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*Neural Control of Movement*

# Multimodal exercise program contributes to balance and motor functions in men and women with Parkinson's disease differently: an intervention study

Margit Mafra[1], Otávio Matheus Werpachowski Lenzi[1], Fábio Souza Silveira[1], Maiara Vargas Schmitt[2], João Filipe de Oliveira[3], Clóvis Arlindo de Sousa[1,2]

*[1]Universidade Regional de Blumenau, Departamento de Educação Física, Laboratório de Motricidade Humana, Blumenau, SC, Brazil; [2]Universidade Regional de Blumenau, Programa de Pós-Graduação Stricto Sensu em Saúde Coletiva, Grupo Interdisciplinar de Pesquisa em Saúde, Blumenau, SC, Brazil; [3]Universidade Regional de Blumenau, Departamento de Medicina, Blumenau, SC, Brazil.*

Associate Editor: Angelina Zanesco. [1]Universidade Metropolitana de Santos, Faculdade de Medicina, Santos, SP, Brazil; [2]Universidade Estadual Paulista "Júlio de Mesquita Filho", Departamento de Educação Física, Instituto de Biociências, Rio Claro, SP, Brazil. E-mail: angelina.zanesco@unesp.br.

**Abstract - Aim:** To verify the effects of a multimodal exercise program on balance and motor functions, and the differences by sex, in people with Parkinson's disease (PD). **Methods:** The intervention study, was composed of 16 people with PD, that were assessed before and after 16 weeks of interventions with the multimodal exercise program. The effects were analyzed generally and by sex, using the Wilcoxon Test. The significance level was established at 5%. **Results:** Overall, there was an improvement in the strength of the lower limbs (LL) ($p = 0.035$) and upper limbs (UL) ($p = 0.009$), functional mobility ($p = 0.003$), gait ($p = 0.050$), balance ($p = 0.001$) and in motor scores of UPDRS III ($p = 0.005$), which categorize motor symptoms of the disease. In regards to sex, women affected muscle strength ($p = 0.044$) and flexibility of LL ($p = 0.028$), gait ($p = 0.018$), and motor aspects of the UPDRS III ($p = 0.042$). The men presented effects in muscle strength of the UL ($p = 0.042$). Women and men had a significant increase in functional mobility ($p = 0.046$ and $p = 0.027$, respectively) and in balance ($p = 0.012$ and $p = 0.042$, respectively). There was no significant difference for both sexes, in body mass and the reach behind the backtest. **Conclusion:** the multimodal exercise program contributed to the improvement in motor function and balance in men and women with PD. Nevertheless, the effects were more significant in women. The comprehension of the differences between men and women grants us a more directional and efficient approach to their treatment.

**Keywords:** Parkinson's disease, physical exercise, multimodal training, motor functions, balance.

## Introduction

Parkinson's disease (PD) is currently one of the greatest challenges in the health area. PD is a neurological disorder, both degenerative and progressive, categorized by the impairment or death of the dopaminergic neurons within the substantia nigra of the brain. The pathophysiological mechanisms of the disease aren't completely elucidated. The PD is multisystemic, with a complex neurophysiological process, and it causes different manifestations in each patient[1,2].

PD is disabling because it compromises motor functions like gait, balance, postural control, and mobility. It also presents several non-motor symptoms, such as alterations in sleep patterns and mood, as well as cognitive deficits[3,4]. Furthermore, it is the fastest-growing neurological disorder in the world, and its causes are attributed to aging, as well as environmental and genetic factors[5]. It is estimated that the global prevalence has more than doubled from 2.5 million people in 1990 to 6.3 million in 2016[6]. It affects around 3% of the population above 65 years of age and up to 5% of people above 85 years of age[7,8].

In this sense, the concern with the quality of interventions applied to this population grows, and the necessity of personalized and effective therapies[2,6]. The exercises can be an excellent strategy to deaccelerate the progression of the disease and should definitely be an essential part of the therapy, as they contribute to the quality of life, aiding the treatment of motor and non-motor symptoms[9-12]. Additionally, exercise reduces the risk of other chronic diseases like diabetes, hypertension, and cardiovascular diseases, which can also compromise the pathogenesis of PD[12,13].

