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Review Article

Crosstalk between movement disorders, sleep disturbances and striatum: A comprehensive review

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Abstract

Movement disorders such as Parkinson's disease frequently present with comorbid sleep disturbances, which exacerbate motor symptoms and reduce patients' quality of life. The striatum, a critical basal ganglia structure, is implicated in both motor control and sleep regulation and represents the key anatomical locus affected in these disorders. While nutritional and exercise interventions have shown promise independently, a significant gap remains in understanding the synergistic molecular crosstalk between these lifestyle modifications and how they collectively target the striatal mechanisms disrupted by sleep deprivation. This review synthesizes evidence to elucidate the integrated, neurobiological effects of combined nutritional and exercise interventions on sleep deprivation-associated movement disorders, emphasizing the striatum's pivotal role. We establish that exercise, through the induction of neurotrophic factors (like BDNF/GDNF) and enhanced dopaminergic signaling (DAT), provides a critical foundation for synaptic repair. This foundation is synergistically amplified by targeted nutritional strategies, such as polyphenols and omega-3s, which augment antioxidant capacity, dampen neuroinflammation (NRF2/NFκB axis), and modulate key receptors (like A2AR) within the striatum. These combined, non-pharmacological approaches more effectively restore striatal homeostasis and redox balance than either intervention alone, resulting in superior improvement in both motor function and sleep quality. Further longitudinal and mechanistic studies (e.g., RCTs with multimodal endpoints) are warranted to refine optimal intervention protocols and personalize therapeutic strategies. Incorporating these findings into clinical guidelines could promote holistic, synergistic management strategies that improve patient outcomes and reduce healthcare costs.

Key Words: Movement disorders, Striatum, Sleep disturbances, Nutritional interventions, Exercise interventions

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Introduction

Movement disorders such as Parkinson's disease, Huntington's disease, and dystonia frequently co-occur with significant sleep disturbances, including insomnia, excessive daytime sleepiness, and rapid eye movement (REM) sleep behavior disorder (Grace A. Bailey et al., 2021a; Bohnen & Hu, 2019). The bi-directional relationship between sleep deprivation and movement disorders is well-documented: not only do motor symptoms worsen as sleep quality declines, but sleep disturbances themselves may precede or exacerbate the onset and severity of movement dysfunctions (Minakawa, 2022). For instance, longitudinal studies in Parkinson's disease have reported that sleep impairments, especially REM sleep behavior disorder and fragmented sleep, are prodromal features and can forecast the later development and progression of motor symptoms (Xu et al., 2022). Medications used to manage movement disorders can further disrupt sleep, compounding the burden on patients and negatively impacting their quality of life (Driver-Dunckley & Adler, 2012). Central to the regulation of movement is the striatum, a subcortical hub within the basal ganglia that governs locomotor control and the fine-tuning of movement parameters (Fieblinger, 2021). Recent research has challenged the traditional view that the striatum is solely responsible for action selection, instead underscoring its cooperative role with the motor cortex in specifying the details of movement execution (Park et al., 2025; Tewari et al., 2016).

Dysfunction within striatal circuitry, particularly involving striatal spiny projection neurons, is implicated in a broad spectrum of movement disorders (Abela & Kurian, 2018; Gittis & Kreitzer, 2012), with striatal atrophy and neurotransmitter imbalances recognized as key pathological features (Lima, 2013; Tang et al., 2023; Thangaleela et al., 2023). In parallel, emerging studies highlight the potential of non-pharmacological intervention, particularly dietary modifications and exercise regimens, to improve both motor and non-motor outcomes among affected individuals (Janssen Daalen et al., 2022; Seixas et al., 2025a). Emerging evidence also supports that combining these lifestyle modifications may offer superior neur-

