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Locomotor Disorders in Patients at Early Stages of Parkinson's Disease: a Quantitative Analysis

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***Abstract*—Several studies have been performed with automatic motion analysis techniques to investigated the locomotor disorders of patients with severe Parkinson's Disease (PD). These are mainly related to steady-state walking. Aim of the present study was to investigate the presence and the degree of these disorders in patients at early stages of PD. For this purpose a group of patients with mild PD (H&Y ≤ 2) and a group of age-matched controls were assessed by means of multifactorial analysis of kinematic and kinetic variables, during the execution of the following motor tasks: steady-state walking, gait initiation and turning around an obstacle. Results showed that PD patients did not differ from controls in steady-state walking, while significant differences emerged in gait initiation and turning strategies. Main differences consisted in a limitation of the amplitude of the imbalance phase and of the first step, and, for the turning task, in a delayed initiation of the turning movement, with an altered head-trunk rotational strategy. It is concluded that patients in early stages of PD do not reveal, during steady state walking, consistent impairments of kinematic and kinetic patterns typical of severe PD patients. Nevertheless, they present significant alterations in transient conditions such as gait initiation and change of walking direction. The above results suggest that a quantitative analysis of locomotor tasks which imply the transition from one condition to another, could provide parameters useful for the characterization of early stage PD patients and, potentially, markers for a precox differential diagnosis respect other neurodegenerative diseases characterized by parkinsonisms.**

I. Introduction

PARKINSON'S Disease (PD) is a neurodegenerative disorder of unknown cause due to the progressive loss of dopaminergic neurons in the Substantia Nigra pars compacta (SNc), a cerebral region of Basal Ganglia (BG). The estimated prevalence of PD is 150/100.000, with an estimated annual incidence of 20/100.000 [1]. Rigidity, akinesia, and tremor represent the main motor symptoms of PD. During the first years of the disease dopaminergic therapies as levodopa and dopamine-agonists are able to relief motor disturbances with a satisfactory clinical benefit for the patient. However, the progression of the disease leads to a severe disability due to the onset of motor fluctuations unresponsive to the pharmacological treatment.

Gait disorders play a key role in the generation of patient's motor disability in the advanced stage of PD, therefore a large number of studies have been performed to characterize walking abnormalities, often making use of automatic motion analysis approaches which allow for a quantitative and objective evaluation. From those studies, it emerges that parkinsonian gait is typically shuffle, with a shortened stride length [2]-[13] and reduced velocity [2]-[6],[8]-[13]. Gait cadence is not altered [6],[10],[11] or, in some cases, it is increased to compensate for stride length reduction [4],[7],[8],[10]. Trunk is forward flexed and presents a limited torsion and lateral bending during walking [6],[14]; moreover, associated arms movements are reduced [6],[10],[11]. Finally, a reduced range of motion (ROM) at lower limb joints are also present [3],[5],[6],[10]. Also kinetic patterns are typically altered in PD patients: reduced peaks of GRF at heel strike and push off and reduced peak of power production at lower limb joint [3]-[6],[11],[12] are the main abnormalities.

A smaller number of studies have analyzed other locomotor tasks that are typically impaired in patients with PD, such as gait initiation and turning around an obstacle. Gait initiation is normally analyzed considering two distinct aspects: the Anticipatory Postural Actions (APA), performed before and in preparation to gait, and the actual motor phase, the first step. Studies [15]-[19] have shown that the duration of APAs (unbalance and unloading phases) are augmented, the backward/lateral displacement of the Centre of Pressure (CoP) is reduced, first step length and velocity are shortened. Moreover, the underlying anticipatory muscular synergy are disrupted: Soleus muscle inhibition and Tibialis Anterior muscle activation are desynchronized, segmented or even absent [15],[16]. As regard "turning", the only two published studies [6],[20] found that, compared to controls, PD patients show the tendency to reduce stride length while approaching the turn and augment the number of steps needed to complete the turn [6]. Moreover, while healthy subjects start the turning maneuver with a rotation of the head towards the final walking direction, then turn the trunk, then the pelvis, and finally change the direction of movements of the feet, PD patients adopt an "an block" strategy, with a simultaneous horizontal rotation of head, trunk and pelvis [6]. Finally, when asked to perform a 90° turn, PD patients tend to realize a smaller change of

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direction, due to the reduced horizontal components of the ground reaction force (GRF) consequence of a limited muscular activation, particularly of TA muscles [20].