Countless exercise modalities are beneficial. However, in PD there are gaps in knowledge to clarify which type, intensity, duration, and frequency of exercises are ideal. A single prescription is unlikely to be suitable for all, given the progression of the disease and its different phenotypes[10,12]. Functional or multimodal training consists in utilizing the main components of exercise like strength, aerobic resistance, and coordination, to improve the development of daily life functional tasks. The combination of different types of exercise can reinforce functional gain, including improvements in gait, functional mobility, balance, postural control, and a decrease in the disease's progression rate[10,12-14].

There is no evidence of how men and women with PD respond to treatment[10,12,13]. The evolution of the pathology presents differences between men and women and manifests distinct motor and non-motor symptoms as the PD progresses[15,16]. PD can be two times more common in men than in women. A protective effect of the female sex hormones, a genetic mechanism associated with sex, and disparities in health care are factors that can contribute to this difference[8,17].

PD tends to start earlier in men, who report more stiffness as a dominant symptom, and, during the disease, they are more prone to developing significant postural alterations like the freezing of gait[15,16]. The motor symptoms develop later in women, which can be attributed to estrogens concentrations. However, women report tremors as an initial motor symptom. The non-motor symptoms seem to be more common and exacerbated in women[16]. The women develop a more accelerated progression of the disease and have higher risks of falling, on the other hand, men seem to present more cognitive deficits. It is a consensus among authors that there is still no full comprehension of what is behind those differences and studies in the area are highly encouraged[15,16].

Observing the clinical variations between men and women with PD, there may be also differences in their response to treatment. Nevertheless, studies that verify this hypothesis are scarce. The very few data found point to differences in several aspects, prompting a more precise investigation in the comparison of the physiological effects of the physical treatment in men and women with PD[18,19].

The identification of sex differences for training is important to adapt the exercises and establish more effective outcomes, and the results can meet the individual and social needs of women and men with PD[15]. In this sense, the objective was to verify the effects of multimodal physical training on motor functions and balance of men and women with PD.

## Methods

*Participants*

Intervention study, pre, and post multimodal physical exercise program, with subsequent stratification by sex, who were submitted to neurological evaluation to assure the diagnosis and to confirm the stage of the disease. All 28 participants with idiopathic PD from the Parkinson's Support Group in the city of Blumenau/SC were evaluated, and only those with values up to 2.5 on the Degree of Disability Scale by Hoehn and Yahr (H&Y)[20] were included. 17 people who met the criteria were invited to participate in the exercise program.

The sample included 16 participants with idiopathic PD who agreed to participate in the exercises, 8 men with an average age of 65.7 years and H&Y scale of 2.2, and 8 women with an age of 65.8 years and H&Y scale of 2.3. The average time of the disease was 3.9 years for the men and 5.7 years for the women ($p = 0.361$).

All individuals were using specific PD medication and didn't present any other significant diseases that could affect their participation in the proposed activities. Individuals who didn't complete at least 75% of the planned training program, would be excluded from the research. There weren't exclusions or abandonments.

The participants agreed to take part in the study and signed an informed consent form. The study was approved by the Ethics Committee of the University of Blumenau (Number: 3.346.878/2019).

*Methodological procedures*

The participants were interviewed and evaluated by trained individuals. The data collection followed a clinical, physical, and functional tests protocol, which was applied before and after the intervention, under the same conditions for localization, time, and medication of the participants.