-oprotection compared to either intervention alone (JAMA Neurology, 2018; Li et al., 2019). Exercise interventions, such as high-intensity aerobic activity, have demonstrated beneficial effects on motor symptoms and may even stabilize disease progression, especially in early stages of Parkinson's disease (Langeskov-Christensen, Franzén, Grøndahl Hvid, et al., 2024). Nutritional interventions also show promise, but the current body of research remains fragmented and less robust, with a clear gap in understanding how these interventions modulate underlying striatal function and their interplay with sleep-related disturbances (Dunk et al., 2022; Yalçin et al., 2025). This review study aims to elucidate the synergistic and interactive effects of nutritional and exercise interventions on sleep deprivation-associated movement disorders, with a focus on the striatum's role as a key mediator. By synthesizing current evidence from preclinical and clinical studies, we seek to unravel how combined interventions or lifestyle modifications may restore striatal neuroplasticity and dopaminergic balance, potentially slowing disease progression and improving motor outcomes (Koehler et al., 2021; Malkki, 2016). Combined interventions or lifestyle modifications may restore striatal neuroplasticity and dopaminergic balance, potentially slowing disease progression and improving motor outcomes. Given the striatum's vulnerability to oxidative stress (Petzinger et al., 2013), and its involvement in the pathophysiology of disorders such as Parkinson's disease and REM sleep behavior disorder (Alushaj et al., 2023), understanding this crosstalk may inform personalized, non-pharmacological therapeutic strategies in managing sleep deprivation-induced motor impairments.

Sleep disturbances in movement disorders

Abnormal sleep and circadian rhythm disorders are prevalent yet often overlooked in patients with movement disorders (Grace A Bailey et al., 2021). This underdiagnosis represents a significant gap in clinical care, as these sleep disturbances can exacerbate the symptoms of movement disorders. The regulation of sleep and circadian rhythms involves specific brain regions, including the forebrain, thalamus, and midbrain dopaminergic neurons, which are also implicated in the pathogenesis of various movement disorders (Tebbe et al., 2024). Previous studies highlight the high prevalence of sleep disorders, particularly in conditions like PD, where estimates suggest that up to 98% of patients experience such disturbances. In contrast, disorders like adult-onset primary dystonia show a different pattern, with sleep issues correlating more closely with psychiatric symptom severity (Eichenseer et al., 2014; Postuma & Berg, 2016).

The physiological aspects of sleep are essential for understanding the manifestation of sleep disorders in patients with movement disorders like Parkinson's disease. Sleep cycles change between non-rapid eye movement (NREM) sleep, which is further divided into stages of light and deep sleep, and rapid eye movement (REM) sleep, where dreaming occurs. Disruptions in these cycles are prevalent among affected individuals, leading to fragmented sleep and reduced overall sleep quality (George & Davis, 2013). Key neurotransmitters, including glutamate and gamma-aminobutyric acid (GABA), are crucial in regulating the sleep-wake cycle. Glutamate acts as an excitatory neurotransmitter that promotes wakefulness and alertness, while GABA serves as the primary inhibitory neurotransmitter, facilitating the onset of sleep by calming neuronal activity. The balance between these neurotransmitters is vital; an imbalance can result in sleep disturbances. For instance, excessive glutamatergic activity may lead to difficulties in initiating or maintaining sleep, while insufficient GABAergic activity can prevent the transition into deeper sleep stages. Additionally, other neurotransmitters, such as serotonin and norepinephrine, play roles in modulating sleep architecture and transitions between NREM and REM sleep (Kaczmarski et al., 2023; Luo et al., 2025).

Several brain regions, including the hypothalamus, thalamus, and brainstem, coordinate these neurotransmitter systems to regulate sleep patterns (Eban-Rothschild et al., 2017; Falup-Pecurariu et al., 2021). For example, the suprachiasmatic nucleus (SCN) in the hypothalamus serves as the body's primary circadian clock, influencing sleep timing and quality based on light exposure (Moore, 2007). Disruptions in these neurotransmitter systems and brain regions can lead to a range of sleep disorders, such as insomnia, REM Sleep Behavior Disorder, and excessive daytime sleepiness, which are commonly observed in patients with movement disorders. Understanding these physiological mechanisms is crucial for developing targeted interventions to improve sleep quality and overall well-being in these patients (Arnulf et al., 2008; Dodet et al., 2024).

