Sleep microstructure as an early marker of neurodegeneration in de novo Parkinson's disease: insights from a polysomnography study

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Objectives To investigate the association between sleep architecture (macro and microstructure) and cerebrospinal fluid (CSF) biomarkers of neurodegeneration in patients with early/de novo drug-naive Parkinson's disease (PD).

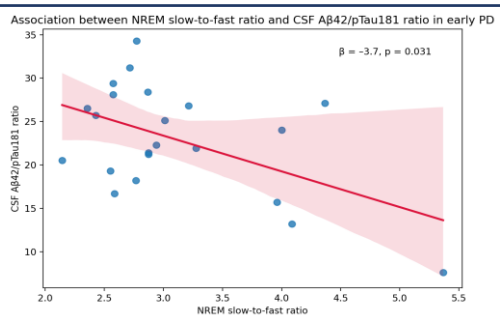
Materials Twenty-five drug-naïve patients with early/de novo PD from our Neurology Clinic in Verona underwent extensive neurological examination, overnight polysomnography and lumbar puncture. CSF was analysed for β-amyloid 1–42 (Aβ42), β-amyloid 1–40 (Aβ40), total tau, and phosphorylated tau (pTau181).

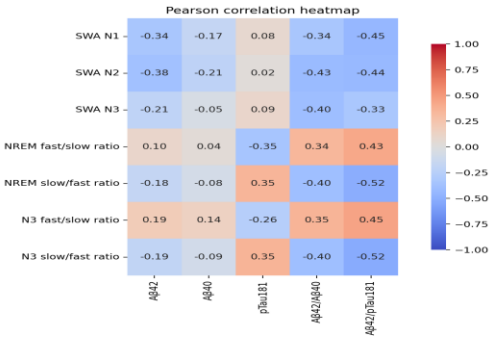
Methods Sleep macrostructure parameters included total sleep time (TST), sleep efficiency (SE), and the percentage of time spent in N1, N2, N3, and REM stages. Microstructural features, extracted from central EEG derivations (C3 and C4), included spectral power, slow wave activity (SWA), and the ratio of slow-to-fast and fast-to-slow frequencies during NREM stages (N1, N2, N3). Associations between sleep parameters and individual CSF markers (Aβ42, Aβ40, tau, pTau181), as well as composite ratios (Aβ42/pTau181 and Aβ42/Aβ40), were explored using Pearson's correlation. Linear regression analyses adjusting for age were also performed.

Results No significant associations were found between sleep macrostructure and CSF biomarkers. In contrast, **sleep microstructure showed robust associations.**
We analyzed central EEG derivations and we found that **the Aβ42/pTau181 ratio positively correlated with the fast-to-slow ratio in NREM and in N3**, and negatively with the slow-to-fast ratio in both NREM and N3 (all **p<0.05**).
SWA in N2 and N1 also negatively correlated with Aβ42/pTau181(**all p<0.05**).
Regression confirmed the predictive role of central derivations slow-to-fast ratio on Aβ42/pTau181 (NREM: β = –3.7, **p=0.031**; N3: β = –2.2, **p=0.033**).
Aβ42/Aβ40 showed similar patterns: negative correlations with slow-to-fast ratio (NREM: r=–0.48; N3: r=–0.44), SWA in N2, and a positive correlation with fast-to-slow ratio (NREM: r=0.42). Regression confirmed NREM slow-to-fast ratio as a predictor of Aβ42/Aβ40 (β = –0.009, R^2 = 0.28, **p=0.037**). No significant associations emerged between spectral parameters and the single biomarkers (Aβ42, Aβ40, tau, pTau181).

Discussion Our findings suggest that spectral imbalances during NREM sleep, particularly **a shift toward lower-frequency dominance, are associated with a more severe neurodegenerative CSF profile**.
This may reflect early thalamo-cortical dysregulation or ineffective slow-wave activity, potentially impairing glymphatic clearance and/or reflecting early pathological changes in PD.

Conclusions These findings suggest that NREM spectral markers could serve as **early electrophysiological indicators of disease progression in de novo PD.** Longitudinal studies are needed to validate their potential role as progression and/or state biomarkers of subtype of PD, i.e. severe phenotype with worse cognitive decline.





Limitations

- Cross sectional design;
- Small sample size;
- Single-center;

References

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