Original Article (short paper)

Does physiotherapy plus cognitive training improve balance in Parkinson's disease? Randomized clinical trial.

Marcelle Brandão Terra[1], Natália Mariano Barboza[1], Isabela Andrelino de Almeida[2], Maria Eduarda Brandão Bueno[1], Suhaila Mahmoud Smaili[1]

[1]*Universidade Estadual de Londrina, Departamento de Fisioterapia, Londrina, PR, Brasil.*
[2]*Escola Nacional de Saúde Pública, Fiocruz, Rio de Janeiro, RJ, Brasil.*

Abstract - Aims: Postural instability is intrinsically related to cognitive dysfunctions in Parkinson's disease (PD), which supports the importance of multimodal treatments. The purpose of this study was to investigate the effectiveness of adding cognitive training to motor physiotherapy in comparison with motor physiotherapy in the balance of individuals with PD. **Methods:** randomized clinical trial, where the individuals were randomized to two treatments: Physiotherapy Group (PG; n=29; M=12; HY= 2.5 [2-3]) executed balance training; Physiotherapy plus Cognitive Training Group (PCG; n=29; 10M; HY= 2.5 [1.5-3]), balance training plus a cognitive training at the end of the therapy. Evaluation instruments: Balance Evaluation Systems Test (BESTest); Unified Parkinson Disease Rating Scale (UPDRS). **Results:** The intragroup analysis revealed that both groups presented improved balance and UPDRS total score after execution of the protocols, but without statistically significant intergroup differences. The effect sizes were small for all the comparisons. **Conclusion:** There was no difference between the proposed treatments (PCG and PG). However, both interventions benefitted the individuals' balance and signs and symptoms of PD, when considered the time effect.

Keywords: Parkinson's disease, postural balance, cognition, rehabilitation.

Introduction

Balance disorders may already be present in the early stages of Parkinson's disease (PD) and tend to worsen gradually as the disease progresses[1]. Evidence indicates that postural instability is the symptom that most correlates with falls and with increased morbidity in this population[2–4]. A complex network plays an important role in balance control, so that information from different sensory systems has to be processed and integrated in order to perform motor adjustments[5]. There are some structures that are particularly central to balance skills: cerebellum, basal ganglia, thalamus, hippocampus, inferior parietal cortex and frontal lobe[6]. Under normal conditions, balance control occurs automatically[7] and relies more on the subcortical structures (basal ganglia and brainstem)[8], but in PD there is an over-inhibition of the motor and premotor regions[8] and an impact in subcortical pathways, which leads to dysfunctional automatic movement control, and can be accompanied by a compensatory shift to more voluntary cortical control[9]. Thereby, considering that posture control and motor planning are impaired among individuals with PD, individuals can use compensatory strategies (increasing sensory information, attention and cognitive demands) to successfully perform a given motor task[8].

Individuals with PD who present postural instability and gait dysfunction as predominant symptoms are more likely to develop cognitive impairments compared to individuals whose main symptom is tremor[10,11]. In particular, impairment of executive functions is closely related to postural instability[12], which is important given that executive functions are associated with other motor control functions such as anticipatory adjustments, planning and motor coordination[13].

Once the relationship between postural instability and cognitive dysfunctions has been established[12,14,15], it becomes important to investigate treatments that combine motor and cognitive tasks in an attempt to offer additional benefits to individuals with PD[16,17]. To our knowledge, there is no clinical trial in the literature which is similar to the one proposed in this study and addresses motor physiotherapy plus specific cognitive training treatment in individuals with PD assessing balance as the primary outcome. Although, there is evidence that dual task training (DTT - concurrent cognitive and motor training) is effective to improve balance in PD[18], in older adults and individuals with parkinsonism[16].

