Appendix 1 Explanation of enrollment samples and related clinical scales

The study cohort consisted of 152 PD and 75 NC participants, all of whom completed the Montreal Cognitive Assessment (MoCA). When considering individuals with values from other assessment scales, such as the Motion Disorder Association Unified Parkinson's Disease Rating Scale (MDS-UPDRS), Hoehn and Yahr Staging (H&Y), University of Pennsylvania Olfactory Recognition Test (UPSIT), Geriatric Depression Scale (GDS), Parkinson's Disease Outcome Scale Autonomy (SCOPA-AUT), etc., the number of participants decreased to 146 in the PD group and 56 in the NC group. Due to the limited number of participants, the main experimental framework of the study did not include data from other scales.

If additional scales are included, the demographic data of the participants are summarized in Table S3. There were significant statistical differences in the results of the MDS-UPDRS, H&Y, UPSIT, MoCA, GDS, and SCOPA-AUT between the two groups of participants. Therefore, the white matter fiber bundles with differential regions between the two groups are related to both advanced cognitive function and motor symptoms, proving that in the early stages of PD, the impact of disease on brain structure has already affected cognitive and motor functions.

Table S1 Inclusion criteria for case selection from PPMI

Case ID	Cases' enrollment year (circle) and examination year (checkmark)						
	2010	2011	2012	2013	2014	2015	2016
3371			○√	√	√		√
3372			○√	√	√		√
3373			○√	√	√		√
.....							
3551	○√	√				√	
3552		○√	√	√		√	
.....							
4136				○√	√		
4139				○√			

PPMI, Parkinson's Progression Markers Initiative.

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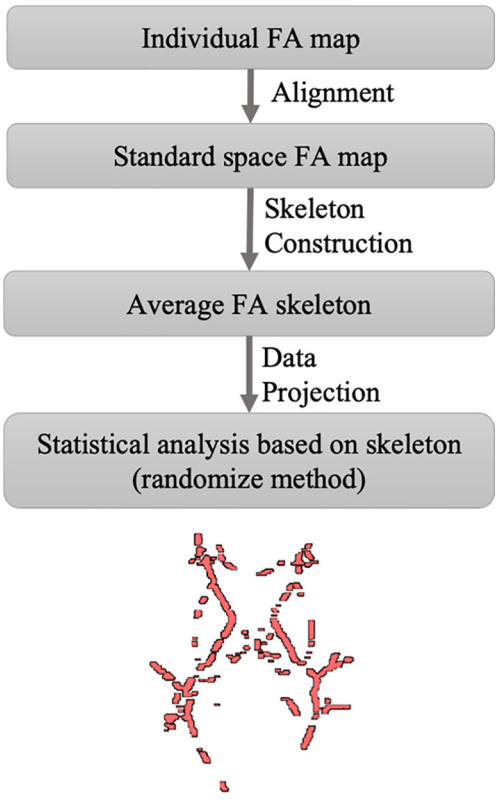

Figure S1 TBSS analysis flowchart. FA, fractional anisotropy; TBSS, tract-based spatial statistics.

Table S2 FA skeleton geometric dimensionality reduction parameters

FA	Image size	No. of voxels	Mean value of voxels (vox.)	No. of vox. >0 (%)	No. of vox. >max/2 (%)	Range of vox.
Before gridded	182×218×182	7221032	0.003±0.040	46,831 (0.65%)	20,808 (44.43%)	[0, 0.94]
After gridded	16×18×16	4608	4.683±18.820	613 (13.3%)	62 (10.11%)	[0, 205.233]

FA, fractional anisotropy.

Table S3 Demographic data summary for participants (non-imaging data)

Demographic/clinical scale	PD (n=146)	NC (n=56)	P	t-value
Gender (male/female)	94/52	40/16	0.041*	–0.946
Age	61.61±9.51	59.97±11.54	0.083	–1.032
Years of education	15.20±3.20	16.04±3.09	0.507	1.682
Duration of disease (months)	6.87±6.94	–	–	–
UPDRS	31.20±13.14	3.63±3.37	<0.001*	–15.493
H&Y	1.6±0.49	0.02±0.13	<0.001*	–23.785
UPSIT	21.75±8.63	34.04±4.51	<0.001*	10.128
MoCA Score	27.62±2.08	28.27±1.15	<0.001*	2.216
GDS	2.35±2.55	1.00±1.36	<0.001*	–3.746
SCOPA	8.75±5.08	5.95±3.70	0.022*	–3.767

Except for the numerical representation of gender (male/female), all other data is represented in the form of mean ± standard deviation. *, P<0.05, considered statistically significant. PD, Parkinson's disease; NC, normal control; UPDRS, Unified Parkinson's Disease Rating Scale; H&Y, Hoehn and Yahr; UPSIT, University of Pennsylvania Smell Identification Test; MoCA, Montreal Cognitive Assessment; GDS, Geriatric Depression Scale, SCOPA, Scales for Outcomes in Parkinson's Disease.

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