

Thalamocortical correlates of sleep spindle and slow oscillation dysfunction in Lewy body disorders

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Article

Keywords: Parkinson's, Dementia with Lewy bodies, Lewy Body Disorders, Sleep spindles, Neuroimaging, EEG

Posted Date: September 25th, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-10904079/v1>

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Additional Declarations: There is **NO** Competing Interest.

Abstract

Sleep disturbances are pervasive in Lewy body disorders (LBD), but their neurophysiological basis remains unclear. Non-rapid eye movement (NREM) sleep offers an objective window into thalamocortical circuit function, minimally confounded by the motor and cognitive fluctuations of wake. Sleep spindles, slow oscillations (SOs) and their coupling reflect complementary aspects of this system, and may be differentially affected in LBD. We characterised NREM microarchitecture in 109 participants (55 controls, 32 Parkinson's disease [PD], 22 dementia with Lewy bodies [DLB]), quantifying spindle density and morphology, SOs, spindle–SO coupling and spectral power, and related these to thalamic volumes and cortical thickness in the 77 participants with MRI, adjusting for age and sex. Macroarchitecture was broadly similar between groups. Slow and fast spindle densities were reduced in LBD and lowest in DLB (all $p_{\text{FDR}} < 0.05$), with PD reductions more prominent for fast spindles. Additionally, DLB showed reduced central and occipital SO density ($p_{\text{FDR}} \leq 0.018$), altered slow spindle–SO coupling, and increased frontal beta power ($p_{\text{FDR}} = 0.004$). Within LBD, reduced thalamic volume was associated with lower spindle density and weaker slow spindle–SO coupling. These dissociable abnormalities of spindle generation and thalamocortical coordination support sleep EEG as an accessible physiological readout of circuit dysfunction in LBD.

Introduction

Lewy body disorders (LBD), encompassing Parkinson's disease (PD) and dementia with Lewy bodies (DLB), are common neurodegenerative disorders in older adults characterized pathologically by the aberrant accumulation of misfolded α -synuclein. PD and DLB present with overlapping motor, cognitive, neuropsychiatric, autonomic, and sleep-wake disturbances, differing primarily in the temporal sequence of symptom onset.¹ Among these features, sleep–wake disturbances are multifaceted^{2–5}, highly prevalent^{2,3}, often emerge early^{6–8}, worsen with disease progression⁹, and represent a major source of disability for patients and burden for caregivers.^{10,11}

Despite their prominence, the neurophysiological basis of sleep disruption in LBD remains incompletely understood. Conventional polysomnographic (PSG) measures of sleep macroarchitecture, including sleep timing and the proportion of time spent in sleep stages, have shown modest group-level differences. In PD, meta-analytic evidence indicates minimal changes in rapid eye movement (REM) and non-rapid eye movement (NREM) stage proportions relative to controls², while in DLB, profound clinical sleep disturbance, including REM sleep behaviour disorder, hypersomnia, and fragmentation, is not adequately captured by standard staging metrics.³ Although these conventional measures provide important clinical information, they are relatively coarse summaries of sleep organisation and may be insensitive to the circuit-level abnormalities occurring in these disorders. Sleep extends beyond a sequence of discrete stages and is a dynamic process characterised by coordinated neuronal activity across distributed circuits.^{12,13} Understanding dysfunction in these circuits therefore requires moving beyond macroarchitectural descriptions to sleep microarchitecture.

NREM sleep is a particularly informative window in which to examine microarchitecture in these disorders. In NREM sleep, the relative withdrawal of monoaminergic and cholinergic tone creates a permissive state in which thalamocortical and cortico-cortical circuit dynamics emerge as organized oscillations.¹⁴ Key features include sleep spindles, slow oscillations (SOs), their temporal coupling, and the spectral composition of the electroencephalographic (EEG) signal. Sleep spindles are 10–16 Hz oscillations generated through reciprocal interactions between thalamic reticular and thalamocortical relay neurons and may provide a functional index of thalamocortical integrity.¹⁵ Slow spindles (SS) and fast spindles (FS; ~11 and ~15 Hz, respectively) occupy distinct frequency ranges and exhibit characteristic topographic distributions, with slow spindles predominating frontally and fast spindles centrally and parietally. They are thought to reflect differences in thalamocortical organization and function.^{16–18} SOs (~1 Hz), generated within cortical networks, coordinate large-scale neuronal excitability and synchronise activity across brain regions.^{19–21} Spindles are temporally coupled with the depolarising phase of SOs, a relationship implicated in systems-level memory consolidation.^{22–24} Spectral power and directional phase relationships provide complementary measures of broader NREM network organisation.^{25–27} Together, these features provide a sensitive, mechanistically grounded window into circuit-level function that is not accessible through conventional sleep staging.

Evidence for disruption of NREM microarchitecture in LBD is emerging but remains incomplete. In PD, reduced spindle density and activity have been reported^{28,29}, with alterations in spindle morphology correlating with cognitive performance and predicting cognitive decline.³⁰ Spindles cluster more tightly around a preferred slow oscillation phase than in controls, without a shift in the preferred phase itself or a change in how often spindles and SOs co-occur³¹, and slow wave activity is also diminished and associated with non-motor symptoms.^{32–35} However, these prior findings have focused predominantly on PD, and often examined individual oscillatory features in isolation. NREM microarchitecture has not been systematically characterised in DLB. It is therefore unclear whether spindle, SO, coupling, and spectral abnormalities differ between PD and DLB, whether they show distinct spatial patterns, and whether they relate to structural vulnerability within thalamocortical networks.

This question is particularly important in the context of LBD neurobiology. The thalamus is affected by α -synuclein pathology and shows broader structural and functional abnormalities³⁶, with alterations across thalamic subdivisions linked to hallmark clinical features of LBD including cognitive and motor manifestations³⁷, visual hallucinations³⁸, and sleep disturbances.³⁹ Widespread cortical thinning has been documented across the LBD spectrum^{40–43}, with DLB exhibiting the most extensive reductions concentrated in posterior cingulate, inferior parietal, precuneus, fusiform, and pericalcarine regions.⁴² Given that sleep spindles and their coordination with SOs reflect thalamocortical circuit dynamics, NREM microarchitecture may provide a non-invasive index of dysfunction within these selectively affected networks. In other disorders of thalamocortical circuitry, such as schizophrenia, spindle deficits are closely linked to reduced thalamic volume and cognitive impairment⁴⁴, supporting the potential of this approach in LBD.

Here, we use overnight polysomnography in a well-characterised cohort of 109 participants (55 healthy controls, 32 PD and 22 DLB) to comprehensively assess NREM sleep microarchitecture and its structural correlates. We quantify sleep spindle and SO densities, spindle–SO coupling and spectral power, together with complementary analyses of spindle and SO morphology, and directional phase relationships using the phase slope index (PSI). We hypothesised that spindle generation and spindle–SO coordination would be disrupted across LBD, with the greatest abnormalities in DLB, and that these changes would be associated particularly with thalamic structural integrity and, more broadly, with thalamocortical network structure.

Results

Participant Characteristics

A total of 109 participants were included: 55 HC, 32 PD, and 22 DLB (Table 1). DLB participants were older than both HC and PD and had a higher proportion of male participants than HC. MMSE was also lower in the DLB group, as expected. Daytime sleepiness was increased in DLB, with higher ESS scores relative to HC and PD ($p = 0.001$) and higher SCOPA-Sleep Daytime scores than PD ($p = 0.036$). SCOPA-Sleep Night scores were lower in DLB than PD ($p = 0.007$). RBD Screening Questionnaire scores did not differ between PD and DLB. Cholinesterase inhibitor use was more frequent in DLB ($p < 0.001$), while antidepressant use was higher in both PD and DLB relative to HC ($p = 0.010$). Levodopa equivalent daily dose did not differ between PD and DLB groups.