In movement disorders, common sleep problems are including REM Sleep Behavior Disorder (RBD), Periodic Limb Movements during Sleep (PLMS), and sleep-related breathing disorders. The severity of sleep disturbances tends to increase with the progression of the disease, particularly in later stages where insomnia and somnolence become more pronounced (Tang et al., 2020). RBD is notably prevalent among PD patients, with studies indicating that approximately 73.5% of those with idiopathic RBD develop neurodegenerative disorders within 12 years (Fereshtehnejad et al., 2019). Patients with both PD and RBD often exhibit more severe motor symptoms, psychiatric issues, and cognitive impairments compared to those without RBD (Parker & Garrity, 2013; Romenets et al., 2012). Imaging studies have shown significant structural changes in brain areas associated with sleep regulation, such as the pontomesencephalic tegmentum and locus coeruleus, suggesting that RBD may serve as a marker for PD disease progression (Boucetta et al., 2016; García-Lorenzo et al., 2013).

Therapeutic management of sleep disorders in PD involves a range of treatments, including dopaminergic therapies, which can both improve and exacerbate sleep issues. While medications like levodopa can enhance sleep duration, dopamine agonists may lead to increased daytime sleepiness and sudden-onset sleep episodes (Comella et al., 2005). Other treatments, such as melatonin and certain antidepressants, have shown promise in alleviating sleep disturbances, though their effectiveness varies among individuals (Videnovic et al., 2014). Overall, the management of sleep disorders in PD requires a comprehensive approach that considers motor symptoms, medication effects, and comorbidities, highlighting the need for further research to optimize treatment strategies (Breen et al., 2014).

Taken together, there is an urgent need for a comprehensive approach to assessing and treating sleep disorders in patients with movement disorders. Understanding the shared pathophysiological mechanisms underlying both motor and sleep-related symptoms is crucial for developing targeted therapeutic strategies. The current study advocates for further research to elucidate the etiology of sleep disturbances across various movement disorders, aiming to improve patient outcomes by addressing sleep issues alongside motor symptoms. Future studies should leverage advancements in wearable technology to enhance diagnostic accuracy and monitor treatment efficacy in real-world settings (Sun et al., 2024). These fundamental disruptions in neurotransmitter balance, particularly involving dopaminergic and GABAergic systems, as well as circadian rhythm regulation, underscore key non-pharmacological targets. Lifestyle modifications, notably exercise and targeted nutrition, hold the potential to modulate these systems by influencing neurotrophic support and cellular homeostasis, thereby providing complementary avenues for managing sleep disturbances in movement disorders (JAMA Neurology, 2018; Kim et al., 2020; Li et al., 2019; Sun et al., 2024).

Reciprocal molecular interactions between movement disorders and sleep disturbances: Parkinson's disease as a paradigm

As discussed, while the hallmark features of PD include motor symptoms such as tremors and rigidity, it is increasingly recognized as a multisystem disorder characterized by various non-motor symptoms. Among these, sleep disturbances are particularly prevalent and debilitating (Munhoz et al., 2015). Studies indicate that nearly 50% of newly diagnosed PD patients report subjective sleep complaints, which can manifest as insomnia, parasomnia, disruptions in wakefulness, and alterations in circadian rhythms (Breen et al., 2014). A multicenter survey revealed that 64.1% of PD patients suffer from sleep problems, making these disturbances the second most frequent non-motor symptom after depression. The high prevalence of sle-

-ep issues underscore the need for a deeper understanding of their implications in PD (Barone et al., 2009).

Significantly, evidence suggests that sleep disturbances may occur years before the onset of classic motor symptoms associated with PD. This finding opens up new avenues for research into the early identification of individuals at risk for PD (Videnovic & Abbott, 2016). Longitudinal studies indicate that individuals with RBD have a progressively increasing risk of developing neurodegenerative disorders, including PD and Lewy body dementia. The cumulative risk of developing PD within 14 years of an RBD diagnosis can be as high as 96.6%. This suggests that monitoring and addressing sleep disturbances in at-risk populations could serve as an early intervention strategy to modify disease progression (Galbiati et al., 2019).