Almost all the results reported above are referred to studies performed in patients in an advanced phase of Parkinson's disease, typically at a stage ≥ 3 according to the Hoehn and Yahr scale [21], which correspond to "significant slowing of movements, impairment of equilibrium on walking/standing, moderately severe dysfunction". Unfortunately, much less information are available for patients at earlier stages of the pathology. A quantitative characterization of locomotor abnormalities in early stages of PD may provide important information on the pathophysiology of the disease and could help in the differential diagnosis respect other neurodegenerative diseases characterized by a similar picture of movement disorders or parkinsonisms, like Lewy Body Disease and Supra Nuclear Palsy. Goal of the present study was therefore to evaluate whether the locomotor abnormalities typically found in PD patients in the advanced phase of the disease, are also present in the early stages.

II. Materials and Methods

A. Subjects

Seven patients with idiopathic PD in the early stage (H&Y score ≤ 2) and a mean age of 65.7(±5.2) and eighteen elderly controls (mean age: 67.7 ± 4.9) voluntarily took part in the study. Diagnosis of PD was done according to [22]. All subjects had given written informed consent and the protocol had been approved by the local Ethical Committee.

Demographic and anthropometrical data are reported in Table I.

TABLE I – Patients characteristics at the time of the study

Patient	Age [yrs]	Sex	Height [cm]	Weight [kg]	UPDRS score	H&Y score
PD1	67	F	161	65	12	I
PD2	67	F	153	65	12	II
PD3	67	M	168	60	15	I
PD4	64	M	160	60	15	II
PD5	55	M	170	74	17	I
PD6	69	M	183	68	20	II
PD7	71	M	175	82	18	II

B. Experimental protocol and data pre-processing

Patients and controls were tested following a protocol consisting of 3 different tests: 1) SW: steady-state walking; 2) TW: turning while walking; 3) GI: initiation of gait. In test SW, subjects were asked to walk at a self-selected velocity along a straight trajectory of about 6 m. A force platform was positioned in the middle of the path in order to record the ground reaction force acting on the foot during walking. As for test TW, the subjects walked straight for 2 m and, when reached the force platform, turned on the left of 90 degrees and continued walking in the new direction. Subjects were instructed to turn using the right foot as pivot. In the gait initiation test, subjects stood upright for two seconds with both feet on the force platform, and then started walking, as soon as they received a verbal cue which specified which leg they had to start with.

The locomotor tasks described above were assessed by an analysis of kinematic and dynamic variables. Kinematic data were recorded using an optoelectronic system (SMART, BTS, Italy), consisting in 9 TV cameras working at a sampling rate of 60 Hz and located around a calibrated volume of 5×3×2 m^3. The position of the subjects' main body segments was determined by means of 29 retro-reflective markers with a diameter of 15 mm, attached in the bony landmarks shown in Fig. 1, following the protocol described in [23]. After the acquisition, markers' coordinates were low-pass filtered (6 Hz cut-off freq.). Anthropometrical parameters were used for the estimation of internal joint centers. These, in turn, enabled calculation of head, trunk and lower limb kinematics. Ground Reaction Forces were measured by means of a dynamometric platform (KISTLER GmbH, Winterthur, Switzerland) embedded in the floor (sampling rate 160 Hz). The resulting signals were used for the calculation of CoP trajectory and the lower limbs joints moments and powers.

