

Work and power reduced in L-dopa naïve patients in the early-stages of Parkinson's disease

Trabalho e potência reduzidos em indivíduos com doença de Parkinson sem L-dopa nos estágios iniciais

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ABSTRACT

Studies which have investigated muscular performance during the initial stages of Parkinson's disease (PD) without L-dopa treatments were not found. **Objective:** to assess whether muscular performance, work and power, of the trunk and lower limbs in L-dopa naïve patients in the early stages of PD was lower than those of healthy subjects and to compare muscular performance between the lower limbs. **Method:** Ten subjects with PD, Hoehn and Yahr (HY) I-II, L-dopa naïve and 10 subjects in the control group were assessed with the isokinetic dynamometer. **Results:** ANOVAs revealed that work and power measures of the trunk, hip, knee, and ankle muscular groups were lower in PD compared with the control group ($p < 0.05$). There were no significant differences in muscular performance between the lower limbs. **Conclusion:** The results suggested the use of specific exercises, as rehabilitation strategies, to improve the ability to produce work and power with this population.

Keywords: Parkinson's disease; muscle strength; Muscle strength dynamometer; rehabilitation; physical therapy speciality.

RESUMO

Estudos que investigaram o desempenho muscular durante os estágios iniciais da doença de Parkinson (DP), sem tratamento com L-dopa não foram encontrados. **Objetivo:** Avaliar se o desempenho muscular, por meio de medidas de trabalho e potência, do tronco e dos membros inferiores em pacientes sem o uso de L-dopa nas fases iniciais da DP é menor do que o de indivíduos saudáveis e comparar o desempenho muscular entre os membros inferiores. **Método:** Dez indivíduos com DP, Hoehn and Yahr (HY) I-II, sem L-dopa e 10 indivíduos do grupo controle foram avaliados com o dinamômetro isocinético. **Resultados:** Medidas de trabalho e potência muscular do tronco, quadril, joelho, tornozelo foram menores no PD em comparação com o grupo controle ($p < 0,05$) e não houve diferenças significativas no desempenho muscular entre os membros inferiores. **Conclusão:** O uso de exercícios específicos, como estratégias de reabilitação, pode melhorar a capacidade de produzir trabalho e potência muscular nesta população.

Palavras-chave: doença de Parkinson; força muscular; Dinamômetro de força muscular; reabilitação; fisioterapia.

Parkinson's disease (PD) is a neuro-degenerative disease in which the progressions of the symptoms are associated with progressive loss of strength and power, which leads to deterioration of physical abilities^{1,2}. Studies that employed measures of peak torque have observed muscular deficits in individuals at various stages of PD, mainly in the intermediate and advanced phases^{3,4}. Usually, these individuals demonstrated bilateral motor impairments, which are associated with deficits in balance and gait and may contribute to immobility and poorer functional performance⁵.

Recently, studies have found that in the early stages, individuals with PD already demonstrate cognitive decline⁶, impaired

planning⁷, altered dynamic postural control⁸, and functional losses when compared to those without the disease⁹. In addition to these impairments, it is possible that muscle deficits may also contribute to the functional losses. However, few studies have investigated muscular performance in individuals in the early stages of PD. Bridgewater and Sharpe¹⁰ showed decreases in trunk extensor torque during the early-stages of PD, which could contribute to the flexed posture observed in the advanced stages. Koller and Kase¹¹ observed decreases in the maximal isotonic knee strength of individuals in the early stages of the disease; however, the hip and ankle muscular groups were not assessed. Furthermore, several studies have

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indicated torque deficits with significant differences between the most- and least-affected lower limbs in the advanced stages of PD^{5,12}. However, these results are controversial regarding the distribution of the weaknesses between the lower limbs in the early stages of PD^{5,13}.

Isokinetic analyses of muscular performance in individuals with PD generally considered only peak torque measures. However, work has been recognized as a more representative measure for the execution of various motor activities, such as gait¹⁴. Some studies have suggested that measures of power are important indicators of muscular performance in PD because they take into account the time to reach peak torque, since bradykinesia is an important deficit observed in these individuals¹².

It is important to note that these studies were in patients with L-dopa treatment. However, few studies have been conducted about newly diagnosed, L-dopa naïve patients and their muscular performance in relation to the variable of work and power. Felows et al. showed exaggerated grip force levels in the early stages of PD, in patients with no exposure to L-dopa medication. However, the patients developed grip force markedly slower than did the control subjects¹⁵.

