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LONGITUDINAL CLINICAL AND NEUROANATOMICAL CHANGES OF PD-MCI REVERTERS

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INTRODUCTION

The aim of this study is to investigate longitudinal clinical and neuroanatomical features of Parkinson's disease (PD) patients who experienced mild cognitive impairment (MCI) but reverted to normal cognition overtime (PD-MCIr) compared to PD with normal cognition (PD-CN), stable MCI (PD-MCIs), and patients who converted to MCI (PD-MCIc) or dementia (PD-Dc).

METHODS

Patients received a comprehensive evaluation including clinical and cognitive/behavioural assessments at study entry and every year or every two years for at least 2 and maximum 3 follow up visits within 4 years. At the end of the observation period (i.e., at last available visit), we classified patients according to their cognitive profile.

Table 1. Sociodemographic, clinical and neuropsychological features of the sample at baseline.

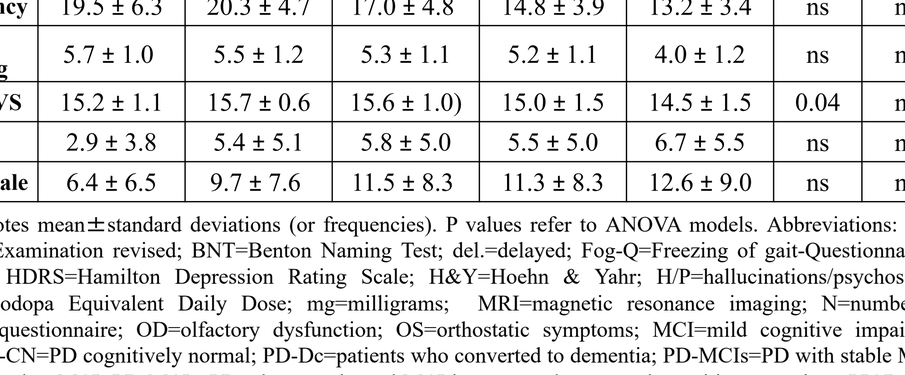
	PD-MCIr	PD-CN	PD-MCIc	PD-MCIs	PD-Dc	*vs* PD-CN	*vs* PD-MCIc	*vs* PD-MCIs	*vs* PD-Dc
N	12	55	37	26	24				
Age at MRI	58.1 ± 8.1	58.3 ± 8.3	62.6 ± 6.3	63.3 ± 5.9	67.3 ± 7.4	ns	ns	0.03	0.002
Sex (% mean)	8 (67)	27 (49)	27 (73)	16 (62)	13 (53)	ns	ns	ns	ns
Education	12.3 ± 1.2	13.8 ± 2.3	12.4 ± 2.2	10.6 ± 2.4	11.5 ± 2.8	0.03	ns	0.02	ns
Age at onset	55.5 ± 8.9	55.6 ± 8.5	58.0 ± 8.4	54.65 ± 7.6	57.7 ± 8.0	ns	ns	ns	ns
PD duration	2.7 ± 2.4	2.7 ± 3.1	4.6 ± 4.6	6.9±5.8	9.6 ± 4.4	ns	ns	0.02	<0.001
LEDD[mg]	259.2 ± 395.7	323.3 ± 368.3	554.1 ± 412.2	675.6 ± 385.6	832.7 ± 251.9	ns	0.03	0.004	<0.001
Clinical motor features									
H&Y	1.4 ± 0.6	1.2 ± 0.5	1.7 ± 0.7	2.0 ± 0.8	2.71 ± 0.51	ns	ns	0.03	<0.001
UPDRS Tot	32.4 ± 12.4	30.6 ± 15.8	41.4 ± 16.5	50.8 ± 20.0	71.23 ± 14.9	ns	ns	0.01	<0.001
UPDRS-II Tot	6.7 ± 3.2	6.4 ± 4.2	8.5 ± 4.5	11.8 ± 5.6	15.1 ± 4.9	ns	ns	0.01	<0.001
UPDRS-III Tot	21.7 ± 8.8	19.2 ± 12.2	28.1 ± 13.0	33.5 ± 14.5	48.9 ± 9.6	ns	ns	0.01	<0.001
Fog-Q	1.6 ± 3.4	1.3 ± 2.4	2.5 ± 3.5	4.4 ± 4.2	6.1 ± 4.3	ns	ns	0.049	0.003
Clinical non-motor features									
RBDSQ	2.2 ± 2.4	2.7 ± 2.5	3.0 ± 2.3	4.5 ± 3.9	4.6 ± 2.8	ns	ns	ns	0.02
UPDRS-I Total	3.6 ± 3.5	4.6 ± 3.3	3.8 ± 3.5)	4.1 ± 4.2	3.8 ± 2.4	ns	ns	ns	ns
UPDRS-I H/P*	0 (0)	2 (4)	3 (8)	8 (31)	15 (63)	ns	ns	ns	<0.001
NMS-Q GS*	4 (33)	36 (65)	11 (30)	18 (69)	23 (96)	0.03	ns	0.03	<0.001
NMS-Q US*	6 (50)	30 (55)	14 (38)	20 (77)	21 (88)	ns	ns	ns	0.01
NMS-Q OD*	2 (17)	12 (22)	11 (30)	7 (27)	8 (33)	ns	ns	ns	ns
NMS-Q SD*	2 (17)	24 (17)	15 (41)	18 (69)	18 (75)	ns	ns	0.002	<0.001
NMS-Q OS*	1 (8)	11 (20)	8 (22)	11 (44)	13 (53)	ns	ns	0.03	0.01
Cognitive features									
ACE-R, Total	91.4 ± 3.8	94.0 ± 3.8	90.8 ± 5.6	84.1 ± 7.8	82.0 ± 7.0	0.03	ns	0.004	<0.001
RAVLT, del.	8.0 ± 3.3	8.3 ± 2.7	7.0 ± 1.6	5.2 ± 2.4	4.6 ± 2.4	ns	ns	0.01	0.001
BNT total	58.3 ± 1.1	58.1 ± 2.4	56.3 ± 4.0	53.8 ± 4.7	52.4 ± 10.9	ns	ns	0.002	ns
Sem. fluency	19.5 ± 6.3	20.3 ± 4.7	17.0 ± 4.8	14.8 ± 3.9	13.2 ± 3.4	ns	ns	0.01	<0.001
Digit ordering	5.7 ± 1.0	5.5 ± 1.2	5.3 ± 1.1	5.2 ± 1.1	4.0 ± 1.2	ns	ns	ns	<0.001
ACE-R, VS	15.2 ± 1.1	15.7 ± 0.6	15.6 ± 1.0)	15.0 ± 1.5	14.5 ± 1.5	0.04	ns	ns	ns
HDRS	2.9 ± 3.8	5.4 ± 5.1	5.8 ± 5.0	5.5 ± 5.0	6.7 ± 5.5	ns	ns	ns	0.04
Apathy scale	6.4 ± 6.5	9.7 ± 7.6	11.5 ± 8.3	11.3 ± 8.3	12.6 ± 9.0	ns	ns	ns	0.04

