Parkinson's Disease: a study of executive dysfunction in relation to the disease stage.

Elisa Montanaro, Laura Rizzi, Francesca Dematteis, Carlo Alberto Artusi, Alberto Romagnolo, Maurizio Zibetti, Mario Giorgio Rizzone, Leonardo Lopiano

Department of Neuroscience, University of Turin, Italy

- ***Objectives***

Parkinson's disease (PD) is a progressive neurodegenerative disorder. Non-motor features are now considered as part of the clinical symptomatology. Specifically, cognitive impairment is a major non-motor symptom of PD that can occur at all stages of the disease (*Cosgrove et al., 2015*). Although there is heterogeneity in the clinical presentation of cognitive impairment in PD, generally cognitive deficits involve executive functions, attention and working memory (*Dirnberger et al., 2013*). Our aim is to explore executive-cognitive profile in idiopathic PD patients considering three phases of the pathology: initial (G1), intermediate (with initial motor fluctuations - G2) and advanced (patients eligible for complex therapy - G3). We focus specifically on changes in superior frontal cortical functions in relation to the phases of the disease, in order to better understand the relationship between executive dysfunction and clinical progression of PD.

- ***Materials***

Patients underwent a neurological evaluation and an extensive neuropsychological assessment investigating five cognitive domains: reasoning, memory, language, attention and executive functions. Frontal-executive functions were evaluated by: Frontal Assessment Battery (FAB), Modified-Wisconsin Card Sorting Test (M-WCST), Trail Making Test (TMT A and B).

- ***Method***

Subjects were divided into three groups corresponding to different disease stages. Descriptive statistics and nonparametric test were used to compare groups.

- ***Results***

Concerning disease stage, our data on forty-five idiopathic PD patients (*see Table 1 for demographic and clinical features*), suggest a greater cognitive impairment with advancing stages of disease (*see Table 2 and Figure 1 for neuropsychological scores*), especially in attentional-executive functions.

- In particular, **G1** and **G2** differ only for **M-WCST perseverations** (*p=0.023*), whereas **G2** and **G3** differ for **FAB** (*p=0.041*) and **TMT B** score (*p=0.041*).
- Initial (**G1**) and advanced PD patients (**G3**) show significant differences for all test considered (**M-WCST categories**: *p=0.037*; **M-WCST perseverations**: *p=0.010*; **TMT B**: *p=0.016*; **TMT B-A**: *p=0.010*; **FAB**: *p=0.001*).
- About memory, **G2** differs from **G3** for **Digit span** (*p=0.001*) and **Bisyllabic word repetition test** (*p=0.018*). Also **Paired associate learning** scores reveal significant differences (**G1** vs **G2**: *p=0.016*; **G1** vs **G3**: *p<0.001*).

	G1	G2	G3
Age	55 (13)	59.13 (7.7)	60.7 (9.1)
Gender (M/F)	10/5	8/7	7/8
Education (years)	12.9 (4.9)	9.4 (3.9)	9.6 (4.3)
Age at diagnosis	51.8 (11.9)	48.9 (7.4)	47.3 (8.8)
PD duration (years)	2.5 (1.6)	10.2 (2.5)	13.3 (2.7)
Dementia (%)	0	6.6	40
Depression (BDI)	6.3 (5.2)	11 (5.7)	11.3 (6.2)
LEDD (mg)	359.8 (222.4)	857.3 (317.3)	1156.7 (379.9)
UPDRS III on	17.2 (7.5)	11.1 (5.4)	16 (8.9)
Motor phenotype (%) *Tremor dominant* *Rigid-akinetic*	 38.5 61.5	 40 60	 7.7 92.3

Table 1: Patients' demographic and clinical features. Mean (standard deviation) or percentage are reported.

	G1	G2	G3
SCREENING			
MMSE	29.1 (1.2)	28.3 (1.2)	27.1 (3.2)
EXECUTIVE FUNCTIONS			
FAB	16.9 (1.1)	15.8 (2)	13.2 (4.1)
TMT B	101.8 (70.3)	175.7 (140)	276.2 (237.4)
TMT B-A	51.8 (42.5)	102.4 (138.3)	193.4 (169.4)
M-WCST categories	5.8 (0.3)	5.4 (1)	4.5 (1.8)
M-WCST perseverations	0.9 (0.8)	2.6 (2.5)	4.7 (4)
ATTENTION			
Digit cancellation test	52 (7)	48.5 (7.9)	41.9 (15)
TMT A	39.2 (22)	59.7 (24.1)	84.3 (58.8)

