DIFFERENTIAL EFFECT OF DOPAMINERGIC TREATMENT ON BRADYKINESIA FEATURES AND LIMB-KINETIC APRAXIA IN PARKINSON'S DISEASE

Martina De Riggi[1], G. Paparella[1-2], A. Cannavacciuolo[1-2], D. Birreci[1], D. Costa[2], M. Passaretti[1], L. Angelini[1,2], M. Bologna[1-2]

[1]Department of Human Neurosciences, Sapienza University of Rome, Rome, Italy

[2]IRCCS Neuromed, Pozzilli (IS), Italy

INTRODUCTION: Bradykinesia is one of the primary motor symptoms in Parkinson's disease (PD). However, other cognitive-motor disorders, such as limb-kinetic apraxia, may contribute to motor dysfunction, influencing the variability in treatment responses.

OBJECTIVES: To investigate the differential effects of dopaminergic therapy on bradykinesia and limb-kinetic apraxia in PD patients using kinematic analysis. Additionally, transcranial magnetic stimulation (TMS) was employed to further elucidate the underlying mechanisms of treatment.

METHODS: Twenty-five patients with PD were assessed in both OFF- and ON-medication states, along with 24 age- and gender-matched healthy controls (HC). Kinematic analysis was performed to evaluate bradykinesia (using a finger-tapping task) and limb-kinetic apraxia (using a 10-second coin rotation task) (***FIG. 1***). Corticospinal excitability was examined through TMS, which measured resting motor thresholds, motor-evoked potential input/output curves, short-interval intracortical inhibition, and interhemispheric inhibition.

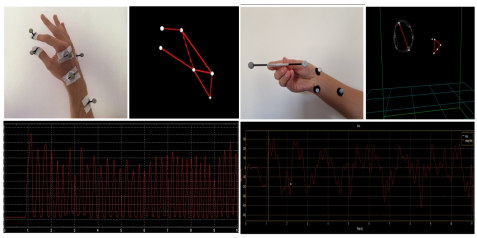

FIG. 1 *Kinematic recordings of coin rotation task and finger tapping. The kinematic system included three infrared cameras and reflective markers fixed on the subject's hands. Several movement parameters were calculated, including movement velocity and amplitude, movement rhythm and the sequence effect.*

RESULTS: In the OFF-medication state, PD patients exhibited slower velocity, progressive reduction in amplitude (sequence effect), and decreased regularity in finger-tapping movements compared to HC. Similarly, slower velocity and altered movement regularity were observed in the coin rotation task in PD patients OFF medication compared to HC. Dopaminergic therapy improved finger-tapping velocity but had no significant effect on other finger-tapping parameters or the coin rotation task, highlighting a differential impact on the two motor tasks (***TABLE 1***) (***FIG. 2***). Increased M1 excitability was associated, to variable extent, with impaired motor performance, such as velocity and/or altered movement regularity, during both the finger-tapping and coin rotation tasks (***FIG. 3***). No correlations were observed in the ON state. Additionally, no correlations were found between changes in kinematic parameters from the OFF to the ON state and the concurrent changes in TMS parameters.

		PD (most affected side)		HC (dominant side)	P-value*	
		ON condition	OFF condition		PD-OFF vs HC	PD (OFF vs ON)
Finger Tapping	N° Mov	49.50±16.17	48.91±14.94	47.13±13.81	0.666	0.731
	Rhytm(CV)	0.13±0.07	0.14±0.09	0.09±0.03	**0.008**	0.561
	Amplitude	43.94±13.82	42.39±10.20	47.69±10.71	0.082	0.617
	Ampl Decr	-0.26±0.31	-0.23±0.21	-0.10±0.25	**0.049**	0.627
	Velocity	990.72±263.88	892.26±225.83	1085.50±171.98	**0.001**	**0.048**
	Vel Decr	4.80±4.02	6.85±4.46	6.20±5.44	0.652	0.082
Coin Rotation Task	N° Mov	4.81±0.69	4.58±0.74	5.45±1.12	**0.002**	0.175
	Rhytm(CV)	0.22±0.08	0.20±0.08	0.14±0.05	**0.002**	0.467
	Velocity	116.95±33.38	111.06±35.91	166.56±34.48	**<0.001**	0.247
	Slope I/O	4.43±1.97	5.03±1.82	3.95±1.93	**0.038**	0.470
	SICI2ms	0.64±0.47	0.62±0.39	0.42±0.39	**0.035**	0.749
	s-IHI	0.92±0.72	1.35±1.17	0.70±0.73	**0.036**	0.146

