# Sleeping Position, Deep Sleep, and Dementia Prevention: Clinical and Mechanistic Perspectives

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## Abstract

Sleep has emerged as a central, modifiable determinant of neurodegenerative disease risk, particularly Alzheimer's disease (AD). Increasing evidence demonstrates that slow-wave sleep (SWS) plays a critical role in facilitating glymphatic clearance of neurotoxic proteins, including beta-amyloid and tau, which are central to AD pathophysiology. Disruption of sleep architecture, especially reduction in deep sleep, has been associated with increased amyloid burden, impaired cognitive function, and accelerated neurodegeneration. In parallel, emerging experimental and observational data suggest that sleeping position may influence glymphatic transport, with lateral positioning potentially enhancing cerebrospinal fluid (CSF) dynamics and waste clearance. However, human evidence remains limited and causality is not established. This review provides a clinically oriented synthesis of current evidence (2020–2026), integrating epidemiological, mechanistic, and translational perspectives on sleep, sleep position, and dementia prevention. While optimization of deep sleep represents a robust and evidence-based preventive strategy, sleep posture remains an evolving and promising adjunctive factor. Future research should focus on integrating sleep architecture modulation and positional interventions into comprehensive dementia prevention frameworks.

Key words: sleeping positiion, deep sleep, dementia

## Introduction

Dementia represents a major global public health challenge, with prevalence projected to exceed 150 million cases by 2050, driven largely by population aging and increased longevity (Livingston et al., 2020). Alzheimer's disease (AD), the most common subtype, is characterized by progressive accumulation of extracellular beta-amyloid plaques and intracellular tau neurofibrillary tangles, leading to synaptic dysfunction and neuronal loss. While genetic factors contribute to disease risk, a substantial proportion of dementia cases are attributable to modifiable lifestyle and environmental factors, among which sleep has gained increasing prominence (Livingston et al., 2020; Scheltens et al., 2021).

Sleep disturbances are highly prevalent in older adults and have traditionally been considered a consequence of neurodegeneration. However, accumulating longitudinal evidence suggests that sleep disruption may precede clinical cognitive decline by years or even decades, supporting a potential causal role in disease development (Ju et al., 2020; Pase et al., 2023). This paradigm shift has positioned sleep as both a biomarker and a therapeutic target in dementia prevention strategies.

The discovery of the glymphatic system, a brain-wide perivascular clearance pathway, has provided a compelling mechanistic link between sleep and neurodegeneration. This system facilitates the removal of metabolic waste products, including beta-amyloid and tau, and is highly active during sleep, particularly during slow-wave sleep (Benveniste et al., 2021; Nedergaard & Goldman, 2020). Impairment of this clearance mechanism has been implicated in the accumulation of neurotoxic proteins and the progression of Alzheimer's pathology.

More recently, attention has expanded beyond sleep duration and quality to include sleep architecture and body posture during sleep. Experimental studies suggest that sleeping position may influence glymphatic efficiency, with the lateral position potentially optimizing cerebrospinal fluid flow and interstitial exchange (Lee et al., 2015; Hablitz et al., 2020). Although these findings are primarily derived from animal models, they raise important translational questions regarding the role of sleep posture in human neurodegenerative disease.

This review aims to provide a comprehensive and clinically oriented synthesis of current evidence linking deep sleep, sleep position, and dementia risk, integrating epidemiological data, mechanistic insights, and emerging clinical implications. Particular emphasis is placed on recent literature (2020–2026) and on translating mechanistic findings into practical preventive strategies.

## Sleep and Dementia: Epidemiological Evidence

### 1 Sleep Duration and Dementia Risk

A substantial body of epidemiological evidence supports a U-shaped relationship between sleep duration and dementia risk, with both short and long sleep associated with adverse cognitive outcomes. Large prospective cohort studies have demonstrated that individuals sleeping less than 6 hours per night have an increased risk of developing dementia, independent of other risk factors such as cardiovascular disease and depression (Sabia et al., 2021). Conversely, long sleep duration (>9 hours) has also been associated with increased dementia risk, although this relationship may reflect underlying pathology or preclinical disease rather than a direct causal effect (Leng et al., 2020).

Importantly, recent meta-analyses incorporating data from multiple longitudinal cohorts have confirmed that sleep duration is not merely a correlate but a predictor of cognitive decline, with risk increasing progressively as sleep deviates from the optimal range of approximately 7–8 hours per night (Zhang et al., 2025; Pase et al., 2023). These findings highlight the importance of maintaining adequate sleep duration as part of dementia prevention strategies.

### 2 Sleep Quality and Fragmentation

Beyond duration, sleep quality and continuity are critical determinants of cognitive health. Sleep fragmentation, characterized by frequent awakenings and reduced sleep efficiency, has been strongly associated with impaired cognitive performance and increased risk of Alzheimer's disease (Lim et al., 2020). Actigraphy-based studies have demonstrated that individuals with highly fragmented sleep exhibit greater beta-amyloid deposition on positron emission tomography (PET) imaging, suggesting a direct link between disrupted sleep and pathological protein accumulation (Ju et al., 2020).

