



Visuospatial Dysfunction And Dementia Risk In Parkinson's Disease

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Abstract

Cognitive decline in Parkinson’s disease (PD) is heterogeneous, and predictors of dementia conversion remain inconsistent. We applied Subtype and Stage Inference (SuStaln) to baseline neuropsychological data from 474 drug-naïve patients with early-stage PD. SuStaln identified three cognitive subtypes: verbal memory-dominant, visuospatial/visual memory-dominant, and frontal/executive-dominant patterns. During follow-up, the visuospatial-dominant subtype showed the highest risk of dementia conversion after 3.5 years. These findings suggest that early visuospatial dysfunction may serve as a clinically useful marker for identifying patients with PD at increased risk of future dementia.

I. Introduction

Cognitive impairment is common in PD, but its clinical course varies widely across patients. Previous studies have reported inconsistent cognitive predictors of dementia conversion, partly because cognitive decline has often been evaluated using selected tests or cross-sectional approaches. A data-driven model that captures the temporal evolution of domain-specific cognitive impairment may help identify patients at high risk of dementia earlier.

II. Methods

We retrospectively analyzed 474 drug-naïve patients with early-stage PD who underwent comprehensive neuropsychological testing at diagnosis. Age- and education-adjusted z-scores from 13 cognitive subtests were entered into the SuStaln model to identify cognitive subtypes and progression sequences. Dementia conversion during follow-up was evaluated, and subtype-specific risk was compared using time-dependent Cox regression analyses.

III. Results

SuStaln identified three cognitive impairment subtypes: Subtype 1, characterized by early verbal memory impairment; Subtype 2, characterized by early visuospatial and visual memory dysfunction; and Subtype 3, characterized by early frontal/executive dysfunction. An additional 158 patients showed no baseline cognitive impairment. During follow-up, dementia conversion was most frequent in Subtype 2. After 3.5 years, Subtype 2 showed a significantly higher risk of dementia conversion than Subtype 1 and Subtype 3.

