Supplementary Material

Cyclic Alternating Pattern and Sleep Microstructure in Parkinson's Disease: A Systematic Review and Meta-Analysis

Supplementary File 1. Full search strategies

Search period: studies published from January 1, 2020, to September 15, 2025.

Databases searched: MEDLINE via OVID, EMBASE via OVID, CINAHL via EBSCOhost, APA PsycArticles via EBSCOhost, and Evidence-Based Medicine (EBM) databases via EBSCOhost.

1. MEDLINE via OVID (records identified: n=168)

#1 (Parkinson Disease[Mesh] OR parkinson* OR PD OR paralysis agitans)
#2 (Polysomnography[Mesh] OR polysomnogr* OR PSG OR sleep study OR sleep monitor*)
#3 (Sleep[Mesh] OR Sleep Stages[Mesh] OR Sleep, REM[Mesh] OR Sleep, Slow-Wave[Mesh] OR Sleep Architecture[Mesh] OR sleep OR sleep stage* OR rem sleep OR slow wave sleep OR nrem sleep)
#4 (Electroencephalography[Mesh] OR electroencephalogr* OR EEG)
#5 ("sleep spindle"[tiab] OR "sigma activity"[tiab] OR "EEG spectral"[tiab] OR "power spectral"[tiab] OR "cyclic alternating pattern"[tiab] OR CAP[tiab] OR "sleep microstructure"[tiab] OR "micro-arousal"[tiab] OR "delta power"[tiab] OR "theta power"[tiab] OR "alpha power"[tiab] OR "beta power"[tiab] OR "gamma power"[tiab])
#6 (#1) AND (#2 OR #3 OR #4) AND #5

2. EMBASE via OVID (records identified: n=311)

#1 (exp Parkinson disease/ OR parkinson*.mp. OR PD.mp. OR paralysis agitans.mp.)
#2 (exp polysomnography/ OR polysomnogr*.mp. OR PSG.mp. OR sleep study.mp. OR sleep monitor*.mp.)
#3 (exp sleep/ OR exp sleep stage/ OR exp rapid eye movement sleep/ OR exp slow wave sleep/ OR exp sleep architecture/ OR sleep.mp. OR sleep stage*.mp. OR rem sleep.mp. OR slow wave sleep.mp. OR nrem sleep.mp.)
#4 (exp electroencephalography/ OR electroencephalogr*.mp. OR EEG.mp.)
#5 ("sleep spindle".mp. OR "sigma activity".mp. OR "EEG spectral".mp. OR "power spectral".mp. OR "cyclic alternating pattern".mp. OR CAP.mp. OR "sleep microstructure".mp. OR "micro-arousal".mp. OR "delta power".mp. OR "theta power".mp. OR "alpha power".mp. OR "beta power".mp. OR "gamma power".mp.)
#6 #1 AND (#2 OR #3 OR #4) AND #5

3. CINAHL via EBSCOhost (records identified: n=21)

((MH "Parkinson Disease") OR TI (parkinson* OR PD OR "paralysis agitans") OR AB (parkinson* OR PD OR "paralysis agitans") OR KW (parkinson* OR PD OR "paralysis agitans")) AND (((MH "Polysomnography") OR TI (polysomnogr* OR PSG OR "sleep study" OR "sleep monitor*") OR AB (polysomnogr* OR PSG OR "sleep study" OR "sleep monitor*") OR KW (polysomnogr* OR PSG OR "sleep study" OR "sleep monitor*")) OR ((MH "Sleep" OR MH "Sleep Stages" OR MH "REM Sleep" OR MH "Slow Wave Sleep" OR MH "Sleep Architecture") OR TI (sleep OR "sleep stage*" OR "rem sleep" OR "slow wave sleep" OR "nrem sleep") OR AB (sleep OR "sleep stage*" OR "rem sleep" OR "slow wave sleep" OR "nrem sleep") OR KW (sleep OR "sleep stage*" OR "rem sleep" OR "slow wave sleep" OR "nrem sleep")) OR ((MH "Electroencephalography") OR TI (electroencephalogr* OR EEG) OR AB (electroencephalogr* OR EEG) OR KW (electroencephalogr* OR EEG))) AND (TI ("sleep spindle" OR "sigma activity" OR "eeg spectral" OR "power spectral" OR "cyclic alternating pattern" OR CAP OR "sleep microstructure" OR "micro-arousal" OR "delta power" OR "theta power" OR "alpha power" OR "beta power" OR "gamma power") OR AB ("sleep spindle" OR "sigma activity" OR "eeg spectral" OR "power spectral" OR "cyclic alternating pattern" OR CAP OR "sleep microstructure" OR "micro-arousal" OR "delta power" OR "theta power" OR "alpha power" OR "beta power" OR "gamma power") OR KW ("sleep spindle" OR "sigma activity" OR "eeg spectral" OR "power spectral" OR "cyclic alternating pattern" OR CAP OR "sleep microstructure" OR "micro-arousal" OR "delta power" OR "theta power" OR "alpha power" OR "beta power" OR "gamma power"))

