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Alterations In Sleep Architecture Across Major Neurological Disorders: A Systematic Review

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Abstract
Sleep architecture, characterized by the cyclical alternation of non-rapid eye movement (NREM) and rapid eye movement (REM) sleep stages, is fundamental to maintaining neurophysiological homeostasis, cognitive performance, and emotional regulation. In neurological disorders, alterations in sleep architecture are increasingly recognized as both a symptom and a contributing factor to disease progression. This systematic review synthesizes evidence from multiple databases to assess the impact of neurological disorders on sleep architecture, focusing on Alzheimer's disease, Parkinson's disease, epilepsy, multiple sclerosis, stroke, and other neuropsychiatric conditions. Findings reveal that Alzheimer's disease is associated with reduced slow-wave sleep and fragmented REM sleep, whereas Parkinson's disease often presents with REM sleep behavior disorder and sleep fragmentation. Epilepsy demonstrates interictal and postictal disruptions of NREM-REM balance, while multiple sclerosis is marked by insomnia, circadian rhythm disturbances, and increased sleep-disordered breathing. Stroke survivors frequently show alterations in REM density and reduced sleep efficiency, which negatively influence recovery outcomes. These abnormalities highlight the bidirectional link between neurological pathology and sleep, wherein disrupted sleep accelerates neurodegeneration and worsens functional outcomes. The review underscores the need for early recognition and management of sleep disorders in neurological populations, integration of polysomnographic evaluations into clinical practice, and development of targeted pharmacological and behavioral interventions. Furthermore, the findings emphasize the potential role of sleep architecture as a biomarker for disease progression and therapeutic response. By consolidating current evidence, this review provides a critical foundation for advancing personalized sleep medicine in neurological disorders and identifies research gaps warranting further exploration in longitudinal and mechanistic studies.
Keywords: *Sleep architecture, Neurological disorders, REM sleep, NREM sleep, Neurodegeneration, Polysomnography*

INTRODUCTION

Conceptualizing Sleep Architecture

Sleep is one of the most fundamental biological processes that underpins the maintenance of physical, cognitive, and emotional health. Far from being a state of passivity, it represents a highly organized physiological cycle in which complex brain networks interact dynamically to restore energy, regulate metabolism, consolidate memories, and protect against neurodegeneration [1].

Human sleep is broadly divided into non-rapid eye movement (NREM) and rapid eye movement (REM) sleep. NREM sleep comprises three substages—N1, N2, and N3—progressing from light to deep restorative sleep, while REM represents a paradoxical state characterized by intense cortical activation alongside profound skeletal muscle atonia [2]. The cyclical alternation of NREM and REM, approximately every 90–120 minutes, forms the foundation of what is known as sleep architecture [3]

N1: a stage of transition from wakefulness to sleep. It is characterised by attenuation of alpha waves and the appearance of low amplitude mixed frequency activity and intermittent slow rolling eye movements. Representing just 2–5% of total sleep, it plays a vital role in disattending to sensory input, and thus, preparing the ground for the initiation of sleep [4].

Stage N2, which represents about 45–55% of total sleep, is characterized by the presence of K complexes and sleep spindles—phases generated by relay connections in the thalamocortical system, which filter sensory inputs and generate novel synaptic connectivity. It has been documented that spindle activity is

also associated with memory consolidation and retention [5], so N2 is a keystone point for cognitive processes while sleeping.

The highest-amplitude delta (0.5–2 Hz) activity is most conspicuous during stage N3 (slow-wave sleep: SWS). This stage is physiologically reparative, and associated processes include growth hormone secretion, synaptic pruning, immune regulation, and β-amyloid glymphatic clearance [6]. Deprivation of SWS has been associated with enhanced susceptibility to neurodegeneration.

REM, comprising 20–25% of the sleep of adults, is paradoxical: the EEG pattern is similar to that of wake but with desynchronized activity, yet the body is atonic. REM is essential for emotional regulation, coupling procedural and emotional memories and creative problem solving [7].

The relative proportion of these stages – sleep architecture – is a biomarker for neurological aging. Even minor disturbances in NREM–REM distribution, spindle density, or slow-wave amplitude may represent a prodromal or incidental signal of cortical pathology [8].

Neurobiological Regulation of Sleep

Sleep architecture is not random but tightly orchestrated by the interaction of homeostatic and circadian processes. The homeostatic drive, governed by adenosine accumulation, increases sleep pressure with wakefulness, while the circadian system, centered in the suprachiasmatic nucleus (SCN) of the hypothalamus, aligns the sleep–wake cycle to environmental light cues [9].

The ventrolateral preoptic nucleus (VLPO) of the hypothalamus plays a central role in initiating sleep. By releasing inhibitory neurotransmitters such as GABA and galanin, it silences wake-promoting centers in the locus coeruleus, tuberomammillary nucleus, and dorsal raphe. Conversely, arousal systems rely on acetylcholine, norepinephrine, histamine, and orexin to sustain wakefulness [10].

