Non-motor features may be either intrinsic to Parkinsonian disturbances) contribute more to quality of life, healthcare costs, and institutionalization rates. Such features are under-recognized and under-treated. Non-motor features may be either intrinsic to Parkinsonian disorders or due in part to medication side effects.

Within the PDD group, five combined motor/non-motor patterns were performed with k-means using non-motor or motor features, or both. Within the PDD group, cluster analyses were performed on all clinical, neuroimaging (striatal dopamine transporter binding ratio (SBR)), and cerebrospinal fluid (CSF) biomarkers (α-synuclein (-syn) tau, phosphorylated at threonine 181, total tau, and β-amyloid 1-42) were obtained in an ongoing observational study of Parkinsonism - the Parkinson’s Progression Markers Initiative (PPMI). Group comparisons of Parkinsonism with dopaminergic deficits (PDD), controls, and participants with Parkinsonian motor features but scans without evidence of dopaminergic deficits (SWEDD)’s were done with ANOVA F-tests, chi-square tests, and post-hoc pairwise tests. Within the PDD group, cluster analyses were performed with k-means using non-motor or motor features, or both.

Key Findings

- α-syn and tau-related markers were lower in PDD than SWEDD.
- SWEDD’s had the most severe autonomic, sleep-related, and impulsive/cognitive symptoms.
- Within the PDD group, four non-motor patterns were observed: Impulsive: presence of impulsive/cognitive behaviors; Sleep-autonomic: most severe non-motor (MDS-UPDRS Part 1), automatic (SCOPA-AUT) and REM sleep disorder symptoms; Cognitive-offactory: performed worst on all cognitive tests and had low UPSIT scores; Mild: no impulsive/cognitive behaviors and the best UPSIT performance.
- Within the PDD group, four motor patterns were observed:
  - Tremor plus bradykinesia: tremor and bradykinesia at the time of diagnosis
  - Tremor without bradykinesia: tremor and no bradykinesia at the time of diagnosis
  - Postural instability: postural instability at the time of diagnosis
  - No tremor: no tremor at the time of diagnosis.
- Within the PDD group, five combined motor/non-motor patterns were observed:
  - Tremor with bradykinesia
  - Tremor without bradykinesia
  - No tremor and mild non-motor features: no tremor at diagnosis and lower severity for several non-motor features
  - Postural instability with sleep and autonomic disturbances: postural instability at the time of diagnosis of the most severe sleep and autonomic symptoms
  - Oldest onset cognitive-offactory: the oldest age of onset of PDD with the worst cognitive and olfactory performance.

Conclusions

To our knowledge, this is the first description of non-motor clinical patterns and underlying biomarkers in early medication-naive Parkinsonism.

In the PDD group, most are Parkinsonian disease. However other Parkinsonian disorders, could, in part, account for clinical patterns observed.

While several studies have reported lower concentrations of α-synuclein in CSF in Parkinsonian Disease, our results suggest this occurs early in PDD, prior to the initiation of anti-Parkinsonian medications.

The fact that non-motor features are prominent in a medication-naive cohort provides strong evidence that such phenomena can be intrinsic to PDD.

Several non-motor symptoms are treatable, including sleep disturbances, autonomic dysfunction, cognitive impairment, and psychiatric disorders. This demonstrates the need for treatment strategies which encompass both motor and non-motor features to begin at diagnosis.

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