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Sleep Architecture Disruption as a Predictor of Cognitive Decline in Parkinson's Disease

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Abstract

Cognitive decline is one of the most consequential non-motor complications of Parkinson's disease (PD), but at diagnosis motor features give little indication of who will progress to mild cognitive impairment or dementia. This short communication synthesizes recent evidence that disrupted sleep architecture is not merely a common accompaniment of PD but a measurable, mechanistically plausible predictor of cognitive trajectory. We trace two converging lines of evidence: reduced slow-wave sleep and frontal EEG delta power are associated with poorer global cognition and executive function in PD, plausibly through impaired glymphatic clearance of misfolded proteins during deep sleep; and REM sleep behavior disorder, a loss of normal REM muscle atonia, is among the strongest known prodromal markers of neurodegeneration, with a large multicentre cohort reporting roughly 6% annual phenoconversion to parkinsonism or dementia. Newer biomarkers, including neurofilament light chain, cardiac MIBG uptake, and quantitative scoring of REM sleep without atonia, are beginning to refine this prediction further, while depression appears to mediate part of the sleep-cognition association. We close by noting that whether treating sleep architecture disruption, through dopaminergic optimization, circadian interventions, or treatment of comorbid sleep apnea, can slow cognitive decline rather than simply improving sleep quality remains an open and clinically important question.

Keywords: sleep architecture; Parkinson's disease; cognitive decline; REM sleep behavior disorder; slow-wave sleep

1. Introduction

Cognitive decline is among the most consequential non-motor complications of Parkinson's disease (PD), yet it remains difficult to anticipate in an individual patient at the time of diagnosis, when motor features alone give little indication of who will progress to mild cognitive impairment or dementia within a few years and who will not [1,2]. Clinical-genetic risk scores combining variants such as *GBA* and *APOE* status with baseline clinical features have improved group-level prediction of cognitive trajectory across pooled cohorts, but they remain population-level tools rather than something a clinician can act on at a single bedside visit, which is part of why an accessible, repeatable physiological marker like sleep architecture is attractive as a complementary predictor [3]. The Movement Disorder Society's own task force criteria for PD-associated mild cognitive impairment (PD-MCI) were written explicitly to standardize a diagnosis that, until then, different centers were making on incompatible grounds, and the criteria's adoption has made it possible to compare cognitive trajectories across cohorts in a way that was simply not feasible a decade earlier [4]. What has changed more recently is the growing conviction, across several independent lines of evidence, that disrupted sleep is not merely a common accompaniment of PD but an active, mechanistically plausible, and measurable contributor to the cognitive trajectory itself.

Sleep in PD is disrupted in ways that go well beyond the insomnia and daytime sleepiness patients often report spontaneously. Polysomnographic studies describe a reduction in slow-wave sleep (SWS) and altered EEG spectral power, a loss of REM sleep's normal muscle atonia (REM sleep behavior disorder, RBD), fragmented sleep architecture with frequent arousals, and disturbed circadian regulation of the sleep-wake cycle, often years before diagnosis and worsening as disease advances [5,6,7]. Several of these disturbances now have direct, quantifiable links to cognitive outcome. This short communication synthesizes that evidence, focusing specifically on which components of sleep architecture disruption have been linked to cognitive decline in PD, through what plausible mechanisms, and how far the field has come toward treating sleep architecture as an actionable predictive biomarker rather than an incidental symptom.

2. Sleep Architecture Changes in Parkinson's Disease

The neuropathological substrate for PD's sleep disturbances is, in outline, the same substrate that produces its motor and cognitive features: the progressive, caudal-to-rostral deposition of misfolded alpha-synuclein first described systematically by Braak and colleagues, who showed that brainstem nuclei governing sleep-wake regulation and REM atonia are affected at stages well before the substantia nigra itself [8]. This staging scheme is why RBD is now understood not as a coincidental comorbidity but as an early marker of the same underlying synucleinopathy that will, in a majority of patients, eventually produce parkinsonism or dementia. Postuma and colleagues' prospective multicentre study of 1,280 patients with idiopathic RBD is the clearest demonstration of this: approximately 6% of patients converted to an overt neurodegenerative syndrome each year, with cumulative conversion exceeding 73.5% by 12 years of follow-up, and the great majority of conversions were to either PD or dementia with Lewy bodies [9]. That single figure reframes RBD from "a sleep disorder some PD patients happen to have" to one of the most powerful prodromal markers currently available in neurodegenerative disease research.