Initially, a complete anamnesis of the participants was done for the sample profiling, as well as to identify the main complaints. The severity of the disease and the clinical and motor characteristics were assessed by an experienced neurologist, using the Hoehn & Yahr[20] staging system and the Movement Disorders Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) part III[21], respectively. Subsequently, the anthropometric evaluation (weight and height) and the assessment with the Rikli & Jones[22] Physical and Functional Fitness Test Protocol, which included the following tests:

- Stand up and sit down on the chair: LL muscle strength and resistance (number of executions in 30 s, without using UL);
- Forearm flexion: UL muscle strength and resistance (number of executions in 30 s)

- Sit down and reach: LL flexibility (distance reached to the toes)
- TUG (Time Up and Go): functional mobility (speed, agility, and dynamic balance while standing up, walking as fast as possible on a 3-m distance, going around a cone, and returning to the chair, while the time is measured in seconds);
- Reach behind the back: UL flexibility (distance in which the hands can reach behind the back);
- 6-min walk: aerobic resistance and gait (traveling the largest distance within 6 min);
- Berg[23] Balance Scale: a static and dynamic balance.

Each participant performed a familiarization test to guarantee that the instructions were understood and to avoid errors during the execution. Standard equipment and procedures were used to measure with precision, before and after the training.

*Multimodal physical exercise program*

The participants performed a multimodal physical exercise program, in the group, with 2 sessions of 60 min per week, for 16 weeks. The program was based on a functional circuit. The components worked in the program were aerobic resistance, muscular strength, balance, motor coordination, agility, and flexibility, enhanced with specific tasks from daily life and double tasks. Entertaining activities, social integration, group dynamics, breathing techniques, and relaxation were included to improve socioemotional aspects and to guarantee adherence.

The program of the present study was planned to respect the physical training principles like individuality, overload, and variability while considering the necessities of the sample. There was an increase in the overload through challenging motor demands and task complexities like a simple to complex motor sequence and single to double tasks. Intensity control through Subjective Effort Perception, Borg Scale. Movements from daily life tasks were used with great amplitude during displacements. Large muscular and multiarticular groups were prioritized while performing resisted exercises. Visual clues were also utilized, as well as several unstable surfaces for gait and dynamic balance exercises. Motor and cognitive learning were stimulated with stimulus variations, different materials, and games. When performing repetitions and executing tasks, as well as considering exercise load and speed, each patient's rhythm was considered.

Organization and training:

- Reception of participants: 5 min

The participants were observed on how they were feeling and if they were in an “on” period of their medication.

This time was made available for them to exchange information and experiences, in addition to being given attention and care through listening.

- Warming up: 5 to 10 min

During this time, they participated in playful activities to develop articular mobility, neuromuscular activation of the muscles that will be used in the exercise program, and functional mobilities (displacements)

- The main part of the program - 40 to 45 min

The structured functional circuit according to the physical components that were worked during the session (muscular strength, aerobic resistance, balance, motor coordination, agility, flexibility), including exercises with functional tasks and double tasks.

- Return to a calm state - 5 to 10 min

Stretching, prioritizing the worked musculature. Relaxation techniques, breathing, massage, and guided meditation. Selfcare and house tasks were also stimulated.

*Statistical analysis*

The Kolmogorov-Smirnov was performed to test data normality. Due to variables comprising abnormal distributions, the medians and the interquartile intervals (percentile 25% and 75%) were analyzed using non-parametrical tests. We used Box-plot to visualize the effect of the exercise program on the variables UPDRS, TUG, 6-min walk, and Berg balance scale, by sex. The Mann-Whitney U Test was initially used to analyze all the participant variables, by sex, for the pre-physical exercise program. Subsequently, the total effects and the effects by sex were analyzed, pre and post-physical exercise program, using the Wilcoxon Test. The effect size was calculated by dividing the z-score over the square root of the sample size. The significance level was established at 5%.

## Result

There were no abandonments during the intervention period and the adherence to the training sessions was 85.6% for the men and 96.7% for the women. There were no significant statistical differences between men and women, before the exercise program, with regard to characteristics, clinical variables, and performance on the tests (Table 1).

Table 2 shows the general results, comparing them before and after the intervention. A significant difference between the two conditions was observed, indicating that the exercise program affected the sit-down and stand-up tests positively ($p = 0.035$), as well as the forearm flexion ($p = 0.009$), TUG ($p = 0.003$), 6-min walk ($p = 0.050$), Berg's balance ($p = 0.001$) and the UPDRS III scores ($p = 0.005$). There were no significant statistical in the flexibility tests (sit and reach, and reach behind the back).

