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Cortical thinning associated with mild cognitive impairment in Parkinson's disease

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OBJECTIVE

To investigate patterns of cortical thinning associated with mild cognitive impairment (MCI) in a large sample of Parkinson's disease (PD) patients and to explore relationships with cognitive deficits**.**

MATERIALS AND METHODS

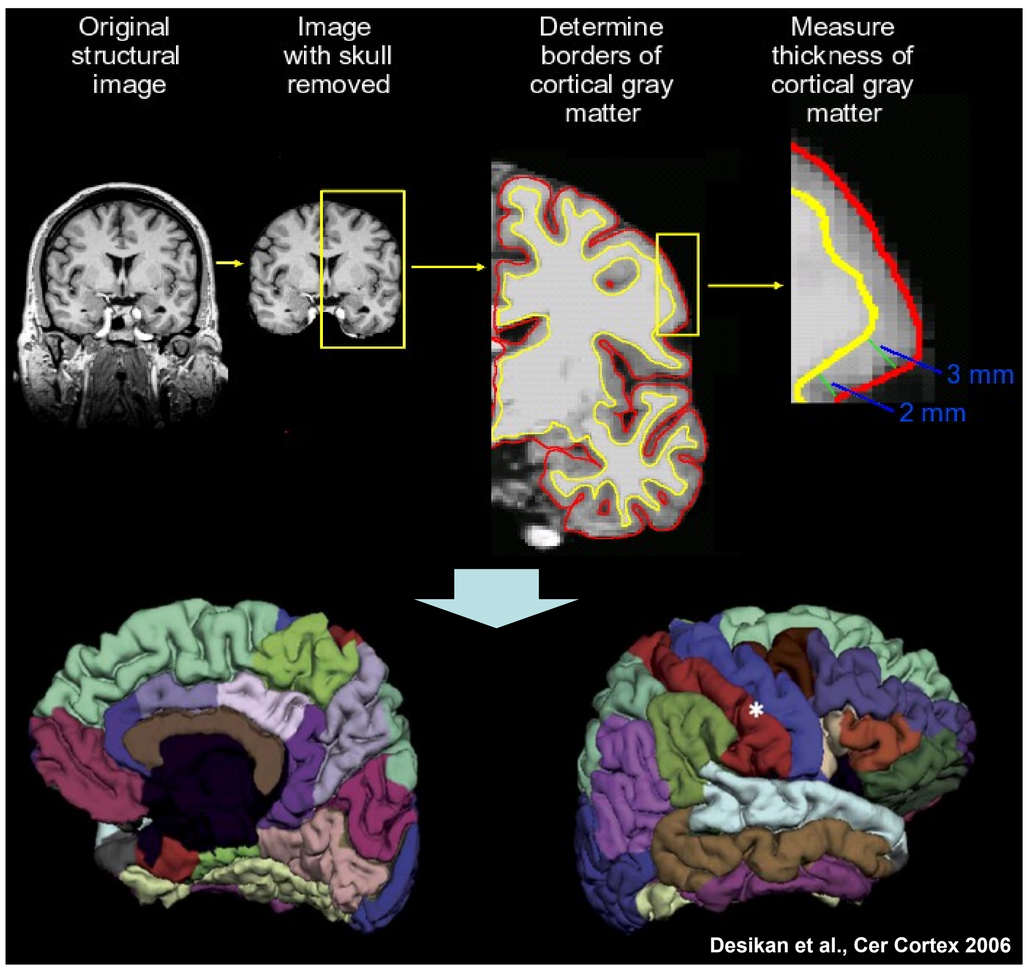
- We included 108 PD patients (54 without cognitive impairment [PD-ncog], and 54 with MCI [PD-MCI]), and 41 healthy controls.
- All patients and controls underwent structural magnetic resonance imaging (MRI) at 1.5 T and a comprehensive clinical and neuropsychological evaluation including tests that assess different cognitive domains: attention and working memory, executive functions, memory, language, and visuospatial functions.
- According to the MDS Task-force criteria (Litvan, et al., 2012), PD-MCI patients had multidomain MCI with 24% having impairment of attention and working memory, 74% of executive functions, 64% of memory, 74% of language and 80% of visual spatial abilities.
- The cortical thickness analysis was performed on the 3D T1-weighted scans using the Freesurfer software package.
- Cortical thickness data were then compared among groups.
- In PD patients, thickness measures of the brain areas that were significantly different between groups were correlated with neuropsychological measures.

Table 1. Demographic and clinical findings of PD patients and healthy controls.