Table 1
Group differences in demographics, clinical data and self-report questionnaires

Clinical Variables	Controls (n = 55)	PD (n = 32)	DLB (n = 22)	p value
Age	66.17 ± 7.54	63.36 ± 8.87	74.73 ± 6.09	< 0.001 ^{b,c}
Education	14.36 ± 3.06	13.80 ± 3.21	12.60 ± 3.63	0.183
Male (n,%)	27 (49.1%)	20 (62.5%)	17 (77.2%)	0.038 ^b
MMSE	28.86 ± 1.75	28.81 ± 1.47	21.90 ± 5.17	< 0.001 ^{b,c}
Questionnaires				
Epworth Sleepiness Scale	5.95 ± 3.95	7.31 ± 4.38	10.83 ± 5.69	0.001 ^{b,c}
SCOPA Sleep Night	-	5.27 ± 3.67	2.00 ± 3.25	0.007
SCOPA Sleep Day	-	3.60 ± 2.87	6.25 ± 4.55	0.036
RBD Screening Questionnaire	-	5.15 ± 3.6	6.38 ± 3.58	0.518
Sensory/Motor				
Sniffin Sticks	-	5.81 ± 2.79	3.47 ± 2.63	0.001
MDS-UPDRS III	-	20.77 ± 10.55	37.70 ± 16.93	0.001
Medications				
LEDD total (mg/d)	-	433 ± 419	267 ± 452	0.131
Benzodiazepines (% on)	3 (5.4%)	4 (12.5%)	2 (9.1%)	0.543
Antidepressants (% on)	0 (0.0%)	5 (15.6%)	5 (22.7%)	0.010 ^{a,b,c}
Cholinesterase Inhibitors (% on)	0 (0.0%)	1 (3.1%)	9 (40.9%)	< 0.001 ^{b,c}
Demographic, clinical and questionnaire data				

Values are displayed as number (proportion as a percentage) or mean±standard deviation.

P values were calculated using non-parametric permutation testing and chi-squared tests where applicable. DLB, dementia with Lewy bodies; HC, healthy controls; LEDD, Levodopa Equivalent Daily Dose; MDS-UPDRS I, Unified Parkinson's Disease Rating Scale Section I; MDS-UPDRS II, Unified Parkinson's Disease Rating Scale Section II; MDS-UPDRS III, Unified Parkinson's Disease Rating Scale Section III; MMSE; The Mini Mental State Examination; PD, Parkinson's disease; RBD, REM Sleep Behaviour Disorder; SCOPA, Scales for Outcomes in Parkinson's disease.

^aPairwise comparisons: significant differences between PD and HC

Pairwise comparisons: significant differences between DLB and HC

Pairwise comparisons: significant differences between DLB and PD

Sleep Macroarchitecture

Sleep macroarchitecture measures are summarised in Table 2. Overall, sleep continuity and stage distribution were broadly comparable across groups. Total sleep time, sleep efficiency, wake after sleep onset (WASO), and REM onset latency did not differ significantly. Sleep latency was shorter in both PD and DLB compared to HC ($p_{FDR}=0.015$). REM sleep proportion differed modestly across groups ($p_{FDR}=0.049$), with lower REM% observed in PD and DLB relative to HC. No significant group differences were identified in the proportions of N1, N2 or N3 sleep.

Respiratory disturbance measures were comparable across groups. The total arousal index was higher in healthy controls than in PD, while the periodic limb movement arousal index was higher in DLB than in PD. These secondary differences were small and are detailed in Table 2.

Sleep macro-architecture data.

Values are displayed as mean±standard deviation.

P values were calculated using non-parametric permutation testing. AHI, Apnea Hypopnea Index; DLB, dementia with Lewy bodies; NREM, Non-rapid Eye Movement Sleep; N1, Sleep stage 1; N2, Sleep stage 2; N3, Sleep Stage 3; RDI, Respiratory Disturbance Index; PLM, Periodic Limb Movement; RERA, Respiratory Effort-Related Arousal; REM, Rapid Eye Movement Sleep; PD, Parkinson's disease; WASO, Wake After Sleep Onset.

Pairwise comparisons: significant differences between PD and HC

Pairwise comparisons: significant differences between DLB and HC

Pairwise comparisons: significant differences between DLB and PD

Sleep spindle density is reduced across LBD

Fast spindle density was markedly reduced across LBD, with significant group differences at every electrode ($p_{FDR}<0.05$; Fig. 1 and Supplementary Table 1) and the largest reductions over central and parietal regions. DLB showed the lowest fast spindle density, significantly below controls at all electrodes and below PD at most derivations (F3, F4, C3, C4, O1, O2), whereas in PD the reduction relative to HC reached significance at frontal, central and parietal but not occipital derivations. At C3, fast spindle density was 1.75 ± 0.91 spindles/min in HC, compared with 1.01 ± 0.74 in PD and 0.27 ± 0.29 in DLB (reductions of 42% and 85%, respectively).

Slow spindle density showed a broadly similar pattern, with widespread group differences across electrodes ($p_{FDR} < 0.05$). DLB had lower slow spindle density than both HC and PD across most derivations, whereas PD–HC differences were less consistent (Supplementary Table 1). To confirm these group differences were not driven by medication use, the spindle-density analyses were repeated with additional adjustment for antidepressant, benzodiazepine and cholinesterase-inhibitor use and levodopa equivalent daily dose; all differences remained significant (Supplementary Table 2). Slow spindle duration was reduced in DLB and PD relative to controls at F4 ($p_{FDR} < 0.001$) and in DLB at O1 ($p_{FDR} = 0.006$); spindle amplitude did not differ significantly between groups after false discovery rate correction.

Centro-occipital slow oscillation deficits are specific to DLB

Group-level SO measures are summarized in Fig. 1 and Supplementary Table 3. In contrast to the more widespread spindle deficits observed across LBD, SO alterations were spatially restricted and observed predominantly in DLB. SO density was lower in DLB compared to HC at the occipital (O1: $p_{FDR} < 0.001$) and central electrodes (C4: $p_{FDR} < 0.001$; C3: $p_{FDR} = 0.010$). No significant differences in SO density were identified between HC and PD at any electrode. SO peak-to-peak amplitude showed reduction in DLB, with HC vs DLB significant differences at O1 ($p_{FDR} = 0.013$). Duration was increased at F3 in DLB ($p_{FDR} = 0.044$). No other differences in SO amplitude, duration or slope survived false discovery rate correction. These reductions in SO density were similarly unchanged after additional adjustment for medication use (Supplementary Table 4).

Spindle-slow oscillation coupling is altered in DLB

The proportion of spindles coupled to a detected SO was comparable across healthy controls, PD and DLB (approximately 27%, 31% and 29% respectively). The coupling differences described below may reflect the reduced number of spindles rather than a failure of spindles to co-occur with SO (Supplementary Table 5).

At the frontal derivation, fast spindles were phase-locked to the rising slope of the SO, approaching the up-state peak, in HC (preferred phase $251^\circ \pm 66^\circ$; $p = 0.52$; Rayleigh $p < 0.001$) and PD ($262^\circ \pm 68^\circ$; $p = 0.49$; Rayleigh $p < 0.001$). In DLB, fast spindle-SO coupling was weaker and its phase distribution did not depart from uniform ($251^\circ \pm 83^\circ$; $p = 0.35$; Rayleigh $p = 0.104$), consistent with the markedly reduced number of fast spindles; DLB fast spindle-SO coupling estimates should therefore be interpreted with caution. Neither coupling magnitude nor preferred phase differed significantly between groups for fast spindles (group $p_{FDR} = 0.15$ and $p_{FDR} = 0.78$, respectively; Fig. 1 and Supplementary Table 6).

For slow spindles, the preferred coupling phase was strongly concentrated in DLB (preferred phase $303^\circ \pm 44^\circ$; $p = 0.74$; Rayleigh $p < 0.001$) but diffuse in healthy controls ($9^\circ \pm 118^\circ$; $p = 0.12$; Rayleigh $p = 0.471$) and PD ($305^\circ \pm 116^\circ$; $p = 0.13$; Rayleigh $p = 0.576$), in whom the phase distribution did not differ from

uniform. Slow spindle-SO coupling magnitude and preferred phase both differed significantly between groups at the frontal derivation (group $p_{FDR} = 0.019$ and $p_{FDR} = 0.031$, respectively), and the group difference in preferred phase was also significant at the central derivation (C3: group $p_{FDR} < 0.001$; Supplementary Table 6). Phase distributions were thus concentrated in DLB but diffuse in HC and PD.

Frontal NREM spectral power is altered in DLB

Differences in NREM spectral power are shown in Fig. 2 and Supplementary Table 7. Significant group differences were confined to the frontal derivation, with no differences identified at C3 or O1 after FDR correction. At F3, beta-band power (16–30 Hz) was higher in DLB than in both HC and PD ($p_{FDR}=0.004$). Frontal theta power (4–8 Hz) was also higher in DLB than in HC only ($p_{FDR}=0.023$). No significant group differences were observed in delta, alpha or sigma power, or in total spectral power during NREM sleep (Supplementary Table 7). The frontal beta increase remained significant after additional adjustment for medication use (Supplementary Table 8).

