STRUCTURAL BRAIN CORRELATES OF COGNITIVE IMPAIRMENT IN PROGRESSIVE SUPRANUCLEAR PALSY

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BACKGROUND

✓Progressive supranuclear palsy syndrome (PSPs) commonly presents cognitive (1, 2) and behavioural disorders (3), beside classical motor symptoms.

✓Previous voxel-based morphometry studies revealed a significant relationship between frontal grey matter (GM) atrophy and deficits in executive functions (4, 5) and social cognition (6). Moreover a recent diffusion-tensor (DT)-MRI study showed that white matter (WM) damage in corpus callosum and frontal WM tracts is significantly related to executive deficits and apathy in these patients (7).

OBJECTIVES

✓To describe the pattern of GM and WM damage in a clinically and neuropsychologically well-characterized sample of PSPs patients using a surface-based method as cortical thickness and DT-MRI respectively.

✓To explore the clinicoanatomical correlations between MRI measures and cognitive features of PSPs patients.

METHODS

Table 1. Demographic and clinical data of PSPs patients and HC.

	HC	PSPs
Number	15	23
Age [years]	69.5 6.8	69.4 7.2
Sex [F/M]	9/6	14/9
Education [years]	12.1 4.9	11.4 4.9
Disease duration [years]	-	4.2 3.1
UPDRS III-motor score [off-status]	-	40.4 13.7
Hoehn and Yahr scale [off-status]	-	3.6 0.8
MMSE (cut-off 24)	28.9 0.9	24.9 4*
Clinical Dementia Rating scale	-	1.2 0.8

Values are means standard deviations.
Abbreviations: *<0.05 *vs* healthy controls (HC); F: female; M: male; MMSE: mini mental state examination; UPDRS III: Unified Parkinson's disease Rating scale III

Table 2. Main neuropsychological findings in PSPs patients.

Cognitive domains	
Executive domain	-1.34 1.0 (-3.36 -0.5)
Fluency domain	-1.44 1.1 (-2.96 -1.61)
Verbal Memory domain	-0.79 1.1 (-2.78 -0.15)
Visuospatial Memory domain	-1.04 0.9 (-2.16 -0.62)
Visuospatial domain	-0.79 1.1 (-6.15 -0.56)
Language domain	-1.24 1.9 (-5.48 -1.10)
Behavioral disturbances	
Neuropsychiatry battery inventory	11.1 11.5
Frontal Behavioral Inventory	17.8 12.7

Values are means standard deviations (range).
Raw cognitive test scores were transformed into Z scores, and the mean Z score for each cognitive domain was calculated.

MRI acquisition and analysis

3T MRI scanner: T2-weighted spin echo (SE); fluid-attenuated inversion recovery; 3D T1-weighted fast field echo; and pulsed-gradient SE echo planar with sensitivity encoding and diffusion gradients applied in 32 non-collinear directions.

✓A surface-based morphometry analysis was used to assess cortical thickness. Both cluster-wise and regions of interest-based analyses were applied.

✓WM damage [fractional anisotropy (FA), and mean (MD), axial (axD), and radial diffusivities (radD)] was measured using a voxel-wise analysis with Tract-Based Spatial Statistics (TBSS) version 1.2 in FSL ($p<0.05$ FWE).

✓A Random Forest (RF) approach was used to identify MRI predictors of cognitive impairment in PSPs at an individual patient level.

RESULTS

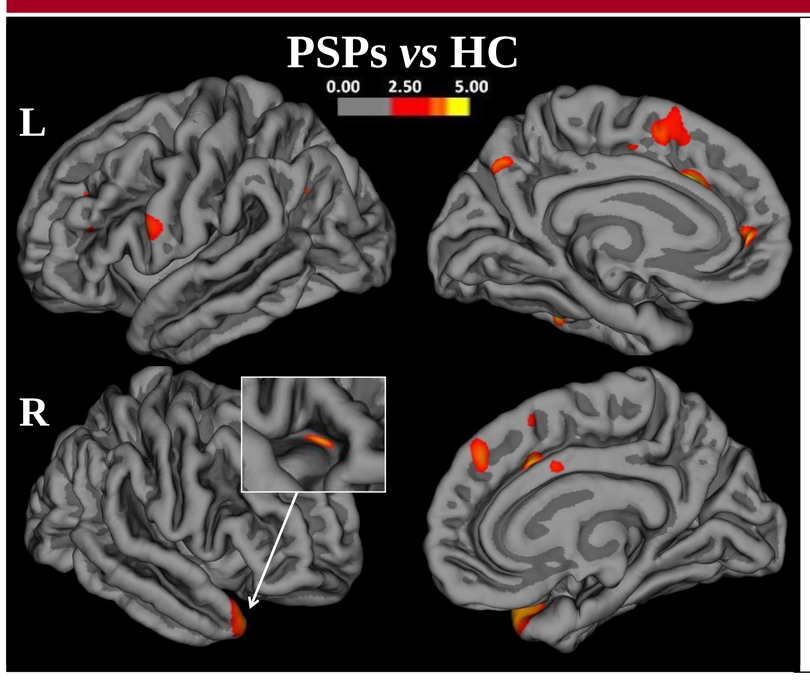

Figure 1. Distribution of the cortical thinning on the pial surface in patients PSPs relative to HC. Results are false-discovery rate corrected for multiple comparisons. Color bar denotes t values. L= left; R= right.

