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Characteristics of punding in Parkinson's disease: a multimodal neuroimaging approach

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INTRODUCTION AND OBJECTIVE

Impulse control disorder (ICD) in Parkinson's disease (PD) is a heterogeneous group of disorders comprising four so-called "major ICDs" (gambling, hypersexuality, compulsive buying, binge eating) and loosely defined ICDs, including dopamine-dysregulation and punding. While there is growing body of evidence showing brain alterations associated to the major ICDs in PD, less light has been shed on punding. This study aimed to assess cerebral cortical thickness, white matter (WM) microstructure integrity, and resting state (RS) functional connectivity in PD-punding patients compared with well-matched (age, gender, education, PD duration, PD age at onset, dopaminergic treatment and cognitive features) PD no-ICD patients and healthy controls.

MATERIALS AND METHODS

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

	PD-punding	PD no-ICD	HC	p PD-punding *vs* HC	p PD no-ICD *vs* HC	p PD-punding *vs* PD no-ICD
Number	22	30	30			
Age at MRI [yrs]	63.1 ± 9.2	63.9 ± 6.6	63.0 ± 9.1	1.00	1.00	1.00
Gender [N, % male]	19 (86%)	21 (70%)	21 (70%)	0.20	1.00	0.20
Education [yrs]	12.1 ± 2.7	11.7 ± 2.3	12.2 ± 2.7	1.00	1.00	1.00
Age at onset [yrs]	54.0 ± 9.8	54.0 ± 7.8				1.00
PD duration [yrs]	9.1 ± 5.4	9.9 ± 5.3				0.61
Side affected at onset [% right]	13 (59%)	18 (60%)				0.43
LEDD [mg]	887.9 ± 348.3	934.8 ± 302.8				0.61
DA LEDD [mg]	269.1 ± 141.2	315.7 ± 177.8				0.32
UPDRS-III	43.1 ± 13.7	47.2 ± 8.0				0.23
Hoehn & Yahr	2.5 ± 0.9	2.6 ± 0.5				0.68
Behavioural features						
HDRS	9.1 ± 3.9	4.5 ± 4.1	3.8 ± 5.0	0.001	1.00	0.001
HAMA	4.4 ± 5.0	5.8 ± 5.8	3.2 ± 3.1	1.00	0.14	0.89
Apathy scale	17.1 ± 5.9	10.9 ± 8.5	1.7 ± 3.6	<0.001	<0.001	0.004
PRS, total score	10.3 ± 3.3	-	-	-	-	-
PRS, hours spent on punding per day	4.6 ±2.0	-	-	-	-	-
PRS, severity score	5.7 ± 2.0	-	-	-	-	-
Global cognition						
MMSE	28.0 ± 1.9	28.1 ± 3.7	29.7 ± 0.7	0.09	0.07	1.00
ACE-R, total	89.3 ± 7.1	89.6 ± 10.6	96.2 ± 2.8	0.01	0.01	1.00

Values are means ± standard deviations or frequencies. P values refer to T-test or ANOVA models. Abbreviations: DA=dopamine agonist; LEDD=levodopa equivalent daily dose; HAMA=Hamilton Anxiety Rating Scale; HC=Healthy Controls; HDRS=Hamilton Depression Rating Scale; mg=milligram; MMSE=Mini Mental State Examination; ACE-R=Addenbrooke's Cognitive Examination-Revised; PRS= Punding Rating Scale; UPDRS-III=Unified Parkinson's Disease Rating Scale III; yrs=years.

MRI acquisition

- ✓ MR 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 analysis

- ✓ Cortical thickness measures from atlas-based cortical regions (Desikan atlas) using FreeSurfer (v. 5.3); DT MRI metrics from main motor, interhemispheric and long associative WM tracts; RS fMRI data using a seed-based approach with habenula and amygdala used as seed regions.

Statistical analysis

- ✓ CT and DT MRI measures: ANOVA models in SPSS, followed by post-hoc pairwise comparisons, false discovery rate (FDR)-corrected for multiple comparisons ($p<0.05$); RS fMRI: between-group comparisons in FSL (adjusted for gray matter maps), family wise error (FWE)-corrected for multiple comparisons ($p<0.05$).