4. APA PsycArticles via EBSCOhost (records identified: n=6)

(DE "Parkinson's Disease" OR TI (parkinson* OR PD OR "paralysis agitans") OR AB (parkinson* OR PD OR "paralysis agitans")) AND ((DE "Polysomnography" OR TI (polysomnogr* OR PSG OR "sleep study" OR "sleep monitor*") OR AB (polysomnogr* OR PSG OR "sleep study" OR "sleep monitor*")) OR (DE "Sleep" OR DE "Sleep Stages" OR DE "REM Sleep" OR DE "Slow Wave Sleep" OR DE "Sleep Architecture" OR TI (sleep OR "sleep stage*" OR "rem sleep" OR "slow wave sleep" OR "nrem sleep") OR AB (sleep OR "sleep stage*" OR "rem sleep" OR "slow wave sleep" OR "nrem sleep")) OR (DE "Electroencephalography" OR TI (electroencephalogr* OR EEG) OR AB (electroencephalogr* OR EEG))) AND (TI ("sleep

spindle" OR "sigma activity" OR "eeg spectral" OR "power spectral" OR "cyclic alternating pattern" OR CAP OR "sleep microstructure" OR "micro-arousal" OR "delta power" OR "theta power" OR "alpha power" OR "beta power" OR "gamma power") OR AB ("sleep spindle" OR "sigma activity" OR "eeg spectral" OR "power spectral" OR "cyclic alternating pattern" OR CAP OR "sleep microstructure" OR "micro-arousal" OR "delta power" OR "theta power" OR "alpha power" OR "beta power" OR "gamma power"))

5. Evidence-Based Medicine (EBM) databases via EBSCOhost (records identified: n=30)

("parkinson disease" OR parkinson* OR PD OR "paralysis agitans") AND ("polysomnography" OR polysomnogr* OR PSG OR "sleep study" OR "sleep monitor*" OR "sleep" OR "sleep stages" OR "rem sleep" OR "slow wave sleep" OR "nrem sleep" OR "sleep architecture" OR "electroencephalography" OR electroencephalogr* OR EEG) AND ("sleep spindle" OR "sigma activity" OR "eeg spectral" OR "power spectral" OR "cyclic alternating pattern" OR CAP OR "sleep microstructure" OR "micro-arousal" OR "delta power" OR "theta power" OR "alpha power" OR "beta power" OR "gamma power")

Total records identified: 536.

Supplementary Table S1. Newcastle-Ottawa Scale item-level scoring for included observational studies (maximum 9 stars)

Study	S1	S2	S3	S4	C1	C2	E1	E2	E3	Total
Doppler et al. (2021)[21]	★	-	★	★	★	★	★	★	-	7
Doppler et al. (2022)[25]	★	-	★	★	★	★	★	★	-	7
Cheng et al. (2025)[16]	★	-	-	★	★	★	★	★	-	6
Dagay et al. (2025)[26]	★	-	★	★	★	-	★	★	-	6

Note: S1 = adequate case definition; S2 = representativeness of cases; S3 = selection of controls; S4 = definition of controls; C1 = main factors controlled; C2 = additional factors controlled; E1 = exposure/outcome ascertainment; E2 = same method of ascertainment; E3 = non-response rate. A star indicates that the item was satisfied; a dash indicates that the item was not satisfied or was not clearly reported. Superscript Arabic numerals indicate reference-list numbers in the main manuscript.

Supplementary Table S2. Leave-one-out sensitivity analyses

Panel A. Macrostructural outcomes.