The relationship between sleep disturbances and PD is likely bidirectional. Chronic sleep disruptions may exacerbate the underlying pathophysiological mechanisms of PD. For instance, sleep fragmentation can impact the efficiency of the glymphatic system, which is responsible for clearing metabolic waste from the brain (Xie et al., 2013). During sleep, the interstitial space in the brain expands, allowing for more effective clearance of neurotoxic proteins like alpha-synuclein, a key contributor to PD pathology (Anandasabapathy, 2012). Conversely, when sleep is disrupted, the lymphatic system's efficiency diminishes, leading to an accumulation of toxic proteins and increased oxidative stress in the central nervous system (CNS). This oxidative stress can further damage dopaminergic neurons, creating a vicious cycle that accelerates the progression of PD (Yang et al., 2020).

In regard to molecular trajectories, the endoplasmic reticulum (ER) stress response highlights the critical role of protein misfolding and aggregation in neurodegenerative diseases such as PD. The maintenance of intracellular protein homeostasis, known as proteostasis, is largely dependent on the proper functioning of the ER (Kaushik & Cuervo, 2015). When proteins misfold and aggregate, they trigger ER stress, leading to the activation of the unfolded protein response (UPR). This adaptive mechanism, initiated by three transmembrane proteins, aims to alleviate the burden of misfolded proteins by reducing protein translation and enhancing the maturation of proteins through the upregulation of specific genes and ER chaperones (Schröder & Kaufman, 2005; Szegezdi et al., 2006).

Previous studies also explored the impact of sleep disturbances on ER stress. Acute sleep deprivation activates the ER stress response in young mice, while aged mice show suppressed UPR activation. This difference suggests that aging may attenuate the cellular response to stress, leading to increased levels of pro-apoptotic proteins in the cerebral cortex of older mice. Given that patients with PD often experience fragmented sleep, it is hypothesized that sleep disturbances exacerbate the burden on

the proteostasis system, potentially accelerating protein aggregation and contributing to the progression of PD (Naidoo et al., 2008; Naidoo et al., 2005).

Other investigations also revealed that exposure to intermittent cyclical hypoxia and reoxygenation, akin to conditions experienced in sleep apnea, induces ER stress in specific brain regions and is linked to impaired motor and cognitive functions. Human studies support these hypotheses, showing that greater sleep fragmentation is associated with an increased risk of Lewy pathology and dopaminergic neuron loss in elderly individuals. However, longitudinal studies are needed to clarify the causal relationships between sleep disorders and PD pathology (Petitjean, 2014).

Additionally, the study addresses the role of oxidative stress in PD. The accumulation of reactive oxygen species (ROS) due to cellular redox imbalance is implicated in mitochondrial dysfunction and neurodegeneration (Phillipson, 2017). Preclinical evidence shows elevated oxidative stress levels in PD patients before significant neuronal loss occurs. Sleep is believed to promote the removal of excessive reactive species, and sleep deprivation has been associated with increased oxidative stress in various animal models. This suggests a potential mechanism linking sleep loss to the pathogenesis of PD through heightened oxidative damage (Al Rubaie, 1994; Li et al., 2019; Singh et al., 2008).

In summary, the study emphasizes the interconnectedness of ER stress, sleep disturbances, glymphatic system dysfunction, and oxidative stress in the progression of neurodegenerative diseases like PD. It highlights the need for further research to elucidate these relationships and their implications for potential therapeutic strategies. Crucially, these pathways—including ER stress, oxidative stress, and glymphatic dysfunction—represent highly promising targets for non-pharmacological interventions (Cosentino & Torres, 2012; "JAMA Neurology," 2021; Scott et al., 2023). For example, targeted nutritional strategies can introduce antioxidants to counter oxidative damage, while exercise is known to enhance cellular resilience by promoting adaptive UPR and improving mitochondrial function, suggesting a convergence of mechanisms that can be therapeutically leveraged.

Striatum's function in the sleep disturbances and movement disorders

The striatum, a critical basal ganglia structure, plays a central role in the pathophysiology of sleep disturbances such as RBD and movement disorders like PD. Multiple studies converge on its importance, highlighting its dysfunction involving dopamine and adenosine receptor systems (Marecek et al., 2024).