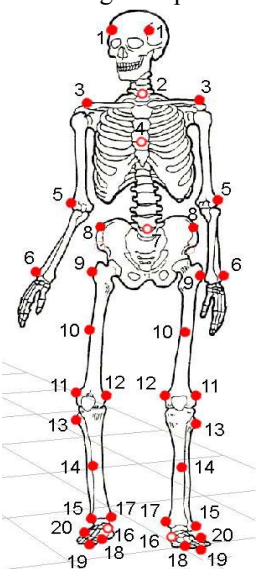

Fig. 1. Markers position on the body

C. Data elaboration

Specific sets of parameters for the characterization of each task analyzed, were automatically extracted by dedicated algorithms. In particular, steady-state walking was described by spatio-temporal gait parameters (walking speed, cadence, stride length, stance and double support phase duration), time-course of hip, knee and ankle joints angles, moments and powers in the sagittal plane, ROM of the hip, knee and ankle joint in the sagittal plane and of the pelvis in all planes.

For the description of test TW, the time-course of head and trunk angles in the transverse plane (horizontal rotation angles) were computed. Subsequently, the two steps which characterize the turning phase were considered: the "approach" step, defined from the left heel strike (T1) to the right heel strike (T2) before direction change, and the "turn step" defined from T2 to the left heel contact after the change of direction (T3). These two steps are schematically represented in Fig. 2a. These variables, in turn, allowed for the calculation of the following parameters: head delay and trunk delay, defined as the time intervals from T1 to the first instant at which, respectively, the head and the upper trunk started to rotate in the new direction and mean horizontal rotation angles of head and upper trunk during both the "approach step" and the "turn step".

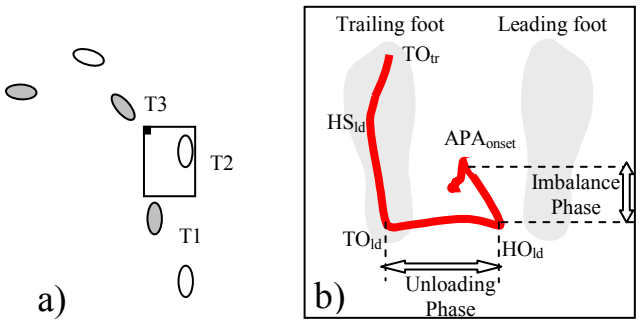

Fig.2. a) Schematic representation of steps during TW task. T1-T2: approach step; T2-T3: turn step. b) CoP trajectory during GI task

As for the gait initiation task, APA phase was subdivided into two sub-phases called "imbalance phase" and "unloading phase", which are represented in Fig. 2b. The parameters extracted to describe the APA phases were: imbalance phase duration (from the instant APAOnset, at which the CoP started moving backward, to the instant of heel-off of the leading foot, HO_{ld}), backward shift of the CoP at HO_{ld} (normalized to the distance between lateral malleolar and fifth metatarsal marker) and duration of the "unloading phase" (from HO_{ld} to the instant of toe-off of the leading foot, TO_{ld}). As for the actual execution of the first step the parameters extracted were: duration of the "first swing phase" (from TO_{ld} to the instant of heel-strike of the leading foot, HS_{ld}), length of the first step (normalized to subject's height), and velocity of the sacrum marker at the instant of heel-strike of the second step, HS_{tr}.

III. Results

A. Steady state walking

The comparison between spatio-temporal gait parameters of PD and control groups, reported in fig.3, revealed a slight reduction in mean gait velocity and cadence, but not in stride length and in the duration of stance and double support phases of gait cycle, which are the most altered parameters of PD patients in the advanced phase (see Introduction). Moreover, the analysis of the profiles of kinematic and kinetic variables (hip, knee and ankle angles, moments and powers, pelvis rotations, GRF components) did not show a significant difference from the control group.

B. Gait initiation

Compared to controls, PD patients showed (see fig.4) a reduced backward displacement of the CoP, but not a shortening of the imbalance and unloading phases, typical of patients in more advanced stages. The analysis of EMG patterns, showed that 5 out of 7 PD patients always presented a physiological anticipatory muscular synergy, with a correct inhibition of Soleus activity and a subsequent bilateral recruitment of Tibialis Anterior muscles. In the remaining two patients TA activation was either monolateral, segmented or even absent, in some trials.

