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BRAIN FUNCTIONAL CONNECTIVITY DISRUPTION IN A LARGE COHORT OF PATIENTS WITH PRIMARY PROGRESSIVE APHASIA

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INTRODUCTION

The three clinical presentations of primary progressive aphasia (PPA) reflect heterogeneous neuropathological substrates which are difficult to be recognized *in vivo*. Resting-state functional MRI (RS-fMRI) is promising for the investigation of brain functional connectivity alterations in PPA. The aim of the present study is to assess the RS functional connectivity patterns associated with each of the three variants of PPA in a large multicenter cohort of patients.

METHODS

Table 1. Clinical and neuropsychological features of the sample.

	HC	nfvPPA	lvPPA	svPPA	P overall
Number	62	40	22	28	-
Age (years)	67.3±5.7	69.3±8.3	69.3±7.6	65.6±8.3	0.17
Sex, females (%)	61%	62%	55%	46%	0.52
Disease duration (years)	-	4.0±3.2	2.6±1.3	4.4±2.5	0.06
Education (years)	12.5±3.5	9.7±5.4#,^	13.1±3.4	11.9±4.3	0.01
CSF, Aβ42 (ng/L)	-	756.1±305.2	384.8±111.2*	708.6±249.6	<0.001
CSF, T-tau (ng/L)	-	358.4±171.9	462.1±289.8	300.5±194.1	0.163
CSF, p-tau (ng/L)	-	54.4±25.6	99.4±79.9*	48.2±18.5	0.01
Global cognition					
MMSE	29.5±0.8*	20.8±7.9	21.1±7.3	21.7±7.2	<0.001
FAB	-	6.3±4.3$	7.2±4.6	10.8±4.9	0.03
Language assessment					
Naming	-	39.7±10.4	38.9±10.8	20.2±13.4*	<0.001
Single word comprehension	-	47±2.2	48±0.0	38.5±10.0*	<0.001
Syntactic comprehension	33.5±2.0*	23.6±6.8	23.7±6.6	22.5±9.1	<0.001
Object knowledge	-	43.4±7.6	46.6±6.8	39.2±7.7^	0.04
Word/Sentence repetition	-	120.9±27.1	128.8±12.2	143.1±12.9*	0.003
Reading	-	26.3±5.1	26.9±5.1	28.8±2.3*	0.03
Writing	-	23.4±6.2$	25.9±5.3	29.1±1.6	0.004

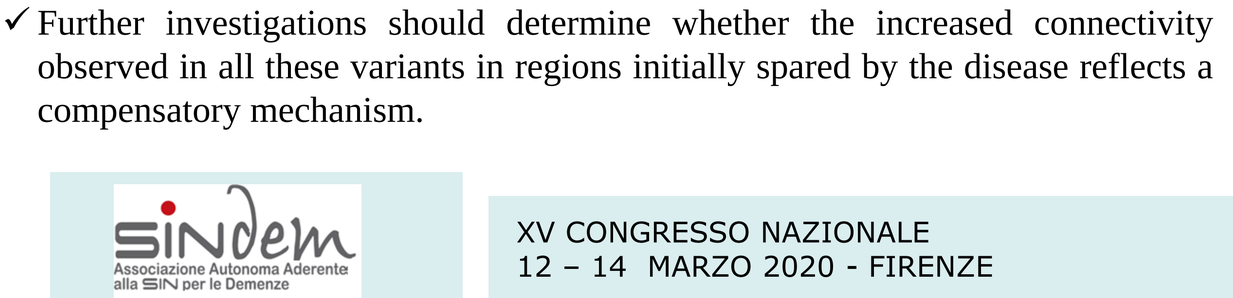
Values denotes mean ± standard deviations (or frequencies). P values refer to ANOVA models. Abbreviations: Aβ42= Amyloid-beta42; CSF=cerebrospinal fluid; FAB=Frontal Assessment Battery; lv/nfv/svPPA=logopenic/nonfluent/semantic variant of Primary Progressive Aphasia; MMSE=Mini Mental State Examination; ng/L=nanogram/Liter; p-Tau/T-tau=phosphorilated/Total tau. * denotes p<0.05 *vs* the other groups; # *vs* HC; ^ *vs* lvPPA; $ *vs* svPPA.

MRI acquisition and analysis

T1-weighted and RS-fMRI sequences were acquired in three different scans (1.5 T Achieva, Philips; 3.0 T Intera, Philips; 3.0 T Ingenia CX, Philips).

Brain networks of interest were identified using an independent component analysis and compared between groups accounting for gray matter atrophy (GIFT and BPM toolboxes, SPM12, **Figure 1**).

Figure 1. Steps of RS-fMRI data preprocessing and analysis.