Outcome	Omitted study	Pooled Hedges' g (95% CI)	p	I^2
WASO	Cheng et al. (2025)[16]	0.072 (-0.295 to 0.438)	0.702	0.0%
WASO	Dagay et al. (2025)[26]	0.670 (-0.648 to 1.988)	0.319	88.0%
WASO	Doppler et al. (2022)[25]	0.707 (-0.517 to 1.931)	0.258	87.6%
Sleep efficiency	Cheng et al. (2025)[16]	0.023 (-0.296 to 0.343)	0.886	0.0%
Sleep efficiency	Dagay et al. (2025)[26]	-0.330 (-1.283 to 0.623)	0.498	83.6%
Sleep efficiency	Doppler et al. (2021)[21]	-0.417 (-1.267 to 0.433)	0.336	81.4%
Sleep efficiency	Doppler et al. (2022)[25]	-0.413 (-1.282 to 0.457)	0.352	81.0%
N1 (%)	Cheng et al. (2025)[16]	-0.236 (-0.882 to 0.410)	0.475	60.6%
N1 (%)	Dagay et al. (2025)[26]	-0.433 (-0.894 to 0.029)	0.066	0.0%
N1 (%)	Doppler et al. (2021)[21]	-0.060 (-0.444 to 0.324)	0.759	0.0%
N2 (%)	Cheng et al. (2025)[16]	-0.101 (-0.487 to 0.285)	0.608	0.0%
N2 (%)	Dagay et al. (2025)[26]	0.460 (-0.432 to 1.353)	0.312	72.5%
N2 (%)	Doppler et al. (2021)[21]	0.352 (-0.707 to 1.412)	0.515	84.8%
AHI	Cheng et al. (2025)[16]	-0.212 (-0.533 to 0.109)	0.195	0.0%
AHI	Dagay et al. (2025)[26]	-0.242 (-0.600 to 0.116)	0.186	0.0%
AHI	Doppler et al. (2021)[21]	-0.101 (-0.420 to 0.218)	0.536	0.0%
AHI	Doppler et al. (2022)[25]	-0.062 (-0.392 to 0.269)	0.715	0.0%
REM sleep (%)	Cheng et al. (2025)[16]	-0.050 (-1.463 to 1.362)	0.944	91.3%
REM sleep (%)	Dagay et al. (2025)[26]	-0.172 (-1.863 to 1.518)	0.842	92.0%
REM sleep (%)	Doppler et al. (2021)[21]	-0.851 (-1.253 to -0.449)	<0.001	0.0%

Panel B. CAP-related outcomes.

Outcome	Omitted study	Pooled Hedges' g (95% CI)	p	I^2
CAP rate	Dagay et al. (2025)[26]	-0.821 (-1.267 to -0.375)	<0.001	0.0%
CAP rate	Doppler et al. (2021)[21]	-0.848 (-1.231 to -0.465)	<0.001	0.0%
CAP rate	Doppler et al. (2022)[25]	-0.856 (-1.259 to -0.454)	<0.001	0.0%
CAP sequence duration	Dagay et al. (2025)[26]	-1.088 (-1.547 to -0.629)	<0.001	0.0%
CAP sequence duration	Doppler et al. (2021)[21]	-0.835 (-1.218 to -0.452)	<0.001	0.0%
CAP sequence duration	Doppler et al. (2022)[25]	-0.917 (-1.385 to -0.450)	<0.001	21.2%
CAP index	Cheng et al. (2025)[16]	-0.858 (-1.262 to -0.454)	<0.001	0.0%
CAP index	Dagay et al. (2025)[26]	-0.741 (-1.213 to -0.270)	0.002	0.0%
CAP index	Doppler et al. (2021)[21]	-0.935 (-1.339 to -0.530)	<0.001	0.0%

Note: Rows omitting Doppler et al. (2021) or Doppler et al. (2022) also served as exploratory sensitivity analyses for potential cohort overlap when both studies contributed to the same outcome. CAP = cyclic alternating pattern; CI = confidence interval; WASO = wake after sleep onset; AHI = apnea-hypopnea index; REM = rapid eye movement.

Supplementary Table S3. Summary of EEG spectral-power and sleep-spindle findings in included studies

First author (year)	Sleep spindle characteristics	EEG spectral-power findings
Cheng et al. (2025)[16]	Not reported.	During N3 non-CAP (NCAP) segments, patients with Parkinson's disease showed lower absolute delta power and higher absolute alpha and beta power than healthy controls ($p < 0.05$). During N3 CAP sequences, phase-specific reductions in absolute delta power were reported in A1, B1, and A3 phases, together with increased absolute beta power in A3, B2, and B3 phases. The authors also described a tonic alpha pattern and a shorter proportion of N3 occupied by high-amplitude delta waves (>=75 µV) in the PD group.
Doppler et al. (2021)[21]	Not reported.	Quantitative spectral-power data were not reported. The study focused on CAP metrics and their association with noradrenergic transporter density in arousal-related brain structures.
Doppler et al. (2022)[25]	Not reported.	Quantitative spectral-power data were not reported. The study evaluated CAP dynamics across prodromal, recent, and established stages of Parkinson's disease.
Dagay et al. (2025)[26]	Not reported.	Quantitative spectral-power data were not reported. The analysis focused on CAP dynamics among individuals stratified by genetic and prodromal risk factors for Parkinson's disease.

Note: Findings were summarized descriptively because sleep-spindle and EEG spectral-power outcomes were not consistently reported across the included studies. CAP = cyclic alternating pattern; EEG = electroencephalographic; N3 = non-rapid eye movement sleep stage 3; NCAP = non-CAP; PD = Parkinson's disease.