Neuropsychological assessment in initial clinical stages of Parkinson disease

Mattia Siciliano[1], R. De Micco[1], M. De Stefano[1], C. Baiano[1], L. Marcuccio[1], A. De Mase[1], C. Passaniti[1], L. Trojano[2,3], G. Tedeschi[1], A. Tessitore[1]

[1] Department of Medical, Surgical, Neurological, Metabolic and Aging Sciences, University of Campania "Luigi Vanvitelli", Naples, Italy.
[2] Department of Psychology, University of Campania "Luigi Vanvitelli", Naples, Italy.
[3] Salvatore Maugeri Foundation, Scientific Institute of Telese, Telese Terme (BN), Italy

OBJECTIVE: To compare cognitive performances in newly diagnosed patients with Parkinson's disease (PD) at Hoehn and Yahr (HY) stage I or stage II at their first medical evaluation.

METHODS: Forty de novo PD patients at HY stage I and 40 patients at HY stage II completed a standardized neuropsychological battery. A multivariate analysis of covariance was used to compare cognitive performance between HY groups. Odds ratios (ORs) were employed to explore the risk of cognitive impairment between HY stages. The prevalence of mild cognitive impairment (MCI) was estimated for patients in HY stage I and II. Finally, we also performed a one-way MANOVA to search for any significant neuropsychological difference between PIGD-dominant and TD groups.

RESULTS: Demographic and clinical characteristics are reported in Table 1. Patients at HY stage I obtained better scores on neuropsychological tests than patients at HY stage II (Wilks' lambda = .562, $F(16, 61) = 2.968$, $p = .001$, $\eta^2 = .438$). Univariate analysis of covariance revealed significant differences between HY stages on Rey's auditory verbal learning test -immediate recall, 10 points Clock Drawing Test, and Rey-Osterrieth Complex Figure Test –copy (Table 2). Odds Ratios (Ors) of having cognitive impairment were greater for HY stage II than stage I group (Table 3). PD-MCI occurred in 7.5% of patients in HY stage I, and in 42.5% of patients in HY stage II. ORs for MCI are 8.22 (95% CI [2.162, 31.271]) times greater for patients at HY stage II than for those at stage I. As for the comparison between PIGD-dominant and TD groups, we did not observe any differences for the main demographic and clinical variables. One-way MANOVA testing for cognitive differences between these two groups did not show any significant difference, Wilks' lambda = .721, $F(15, 52) = 1.342$, $p = .212$.

DISCUSSION AND CONCLUSIONS: Our results demonstrate that at the time of first diagnosis, motor impairment of de novo PD patients is significantly associated with reduced performances on cognitive tests, particularly in memory, executive, and visuospatial domains. In addition, our study suggests that de novo PD patients at a HY stage II have a higher risk of cognitive impairment than the patients in HY stage I. Compared with those at HY stage I, patients at HY stage II had higher odds ratio of having attention, memory, visuospatial, and executive dysfunctions. Moreover, in the present study we did not find any significant differences between PIGD-dominant and TD group on neuropsychological tests. Taken together, our results suggest that the rate of motor impairment, closely related to prevalence of MCI, may contribute to identify those patients most likely to benefit from early intervention to maintain cognitive performances.

Table 1. Demographic and clinical characteristics of the patients in Hoehn & Yahr stage I vs. stage II; data are reported as mean standard deviation or as counts (and

	HY stage I (N = 40)	HY stage II (N = 40)	F/χ^2	p
Age at onset	61.03 ± 8.61	63.57 ± 7.35	2.010	.160
Education, years	11.10 ± 3.77	9.83 ± 4.61	1.828	.180
Male sex	22 (55%)	28 (70%)	1.920	.166
Disease duration, months	14.60 ± 6.45	17.43 ± 7.21	3.406	.069
UPDRS III	15.02 ± 5.29	24.45 ± 6.46	50.856	**>.0001**
Tremor score	2.18 ± 2.5	2.23 ± 2.78	.007	.933
Rigidity score	2.78 ± 2.17	5.20 ± 3.37	14.576	**>.0001**
Bradykinesia score	7.20 ± 3.53	12.28 ± 4.40	32.288	**>.0001**
Gait/Postural stability score	.90 ± .928	2.62 ± 1.62	33.889	**>.0001**
Epworth Sleepiness Scale (ESS)	3.68 ± 2.729	4.28 ± 3.731	.622	.433
Beck Depression Inventory (BDI)	6.78 ± 4.131	8.34 ± 6.494	.940	.232
Side of onset:			1.251	.263
Left	22 (55%)	17 (42.5%)		
Right	18 (45%)	23 (57.5%)		
PD subtype classification:			3.242	.198
Tremor-D	16 (40%)	10 (25%)		
PIGD-D	17 (42.5%)	25 (62.5%)		
Not determined	7 (17.5%)	5 (12.5%)		
WMH load	265.4 ± 399.5	315.2 ± 479.3	.236	.629

Note. Significant differences according to Bonferroni criterion (.05/14 = .003) are shown in bold; UPDRS, Unified Parkinson's Disease Rating Scale; PD, Parkinson's disease; Tremor-D, Tremor-Dominant form; PIGD-D, Postural Instability Gait Disorder-Dominant; WMH, white matter hyperintensity.

Table 2. Cognitive performance of the patients in Hoehn & Yahr stage I vs. stage II group; data are reported as mean standard deviation.