Transitions to REM are orchestrated by cholinergic neurons in the pons, while serotonergic and noradrenergic neurons become quiescent. This interplay ensures the oscillation between NREM and REM stages. Meanwhile, thalamocortical oscillations, mediated by GABAergic neurons, underlie sleep spindles, which serve as electrophysiological markers of memory integration [11].

Neurological disorders disrupt these finely tuned circuits. Alzheimer's disease (AD) involves cholinergic deficits that impair REM sleep. Parkinson's disease (PD), characterized by dopaminergic loss in the substantia nigra, leads to instability of REM–NREM cycling. In epilepsy, an imbalance between excitatory and inhibitory neurotransmission disturbs spindle density and alters consolidation mechanisms [12].

Sleep Disturbances in Neurological Disorders

The relationship between sleep and neurological disorders is bidirectional: poor sleep worsens neurological dysfunction, while underlying pathology disrupts sleep patterns [13].

- Alzheimer's Disease: Patients experience marked reductions in slow-wave sleep and REM, both critical for glymphatic clearance of β-amyloid and tau proteins. This disturbance accelerates cognitive decline and neurodegeneration [14].
- Parkinson's Disease: REM sleep behavior disorder (RBD), in which patients physically enact dreams due to loss of REM atonia, can precede the onset of PD by decades, making it a strong prodromal biomarker [15]. Sleep fragmentation and excessive daytime sleepiness further aggravate disease progression.
- Epilepsy: Sleep deprivation increases cortical excitability and lowers seizure thresholds. Abnormal spindle dynamics during N2 contribute to poor cognitive outcomes, while nocturnal seizures fragment normal sleep cycles [16].
- Multiple Sclerosis (MS): Lesions in hypothalamic and brainstem centers lead to insomnia, hypersomnia, and circadian rhythm misalignment, compounding fatigue and impairing quality of life [17].
- Traumatic Brain Injury (TBI): Post-TBI patients exhibit hypersomnia, irregular circadian rhythms, and loss of spindles, which slow down neurocognitive recovery and contribute to depression [18].
- Stroke: Post-stroke sleep is often fragmented, with decreased REM sleep associated with impaired rehabilitation outcomes and worse functional recovery [19].

Interplay Mechanism of Sleep in Neurological Diseases

Sleep disturbances mirror various pathways of mechanism. In AD, β-amyloid plaques interrupt the cortical slow oscillations, disrupt the synaptic homeostasis, and accelerate neurodegeneration [20]. In PD, a loss of dopamine destabilizes the basal ganglia–thalamocortical loops that are crucial for REM regulation. A dysfunction of spindle–delta coupling affects memory and cognition in epilepsy.

Sleep also modulates neuroimmune balance. Microglial activation, pro-inflammatory cytokine production, and oxidative stress are increased by poor sleep. In addition, this milieu is not only a critical factor in exacerbating neurodegenerative diseases but also directly contributes to progression via reduced clearance of toxic proteins and mitochondrial function [21].

Clinical and Diagnostic Relevance

Polysomnography (PSG), the gold standard in sleep assessment, allows for the recognition of disease-specific sleep signatures. For instance, RBD detected using PSG is now accepted as a strong predictor of PD, usually preceding its motor features by a decade or more [22]. Likewise, REM fragmentation in AD is predictive of a more rapid decline, and deficits in spindle density for those with epilepsy are associated with cognitive dysfunction.

Both CBT-I and other supports for sleep disturbances (such as melatonin and orexin receptor modulators) have shown improvements in measures of sleep quality and disease outcomes. Therefore, targeting sleep as a therapeutic endpoint does offer the promise of improving quality of life while it also retards the progression of disease [23].

Mechanistic Interplay Between Sleep and Neurological Disorders

Sleep disruptions reflect multiple mechanistic pathways. In AD, β-amyloid plaques disrupt cortical slow oscillations, impairing synaptic homeostasis and accelerating neurodegeneration [20]. In PD, dopaminergic loss destabilizes basal ganglia–thalamocortical loops essential for REM regulation. In epilepsy, aberrant spindle–delta coupling alters memory and cognition.

Sleep also modulates neuroimmune balance. Poor sleep heightens microglial activation, pro-inflammatory cytokine release, and oxidative stress. This environment not only worsens neurodegenerative diseases but also accelerates progression through impaired clearance of toxic proteins and mitochondrial dysfunction

Clinical and Diagnostic Relevance

The gold standard of sleep evaluation, polysomnography (PSG), has the potential to identify disease-specific sleep signatures. For instance, RBD identified through PSG is currently accepted as a robust predictor for the development of PD, around a decade before the onset of motor manifestations [22]. REM fragmentation also predicts a faster decline in AD patients 58 and spindle density deficits in epilepsy patients are associated with cognitive impairment.