In PD patients with clinically probable RBD (cpRBD), dopaminergic depletion in the striatal regions, particularly the putamen and caudate nucleus, is more pronounced than in those without RBD. Chung, Lee (Hyeon et al., 2017) observed that PD patients with RBD exhibited lower dopamine transporter (DAT) activity in the putamen, specifically on the less-affected side, along with more severe and asymmetrical motor symptoms, which suggests that RBD might represent a distinct PD subtype with malignant motor features. Supporting this, Wang, Chang (Mameli et al., 2025) showed that de novo PD patients with probable RBD had significantly reduced DAT binding in the caudate and putamen, correlating with increased non-motor symptoms such as depression and constipation, indicating greater striatal dopaminergic dysfunction and potentially faster disease progression.

Further elaborating on the clinical phenotypes, Cicero, Terravecchia (Cicero et al., 2025) confirmed different patterns of striatal dopaminergic dysfunction depending on the timing of RBD onset relative to motor symptoms. Specifically, patients with RBD onset before motor signs (PD-RBDpre) had more symmetrical motor impairment, lower caudate DAT binding, and more cognitive deficits compared to those with RBD onset following motor symptoms or no RBD, supporting the "body-first" versus "brain-first" Parkinson's disease phenotype model. Kim,(Kim et al., 2020) also reported that likely-RBD in early PD predicted a faster decline of striatal dopamine, especially in the more affected striatum, reinforcing that RBD associates with accelerated dopaminergic denervation and worse prognosis.

Other studies also demonstrated that in idiopathic RBD (iRBD), reduced DAT uptake in the striatum and putamen precedes overt PD or other synucleinopathies, emphasizing its role as a subclinical biomarker for neurodegeneration involving the nigrostriatal pathway (Arnaldi et al., 2015; Iranzo, 2013; Iranzo et al., 2011). Li, Kang (Li et al., 2017) supported this by correlating reduced DAT uptake with shorter progression-free survival in iRBD patients developing synucleinopathies. Additionally, Sun, Lai (Martinez-Martin, 2020) found increased iron deposition in the striatum (especially substantia nigra and putamen) in iRBD and PD patients, which correlates with disease progression and may reflect underlying neurodegeneration contributing to both motor and sleep disturbances. Electrophysiological and neurochemical studies demonstrate that striatal dopamine levels fluctuate with vigilance states: dopamine is highest during wakefulness, decreases during non-REM sleep, and is lowest in REM sleep. External stimuli can induce striatal dopamine release, and wake-promoting agents like modafinil increase striatal dopamine levels, whereas caffeine does not, highlighting the tight link between striatal dopamine and sleep-wake regulation (Al Mughairbi, 2019).

Adenosine, a neuromodulator involved in promoting sleep, particularly

particularly slow-wave sleep, interacts closely with striatal dopamine pathways. The adenosine A2A receptor (A2AR) is highly expressed in the striatum's GABAergic medium spiny neurons and negatively modulates dopamine D2 receptor signaling, which is critical for motor control and PD pathophysiology (Blutstein & Haydon, 2012; Cunha, 2008; Van Dort et al., 2009). Studies show that lower serum adenosine and GABA levels are associated with worse sleep quality in PD patients, suggesting deficient adenosine signaling may contribute to sleep disturbances (Ogrodnik et al., 2023). Sun, Lai (Sun et al., 2020) findings of disrupted striatal dopamine signaling in RBD and PD could be partly explained by altered adenosine receptor activity. Mishina, Ishiwata (Mishina et al., 2011) demonstrated that in PD, A2ARs are asymmetrically decreased in the putamen on the more affected side at early stages but are upregulated after antiparkinsonian therapy and in patients with dyskinesia, implicating A2ARs in compensatory and pathologic changes of dopaminergic signaling in the striatum. Moreover, Villar-Menéndez, Porta (Villar-Menéndez et al., 2014) found increased A2AR protein levels in the putamen in early and incidental PD cases, possibly regulated post-transcriptionally via microRNAs, highlighting the complex regulation of A2AR in PD progression. Moreover, Yuan, Wang (Yuan et al., 2017) identified that activation of striatal A2AR neurons promotes non-REM sleep through their inhibitory projections to parvalbumin neurons in the external globus pallidus, elucidating a neural circuit by which the striatum modulates sleep-wake states. This shows that altered A2AR signaling in the striatum can impact both sleep regulation and motor control, possibly contributing to PD sleep disturbances. Lastly, Salamone, Ishiwari (Salamone, 2010) demonstrated that A2AR antagonists can alleviate motor dysfunction in PD animal models by modulating dopamine-adenosine interactions within specific striatal subregions, affecting locomotion and tremor. These findings underline the therapeutic potential of targeting striatal A2ARs to manage both motor and sleep symptoms in PD.

