White matter lesions and Mild Cognitive Impairment in Parkinson's disease: the PArkinson's disease COgnitive impairment Study

Edoardo Cicero[1], Roberta Baschi[2], Brigida Fierro[2], Cesare Gagliardo[3], Antonella Luca[1], Francesco Le Pira[1], Alessandra Nicoletti[1], Vincenzo Restivo[2], Mario Zappia[1], Roberto Monastero[2]

[1]Dipartimento G.F. Ingrassia, Sezione di Neuroscienze, Università Degli Studi di Catania, Italia
[2]Dipartimento di Biomedicina Sperimentale e Neuroscienze Cliniche, Università degli Studi di Palermo, Italia
[3]Dipartimento di Biopatologia e Biotecnologie mediche, Università degli Studi di Palermo, Italia

Introduction

The burden of cognitive impairment in Parkinson's disease (PD) represents a major cause of disability. The severity may range from Mild Cognitive Impairment (PD-MCI) to Dementia (PDD). One of the risk factors associated with dementia and cognitive impariment in the elderly population are White Matter Lesions (WML). While the undergoing processes that may cause white matter lesions are already known, the role they have in the cognitive decline in PD still has to be defined.

Materials and Methods

The **PA**rkinson's disease **CO**gnitive impairment **S**tudy (PACOS) is a multicenter study involving two Movement Disorder centers located in Southern Italy. Patients affected by PD diagnosed according to the Gelb's diagnostic criteria, were consecutively enrolled in the study. PD-MCI was diagnosed with modified level-II Litvan's criteria. PDD was diagnosed according to the Emre's criteria. PD severity was evaluated with the Unified Parkinson's Disease Rating Scale – Motor Evaluation (UPDRS-ME) and the Hoehn-Yahr (HY) scale. WML evaluation was carried out with the Wahlund visual rating scale. We compared the clinical features and the Wahlund scores of the patients with PDD , PD-MCI and PD with normal cognition (PD-NC). We then performed a separate analysis on the PD-MCI subjects that showed a score >1 at the Wahlund scale. Univariate and multivariate logistic regression analysis was used to test the association between variables.

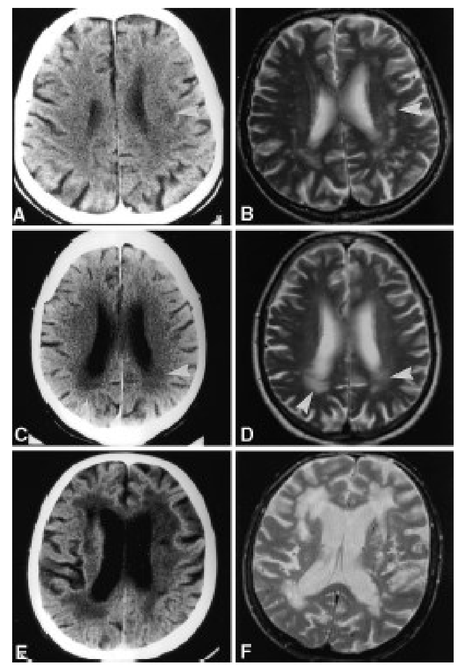


Figure 1. A through F, Examples of the rating scores 1, 2, and 3 from CT and MRI scans. Each pair of images (CT/MRI) refers to the same patient. The lesions are chosen from matching slices. Note that the slice angulation differs between CT and MRI (T2-weighted MRI images are shown). For a rating score of 1, a single lesion is clearly seen on CT (A) (see arrow); on MRI (B), additional lesions are rated as 2; rating score 2 is exemplified in C and D (see arrows); rating score 3 is shown in E and F.

Results

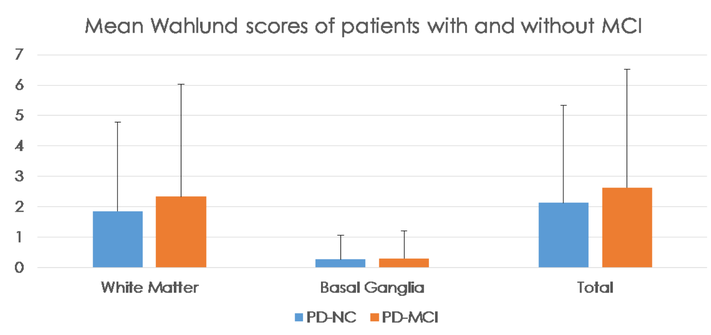
The study included 627 PD patients of whom 585 (57.6 % men; mean age 67.6 ± 9.6 years) underwent a neuroimaging study and were included in the analysis. The mean age at onset was 64.2 ± 10.5 years with a mean disease duration of 3.4 ± 4.7 years; the mean UPRDS-ME score was 25.8 ± 13.5 with a mean HY stage of 2.0 ± 0.7. Fifty-three patients out of the 585 enrolled (9.1%) were classified as PDD (age 71.3 ± 8.2 years; disease duration 6.8 ± 7.2 years) and 281 (48.1%) as PD-MCI (age 69.8 ± 8.2 years; disease duration 3.4 ± 4.3 years).