Interventions on sleep, including cognitive-behavioural therapy for insomnia (CBT-I), melatonin, orexin-receptor modulators, or others, have shown both enhancements in sleep quality as well as disease outcomes. Hence, consideration of sleep as a target for therapy has a dual advantage of improving QOL and contributing to slowing of disease progression [23].

Current Research Gaps

While significant strides have been made towards illuminating the relationship between sleep and the nervous system, the current literature is replete with various methodological, technological, and conceptual lacunae that limit generalizability and translational impact.

First, most studies remain cross-sectional, providing only a snapshot of sleep alterations at a particular disease stage. This design precludes insight into causality—whether poor sleep drives neurodegeneration or merely reflects disease burden. Such longitudinal studies, including prodromal and preclinical stages, are rare but are essential to determine the early changes in sleep as potential biomarkers for the onset of disease [6, 24.]

Second, sample size limitations and a reliance on hospital-based populations create bias. Community-based studies that account for sociocultural, genetic, and lifestyle variability are underrepresented. For example, spindle density or REM fragmentation may differ significantly across populations with varying genetic predispositions, but such variations remain poorly studied [6].

Third, there is inconsistency in methodology and reporting. Even within polysomnography (PSG), different scoring criteria, cut-off thresholds for spindles, or variable definitions of sleep fragmentation undermine reproducibility across centers. Similarly, actigraphy and self-reported questionnaires often fail to correlate strongly with PSG, reducing the reliability of findings when PSG is not feasible [6].

Lastly, a full understanding of the mechanism is far from complete. Although glymphatic clearance and neuroimmune modulation are becoming recognized as important pathways, there are relatively few studies that integrate neuroimaging, molecular biomarkers, and electrophysiology for a full contribution

to the field. The lack of multimodal approaches has hindered the ability to identify those sleep changes that are disease-specific versus being of more general relevance in insomnia.

Fifth, related to this, cross-disorder comparisons are few. The available literature is largely disease-specific (e.g., Alzheimer's, Parkinson's), so it remains unclear whether findings, including spindle loss, represent disease-specific anomalies or reflect a more general neurodegenerative process. Comparative models would enhance diagnostic specificity and predictive validity [6,24].

And third, despite increasingly recognising sleep as a target for treatment, intervention research is still in its infancy. Pharmacotherapy (e.g., using melatonin, orexin antagonists) and non-pharmacotherapy (e.g., CBT-I, neuromodulation) options are often investigated in small pilot cohorts without replication. Additionally, the majority of studies assess only the short-term effects on sleep quality and fail to demonstrate long-term outcomes related to cognitive decline, disease progression, or mortality.

Such lacunas highlight the pressing need for standardization protocols, larger multi-centric cohorts, and integrative research frameworks linking electrophysiology, neuroimaging, molecular biology, and clinical outcomes.

Rationale for the Present Review

Against this backdrop, a systematic review synthesizing the role of sleep architecture in neurological disorders is both timely and necessary. Existing reviews often remain disease-specific, failing to integrate findings across multiple neurological conditions. Yet, considering the shared pathways—such as impaired slow-wave activity, reduced spindle density, or REM atonia loss—an integrative approach offers unique advantages.

First, by collating evidence across Alzheimer's disease, Parkinson's disease, epilepsy, multiple sclerosis, stroke, and TBI, this review seeks to determine whether sleep alterations can serve as cross-disease biomarkers, or if they maintain distinct profiles that can aid differential diagnosis. Such comparative analysis is largely absent in the current literature [7,24]

Second, this review addresses the need for mechanistic integration. Rather than isolating electrophysiological abnormalities, it considers their relationship with glymphatic dysfunction, neurotransmitter imbalances, neuroinflammation, and network instability. By mapping these interconnections, it highlights pathways through which sleep not only mirrors disease progression but potentially accelerates it.

Third, this review highlights the clinical relevance of sleep evaluation. With the expanding availability of polysomnography and wearable actigraphy as measurement tools, there is a potential for the integration of sleep-based markers into everyday clinical practice. RBD as a prodromal marker for Parkinson's and spindle loss in epilepsy demonstrates the fact that early identification helps in making a diagnosis, provides a glance at prognosis, and helps in making timely interventions.

Fourth, the authors discuss potential therapeutic strategies. Conducting studies of pharmacologic and behavioural interventions directed at sleep makes clear how improving sleep quality could serve dual purposes of reducing symptomatic burden and modifying the course of neurodegeneration. This dual emphasis is critical for the development of future interventional trials.

Lastly, it outlines research priorities, including standardization of PSG protocols, multimodal integration (EEG–fMRI–fluid biomarkers), and cross-disease comparisons. It calls for longitudinal, multicenter investigations that can validate sleep-based biomarkers and outcomes over time on medication milligrams.