Systematic reviews and meta-analyses have shown that physiotherapy leads to benefits on balance of people of PD[19–22] and the most used therapeutic approaches include: specific balance training, resistance exercises and

walking or treadmill training, which can be performed statically, dynamically or in functional activities, with the exploration of postural reactions and assistive technology[19]. These benefits are especially verified when individuals are inserted into therapeutic programs with challenging exercises, with treatment principles that include sensory integration, anticipatory postural adjustments, motor agility, stability limits, dual-task, progressive difficulty, and direct supervision by the therapist[14]. Regarding cognitive training in PD, the main approaches applied are computerized resources, paper-pencil activities, and non-invasive brain stimulation, as well as interventions that combine different forms of treatment (multimodal)[23]. A recent systematic review showed that cognitive training is effective in improving cognition in healthy older adults[24] and in individuals with mild cognitive impairment[25]. In PD, a recent meta-analysis has suggested that cognitive training leads to improvements in cognitive performance, but affirms the need for new randomized trials so that the efficacy for this outcome in PD is better investigated[26].

Thus, the objectives of this study were: (1) to verify the effectiveness of adding cognitive training to motor physiotherapy compared to motor physiotherapy in balance, motor symptoms and activities of daily living in individuals with Parkinson's disease; (2) to investigate the effectiveness of both treatments after 3-month follow-up, on balance, motor symptoms and activities of daily living. The following hypothesis was proposed: (1) physiotherapy plus specific cognitive training is more effective for balance, activities of daily living and motor symptons when compared to isolated physiotherapy.

Methods

Trial design

This is a randomized controlled trial, parallel, with group allocation concealed and blinded to the principal assessor. The allocation ratio was 1:1. Approval for the study was obtained from the ethics committee for research involving human beings of UEL (1.356.676), registered in the Brazilian Registry of Clinical Trials (REBEC) under number RBR-43SJZ7 and conducted according to the standards established by the CONSORT Statement[27].

Participants

Individuals were recruited from the Neurology Medical Clinic of the *Hospital de Clínicas* of UEL. Eligibility criteria were: medical diagnosis of PD according to the London Brain Bank criteria[28], aged over 50 years, classified between stages 1.5 to 3 of the Modified Hoehn & Yahr scale[29], absence of cognitive deficit, characterized by the Mini Mental State Examination (MMSE)[30] and of other neurological or musculoskeletal disorders that could interfere in the individuals' assessment or treatment, absence of disorders that might affect locomotion and no engagement in other rehabilitation programs. The study was executed from March 2015 to March 2017 at the State University of Londrina (UEL), in association with the Ágape social center (CASA) in Londrina, Paraná, Brazil.

Interventions

The intervention program consisted of 32 sessions (four months), offered twice a week. Physiotherapy Group (PG) received 60 minutes and Physiotherapy plus Cognitive Training Group (PCG) 90 minutes of therapy (60 minutes like PG plus 30 minutes of cognitive training). Both groups were directly supervised, with a ratio of one physiotherapist for each participant, in the motor training. Cognitive training was also supervised by physiotherapists, but with a ratio of one therapist for two participants. The details of the interventions are described in the Appendix 1.

a) Physiotherapy group (PG)

The PG intervention protocol focused on balance training, sensory integration, agility and motor coordination, stability limits, anticipatory and reactive postural adjustments, functional independence and gait improvement, based on the study published by Santos et al[31] Sessions were divided into four blocks, with a gradual increase in the complexity of the exercises, such as the support base, use of more unstable therapeutic resources (foam, trampoline, ball) of exercises for agility and motor coordination, and elaboration of gait circuits.

b) Physiotherapy plus Cognitive Training Group (PCG)

The PCG intervention protocol was performed in two stages. First, the same protocol was used in the PG and, at the end of each session, 30 minutes of cognitive stimulation activities were added, which took place as follows: the participants sat at the table in group, but the tasks were performed individually, with three cognitive activities being performed face-to-face and supervised by physiotherapists, and participants receiving three more activities to perform at home and bring to the subsequent session for joint and supervised correction before performing any new tasks. The level of exercises difficulty was gradually increased. In each session we sought to stimulate different cognitive domains. The tasks were delivered to patients at the end of the session, and in the next session they were brought in for correction. There was a sheet for controlling the delivery of activities. The cognitive domains were: executive function, perceptual and visuospatial function, visual attention, mental flexibility, motor planning sequencing, selective attention. The sessions involved paper-pencil tasks in which the individuals performed activities such as interpreting figures, making associations between them, solving problems and performing simple calculations, recognizing and circling equal figures among similar images, searching for images

amidst different backgrounds, cutting out figures and assembling puzzles by gluing them to the right places and memory activities[32].

