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DOPAMINERGIC REGULATION OF SLEEP ARCHITECTURE AND DREAM GENERATION: FROM NEUROPSYCHIATRIC PATHOLOGY TO THE THERAPEUTIC POTENTIAL OF EXERCISE – A NARRATIVE REVIEW

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ABSTRACT

Classically viewed as the primary mediator of reward, motivation, and exercise-induced euphoria, dopamine actually exerts highly nuanced, region- and receptor-specific effects on sleep architecture and dream generation. This narrative review synthesizes current literature from major scientific databases up to 2026 to elucidate how localized dopaminergic signaling acts as a homeostatic gatekeeper of overnight neurological restoration, and how its disruption drives sleep pathology across a broad clinical spectrum. Pathological breakdowns in dopaminergic pathways manifest as profound sleep fragmentation in Parkinson's disease, circadian and phenomenological disturbances in schizophrenia, receptor desensitization linked to anhedonia in Major Depressive Disorder, neuroendocrine-driven hypersomnia in hyperprolactinemia, and failed fear extinction fueling recurrent nightmares in Post-Traumatic Stress Disorder. Crucially, this study evaluates the translational potential of physical exercise—particularly high-intensity interval training (HIIT)—as a non-pharmacological intervention. While respecting evolutionary limits in healthy organisms via the natural ceiling hypothesis, exercise opens a therapeutic window in deficit states, upregulating D₂ receptor density, stabilizing sleep microstructure through expanded N2 stages and sleep spindle activity, and enhancing slow-wave sleep. This prolongation of deep sleep ultimately accelerates glymphatic clearance, facilitating the convective removal of neurotoxic aggregates such as α -synuclein. By bridging the gap between exercise physiology, translational neurology, and sleep medicine, this review establishes a cohesive mechanistic framework for utilizing structured physical activity to protect vulnerable neural networks and transform the clinical management of complex motor and neuropsychiatric disorders.

KEYWORDS

Dopamine, Exercise Signaling, Sleep Regulation, Sleep Disorder

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1. Aim of the study

The primary aim of this study is to comprehensively analyze and synthesize the current scientific literature regarding the complex, non-linear role of the dopaminergic system in regulating sleep architecture and dream generation, shifting the paradigm from dopamine as a simple waking stimulant to a nuanced neurochemical gatekeeper. Furthermore, this study aims to evaluate the translational potential of physical exercise—particularly high-intensity interval training (HIIT)—as a non-pharmacological intervention capable of remodeling receptor plasticity, stabilizing sleep microstructure, and accelerating the glymphatic clearance of neurotoxic proteins like α -synuclein.

2. Introduction

Classically conceptualized as the quintessential neurotransmitter of reward, motivation, and behavioral reinforcement, dopamine has long been celebrated as the primary "pleasure molecule" of the central nervous system. In the realms of sports science and exercise physiology, this catecholamine is traditionally recognized for its pivotal role in driving motor coordination, fueling competitive drive, and mediating the profound sense of satisfaction and psychological euphoria—often termed the "runner's high"—associated with acute physical exertion. This conventional perspective views dopamine primarily as a unidirectional, activating agent that pairs behavioral output with hedonic validation and alertness.

However, contemporary translational neurology reveals a far more intricate and compartmentalized neurochemical reality. Dopamine does not act as a homogenous stimulant; rather, its physiological consequences are strictly dependent on localized neuroanatomy, receptor subtype expression, and fluctuating synaptic concentrations. Within the mesolimbic, mesocortical, and nigrostriatal pathways, the functional outcome of dopaminergic transmission is highly nuanced. This is most vividly demonstrated at the receptor level, where excitatory D₁ receptors consistently promote wakefulness, whereas inhibitory D₂ receptors exhibit

a complex biphasic profile—potentiating deep sleep at low concentrations via autoreceptor stimulation, yet forcing the brain into hyperarousal when saturated.