Given the short- and long-term complications in performance of functional tasks affecting individuals with Parkinson's disease, the current research supports the delivery of rehabilitation interventions early in the disease's progress. Studies suggested that rehabilitation can maintain mobility and prevent secondary impairments of neuromuscular systems associated with reduced physical activity^{5,16}. Therefore, the analysis of muscular performance in the early stages may help to identify earlier, prevent, or delay muscular abnormalities and decline.

Hence, the main purpose of the present study is to evaluate and compare muscular performance by measuring work and power of the trunk and lower limbs, between individuals in the early stages of PD without L-dopa treatments and individuals without PD. Specifically, the aims were to investigate if there are significant differences between work and power measures of the trunk, hip, knee, and ankle muscular groups within individuals between the most and least affected lower limbs.

In PD, a nigral dopaminergic deficit results in reduction of the excitatory drive to the motor cortex and disruption of the cortical activation of the muscle¹⁷ and may manifest as bradykinesia and muscle weakness. Therefore, if muscular performance in the early stages of PD without L-dopa treatment is decreased, it may be treated and loss and disability in the advanced stages may be decreased.

METHOD

Subjects

This was a two-group comparison study, where participants with PD were compared with individuals without PD in a control group. The study comprised a convenience sample

including 10 individuals without PD recruited in the community and 10 individuals with PD recruited at the Movement Disorder Clinic of the University Hospital during medical appointments. Outcomes were measured by the research assistant who was blinded to recruitment and the aims of the study. Individuals with PD were diagnosed by movement disorder neurologists according to the United Kingdom Brain Bank criteria.

The PD group was comprised of 10 individuals (eight men and two women), who were at stages one to two of the modified Hoehn and Yahr (HY) scale¹⁸. These individuals had never taken L-dopa (L-dopa naïve) medication; however, they were taking other drugs, such as dopaminergic agonists and amantadine. Five individuals with PD were classified in stage 2, two in stage 1, and three in stage 1.5 of the HY modified scale. Regarding their medications, two subjects did not use any medications, three were using dopamine agonists, and five were taking dopamine agonists plus amantadine.

The control group consisted of 10 subjects without PD, matched by age, gender, physical activity, and body mass index (BMI). Persons were classified as physical activity according to Physical Activity Trends¹⁹. Subjects were excluded if they had other neurological or systemic disorders; histories of trunk, knee, hip, and ankle surgeries; and detectable cognitive impairments, as determined by their Mini-Mental State Examination scores < 24²⁰. The study was approved by the institutional ethical review committee and all participants provided their consent.

There were no significant differences between the groups for the variables related to age, height, BMI (Table 1). In both groups, seven subjects were inactive and three patients reported some activity during the preceding month but not enough to be classified as moderate or vigorous. So, they were classified as insufficient¹⁹.

Procedures

The PD participants were assessed approximately one hour after taking their usual medications. Initially, demographic and anthropometric data related to age, body mass, physical activity and height, were obtained for characterization purposes for both groups. Clinical information was also collected regarding their motor capacity levels and activity of daily living of the Unified Parkinson's Disease Rating Scale (UPDRS)²¹.

Outcome measures

The muscular performance of both groups was assessed with the isokinetic Biodex System 3 Pro (Biodex, Shirley, NY). All tests were performed by the same examiner and the measurements were bilaterally obtained. Trunk, knee, and ankle joints were assessed in the seated position, while the hip joint was evaluated in the supine position. During the evaluations, the subjects were appropriately positioned and stabilized with belts. For the lower limb joints, the selected angular speeds were 30°/s and 90°/s in the concentric-concentric

Table 1. Descriptive statistics and comparisons between the control and PD groups (n = 10) regarding their demographic, anthropometric, and clinical variables. Means \pm standard deviations (95% confidence intervals).

Variable	Control group (95%CI)	PD group (95%CI)
Age (years)	59.4 \pm 6.9 (54.4-64.3)	59.4 \pm 6.7 (54.5-64.2)
Height (m)	1.67 \pm 0.07 (1.62-1.72)	1.67 \pm 0.08 (1.61-1.73)
Body mass (Kg)	76.3 \pm 10.5 (68.7-83.8)	69.7 \pm 16.0 (58.2-80.1)
Body mass index	27.1 \pm 2.5 (25.3-29.9)	25.3 \pm 4.01 (22.4-28.1)
Time since diagnosis (years)	N/A	2.2 (1.40)
UPDRS – motor (0-108)	N/A	19.0 (8.55)
Physical activity	Inactive (n = 7) Insufficient (n = 3)	Inactive (n = 7) Insufficient (n = 3)

N/A: not applicable; UPDRS: Unified Parkinson's disease rating scale.

modes. These angular speeds were chosen, since they have commonly been used in previous studies in individuals with PD^{4,11,12} and are more comprehensive performance indicators. For the trunk, the evaluated speed was 120°/s.