Table 3 shows the comparison between pre and post-intervention between men and women. The forearm flexion ($p = 0.042$), TUG ($p = 0.027$), and Berg scale ($p = 0.042$) all had a significant effect on men. The women had a significant effect on the sit-down and stand-up test ($p = 0.044$), the sit-down and reach test ($p = 0.028$), the 6-

**Table 1** - Characteristics of the sample, pre multimodal physical program, by sex. Blumenau, SC, Brazil.

| Variables | Male | | Female | | p-value* |
|---|---|---|---|---|---|
| | Median | Interquartile Interval (p25 / p75) | Median | Interquartile Interval (p25 / p75) | |
| Age (years) | 64.50 | (59.50 / 73.25) | 65.50 | 57.25 / 74.00) | 0.959 |
| Body mass (kg) | 75.50 | (63.63 / 89.20) | 66.60 | (64.60 / 84.65) | 0.662 |
| Time of disease (months) | 48.00 | (24.00 / 69.00) | 60.00 | (15.00 / 132.00) | 0.645 |
| Hoehn e Yahr | 2.00 | (2.00 / 2.50) | 2.25 | (2.00 / 2.50) | 0.694 |
| UPDRS (medical exam - part III) | 29.00 | (27.00 / 37.00) | 36.50 | (18.75 / 44.50) | 0.867 |
| Stand up and sit down for 30 s (repetitions) | 10.00 | (9.25 / 13.00) | 9.00 | (6.00 / 10.00) | 0.094 |
| Forearm flexion 30 s (repetitions) | 11.00 | (7.75 / 11.00) | 10.00 | (7.00 / 10.00) | 0.121 |
| Static balance 30 s | 30.00 | (30.00 / 30.00) | 30.00 | (30.00 / 30.00) | 0.336 |
| Sit down and reach (cm) | -12.50 | (-18.25 / 2.25) | -14.00 | (-17.00 / -8.00) | 0.536 |
| Reach behind the back (cm) | -22.50 | (-29.75 / -13.13) | -12.00 | (-26.00 / -9.00) | 0.336 |
| TUG (s) | 9.00 | (7.00 / 11.25) | 12.00 | (10.00 / 13.00) | 0.054 |
| 6-min walk (m) | 485.00 | (312.50 / 525.00) | 320.00 | (290.00 / 420.00) | 0.189 |
| Berg Scale | 51.50 | (48.00 / 55.50) | 50.00 | (42.00 / 54.75) | 0.382 |

UPDRS: Unified Parkinson's Disease Rating Scale; TUG: Timed Up and Go.
*Mann-Whitney U Test.

**Table 2** - Median and interquartile interval pre and post-multimodal exercise. Blumenau, SC, Brazil.

| Variables | Pre | | Post | | p-value* | Effect size (r)*** |
|---|---|---|---|---|---|---|
| | Median | Interquartile Interval (p25 / p75) | Median | Interquartile Interval (p25 / p75) | | |
| Body mass (kg) | 72.50 | (65.70 / 85.10) | 68.90 | (63.60 / 86.20) | 0.247 | -0.290 |
| Hoehn e Yahr | 2.00 | (2.00 / 2.50) | 2.00 | (2.00 / 2.50) | 0.102 | -0.408 |
| UPDRS (medical exam - part III) | 33.00 | (26.00 / 40.00) | 27.00 | (17.00 / 40.00) | 0.005** | -0.700 |
| Stand up and sit down for 30 s (repetitions) | 10.00 | (9.00 / 11.00) | 11.00 | (10.00 / 12.00) | 0.035** | -0.527 |
| Forearm flexion 30 s (repetitions) | 10.00 | (7.00 / 11.00) | 11.00 | (10.00 / 13.00) | 0.009** | -0.655 |
| Static Balance 30 s | 30.00 | (20.00 / 30.00) | 30.00 | (30.00 / 30.00) | 0.109 | -0.401 |
| Sit down and reach (cm) | -13.00 | (-17.00 / 0.00) | -7.00 | (-14.00 / 0.00) | 0.077 | -0.442 |
| Reach behind the back (cm) | -14.00 | (-29.00 / -11.50) | -15.50 | (-21.25 / -4.63) | 0.099 | -0.118 |
| TUG (s) | 10.00 | (9.00 / 13.00) | 8.00 | (6.00 / 11.00) | 0.003** | -0.738 |
| 6-min walk (m) | 370.00 | (300.00 / 510.00) | 460.00 | (410.00 / 540.00) | 0.050** | -0.489 |
| Berg Scale | 51.00 | (45.50 / 54.75) | 56.00 | (55.25 / 56.00) | 0.001** | -0.796 |

