PN 331

THE CEREBRAL STRUCTURAL AND FUNCTIONAL SIGNATURES OF IMPULSE CONTROL DISORDER IN PARKINSON'S DISEASE

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INTRODUCTION AND OBJECTIVE

Impulse control disorder (ICD) is frequent in patients affected by Parkinson's disease (PD). Compared with PD without ICD (PD no-ICD), PD-ICD patients are characterized by more severe psychiatric symptoms and cerebral structural alterations in the meso-cortico-limbic circuit. However, while comparing the two groups of PD patients, few studies have taken into account the motor impairment severity, disease duration and cognitive status. Our aim was to assess cortical thickness (CT) measures, white matter (WM) microstructural damage and resting state (RS) functional connectivity in PD-ICD patients compared with healthy controls (HC) and PD no-ICD cases matched for disease stage, motor impairment, and cognitive features.

MATERIALS AND METHODS

Table 1. Sociodemographic and cognitive features of patients and healthy controls

	PD-ICD	PD no-ICD	HC	p value
N	35	50	50	
Age	62.0 ± 10.4	61.5 ± 8.9	59.0 ± 12.4	0.36
Gender, males (%)	30 (86)	36 (72)	35 (70)	0.22
Education	12.7 ± 2.6	12.2 ± 2.3	13.2 ± 2.8	0.19
PD duration, years	9.5 ± 5.2	9.0 ± 6.1	-	0.67
UPDRS-III	47.2 ± 15.5	43.5 ± 12.4	-	0.25
H&Y	2.7 ± 0.8	2.5 ± 0.7	-	0.11
QUIP, total	21.9 ± 10.2	-	-	-
ICD duration, years	3.3 ± 2.1	-	-	-
Global cognition				
MMSE	28.3 ± 1.8	28.1 ± 1.4	29.7 ± 0.7*	<0.001
Memory				
RAVLT, immediate recall	37.5 ± 10.8	36.5 ± 10.4	44.8 ± 10.4*	0.001
RAVLT, delayed recall	6.7 ± 3.1	6.3 ± 2.7	8.7 ± 2.8*	<0.001
Language				
ACE-R, language	24.3 ± 2.2	23.6 ± 2.4	25.9 ± 0.3*	<0.001
Executive functions				
Phonemic fluency	31.9 ± 9.2	33.0 ± 9.5	40.0 ± 8.2*	<0.001
Semantic fluency	16.8 ± 4.4	16.7 ± 5.1	19.7 ± 4.5*	0.01
Visuospatial abilities				
ACE-R, visuospatial	14.8 ± 1.7	15.2 ± 1.1	15.8 ± 0.4*	0.01
Mood and behavior				
HDRS	9.8 ± 5.4*	5.7 ± 5.4	3.6 ± 4.9	<0.001
HAMA	6.0 ± 6.5	6.9 ± 6.0	3.4 ± 3.8°	0.02
Apathy Evaluation Scale	16.1 ± 6.2*	10.7 ± 8.9*	1.9 ± 3.5*	<0.001

Values are means ± standard deviations or frequencies (%). P values refer to T-test or ANOVA models. Post-hoc analyses are shown as following: *p<0.05 *vs* each other group; °p<0.05 *vs* PD no-ICD patients. Abbreviations. ACE-R=Addenbrooke's Cognitive Examination-Revised; HAMA=Hamilton Anxiety Rating Scale; HDRS=Hamilton Depression Rating Scale; H&Y=Hoehn and Yahr Scale; MMSE=Mini Mental State Examination; QUIP=Questionnaire for Impulsive-Compulsive Disorders; RAVLT=Rey Auditory Verbal Learning Test; UPDRS-III=Unified Parkinson's Disease Rating Scale III.

MRI acquisition

✓All patients underwent the following sequences: T1-weighted, Diffusion Tensor (DT), and T2*-weighted single-shot echo planar imaging (EPI) for RS fMRI on a 1.5 T scanner (Philips Medical Systems, Achieva).

MRI preprocessing

✓MRI metrics of CT 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).
✓RS fMRI data analysis of brain networks using FSL (MELODIC).

