PN 440

MULTIMODAL STRUCTURAL MRI DIFFERENTIATES *IN VIVO* THE THREE CLINICAL VARIANTS OF PRIMARY PROGRESSIVE APHASIA

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INTRODUCTION AND OBJECTIVE

Primary progressive aphasia (PPA) is a language disorder that involves changes in the ability to speak, read, write and understand what others are saying. PPA has been stratified according to clinical phenomenology into three subtypes: nonfluent and/or agrammatic PPA (NFvPPA), semantic PPA (SvPPA), and logopenic PPA (LvPPA). Each variant is associated with specific pattern of cognitive deficit, however they may present with overlapping pattern of brain alterations. Our aim was to investigate, in a large sample of PPA, structural (cortical thickness and white matter [WM] tract microstructure) differences between the three clinical variants.

MATERIALS AND METHODS

Table 1. Demographic and clinical features of PPA patients and healthy controls (HC).

	NFvPPA	LvPPA	SvPPA	HC	p	p NFvPPA *vs* HC	p LvPPA *vs* HC	p SvPPA *vs* HC	P NFvPPA *vs* LvPPA	p NFvPPA *vs* SvPPA	p LvPPA *vs* SvPPA
N	28	15	16	50							
Age at MRI, years	70.0 ± 6.9 (57-82)	67.3 ± 8.3 (52-80)	65.1 ± 6.4 (52-74)	66.7 ± 7.7 (47-81)	0.16	0.38	1.00	1.00	1.00	0.24	1.00
Age at onset, years	67.1±6.9 (55-81)	64.9±7.6 (52-77)	61.1±6.3 (49-70)	-	**0.03**	-	-	-	1.00	**0.03**	0.41
Disease duration, months	31.2±16.1 (7-66)	36.5±27.6 (5-116)	46.6±18.6 (18-84)	-	**0.06**	-	-	-	1.00	**0.06**	0.51
Education, years	8.4 ± 5.2 (0-22)	12.3 ±4.5 (5-18)	10.9 ± 4.8 (5-18)	11.0 ± 3.4 (5-17)	**0.03**	0.12	1.00	1.00	**0.04**	0.51	1.00
Gender, women	18 (64%)	9 (60%)	9 (56%)	30 (60%)	0.961	0.71	1.00	0.79	0.78	0.60	0.83
MMSE	23.0± 5.5 (6-30)	24.0 ±5.8 (10-29)	23.3 ± 5.7 (7-29)	29.3 ± 0.8 (28-30)	**<0.001**	**<0.001**	**0.02**	**0.002**	1.00	1.00	1.00

Numbers are mean ± standard deviation (range) or frequencies (%). P values refer to ANOVA models, followed by post-hoc pairwise comparisons. Abbreviations: MMSE=Mini-Mental State Examination; MRI= Magnetic Resonance Imaging.

MRI acquisition

- ✓ All subjects underwent 3D T1-weighted and Diffusion Tensor (DT) MRI on a 3 T scanner (Philips Medical Systems, Intera).

MRI preprocessing

- ✓ MRI metrics of cortical thickness from atlas-based cortical regions (Desikan atlas) using FreeSurfer (v. 5.3).
- ✓ DT MRI metrics from the main motor, interhemispheric and long associative WM tracts using FSL (v. 4.1.7; probtrackx).