This intricate, non-linear behavior carries vast clinical implications, particularly concerning the regulation of sleep architecture and the generation of dream content. Far from being a simple daytime wakefulness promoter, the dopaminergic system acts as a homeostatic gatekeeper of overnight neurological restoration. Consequently, when dopaminergic networks suffer from localized dysregulation, deficiency, or hyperactivation, they become central drivers of sleep pathology across a diverse spectrum of neuropsychiatric and neurodegenerative conditions. From the profound sleep fragmentation and nocturnal "off-time" awakenings in Parkinson's disease to the altered dream phenomenology and circadian rhythm disruptions in schizophrenia, the receptor desensitization underpinning anhedonia in Major Depressive Disorder, and the disrupted fear extinction learning that fuels recurrent nightmares in Post-Traumatic Stress Disorder, aberrant dopamine signaling fundamentally distorts the sleeping brain. By exploring these localized mechanisms, alongside the neuroprotective capacity of structured physical exercise to remodel receptor plasticity and facilitate glymphatic clearance, this paper aims to elucidate how the fine-tuning of dopamine remains essential for harmonizing movement, sleep homeostasis, and clinical recovery.

3. Material and methods of research

This study was designed as a comprehensive narrative review evaluating the current state of literature on the intersection of the dopaminergic system, sleep architecture, neuropsychiatric disorders, and exercise physiology. To gather relevant data, a rigorous search of major electronic databases—including PubMed/MEDLINE, PubMed Central (PMC), Scopus, and Google Scholar—was conducted for peer-reviewed articles published from database inception up to early 2026. The search strategy utilized combinations of Medical Subject Headings (MeSH) terms and specific keywords, including: "dopamine", "D1 and D2 receptors", "sleep architecture", "REM sleep", "Parkinson's disease", "schizophrenia", "major depressive disorder", "PTSD", "high-intensity interval training (HIIT)", and "glymphatic clearance".

Inclusion criteria were strictly restricted to peer-reviewed original research articles (comprising both preclinical rodent models and clinical human trials), systematic reviews, and meta-analyses published in the English language. Articles were selected if they directly addressed the neurobiological mechanisms linking dopaminergic pathways to sleep homeostasis, oneiric generation, or exercise-induced neuroplasticity. Literature focusing exclusively on peripheral dopaminergic functions or unrelated sleep disorders (such as obstructive sleep apnea) was excluded. Document selection prioritized methodological rigor, sample size reliability, and recent advancements in translational neurology, with a specific focus on novel discoveries regarding glymphatic protein clearance and receptor-level sexual dimorphism. Ultimately, data from the selected literature were qualitatively synthesized and organized into thematic sections outlining physiological baselines, pathological disruptions, and non-pharmacological interventions to provide a cohesive mechanistic framework.

4. Results

For sports medicine and translational neurology, this duality provides a starting point for understanding how physical exercise, overtraining, and metabolic interventions (such as ketosis) influence neuroplasticity, recovery, and the treatment of clinical motor and neuropsychiatric disorders.

4.1. Neuroanatomy of the Dopaminergic System and D1/D2 Receptors in Dream Generation

The mesolimbic pathway—projecting from the ventral tegmental area (VTA) to the nucleus accumbens (NAc)—assigns emotional and motivational salience to dream content [1], with phasic dopamine (DA) release in the NAc core actively promoting REM sleep and modulating muscle atonia mechanisms [2]. Concurrently, DA signaling within the basolateral amygdala (BLA) acts as a critical trigger for REM sleep initiation and shapes the emotional intensity of dreams [3].

Anatomically, the neural networks driving dream generation are distinct from core REM-permissive structures. According to the Reward Activation Model, the sleep-associated hyperactivation of the mesocortical-mesolimbic dopaminergic network drives the offline reprocessing of memories with high survival and emotional value. During REM sleep, VTA dopaminergic neurons exhibit burst-firing patterns that mimic waking reward anticipation, causing substantial phasic DA release in the NAc [4].

At the receptor level, while dopamine D₁ receptors consistently promote arousal in a dose-dependent manner, D₂ receptors exhibit a complex biphasic effect, facilitating sleep at low doses and driving wakefulness at high doses [5].

Table 1. DA receptors classes, their functions and key locations for sleep regulation.