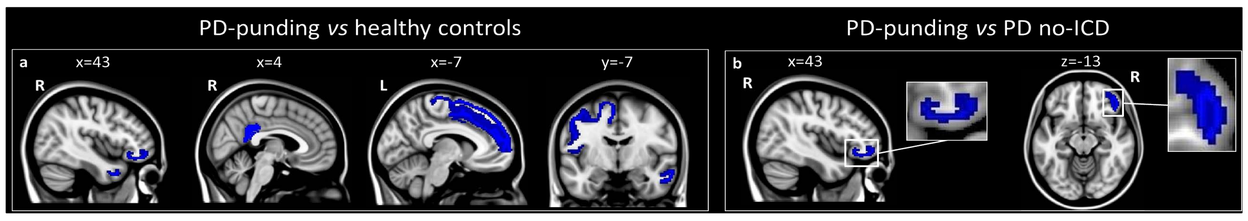
RESULTS: clinical findings

All PD patients showed more severe apathy and performed worse in tests assessing global cognition and working memory compared to controls. Additionally, PD-punding patients showed higher scores in the scales assessing depression and apathy compared to both PD no-ICD and control groups (Table 1). Also, PD-punding patients showed further deficits in several tests assessing visuospatial abilities and executive functions, and PD-no ICD in a test assessing language.

MRI RESULTS

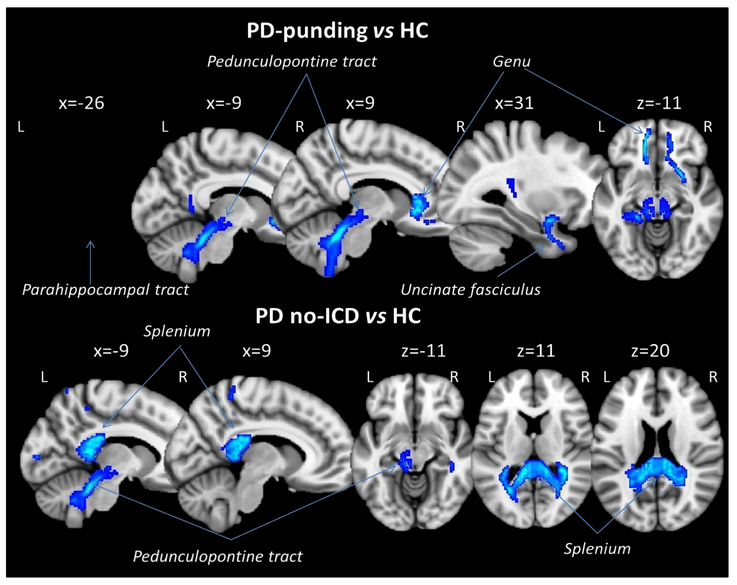
Cortical thickness and white matter (WM) damage

Figure 1. Cortical thinning pattern in PD punding *vs* controls (a) and PD no-ICD (b)



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.

Figure 2. WM tract damage in PD punding and PD no-ICD patents patients *vs* controls



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.

RS functional connectivity

Figure 3. Regions where PD-punding patients showed enhanced (cold colors) or reduced (warm colors) functional connectivity with the bilateral habenula compared to healthy controls (upper panel) and PD no-ICD patients (lower panel).