Collectively, these studies represented the striatum as a pivotal locus where dopaminergic and adenosinergic dysfunction converge to drive both sleep disturbances like RBD and motor impairments in PD and related synucleinopathies. Early striatal dopamine depletion, detectable by reduced DAT binding mainly in the putamen and caudate nucleus, correlates with RBD presence, cognitive changes, and accelerated disease progression. Concurrently, altered levels and receptor expression of adenosine, particularly the A2AR, influence the striatum's inhibitory output circuits affecting sleep homeostasis and motor control. The interaction between dopamine and adenosine systems in the striatum mediates complex effects on locomotion, sleep-wake regulation, and disease progression, making these receptors promising biomarkers and therapeutic targets in PD and associated sleep disorders.

This multifaceted striatal dysfunction, which characterized by dopaminergic denervation, altered adenosine receptor expression, neurochemical imbalance, and neurodegenerative changes such as iron accumulation, underpins the clinical manifestations and progression of sleep disturbances and movement disorders in PD and idiopathic RBD. Early identification and modulation of these striatal neurotransmitter systems could guide personalized treatments to improve both motor and non-motor symptoms. The crucial involvement of striatal dopaminergic denervation and A2AR dysregulation in both motor and sleep pathology establishes these pathways as highly specific targets for non-pharmacological interventions (Bloem et al., 2020; Chen et al., 2023; Langeskov-Christensen, Franzén, Grøndahl Hvid, et al., 2024; Moretti et al., 2015). Exercise is uniquely positioned to enhance dopamine release and neurotrophic factor (BDNF/GDNF) signaling, directly counteracting denervation, while nutritional components can act as natural A2AR antagonists or provide metabolic support to rebalance neurochemical circuits, thus bridging the gap between pathophysiology and synergistic therapeutic strategies.

Integrated Pharmacological, Nutritional, and Exercise Strategies for Striatal Restoration in Movement Disorder–Related Sleep Disturbances

Sleep disturbances in movement disorders, particularly Parkinson's disease (PD), derive primarily from perturbations in striatal dopaminergic signaling, oxidative stress, and neuroinflammation (Zuzuárregui & During, 2020). Mounting evidence indicates that pharmacologic agents, dietary interventions, and structured exercise collaborate on these molecular axes, suggesting a shared mechanistic foundation. Dopaminergic medications recalibrate neurotransmission, dietary antioxidants dampen microglial activation and lipid peroxidation, and exercise enhances neurotrophic and antioxidative defense via brain derived neurotrophic factor (BDNF) and nuclear factor erythroid 2–related factor 2 (NRF2) induction (Davinelli et al., 2024; Duan et al., 2025; Seixas et al., 2025b). This cross modulation among neurotransmitter, inflammatory, and metabolic networks underpins a unifying therapeutic strategy—one that restores redox homeostasis and promotes neural plasticity, both of which are essential for sleep regulation via the striatal–hypothalamic circuitry.

Pharmacological and neuromodulatory anchors

Dopaminergic pharmacotherapy remains the cornerstone of clinical management, yet should be interpreted as one dimension within a multi layered intervention model. Agents such as Madopar (levodopa–benserazide) and pramipexole enhance dopaminergic tone and normalize circadian periodicity, contributing to shorter sleep latency and improved continuity (Grace A. Bailey et al., 2021b). Orexin receptor antagonists, incl-

-uding suvorexant and lemborexant, further refine sleep architecture by selectively inhibiting arousal networks interfaced with striatal output pathways (Raheel et al., 2024). In parallel, modulation of the adenosine A_2A receptor provides a pharmacologic conduit linking energy metabolism and dopaminergic signaling, facilitating non REM restoration and attenuating motor hyperarousal (Chen et al., 2023). Noninvasive neuromodulation via transcranial magnetic stimulation and transcranial direct current stimulation complements these agents by re synchronizing cortico striatal rhythms that are frequently misaligned in PD sleep dysfunction (Xia et al., 2025).