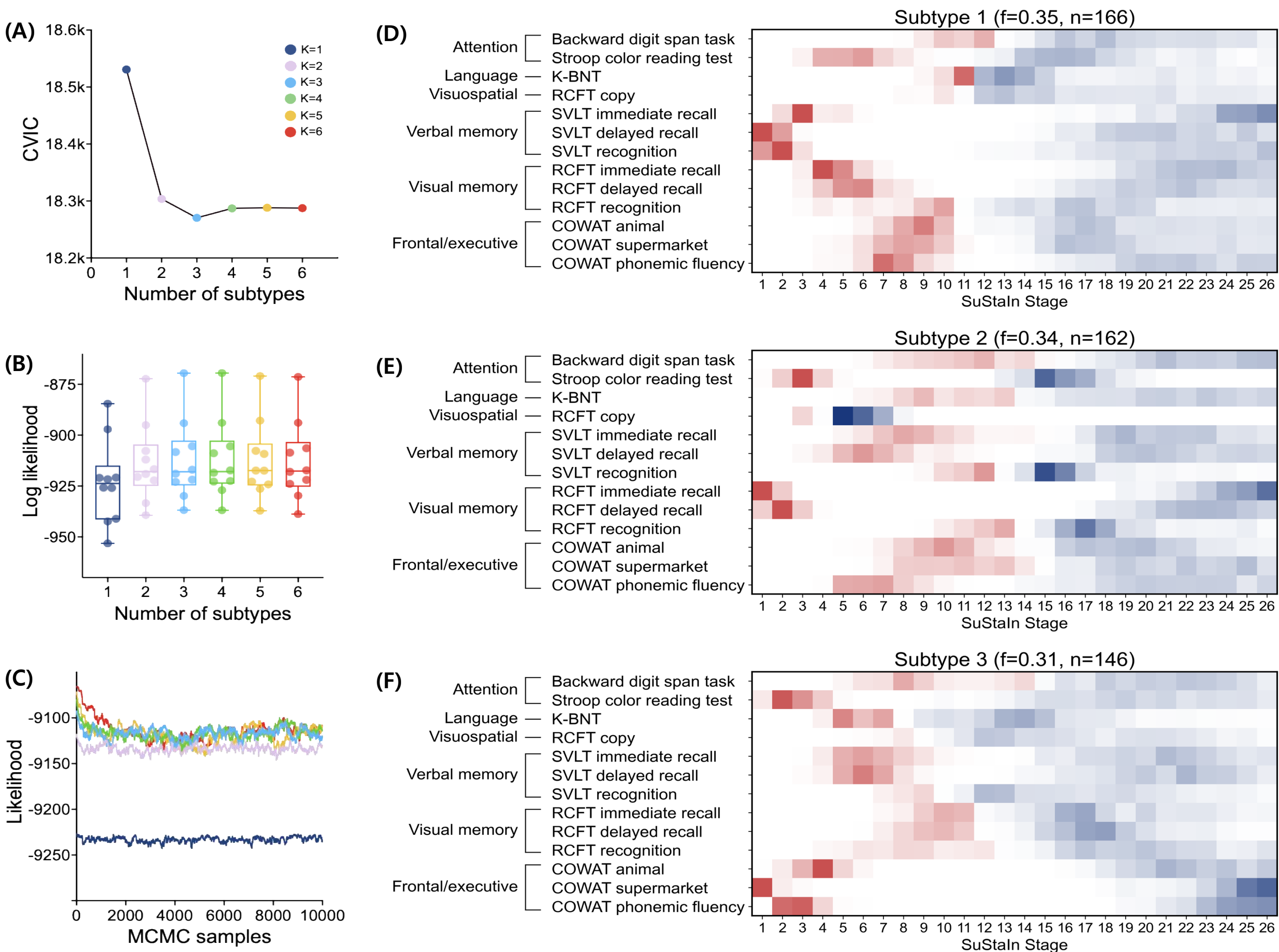


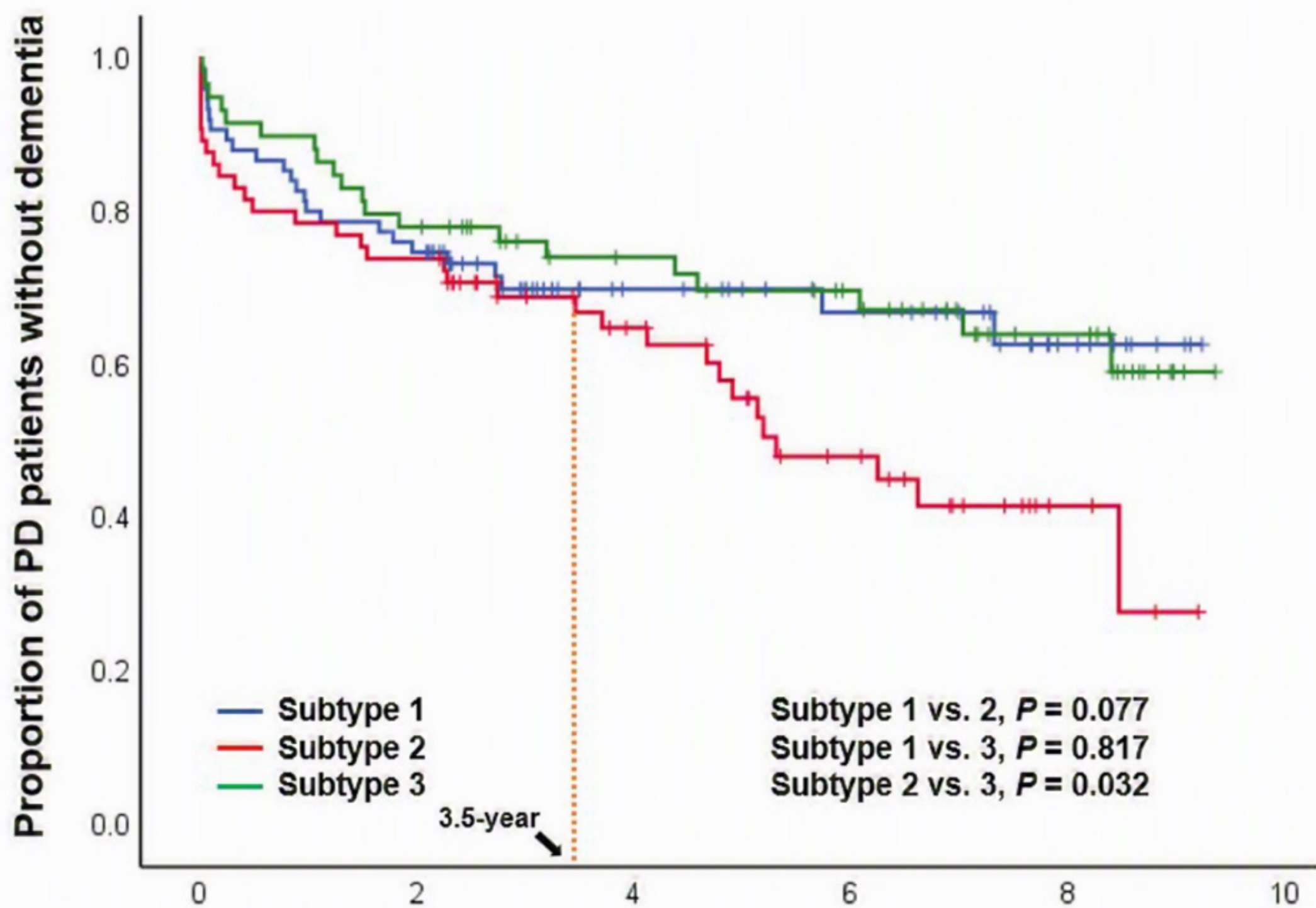
Figure 1. Identified cognitive subtypes in early-stage Parkinson’s disease. (A–C) Ten-fold cross-validation supported a three-subtype model: CVIC reached its minimum (A), log-likelihood plateaued (B), and MCMC traces showed no further improvement beyond this model (C). (D–F) Subtype-specific PVDs illustrate the probabilistic ordering of cognitive decline across sequential SuStaln stages. Red and blue indicate z-score events of 1 and 3, respectively, with blue representing more advanced impairment. Color opacity reflects certainty in event ordering.