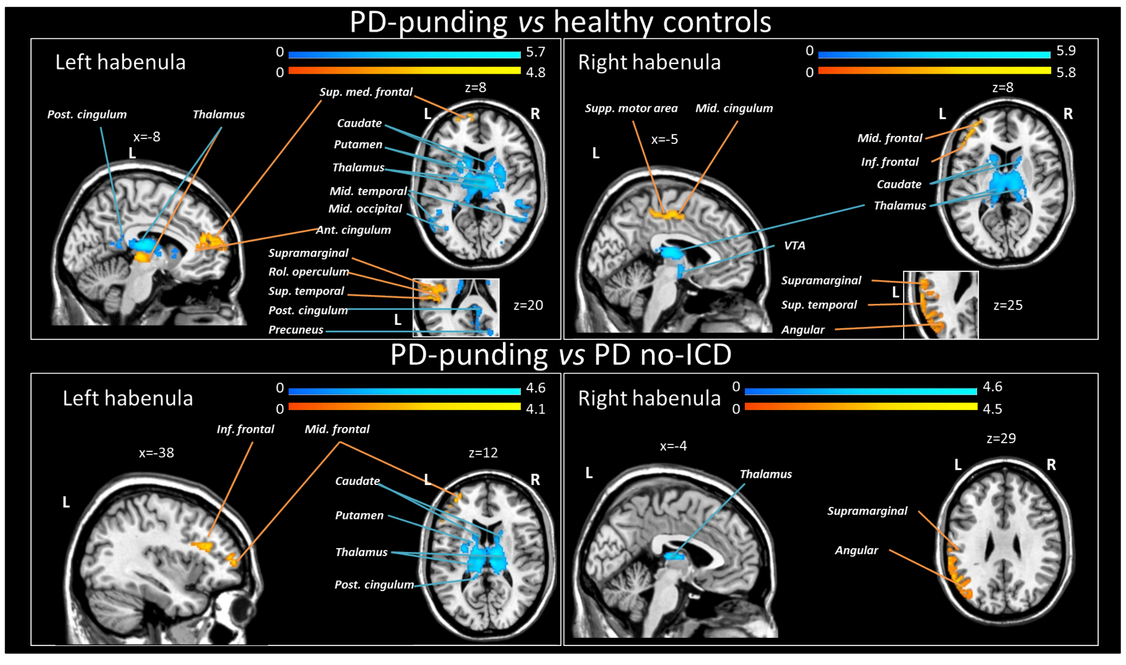
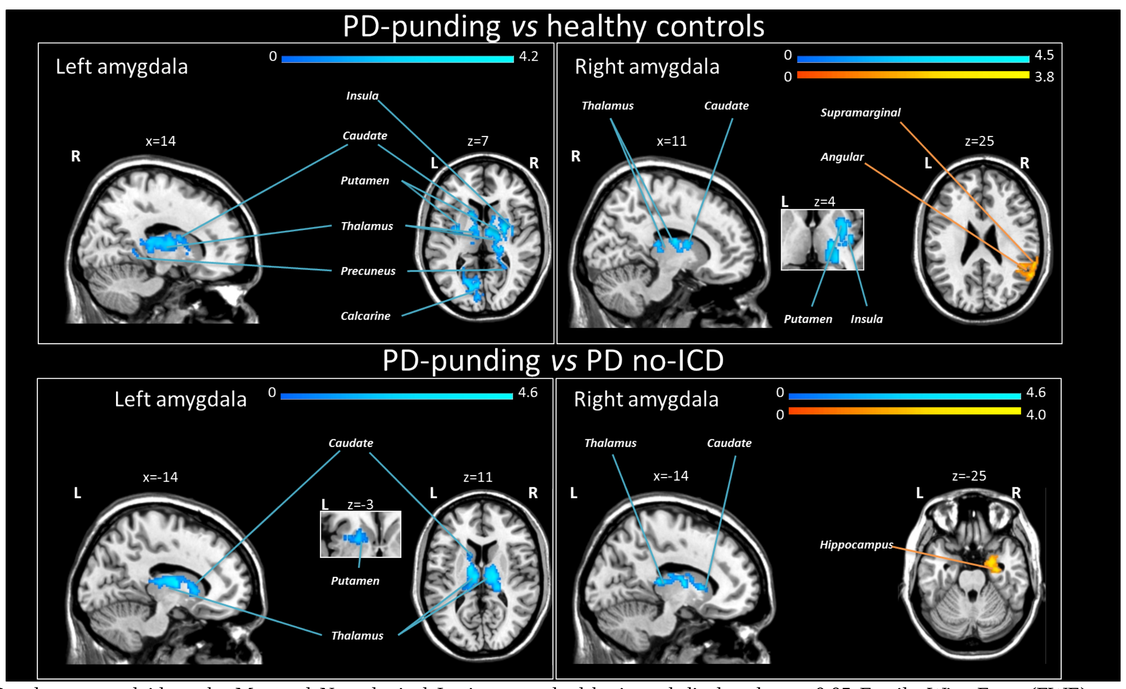


Figure 4. Regions where PD-punding patients showed enhanced (cold colors) or reduced (warm colors) functional connectivity with the bilateral amygdala compared to healthy controls (upper panel) and PD no-ICD patients (lower panel).



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

CONCLUSIONS

PD-punding is associated with a disconnection between brain regions which modulate the reward circuit and the frontal cortex, and a hyperconnectivity between these regions and those at the subcortical level. In PD-punding patients, these alterations may reflect their typical repetitive behavior regardless the reward. This study offers opportunity for the detection of PD patients at risk to develop punding.

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