Beyond RBD, patients with PD show reduced SWS and altered EEG delta-band spectral power relative to age-matched controls, together with more fragmented sleep architecture and, in more advanced or dementia-associated disease, disturbances in hypocretin (orexin) signaling that track with excessive daytime sleepiness [5,10]. Circadian regulation is disturbed as well: core clock gene expression, melatonin rhythm timing, and rest-activity cycles measured by actigraphy all show abnormalities in PD that appear to worsen with disease progression and that plausibly compound the effects of fragmented nighttime sleep by desynchronizing the timing of whatever restorative sleep still occurs [7]. Recognizing this constellation as a single interconnected system, rather than a list of independent symptoms, is what has allowed the field to start asking a more pointed question: which of these specific architectural changes actually predicts cognitive outcome, and through what mechanism.

3. Mechanistic Links Between Sleep Disruption and Cognitive Decline

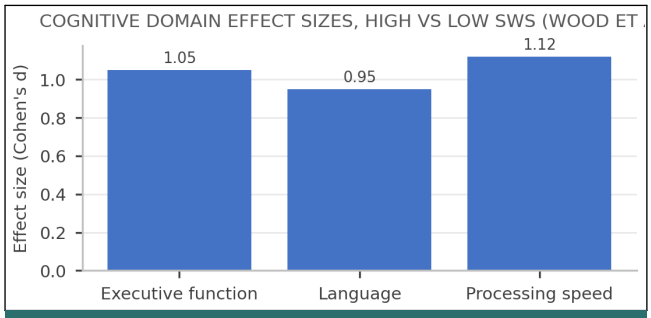

Figure 1: Between-group effect sizes (Cohen's d) for cognitive domain performance, high slow-wave sleep (SWS) versus low SWS groups, in a polysomnographic study of 32 patients with Parkinson's disease. Larger values indicate a larger cognitive advantage for the high-SWS group [10].

Two mechanistic accounts, not mutually exclusive, dominate current thinking about how disrupted sleep architecture could causally contribute to cognitive decline in PD rather than merely co-occurring with it. The first concerns glymphatic clearance. Xie and colleagues' foundational work in mice showed that the brain's interstitial space expands substantially during sleep, and specifically during slow-wave sleep, increasing convective clearance of interstitial solutes, including amyloid-beta, by roughly two-fold relative to the awake state [11]. If SWS is the sleep stage during which the brain clears misfolded and aggregation-prone proteins most efficiently, then the SWS reduction documented in PD patients is not a neutral bystander finding; it implies reduced clearance capacity precisely when the burden of alpha-synuclein and often co-existing amyloid pathology is accumulating. Morawska and colleagues tested this logic directly in a mouse model of PD, showing that enhancing slow-wave activity reduced synucleinopathy and favorably shifted proteostatic processes relative to untreated animals, which is about as close as the current literature comes to a causal experimental demonstration that slow-wave sleep quantity or quality can influence the underlying pathological burden rather than just correlating with it [12].