NREM directional connectivity may be disrupted in LBD

Phase slope index (PSI) analyses identified group differences in directed phase relationships during NREM sleep at 20 electrode-by-frequency combinations after FDR correction, concentrated in the delta (1–5 Hz) and sigma (11–17 Hz) ranges (Supplementary Table 9). Across the spectrum, frontal and central derivations tended to show positive PSI (outgoing, source-like) and parietal and occipital derivations negative PSI (incoming, sink-like); this frontoposterior organisation was attenuated in the LBD groups, most clearly in the sigma band. In the 13–17 Hz sigma band, PSI at Fz was lower in PD than in healthy controls (2.38 ± 2.62 versus 4.96 ± 3.87), and posterior PSI shifted from negative in healthy controls (O1: -3.41 ± 3.29 ; O2: -3.86 ± 3.17) to near zero or positive in DLB (O1: 0.23 ± 1.53 ; O2: 0.71 ± 1.30). Given the number of electrode-by-frequency comparisons and the spatial limitations of scalp EEG, these findings were considered exploratory.

Thalamic and cortical structure differs across LBD

Structural magnetic resonance imaging (MRI) was available for 77 participants: 45 healthy controls, 16 with PD and 16 with DLB. Bilateral thalamic volumes differed across groups in all examined nuclei (all $p_{FDR}<0.001$; Fig. 3 and Supplementary Table 10). Post-hoc comparisons demonstrated a consistent pattern of graded atrophy, with both PD and DLB showing reduced volumes relative to healthy controls. All nuclei were significantly smaller in DLB compared to HC (all $p_{FDR}<0.001$), while PD also exhibited bilateral reductions across all nuclei relative to HC (all $p_{FDR}<0.05$). Direct differences between PD and DLB were limited to the right ventral latero-dorsal nucleus ($p_{FDR}=0.026$).

Significant cortical thinning was demonstrated in 54 of 68 parcels (all $p_{FDR}<0.05$; Fig. 3 and Supplementary Table 11). These effects were predominantly driven by DLB, which showed widespread

reductions relative to HC across posterior and association cortices, including bilateral posterior cingulate, precuneus, precentral, paracentral, superior and middle temporal, lingual, and pericalcarine regions (all $p_{FDR} < 0.001$). Cortical thinning in PD was more restricted. Direct differences between PD and DLB were identified only in the left supramarginal and right pars opercularis regions ($p_{FDR} < 0.05$). Global cortical thickness was reduced in both PD and DLB groups relative to HC (HC: 2.42 ± 0.11 mm; PD: 2.34 ± 0.12 mm; DLB: 2.20 ± 0.09 mm; $F = 19.52$, $p < 0.001$).

Thalamic volume is associated with spindle density and slow spindle coupling in LBD

Within the combined LBD cohort, larger thalamic volumes were associated with greater spindle density after adjustment for age and sex (Fig. 3 and Supplementary Table 12). Slow spindle density at F3 and C3 was positively associated with volume across all thalamic nuclei (all $p_{FDR} < 0.05$; Fig. 3 (bottom left)/Supplementary Table 12), with the strongest effects observed in the left ventral anterior (F3: $p_{FDR} = 0.006$; C3: $p_{FDR} = 0.011$) and left ventral latero-dorsal nuclei (F3: $p_{FDR} = 0.004$; C3: $p_{FDR} = 0.007$). Associations with fast spindle density were more spatially restricted, reaching significance primarily at C3, where larger volumes across the examined thalamic nuclei were associated with greater fast spindle density (all $p_{FDR} < 0.05$). The largest effects were again observed in the ventral anterior and ventral latero-dorsal nuclei. In an exploratory sensitivity analysis within the LBD cohort additionally adjusting for diagnosis, no association survived FDR correction; however, central fast spindle density remained associated at an uncorrected level, with the left central lateral–lateral posterior–medial pulvinar ($\beta = 0.272$, $p = 0.028$) and the bilateral ventral latero-ventral nuclei (left: $\beta = 0.216$, $p = 0.042$; right: $\beta = 0.288$, $p = 0.018$; Supplementary Table 13). Thalamic volumes were also associated with greater slow spindle–SO coupling magnitude across the examined nuclei (Supplementary Table 14). The strongest associations were observed in the left ventral anterior ($\beta = 0.105$, $p = 0.001$) and left ventral latero-dorsal nuclei ($\beta = 0.091$, $p = 0.001$). Thalamic volume was not significantly associated with fast spindle coupling magnitude.

Thalamic structure was associated principally with spindle density and the consistency of slow spindle–slow oscillation coupling and no significant associations were observed between thalamic volume and slow oscillation density after false discovery rate correction (Supplementary Table 15).

Cortical thickness is associated with spindle–SO coupling in LBD

Slow spindle–SO coupling magnitude was positively associated with global cortical thickness across LBD ($p = 0.049$; Supplementary Table 16). No significant associations were identified for fast spindle–SO coupling magnitude. Furthermore, global cortical thickness was not significantly associated with slow or fast spindle density (Fig. 3; Supplementary Table 17) or SO density (Supplementary Table 18) after FDR correction.

Top left: Group differences in thalamic nucleus volume, displayed as subcortical atlas renderings for the left and right hemispheres and colour-coded by $-\log_{10}(p)$ from age- and sex-adjusted analysis of covariance; darker shading indicates greater statistical significance. Below each rendering, heatmaps show $-\log_{10}(p)$ for each pairwise post-hoc comparison (HC vs PD, HC vs DLB, PD vs DLB) across the seven thalamic nuclei, separately for each hemisphere. **Top right:** Group differences in regional cortical thickness rendered on inflated cortical surface reconstructions and colour-coded by statistical significance ($-\log_{10}(p)$); warmer colours indicate greater significance. **Bottom left:** Age- and sex-adjusted associations between thalamic nucleus volume and spindle density in the combined LBD cohort, shown separately for the left and right hemispheres. Rows correspond to slow- and fast-spindle density at the frontal (F3) and central (C3) derivations; columns to the seven thalamic nuclei. Cells are coloured by the standardised regression coefficient (β) where the association was significant ($p < 0.05$); non-significant associations are left uncoloured. **Bottom right:** Scatterplots of spindle density against global cortical thickness in the combined LBD cohort (PD, orange; DLB, purple) for slow spindles (SS) and fast spindles (FS) at the frontal (F3) and central (C3) derivations (inset heads indicate the derivation). Solid lines show the linear fit with 95% confidence interval; β and p values are from the age- and sex-adjusted linear regression model. Abbreviations: AN, anterior; ANCOVA, analysis of covariance; C3/F3, central/frontal EEG derivations; CLp, central lateral / lateral posterior / medial pulvinar; DLB, dementia with Lewy bodies; FS, fast spindle; HC, healthy controls; LBD, Lewy body disorders; MD, mediodorsal; NREM, non-rapid eye movement; PD, Parkinson's disease; Pul, pulvinar; SS, slow spindle; VA, ventral anterior; VLD, ventral latero-dorsal; VLV, ventral latero-ventral.

Associations with clinical measures

Correlations between sleep physiological measures and clinical severity showed several trend-level effects that did not survive FDR correction (see Supplementary Table 19). Slow spindle density at F3 was negatively associated with motor severity (MDS-UPDRS-III; $\beta = -0.022$, $p = 0.004$, $p_{\text{FDR}} = 0.057$), and slow spindle density at C3 showed a positive trend with global cognition (MMSE; $\beta = 0.042$, $p = 0.006$, $p_{\text{FDR}} = 0.086$).

Discussion

In this study, we identified distinct abnormalities in NREM sleep microarchitecture across PD and especially DLB. Sleep spindle density was reduced in both disorders, with the greatest reductions in DLB, whereas SO abnormalities were more spatially restricted and predominantly observed in DLB. In DLB, the coordination of the few surviving spindles with SOs was altered rather than uniformly reduced, while the proportion of total spindles coupled to SOs was preserved across groups. Interestingly, these features mapped onto specific structural substrates. Within the LBD cohort, smaller thalamic volumes were associated with lower spindle density and weaker slow spindle–SO coupling, while global cortical thinning showed a more exploratory association with weaker spindle–SO coupling. Together, these findings suggest that spindle-generating circuitry is affected across LBD, with more extensive disruption of coordinated thalamocortical activity in DLB.