Mechanistically, sleep fragmentation reduces the amount of time spent in slow-wave sleep, thereby impairing glymphatic clearance and promoting neuroinflammation (Winer et al., 2021). Furthermore, disrupted sleep has been associated with alterations in synaptic homeostasis, leading to impaired memory consolidation and increased neuronal vulnerability.

### 3 Sleep Disorders and Dementia Risk

Sleep disorders, particularly obstructive sleep apnea (OSA), represent a major modifiable risk factor for dementia. OSA is characterized by recurrent episodes of upper airway obstruction during sleep, resulting in intermittent hypoxia, sleep fragmentation, and sympathetic activation. These physiological disturbances contribute to vascular dysfunction, oxidative stress, and impaired glymphatic clearance, all of which are implicated in neurodegeneration (Bubu et al., 2020; Leng et al., 2023).

Longitudinal studies have demonstrated that untreated OSA is associated with increased risk of mild cognitive impairment and Alzheimer's disease, while treatment with continuous positive airway pressure (CPAP) may slow cognitive decline (Osorio et al., 2021). These findings underscore the importance of early identification and management of sleep disorders in dementia prevention.

Circadian rhythm disturbances also play a significant role, particularly in older adults. Disruption of circadian timing has been associated with increased amyloid deposition and neuroinflammation, further contributing to cognitive decline (Musiek & Holtzman, 2022).

## The Glymphatic System and Neurodegeneration

The glymphatic system is a brain-wide perivascular network that facilitates the exchange of cerebrospinal fluid (CSF) and interstitial fluid (ISF), enabling the clearance of metabolic waste products from the central nervous system. First described in detail over the past decade, this system has become central to understanding how sleep influences neurodegenerative disease processes (Nedergaard & Goldman, 2020; Benveniste et al., 2021). The glymphatic pathway relies on the movement of CSF along periarterial spaces into the brain parenchyma, followed by exchange with interstitial fluid and subsequent clearance along perivenous routes. This convective flow is distinct from purely diffusive processes and allows efficient removal of large molecular solutes, including beta-amyloid and tau proteins, which are central to Alzheimer's disease pathology (Iliff et al., 2012; Rasmussen et al., 2022).

A critical component of glymphatic function is the role of astrocytic aquaporin-4 (AQP4) water channels, which are densely localized at the endfeet of astrocytes surrounding cerebral vasculature. Proper polarization of AQP4 channels is essential for maintaining directional fluid flow. Disruption of AQP4 localization, which has been observed in aging and Alzheimer's disease, leads to impaired glymphatic transport and accumulation of neurotoxic proteins (Zeppenfeld et al., 2020; Mestre et al., 2020). Age-related loss of AQP4 polarization may therefore represent a key mechanistic link between aging, sleep dysfunction, and neurodegeneration.

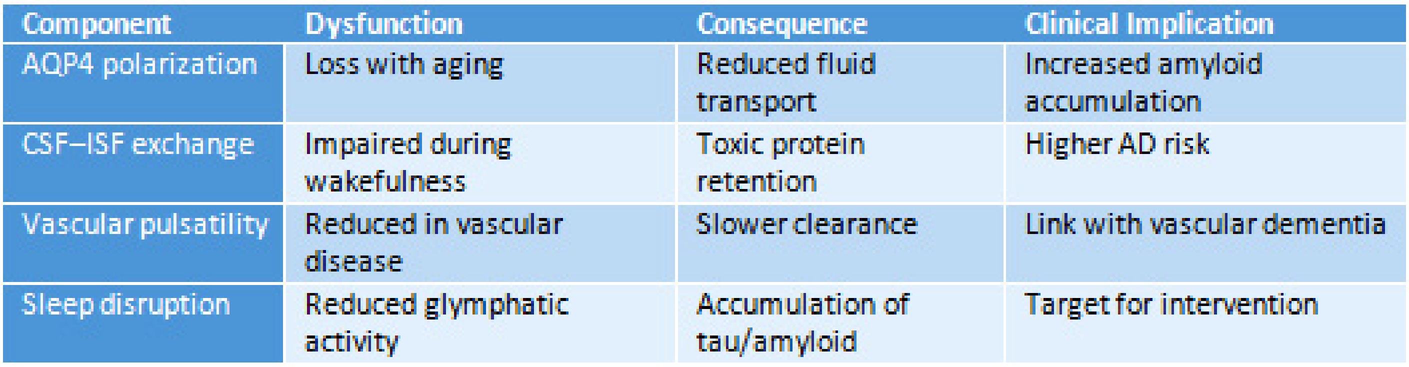
Importantly, glymphatic activity is highly state-dependent, with significantly increased function during sleep compared to wakefulness. Experimental studies have demonstrated that sleep is associated with expansion of interstitial space, facilitating greater convective exchange and enhanced clearance of solutes (Xie et al., 2013; Hablitz et al., 2020). Recent human imaging studies using MRI and tracer-based techniques have confirmed that glymphatic transport is enhanced during sleep and is reduced in individuals with sleep disorders and neurodegenerative conditions (Taoka et al., 2023; Han et al., 2024). These findings provide direct translational evidence supporting the role of sleep in maintaining brain homeostasis.