As regard the motor phase, results show that even at early stages of the pathology, PD patients perform a first step characterized by a significant reduction of length, increase of swing duration and a consequent reduction of body velocity.

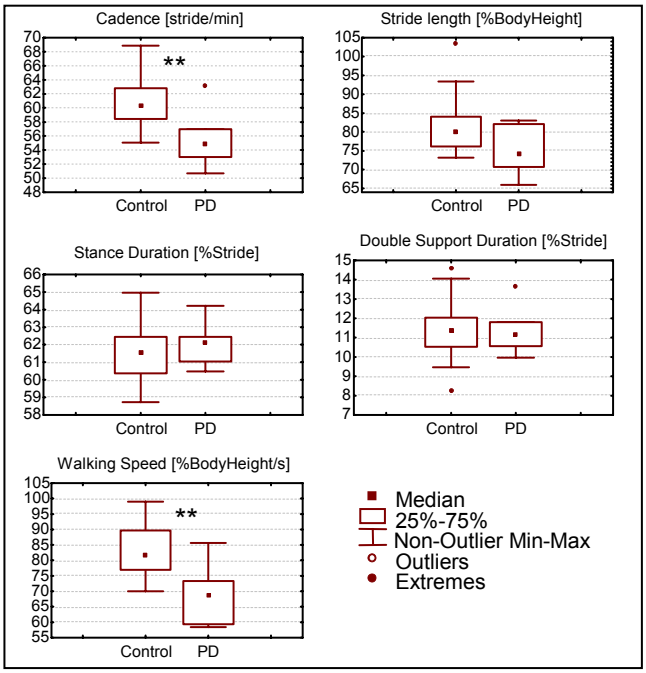

Fig.3. Spatio-temporal parameters of SW task: comparison between PD patients and control group. ** p<0.01 (Mann-Whitney U test)

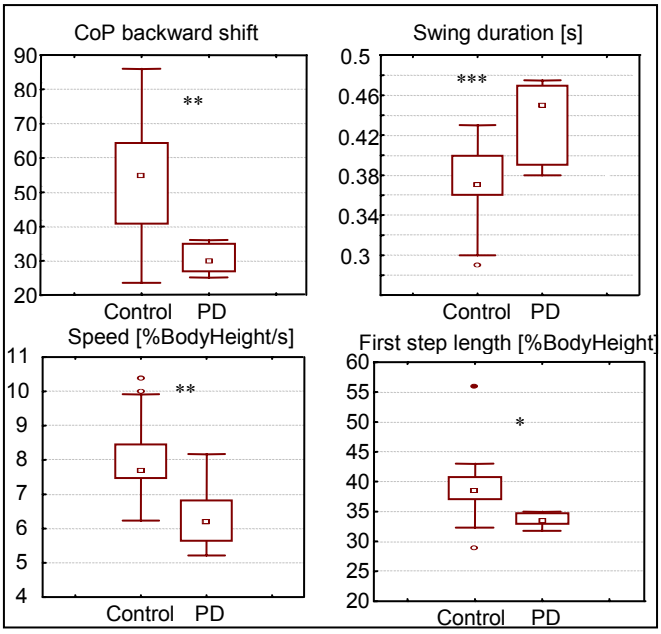

Fig.4. GI task: comparison between PD patients and control group. *** p<0.001, ** p<0.01, * p<0.05 (Mann-Whitney U test)

C. Turning

Results of locomotor task with turning, showed in fig. 5, revealed that PD patients considered in the present study adopt a strategy similar to that of patients in the advanced stages: they delayed the initiation of turning at the step that actually reached the turning target, and rotated the head and the trunk almost simultaneously (average delay 40 ms), and at a smaller angular amplitude compared to controls.