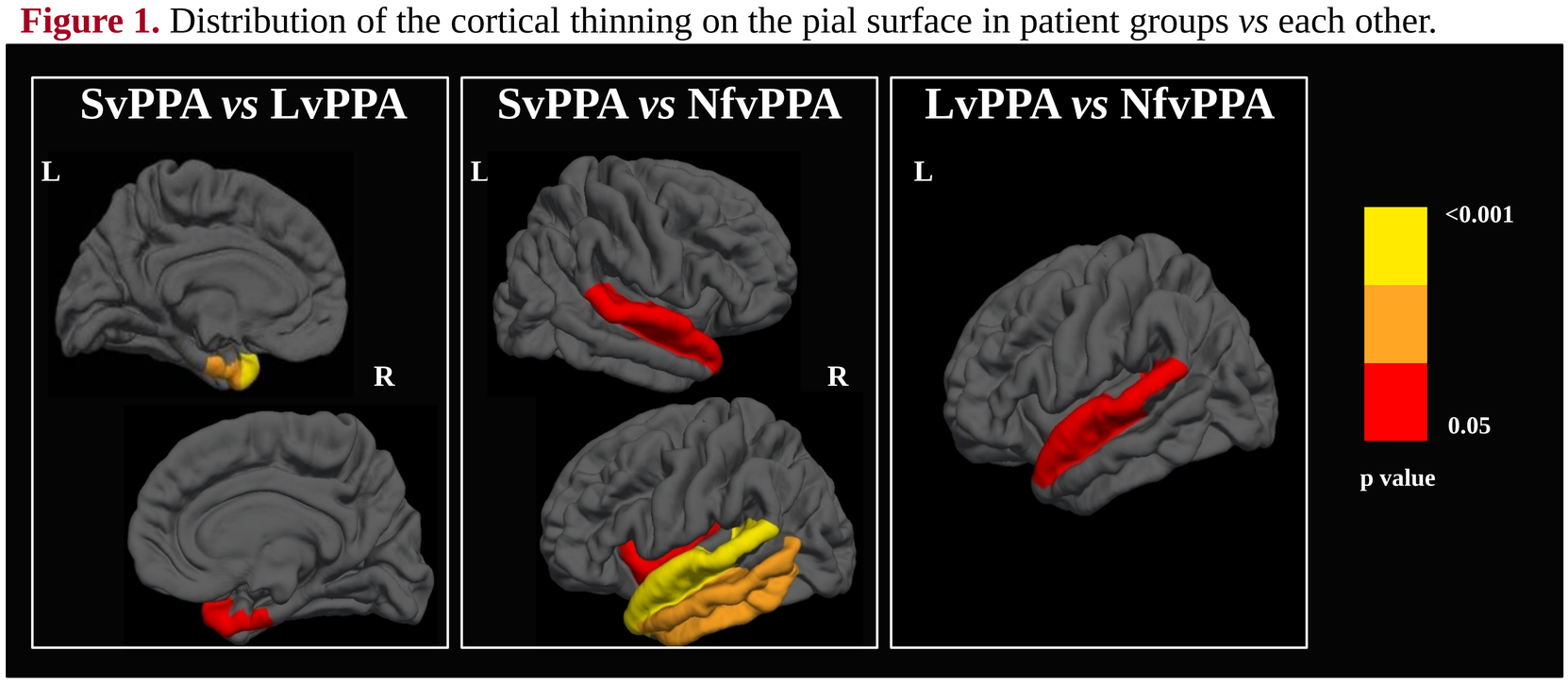
Statistical analysis

All MRI features were compared between groups using ANCOVA models, including disease duration as confounding variable.