Table 1. Clinical and imaging characteristics of the three cognitive subtypes. Subtype 2 demonstrated predominant visuospatial dysfunction accompanied by greater striatal dopaminergic deficits and posterior cortical hypoperfusion. Values are presented as mean ± SD, estimated mean (SE), or n (%).

	Parameter	Subtype 1 N=121	Subtype 2 N=108	Subtype 3 N=87	p-value
Demographics	Age, years	70.92 ± 8.49	73.43 ± 7.05	72.40 ± 9.90	0.054
	Female, n (%)	51 (42.1%)	67 (62.0%)	32 (36.8%)	<0.001
Global cognition	K-MMSE	25.98 ± 3.04	25.20 ± 3.11	25.52 ± 3.97	0.208
	CDR-SB	1.62 ± 1.39	2.00 ± 1.72	1.42 ± 1.52	0.033
Visuospatial	RCFT copy	−0.29 ± 0.81	−2.23 ± 2.03	−0.36 ± 0.87	<0.001
Verbal memory	SVLT delayed recall	−1.52 ± 0.67	−0.76 ± 1.07	−0.71 ± 0.85	<0.001
Visual memory	RCFT delayed recall	−0.85 ± 0.86	−1.37 ± 0.59	−0.21 ± 0.92	<0.001
Frontal/executive	COWAT-supermarket	−0.63 ± 0.91	−0.54 ± 0.89	−1.23 ± 0.62	<0.001
Striatal DAT	Anterior caudate	3.030 (0.074)	2.694 (0.079)	2.872 (0.087)	0.009
	Posterior caudate	1.916 (0.046)	1.712 (0.050)	1.811 (0.055)	0.012
	Ventral striatum	3.135 (0.092)	2.749 (0.099)	2.844 (0.109)	0.013
Perfusion	Parietal cortex	0.948 (0.005)	0.927 (0.005)	0.941 (0.006)	0.022
	Occipital cortex	1.018 (0.007)	0.994 (0.007)	1.014 (0.008)	0.033
	Precuneus	1.002 (0.007)	0.980 (0.007)	1.006 (0.008)	0.023

Research highlights

- SuStaln identified three distinct cognitive subtypes in early-stage Parkinson’s disease.
- Early visuospatial dysfunction was associated with the highest risk of dementia conversion.
- This data-driven approach may help identify patients who require closer monitoring and personalized care.



Time (years)						
No. at risk	0	2	4	6	8	10
Subtype 1	75	56	29	22	9	0
Subtype 2	65	48	30	4	1	0
Subtype 3	59	46	34	28	16	0
No. of event	0	2	4	6	8	10
Subtype 1	0	19	22	23	24	24
Subtype 2	0	17	22	31	32	32
Subtype 3	0	13	15	17	19	20

Figure 3. Dementia conversion risk by cognitive subtype. Kaplan–Meier curves show that Subtype 2 had a higher risk of dementia conversion than Subtypes 1 and 3, with the separation becoming prominent after 3.5 years. Crosses indicate censored cases.

IV. Conclusion

Data-driven cognitive subtyping revealed distinct trajectories of cognitive decline in early-stage PD. Early visuospatial dysfunction may indicate an increased risk of future dementia conversion and could help guide personalized monitoring strategies in clinical practice.

V. References

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