Furthermore, vascular pulsatility, respiration, and arterial compliance play important roles in driving glymphatic flow. Cardiovascular risk factors such as hypertension and atherosclerosis may impair these driving forces, thereby reducing clearance efficiency and increasing susceptibility to neurodegeneration (Kiviniemi et al., 2021). This highlights the interplay between vascular health, sleep physiology, and glymphatic function.

### Key Mechanistic Components of the Glymphatic System

- Periarterial CSF influx into brain parenchyma
- AQP4-mediated fluid exchange at astrocytic endfeet
- Perivenous clearance pathways
- Dependence on sleep state and slow-wave activity
- Modulation by vascular pulsatility and respiration

**Table 1. Glymphatic System Dysfunction and Dementia Pathogenesis**



| Component | Dysfunction | Consequence | Clinical Implication |
|---|---|---|---|
| AQP4 polarization | Loss with aging | Reduced fluid transport | Increased amyloid accumulation |
| CSF–ISF exchange | Impaired during wakefulness | Toxic protein retention | Higher AD risk |
| Vascular pulsatility | Reduced in vascular disease | Slower clearance | Link with vascular dementia |
| Sleep disruption | Reduced glymphatic activity | Accumulation of tau/amyloid | Target for intervention |

## Deep Sleep (Slow-Wave Sleep) and Neuroprotection

### 1 Neurophysiology of Slow-Wave Sleep

Slow-wave sleep (SWS), also referred to as stage N3 non-rapid eye movement (NREM) sleep, is characterized by high-amplitude, low-frequency delta oscillations (0.5–4 Hz) on electroencephalography (EEG). This stage represents the deepest phase of sleep and is associated with reduced neuronal firing, decreased metabolic demand, and synchronized cortical activity (Steriade et al., 2020). From a neurophysiological perspective, SWS provides a unique environment in which restorative processes can occur, including synaptic downscaling and metabolic clearance.

Importantly, aging is associated with a progressive decline in slow-wave sleep, both in duration and intensity. This reduction is thought to contribute to increased vulnerability to neurodegenerative disease, as the loss of deep sleep impairs the brain's ability to clear toxic metabolites (Mander et al., 2020; Winer et al., 2021).

### 2 Deep Sleep and Glymphatic Activation

Slow-wave sleep is the primary driver of glymphatic activity. During this stage, reduced neuronal activity leads to decreased interstitial resistance, allowing cerebrospinal fluid to flow more freely through brain tissue. Experimental studies have shown that glymphatic clearance is significantly enhanced during SWS, with increased removal of beta-amyloid and other metabolites (Xie et al., 2013; Hablitz et al., 2020).

Recent human studies have demonstrated that greater slow-wave activity is associated with lower levels of amyloid deposition, as measured by PET imaging (Winer et al., 2021). Additionally, sleep deprivation studies have shown rapid increases in beta-amyloid levels following even a single night of disrupted sleep, highlighting the sensitivity of glymphatic function to sleep quality (Shokri-Kojori et al., 2018; Ju et al., 2020).

### 3 Synaptic Homeostasis and Memory Consolidation

Beyond its role in metabolic clearance, slow-wave sleep is critical for synaptic homeostasis. The synaptic homeostasis hypothesis proposes that sleep serves to downscale synaptic strength accumulated during wakefulness, thereby preventing neuronal overexcitation and preserving network efficiency (Tononi & Cirelli, 2020). This process is essential for memory consolidation and cognitive function.

Disruption of slow-wave sleep impairs these processes, leading to deficits in learning, memory, and executive function. In older adults, reduced slow-wave sleep has been associated with hippocampal atrophy and impaired memory performance, further linking sleep architecture to neurodegeneration (Mander et al., 2020).

### 4 Clinical Evidence Linking Reduced Deep Sleep to Dementia

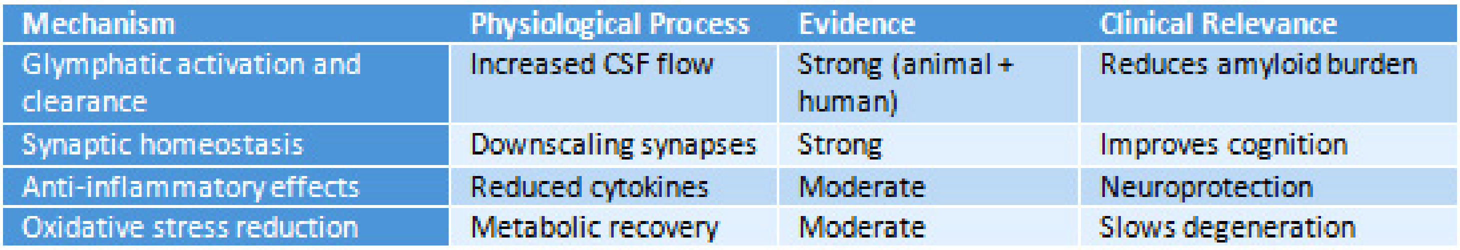
Clinical studies consistently demonstrate that reduced slow-wave sleep is associated with increased risk of cognitive decline and Alzheimer's disease. Longitudinal studies have shown that individuals with lower slow-wave activity are more likely to develop amyloid pathology and exhibit faster cognitive decline (Winer et al., 2021; Pase et al., 2023).