Spindle deficits are a transdiagnostic feature of LBD and relate to thalamic integrity

A central finding of this study was the widespread reduction in both slow and fast spindle density across LBD, with DLB exhibiting markedly greater deficits than PD. Fast spindle reductions were significant in both patient groups relative to controls, while slow spindle deficits were most severe in DLB. This pattern provides direct comparative evidence that spindle disruption occurs across both conditions, while suggesting more extensive impairment of spindle-generating circuitry in DLB.

These observations extend findings from prior work in PD demonstrating reduced spindle density in early disease and in prodromal populations with isolated REM sleep behaviour disorder, with evidence that lower spindle density predicts subsequent cognitive decline and dementia.^{28–30} By demonstrating that spindle deficits are present in both PD and DLB, but substantially more pronounced in DLB, our findings therefore support spindle disruption as a transdiagnostic marker of thalamocortical dysfunction in LBD.

Spindle density was positively associated with thalamic volume across the examined nuclei in LBD, with the strongest associations in the ventral anterior and ventral latero-dorsal nuclei, regions with dense reciprocal connections to prefrontal and motor association cortices⁴⁵. Given that sleep spindles emerge from reciprocal interactions between thalamocortical relay neurons and inhibitory neurons of the thalamic reticular nucleus^{15,46–48} these findings provide *in vivo* support for disruption of spindle-generating circuitry in LBD. The relative preservation of spindle amplitude despite pronounced reductions in density further suggests that the capacity to generate individual spindle events remains at least partly intact, while their initiation or recruitment becomes less frequent. These associations were attenuated when diagnostic group was included, with only central fast-spindle density remaining nominally associated with ventral and central-lateral/pulvinar nuclei; this may partly reflect the greater deficits in DLB, or reduced power once group is modelled.

Thalamic volume was also associated with slow spindle–SO coupling magnitude, suggesting that thalamic integrity relates not only to spindle generation but also to the consistency with which spindles are coordinated with cortical SOs. These structural changes likely capture several forms of recognized thalamic vulnerability in LBD. Molecular and synaptic abnormalities can occur despite relatively modest local Lewy pathology⁴⁹, while thalamic function may also be affected by degeneration of cholinergic projections from the pedunculopontine and laterodorsal tegmental nuclei^{50,51} and by deafferentation within interconnected basal ganglia, brainstem and cortical networks. The involvement of higher-order nuclei, including the pulvinar, further implicates thalamic systems involved in attention, corticocortical communication and large-scale network integration.^{52,53} Together, these widespread volumetric associations, preserved spindle amplitude and greater abnormalities in DLB support a model of impaired thalamocortical recruitment and coordination rather than failure of a single nucleus or pathological process.

Localised SO deficits in LBD

In contrast to the widespread spindle deficits observed across both patient groups, SO abnormalities were spatially restricted and most pronounced in DLB, with reductions in SO density confined to occipital and central electrodes and no significant differences observed between PD and healthy controls. This topographic specificity is broadly consistent with the well-established posterior-dominant pattern of cortical atrophy in DLB, particularly affecting parietal and occipital association cortices.^{54,55} From a mechanistic perspective, this regional pattern is consistent with the known dependence of SO generation on local cortical network integrity, as slow waves arise from synchronized transitions between neuronal up- and down-states within corticocortical circuits rather than global sleep drive.^{46,56} The relative preservation of slow oscillations in PD also argues against a uniform reduction in all NREM oscillatory activity and supports a more selective, or a gradient-like, disruption of sleep microarchitecture.

Spindle–SO coupling is altered in DLB

A more nuanced picture emerged for spindle–SO coupling than a simple reduction. Spindles that were generated continued to arrive during SO at comparable rates across groups. The coupling changes we observed are predominantly derived from the profound loss of spindles rather than a failure of co-occurrence. Apparent group differences in raw phase-locking strength were moreover confounded by the differences in spindle numbers between groups where the resultant vector length was altered due to the few available events.⁵⁷ Even after surrogate correction, the fast-spindle comparison was uninterpretable in DLB owing to the near-absence of fast spindles. Unexpectedly, the residual slow spindles in DLB were more phase-concentrated to the slow oscillation than in controls or PD. Rather than enhanced coordination, this most plausibly reflects a higher concentration of phase-locked spindles, driven by a small surviving population of stereotyped slow spindles, and cautions against interpreting greater phase-locking as preserved thalamocortical function. Taken together, these observations reframe the coupling result: the dominant abnormality across LBD is the loss of spindles themselves, with the coordination of the few remaining events altered rather than uniformly reduced.

The association between slow spindle–slow oscillation coupling magnitude and global cortical thickness across LBD is consistent with a contribution from distributed cortical networks; a comparable link between cortical atrophy and degraded slow wave–spindle coupling has been reported in ageing.⁵⁸ Alongside the parallel thalamic-volume association, this points to both cortical and thalamic integrity supporting the temporal alignment of spindles with the slow oscillation through reciprocal corticothalamic loops.⁵⁹

Frontal beta activity is altered in DLB

Beyond spindle and slow oscillation abnormalities, DLB was associated with increased frontal beta power during NREM sleep. Pathological beta activity is well recognised in basal ganglia–cortical circuits in PD and can persist across sleep states, but its expression in scalp-recorded sleep EEG remains less well understood.^{34,60–63} The greater beta elevation in DLB than in PD suggests that it may reflect broader state-independent network dysregulation rather than motor disease severity alone. The elevation

remained significant after adjustment for medication use, arguing against a pharmacological explanation. We did not examine the structural correlates of frontal beta power, and functional or neurochemical abnormalities within basal ganglia–thalamocortical and neuromodulatory systems remain plausible substrates for future work to test directly.

Frontoposterior directional connectivity is disrupted across the disease spectrum

Exploratory analyses of the phase slope index provided complementary evidence of altered network organisation, particularly within the sigma range. The usual pattern of frontal and central outgoing directionality and posterior incoming directionality was attenuated in PD and more clearly disrupted in DLB. Although scalp EEG cannot identify the anatomical pathways underlying these phase relationships, the findings are consistent with reduced organisation of frontoposterior activity during NREM sleep. Together with the spindle and coupling abnormalities, these results suggest that DLB involves disruption not only of individual oscillatory events but also of their coordination across distributed brain networks.

Clinical and biomarker implications

Collectively, our findings highlight the potential of sleep EEG as a low-cost, scalable, and mechanistically informative tool in LBD. Different NREM features appear to capture distinct neurobiological processes. Because many patients with LBD already undergo polysomnography as part of clinical assessment, these measures could potentially be extracted from routine recordings without additional invasive or costly investigations. However, their value for diagnosis, prognosis, disease staging or treatment stratification will require longitudinal validation and demonstration of reliability across recording systems and cohorts. The absence of clinical associations surviving correction may reflect limited power and the use of broad measures such as the MMSE and MDS-UPDRS III, which may not capture the specific cognitive and circuit functions indexed by NREM oscillations.

Limitations and future directions

Several limitations should be acknowledged. The cross-sectional design precludes causal or longitudinal inference, and prospective studies, particularly in prodromal populations with isolated REM sleep behaviour disorder, are required to determine whether these EEG markers predict disease onset, subtype, and progression. The DLB sample was modest in size, which may have reduced sensitivity to detect more subtle effects, particularly for the structural correlation analyses. EEG data were acquired across three recording systems with different sampling rates and although recordings were harmonised prior to analysis, the potential contribution of recording platform to inter-individual variability cannot be fully excluded. Medication use, including dopaminergic, cholinergic, and other psychoactive agents, may have influenced sleep physiology and cannot be fully disentangled from disease effects in a clinically representative cohort of this kind. Finally, while structural MRI provides important anatomical context, integration with functional neuroimaging and molecular markers of dopaminergic and cholinergic integrity would substantially clarify the mechanisms underlying the observed electrophysiological abnormalities, particularly for the beta power and connectivity findings.

Future research should prioritise longitudinal cohorts and prodromal populations, particularly individuals with isolated REM sleep behaviour disorder, to establish whether NREM microarchitectural abnormalities precede clinical diagnosis and predict disease subtype. Multimodal approaches integrating sleep EEG with dopaminergic and cholinergic PET imaging will be critical for directly linking oscillatory dynamics to specific neurotransmitter pathologies, an essential step in validating these measures as mechanistically grounded biomarkers. Diffusion imaging could complement our volumetric measures by mapping locus coeruleus–thalamo-cortical circuit integrity and, through perivascular indices, its association with these neurophysiological signatures. Extending this framework across the Alzheimer's disease continuum may help dissociate Alzheimer- from Parkinson-related contributions in DLB. High-density EEG or simultaneous EEG–fMRI during sleep would enable source localisation of the connectivity moving beyond scalp-level observations toward circuit-specific characterisation.