	G1	G2	G3
MEMORY			
Bisyllabic word repetition test	4.5 (1)	4.5 (0.7)	3.7 (0.9)
Digit span	5.9 (1)	5.7 (1)	5 (0.8)
Corsi's block tapping test	4.5 (1)	4.7 (0.9)	4.1 (1)
Paired associate learning	14.6 (2)	11.3 (3.3)	10.2 (3.6)
REASONING			
Raven coloured matrices test	33 (3)	29.4 (5.1)	27.2 (8.2)
LANGUAGE			
Phonemic verbal fluency	40.3 (9.1)	37.1 (13.5)	20.9 (8.3)
Category verbal fluency	24.8 (6.4)	20.7 (4.5)	20.1 (8.2)

Table 2: Neuropsychological results. Mean (standard deviation).

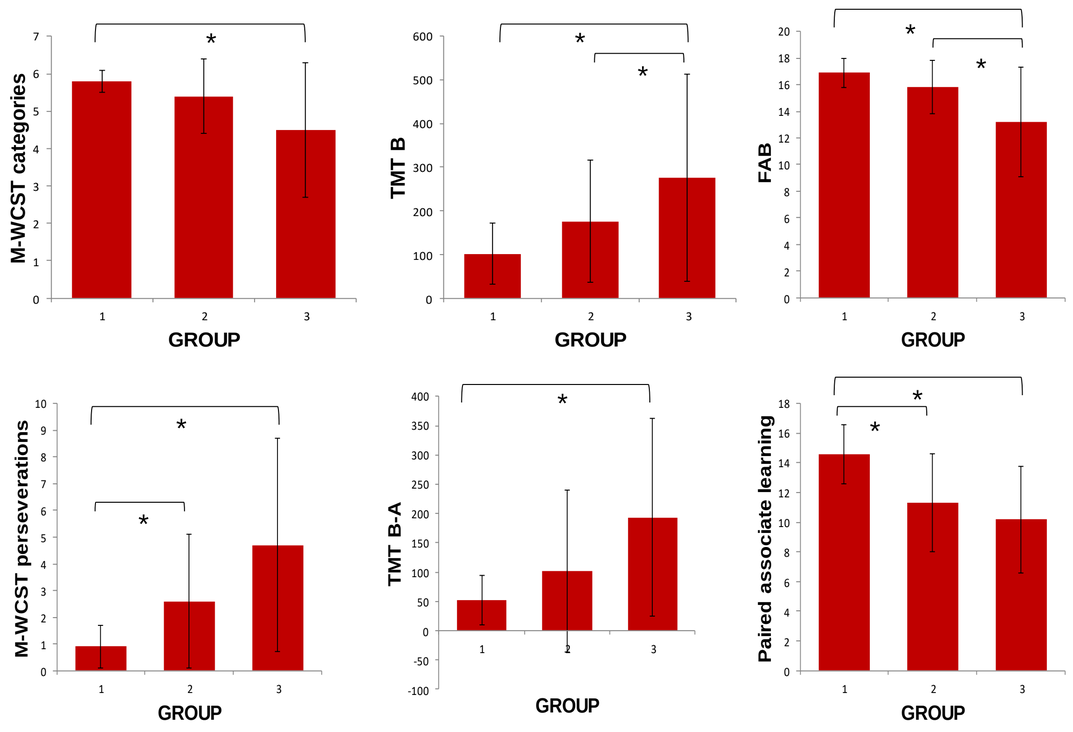

Figure 1: Graphic representation of neuropsychological scores.* Significant difference *(p < 0.05)*.

- ***Discussion***

Referring to global cognitive status our results indicate a greater impairment in advanced PD patients. Furthermore, our data seem to suggest a **temporal relationship between PD stages and executive-cognitive profile** with an earlier worsening in some skills, like **associative learning** and **perseverative behaviour**, followed by **set shifting** changes. **Cognitive flexibility** and **categorization**, instead, remains preserved for a longer period of time.

- ***Conclusions***

Our study contributes to a better understanding of **cognitive features associated to clinical progression of PD**, which often represents an important cause of disability and caregiver distress.

References: - Cosgrove J., Alty J.E., Jamieson S. Cognitive impairment in Parkinson's disease. Postgrad Med J 2015; 91: 212–220;
- Dirnberger G., Jahanshahi M. Executive dysfunction in Parkinson's disease: A review. Journal of Neuropsychology 2013; 7: 193-224.