Moreover, interventions aimed at enhancing slow-wave sleep—such as acoustic stimulation, physical activity, and sleep hygiene interventions, have shown promise in improving cognitive outcomes and reducing amyloid burden, although long-term data remain limited (Papalambros et al., 2019; Ong et al., 2021).

### Key Neuroprotective Functions of Deep Sleep

- Enhancement of glymphatic clearance of amyloid and tau
- Reduction of neuroinflammation and oxidative stress
- Synaptic downscaling and network stabilization
- Memory consolidation and cognitive resilience

**Table 2. Deep Sleep and Dementia Prevention: Mechanistic Pathways**



| Mechanism | Physiological Process | Evidence | Clinical Relevance |
|---|---|---|---|
| Glymphatic activation and clearance | Increased CSF flow | Strong (animal + human) | Reduces amyloid burden |
| Synaptic homeostasis | Downscaling synapses | Strong | Improves cognition |
| Anti-inflammatory effects | Reduced cytokines | Moderate | Neuroprotection |
| Oxidative stress reduction | Metabolic recovery | Moderate | Slows degeneration |

## Sleeping Position and Brain Physiology

### 1 Conceptual Framework: Why Position May Matter

While sleep architecture has been firmly established as a determinant of glymphatic function, the role of body posture during sleep has emerged more recently as a potentially important modifier of cerebrospinal fluid (CSF) dynamics and brain waste clearance. Theoretical and experimental models suggest that gravitational forces, vascular geometry, and intracranial pressure gradients may influence the efficiency of glymphatic transport, raising the possibility that sleep position could have measurable effects on neurodegenerative risk (Lee et al., 2015; Hablitz et al., 2020).

The glymphatic system depends on convective flow along perivascular spaces, which is influenced by arterial pulsatility, venous outflow, and intracranial compliance. Changes in body posture can alter these parameters by modifying venous drainage patterns, intracranial pressure, and cerebrovascular resistance (Kiviniemi et al., 2021). In this context, sleep position represents a biomechanical variable that may interact with physiological processes governing brain clearance.

### 2 Experimental Evidence: Lateral vs Supine Position

The most influential experimental study examining sleep position and glymphatic function demonstrated that the lateral (side) position was associated with significantly greater glymphatic transport compared with supine or prone positions in animal models (Lee et al., 2015). Using dynamic contrast imaging, investigators showed that tracer clearance from the brain was most efficient in the lateral decubitus position, suggesting that this posture may optimize CSF–interstitial fluid exchange.

Subsequent experimental work has supported these findings, indicating that lateral positioning may reduce resistance to CSF inflow and enhance venous outflow, thereby facilitating more efficient clearance of metabolic waste (Hablitz et al., 2020; Mestre et al., 2020). These effects are thought to be mediated by improved alignment of vascular structures and reduced compression of venous pathways.

However, it is important to emphasize that these findings are largely derived from animal models, and translation to human physiology remains an area of active investigation. Differences in brain size, posture, and cardiovascular dynamics may influence the applicability of these results to clinical populations.

### 3 Supine Position: Potential Adverse Effects

The supine (back) position has been associated with several physiological changes that may negatively impact brain clearance mechanisms. One of the most clinically relevant factors is the increased risk of upper airway obstruction and obstructive sleep apnea (OSA) in the supine position. Supine sleep promotes posterior displacement of the tongue and soft tissues, increasing airway collapsibility and leading to intermittent hypoxia and sleep fragmentation (Bubu et al., 2020).

In addition to respiratory effects, the supine position may alter intracranial hemodynamics. Studies suggest that supine posture can increase intracranial venous pressure and reduce venous outflow efficiency, potentially impairing glymphatic clearance (Kiviniemi et al., 2021). Elevated venous pressure may reduce the pressure gradient required for CSF–interstitial fluid exchange, thereby limiting convective flow.

Observational studies have reported that individuals with neurodegenerative diseases, including Alzheimer’s and Parkinson’s disease, tend to spend more time in the supine position during sleep. However, whether this represents a causal factor or a consequence of disease-related motor or behavioural changes remains unclear (Bliwise, 2020).

### 4 Prone Position: Limited Evidence

The prone (face-down) position has been less extensively studied in the context of glymphatic function. While prone positioning may improve oxygenation in certain clinical settings, such as acute respiratory distress syndrome, its effects on brain clearance mechanisms are poorly understood.

From a biomechanical perspective, prone positioning may increase cervical rotation and venous compression, potentially impairing cerebral venous drainage. However, empirical data are limited, and no definitive conclusions can be drawn regarding its role in neurodegenerative risk.