	HY stage I (N = 40)	HY stage II (N = 40)	F	p	η^2
Attention/Working memory					
TMT-A[a]	43.93±17.71	63.53±42.75	3.509	.065	.044
TMT-B	122.13±57.65	163.62±96.11	2.416	.124	.031
Digit Span forward[a]	5.48±1.08	5.13±1.04	.658	.420	.009
Memory					
RAVLT-immediate recall	38.2±8.38	29.08±9.36	16.307	**<.0001**	.177
RAVLT-delayed recall[a]	7.05±2.49	5.28±3.07	4.602	.035	.057
RAVLT-recognition	13.07±2.56	12.2±2.88	.953	.332	.012
ROCF-immediate recall	9.58±6.26	7.49±6.21	.762	.385	.010
Prose recall test[a]	9.85±3.6	7.3±3.62	7.027	.010	.085
Executive function					
Letter fluency task[a]	29.5±10.96	23.88±10.96	2.196	.143	.028
Category fluency task	36.23±6.85	31.85±8.10	3.365	.071	.042
MCST-perseverative errors	4.23±6.71	5.75±7.74	.039	.845	.001
MCST-number of categories achieved[a]	4.85±1.77	4.08±1.88	1.180	.281	.015
10 points CDT	8.23±1.33	6.60±2.36	9.558	**.002**	.112
Frontal Assessment Battery (FAB)	15.48±1.72	13.78±2.93	5.646	.020	.069
Visuospatial function					
ROCF-copy[a]	28.95±6.13	20.51±9.14	19.784	**<.0001**	.207
Language					
Boston Naming Test (BNT)	45.92±4.92	42.09±6.66	5.498	.022	.067

Note. a, tests used for the diagnosis of Parkinson's Disease-Mild Cognitive Impairment according to the Movement Disorder Society Task Force Level I criteria; significant differences according to Bonferroni criterion (.05/16 = .003) are shown in bold; η^2, Eta-squared; TMT, Trail Making Test; RAVLT, Rey's Auditory Verbal Learning Test; MCST (Nelson's modification), Modified Card Sorting Test; CDT, Clock Drawing Test; ROCF, Rey-Osterrieth Complex Figure Test.

Table 3. Relationship between the HY stages and risk of cognitive impairment – HY stage I and HY stage II.

	HY stage I N (%)	HY stage II N (%)	OR	p	[95% CI]
Attention/Working memory					
TMT-A					
> - 1.5 SD	39 (97.5)	31 (77.5)	11.323	**.025**	[1.360, 94.248]
< - 1.5 SD	1 (2.5)	9 (22.5)			
TMT-B					
> - 1.5 SD	39 (97.5)	35 (87.5)	5.571	.125	[.620, 50.031]
< - 1.5 SD	1 (2.5)	5 (12.5)			
Digit Span forward					
> - 1.5 SD	39 (97.5)	39 (97.5)	1	1	[.060, 16.562]
< - 1.5 SD	1 (2.5)	1 (2.5)			
Memory					
RAVLT-immediate recall					
> - 1.5 SD	36 (90)	20 (50)	9.000	**>.0001**	[2.698, 30.021]
< - 1.5 SD	4 (10)	20 (50)			
RAVLT-delayed recall					
> - 1.5 SD	35 (87.5)	27 (67.5)	3.370	**.038**	[1.070, 10.613]
< - 1.5 SD	5 (12.5)	13 (32.5)			
ROCF-immediate recall					
> - 1.5 SD	19 (47.5)	15 (37.5)	1.508	.367	[.618, 3.678]
< - 1.5 SD	21 (52.5)	25 (62.5)			
Prose recall test					
> - 1.5 SD	25 (62.5)	16 (40)	2.500	**.046**	[1.016, 6.149]
< - 1.5 SD	15 (37.5)	24 (60)			
Executive functions Letter fluency task					
> - 1.5 SD	37 (92.5)	30 (75)	4.111	**.044**	[1.037, 16.295]
< - 1.5 SD	3 (7.5)	10 (25)			
Category fluency task					
> - 1.5 SD	38 (95)	30 (75)	6.333	**.023**	[1.289, 31.115]
< - 1.5 SD	2 (5)	10 (25)			
MCST-perseverative errors					
> - 1.5 SD	31 (77.5)	29 (72.5)	1.307	.606	[.473, 3.609]
< - 1.5 SD	9 (22.5)	11 (27.5)			
MCST-number of categories achieved					
> - 1.5 SD	29 (72.5)	25 (62.5)	1.582	.341	[.615, 4.066]
< - 1.5 SD	11 (27.5)	15 (37.5)			
10 points CDT					
> - 1.5 SD	38 (95)	28 (70)	8.143	**.009**	[1.686, 39.317]
< - 1.5 SD	2 (5)	12 (30)			
Frontal Assessment Battery (FAB)					
> - 1.5 SD	37 (92.5)	26 (65)	6.641	**.006**	[1.732, 25.465]
< - 1.5 SD	3 (7.5)	14 (35)			
Visuospatial functions					
ROCF-copy					
> - 1.5 SD	28 (70)	12 (30)	5.444	**.001**	[2.092, 14.168]
< - 1.5 SD	12 (30)	28 (70)			
Language					
High BNT score	37 (92.5)	35 (87.5)	1.762	.460	[.392, 7.929]
Low BNT score	3 (7.5)	5 (12.5)			

Note. OR, Odds Ratio; SD, Standard Deviation; TMT, Trail Making Test; RAVLT, Rey's Auditory Verbal Learning Test; MCST (Nelson's modification), Modified Card Sorting Test; CDT, Clock Drawing Test; ROCF, Rey-Osterrieth Complex Figure Test.