	Healthy controls	PD-MCI	PD-ncog	PD-MCI *vs* controls	PD-ncog *vs* controls	PD-MCI *vs* PD-ncog
Number	41	54	54	-	-	-
Right-handed	41	52	51	0.46	0.13	0.37
Men/women	15/26	29/25	29/25	0.1	0.1	1
Age at MRI, ys	63 ± 8 (49-77)	64 ± 9 (39-81)	63 ± 7 (47-83)	0.48	0.94	0.39
Education, ys	13.5 ± 2.9 (8-18)	10.9 ± 2.4 (8-16)	11.8 ± 2.2 (8-17)	<0.001	0.001	0.15
Age at onset, ys	-	58.2 ± 9.3 (38-76)	58.7 ± 8.0 (44-74)	-	-	0.89
Disease duration, ys	-	6.2 ± 4.9 (1-22)	4.6 ± 4.4 (1-19)	-	-	0.06
UPDRS III	-	37.2 ± 16.3 (12-76)	26.3 ± 14 (7-61)	-	-	<0.001
UPDRS total	-	55.8 ± 21.9 (16-102)	39.1 ± 18.4 (11-86)	-	-	<0.001
H&Y	-	2.1 ± 0.9 (1-4)	1.6 ± 0.8 (1-3)	-	-	0.01
Motor phenotype, tremor dominant/rigid akinetic	-	23/29	22/30	-	-	0.98
Asymmetry, asymmetric/ symmetric	-	52/2	51/3	-	-	0.65
Side of onset, right/left/ symmetric	-	31/21/1	35/17/2	-	-	0.61
LEDD	-	690.5 ± 433.8 (0-1560)	447.4 ± 356.4 (0-1200)	-	-	0.004

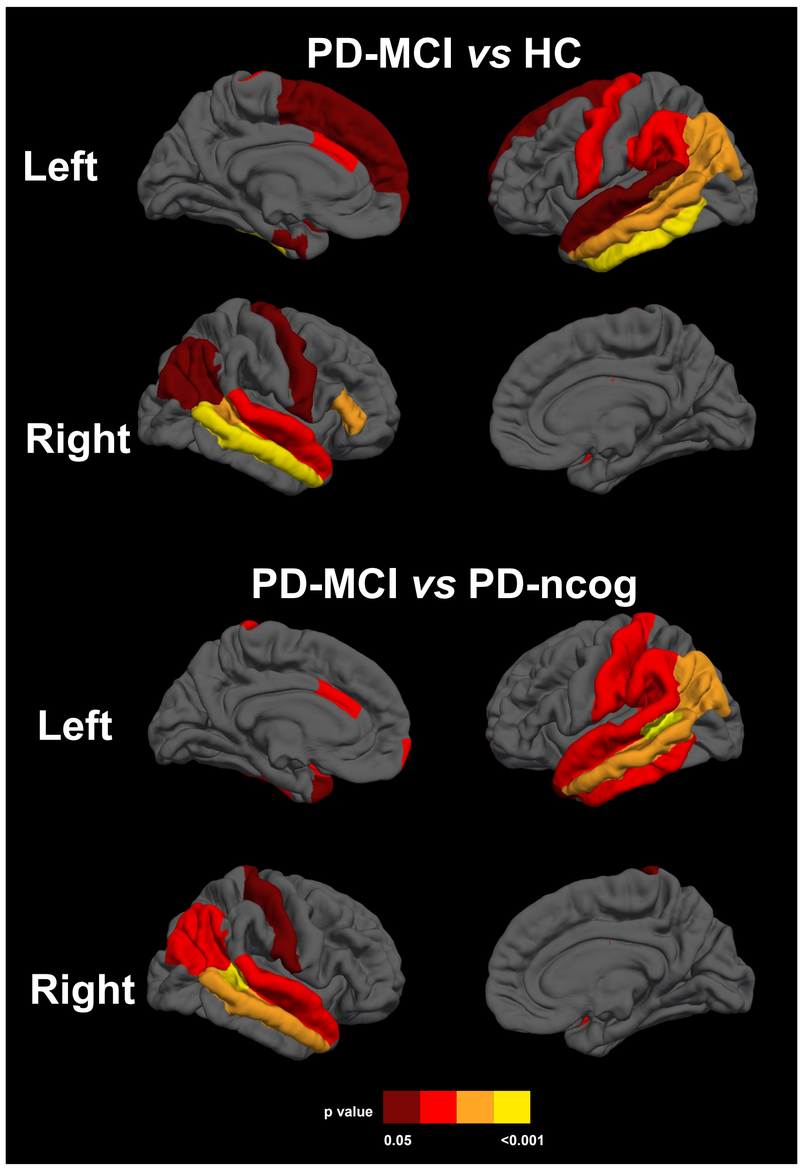
Numbers are mean ± standard deviation (range) or number. P values refer to ANOVA models, followed by post-hoc pairwise comparisons. Abbreviations: H&Y: Hoehn & Yahr scale; LEDD: Levodopa Equivalent Daily Dose; PD-MCI: PD patients with mild cognitive impairment; PD-ncog: PD patients with no cognitive impairment; UPDRS: Unified Parkinson's Disease Rating Scale; ys: years.