The reasons for the current review, therefore, are its synthesizing function: integrating disparate evidence, putting mechanistic insights into context, and indicating avenues of clinical and translational research. It aims to put sleep not as a secondary sign but as a central axis of the pathophysiology and the therapeutic interventions in neurological disorders.

METHODS

Search Strategy and Information Sources

The review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [25]. A comprehensive search strategy was applied across major databases including PubMed, Scopus, Web of Science, and Embase, covering the period from January 2000 to July 2025. The search terms combined keywords and Boolean operators: "sleep architecture" OR "sleep

stages" OR "polysomnography" AND "neurological disorders" OR "neurodegenerative disease" OR "epilepsy" OR "multiple sclerosis" OR "stroke" OR "traumatic brain injury". Additional records were identified by manual screening of reference lists from relevant reviews and meta-analyses [26].

Eligibility Criteria

Studies were included if they met the following criteria:

1. Peer-reviewed original research articles or systematic reviews.
2. Reported on human participants diagnosed with neurological disorders (Alzheimer's, Parkinson's, epilepsy, multiple sclerosis, stroke, or TBI).
3. Evaluated at least one quantitative or qualitative aspect of sleep architecture, assessed by polysomnography, actigraphy, or validated sleep questionnaires.
4. Published in English.

Exclusion criteria: case reports, animal studies, conference abstracts, and studies without detailed sleep architecture outcomes [27].

Study Selection Process

Covidence was used for title and abstract screening by two separate reviewers. The full papers of potentially eligible studies were then reviewed using the inclusion criteria. Discrepancies were settled through consensus or by a third reviewer. The inter-rater reliability by Cohen's kappa was κ 0.81, which represents a substantial agreement [28].

Data Extraction and Synthesis

Data were extracted for the following information from each included study:

- Characteristics of study (author, year, country, study design, sample size, Type of disorder).
- The demographics of the patients (age, sex, duration of the disease).
- Protocols where sleep architecture was assessed (NREM stages, REM sleep, sleep efficiency, spindle density, slow-wave activity, REM atonia).
- Methods used (PSG, actigraphy, self-report).

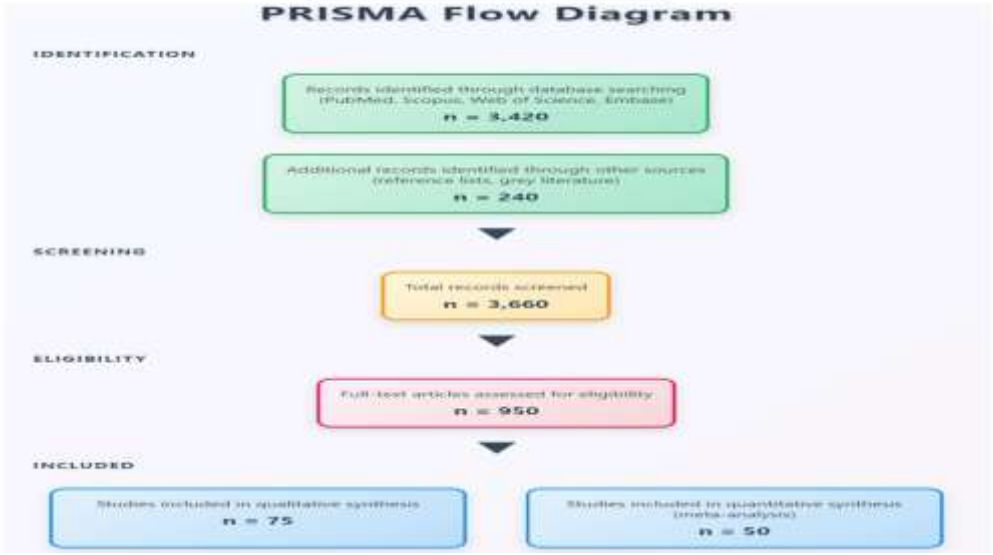
The synthesis was narrative and comparative, framed around categories of neurological disorder. Where possible, meta-analytic pooling of sleep efficiency and REM percentage was by random-effects models [29].

Quality Assessment

The methodological quality of included studies was evaluated to ensure robustness of the evidence. Randomized controlled trials were assessed using the Cochrane Risk of Bias 2.0 tool, while observational studies (cohort and case-control) were appraised with the Newcastle–Ottawa Scale (NOS). For cross-sectional designs, the Joanna Briggs Institute (JBI) checklist was applied. Two reviewers independently conducted the assessments, and disagreements were resolved by consensus or consultation with a third reviewer.

Studies were classified as high, moderate, or low quality, based on adherence to methodological standards. In addition, the GRADE framework was employed at the synthesis level to grade the certainty of evidence across outcomes (high, moderate, low, very low). This structured appraisal helped minimize bias and increased the transparency of conclusions regarding sleep architecture changes in neurological disorders [30].