TABLE 1 *Kinematic variables of finger tapping and coin rotation task movements and TMS in patients with Parkinson's disease (PD) and in healthy controls (HC). *P-values by unpaired, one tailed t-tests. Significant P-values are in bold. N°Mov: number of movements; CV: coefficient of variation; I/O: input/output.*

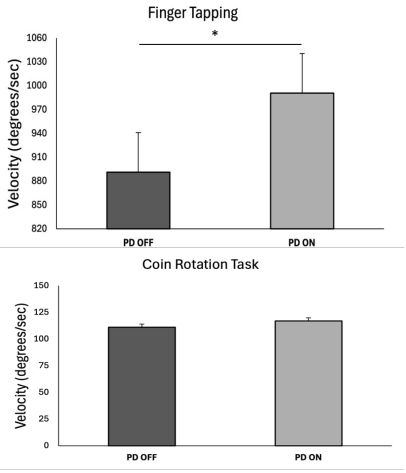

FIG. 2 *Kinematic analysis of movement velocity during the finger tapping and coin rotation tasks in Parkinson's disease (PD) patients in the OFF and ON medication states. Asterisk indicates P<0.05 from paired t-test.*

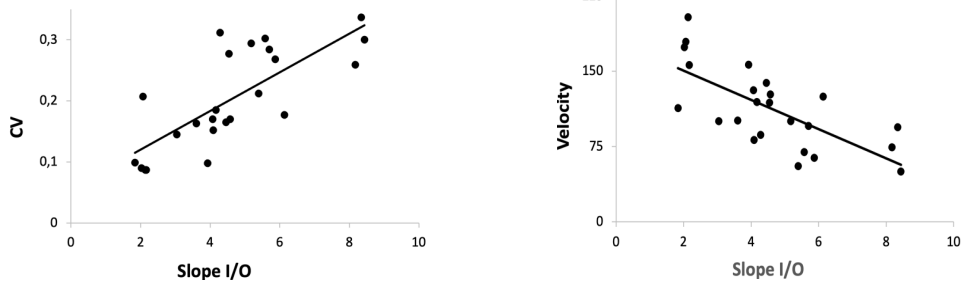

FIG. 3 *Correlations between neurophysiological and kinematic data in Parkinson's disease (PD), assessed on the most affected side during the OFF condition. Velocity (expressed in °/s) and coefficient of variation (CV) (i.e. rhythm) (x axis); slope input/output (slope I/O) (y axis). Higher M1 excitability, i.e. steeper input-output MEP curve, was associated with decreased velocity and increased irregularity during the motor task (r = -0.44 and 0.62, respectively; both Ps < 0.05).*

CONCLUSIONS: The differential impact of treatment on bradykinesia and limb-kinetic apraxia in PD may suggest distinct pathophysiological mechanisms possibly involving distributed cortical and subcortical systems with varying sensitivity to dopaminergic therapy.

MAJOR REFERENCES: (***1***) *Bologna M, Guerra A, Paparella G, Giordo L, Alunni Fegatelli D, Vestri AR, Rothwell JC, Berardelli A. Neurophysiological correlates of bradykinesia in Parkinson's disease. Brain. 2018 Aug 1;141(8):2432-2444. doi: 10.1093/brain/awy155. PMID: 29901693;* (***2***) *Heilman KM. Hugo Liepmann, Parkinson's disease and upper limb apraxia. Cortex. 2020 Oct;131:79-86. doi: 10.1016/j.cortex.2020.05.017. Epub 2020 Jul 21. PMID: 32801083;* (***3***) *Gebhardt A, Vanbellingen T, Baronti F, Kersten B, Bohlhalter S. Poor dopaminergic response of impaired dexterity in Parkinson's disease: Bradykinesia or limb kinetic apraxia? Mov Disord. 2008 Sep 15;23(12):1701-6. doi: 10.1002/mds.22199. PMID: 18649388.*