Values denotes mean±standard deviations (or frequencies). P values refer to ANOVA models. Abbreviations: ACE-R=Addenbrooke's Cognitive Examination revised; BNT=Benton Naming Test; del.=delayed; Fog-Q=Freezing of gait-Questionnaire; GS=gastrointestinal symptoms; HDRS=Hamilton Depression Rating Scale; H&Y=Hoehn & Yahr; H/P=hallucinations/psychosis; IND=Indeterminate; LEDD=Levodopa Equivalent Daily Dose; mg=milligrams; MRI=magnetic resonance imaging; N=number; NMS-Q=Non-motor symptoms questionnaire; OD=olfactory dysfunction; OS=orthostatic symptoms; MCI=mild cognitive impairment; PD=Parkinson's disease; PD-CN=PD cognitively normal; PD-Dc=patients who converted to dementia; PD-MCIs=PD with stable MCI; PD-MCIc=patients who converted to MCI; PD-MCIr=PD who experienced MCI but reverted to normal cognition over time; PIGD=Postural instability and gait disorder; RAVLT=Rey Auditory Verbal Learning Test; RBDSQ=Rem sleep behavior disorder screening questionnaire; SD=sexual dysfunction; Sem.=semantic; UPDRS=Unified Parkinson's Disease Rating Scale; US=urinary symptoms; VS=visuospatial. *Percentage of patients with the presence of symptoms. Age at MRI/onset, PD duration, Education values are expressed in years.

MRI preprocessing and analysis

- ✓ At each visit all patients underwent a MRI scan (T1-weighted sequences acquired in a 1.5 T Philips Achieva scanner).
- ✓ Baseline cortical thickness (**Figure 1**) and subcortical volumetry was obtained from all patients and compared between groups.
- ✓ Cortical thinning and volume loss overtime was investigated within and between groups.

Figure 1. Steps of the cortical thickness preprocessing (FreeSurfer image analysis suite, version 5.3)



RESULTS

Figure 2. Clinical, motor and non-motor features of PD-MCIr compared to the other groups at the last available visit.