The second mechanistic account is more directly clinical: sleep disruption degrades the neural substrate for the attentional, executive, and consolidation processes that cognitive testing measures, independent of any effect on protein clearance. Wood and colleagues' polysomnographic study of 32 PD patients found that participants in a high-SWS group had significantly better global cognitive performance than those in a low-SWS group ($p = 0.01$, effect size $r = 0.45$), with particularly large between-group differences in executive function (Cohen's $d = 1.05$), language ($d = 0.95$), and processing speed ($d = 1.12$); frontal EEG delta power during N3 sleep was independently correlated with both the composite cognitive score and executive function specifically [10]. Because frontal-executive circuits are exactly the circuits most consistently implicated in PD-associated cognitive impairment, this frontal delta-power association is a plausible physiological bridge between a polysomnographic measurement and a specific, clinically recognizable cognitive phenotype, rather than a generic "sleep is good for the brain" association. Outside PD specifically, Lim and colleagues' prospective study of community-dwelling older adults found that more fragmented sleep, measured objectively by actigraphy, predicted a substantially elevated risk of incident Alzheimer's disease and more rapid cognitive decline over follow-up, a finding that has since anchored much of the broader sleep-and-neurodegeneration literature and that is entirely consistent with, even if not specific to, what is now being observed in PD cohorts [13]. Obstructive sleep apnea (OSA) offers a further, partially independent route to the same endpoint: OSA-related intermittent hypoxia and sleep fragmentation are associated with accelerated cognitive decline and altered Alzheimer's-pathology biomarkers in systematic reviews of the general older population, and because OSA is common and often unrecognized in PD, it represents a mechanistically distinct, and in principle treatable, contributor to the same clinical picture [14].

4. Sleep Biomarkers as Predictors of Cognitive Decline

The predictive value of RBD specifically extends beyond the binary question of whether phenoconversion occurs at all. Neurofilament light chain, a nonspecific marker of axonal injury, and reduced cardiac MIBG uptake, a marker of cardiac sympathetic denervation, have each been shown to add predictive information for phenoconversion timing and outcome type beyond clinical assessment alone in isolated RBD cohorts, suggesting that RBD's prognostic value can be sharpened by combining it with orthogonal biomarkers rather than treated as a single all-or-nothing risk flag [15]. Quantitative electromyographic scoring of REM sleep without atonia, the polysomnographic hallmark underlying an RBD diagnosis, has similarly been shown to improve prediction of which patients with isolated RBD will go on to develop an overt

alpha-synucleinopathy, refining a diagnosis that was historically made in a more binary, visually-scored fashion into a graded, quantitative risk marker [16]. Table 1 summarizes several of these predictive sleep-architecture markers alongside the study designs that established them, to make explicit how heterogeneous the underlying evidence base still is even as the individual findings converge on the same broad conclusion.

Table 1: Representative sleep-architecture markers studied as predictors of cognitive or neurodegenerative outcome in Parkinson's disease and related synucleinopathies. [9,10,15,16,5].

Sleep marker	Source	Study design	Reported predictive/associative finding
REM sleep behavior disorder (clinical diagnosis)	Postuma et al. [9]	Prospective multicentre cohort, n=1280 idiopathic RBD	~6% per year phenoconverted to PD, DLB or MSA; >73.5% cumulative by 12 years
Slow-wave sleep % and frontal EEG delta power	Wood et al. [10]	Polysomnography + neurocognitive battery, n=32 PD	High-SWS group had better global cognition (p=0.01, r=0.45) and executive function (d=1.05)
Neurofilament light chain, cardiac MIBG uptake	Park et al. [15]	Isolated RBD cohort, biomarker + follow-up	Added predictive value for phenoconversion beyond clinical assessment alone
Quantitative REM sleep without atonia (EMG scoring)	Noh et al. [16]	Polysomnographic EMG quantification, isolated RBD	Continuous atonia-loss scoring improved prediction of phenoconversion over visual scoring
CSF hypocretin, sleep architecture	Compta et al. [5]	Cross-sectional, PD with dementia vs PD vs controls	Lower CSF hypocretin and altered architecture associated with daytime sleepiness in PD dementia

Depression is a further complicating and clinically important factor: a recent analysis found that sleep disturbance statistically mediates a meaningful portion of the association between depressive symptoms and cognitive decline in PD, which matters practically because depression and sleep disturbance are both common, both under-recognized, and both are, in principle, treatable, unlike the underlying neurodegenerative process itself [17]. This mediation finding is a useful corrective against treating sleep architecture purely as a passive biomarker: at least some of its predictive association with cognition plausibly runs through a modifiable mood pathway rather than through fixed neurodegenerative burden alone, which has direct implications for how aggressively clinicians should screen for and treat depression and sleep disturbance jointly in early PD.