RESULTS

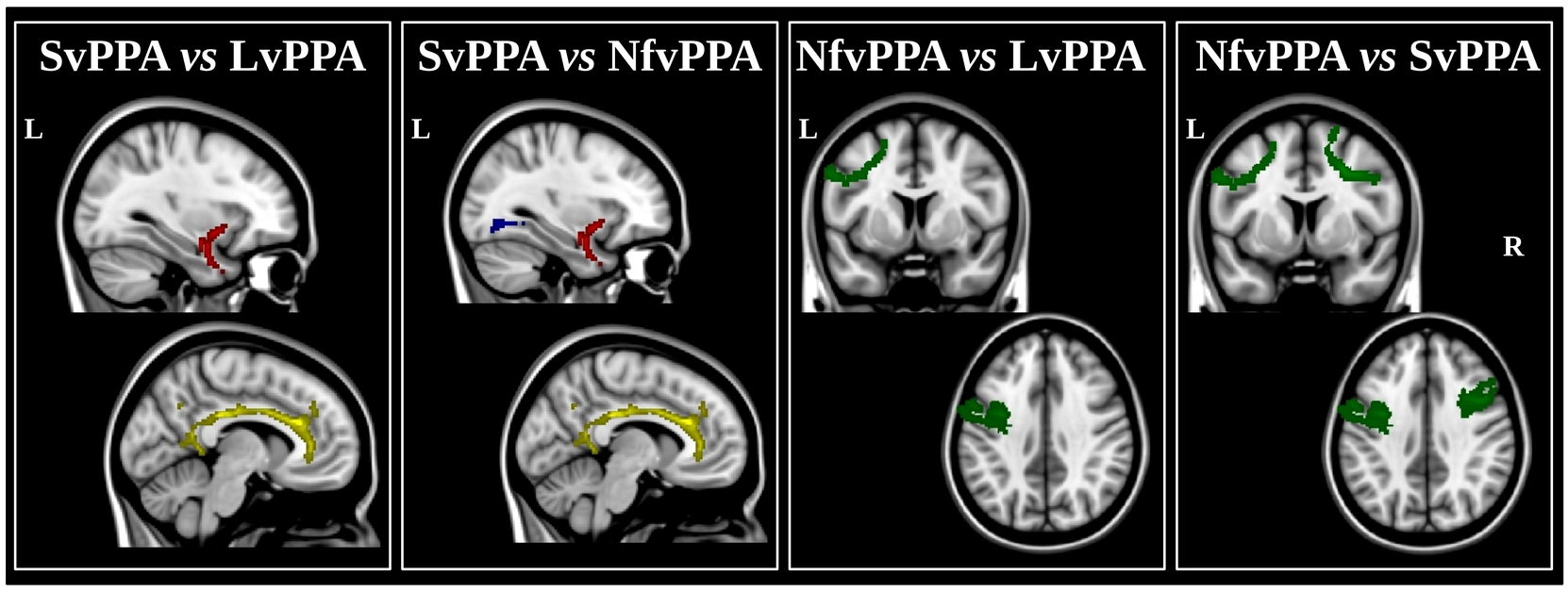
Compared with controls, all patients showed cortical thinning of the bilateral superior, inferior, and orbital frontal gyri, superior and middle temporal gyri, and temporal pole, left inferior temporal gyrus and entorhinal cortex; and a common widespread pattern of WM damage involving the bilateral cingulum, left uncinate, inferior and superior longitudinal fasciculi. Relative to controls, each patients group showed further variant-specific structural alterations (cortical thinning of the left pars opercularis in NFvPPA, left superior temporal and temporal pole in SvPPA, and left precuneus in LvPPA) which reflect their clinical and neuropsychological features.

Figure 1. Distribution of the cortical thinning on the pial surface in patient groups *vs* each other.



Results are false-discovery rate corrected for multiple comparisons and adjusted for subject's disease duration. Colors represent p values: yellow=0.001≥ p < 0.01; orange=0.01≥ p ≤ 0.02; red=0.02 > p < 0.05. L=left; R=right.

Figure 2. White matter tract damage in patient groups *vs* each other.



Colours indicate WM tract damage (blue: inferior longitudinal fasciculus; green: frontal aslant; red: uncinate; yellow: cingulum). Results are overlaid on the Montreal Neurological Institute standard brain and shown at p<0.05 corrected for False Discovery Rate; R=right; L=left.

CONCLUSIONS

In a large cohort of PPA patients, we demonstrated that structural MRI is powerful for distinguishing the PPA variants *in vivo*. NfvPPA and svPPA showed distinct MRI profiles. Specifically, nfvPPA is characterized by a prevalent WM damage mainly located in the frontal aslant tract, while svPPA showed a prevalent cortical damage of the anterior temporal lobe and microstructural alterations of the main temporal WM connections. Noteworthy, these data suggest that the involvement of the frontal aslant tract could be crucial for distinguishing nfvPPA from lvPPA cases, which can be challenging in the clinical practice.

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