PN 441

FUNCTIONAL AND STRUCTURAL BRAIN ALTERATIONS IN TWO INDEPENDENT SAMPLES OF PATIENTS WITH POSTERIOR CORTICAL ATROPHY

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INTRODUCTION AND OBJECTIVE

Posterior cortical atrophy (PCA) is an atypical variant of Alzheimer's disease characterized by an early age of onset, visuospatial impairment and posterior occipital-temporal-parietal atrophy. Up to date, the brain functional connectivity in PCA patients has been poorly investigated. This study assessed resting state (RS) functional connectivity and structural brain alterations in two independent samples of patients with PCA compared with age-matched healthy controls.

MATERIALS AND METHODS

Table 1. Demographic and clinical features of patients and healthy controls.

	1.5 T			3 T			
	PCA	**HC**	**p**	**PCA**	**HC**	**p**	**p (1.5-3 T)**
Number	8	24		13	20		
Gender, males (%)	5 (63%)	14 (58%)	0.84	4 (31%)	7 (35%)	0.80	0.15
Age at MRI	60.2 ± 4.7	60.9 ± 6.7	0.78	61.9 ± 6.0	62.0 ± 2.8	0.97	0.50
Education	13.6 ± 2.26	13.0 ± 3.1	0.63	9.5 ± 3.2	16.0 ± 4.7	<0.001	<0.01
Age at onset	55.4 ± 4.8	-	-	58.5 ± 6.6	-	-	0.26
Disease duration	4.8 ± 1.6	-	-	3.4 ± 1.1	-	-	0.02
CSF, $A\beta_{42}$	552.0 ± 229.0	-	-	369.4 ± 180.4	-	-	NA
CSF, T-Tau	502.7 ± 174.6	-	-	339.0 ± 192.6	-	-	NA
CSF, p-Tau	79.4 ± 12.6	-	-	103.1 ± 100.9	-	-	NA
CDR	1.9 ± 0.9	-	-	1.2 ± 0.4	-	-	0.07
ADL	34.8 ± 25.0	-	-	5.3 ± 1.1	-	-	NA

Values denote means ± standard deviations or frequencies (%). **Abbreviations:** Aβ=Amyloid-beta; ADL=Activities of Daily Living; CDR=Clinical Dementia Rating Scale; CSF=Cerebrospinal Fluid; HC=Healthy Controls; MRI=Magnetic Resonance Imaging; NA=Not applicable (different cut off references); PCA=Posterior Cortical Atrophy; p-Tau=phosphorylated Tau; T-Tau=Total Tau.
CSF normal values: 1.5 T: $A\beta_{42}$>563.1 ng/L; T-tau<244.7 ng/L; p-Tau<83.4 ng/L; 3 T: $A\beta_{42}$>500 ng/L; T-tau<450 ng/L; p-Tau<61 ng/L.

All subjects underwent the following sequences: 3D T1-weighted, Diffusion Tensor (DT) MRI, and RS fMRI on a 1.5 T (Philips Medical Systems, Achieva) or 3 T (Philips Medical Systems, Intera) scanners.

MRI analysis

Voxel-Based Morphometry (VBM) in SPM8 to assess gray matter (GM) atrophy.

DT MRI metrics from the main motor, interhemispheric and long associative WM tracts using FSL (v. 4.1.7; probtrackx).

RS fMRI data analysis of brain networks using FSL (MELODIC).