NREM sleep abnormalities in LBD extend beyond conventional sleep architecture to involve spindle generation and the temporal coordination of thalamic and cortical oscillations. Across the LBD spectrum, spindle density was reduced, while slow oscillation and spindle–slow oscillation coupling abnormalities were most prominent in DLB. Their associations with thalamic volume, and more exploratory relationships with cortical thickness, support widespread disruption of thalamocortical circuitry. These findings highlight sleep EEG as a non-invasive and accessible framework for investigating and monitoring circuit dysfunction in LBD.

Methods

Study Design and Participants

Participants with a clinical diagnosis of either DLB or PD were recruited from the Brain and Mind Centre, University of Sydney, together with healthy controls (HC). All participants were assessed by a specialist neurologist; PD and DLB diagnoses were made in accordance with current clinical consensus criteria.^{64,65} HC participants had no evidence of cognitive impairment on formal neuropsychological testing and were screened to exclude sleep, psychiatric, or neurological disorders. None of the HC participants were receiving serotonergic or noradrenergic reuptake inhibitors, or antipsychotic medications at the time of assessment. All assessments, including PSG and imaging, were conducted while participants remained on their usual anti-parkinsonian medications, with dopaminergic dose equivalents calculated using standard conversion formulas.

All participants provided written informed consent in accordance with the Declaration of Helsinki. The study was approved by the University of Sydney Human Research Ethics Committee.

Polysomnographic Data Acquisition

Overnight laboratory PSG was conducted at the Woolcock Institute of Medical Research, Sydney. Participants were instructed to maintain their habitual sleep schedule in the week prior to the study and

retired at their self-reported habitual bedtime, with morning awakening occurring naturally without enforced wake time. In accordance with the SINBAR guidelines⁶⁶, adopted given the high prevalence of RBD across the LBD spectrum, EEG was recorded according to the international 10–20 system, including referential derivations at F3, F4, C3, C4, O1, and O2, each referenced to the contralateral mastoid (M1 or M2). Additional electrodes were placed at F_Z, C_Z, and P_Z to allow for full midline coverage. EEG data were acquired across three clinical recording systems: 512 Hz (Sandman Elite), 256 Hz (Compumedics Graef), or 200 Hz (Respironics Alice-5), depending on the platform in use at the time of recording. To ensure uniformity, recordings were downsampled to a common rate of 200 Hz prior to analysis. Standard PSG channels additionally included bilateral electro-oculography (EOG), submental and bilateral anterior tibialis electromyography (EMG), electrocardiography (ECG), nasal pressure transducer, thoracic and abdominal inductance belts, body position sensors, and finger pulse oximetry. Sleep stages were manually scored in 30-second epochs by a certified polysomnographic technician according to the American Academy of Sleep Medicine (AASM) criteria.⁶⁷

Sleep EEG Analysis

Pre-processing and Staging

All EEG processing was performed using Luna⁶⁸ (v1.3.4; <http://zzz.bwh.harvard.edu/luna/>), an open-source package for polysomnographic signal analysis. EEG channels were re-referenced to average mastoids and bandpass filtered between 0.3 and 35 Hz. Following frequency down-sampling, artefact rejection was performed in a staged procedure. Channels exhibiting gross or persistent artefact, defined as exceeding 2 SD from the cross-channel mean on any of the three Hjorth parameters (activity, mobility, complexity) in more than 30% of epochs, were excluded, epochs were flagged as artefactual if they exceeded 4 SD on the same Hjorth parameters across all EEG channels, had maximum amplitudes above 500 μ V, or contained flat or clipped signals for more than 10% of the epoch. Finally, within-channel outlier epochs were identified using a 4 SD threshold on Hjorth parameters; epochs flagged in at least one channel were excluded from all channels, ensuring a consistent epoch set across the montage. Cleaned data were visually inspected prior to analysis. All N2 and N3 sleep epochs were analysed as a single consolidated stage. Sleep stage discrimination is increasingly unreliable in older adults and those with neurodegeneration, where N2 and N3 boundaries are frequently conflated⁶⁹; pooling NREM epochs avoids these artefacts and improves analytic reliability.

Sleep Spindle Detection

Sleep spindles were detected using a wavelet-based algorithm with separate identification of slow (SS; centre frequency 11 Hz) and fast spindles (FS; centre frequency 15 Hz), in each case detecting spindles within ± 2 Hz of the target frequencies, as described by Purcell et al. (2017).¹⁶ These centre frequencies

were selected to minimise spectral overlap between SS and FS populations and to maximise their known topographic and coupling differences. Spindle detection was applied to N2 and N3 sleep epochs only.

Putative spindles were identified from the magnitude of the temporally smoothed wavelet coefficient (Morlet wavelet; smoothing window = 0.1s). For each channel, a baseline was defined as the mean of this smoothed wavelet-coefficient magnitude across all artefact-free NREM sample epochs. Intervals were detected as spindles where a channel simultaneously exceeded (1) $4.5 \times$ this mean for at least 300 ms and (2) $2 \times$ the mean for at least 500 ms. Events exceeding 3 s in duration were rejected; consecutive events occurring within 500 ms were merged, unless the merged spindle exceeded 3 s. Putative spindles were additionally excluded if the relative increase in non-spindle band activity (delta, theta, and beta) was greater than the corresponding increase in spindle-frequency activity, ensuring detected events reflected genuine sigma-band oscillations rather than broadband amplitude increases. For each spindle type and channel, we computed spindle density (count per minute of NREM sleep), mean peak-to-peak amplitude (μV) and duration (s).

Slow Oscillation Detection

SOs were detected from EEG signals bandpass filtered between 0.3 and 4 Hz. Zero-crossings of the filtered signal were identified and putative SOs were accepted if; the interval from a downward to subsequent upward zero-crossing (negative half-wave) was between 0.3 and 1.5 s, and; the interval from an upward to subsequent downward zero-crossing (positive half-wave) did not exceed 1.0 s. Adaptive, participant-specific amplitude thresholds were applied, requiring the negative peak and peak-to-peak amplitude to exceed twice the individual and channel-specific mean.⁷⁰ SO density was expressed as count per minute of NREM sleep. Additional secondary measures were calculated including mean negative peak amplitude (μV), mean peak-to-peak amplitude (μV), mean duration (s), and mean negative-to-positive peak slope ($\mu\text{V/s}$).

Spindle–SO Temporal Coupling

Spindle–SO coupling was assessed separately for slow and fast spindles at each derivation. For every detected spindle, the instantaneous phase of the concurrent SO was estimated by Hilbert transform of the 0.3–4 Hz band-pass-filtered signal, and the SO phase at the peak of the spindle envelope was recorded. The SO trough and up-state fall at approximately 90° and 270° respectively. The proportion of spindles overlapping a detected SO was calculated as a descriptive index of whether spindles arrived during SOs (co-occurrence rate). Preferred coupling phase and phase-locking strength were quantified using circular statistics: the circular mean provided the preferred phase angle, the mean resultant vector length (ρ) indexed phase concentration, and the Rayleigh test assessed departure from uniformity. Because the resultant vector length is upward-biased when few events are available, coupling magnitude was expressed as a surrogate-corrected z-score relative to a null distribution generated by shuffling spindle peak times within NREM sleep over 10,000 iterations.

Spectral Power Analysis

Spectral power was estimated over the frequency range 0.5–30 Hz using Welch's method. For each 30-second epoch, power spectra were computed using fast Fourier transform (FFT) applied to 4-second sub-segments, windowed with a Tukey taper ($\alpha = 0.5$) and 50% overlap. Power estimates were averaged across all artefact-free NREM epochs per participant. Band-limited power was extracted for canonical frequency ranges: slow oscillation (SO; 0.5–1.0 Hz), delta (1.0–4.0 Hz), theta (4.0–8.0 Hz), alpha (8.0–12.0 Hz), slow sigma (12.0–15.0 Hz), fast sigma (15.0–16.0 Hz), and beta (16.0–30.0 Hz).

To reduce redundancy and multiple comparisons, hemispheric differences were first assessed and no significant left–right effects were observed across frequency bands (all $p > 0.05$). Accordingly, spectral analyses were conducted using representative electrodes for frontal (F3), central (C3), and occipital (O1) regions.