UPDRS: Unified Parkinson's Disease Rating Scale; TUG: Timed Up and Go.
*Wilcoxon Test;
**Significant statistical difference;
***small ≤ 0.30, medium ≤0.50, large >0.50.

min walk (p = 0.018), and TUG (p = 0.046), and the Berg Scale (p = 0.012). Women also presented effects on the UPDRS III motor scores (p = 0.042) (Figure 1). There was no significant difference in the body mass and the reach behind the backtest, for both men and women.

## Discussion

The findings in the present study confirmed our hypotheses about the positive effects of the multimodal training, during 16 weeks, for balance and motor function of men and women with mild to moderate stage PD, while no drug-related alteration was made. There was a significant improvement in thein the TUG and Berg Scale, which assesses functional mobility and balance. There was also a significant improvement in the UPDRS motor scores and the stand-up and sit down, forearm flexion, and 6-min walk tests. Substantial effects were observed in women, who gained a significant improvement on the sit and reach test, the stand, and sit-down test, and the 6-min walk, in addition to the UPDRS motor scores. The men stood out only in the muscle strength forearm flexion test.

**Table 3** - Median and interquartile interval pre and post multimodal exercise, by sex. Blumenau, SC, Brazil.

| Variables | | Male | | p-valor* | Effect size (r)*** | Female | | p-value* | Effect size (r)*** |
|---|---|---|---|---|---|---|---|---|---|
| | | Median | Interquartile Interval (p25 / p75) | | | Median | Interquartile Interval (p25 / p75) | | |
| Body Mass (kg) | Pre | 75.50 | (63.63 / 89.20) | 0.345 | -0.334 | 66.60 | (64.60 / 84.65) | 0.684 | -0.144 |
| | Post | 79.90 | (60.70 / 91.40) | | | 65.70 | (63.75 / 82.98) | | |
| Hoehn e Yahr | Pre | 2.00 | (2.00 / 2.50) | 0.157 | -0.500 | 2.25 | (2.00 / 2.50) | 0.317 | -0.354 |
| | Post | 2.00 | (2.00 / 2.50) | | | 2.00 | (2.00 / 2.38) | | |
| UPDRS (medical exam - part III) | Pre | 29.00 | (27.00 / 37.00) | 0.058 | -0.669 | 36.50 | (18.75 / 44.50) | 0.042** | -0.717 |
| | Post | 23.00 | (18.00 / 40.00) | | | 29.50 | (11.75 / 38.75) | | |
| Stand up and sit down for 30 s (repetitions) | Pre | 10.00 | (9.25 / 13.00) | 0.340 | -0.337 | 9.00 | (6.00 / 10.00) | 0.044** | -0.712 |
| | Post | 12.00 | (10.00 / 13.00) | | | 11.00 | (10.00 / 11.00) | | |
| Forearm flexion 30 s (repetitions) | Pre | 11.00 | (7.75 / 15.00) | 0.042** | -0.718 | 10.00 | (7.00 / 10.00) | 0.102 | -0.577 |
| | Post | 13.00 | (8.00 / 16.00) | | | 10.50 | (10.00 / 11.75) | | |
| Static balance 30 s | Pre | 30.00 | (30.00 / 30.00) | 0.317 | -0.354 | 30.00 | (0.00 / 30.00) | 0.180 | -0.474 |
| | Post | 30.00 | (30.00 / 30.00) | | | 30.00 | (20.25 / 30.00) | | |
| Sit down and reach (cm) | Pre | -12.50 | (-18.25 / 2.25) | 0.752 | -0.111 | -14.00 | (-17.00 / -8.00) | 0.027** | -0.780 |
| | Post | -12.00 | (-16.00 / 3.00) | | | -6.00 | (-10.00 / -1.50) | | |
| Reach behind the back (cm) | Pre | -22.50 | (-29.75/-13.13) | 0.362 | -0.479 | -12.00 | (-26.00 / -9.00) | 0.176 | -0.543 |
| | Post | -18.50 | (-23.88/-14.25) | | | -11.00 | (-17.50 / -2.25) | | |
| TUG (s) | Pre | 9.00 | (7.00 / 11.25) | 0.027** | -0.780 | 12.00 | (10.00 / 13.00) | 0.046** | -0.706 |
| | Post | 7.00 | (5.00 / 8.00) | | | 10.00 | (7.50 / 11.00) | | |
| 6-min Walk (m) | Pre | 485.00 | (312.50/525.00) | 0.753 | -0.111 | 320.00 | (290.00 / 420.00) | 0.018** | -0.838 |
| | Post | 470.00 | (330.00/580.00) | | | 450.00 | (415.00 / 532.50) | | |
| Berg Scale | Pre | 51.50 | (48.00 / 55.50) | 0.042** | -0.718 | 50.00 | (42.00 / 54.75) | 0.012** | -0.893 |
| | Post | 56.00 | (52.75 / 56.00) | | | 56.00 | (53.75 / 56.00) | | |