Statistical analysis

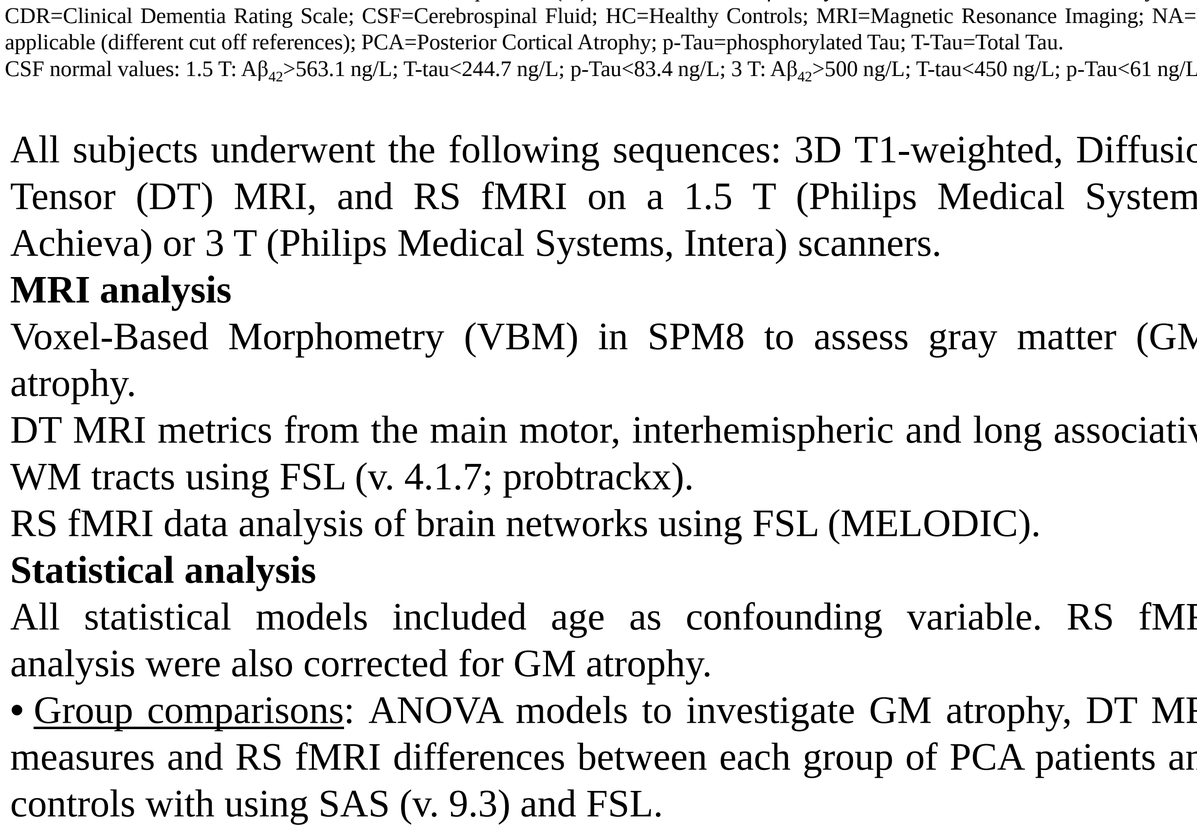
All statistical models included age as confounding variable. RS fMRI analysis were also corrected for GM atrophy.

• Group comparisons: ANOVA models to investigate GM atrophy, DT MRI measures and RS fMRI differences between each group of PCA patients and controls with using SAS (v. 9.3) and FSL.

• Correlations: Multiple regression models to assess the relationships between structural, functional and clinical variables using SAS.