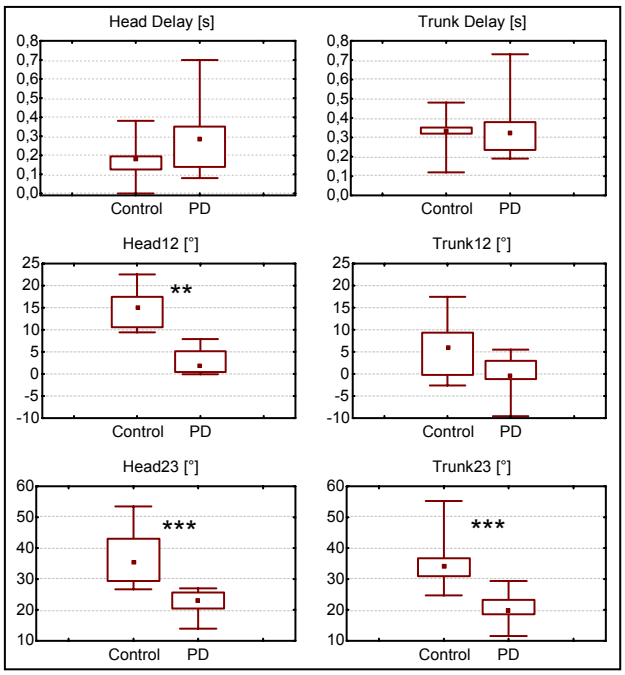

Fig.5. TW task: comparison between PD patients and control group. *** p<0.001, ** p<0.01 (Mann-Whitney U test)

IV. Discussion and Conclusions

Differential diagnosis of idiopathic PD and other neurodegenerative diseases with parkinsonism is not always easy to be done by clinical examinations and sometimes it takes years. Obviously, an earlier diagnosis allows for a faster definition of the correct therapeutic intervention and of the rehabilitative treatments useful to prevent secondary complications. Unfortunately, most of the studies carried out to characterize motor disorders of PD patients have been performed on patients in the advanced stages. The present study, specifically devoted to PD patients in early phases of the disease, is a first attempt to face these aspects.

Results showed that early stage PD patients walk with almost normal kinematic and kinetic patterns, at a slightly reduced velocity due to a reduced gait cadence. On the contrary, significant abnormalities are found in the motor strategies during transitional phases, like gait initiation and turning. In particular, Anticipatory Postural Actions and the coordination of head-trunk rotations are altered compared to age-matched controls.

It might be concluded that a quantitative analysis of locomotor tasks which imply the transition from one condition to another, could provide useful information for the characterization of PD patients also in the early stages of the pathology, when the typical parkinsonian symptoms (bradykinesia, akinesia, rigidity, tremor, disorders of equilibrium, freezing of gait, etc.) are not yet clearly manifested.

References

[1] Schapira AH. Science, medicine, and the future: Parkinson's disease. *Br Med J* vol. 318, pp. 311-314, 1999.

[2] Ferrarin M., Lopiano L. ,Rizzone M., et al., Quantitative analysis of gait in Parkinson's disease: a pilot study on the effects of bilateral sub-thalamic stimulation, *Gait Posture* vol.16, n.2, pp.135-148, 2002.

[3] Ferrarin M., Rizzone M., Bergamasco B., Lanotte M., Recalcati M., Pedotti A., Lopiano L., Effects of bilateral subthalamic stimulation on gait kinematics and kinetics in Parkinson's disease, *Exp Brain Res* vol.160, n. 4, pp.517-527, 2005.

[4] Kimmeskamp S., Hennig E.M., Heel to toe motion characteristics in Parkinson patients during free walking, *Clin Biomech*. Vol.16, pp.806-812, 2001.

[5] Mitoma H., Hayashir R., Yanagisawa N., Tsukagoshi H., Characteristics of parkinsonian and ataxic gaits: a study using surface electomyograms, angular displacements and floor reaction forces, *J Neurol Sci*, vol.174, pp.22-39, 2000.

[6] Morris M.E., Huxham F., McGinley J., Dodd K., Iansek R., The biomechanics and motor control of gait in Parkinson's disease, *Clin Biomech*., vol. 16, pp.459-70, 2001.