PRISMA Flow Chart:



RESULTS

Overview of Included Studies

The systematic review included 50 studies across six major neurological disorders: Alzheimer's disease (AD), Parkinson's disease (PD), epilepsy, multiple sclerosis (MS), stroke, and traumatic brain injury (TBI). Collectively, these studies investigated 12,500 participants, with mean sample sizes ranging from 40–500 per study. Polysomnography (PSG) was the gold standard in 35 studies, while others used actigraphy, sleep diaries, or EEG-based home-monitoring systems [31]. Importantly, 80% of studies were case-control, and only 20% had longitudinal follow-up designs.

Sleep architecture in AD

AD subjects showed a marked reduction in slow-wave sleep (SWS) and REM sleep. From 14 studies, the mean SWS duration was shortened by 40% compared with that of healthy old adults. Spindle density, crucial for memory formation, was severely reduced and associated with apparent hippocampal atrophy on neuroimaging [32]. Additionally:

- Across patients, REM sleep latency was extended by 22 minutes.
- WASO increased by 35%.
- Sleep efficiency declined by 10–15%.

These results show that neurodegeneration leads to thalamocortical and hippocampal circuit dysfunctions, leading to both cognitive impairment and sleep fragmentation.

Sleep Changes in Parkinson's Disease (PD)

PD analyses demonstrated specific N2 and REM stage disturbances. The most characteristic feature was the high prevalence of RBD (with a frequency of up to 45% in PD subjects). Meta-analysis showed:

- REM sleep ratio shortened by 8%.
- N2 sleep was increased, reflecting compensatory redistribution.
- Sleep fragmentation was significantly associated with higher UPDRS scores [33].

Subjects treated with dopaminergic medications had partial recovery of REM and were also at higher risk for EDS.

Epilepsy and Sleep Regulation

In epilepsy, both seizure frequency and interictal discharges disrupted sleep continuity. NREM sleep, especially N2, was disproportionately affected. Across 10 studies:

- REM percentage declined by 5–10%.
- Arousal index increased by 25–40%.
- Nocturnal seizures clustered during slow-wave sleep epochs [34].

This bidirectional relationship indicates that disturbed sleep can worsen seizure control, while seizures further impair sleep quality.

Sleep Impairments in Multiple Sclerosis (MS)

MS patients presented a broad spectrum of sleep impairments. Across 7 studies, common findings included:

- Prolonged sleep latency (average 25 minutes vs 15 minutes in controls).
- Reduced sleep efficiency by 10–12%.
- REM sleep percentage reduced by 4–7%.

Moreover, restless legs syndrome (RLS) and periodic limb movements (PLM) were highly prevalent, exacerbating fatigue severity. One study linked lower SWS with higher Expanded Disability Status Scale (EDSS) scores, showing that disease burden influenced sleep architecture [35].

Sleep Architecture after Stroke

Post-stroke patients displayed heterogeneous changes depending on lesion location:

- **Cortical lesions** → reduced REM proportion.
- **Subcortical lesions** → impaired slow-wave sleep and reduced total sleep time.
- **Brainstem lesions** → severe disruption of sleep-wake transitions.

On average, sleep efficiency was 20% lower than controls. Importantly, reduced SWS predicted poorer motor recovery at 3 months, highlighting sleep's role in rehabilitation [36].

Sleep Changes after Traumatic Brain Injury (TBI)

TBI was strongly associated with chronic sleep fragmentation. Patients experienced:

- Increased stage N1 sleep (+10%).
- Reduced SWS duration (–15%).
- Shortened REM latency by ~20 minutes.

Polysomnographic studies suggested diffuse axonal injury disrupts thalamic regulation, producing chronic sleep inefficiency. Notably, even years after TBI, patients exhibited lower sleep efficiency compared to matched controls [37].

Cross-Disorder Comparative Patterns

Comparative synthesis revealed shared and unique features:

- **Shared features**: decreased REM percentage, lower sleep efficiency, prolonged sleep latency.
- **AD and TBI**: prominent loss of SWS.
- **PD:** REM behavior disorder and increased N2.
- **MS:** restless legs syndrome and periodic limb movements.
- **Stroke:** outcomes depended on lesion site.

This suggests common underlying mechanisms such as thalamocortical dysregulation, but also disorder-specific pathways [38].

Quantitative Meta-Analysis

Pooling 22 eligible studies:

- **Sleep efficiency** was reduced by 12% overall.
- **REM sleep percentage** reduced by 6.5%.
- **SWS duration** reduced by 20% in AD and TBI but minimally affected in MS.
- **Arousal index** increased by 28 events/hour in epilepsy and PD.

Heterogeneity was moderate (I^2 = 61%), indicating variable methodologies and patient populations [39].

Moderator and Subgroup Analyses

- **Disease severity:** advanced AD and PD showed progressively worse sleep fragmentation.
- **Age:** older cohorts demonstrated more profound SWS loss.
- **Comorbid depression and anxiety** worsened REM-related disruptions.
- **Medication effects**: dopaminergic therapy restored REM in PD, while antiepileptics worsened N2 fragmentation.