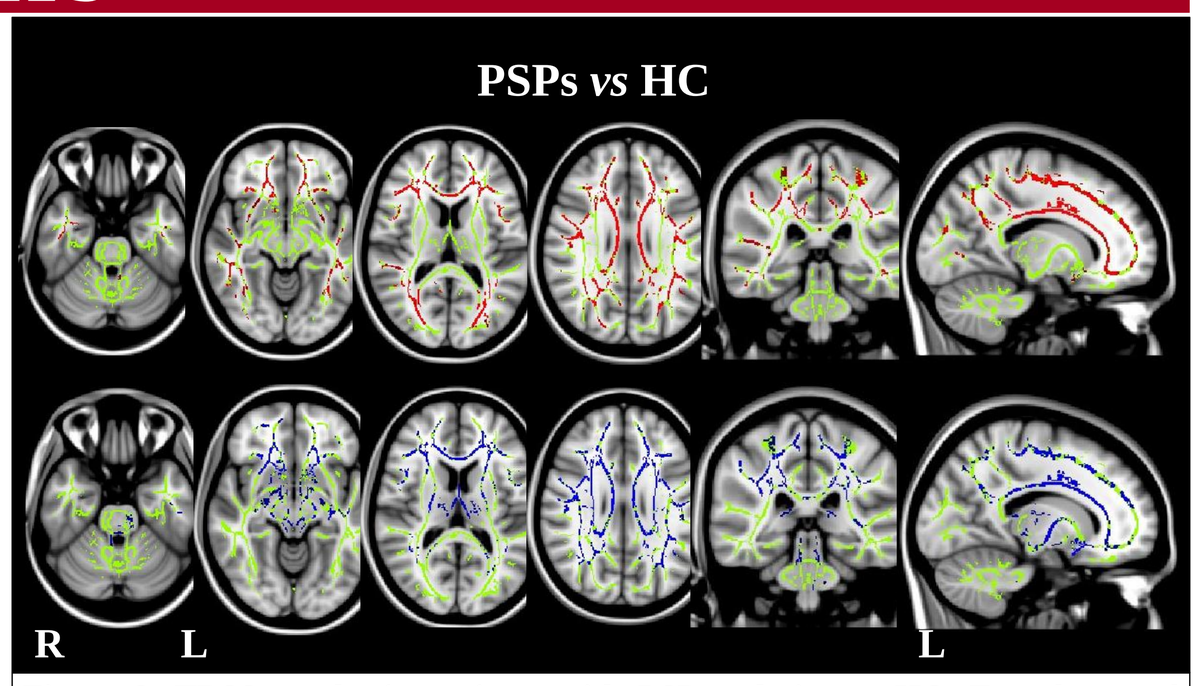

Figure 2. TBSS results in patients with PSPs relative to HC. Top: decreased fractional anisotropy (FA) in PSPs patients *vs* HC is shown in red. Bottom: increased mean diffusivity (MD) in PSPs patients *vs* HC is shown in blue. Results are overlaid on the sagittal, coronal and axial sections of the Montreal Neurological Institute standard brain in radiological convention (right is left), and displayed at $p<0.05$ FWE. The white matter skeleton is shown in green. L= left; R= right.

RANDOM FOREST ANALYSIS

EXECUTIVE DOMAIN	**NVI**
Left external capsule FA	100.00
Body of corpus callosum MD	89.45
Left external capsule raD	65.28

VERBAL MEMORY DOMAIN	**NVI**
Body of corpus callosum MD	100.00
Pontine crossing tracts MD	95.13
Left cingulum raD	76.78

FLUENCY DOMAIN	**NVI**
Left external capsule FA	100.00
Pontine crossing tracts MD	85.39
Left external capsule raD	38.97

VISUOSPATIAL MEMORY DOMAIN	**NVI**
Right external capsule raD	100.00
Left external capsule raD	66.92
Left external capsule MD	64.48

LANGUAGE DOMAIN	**NVI**
Left external capsule FA	100.00
Left corticospinal tract raD	88.33
Body of corpus callosum raD	82.96

Abbreviations: axD: axial diffusivity; FA: fractional anisotropy; MD: mean diffusivity; NVI: normalized variable importance; radD: radial diffusivity

CONCLUSIONS

✓PSPs patients showed a focal cortical thinning within dorsolateral anterior regions, while WM degeneration was more severe and distributed involving the main motor and extramotor tracts.

✓WM measures were highly associated with neuropsychological features in patients with PSPs.

✓DT MRI might be a useful tool to explore the impact of WM damage in the genesis and progression of PSPs and the relationship between the involvement of specific WM tracts and cognitive deficits in this disease.

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