[7] Morris M.E., Iansek R., Matyas T.A., Summers J.J., Ability to modulate walking cadence remains intact in Parkinson's disease, *J Neurol Neurosurg Psychiatry*, vol.57, n.12, pp.1532-1534, 1994.

[8] Morris M.E., Iansek R., Matyas T.A., Summers J.J., Stride length regulation in Parkinson's disease: normalization strategies and underlying mechanisms, *Brain* vol.119, pp.551-568, 1996.

[9] Morris M.E., Iansek R., Matyas T.A., Summers J.J., The pathogenesis of gait hypokinesia in Parkinson's disease, *Brain* vol.117, n.5, pp.1169-1181, 1994.

[10] Morris M.E., Iansek R., McGinley J., Matyas T., Huxham F., Three dimensional gait biomechanics in Parkinson's disease: evidence for a centrally mediated amplitude regulation disorder, *Mov Disord*, vol.20, n.1, pp.40-50, 2005.

[11] Morris M.E., McGinley J., Huxham F., Collier J., Iansek R., Constraints on the kinetic, kinematic and spatiotemporal parameters of gait in Parkinson's disease, *Hum Mov Sci*,.vol.18, pp.461-483, 1999.

[12] Nieuwboer A., De Weerdt W., Dom R., Peeraer L., Lesaffre E., Hilde F., Baunach B., Plantar force distribution in parkinsonian gait: a comparison between patients and age-matched control subjects, *Scand J Rehabil Med.* , vol.31, pp.185-192, 1999.

[13] Vieregge P., Stolze H., Klein C., Heberlein I., Gait quantitation in Parkinson's disease – locomotor disability and correlation to clinical rating scales, *Neural Transm*, vol.104, n.2, pp.237-248, 1997.

[14] Ferrarin M., Rizzone M., Lopiano L., Recalcati M., Pedotti A., Effects of subthalamic nucleus stimulation and L-dopa in trunk kinematics of patients with Parkinson's disease, *Gait Posture*, vol.19, n.2, pp.164-171, 2004.

[15] Crenna P, Frigo C, Giovannini P, Piccolo I, The initiation of gait in Parkinson's disease. In: Berardelli A, Benecke R, Manfredi M and Marsden CD (eds) Motor Disturbances II. Academic Press, London San Diego, pp.161-173, 1990

[16] Gantchev N, Viallet F, Aurenty R, Massion J, Impairment of posturo-kinetic co-ordination during initiation of forward oriented stepping movements in parkinsonian patients, *Electroencephalog. Clin. Neurophysiol* , vol.101, pp.110-120, 1996.

[17] Halliday S.E., Winter D.A., Frank J.S., Patla A.E., Prince F., The initiation of gait in young, elderly, and Parkinson's disease subjects, *Gait Posture*,vol. 8, pp.8-14, 1998.

[18] Burleigh-Jacobs A., Horak F.B., Nutt J.G., Obeso J.A., Step initiation in Parkinson's disease: influence of levodopa and external sensory triggers, *Mov Disord*, vol.12, n.2, pp.206-215, 1997.

[19] Crenna P., Carpinella I., Rabuffetti M., Rizzone M., Lopiano L., Lanotte M., Ferrarin M., Impact of Subthalamic Nucleus stimulation on the initiation of gait in Parkinson's disease, *Exp Brain Res*, 2006 (in press).

[20] Vaugoyeau M., Viallet F., Mesure S., Massion J., Coordination of axial rotation and step execution: deficits in Parkinson's disease, *Gait Posture*,vol.18, pp.150-157, 2003.

[21] Hoehn MM, Yahr MD. Parkinsonism: onset, progression and mortality. *Neurology*, vol.17, pp.427-437, 1967.

[22] Calne DB, Snow BJ, Lee C. Criteria for diagnosing Parkinson's disease. *Ann Neurol,* vol.32, Suppl, pp.S125-S127, 1992.

[23] Rabuffetti M, Crenna P, A modular protocol for the analysis of movement in children, *Gait Posture*, vol.20, pp.S77-S78, 2004.