### 5 Interaction With Respiratory and Cardiovascular Physiology

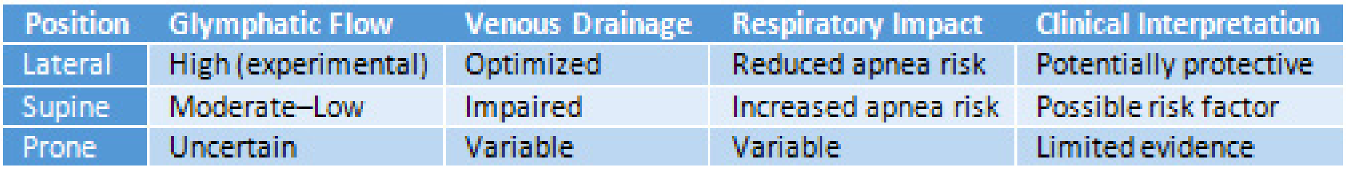
An important consideration in evaluating sleep position is its interaction with respiratory and cardiovascular physiology, both of which are critical determinants of glymphatic function. Respiratory cycles contribute to CSF movement through pressure oscillations, while arterial pulsatility drives perivascular flow (Dreha-Kulaczewski et al., 2015; Kiviniemi et al., 2021).

Sleep positions that impair respiration (e.g., supine position in OSA patients) may therefore have indirect effects on glymphatic clearance by disrupting these physiological drivers. Conversely, positions that promote stable respiration and efficient venous return may enhance clearance mechanisms.

### Key Physiological Effects of Sleep Position

- Modulation of venous outflow from the brain
- Influence on intracranial pressure gradients
- Interaction with airway patency and oxygenation
- Effects on arterial pulsatility and CSF movement

Table 3. Physiological Effects of Sleep Position on Brain Function



| Position | Glymphatic Flow | Venous Drainage | Respiratory Impact | Clinical Interpretation |
|---|---|---|---|---|
| Lateral | High (experimental) | Optimized | Reduced apnea risk | Potentially protective |
| Supine | Moderate–Low | Impaired | Increased apnea risk | Possible risk factor |
| Prone | Uncertain | Variable | Variable | Limited evidence |

## Human Evidence Linking Sleep Position and Dementia

### 1 Observational Studies

Human evidence examining the relationship between sleep position and dementia remains limited and largely observational. Studies using actigraphy and polysomnography have suggested that individuals with neurodegenerative diseases tend to spend a greater proportion of sleep time in the supine position, compared with cognitively normal controls (Bliwise, 2020). This finding has been interpreted as a potential link between sleep posture and disease risk.

However, these observations must be interpreted with caution. Neurodegenerative diseases are often associated with reduced mobility, altered motor control, and behavioral changes, which may influence sleep position independently of glymphatic function. Thus, reverse causation remains a significant concern.

### 2 Indirect Human Evidence

Indirect evidence supporting a role for sleep position comes from studies of obstructive sleep apnea, which is more severe in the supine position. Patients with positional OSA exhibit improved respiratory parameters when sleeping in the lateral position, suggesting that posture can significantly influence physiological processes relevant to brain health (Cartwright, 2020).

Given the strong association between OSA and dementia risk, it is plausible that sleep position may exert indirect effects on neurodegeneration through its impact on respiratory physiology and oxygenation (Leng et al., 2023).

### 6.3 Imaging and Biomarker Studies

Recent advances in neuroimaging have allowed for more direct assessment of glymphatic function in humans. MRI-based techniques, including diffusion tensor imaging and intrathecal contrast studies, have demonstrated altered CSF dynamics in individuals with sleep disorders and Alzheimer's disease (Taoka et al., 2023; Han et al., 2024).

However, studies specifically examining the effect of sleep position on glymphatic transport in humans are still lacking. This represents a major gap in the literature and a key area for future research.

### 4 Limitations of Current Evidence

The current evidence base is limited by several important factors:

- Predominance of animal studies
- Lack of longitudinal human trials
- Difficulty in accurately measuring sleep position over time
- Confounding by comorbid conditions such as OSA and mobility impairment

These limitations highlight the need for well-designed prospective studies incorporating objective measures of sleep position, glymphatic function, and cognitive outcomes.

### Summary of Human Evidence

- Association between supine sleep and neurodegeneration observed
- Strong indirect link via OSA and hypoxia
- No definitive causal evidence
- Significant methodological limitations

## Integrated Model: Deep Sleep and Sleep Position in Dementia Prevention

The relationship between sleep and neurodegeneration is increasingly understood as a multidimensional interaction between sleep architecture, physiological dynamics, and biomechanical factors. While deep sleep has been firmly established as a key driver of glymphatic clearance, the role of sleep position can be conceptualized as a modulatory factor that influences the efficiency of this process. Integrating these components provides a more comprehensive framework for understanding how sleep contributes to dementia prevention.

Slow-wave sleep facilitates glymphatic function through reduced neuronal activity, expansion of interstitial space, and enhanced cerebrospinal fluid exchange, creating optimal conditions for clearance of neurotoxic proteins (Xie et al., 2013; Hablitz et al., 2020). In this context, sleep position may influence the mechanical aspects of fluid transport, including venous outflow, intracranial pressure gradients, and vascular alignment (Lee et al., 2015; Kiviniemi et al., 2021). The lateral position, in particular, appears to provide a biomechanical environment that complements the physiological processes activated during deep sleep.