Functional Connectivity

An exploratory analysis of functional connectivity between EEG channels was assessed using the phase slope index, a frequency-domain measure of directed interactions that reduces the influence of volume conduction by relying on the imaginary component of coherence and non-zero lagged phase differences. PSI captures the consistency of phase lead–lag relationships across neighbouring frequencies, such that positive values indicate a leading (source) signal and negative values indicate a lagging (receiving) signal.

For each participant, 10 minutes of NREM (20 epochs) were randomly selected. Within each 30-second epoch, PSI was estimated from 3 to 20 Hz in 1 Hz steps, using a 5 Hz sliding frequency window to derive the local phase slope. Spectral estimates were calculated from 4-second segments with 50% overlap. PSI values were normalised within each epoch using the standard deviation of the estimator and subsequently averaged across epochs.⁷¹

To summarise directional connectivity at the channel level, a net PSI metric was calculated for each electrode by summing PSI values across all connections involving that channel. This approach provides a single estimate of directional balance, where positive values reflect a predominance of outgoing (source-like) influences and negative values reflect incoming (sink-like) influences.

Clinical Assessments

Clinical assessment was completed within four months of the overnight PSG recording by a subspecialist neurologist. Motor severity was quantified using the Movement Disorder Society Unified Parkinson's Disease Rating Scale Part III (MDS-UPDRS III). Subjective daytime sleepiness was assessed using the Epworth Sleepiness Scale (ESS) and nocturnal and daytime sleep symptoms were evaluated

using the corresponding Scales for Outcomes in Parkinson's Disease–Sleep (SCOPA-Sleep) subscales. Global cognitive status was assessed with the Mini-Mental State Examination (MMSE). Clinical associations were considered secondary analyses.

MRI Data Acquisition and Processing

Structural magnetic resonance imaging (MRI) was available for 77 participants: 45 healthy controls, 16 with PD and 16 with DLB. Imaging was performed on a 3-Tesla General Electric scanner using a sagittal three-dimensional T1-weighted sequence (echo time [TE] = 2.7 ms, repetition time [TR] = 7.2 ms, acquisition matrix = 256 × 256, 200 contiguous slices, 1 mm isotropic resolution).

T1-weighted images were processed using the Computational Anatomy Toolbox (CAT12) implemented in SPM12 (Wellcome Centre for Human Neuroimaging, London, UK) running in MATLAB R2023a (MathWorks, Natick, MA). Images were bias-corrected, segmented into grey matter, white matter, and cerebrospinal fluid, and spatially normalised using the standard CAT12 pipeline.

Thalamic volumes were extracted using atlas-based parcellation according to the in-vivo probabilistic atlas of human thalamic nuclei in the Human Connectome Project⁷², yielding regional estimates for thalamic subdivisions in native space. Total intracranial volume (TIV) was estimated within CAT12, and thalamic volumes were adjusted for TIV using the residuals method.⁷³ Cortical thickness was estimated using the surface-based reconstruction implemented in CAT12. Vertex-wise thickness measures were derived from the distance between the white matter and pial surfaces and mapped to a standard surface template. Regional cortical thickness estimates were extracted according to the Desikan–Killiany atlas⁷⁴ for statistical analysis.

Subcortical structures were visualised using the subcortex_visualization toolbox⁷⁵ (github.com/anniegbyrant/subcortex_visualization) and cortical thickness was displayed using yabplot (github.com/teanijarv/yabplot).

Statistical Analysis

All statistical analyses were performed in R (version 4.5.3). Continuous variables are reported as mean ± standard deviation unless otherwise specified.

Demographic, clinical and conventional polysomnographic variables were compared across diagnostic groups using one-way analysis of variance (ANOVA) for continuous variables and χ^2 tests for categorical variables, with post-hoc pairwise comparisons corrected for multiple comparisons using the Benjamini–Hochberg false discovery rate (FDR) method.

Group differences in EEG-derived and MRI measures were assessed using permutation-based analysis of covariance (ANCOVA) with 10,000 permutations and age and sex included as covariates,

implemented separately for each electrode and metric. Post-hoc pairwise group comparisons were conducted on residuals derived from the covariate-adjusted models, with inference based on the two-tailed permutation distribution of the signed t-statistic. The one exception was spindle–SO preferred coupling phase, a circular measure, for which group differences were assessed using the Watson–Wheeler test and interpreted alongside the per-group mean resultant vector length and Rayleigh test results; spindle–SO coupling magnitude was analysed within the permutation-ANCOVA framework described above.

To limit redundant comparisons, spectral analyses were restricted to representative frontal, central and occipital derivations (F3, C3 and O1), while spindle, SO and coupling analyses were performed across the available electrode montage. FDR correction was applied separately within each prespecified outcome family: spectral power, slow spindle measures, fast spindle measures, slow oscillation measures, spindle–SO coupling measures, thalamic nucleus volumes, and regional cortical thickness. Statistical significance was defined as $pFDR < 0.05$ throughout.

To confirm that group differences were not attributable to medication, the spindle-density, slow-oscillation-density and frontal beta-power analyses were repeated within the same permutation-ANCOVA framework with additional adjustment for antidepressant, benzodiazepine and cholinesterase-inhibitor use and levodopa equivalent daily dose (LEDD).

Associations between sleep EEG measures and structural or clinical variables were examined across the combined LBD cohort (PD and DLB) using general linear models adjusted for age and sex, with separate models constructed for thalamic nucleus volumes and cortical thickness measures. FDR correction was applied within each structural family for a given EEG measure, that is, across thalamic nuclei and across cortical parcels respectively. These analyses were restricted to the frontal (F3) and central (C3) derivations, selected a priori on the basis of the well-established topographic segregation of slow and fast spindles (frontal and centroparietal predominant, respectively)¹⁶ and the frontal predominance of slow oscillations.⁵⁶ As no significant hemispheric asymmetry was observed, these single derivations were considered sufficient to capture spatially distinct but functionally relevant regions while limiting multiple comparisons. As a sensitivity analysis, the thalamus–spindle models were repeated with additional adjustment for diagnostic group.

Data and Code Availability

A key resources table, de-identified derived data supporting the reported findings, a data dictionary, and analysis code are available on Zenodo at <https://doi.org/10.5281/zenodo.22121856>. Raw participant-level data are not openly available because they contain sensitive human participant information and are subject to ethics, consent and privacy restrictions. Requests for access to restricted data may be directed to the corresponding author and will be reviewed by the relevant institutional committee.

Declarations

Acknowledgements

We would like to acknowledge participants and caregivers for their efforts participating in this study.

Funding

JA and AI are recipients of the Australian Postgraduate Award. LC is the recipient of the Bierzonski Burczyk Foundation Postgraduate Research Scholarship. AK is supported by the Australian Rotary Health of Belconnen 50th Anniversary PhD scholarship (SC4968). SLN is supported by the Dementia Leadership Fellowship (APP1135639). ALD is supported by a National Health and Medical Research Council Emerging Leadership Fellowship (2008001) RRG is supported by a National Health and Medical Research Council Leadership Fellowship (1197439). SJGL is supported by a National Health and Medical Research Council Leadership Fellowship (1195830) and has received research funding from the Michael J. Fox Foundation and the Australian Research Council, as well as consulting for Pharmaxis Ltd. EM is supported by a National Health and Medical Research Council Emerging Leadership Fellowship (2008565), the U.S. Department of Defense Congressionally Directed Medical Research Program Early Investigator Grant (PD220061) and the University of Sydney Horizon Fellowship. This work was also supported in part by Aligning Science Across Parkinson's (027449) through the Michael J. Fox Foundation for Parkinson's Research.

Author Contributions

Author roles included: conception and design of the study (JA, RRG, SJGL, EM); acquisition and analysis of data (JA, LC, AK, AI, GC); and final approval of manuscript and/or figures (JA, LC, AK, AI, GC, AL, SLN, ALD, RRG, SJGL, EM). All authors declare accountability for the work contained in the manuscript.

Competing Interests

All authors declare no financial or non-financial competing interests.

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Table 2

Table 2 is available in the Supplementary Files section.