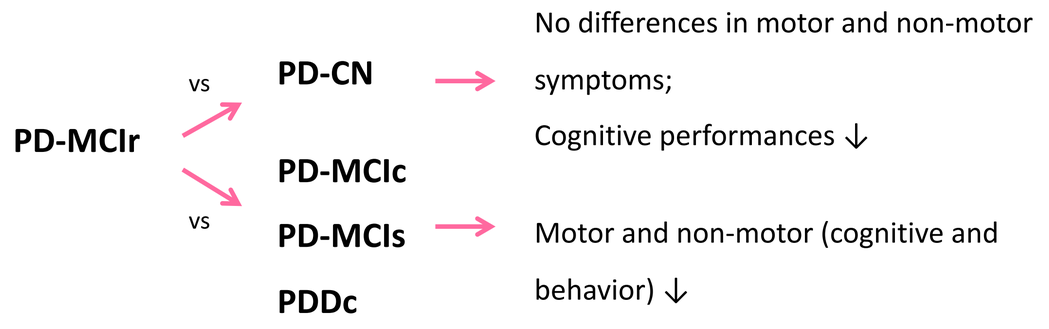


Figure 3. Patterns of cortical thickness and volumetry of PD-MCIr group compared with the other groups of patients at baseline. Findings are shown at $p<0.05$ corrected for multiple comparisons using Monte Carlo correction. Colour bar represents t-values.