Receptor Type	Class (G Protein)	Main Behavioral Function in Sleep-Wake Cycle	Key Locations for Sleep Regulation
D ₁	Gs (Excitatory)	Direct induction of wakefulness (dose-dependent), emergence from anesthesia.	Medial prefrontal cortex, caudate nucleus, NAc
D ₂	Gi/Go (Inhibitory)	Biphasic effect. Stimulation of autoreceptors promotes deep sleep; saturation forces the brain into wakefulness.	VTA, NAc, DRN

4.2. The Impact of Dopamine Deficiency on Sleep in Parkinson's Disease

In Parkinson's disease (PD), progressive nigrostriatal dopamine depletion severely impairs sleep architecture, causing reduced sleep efficiency, prolonged sleep latency, excessive daytime sleepiness (EDS), and marked reductions in both N3 slow-wave sleep and REM sleep stages [6]. Nocturnal hypokinesia, muscle rigidity, and tremors fragment sleep homeostasis, frequently inducing painful dystonia and sleep-maintenance insomnia [7; 8]. Furthermore, functional neuroimaging demonstrates that decreased presynaptic dopamine transporter (DAT) uptake within the striatum strongly correlates with the pathogenesis and clinical progression of REM sleep behavior disorder (RBD) [9].

While symptomatic therapy with the dopamine precursor levodopa can initially facilitate sleep onset by reducing motor restlessness, its narrow therapeutic window induces severe sleep disruption in advanced stages. Natural pharmacokinetic fluctuations and nocturnal "off-time" drug clearance trigger frequent, uncontrolled awakenings during the second half of the night, significantly elevating the Wakefulness After Sleep Onset (WASO) index [7]. Consequently, escalating doses of chronic levodopa negatively correlate with subjective sleep quality, creating a clinical cycle of nocturnal hyperstimulation and daytime exhaustion [7].

4.3. Sleep Architecture, Genetic Predispositions, and Dream Content in Schizophrenia

Sleep and circadian rhythm disruption (SCRD) is a pervasive feature of schizophrenia, including advanced or delayed sleep phases, highly fragmented sleep patterns, and non-24-hour rhythms that fail to entrain to the external light-dark cycle. It affects up to 80% of patients and acts as a prominent predictor of symptom severity and psychosocial impairment [10]. At the molecular level, this dysregulation is evidenced by the loss of rhythmic expression of core circadian clock genes, such as CRY1 and PER2, in the peripheral cells of patients with chronic schizophrenia [11]. Genome-wide association studies have identified links between mutations in clock genes (e.g., CLOCK, PER2, PER3) and an increased risk of developing the disorder [10]. Furthermore, in the sleep architecture of individuals with schizophrenia there is a significant reduction in sleep spindle density and activity during NREM sleep, leading to declarative and procedural memory impairments [12].

The phenomenological similarities between the waking state of psychotic patients—marked by hallucinations and delusions—and the physiological state of REM sleep have led researchers to hypothesize that psychosis shares fundamental neurobiological overlaps with the dreaming brain. Both states feature a relative hyperactivation of limbic and paralimbic structures (e.g., the amygdala and anterior cingulate cortex) alongside a hypometabolism of the dorsolateral prefrontal cortex. This specific cerebral activation pattern leads to diminished executive control, loss of self-reflective awareness, and severely impaired reality testing [13]. Mirroring patients with schizophrenia waking social deficits, their dreams feature fewer friends and familiar characters, while displaying more negative and violent themes where the dreamer frequently perceives themselves as the victim of external hostility [14].

4.4. The Dopaminergic System, Sleep Disorders, and Anhedonia in Major Depressive Disorder

In Major Depressive Disorder (MDD), dysregulation of the mesolimbic dopaminergic reward pathway disrupts sleep macrostructure, characteristically manifesting as reduced sleep efficiency, diminished slow-wave sleep (SWS), shortened REM sleep latency, and elevated REM density [15; 16]. Chronic sleep fragmentation and insomnia compromise the structural and functional integrity of these dopaminergic networks, inducing a profound downregulation of dopamine D₂ and D₃ receptors within the ventral striatum [17].

This receptor desensitization blunts the processing of reward-related stimuli, clinically driving core depressive symptoms such as anhedonia (the loss of pleasure) and aboulia (the lack of volition) [17; 18]. Furthermore, the low-grade systemic inflammation frequently comorbid with MDD impairs functional connectivity across corticostriatal circuits, directly interfering with baseline dopamine signaling and reinforcing treatment-resistant depressive phenotypes [19].

4.5. Hyperprolactinemia, Dopamine Deficiency, and Sleep Homeostasis

The hypothalamic-pituitary-prolactin axis serves as a critical neuroendocrine regulator of the sleep-wake cycle, wherein prolactin (PRL) secretion is tonically suppressed by hypothalamic dopamine binding to lactotroph D₂ receptors (D₂R) [20; 21]. Pathological hyperprolactinemia removes this inhibitory brake, establishing a hypodopaminergic state that triggers the downregulation and desensitization of central D₂Rs, heavily predisposing patients to mood disorders and severe sleep-wake disturbances [20]. While physiological PRL release naturally peaks during NREM sleep, chronic hyperprolactinemia pathologically distorts sleep architecture by extending deep NREM stages into the late sleep cycle and aberrantly enhancing REM sleep [22].