UPDRS: Unified Parkinson's Disease Rating Scale; TUG: Timed Up and Go.
*Wilcoxon Test;
**Significant statistical difference;
***small ≤ 0.30, medium ≤ 0.50, large > 0.50.

The difference in the tests between men and women observed in the study could not be sustained in the current literature. The researchers presented heterogeneous samples and generalized results, which limits the comprehension of the ones who benefit from a specific type of intervention. Furthermore, there is no standardized program that can be replicated.

The results in this study affected daily life tasks and functional performances positively like walking, turning, sitting, and reaching, especially in women. The findings were relevant, considering that keeping autonomy and improving functional capacity has been the most important objective of interventions in PD[13,23,24].

People with PD[25] are more concerned with the impact of the disease on their daily lives than with the clinical aspects of the disease. The leading necessity indicated was functional independence. Our study verified the impact of exercises on the clinical characteristics of the disease and the functional performance for activities of daily living. These results, according to the literature, should be interpreted considering sex[23,26].

The pre and post-intervention results revealed the potential benefits in women and the higher adherence to the program (96,7%) could be one of the main contributing factors. The adherence factor is intimately related to motivation. The motivation component contributes to harder task performances and reduces the mental and physical load of the effort that is put into the exercises, generating more participation, assiduity, and better results[27]. The correlation between motivation and adherence to an exercise intervention program can be the subject of future research.

Individuals with higher severity of PD can benefit more from the exercises[12,13]. The significant improvement in women in the sample is presumably justified by the motivation and adherence to the intervention, considering