Figures

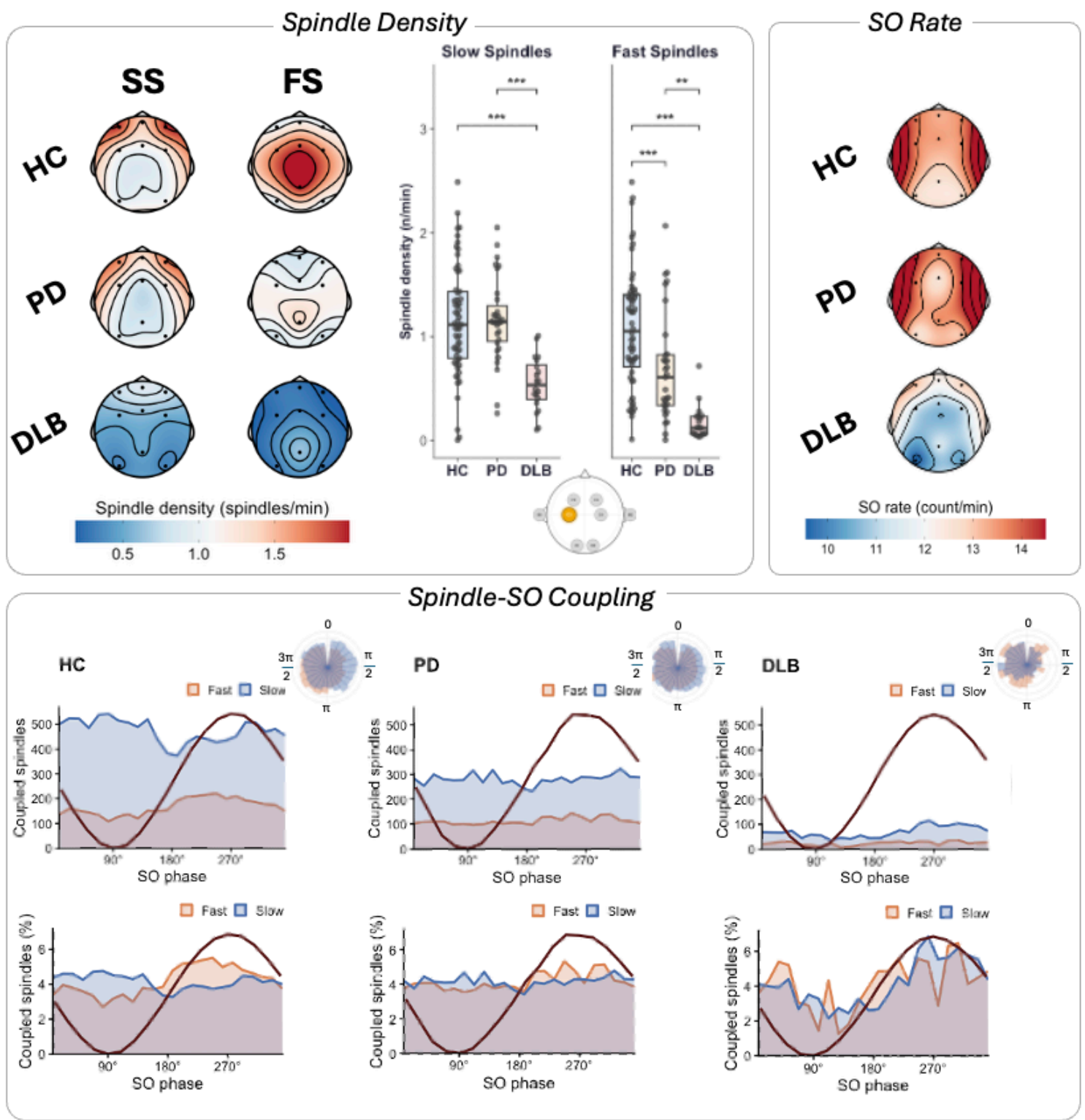


Figure 1

NREM sleep microarchitectural alterations across Lewy body disorders. Sleep spindle density, slow oscillation (SO) rate, and spindle–SO coupling during non-rapid eye movement (NREM) sleep in healthy controls (HC), Parkinson's disease (PD) and dementia with Lewy bodies (DLB). **Top left:** Topographic distributions of slow spindle (SS) and fast spindle (FS) density (spindles/min) across all electrodes for each group, displayed as interpolated scalp maps; warmer colours indicate higher density (colour scale, spindles/min). **Top centre:** Boxplots (median, interquartile range and whiskers) with individual data points showing slow- and fast-spindle density at the C3 electrode, a representative central derivation. Horizontal brackets denote pairwise group differences surviving false discovery rate (FDR) correction ($*** p < 0.001$, $** p < 0.01$). **Top right:** Topographic distributions of SO rate (count/min) across all electrodes for each group, displayed as interpolated scalp maps; warmer colours indicate higher rate (colour scale, count/min). **Bottom:** For each group, spindle–SO coupling at the frontal (F3) derivation, shown separately for slow (blue) and fast (orange) spindles with the mean SO waveform overlaid (dark red); the SO trough and up-state fall at approximately 90° and 270° respectively. Within each group, the upper plot shows the number of SO-coupled spindles as a function of SO phase ($0-360^\circ$), and the lower plot shows the same distribution expressed as a percentage of that group's coupled spindles (normalised within each spindle type). The polar histograms (top right of each group) show the preferred SO phase at maximum spindle amplitude for slow and fast spindles (petals scaled to the largest bin in each plot). Abbreviations: DLB, dementia with Lewy bodies; FDR, false discovery rate; FS, fast spindle; HC, healthy controls; NREM, non-rapid eye movement; PD, Parkinson's disease; SO, slow oscillation; SS, slow spindle.