Figure 1. Pipeline for 3D T1-weighted image processing to measure the thickness of cortical gray matter.



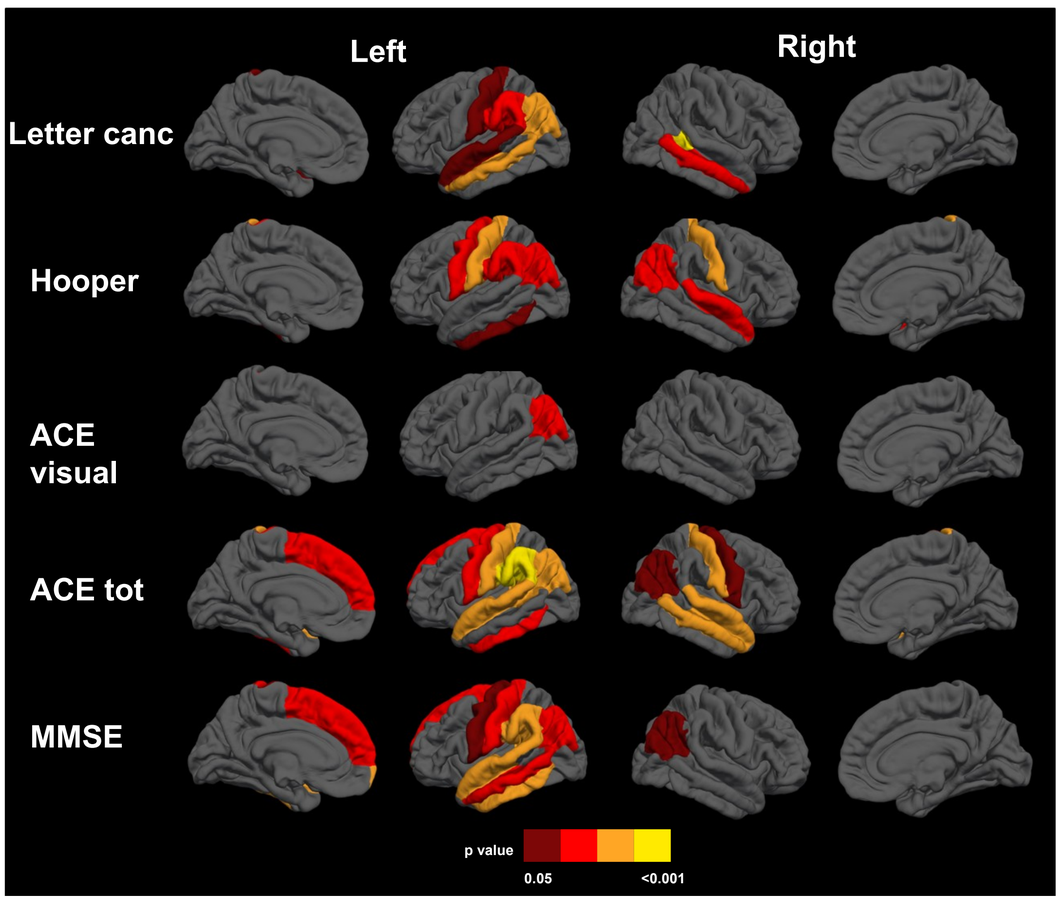
RESULTS

Figure 2. Group comparisons. Areas of reduced cortical thickness in PD-MCI *vs* healthy controls (HC) or PD-ncog.



There were no significant differences of cortical thickness between PD-ncog and HC.

Figure 3. Correlations. Areas where cortical thinning was associated to a worse performance in a neurpsychological test. The neuropsychological tests are indicated on the left side.



Abbreviations: Letter canc= letter cancellation test; Hooper= Hooper's test; ACE= Addenbrooke's Cognitive Examination-Revised; MMSE= Mini Mental State Examination.

CONCLUSIONS

- MCI in PD is associated with cortical thinning.
- Moreover, we showed that cortical atrophy correlates with the performance in neuropsychological tests involving executive functions and visual spatial abilities that typically are deficient in PD patients with cognitive impairment.
- The fronto-temporo-parietal atrophy pattern that was identified in this study might be used as a surrogate marker of cognitive impairment in nondemented PD patients.
- Longitudinal studies are warranted to better understand the relationship between cortical thinning and the progression of cognitive impairment in PD.

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