The range of motion was determined for each joint and the participants were familiarized with the equipment and procedures, by performing three sub-maximal repetitions before the evaluations. The tests consisted of five maximal repetitions at 30°/s and 10 repetitions at 90°/s, with a rest period of 1.5 minutes between each evaluated speed. For the trunk, the subjects performed the same familiarization procedures and five repetitions were assessed at the determined speed. A five to seven minute rest interval was given between each joint evaluation. Throughout the assessments, the subjects received verbal encouragement to perform with their greatest possible efforts. The variables selected for analyses were work, in Joules and power, in Watts, both normalized by the subjects' body mass. Work was calculated as torque x angular displacement and reflects the ability to produce and sustain torque throughout a determined range of motion. Power measurement reflects how much force the participant can generate for a given speed of contraction.

Data analyses

Descriptive statistics and tests for normality (Shapiro-Wilk) were carried out for all variables. Multifactorial repeated measure analyses of variance (ANOVA 2x2), followed by planned contrasts were employed to investigate the main and interaction effects between the PD and control groups and the sides for the outcome variables of work and power, with a significance level of α can 0.05. The Mann-Whitney-U test was employed to investigate differences between the groups regarding muscular performance of the trunk.

RESULTS

Isokinetic work

Work measures of the trunk, hip, knee, and ankle flexors and extensors for the PD and control groups are shown in Table 2. The PD group generated less work than the control

group for the trunk flexion and extension movements and demonstrated significant decreases in the work of the hip flexor/extensors, knee flexors, and ankle plantar flexors at all evaluated speeds. For the knee extensors, significant differences were observed only at the speed of 90°/s. No significant differences were observed for the ankle dorsiflexors for all evaluated speeds.

Isokinetic power

Table 3 shows the power values generated by the trunk and lower limb joints. The PD group also generated less power than the control group for the trunk flexion and extension movements and demonstrated significant decreases in power of the hip flexor/extensors, knee flexors, and ankle plantar flexors for all evaluated speeds. For the knee extensors, significant differences were observed only at the speed of 90°/s. No significant differences were observed for the ankle dorsiflexors for all evaluated speeds.

DISCUSSION

In the present study, L-dopa naïve individuals in the early stages of PD demonstrated poorer muscular performance of the trunk and lower limbs, when compared with those without the disease. These findings are important, since previous studies have reported torque deficits, mainly, in individuals in the intermediate and advanced stages of the disease^{3,4}. The muscular performance variables in the early-stages of PD have been scarcely investigated and the studies which analyzed these parameters^{10,11} did not control for the physical activity and the participants were using L-dopa therapy, which may have affected their results. The effects of levodopa in improving muscular strength were previously reported²². Individuals with PD included in the present study were in the typical early stages of the disease (HY I to II), did not use levodopa-based medications, and had physical activity similar to the control group. The use of well-established inclusion criteria and the process of matching the groups allowed the detection of deficits in muscular performance of the trunk and lower limbs in the early stages of PD.

Table 2. Isokinetic work, in Joules/Kg, produced by the trunk and lower limb muscular groups of the control and PD groups. Means (standard deviations).

Muscular Group	Speed (°/s)	Control group (n = 10)		PD group (n = 10)		p-value
		Non-dominant	Dominant	Most affected	Least affected	
Trunk flexors	120	74.6 (25.4)		20.5 (15.8)		0.0001
Trunk extensors		111.9 (72.2)		27.7 (26.8)		0.002
Hip flexors	30	133.1 (31.4)	145.3 (39.8)	100.1 (26.2)	102.5 (26.0)	0.009
	90	111.9 (34.2)	118.7 (37.7)	57.2 (19.6)	64.6 (23.7)	0.001
Hip extensors	30	152.7 (40.3)	156.1 (30.4)	115.7 (43.4)	100.2 (33.0)	0.008
	90	125.9 (56.3)	133.8 (55.9)	64.9 (38.2)	69.0 (40.1)	0.009
Knee flexors	30	106.6 (18.9)	107.7 (21.8)	76.6 (25.5)	83.9 (25.9)	0.014
	90	85.2 (21.5)	92.5 (19.6)	45.9 (19.2)	50.3 (20.2)	0.0001
Knee extensors	30	192.7 (38.2)	196.2 (36.0)	155.7 (48.6)	167.9 (29.8)	0.064
	90	164.4 (37.5)	169.2 (38.8)	114.1 (37.4)	129.0 (28.5)	0.007
Ankle plantarflexors	30	66.3 (17.8)	68.3 (16.6)	37.6 (17.7)	47.0 (21.8)	0.005
	90	36.9 (13.7)	41.5 (16.3)	19.8 (9.1)	27.6 (16.3)	0.017
Ankle dorsiflexors	30	21.7 (8.3)	21.6 (4.8)	18.4 (6.7)	17.8 (5.7)	0.18
	90	11.8 (1.8)	13.5 (4.6)	10.1 (4.1)	11.8 (3.4)	0.26