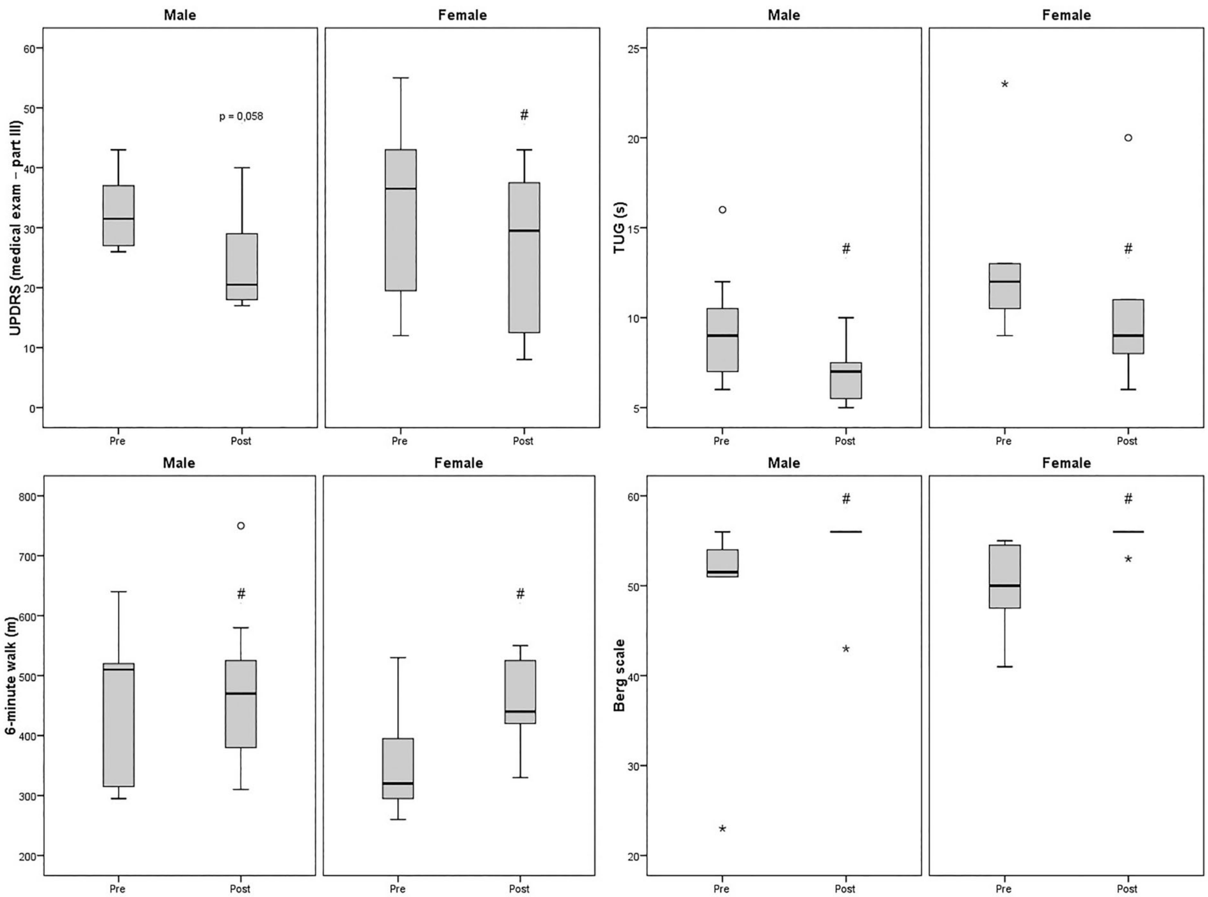


**Figure 1** - Box-plot with the values pre and post of UPDRS III motor scores, TUG, 6-min walk, and Berg balance scale. # Significant difference concerning the pre multimodal exercise program ($p < 0.05$).

they presented the worst UPDRS scores and longer time with the disease. One of the few studies[18] that evaluated the effects of multimodal training by sex found that men had better results. Men improved strength and coordination when compared to women, who only presented effects in strength. However, men presented the worst pre-intervention motor UPDRS, which could have influenced the results. Other studies suggest that women have higher bioavailability and response to levodopa[28]. Considering that physical exercise can be a dopamine stimulating[29], perhaps it can also be attributed to the greater motor effect in women, demanding more investigation.

The present study found that TUG improved significantly in both sexes and the 6-min walk test significantly improved only in women. The present study found that TUG improved significantly in both sexes and the 6-min walk test improved only in women. Women displayed a significant increase in the distance of the 6-min walk test, positively affecting gait and cardiorespiratory capacity. In people with PD, the gait speed is slower in women, compared to men, who tend to demonstrate a more severe bradykinesia[20]. Muscular strength is inferior when compared to men, revealing the crucial need for improvement of these parameters for women because they directly impact physical functions[20,23].