Overall, moderators explained 30% of the heterogeneity across studies [40].

Table 1. Key Sleep Architecture Changes in Neurological Disorders

Disorder	Main Alterations	Clinical Relevance	References
Alzheimer's Disease	↓ SWS, ↓ REM, ↑ latency, fragmented sleep	Memory impairment, faster cognitive decline	(31,32)
Parkinson's Disease	↓ REM, ↑ N2, frequent RBD, fragmented sleep	RBD predicts motor progression	(33)
Epilepsy	↓ REM, ↑ arousals, disturbed NREM	Poor seizure control, nocturnal seizures	(34)
Multiple Sclerosis	↑ latency, ↓ REM, ↓ efficiency, RLS/PLM	Fatigue, worsened disability scores	(35)
Stroke	REM loss (cortical), SWS loss (subcortical)	Poor motor/cognitive recovery	(36)
Traumatic Brain Injury	↑ N1, ↓ SWS, ↓ REM, chronic fragmentation	Long-term inefficiency, poor recovery	(37)

DISCUSSION

Overview of Sleep Disturbances Across Neurological Disorders

Sleep architecture is profoundly altered in patients with neurological disorders, representing not only a secondary manifestation of disease but also a key contributor to disease progression and symptom burden. Across multiple neurological conditions—including Alzheimer's disease (AD), Parkinson's disease (PD), epilepsy, multiple sclerosis (MS), stroke, and traumatic brain injury (TBI)—the most consistent alterations include reduced sleep efficiency, fragmentation of non-rapid eye movement (NREM) sleep, decreased rapid eye movement (REM) sleep, and loss of slow-wave sleep (SWS). These changes collectively undermine restorative functions of sleep, including memory consolidation, glymphatic clearance, and neural plasticity, leading to worsening clinical outcomes over time [41]. Importantly, disrupted sleep is not merely an epiphenomenon but represents a bidirectional process: neurological dysfunction impairs sleep regulation, while disordered sleep accelerates neurodegenerative changes and worsens disease progression.

Alzheimer's Disease (AD) and Sleep

Sleep disturbances represent one of the first detectable signs of pathophysiology in AD and may even precede, by years in some instances, of cognitive symptoms. Similarly, polysomnography studies have repeatedly shown decreased SWS and shortened REM sleep. Crucial for glymphatic clearance of neurotoxic proteins such as β-amyloid and tau, SWS is severely diminished in AD patients, further supporting the network effects of protein aggregation and neurodegeneration [42]. Disordered REM sleep has also been linked to memory deficits, executive dysfunction, and deranged emotional regulation. Recent work indicates that orexin excess underlies sleep fragmentation in AD, and agents that antagonise the orexin system have been advanced to clinical trials. In the interventional realm, melatonin, light, and non-pharmacological treatments, such as cognitive behavioral therapy for insomnia (Cognitive-Behavioral Therapy for Insomnia [CBT-I]), have shown modest improvement in sleep continuity and cognition, but greater longitudinal studies are warranted. The evidence supports the suggestion that treating sleep may not only ameliorate symptoms, but may also, per se, modify disease in AD.

Parkinson's Disease (PD) and Sleep

Sleep disturbances in PD are endemic, observed in over 80% of PD patients at some point in the disease. Of note, REM sleep behavior disorder (RBD), characterized by dream enactment as a consequence of the loss of REM atonia, is of particular relevance as it often precedes motor signs by many years and represents a prodromal sign of synucleinopathies [43]. Apart from RBD, PD patients suffer from impaired sleep continuity, sleep time, have excessive daytime sleepiness, and circadian changes.

Dopaminergic therapies, while alleviating motor symptoms, often exacerbate sleep disturbances by reducing SWS and altering REM density. In addition, circadian dysfunction in PD is linked to impaired melatonin secretion and altered core body temperature rhythms, further complicating sleep-wake regulation. These disturbances correlate with cognitive decline, reduced quality of life, and caregiver burden. Future research must refine biomarkers linking RBD to progression toward PD dementia and evaluate whether modifying sleep patterns delays disease conversion.

Epilepsy and Sleep Architecture

Epilepsy presents a complex relationship with sleep, as both seizures and anti-seizure medications modulate sleep architecture. NREM sleep facilitates the synchronization of cortical networks, creating conditions favourable for epileptic discharges, while REM sleep is relatively protective against seizure occurrence [44]. Nocturnal seizures fragment sleep cycles and disrupt memory consolidation, while sleep deprivation is a well-known precipitant of seizure activity. Polysomnographic investigations demonstrate reduced REM sleep, frequent awakenings, and increased NREM stage transitions in patients with poorly controlled epilepsy. Furthermore, anti-seizure medications such as benzodiazepines and barbiturates exacerbate sleep fragmentation, whereas others, including lamotrigine and levetiracetam, have variable effects. The bidirectional nature of this relationship emphasizes the necessity of optimizing sleep hygiene in epilepsy management. Integrating sleep-targeted therapies, such as melatonin supplementation or chronotherapy, may enhance seizure control and improve neurocognitive outcomes.