RESULTS

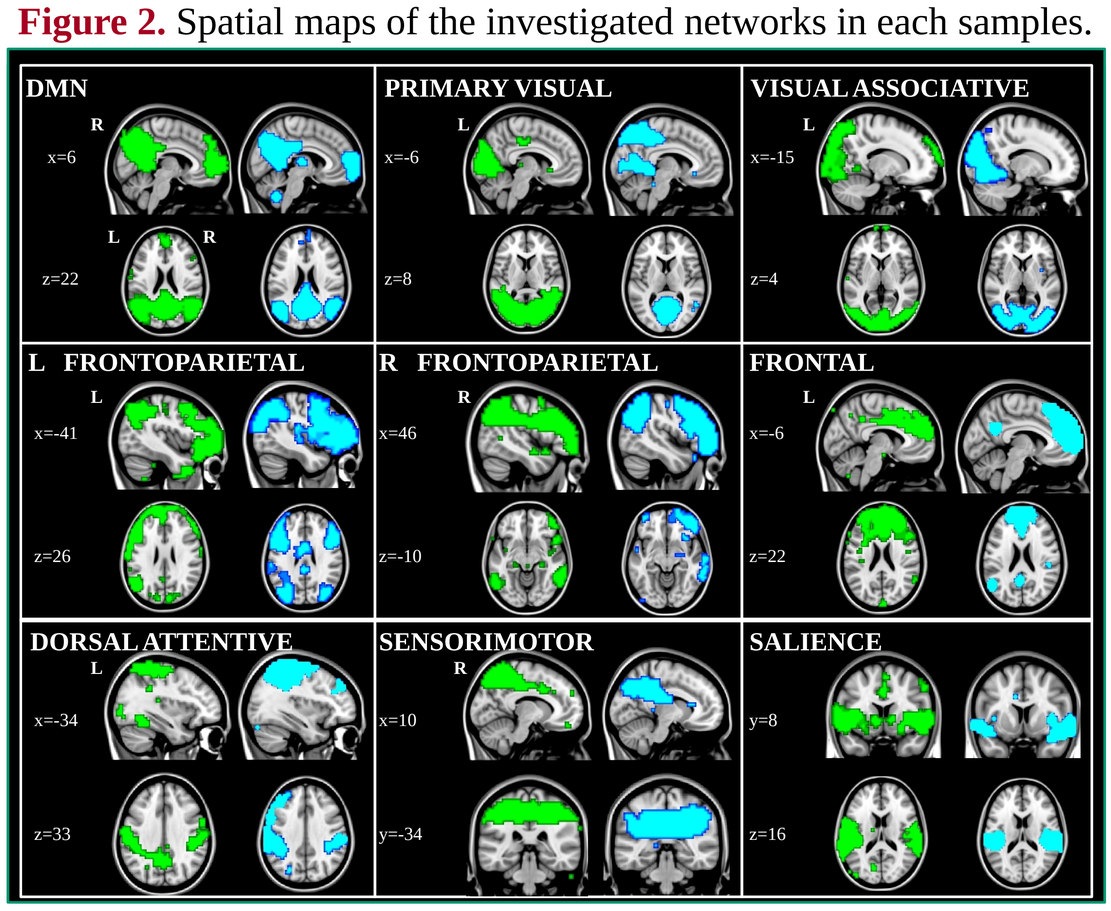
Figure 1. GM atrophy and WM tract damage in patients *vs* controls.



Colours indicate GM atrophy (red to yellow) and white matter (WM) tract damage (green). Results are overlaid on the Montreal Neurological Institute standard brain. Patterns of damage represent findings of VBM for GM (p<0.05 Family Wise Error-corrected within 20 contiguous voxels; Coloured bars denote T-values) and tractography for WM (p<0.05 Bonferroni corrected). L=left; R=Right. Negative numbers denote the left side.