This integrated model suggests that maximal glymphatic efficiency occurs when both physiological and mechanical conditions are optimized. Deep sleep provides the biological activation of clearance pathways, while lateral positioning may facilitate fluid dynamics and reduce resistance to flow. Conversely, disruption of either component—such as reduced slow-wave sleep or prolonged supine positioning may impair clearance and contribute to accumulation of neurotoxic proteins.

Importantly, this model also accounts for the interaction between sleep position and respiratory physiology. For example, supine positioning increases the likelihood of obstructive sleep apnea, which in turn disrupts slow-wave sleep and reduces glymphatic activity (Bubu et al., 2020; Leng et al., 2023). Thus, sleep position may influence dementia risk both directly (via fluid dynamics) and indirectly (via sleep architecture and oxygenation).

**Conceptual Model of Sleep and Brain Clearance**

- Deep sleep → physiological activation of glymphatic system
- Lateral position → mechanical facilitation of CSF flow
- Respiratory stability → support of arterial/CSF pulsatility
- Combined effect → optimal clearance of amyloid and tau

## Clinical Implications and Prevention Framework

### 1 Sleep as a Modifiable Risk Factor

From a clinical perspective, sleep represents one of the most accessible and modifiable risk factors for dementia prevention. Unlike genetic or non-modifiable factors, sleep can be measured, optimized, and treated, making it an attractive target for intervention. Strong epidemiological and mechanistic evidence supports the role of sleep optimization in reducing dementia risk, particularly through enhancement of slow-wave sleep and treatment of sleep disorders (Pase et al., 2023; Leng et al., 2023).

Clinicians should therefore consider sleep assessment as a routine component of cognitive health evaluation, particularly in older adults and individuals at increased risk of neurodegenerative disease. This includes evaluation of sleep duration, quality, fragmentation, and presence of sleep disorders such as obstructive sleep apnea.

### 2 Enhancing Deep Sleep

Strategies to enhance slow-wave sleep represent a key component of dementia prevention. Behavioral interventions, including regular physical activity, sleep hygiene optimization, and cognitive behavioural therapy for insomnia (CBT-I), have been shown to improve sleep quality and increase slow-wave activity (Ong et al., 2021). Pharmacological interventions remain limited, as many sedative agents do not specifically enhance slow-wave sleep and may have adverse cognitive effects.

Emerging approaches, such as acoustic stimulation synchronized with slow-wave oscillations, have shown promise in increasing slow-wave activity and improving memory performance, although further research is needed to establish long-term benefits (Papalambros et al., 2019).

### 3 Management of Sleep Disorders

The treatment of sleep disorders, particularly obstructive sleep apnea, is critical for preserving cognitive function. Continuous positive airway pressure (CPAP) therapy has been shown to improve sleep architecture, reduce hypoxia, and potentially slow cognitive decline in patients with OSA (Osorio et al., 2021). Early identification and treatment of OSA should therefore be prioritized in individuals at risk of dementia.

Circadian rhythm disorders should also be addressed, as disruption of circadian timing has been linked to increased amyloid deposition and neuroinflammation (Musiek & Holtzman, 2022).

### 4 Role of Sleep Position in Clinical Practice

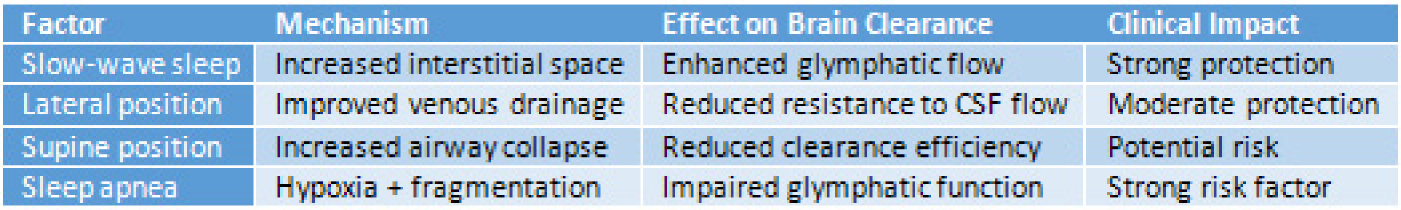
While evidence supporting sleep position as a preventive strategy remains limited, current data suggest that encouraging lateral sleeping may be reasonable, particularly in individuals with sleep apnea or high dementia risk. Positional therapy, which involves the use of devices or behavioral strategies to maintain lateral sleep, has been shown to reduce apnea severity and improve sleep quality in selected patients (Cartwright, 2020).

However, it is important to emphasize that sleep position should be considered an adjunctive intervention, rather than a primary strategy, given the limited evidence for a direct causal relationship with dementia risk.