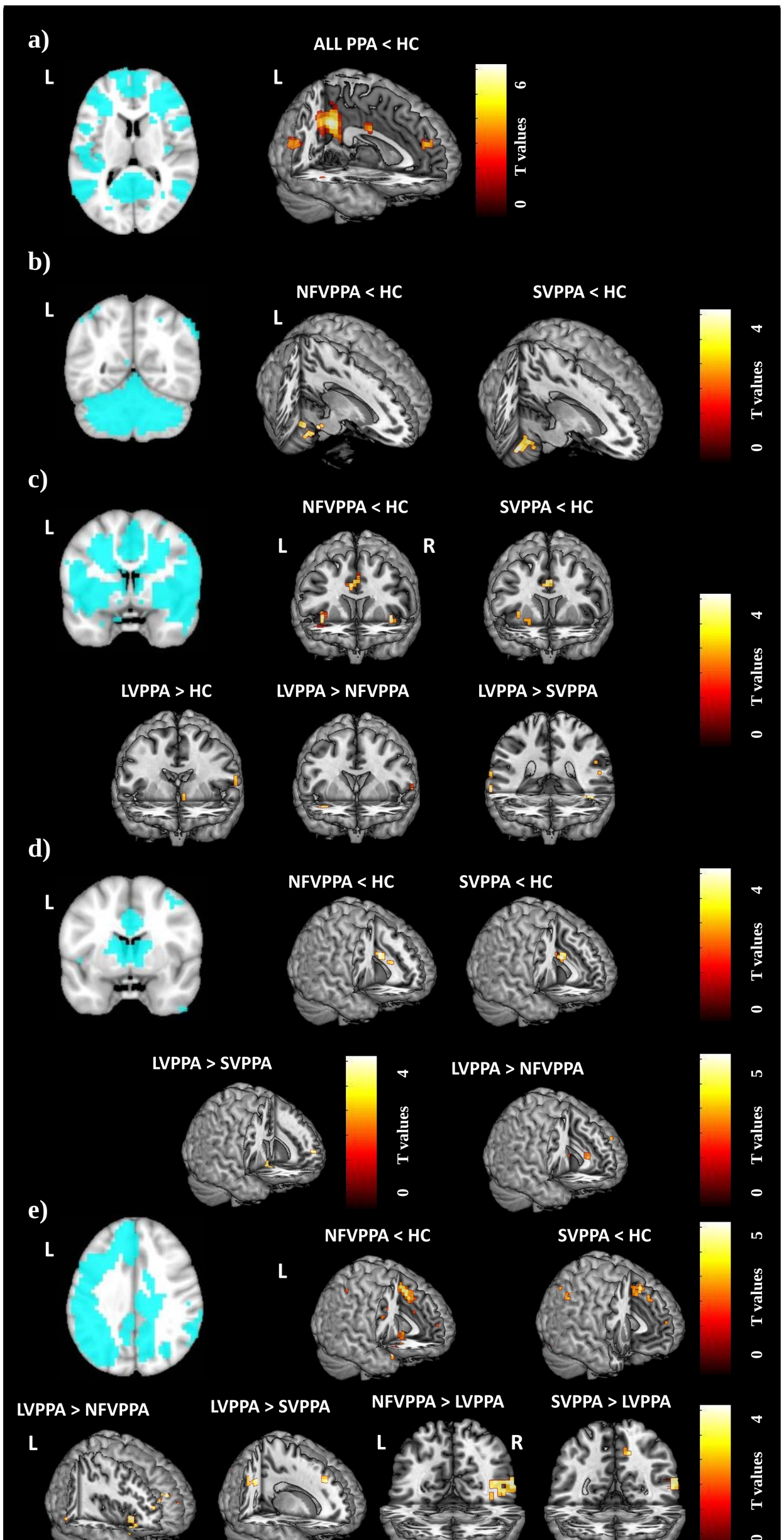


CONCLUSIONS

- ✓ PPA variants share a common pattern of altered functional connectivity within the DMN, suggesting that this network is affected in PPA regardless the underlined pathology.
- ✓ NfvPPA and svPPA showed common alterations within the cerebellar network (in regions known to be involved in high-cognitive functions and functionally connected with frontal areas), frontal and frontoparietal networks, which reflect their common frontotemporal degeneration.
- ✓ lvPPA showed increased connectivity in anterior brain regions within the salience and frontostrial networks as observed in Alzheimer's disease.
- ✓ Further investigations should determine whether the increased connectivity observed in all these variants in regions initially spared by the disease reflects a compensatory mechanism.

RESULTS

Figure 2. Functional connectivity differences between PPA variants and HC. Results are overlaid on the 3D Montreal Neurological Institute template in neurological convention (right is right). Coloured bars denote T-values. Significance is set at p<0.001 uncorrected for multiple comparisons.
Networks of interest are shown at the left side of the panel in cyan colour: a) Default Mode Network (DMN); b) Cerebellar network; c) Salience network; d) Fronto-striatal network; e) left Fronto-parietal network.



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