Statistical analysis

All statistical models included age as confounding variable.

1.Group comparisons

✓To investigate regional CT, DT MRI measures and RS fMRI differences between PD patients with and without ICD and HC groups using ANOVA models in SAS (v. 9.3) and FSL.

2. Correlations

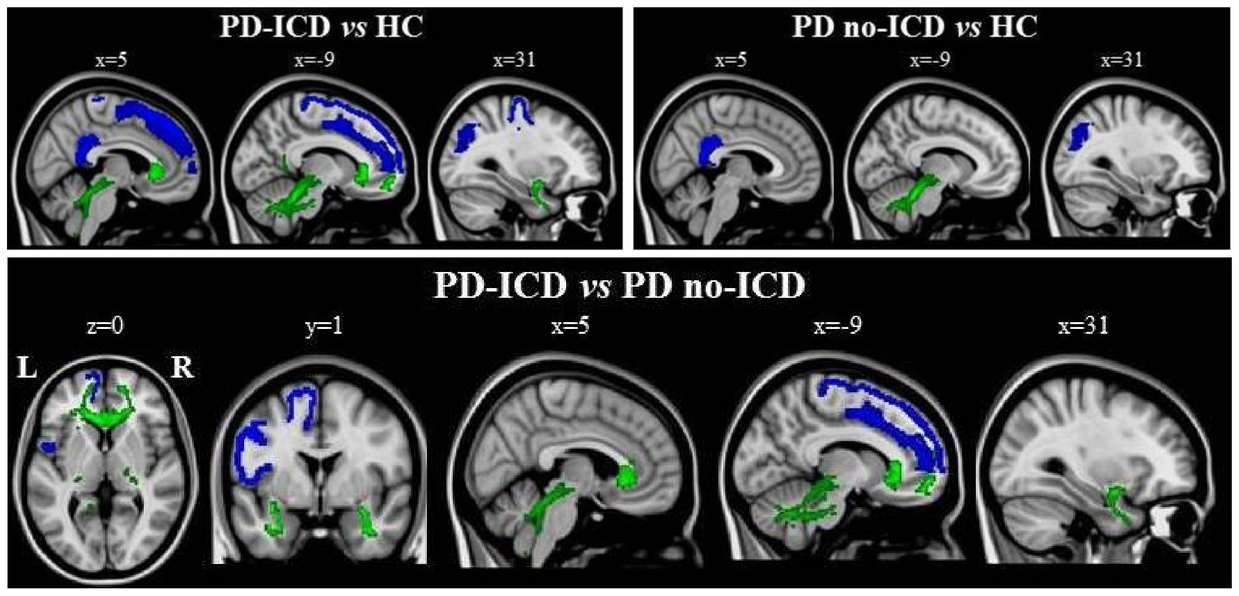
✓Multiple regression models to assess the relationships between structural, functional MRI and clinical variables using SAS.

RESULTS

Clinical findings. Compared to HC and to PD no-ICD, PD-ICD patients showed more depressive and apathetic symptoms. On the contrary, compared to HC, PD no-ICD patients showed more severe anxiety.