Synergistic diet–exercise interactions

The interaction between diet and exercise has emerged as a principal determinant of striatal resilience and sleep homeostasis. Exercise induced BDNF expression fosters synaptic repair and neuronal survival, while concurrent intake of polyphenol and omega 3 rich foods amplifies this pathway by augmenting antioxidant capacity and mitochondrial integrity (Bishop et al., 2025; Langeskov-Christensen, Franzén, Hvid, et al., 2024; Ruegsegger et al., 2023). Such bidirectional reinforcement extends to NRF2 activation: aerobic training elevates endogenous glutathione peroxidase and superoxide dismutase, effects potentiated by dietary cofactors such as flavonoids, curcumin, and coenzyme Q10 (Castro et al., 2022; Paterno et al., 2024). Studies employing combined treadmill and polyphenol-based regimens report superior outcomes in dopamine neuron preservation and sleep efficiency compared with isolated exercise or nutritional therapy (Armeli et al., 2021). Together, these data substantiate a genuine diet–exercise synergy, capable of simultaneously engaging dopaminergic repair, redox signaling, and circadian gene regulation (see Table 1).

Exercise modalities and striatal neurobiology

The mechanistic benefits of physical activity differ by modality, intensity, and duration, each profile distinct striatal neurobiological signatures. Aerobic exercise enhances dopamine turnover and transporter (DAT) regulation, promoting restoration of synaptic efficiency within dorsal striatal nuclei (Dunk et al., 2023). Beyond neurotransmission, sustained aerobic regimens upregulate mitochondrial electron transport proteins and elevate cortical BDNF, mechanistically accounting for improved vigilance and reduced sleep fragmentation. In contrast, resistance training exerts metabolic and anti-inflammatory benefits, improving insulin sensitivity and thereby indirectly supporting dopaminergic receptor density and neuronal energy supply (Rust et al., 2025). Mind–body regimens, notably Tai Chi and yoga, couple mild physical exertion with autonomic modulation; through reduced cortisol and sympathetic tone, they facilitate deeper slow-wave sleep and enhanced motor coordinat-

-ion (Ahmad et al., 2023). High intensity interval training (HIIT), although less studied clinically, appears to stimulate both BDNF and glial cell–derived neurotrophic factor (GDNF) expression, accelerating dopaminergic synaptic recovery and mitochondrial fission–fusion balance (Wang et al., 2023). Collectively, these data demonstrate that exercise modality determines the neurobiological pathway engaged dopaminergic, inflammatory, or oxidative each converging upon sleep–wake stability through striatal restoration, as summarized in Table 1.

Personalized nutrition and cautions

Nutritional adherence remains a critical modifiable determinant of therapeutic success. Mediterranean and MIND style diets, emphasizing unsaturated fats, plant-based antioxidants, and polyphenols, consistently associate with improved sleep metrics and slower PD progression (Morkovin et al., 2024; Pekdemir et al., 2024; Zhao et al., 2024). These diets attenuate oxidative stress and lipid peroxidation, conditions strongly linked to dopaminergic depletion and circadian instability. Nevertheless, a nuanced interpretation is warranted for certain compounds such as caffeine. In a longitudinal imaging analysis, it was demonstrated that chronic coffee consumption was associated with an 8–15 % reduction in striatal dopamine transporter binding, a change considered compensatory rather than degenerative (Ernst et al., 2024). Hence, excessive or unregulated caffeine intake may modify dopaminergic receptor sensitivity without necessarily conferring neuroprotective benefit. Such findings highlight the need for personalized nutrition protocols that calibrate bioactive intake to an individual's genetic and metabolic context rather than relying on generalized dietary assumptions.