5. Clinical and Research Implications

If sleep architecture disruption is genuinely on the causal pathway to cognitive decline, at least in part, then interventions aimed at sleep should in principle be testable as cognition-protective strategies, not merely as symptomatic comfort measures. The evidence here remains preliminary but is not absent. Chaudhuri and colleagues' meta-analysis of levodopa-carbidopa intestinal gel therapy over 24 months of follow-up found improvements in non-motor symptom burden, including sleep-related measures, alongside reductions in dyskinesia, indicating that optimizing dopaminergic therapy itself can meaningfully improve sleep in advanced PD even though the trial was not designed around cognitive endpoints specifically [18]. A randomized controlled trial of timed bright light therapy for PD-associated sleep disturbance and daytime sleepiness likewise demonstrated that a low-cost, non-pharmacological circadian intervention can measurably improve sleep-related outcomes in this population, which is encouraging precisely because it is a chronobiological rather than dopaminergic mechanism, and one that could in principle be layered onto standard PD treatment without added medication burden [19]. Neither trial, it should be said plainly, was designed to demonstrate that improving sleep prevents or slows cognitive decline in PD; that causal question remains open, and answering it will require prospective trials with cognitive endpoints specifically, adequately powered and followed for long enough to detect a meaningful difference in cognitive trajectory rather than sleep quality alone.

The broader clinical picture painted by non-motor symptom research in PD, dating back to Chaudhuri and Schapira's influential framing of non-motor features as central rather than peripheral to the disease's dopaminergic and non-dopaminergic pathophysiology, supports treating sleep architecture assessment as a routine part of cognitive risk stratification rather than an optional add-on pursued only when a patient spontaneously reports insomnia [20]. In practice this would mean incorporating structured sleep history, and where feasible actigraphy or polysomnography, into the same visits where PD-MCI screening under the MDS criteria is performed [4], rather than treating cognitive and sleep assessment as separate clinical tracks that happen to be managed by the same specialty.

6. Conclusion

The literature synthesized here supports a specific, moderately confident claim rather than a sweeping one: several distinct components of sleep architecture disruption in Parkinson's disease, reduced slow-wave sleep and delta spectral power, REM sleep behavior disorder and REM sleep without atonia, and circadian and hypocretin dysregulation, each show a real, biologically plausible, and in some cases quantitatively substantial association with cognitive outcome, through at least two partially distinct mechanisms (impaired glymphatic clearance of pathological proteins, and direct degradation of the neural circuits supporting executive and attentional function) [11,12,10]. RBD in particular has matured into one of the field's most robust prodromal markers, with phenoconversion rates now characterized precisely enough to inform trial design, and with newer biomarkers such as neurofilament light chain and quantitative REM-without-atonia scoring beginning to refine that prediction further [9,15,16]. What remains genuinely open is the therapeutic question: whether intervening on sleep architecture, through dopaminergic optimization, circadian interventions such as timed light therapy, or treatment of comorbid OSA and depression, can meaningfully slow cognitive decline rather than simply improving sleep quality and daytime function in their own right [18,19,14,17]. That question deserves a properly powered, cognition-endpoint-driven trial, and until one exists, sleep architecture disruption should be read as one of the field's more promising predictive biomarkers for cognitive decline in Parkinson's disease, rather than as an established target for its prevention.

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Conflict of Interest

The authors declare that they have no competing interests relevant to this work.

Data Availability Statement

No new data were generated for this article, which is a short literature synthesis. All findings discussed are drawn from the cited published sources, and readers should consult those original publications for their underlying data.

Ethical Approval

Not applicable. This article did not involve human participants, animal subjects, or the collection of any primary data.

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