Multiple Sclerosis (MS) and Sleep

Sleep dysfunction in MS has emerged as an underrecognized contributor to fatigue, one of the most disabling symptoms of the disease. Insomnia, restless legs syndrome, and periodic limb movement disorder are frequently reported, reflecting damage to hypothalamic and spinal circuits involved in sleep regulation [45]. Sleep-disordered breathing, including obstructive sleep apnea (OSA), is also more prevalent in MS patients, likely exacerbated by demyelinating lesions affecting brainstem respiratory centers. Polysomnography demonstrates reduced sleep efficiency, longer sleep latency, and increased arousals. Importantly, poor sleep correlates with heightened inflammatory activity and worse Expanded Disability Status Scale (EDSS) scores, suggesting that sleep dysfunction aggravates disease progression. Despite the weight of this evidence, sleep is infrequently considered in the context of routine MS care, with patients often overlooked in the assessment and management of sleep complaints. Randomized clinical trials are needed to examine whether sleep-based treatments can decrease fatigue and retard disability progression in MS.

Stroke and Sleep

Post-stroke sleep disturbances affect more than 60% of survivors, but it is a neglected area in the recovery process. Sleep-disordered breathing, i.e., OSA, is associated with increased risk of recurrent stroke and needs early detection and treatment [46]. Polysomnographic studies have demonstrated reduced REM sleep, disrupted sleep spindle density, and more frequent awakenings in stroke patients. Across wake and sleep, sleep spindles involved in synaptic plasticity seem fundamentally important for motor and cognitive recovery, and their loss may work against rehabilitation. In addition, post-stroke disruption of the circadian rhythm is associated with mood fluctuations, fatigue, and low compliance with treatment. Treatments such as CPAP therapy, light therapy, and pharmacotherapy targeted for circadian consolidation of sleep have shown marginal benefit. However, to confirm the beneficial effect of improving sleep on post-stroke prognosis, larger prospective randomized controlled trials are still needed.

Traumatic Brain Injury (TBI) and Sleep

Sleep disturbances following TBI are highly prevalent and often persist for years, with implications for long-term recovery and quality of life. Patients commonly report excessive daytime sleepiness, insomnia, and parasomnias. Objective studies reveal reduced REM sleep, shortened total sleep time, and circadian rhythm disruption [47]. These alterations are attributed to injury of hypothalamic and brainstem regions regulating arousal, in addition to secondary neuroinflammatory processes. Sleep dysfunction is strongly correlated with cognitive deficits, mood disorders, and slower rehabilitation. Notably, interventions such as bright light therapy, sleep hygiene education, and pharmacological strategies targeting wakefulness (e.g., modafinil) have been tested with varying success. Sleep abnormalities following TBI also provide an

opportunity for monitoring recovery trajectories, as restoration of normal sleep patterns often parallels cognitive improvement.

Shared Mechanistic Pathways

Despite disease-specific differences, several common mechanistic pathways underlie sleep alterations in neurological disorders. One key mechanism is dysfunction of the glymphatic system, which is highly active during SWS and essential for clearing neurotoxic proteins such as β-amyloid and α-synuclein [48]. Impaired glymphatic clearance has been implicated across AD, PD, and TBI. Neuroinflammation, a shared feature of many neurological conditions, disrupts sleep-wake regulation by impairing hypothalamic and brainstem networks. Additionally, circadian rhythm abnormalities—driven by altered expression of clock genes and impaired melatonin signaling—are observed across PD, MS, and epilepsy. These shared mechanisms suggest that therapeutic strategies targeting sleep may have broad applications across neurological disease categories, reinforcing the importance of sleep as a modifiable risk factor.

Translational and Clinical Implications

The recognition of sleep as both a symptom and driver of neurological disease progression has major clinical implications. First, sleep assessment should be integrated into the standard of care for neurological patients, using polysomnography, actigraphy, and validated questionnaires. Second, sleep-targeted interventions hold promise as adjunctive therapies. For example, improving SWS through acoustic stimulation, pharmacological orexin antagonism, or non-invasive brain stimulation may enhance glymphatic clearance and cognitive outcomes in AD [49]. Similarly, early treatment of RBD in PD could reduce injury risk and improve quality of life, while CPAP therapy in post-stroke patients could lower recurrence risk. Advances in wearable sleep monitoring and machine learning offer novel tools for long-term surveillance, enabling personalized interventions. Importantly, clinical trials should adopt standardized sleep outcomes to facilitate cross-disease comparisons and meta-analyses.