The convergent action of pharmacologic, dietary, and physical interventions reveals a systems level therapeutic network that restores striatal function and normalizes sleep–wake architecture. Each domain—drug, diet, and exercise—addresses a primary facet of dopaminergic, inflammatory, or oxidative imbalance, yet their integrated application achieves a multiplicative rather than additive effect. This paradigm shifts from isolated to synergistic pathway engagement marks an essential evolution in neuro-rehabilitative strategy for movement disorder–related sleep dysfunction.

Future perspectives and conclusions

Building on the synthesized findings of this review, which confirm that striatal dysfunction is the common nexus driving the co-morbidity of sleep disturbances and movement impairments, we advocate for a fundamental shift toward integrated, lifestyle-based neurorehabilitation. The most pressing need for future research is to validate these proposed synergistic mechanisms through rigorous, mechanistically-driven clinical trial. We propose

Table 1. Mapping of molecular mechanisms, modulators, and therapeutic outcomes in striatal sleep disturbances.

Pathway / Mechanism	Primary Modulators	Mechanistic Effect	Therapeutic Outcome	Refs
Dopaminergic signaling (DAT, D_2 receptors)	Dopaminergic drugs aerobic training	Stabilization of dopamine cycling	Shorter sleep latency, improved motor control	(Grace A. Bailey et al., 2021b; Dunk et al., 2023; Langeskov-Christensen, Franzén, Hvid, et al., 2024)
Oxidative stress / NRF2 axis	Exercise polyphenol-rich diet	↑ Antioxidant enzymes (SOD, GPx)	Reduced neurodegeneration better sleep continuity	(Bishop et al., 2025; Duan et al., 2025; Paterno et al., 2024)
BDNF / TrkB neurotrophic axis	Exercise omega-3s β-glucans	Synaptic plasticity, neurogenesis	REM restoration	(Armeli et al., 2021; Castro et al., 2022; Ruegsegger et al., 2023)
Mitochondrial metabolism	Aerobic + resistance exercise CoQ10	↑ ATP production ↓ ROS	Circadian stability	(Li et al., 2020; Rust et al., 2025)
Neuroinflammation (NF-κB, cytokines)	Exercise vitamins E/C flavonoids	↓ IL-6, TNF-α	Reduced arousal improved sleep quality	(Ahmad et al., 2023; Morkovin et al., 2024; Wang et al., 2023)
Adenosine / orexin systems	A_2A antagonists orexin inhibitors	Balanced arousal–sleep signaling	Enhanced efficiency	(Chen et al., 2023; Raheel et al., 2024; Zhao et al., 2024)
Caffeine–adenosine interplay	Controlled coffee intake	DAT modulation, compensatory desensitization	Neutral or protective adaptation	(Ernst et al., 2024)

that future studies must prioritize Randomized Controlled Trials (RCTs) employing a three-arm design—comparing exercise-alone, nutrition-alone, and combined interventions—with patient cohorts carefully stratified by factors such as REM Sleep Behavior Disorder (RBD) status and disease stage to account for clinical heterogeneity. Crucially, these trials must leverage multimodal endpoints to provide actionable clinical and molecular data, specifically utilizing DAT PET/SPECT and MRI/fMRI for quantitative neuroimaging of striatal signaling and connectivity, integrating Polysomnography (PSG) and actigraphy for objective sleep architecture tracking, and conducting nested mechanistic substudies employing multi-omics and advanced serum/CSF biomarkers (e.g., BDNF, oxidative stress markers) to precisely correlate clinical outcomes with the modulation of cellular stress pathways. By adopting these specific, high-resolution study designs, the field can establish evidence-based, personalized protocols that optimize the timing and intensity of combined interventions. Addressing the bidirectional relationship among sleep, striatal function, and motor impairment will significantly advance the transition toward a holistic, precision-based management paradigm, ultimately maximizing the quality of life for this vulnerable patient population.

What is already known on this subject?

Movement disorders such as Parkinson's disease, Huntington's disease, and dystonia frequently co-occur with significant sleep disturbances, including insomnia, excessive daytime sleepiness, and rapid eye movement.

What this study adds?

Striatal dysfunction is the common nexus driving the co-morbidity of sleep disturbances and movement impairments, we advocate for a fundamental shift toward integrated, lifestyle-based neurorehabilitation.

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