p-value: differences between the groups.

Table 3. Isokinetic power, in Watts/Kg produced by the trunk and lower limb muscular groups of the control and PD groups. Means (standard deviations).

Muscular Group	Speed (°/s)	Control Group (n = 10)		PD Group (n = 10)		p-value
		Non-dominant	Dominant	Most affected	Least affected	
Trunk flexors	120	88.3 (39.6)		18.7 (18.0)		0.0001
Trunk extensors		141.0 (105.8)		27.4 (29.8)		0.002
Hip flexors	30	31.9 (8.4)	31.9 (9.5)	20.2 (7.8)	20.9 (8.0)	0.006
	90	66.4 (25.1)	70.2 (29.5)	27.5 (14.1)	31.9 (17.8)	0.001
Hip extensors	30	42.0 (13.5)	41.4 (10.2)	24.0 (8.9)	22.4 (5.7)	0.0001
	90	73.7 (37.3)	79.4 (31.3)	31.9 (17.7)	35.4 (18.8)	0.002
Knee flexors	30	31.9 (8.4)	31.9 (9.5)	20.2 (7.8)	20.9 (8.0)	0.001
	90	66.4 (25.1)	70.2 (29.5)	27.5 (14.1)	31.9 (17.8)	0.001
Knee extensors	30	47.2 (12.1)	48.1 (12.6)	36.6 (11.5)	39.7 (7.0)	0.06
	90	102.4 (30.2)	104.8 (33.8)	64.8 (27.4)	76.1 (18.4)	0.013
Ankle plantarflexors	30	29.0 (11.1)	30.4 (9.5)	11.5 (4.6)	14.8 (5.1)	0.0001
	90	33.2 (15.7)	37.8 (19.7)	11.4 (8.6)	18.5 (11.0)	0.003
Ankle dorsiflexors	30	8.6 (3.1)	9.4 (2.9)	7.1 (2.7)	8.0 (3.6)	0.28
	90	10.3 (3.8)	12.6 (5.1)	8.7 (4.0)	10.3 (3.7)	0.30

p-value: differences between the groups.

The PD group demonstrated significantly decreased capacities to generate work and power, compared to the control group in all tested speeds. Unfortunately, comparable studies concerning isokinetic work with PD subjects were not found. Similar to work, measures of power were also significantly lower in the PD group. Measurement of power using isokinetic dynamometry reflects how much force the participant can generate for a given speed of contraction. It is, therefore, possible to argue that individuals with PD were not able to produce torque through range at that low and high speed.

The PD group demonstrated poorer muscular performance for all muscular groups of the trunk and hip for all investigated speeds. Bridgewater and Sharpe¹⁰ found significant decreases in trunk extensor torques and suggested that there were greater axial strength declines in subjects

with PD in the early stages. However, they did not assess the lower limb muscles. Another study, which analyzed peak torque measures of the trunk and lower limbs, also reported poorer performance of the proximal muscles in relation to the distal ones in individuals mildly affected by PD²³. In the present study, knee extensors at 30°/s and ankle dorsiflexors at both speeds demonstrated no significant differences in performance, compared to the control group. However, these findings could be attributed to the small sample size, which might have increased the likelihood of type-II errors. Other responsible factors were not directly determined but may be explained by age and disease-associated impairments. The selective atrophy of type II fibres with advancing age may partly explain poorer performance at high speeds²⁴. Interestingly, muscles biopsies from persons with PD have

shown increased type-I fibres and decreased type-II²⁵. In addition, patients with PD exhibit multiple agonist bursting during the acceleration phase of movement and increased antagonistic movement²⁶. These abnormal activation patterns may result in the prolonged planning of the tested movement, contributing to the lack of differences at a slower rate in the knee extensors. In the ankle, age induces neural changes as decline of 39% in estimated motor unit number in the tibial anterior. However, this can be compensated by collateral reinnervation of muscle fibers and larger size of the remaining motor units²⁴. So, this could contribute to a better ankle performance compared to the hip. Nallegowda et al.²⁷ also observed no differences in ankle dorsiflexor peak torque values between the groups at 90°/s, 120°/s, and 150°/s speeds for individuals with mild PD. Future studies aiming to better evaluate the relationships between axial and distal muscles in PD should include a larger sample.