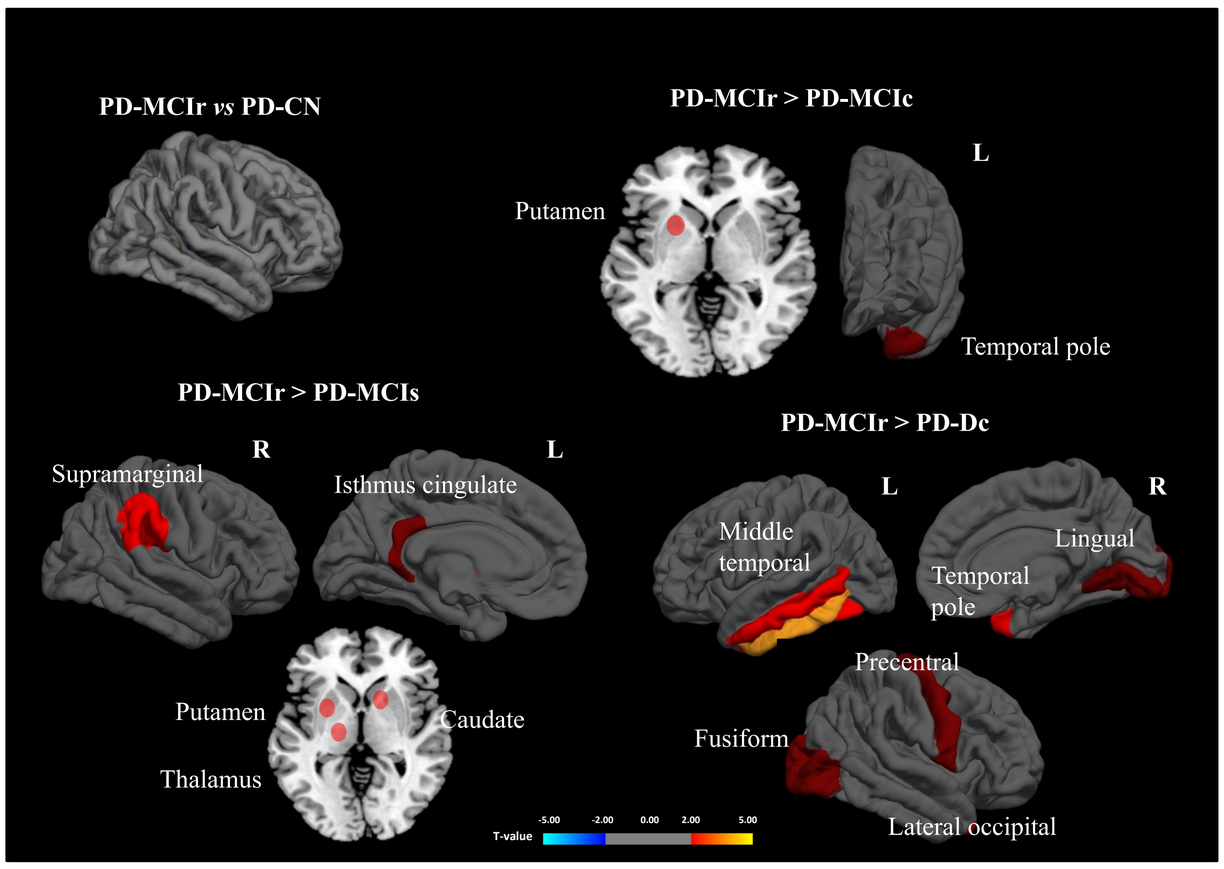
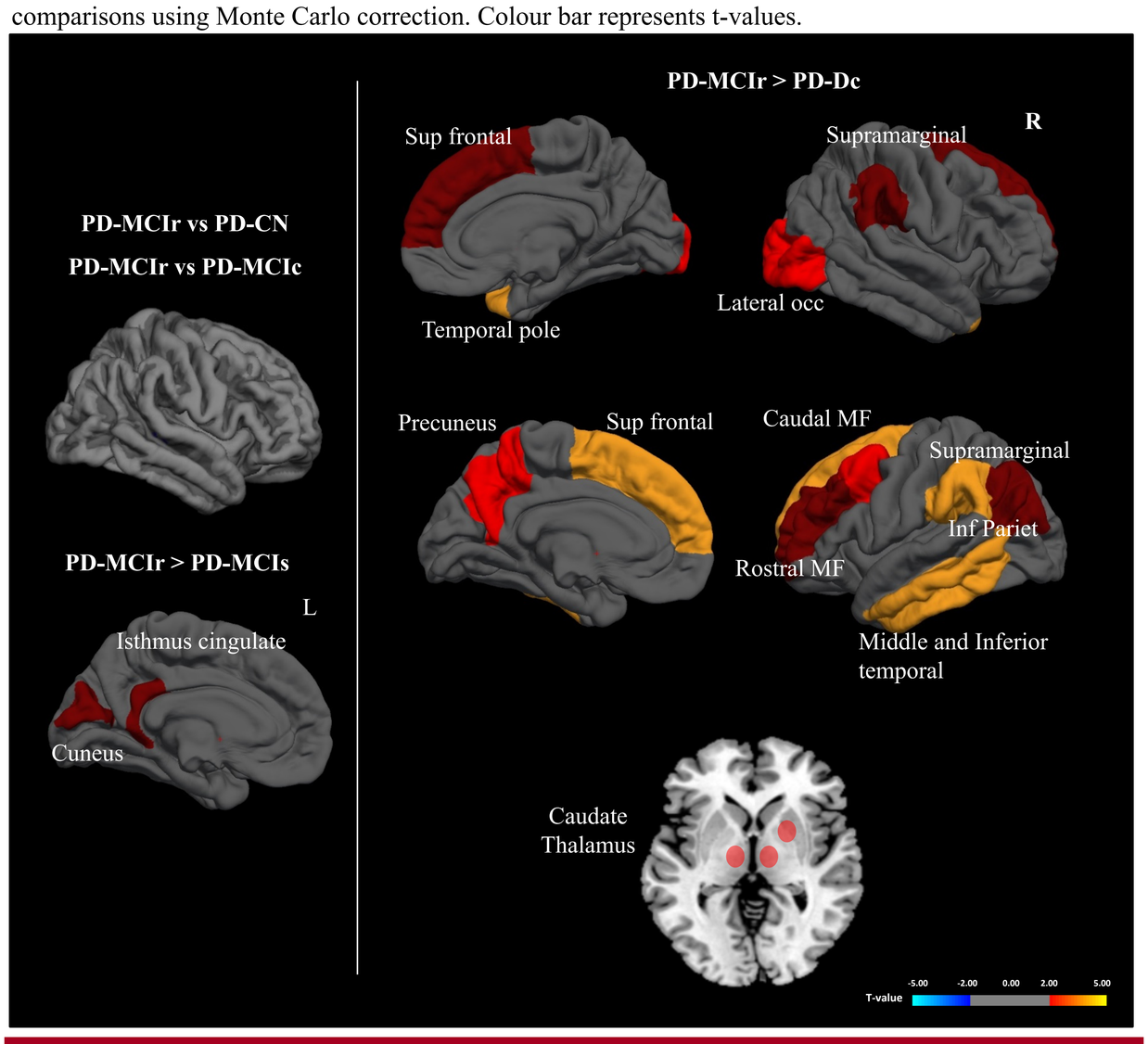


Figure 4. Group-by-time interaction analysis. Findings are shown at $p<0.05$ corrected for multiple comparisons using Monte Carlo correction. Colour bar represents t-values.



CONCLUSIONS

- ✓ PD-MCIr is associated to a mild phenotype and a relatively preserved brain structure relative to patients with a progressive cognitive decline.
- ✓ The PD-MCIr group remains similar to PD-CN cases overtime, except for a cognitive vulnerability that in this group seems to be independent of the progression of motor and (other) non-motor disturbances.
- ✓ This work increases the knowledge on clinical and neuroanatomical features overtime of this specific group of PD.

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