MRI findings: Cortical thickness and white matter tract damage

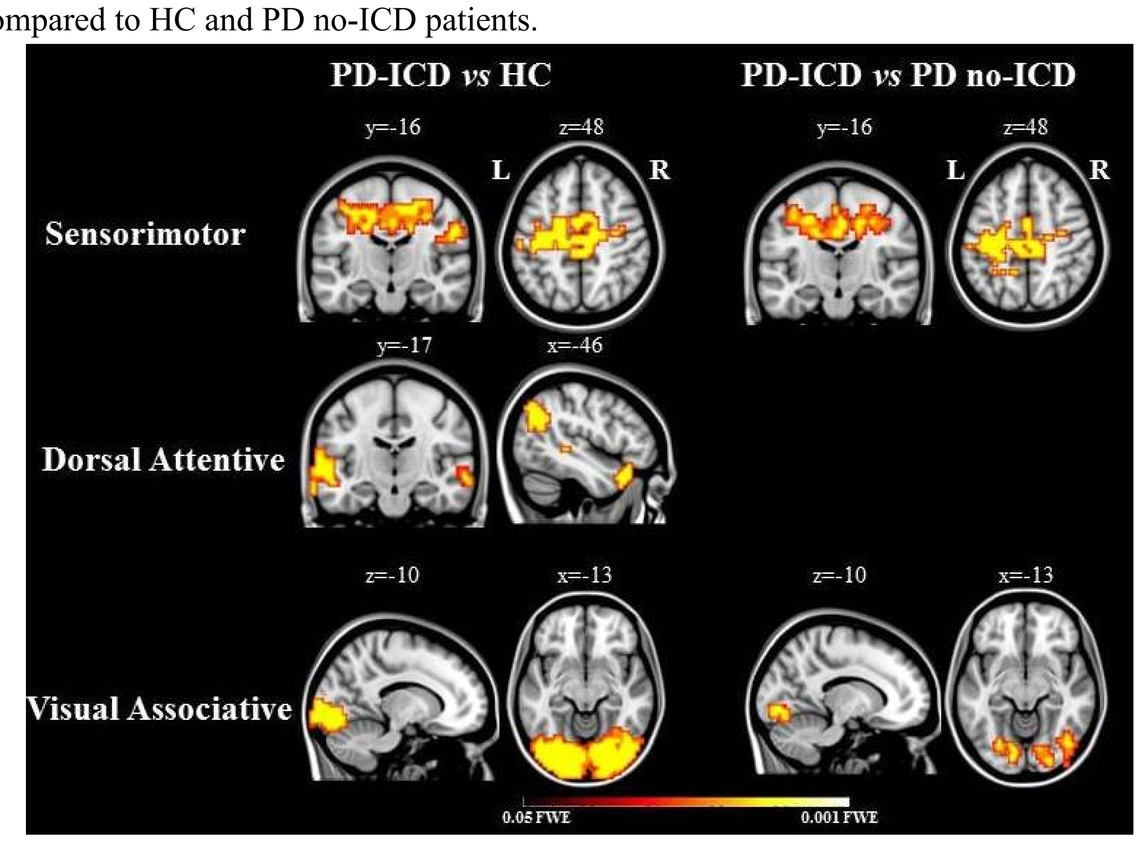
Figure 1. Regional cortical thinning and white matter tract damage in patients *vs* controls.



Colours indicate cortical thinning (blue) and white matter tract damage (green). 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; x=sagittal views, negative numbers denote the left side; y=coronal view; z=axial views.

MRI findings: RS functional connectivity

Figure 2. Increased functional connectivity within the investigated networks in PD-ICD compared to HC and PD no-ICD patients.



Results are overlaid on the Montreal Neurological Institute standard brain and dysplayed at p<0.05 family wise error (FWE) corrected for multiple comparisons. Coloured bar denotes p values. R=right; L=left; x=sagittal views, negative numbers denote the left side; y=coronal view; z=axial views.

Correlations. In PD-ICD patients: longer duration of ICD was associated with greater WM damage of the right uncinate fasciculus; the severity of their depressive symptoms was associated to the WM damage of the genu of the corpus callosum, left parahippocampal bundle and right uncinate fasciculus; the increased RS connectivity within the dorsal attentive and visual associative networks was associated to the cortical thinning of the left superior frontal and inferior temporal lobes.

CONCLUSIONS

✓This study offers a comprehensive picture of the cerebral structural and functional features of PD-ICD patients.
✓PD-ICD patients showed a widespread pattern of cortical thinning and WM damage involving frontal, meso-limbic and motor circuits.
✓In PD-ICD patients, the structural damage of crucial limbic regions was associated with the patient clinical features.
✓RS fMRI data confirmed that PD-ICD patients are characterized by an hyperconnectivity in motor and cognitive-related brain networks.
✓The RS fMRI hyperconnectivity in PD-ICD patients is related to their structural damage, thus excluding the hypothesis of a compensatory mechanism.
✓A multimodal neuroimaging approach is promising for understanding the mechanisms associated with ICD and for the detection of PD patients at risk to develop ICD.