The comparisons between the lower limbs showed symmetrical performance for both groups, regardless of the evaluated speeds. Previous studies demonstrated greater deficits in peak torque of the knee extensor and flexor muscles of the most affected limbs in the early-stages of PD patients during high^{12,13} and low¹² speeds. However, some participants used levodopa-based drugs, while others did not take any medications. It is possible that this heterogeneity of medications may have created a tendency for lower limb asymmetries. Pedersen and Oberg²⁸ showed that the observed differences in peak torques between the lower limbs of individuals in the early-stages of PD, disappeared after the withdrawal of the medications. They reported that the decreases in peak torque were the same for both limbs without medication effects and were not associated with the most affected side. Corroborating the results of the present study, Nogaki et al.³ also observed no differences in knee extension and flexion peak torque values between the lower limb muscular groups at 30°/s, 90°/s, and 180°/s speeds for individuals with mild PD. The observed asymmetries occurred at high speeds and with individuals in the advanced stages³. Asymmetrical depletion of dopamine in the substantia nigra²⁹ is associated with asymmetric motor features of PD. Frazzita et al. showed that Parkinsonian patients in stage 3 HY exhibited muscular weakness on the right side, but not on the left side, as compared to controls³⁰. The observed absence of asymmetries in muscular performance between the lower limbs in the early-stages suggests that such asymmetries could be particularly found in the intermediate and advanced stages of PD. We hypothesized that the depletion of dopamine and some factors such as rigidity, tremor, bradykinesia and executive deficits that would interfere with the ability to rapidly generate appropriate torques may not be so exacerbated as in the later stages of PD. Furthermore, it is important to recognize that dynamic postural control during turning is altered even in the early stages of PD. In our study, we decided investigated hip, knee, ankle, and spinal groups of

muscles because these are the major muscle groups that control locomotion and posture.

It has been suggested that isokinetic methods may be influenced by bradykinesia, especially, at high angular speeds³. Furthermore, this test speed may require a smaller motor planning time, the processing of which is classically affected in PD⁷. These might represent limitations of the present study.

The present findings can be relevant to clinical practice. From a rehabilitation perspective, it is critical that prevention is the preferred strategy³¹. Giladi suggested that a person with movement disorders will develop gait deficit only if all compensatory reserves have been depleted³¹. Prevention represents strengthening of the cognitive, sensory and motor compensatory reserves³¹. In this case, the aims of the treatment should be at decreasing disability by preserving and improving the function of compromised or diseased systems. This may be act to maintain the motor system in the advanced stages of the disease³¹. Additionally, according to the physical therapy international guidelines, one of the goals of physical therapy in the early stages is preserving or improving physical capacity (aerobic capacity, muscle strength, and joint mobility)⁵. The decreased work and power generation observed in the early stages of PD suggest the need for early interventions that improve the muscular performance of these individuals. Recently, Corcos et al.³² observed improve in muscular strength and a 7.3 points decrease in UPDRS-III scores, which is a moderate clinically important change, after a 24-month progressive resistance exercise program (PRE). PRE progressively increased the resistance over time and each repetition lasted 6-9 seconds, that is, at slow speeds³². The authors hypothesized that PRE may lead to experience-dependent plasticity in the basal ganglia and corticomotor pathways, which could contribute to improving signs and motor performance. On other hand, evidence that resistance training during which the concentric component of the movement is performed as quickly as possible may be critical for gains in power and recovering quickly from a loss of balance in order to avoid falling in people with Parkinson's disease². Our findings suggest that the incorporation of higher speed muscular training sessions within a PRE program will be an optimal training method to integrate the various aspects of the neuromuscular system in early stages of the disease. In summary, this training regime can bring about changes in the motor sign, work and power measures, physical in the early stages of neurodegenerative movement disorders maintaining patient mobility and independence in the advanced stages of movement disorders.

In conclusion, L-dopa naïve individuals in the early stages of PD demonstrated poorer muscular performance of the trunk and lower limbs, when compared with those without the disease. Besides, the comparisons between the lower limbs showed symmetrical performance for both groups. Clinical studies should investigate whether interventions designed to improve muscular resources would minimize losses muscular and functional performances in this population.

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