PD-MCI vs PD-NC

The clinical features and the Wahlund scores of the PD subjects with or without MCI are shown in Table 1. At the univariate analysis age, age at onset, UPDRS-ME, Hoeh-Yahr and Postural Instability Gait Disorder (PIGD) phenotype correlated with PD-MCI. However, no significant associations have been found with Wahlund scores.

Table 1. Clinical features of PD patients with and without MCI (N=532)

			Univariate analysis		
	PD-NC N=251	**PD-MCI N=281**	**OR**	**95% CI**	**P-value**
Sex	138 (55.2%)	175 (62.3%)	1.34	.95-1.89	0.1
Age	64.9±10.0	69.6± 8.9	1.05	1.03-1.07	**<0.0001**
Age at onset	62.1±10.6	66.3±9.8	1.04	1.02-1.06	**<0.0001**
Disease duration	2.8±3.9	3.2±4.2	1.03	0.98-1.07	0.2
UPDRS-ME	22.6±11.7	25.8±12.7	1.02	1.01-1.04	**0.003**
Hoehn-Yahr Score	1.8±0.6	2.0±0.6	1.66	1.22 -2.25	**0.001**
Clinical Phenotype					
Tremor Dominant (TD)	87 (36.2%)	71 (25.9%)	1		
PIGD	128 (53.3%)	171 (62.4%)	1.64	1.11-2.41	**0.01**
Mixed	25 (10.4%)	32 (11.7%)	1.57	0.85-2.89	0.1
Wahlund Score					
Mean Basal Ganglia	0.3±0.9	0.3 ±1.0	1.04	0.86-1.25	0.6
Mean White Matter	1.7±3.0	2.3 ±3.7	1.04	0.99-1.10	0.1
Mean Total	2,1±3.2	2.6 ±4.0	1.04	1.0-1.1	0.1

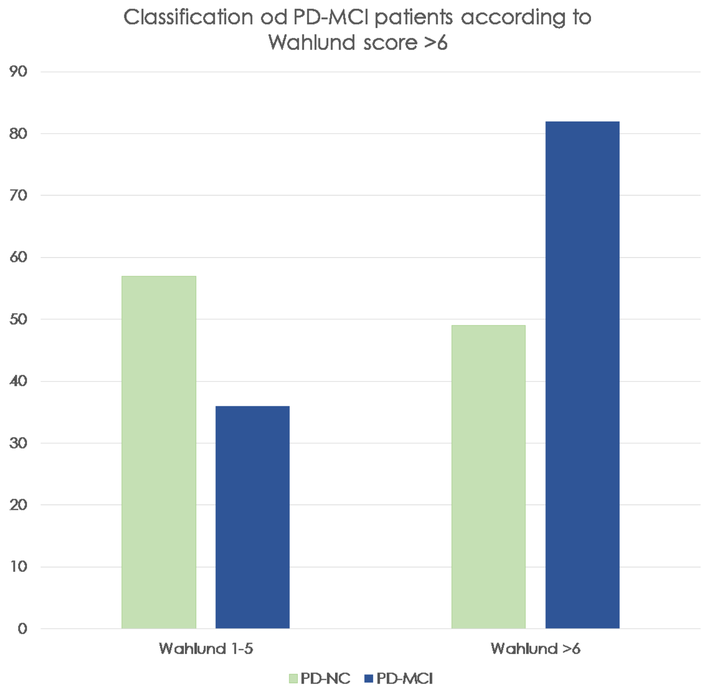


PD-MCI vs PD-NC when Wahlund total score > 1

The multivariate analysis showed a significant association with PD-MCI in subjects with a higher Wahlund score.

Table 2. Multivariate analysis of the PD-MCI patients with cerebrovascular disease with and without MCI (N=224)

	Multivariate Analysis		
	OR	**95% CI**	**P-value**
Sex	1.68	0.94-3.00	0.08
Age	1.06	1.01-1.10	**0.007**
Disease duration	1.05	0.98-1.13	0.2
UPDRS-ME	1.03	1.01-1.06	**0.01**
Wahlund Score Total			
1-5	1		
≥6	2.91	1.50-5.64	**0.001**



PDD vs PD-NC

The multivariate analysis showed a significant association between PDD and the Wahlund Basal Ganglia score.

Table 3. Multivariate analysis of the PD patients with or without PDD. (N=304)

	Multivariate Analysis		
	OR	95% CI	P-value
Age	1.08	1.03-1.13	**0.002**
Hoehn-Yahr Score	10.2	4.69-22.29	**<0,000**
Clinical Phenotype			
TD	1		
PIGD	1.21	0.45-3.22	0.7
Mixed	1.43	0.32-06.29	0.6
Wahlund Score			
Basal Ganglia	3.89	1.39- 10.8	**0.009**
White matter	1.78	0.77-4.09	0.1

Conclusions

Our study shows that among PD subjects with cerebrovascular disease those who have a significant WML burden (Wahlund > 6) have a higher risk for the development of MCI. Higher Wahlund Basal Ganglia score values are also associated with a higher risk of developing PDD. Since most of the risk factors associated with WML are preventable it is important treat them in order to reduce the risk of cognitive impairment in subjects with Parkinson's disease.

References

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