The previously mentioned results along with the improvement in gait, in the women in our study, reduced the UPDRS motor scores significantly. These findings corroborate with Vieira et al.[30] study, which concludes that muscular strength reduces bradykinesia and improves functional development, and can be mediated by the enhancement of neuromuscular activation. Nevertheless, the authors haven't evaluated these effects by sex. In addition, the women in the present sample also showed a significant result in the stand-up and sit-down tests, which had an impact on the improvement of lower limb muscle strength. This fact may also have had a positive impact on PD clinical scores.

The sit and reach flexibility test, in the present study, showed a significant improvement only in women. This result contributes extensively to the functionality of daily routines. Flexibility is an important component of physical function and when combined with strength and balance exercises, it can improve axial alterations[31,32]. Flexibility and balance have been used as part of the multimodal training to improve functional mobility and reduce falling risks. Furthermore, flexibility contributes to the improvement of other motor abilities such as coordination and agility[31,32].

In our study, muscle strength measured with the forearm flexion test showed significant improvement only in men. Moderate-intensity resistance training 2 to 3 times a week for 8 to 10 weeks can result in significant improvements in strength, balance, and improvement in motor symptoms in people with PD of both sexes[33]. Nevertheless, the men in our study did not improve their gait, lower limb strength and endurance, and flexibility. This reinforces the need to combine other exercises for improvements in these variables. In addition to the motivation and adherence mentioned above

Men and women showed significant improvements in the Berg Balance Scale. The improvements related to balance and gait can be related to the double task activities, performed during the training. The double task training presented benefits associated with axial alterations, involving gait, balance, and posture. Challenging motor tilt and dual-task exercises in a training program for individuals with PD, with light and moderate severities, positively impacted balance, gait speed, and performance of motor tasks[34].

We emphasize the prevalence and the impact of the axial alterations in PD individuals, and the significance of including balance, gait, and muscular strength exercises with the double task in a training program[35-38]. Training should contain specific tasks in the context of the necessities of each participant, with varied and challenging stimuli. The double tasks exercises can contribute to relevant and consistent improvements[34,36,38].

The multimodal training, which encompasses three or more combined modalities, produces benefits for motor and non-motor symptoms, functional capabilities, and disease severity[11-13]. When the training is highly challenging, it induces neuroplasticity, and modulates the neurogenesis, synaptogenesis, improved metabolism, and angiogenesis, with a potential of deferring the progression of the disease[11,38-40]. However, for effective and lasting clinical improvements (in motor UPDRS for example), the authors suggest a physical exercise program that has a duration of at least six months[11]. On the other hand, this study showed that a four-month program was effective in improving several measures, especially in women.

The present study offers a preliminary evaluation of the effect of the differences in gender on multimodal exercise. These differences between men and women put in perspective the risk of generalizing the results, which can create subrepresentation when analyzing each sex individually. However, the lack of a control group and the small size of the sample are limitations that can be better investigated in future studies. The researchers' choice due to the absence of the control group in the present intervention was due to the difficulty of finding a greater number of people with PD, which resulted in small sample size, and also due to the importance and need for all people with PD could receive the intervention with multimodal exercises.

Given the evidence presented here, new exercise programs ought to be elaborated with a suitable approach for men and women with PD, moreover, these exercise programs should be assimilated into the treatment routine for better management of symptoms and daily life activities. This study also offers relevant information so that other healthcare professionals can promote sustainable development and incentive of the above-mentioned practice, contributing to an improvement of quality of life and reduction of the burden of patients and their families.

## Conclusion

The multimodal training program showed significant effects on balance and motor functions of men and women with PD, even if the magnitude of the improvements accomplished in the program was different between the sexes. The outcomes were more important in women than in men, because women demonstrated improvements in functional mobility, flexibility, and motor characteristics of the disease. The insight into these differences between them is important for the orientation and implementation of more efficient physical programs, with the urgency and common effort of additional treatments for managing the disease while taking the differences between both men and women with PD into account.

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*Corresponding author*

Margit Mafra, Universidade Regional de Blumenau, Departamento de Educação Física, Laboratório de Motricidade Humana, Blumenau, SC, Brazil.
E-mail: margit.mafra@gmail.com.

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