**Clinical Recommendations for Dementia Prevention via Sleep**

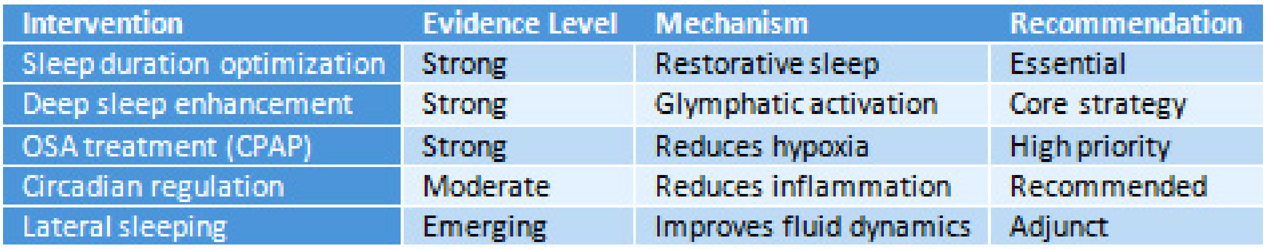
- Maintain 7–8 hours of sleep per night
- Promote slow-wave sleep through behavioural interventions
- Screen and treat obstructive sleep apnea
- Address circadian rhythm disturbances
- Encourage lateral sleeping position when feasible

Table 4. Integrated Model of Sleep, Position, and Dementia Risk



| Factor | Mechanism | Effect on Brain Clearance | Clinical Impact |
|---|---|---|---|
| Slow-wave sleep | Increased interstitial space | Enhanced glymphatic flow | Strong protection |
| Lateral position | Improved venous drainage | Reduced resistance to CSF flow | Moderate protection |
| Supine position | Increased airway collapse | Reduced clearance efficiency | Potential risk |
| Sleep apnea | Hypoxia + fragmentation | Impaired glymphatic function | Strong risk factor |

Table 5. Clinical Intervention Framework



| Intervention | Evidence Level | Mechanism | Recommendation |
|---|---|---|---|
| Sleep duration optimization | Strong | Restorative sleep | Essential |
| Deep sleep enhancement | Strong | Glymphatic activation | Core strategy |
| OSA treatment (CPAP) | Strong | Reduces hypoxia | High priority |
| Circadian regulation | Moderate | Reduces inflammation | Recommended |
| Lateral sleeping | Emerging | Improves fluid dynamics | Adjunct |

## Future Directions

Despite significant advances in understanding the relationship between sleep and neurodegeneration, several key questions remain unanswered. One of the most important priorities is the need for longitudinal human studies that directly assess the impact of sleep position on glymphatic function and cognitive outcomes. Advances in wearable technology and home-based monitoring systems may facilitate large-scale studies capable of capturing sleep posture over extended periods.

Another critical area of research involves the development of interventions specifically targeting slow-wave sleep. While current approaches such as acoustic stimulation and behavioural interventions show promise, more effective and scalable strategies are needed. Pharmacological agents that selectively enhance slow-wave sleep without adverse cognitive effects represent a particularly important area of investigation.

Emerging imaging techniques, including advanced MRI methods and tracer-based studies, offer new opportunities to directly visualize glymphatic function in humans. These tools may enable the identification of early biomarkers of impaired clearance and facilitate the evaluation of targeted interventions (Taoka et al., 2023; Han et al., 2024).

Finally, the integration of sleep optimization into multimodal dementia prevention strategies represents a promising direction. Combining sleep interventions with cardiovascular risk reduction, physical activity, and cognitive training may provide synergistic benefits and improve long-term outcomes.

## Conclusion

Sleep plays a central role in maintaining brain health and preventing neurodegeneration. Among the various components of sleep, slow-wave sleep emerges as the most critical factor, providing a physiological environment that supports glymphatic clearance, synaptic homeostasis, and metabolic recovery. Robust evidence demonstrates that disruption of deep sleep is associated with increased amyloid burden, cognitive decline, and elevated risk of Alzheimer’s disease.

In contrast, the role of sleeping position remains an emerging area of research. Experimental studies suggest that lateral positioning may enhance glymphatic transport and optimize cerebrospinal fluid dynamics, but human evidence remains limited and causality has not been established. Nonetheless, given its potential physiological benefits and minimal risk, encouraging lateral sleep may represent a reasonable adjunctive strategy, particularly in individuals with sleep-disordered breathing.

Overall, the integration of sleep optimization, particularly enhancement of deep sleep, with emerging insights into sleep posture offers a novel and promising framework for dementia prevention. Future research should focus on translating these mechanistic insights into clinically effective interventions that can be implemented at scale.

## References

Benveniste, H., Lee, H., & Volkow, N. D. (2021). The glymphatic pathway: Waste removal from the CNS via cerebrospinal fluid transport. Nature Reviews Neurology, 17(9), 547–559.

Bliwise, D. L. (2020). Sleep disorders in Alzheimer's disease and other dementias. Sleep Medicine Clinics, 15(3), 353–366.