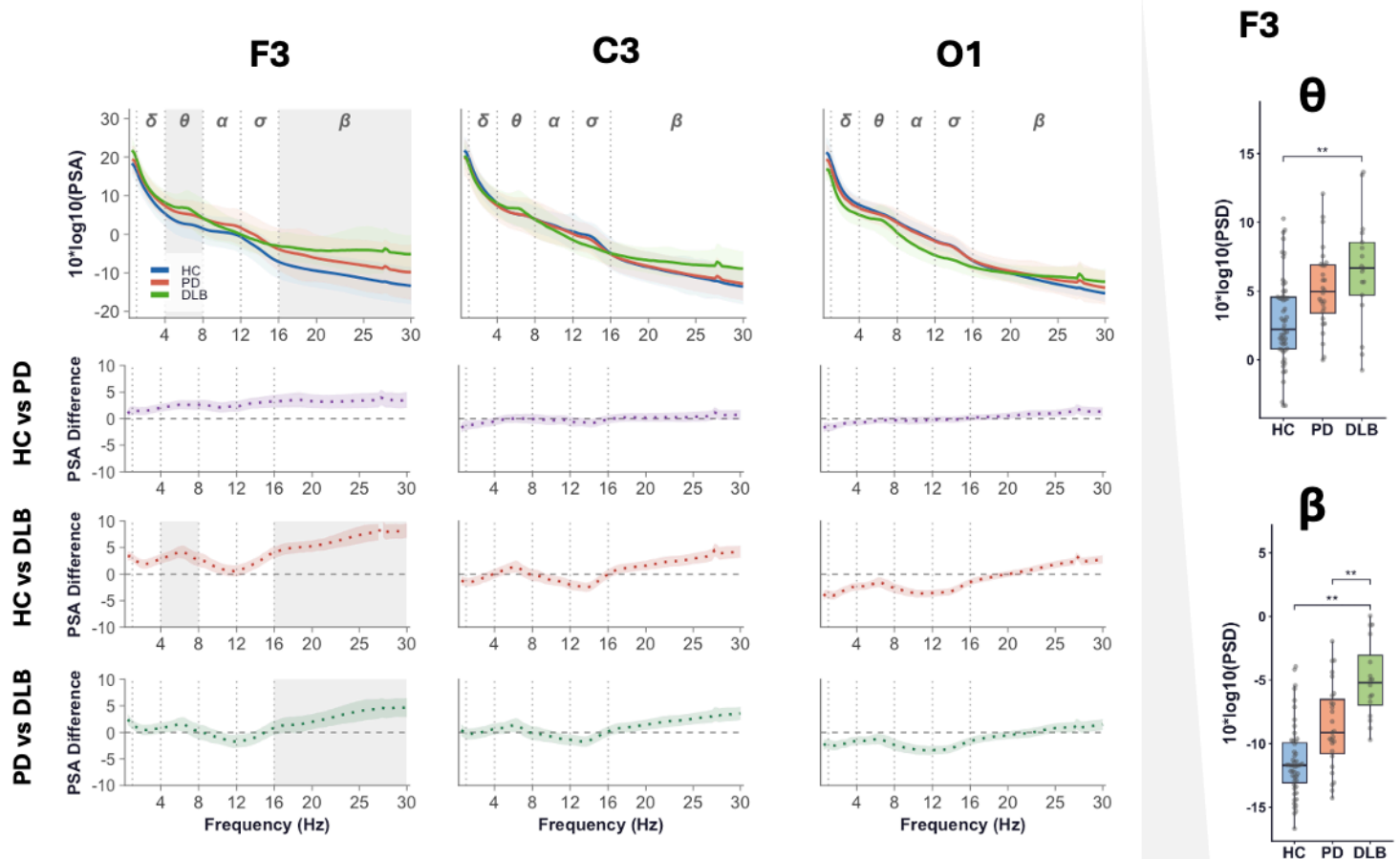


Figure 2

Altered frontal NREM spectral power in dementia with Lewy bodies. **Top row:** Mean NREM power spectral density (PSD, expressed as $10 \cdot \log_{10}[\text{PSD}]$, dB) from 1–30 Hz at representative frontal (F3), central (C3) and occipital (O1) derivations, shown separately for HC (blue), PD (orange) and DLB (green). Shaded ribbons represent ± 1 standard deviation (SD). Vertical dotted lines denote canonical frequency-band boundaries: delta (δ), theta (θ), alpha (α), sigma (σ) and beta (β). Grey shaded regions at F3 highlight the theta (4–8 Hz) and beta (16–30 Hz) bands. **Lower three rows:** Difference in mean PSD between each group pair (HC vs PD, HC vs DLB and PD vs DLB), with positive values indicating greater power in the second group of each labelled pair. Dotted coloured lines show the mean difference and shaded ribbons the standard error (SE) of the difference; grey shaded regions highlight frequency bands with significant group differences after false discovery rate (FDR) correction. **Right:** Individual-level frontal PSD within the theta (4–8 Hz) and beta (16–30 Hz) bands, shown as boxplots (median, interquartile range and whiskers) with individual data points overlaid at F3. Horizontal brackets denote FDR-corrected pairwise group differences, covaried for age and sex (*** $p < 0.001$, ** $p < 0.01$, * $p < 0.05$). Abbreviations: DLB, dementia with Lewy bodies; FDR, false discovery rate; F3/C3/O1, frontal/central/occipital EEG derivations; HC, healthy controls; NREM, non-rapid eye movement; PD, Parkinson's disease; PSD, power spectral density; SD, standard deviation; SE, standard error; δ , delta; θ , theta; α , alpha; σ , sigma; β , beta.

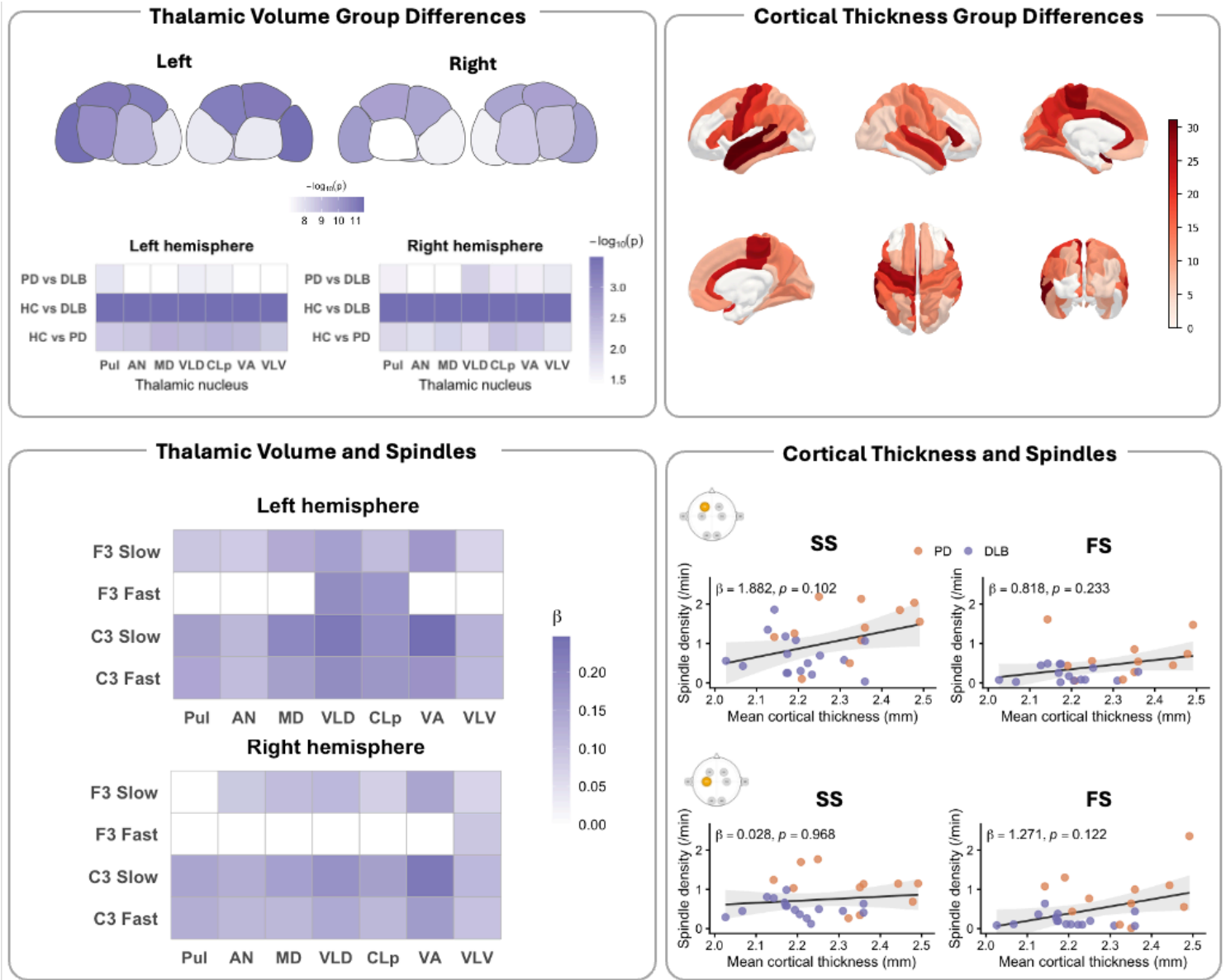


Figure 3

Structural thalamocortical correlates of NREM sleep microarchitecture in Lewy body disorders.

Top left: Group differences in thalamic nucleus volume, displayed as subcortical atlas renderings for the left and right hemispheres and colour-coded by $-\log_{10}(p)$ from age- and sex-adjusted analysis of covariance; darker shading indicates greater statistical significance. Below each rendering, heatmaps show $-\log_{10}(p)$ for each pairwise post-hoc comparison (HC vs PD, HC vs DLB, PD vs DLB) across the seven thalamic nuclei, separately for each hemisphere. **Top right:** Group differences in regional cortical thickness rendered on inflated cortical surface reconstructions and colour-coded by statistical significance ($-\log_{10}(p)$); warmer colours indicate greater significance. **Bottom left:** Age- and sex-adjusted associations between thalamic nucleus volume and spindle density in the combined LBD cohort, shown separately for the left and right hemispheres. Rows correspond to slow- and fast-spindle density at the frontal (F3) and central (C3) derivations; columns to the seven thalamic nuclei. Cells are coloured by the standardised regression coefficient (β) where the association was significant ($p < 0.05$); non-significant

associations are left uncoloured. **Bottom right:** Scatterplots of spindle density against global cortical thickness in the combined LBD cohort (PD, orange; DLB, purple) for slow spindles (SS) and fast spindles (FS) at the frontal (F3) and central (C3) derivations (inset heads indicate the derivation). Solid lines show the linear fit with 95% confidence interval; β and p values are from the age- and sex-adjusted linear regression model. Abbreviations: AN, anterior; ANCOVA, analysis of covariance; C3/F3, central/frontal EEG derivations; CLp, central lateral / lateral posterior / medial pulvinar; DLB, dementia with Lewy bodies; FS, fast spindle; HC, healthy controls; LBD, Lewy body disorders; MD, mediodorsal; NREM, non-rapid eye movement; PD, Parkinson's disease; Pul, pulvinar; SS, slow spindle; VA, ventral anterior; VLD, ventral latero-dorsal; VLV, ventral latero-ventral.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [NREMLBDSupplementaryMaterial.docx](#)
- [Table2.docx](#)