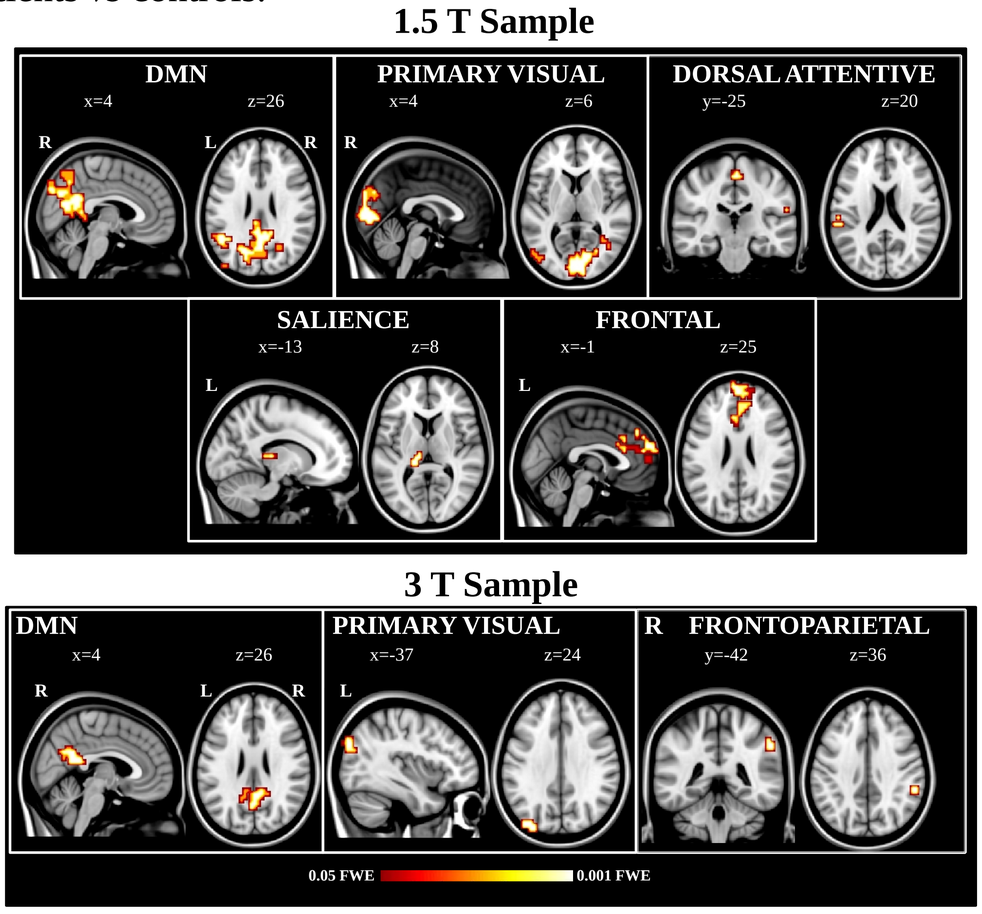
RESULTS

Figure 2. Spatial maps of the investigated networks in each samples.



Colours indicate spatial maps of 1.5 T (green) and 3 T (cyan) samples. Maps are overlaid on the Montreal Neurological Institute standard brain. DMN=Default Mode Network; R=right; L=left; x=sagittal views, negative numbers denote the left side; y=coronal view; z=axial views.

Figure 3. Reduced functional connectivity within the investigated networks in PCA patients *vs* controls.



Results are overlaid on the Montreal Neurological Institute standard brain and displayed at p<0.05 Family Wise Error-corrected. Colour bars denote p values. R=right; L=left; x=sagittal views, negative numbers denote the left side; y=coronal view; z=axial views.

Correlations: In the 1.5 T PCA group, the reduced RS functional connectivity of the left middle occipital gyrus within the DMN was associated with the increased mean diffusivity (MD) of the right superior longitudinal fasciculus. In the 3.0 T PCA group, the reduced RS functional connectivity of the right precuneus within the DMN was associated with the increased MD and axial diffusivity of the left inferior longitudinal fasciculus.

CONCLUSIONS

- ✓ This study provides a comprehensive picture of the cerebral structural and functional features of PCA patients.
- ✓ Microstructural WM damage is more widely distributed than expected on the basis of cortical atrophy in PCA.
- ✓ In PCA, altered functional connectivity involves the most posterior regions of the visual and the default-mode network.
- ✓ Patients with longer disease duration (Sample 1.5 T) showed further alterations in the frontostriatal and parietal regions, likely suggesting the progression of the disease.
- ✓ A multimodal neuroimaging approach is promising for understanding the mechanisms associated with PCA.

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