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Association of specific biotypes in patients with Parkinson disease and disease progression

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Study question

Do distinct neuroanatomical biotypes exist among patients with newly diagnosed with Parkinson disease (PD) and can they explain interindividual differences in longitudinal progression?

What is known and what this paper adds

Subtypes of PD have previously been defined mainly according to clinical symptoms and demographic characteristics. An alternative classification based on shared neuroanatomical signatures provides an opportunity to examine biological heterogeneity in vivo. This investigation's results show that neuroanatomical biotypes exist in PD with distinct clinical and neuroanatomical pattern and that they may be useful for prognosis.

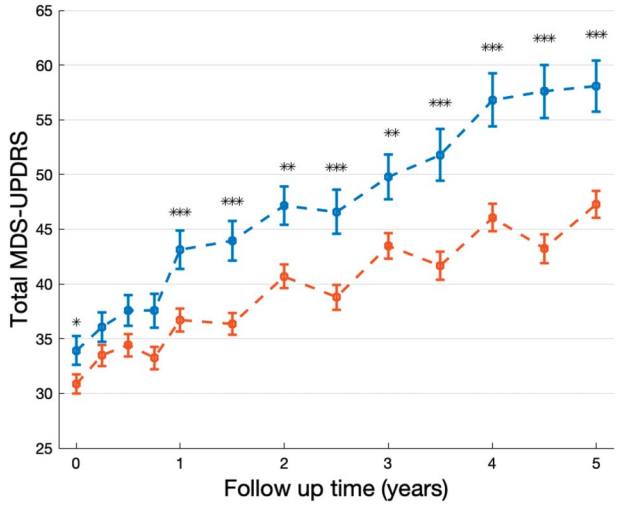
Methods

These clustering analyses relied on data from 314 patients with PD (65.9% male; mean baseline age, 61.0 ± 9.5 years; mean baseline PD duration, 6.9 ± 6.8 months) and 143 age- and sex-matched healthy controls (HCs) who participated in the Parkinson's Progression Markers Initiative (PPMI). At baseline, the PPMI participants underwent clinical assessments with the Movement Disorder Society–Sponsored Revision of the Unified PD Rating Scale (MDS-UPDRS) and T1-weighted MRI scans sequences. Deformation-based morphometry was used for voxel-level analyses of the MRI neuroanatomy data to identify neuroanatomical biotypes, the primary outcome of the study. Spearman rank correlation analysis was used to identify neuroanatomic features with deformation values that significantly ($p < 0.01$) correlated with various MDS-UPDRS scores. Biotypes based on those neuroanatomic features were identified using hierarchical clustering and the relationship between biotypes and disease progression over 5 years of follow-up was assessed with linear mixed models.

Results and study limitations

The clustering analyses identified 2 neuroanatomic biotypes: biotype 1 (n = 114) with subcortical brain volumes smaller than those of HCs; biotype 2 (n = 200) with subcortical brain volumes larger in PD patients than HC. Biotype 1 had more severe motor impairment, autonomic dysfunction, and very much worse REM sleep behavior disorder than biotype 2 at baseline. Although disease duration at initial visit and follow-up were similar between biotypes, PD patients with smaller subcortical brain volume had poorer prognosis, with more rapid decline in several clinical domains and in dopamine functional neuroimaging over an average of 5 years. These results derive from a single cohort of patients and lack of follow-up neuroimaging data for longitudinal analysis are study limitations.

Figure Progression in total MDS-UPDRS score for biotypes 1 (blue) and 2 (red)



*$p < 0.05$; **$p < 0.01$; ***$p < 0.005$.

Study funding and competing interests

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