This attenuation of dopaminergic arousal, coupled with the direct soporific effects of elevated circulating PRL, shifts the homeostatic balance toward hypersomnia, manifesting clinically as severe fatigue and excessive daytime sleepiness (EDS) [20; 23]. Polysomnographic evaluations confirm that hyperprolactinemic patients experience significantly prolonged total sleep times and sleep periods, independent of alternative respiratory or psychiatric etiologies [23].

Standard pharmacological management relies on D₂ receptor agonists (e.g., cabergoline, bromocriptine) to suppress PRL hypersecretion and normalize systemic dopaminergic tone, thereby restoring physiological sleep architecture and enhancing daytime alertness [20; 21]. However, because these dopaminergic agents possess dose-dependent biphasic effects—where low doses promote sedation and high doses trigger insomnia—precise clinical titration remains critical to optimize therapeutic sleep-wake outcomes [20].

4.6. Dopaminergic Mechanisms of Persistent Dreams and Nightmares in PTSD

Beyond hyperactive noradrenergic signaling during REM sleep, the dopaminergic system critically drives the pathogenesis of recurrent, trauma-related nightmares in Post-Traumatic Stress Disorder (PTSD) [24]. When conceptualized within the spectrum of Reward Deficiency Syndrome (RDS), a genetic hypodopaminergic trait disrupts the dopamine-modulated synaptic plasticity required for the consolidation of fear extinction learning [24]. Consequently, traumatic memories fail to undergo physiological overnight emotional depotentiation, retaining a severe affective charge that persistently intrudes into sleep [24].

Simultaneously, aberrant dopaminergic activation within mesolimbic pathways and the amygdala fuels the intense emotionality, vividness, and compromised metacognitive control characteristic of terrifying lucid nightmares [25]. While conventional interventions utilize alpha-1 adrenergic antagonists like prazosin to damp nocturnal noradrenergic tone, targeting the underlying dopaminergic deficit provides a highly effective therapeutic alternative.

Clinical evidence indicates that enhancing dopaminergic transmission via pro-dopamine regulators (such as the neuronutrient complex KB220Z) restores homeostatic signaling and functional connectivity across crucial reward networks, including the nucleus accumbens, anterior cingulate gyrus, and hippocampus [24]. This induction of dopamine homeostasis promotes the neuroplasticity necessary for effective fear extinction, mitigating trauma-induced epigenetic insults and transforming terrifying nightmares into neutral or pleasant oneiric experiences [24].

4.7. Exercise Physiology: Neurochemical Adaptations, Sleep Microstructure, and Glymphatic Clearance

4.7.1. HIIT-Induced Adaptations vs. the Natural Ceiling Hypothesis

High-intensity physical exercise, such as high-intensity interval training (HIIT), exhibits a unique ability to selectively modify receptor plasticity in the brain. Studies on animal models subjected to a chronic HIIT protocol demonstrated a significant 16% increase in the binding density of dopamine D₂ receptors (D₂R) specifically in the shell of the nucleus accumbens (NAc Shell). The NAc Shell constitutes a crucial component of the mesolimbic dopaminergic pathway, which is responsible for motivational control, reward perception, and the inhibition of impulsivity. The upregulation of D₂R receptors in this region induced by HIIT promotes mood stabilization and counteracts compulsive behaviors [26].

Interestingly, chronic HIIT does not show a significant effect on the density of dopamine D₁ receptors (D₁R) or on tyrosine hydroxylase (TH) expression levels in healthy control groups. This phenomenon is explained by the natural ceiling hypothesis. According to this assumption, healthy organisms without neurochemical pathologies are close to their optimal, evolutionary limit of dopaminergic transmission [26]. Consequently, further stimulation of DA synthesis via TH upregulation is blocked by homeostatic feedback loops to prevent the neurotoxic accumulation of free dopamine in the cytosol.

