑ (about +40 min)	Lower	↑ AD significantly
REM Latency (REML)	Longer	Shorter	↑ AD significantly
N1 %	Higher	Lower	↑ AD significantly
N2 %	No significant difference		—
Number of Awakenings	Higher	Lower	↑ AD significantly

Table 1 shows that AD patients fall asleep more slowly, have almost no deep N3 sleep, and sleep less efficiently. Although the REM difference looks small, reductions in REM have been linked with future dementia risk [4].

2.3. EEG evidence

EEG gives more detailed evidence. From Figure 1, Alzheimer's disease (AD) and mild cognitive impairment (MCI) patients show EEG slowing: higher delta/theta power and lower alpha/beta than healthy controls (HC). Sleep spindle activity is also diminished, indicating thalamocortical circuit dysfunction [5]. Coupling between slow waves and spindles is abnormal in early AD, and this predicts memory decline [6].



Figure 1. EEG spectral changes in AD compared to controls [5]

EEG frequency characteristics and spindle density are also suggested as potential electrophysiological biomarkers for Alzheimer's Disease [7]. These results suggest that EEG may be a cheap and non-invasive tool for early diagnosis.

3. Neurophysiological mechanisms underlying sleep changes

3.1. SWS reduction and hippocampal degeneration

Slow-wave sleep (SWS) mainly depends on networks between the hippocampus and cortex. In AD, the hippocampus and the medial prefrontal cortex shrink, breaking the normal slow oscillations. Impaired coupling between slow oscillations and theta bursts correlates with accelerated cognitive decline, suggesting that neuropathology directly modulates sleep architecture [8]. Having less SWS also means the brain clears less waste at night through the glymphatic system, and that can make amyloid build up more quickly.

3.2. REM delay and neurotransmitter systems

Cholinergic neurons control REM sleep in the brainstem and orexin neurons in the hypothalamus. Many cholinergic neurons are lost in AD, making REM take longer to start. At the same time, orexin levels go up, and this makes REM more broken and unstable [7]. Because of that, patients usually have longer REM latency and fewer steady REM periods. So these neurotransmitter changes explain many of the REM problems we see in AD.

3.3. Amyloid and tau effects on sleep centers

Poor sleep promotes amyloid build-up because glymphatic clearance is most active during SWS [9]. Concurrently, the deposition of amyloid plaques and neurofibrillary tangles within sleep-regulating brain regions, such as the hypothalamus and locus coeruleus, exacerbates the disruption of sleep-wake cycles [9].

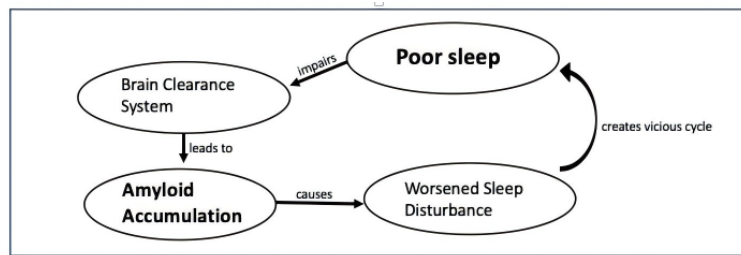


Figure 2. Bidirectional relation between sleep and AD pathology [9]

This shows a vicious cycle: pathology worsens sleep, and bad sleep accelerates pathology [6,9].

4. Predictive value of sleep changes in AD

4.1. Multimodal predictive models

Longitudinal research indicates that poor sleep architecture may serve as a predictive biomarker for future dementia development. For instance, reduced REM sleep duration correlates with an elevated dementia risk, with each percentage point decrease in REM sleep potentially increasing the risk by approximately 9% [3]. EEG sleep measures with cerebrospinal fluid (CSF) and magnetic resonance imaging (MRI), and this made their model more accurate, from about 0.84 to 0.90 AUC [8].

Machine learning is also becoming popular in this field. Researchers tested a semi-supervised deep learning method on PSG data, and it could detect AD with over 90% accuracy [2]. Reviews also point out that EEG-based AI models are a growing trend for early detection [10]. These kinds of methods could maybe make it possible to screen large groups of people in the future, even with simple home devices.

4.2. Clinical challenges and ethics

Still, there are many challenges. Sleep problems are widespread in older adults and not always AD [2]. Insomnia, stress, or other diseases may cause similar PSG patterns [2]. This makes specificity low. PSG is expensive and impractical for routine screening, while consumer devices may lack precision.

There are also ethical issues. Communicating an "Alzheimer's Disease risk" to patients solely on the basis of sleep metrics may precipitate undue anxiety, particularly given the current absence of a definitive cure [3,11]. Long-term data collection also raises privacy questions. Therefore, sleep metrics should be used together with other biomarkers.

5. Conclusion

Alzheimer's disease changes sleep a lot, even in the early stage. Compared with normal aging, patients usually have less slow-wave sleep (SWS) and REM, take longer to fall asleep, and have more broken nights. EEG also shows slower rhythms and fewer spindles. These changes mostly come from brain damage in the hippocampus and cortex, neurotransmitter problems, and amyloid and tau building up in sleep centers. Poor sleep and disease push each other, worsening the decline over time.

More recent studies suggest that sleep itself can be used as a biomarker. Less REM, abnormal coupling between spindles and slow waves, and low efficiency predict cognitive decline. Machine

learning studies with PSG and EEG also report strong accuracy. Integrating sleep metrics with cerebrospinal fluid assays and magnetic resonance imaging enhances predictive accuracy, potentially facilitating early identification of individuals at elevated risk.

Undoubtedly, numerous challenges persist. It is difficult to tell which sleep changes are from normal aging and which are from AD. There are also ethical issues and problems with collecting large-scale data. However, sleep is attractive because it is non-invasive and can be improved. If future work shows that better sleep can slow down AD, then sleep will not only be a symptom but maybe also a way to fight the disease.

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