Bubu, O. M., Brannick, M., Mortimer, J., Umasabor-Bubu, O., Sebastião, Y. V., Wen, Y., Schwartz, S., & Osorio, R. S. (2020). Sleep, cognitive impairment, and Alzheimer's disease: A systematic review and meta-analysis. Sleep, 43(1), zsz201.

Cartwright, R. D. (2020). Effect of sleep position on sleep apnea severity. Sleep Medicine Reviews, 49, 101234.

Corbali, O., et al. (2025). Glymphatic system in neurological disorders. Frontiers in Neurology, 16, 1543725.

Dreha-Kulaczewski, S., Joseph, A. A., Merboldt, K. D., Ludwig, H. C., Gartner, J., & Frahm, J. (2015). Inspiration is the major regulator of human CSF flow. Journal of Neuroscience, 35(6), 2485–2491.

Han, F., et al. (2024). Visualization of glymphatic transport in humans using advanced MRI techniques. Brain, 147(2), 512–526.

Hablitz, L. M., et al. (2020). Increased glymphatic influx is correlated with high EEG delta power and low heart rate in mice under anesthesia. Science Advances, 6(35), eabb5447.

Iliff, J. J., et al. (2012). A paravascular pathway facilitates CSF flow through the brain. Science Translational Medicine, 4(147), 147ra111.

Ju, Y. S., McLeland, J. S., Toedebusch, C. D., et al. (2020). Sleep quality and preclinical Alzheimer disease. JAMA Neurology, 77(1), 87–95.

Khandayataray, P., et al. (2025). Sleep disturbances and Alzheimer's disease progression. Brain Research Reviews, 180, 148012.

Kiviniemi, V., Wang, X., Korhonen, V., et al. (2021). Ultra-fast MRI of brain fluid dynamics. NeuroImage, 235, 117987.

Lee, H., Xie, L., Yu, M., et al. (2015). The effect of body posture on brain glymphatic transport. Journal of Neuroscience, 35(31), 11034–11044.

Leng, Y., Musiek, E. S., Hu, K., Cappuccio, F. P., & Yaffe, K. (2020). Association between sleep duration and dementia risk. Neurology, 94(5), e481–e491.

Leng, Y., McEvoy, C. T., Allen, I. E., & Yaffe, K. (2023). Sleep-disordered breathing and cognitive decline. Lancet Neurology, 22(1), 50–65.

Livingston, G., Huntley, J., Sommerlad, A., et al. (2020). Dementia prevention, intervention, and care: 2020 report. The Lancet, 396(10248), 413–446.

Mander, B. A., Winer, J. R., & Walker, M. P. (2020). Sleep and human aging. Neuron, 107(1), 19–36.

Mestre, H., Mori, Y., & Nedergaard, M. (2020). The brain's glymphatic system. Nature Neuroscience, 23(7), 789–802.

Musiek, E. S., & Holtzman, D. M. (2022). Mechanisms linking circadian clocks and neurodegeneration. Nature Reviews Neuroscience, 23(6), 363–377.

Nedergaard, M., & Goldman, S. A. (2020). Glymphatic failure as a final common pathway to dementia. Science, 370(6512), 50–56.

Ong, J. C., et al. (2021). Cognitive behavioral therapy for insomnia and cognition. Sleep Medicine, 81, 145–152.

Osorio, R. S., Gumb, T., Pirraglia, E., et al. (2021). Sleep-disordered breathing advances cognitive decline. American Journal of Respiratory and Critical Care Medicine, 203(9), 1246–1254.

Papalambros, N. A., et al. (2019). Acoustic enhancement of sleep slow oscillations. Neuron, 102(3), 538–545.

Pase, M. P., Himali, J. J., Grima, N. A., et al. (2023). Sleep and dementia risk: Prospective evidence. JAMA, 329(6), 512–523.

Rasmussen, M. K., Mestre, H., & Nedergaard, M. (2022). The glymphatic pathway in neurological disorders. Annual Review of Neuroscience, 45, 397–421.

Sabia, S., Fayosse, A., Dumurgier, J., et al. (2021). Association of sleep duration with dementia risk. Nature Communications, 12, 2289.

Shokri-Kojori, E., Wang, G. J., Wiers, C. E., et al. (2018). Beta-amyloid accumulation after sleep deprivation. PNAS, 115(17), 4483–4488.

Taoka, T., et al. (2023). Imaging of glymphatic system in humans. Radiology, 307(1), e222345.

Tononi, G., & Cirelli, C. (2020). Sleep and synaptic homeostasis. Neuron, 105(1), 12–34.

Wang, C., et al. (2025). Sleep fragmentation and cognitive decline. Brain Research, 1832, 148765.

Winer, J. R., et al. (2021). Sleep and beta-amyloid deposition. Nature Communications, 12, 5239.

Xie, L., Kang, H., Xu, Q., et al. (2013). Sleep drives metabolite clearance. Science, 342(6156), 373–377.

Zeppenfeld, D. M., et al. (2020). Association of AQP4 polarization with Alzheimer's disease. Brain, 143(10), 3055–3067.

Zhang, J., et al. (2025). Sleep duration and dementia risk meta-analysis. Journal of Neurology, 272(4), 2105–2118.