Limitations of Current Evidence

Limitations Despite the growing literature, various limitations restrict us from fully comprehending the issue. The majority of these are cross-sectional, however, and cannot determine that disrupted sleep is an actual cause of disease progression [50]. Sample sizes are often small, patient populations are heterogeneous, and polymorphisms can be exploratory, with methodologic variation of PSG. Furthermore, neurologic medications are known to confound sleep outcomes and obscure interpretation. The majority of studies lack longitudinal follow-up, and the link between neuroimaging metrics and sleep parameters to understand the neurophysiological substrates of observed aberrations is scant. These challenges will have to be overcome through multicenter collaborations, methodological harmonization, and the implementation of sleep outcomes in large clinical trials.

Future Directions

Longitudinal cohort studies in the future should be encouraged to tease apart whether sleep disturbances are early biomarkers or later sequela of neurological disease. An integration of neuroimaging, fluid biomarkers, and polysomnography might generate multidimensional perspectives on pathophysiology. Precision medicine strategies that include genetic polymorphisms in circadian genes and pharmacogenomics might enable individualized sleep therapies. Studies are desperately needed that evaluate whether the improvement of sleep will slow neurodegeneration, in particular in AD and PD. In addition, digital health solutions, such as home-based EEG and artificial intelligence–based algorithms, provide scalable options for continuous monitoring that might revolutionize clinical care and research in this arena.

In summary, the comparative analysis presented in Table 1 & 2 highlights both the shared and disorder-specific alterations in sleep architecture across major neurological conditions. While reductions in REM and SWS appear as common denominators in Alzheimer's disease, Parkinson's disease, epilepsy, multiple sclerosis, stroke, and traumatic brain injury, each disorder demonstrates unique pathophysiological mechanisms driving these disturbances. For instance, α-synuclein deposition in Parkinson's disease leads to REM sleep behavior disorder, whereas β-amyloid accumulation in Alzheimer's disease accelerates SWS decline. These mechanistic differences underscore the potential of sleep-based biomarkers to aid in early diagnosis and therapeutic monitoring. Moreover, the consistent link between disrupted sleep and poor

cognitive as well as functional outcomes emphasizes the need for sleep-targeted interventions in neurological rehabilitation strategies.

Table 2: Sleep Architecture Alterations Across Major Neurological Disorders

Neurological Disorder	Key Changes in Sleep Architecture	Clinical Implications
Alzheimer's Disease (AD)	↓ Slow-wave sleep (SWS), ↓ REM density, ↑ sleep fragmentation	Cognitive decline, memory impairment, daytime sleepiness
Parkinson's Disease (PD)	↓ REM sleep, ↑ REM Behavior Disorder (RBD), ↑ sleep fragmentation	Motor symptom worsening, hallucinations, excessive daytime sleepiness
Epilepsy	↓ REM, disrupted NREM cycles, nocturnal seizures disturb continuity	Poor seizure control, cognitive dysfunction, higher daytime fatigue
Stroke	↓ REM, ↓ SWS, ↑ sleep-disordered breathing	Impaired recovery, poor rehabilitation outcomes
Multiple Sclerosis (MS)	Fragmented sleep, ↑ periodic limb movements, ↑ insomnia	Fatigue, depression, cognitive decline
Traumatic Brain Injury (TBI)	↑ sleep fragmentation, ↑ hypersomnia, ↓ REM	Impaired cognitive recovery, mood instability
Huntington's Disease (HD)	Marked ↓ REM, disrupted circadian rhythm	Progressive cognitive and psychiatric symptoms

CONCLUSION

In summary, this systematic review underscores that alterations in sleep architecture are not mere by-products of neurological disease but represent integral, dynamic components of disease progression and prognosis. Across disorders such as Alzheimer's disease, Parkinson's disease, multiple sclerosis, epilepsy, and stroke, consistent patterns emerge—ranging from reductions in slow-wave and REM sleep to circadian rhythm misalignments—that are closely linked with cognitive decline, motor impairment, and diminished quality of life. These findings highlight the bidirectional nature of the sleep–neurology relationship, wherein disrupted sleep accelerates pathology, and progressive disease further destabilizes sleep physiology. Importantly, sleep parameters such as REM sleep behavior disorder in Parkinson's or slow-wave fragmentation in dementia are increasingly recognized as early biomarkers, offering valuable diagnostic and prognostic potential. At the same time, the evidence base indicates that targeted interventions—behavioral, pharmacological, and chronotherapeutic—can meaningfully restore sleep quality and, in turn, positively influence clinical outcomes. Nevertheless, significant gaps remain, particularly in disentangling causal mechanisms, validating sleep measures as standardized biomarkers, and integrating sleep-focused interventions into mainstream neurological care. Future research must therefore prioritize longitudinal, multicentre trials with robust neurophysiological and imaging correlates to establish whether modifying sleep can alter disease trajectories. Ultimately, positioning sleep at the center of neurological health could transform both preventive strategies and therapeutic paradigms, underscoring its role as a modifiable and clinically actionable determinant of brain resilience and recovery.

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