The situation is completely different in disease models (e.g., Parkinson's disease or addictions), where baseline dopaminergic transmission is drastically reduced. In such deficit states, the same HIIT protocol exhibits a wide therapeutic window, leading to a marked increase in TH expression, DAT density, and dopamine receptors, effectively restoring homeostasis to the motor and reward systems [27].

Additionally, D₂R receptor adaptations induced by HIIT exhibit distinct sexual dimorphism. In the ventral caudate-putamen (V CPU)—a structure crucial for precise motor control—males showed an average of 14% higher D₂R binding compared to females subjected to the same training regimen. This suggests that the interaction of sex hormones with the mechanical and metabolic stress induced by HIIT may differentiate the rate of transcription and translocation of dopamine receptors to the synaptic membrane.

An important methodological aspect confirming the safety of HIIT protocols is the absence of changes in corticosterone levels and the lack of body weight loss in the studied subjects, which rules out the occurrence of overtraining syndrome and confirms that the induced plasticity represents a physiological adaptation [26].

A study demonstrates that excessive exercise causes profound fatigue by depleting a vital muscle protein (REV-ERB- α), which disrupts a key metabolic pathway and triggers a shift from brain-protecting to neurotoxic chemical levels, thereby establishing a clear biological link between physical exhaustion and brain dysfunction [28].

4.7.2. The impact of physical exercise on sleep microstructure and glymphatic drainage

Regarding changes in the electroencephalographic spectrum and the stabilization of the N2 stage, the application of objective measurement methods, such as polysomnography (PSG) coupled with actigraphy, has allowed for an accurate characterization of the impact of daily physical activity on human sleep microstructure. It has been demonstrated that a higher average daily step count directly correlates with an increase in total sleep efficiency (SE) and a significant prolongation of NREM sleep stage N2 duration. Concurrently, a distinct shortening of Wakefulness After Sleep Onset (WASO) has been observed [29].

Stage N2, which quantitatively constitutes the largest part of the night (50–60% of total sleep time), plays a crucial role as a transition phase to deep sleep. The physical activity-induced increase in the duration of stage N2 is associated with specific changes in the bioelectrical activity of the brain, most notably the enhancement of sigma band power (11–16 Hz). This band is responsible for generating sleep spindles in stage N2, which serve as an electrophysiological marker of synaptic plasticity, regulating the transfer of information from the hippocampus to the neocortex and isolating the thalamus from sensory stimuli to prevent awakening. Additionally, there is an enhancement of theta band power (4–9 Hz), where higher activity during REM and NREM sleep supports sleep stabilization, the selective modeling of synaptic connections, and the consolidation of both declarative and procedural (motor) memory [29].

4.7.3. The Glymphatic System and the Clearance of Neurotoxic Proteins

One of the most significant discoveries in the neurophysiology of sleep is the demonstration of the role of deep slow-wave sleep (SWS) in clearing toxic metabolites from the brain's interstitial space. This process, occurring within the glymphatic system, relies on the convective flow of cerebrospinal fluid (CSF) driven by arterial pulsation. Physical exercise stimulates the secretion of brain-derived neurotrophic factor (BDNF), whose levels strongly and positively correlate with the duration of SWS. An increase in the proportion of slow-wave sleep induced by training enables the effective clearance of pathological proteins, including α -synuclein. The aggregation of this protein is considered a key contributor to neurodegeneration of dopaminergic neurons in the substantia nigra. It has been shown that a single night of sleep deprivation causes an increase in α -synuclein concentration in the brain by as much as 36% [30].

Therefore, ensuring a stable SWS phase through regular aerobic and resistance training constitutes a key, non-pharmacological neuroprotective strategy that protects against damage to dopaminergic neurons and prevents the development of motor and cognitive impairments [31].

Table 2. Key neurochemical, microstructural, and glymphatic adaptations induced by exercise.

Physiological Dimension	Neurochemical & Microstructural Adaptations	Clinical & Functional Impact
HIIT & Receptor Plasticity	• +16% D₂R binding density in NAc Shell. • No change in D₁R or TH in controls (Natural Ceiling Hypothesis). • Marked increase in TH, DAT, and DA receptors in pathological models (PD/addiction).	• Promotes mood stabilization and counteracts compulsive behaviors. • Prevents cytosolic neurotoxicity in healthy states. • Restores baseline motor and reward signaling in DA-deficient brains.
Sexual Dimorphism & Safety	• Males exhibit 14% higher D₂R binding in V CPU compared to females. • Stable corticosterone levels and no body weight loss.	• Suggests sex hormones modulate DA receptor transcription/translocation. • Rules out overtraining syndrome, confirming physiological adaptation.
Excessive Exercise Exhaustion	• Severe depletion of muscle protein REV-ERB-α. • Metabolic shift from neuroprotective to neurotoxic chemical levels.	• Establishes direct biological link between physical overexertion and central brain dysfunction.
Sleep Microstructure	• Higher step count correlates with higher SE and prolonged N2 stage. • Shortened WASO. • Enhanced sigma (11–16 Hz) and theta (4–9 Hz) band power.	• Enhances sleep spindles, driving synaptic plasticity and memory consolidation. • Isolates thalamus from sensory stimuli, preventing awakenings.
Glymphatic Clearance	• BDNF secretion prolongs Slow-Wave Sleep (SWS). • Enhances convective CSF flow driven by arterial pulsation.	• Maximizes clearance of pathological proteins (e.g., α-synuclein). • Non-pharmacological shield against Parkinsonian neurodegeneration.

5. Discussion

A primary limitation is the heavy reliance on preclinical animal models to map receptor-level adaptations, such as the specific increase in D₂ receptor density post-HIIT. Direct longitudinal replication in humans remains scarce, leaving it unclear whether the natural ceiling hypothesis operates under identical homeostatic feedback loops in the human brain. Future research must utilize non-invasive molecular imaging, such as PET or SPECT scans, to track real-time dopaminergic changes in clinical cohorts. Furthermore, while current data highlights a distinct sexual dimorphism in receptor binding, the exact molecular cross-talk between fluctuating sex hormones and the metabolic stress of high-intensity exercise remains unresolved, requiring future trials to strictly control for sex-specific endocrine profiles.

While the relationship between SWS, BDNF secretion, and α -synuclein clearance is well-documented in animals, capturing human glymphatic dynamics in vivo presents severe methodological hurdles. Current human studies rely heavily on peripheral cerebrospinal fluid markers or proxy polysomnographic data rather than direct visualization of neurofluid flow. Developing advanced neuroimaging sequences, such as diffusion-prepared neurofluid MRI, will be paramount to definitively proving the neuroprotective and sleep-stabilizing efficacy of exercise in human clinical populations.

6. Conclusions

The intricate interplay between the dopaminergic system, sleep architecture, and oneiric activity represents a fundamental axis connecting healthy neurobiology to severe neuropsychiatric and neurodegenerative pathologies. Dopamine signaling acts as a master regulator of the sleep-wake cycle and dream generation, characterized by a receptor-specific modulation where D₁ receptors consistently drive arousal, while D₂ receptors exhibit a crucial biphasic effect across the mesolimbic and mesocortical pathways. When this dopaminergic homeostasis is disrupted, it serves as a unifying pathological marker across a broad clinical spectrum, manifesting as severe sleep fragmentation in Parkinson's disease, circadian clock mutations in schizophrenia, receptor desensitization driving anhedonia in Major Depressive Disorder, neuroendocrine disturbances in hyperprolactinemia, and impaired fear extinction in PTSD.

In this context, exercise physiology offers a powerful, non-pharmacological strategy to remodel neurochemical plasticity and restore baseline signaling. High-Intensity Interval Training (HIIT) demonstrates a unique capacity to selectively upregulate D₂ receptor density and tyrosine hydroxylase expression; while it respects evolutionary limits in healthy organisms as dictated by the natural ceiling hypothesis, it opens a wide therapeutic window in pathological deficit states. Furthermore, regular physical activity directly optimizes sleep microstructure by expanding the N2 stage, increasing sleep spindle density, and enhancing slow-wave sleep (SWS). This prolongation of deep sleep ultimately accelerates glymphatic clearance, facilitating the convective removal of neurotoxic aggregates such as α -synuclein and establishing a robust neuroprotective shield against progressive neurodegeneration.

Ultimately, while clinical interventions must carefully navigate the biological boundaries between optimal adaptation and physical exhaustion—such as the neurotoxic risks associated with REV-ERB- α depletion—bridging the gap between exercise physiology, translational neurology, and sleep medicine provides a promising, holistic frontier. Harmonizing these systems offers innovative pathways for enhancing neuroplasticity, protecting vulnerable dopaminergic networks, and transforming the clinical management of complex motor and neuropsychiatric disorders.

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