Outcomes

All evaluations were performed with the participants in the "on" phase of medication (one hour after the drug administration), at the same time and by the same evaluator in the pre-intervention, post-intervention (after four months of treatment) and follow-up (three months after the end of the intervention). The researchers first carried out a telephone triage with standardized questions about the diagnostic confirmation of PD, diagnosis time, current medication, current participation in rehabilitation programs, independence for walking and activities of daily living, personal background and interest in physiotherapy. The patients screened for the interview were evaluated to see if they met the inclusion criteria. On the first day, baseline demographic information were collected: 1) demographic data - age, body mass, height, body mass index (BMI), time of diagnosis, Levodopa equivalent daily dose, level of education; 2) cognitive assessment through MMSE, with cut points stablished by Bertolluci et. al.[33], determined according to the educational level of the participants: 13 points for illiterate, 18 points for low to medium and 26 points to high schooling[33] 3) modified Hoehn & Yahr Scale[29] 4) Geriatric Depressive Scale[34]. The primary outcome measure was the Balance Evaluation Systems Test (BESTest)[35] total and subsection scores for assessing balance performance. The subections are: Section I= Biomechanical constraints; Section II= Stability limits/Verticality; Section III= Anticipatory postural adjustments; Section IV= Postural responses; Section V = Sensory orientation; Section VI= Stability in gait[35]. We used the standardized instructions of the BESTest[35]. The secondary outcome measured was disease severity using the domain II (activities of daily living – ADL) and domain III (motor exam) of the Unified Parkinson Disease Rating Scale (UPDRS)[36].

Sample size

Using the web-based G*power 3.1.9 software and based on the effect size obtained in a previous study[37] for BESTest total score, and assuming a 5% type I error and 95% power, the sample size required to ensure adequate statistical power was 22. Anticipating a 15% attrition rate, the total sample size value was 26[37].

Randomization

Participants were recruited and then allocated into one of the two groups randomly. The randomization procedure was done as follows: First, a random table of numbers was generated using the random sequence generator procedure (from the www.random.org website) considering 58 individuals equally divided in two groups Physiotherapy plus Cognitive Training Group (PCG) or Physiotherapy Group (PG); then, the sequence was included by an independent, blinded researcher into identical opaque sealed envelopes. Neither the participant nor the researcher was aware of possible group allocation until the opening of the envelope in front of the participant. An independent researcher was responsible for randomization.

Blinding

The physiotherapists who supervised the treatment and performed the assessments were not blind to the treatment conditions, for convenience reasons. Participants were not informed of the specific hypothesis of the study and may be considered blind with regard to their allocation.

Statistical methods

The descriptive data were presented as means and standard deviations or medians and interquartile ranges, according to the normality distribution, analyzed by the Shapiro-Wilk test. The chi-square test was performed to analyze the categorical variable gender. The comparison of the demographic data of the individuals was analyzed by means of the t-test for independent samples or Mann-Whitney U test, according to the normality of the data.

For data with normal distribution, two-way variance analysis of repeated measures (ANOVA) was applied for the variables group, time and group X time, using Sidak's post-test. For data with non-normal distribution, the Friedman test was used to compare the moments (pre, post and follow-up). For intergroup analysis, the difference of means was calculated between post-pre, follow-up-pre and follow-up-post for successive analysis by means of the Mann-Whitney test. To verify the magnitude of the changes after the intervention, the effect size was calculated, based on Cohen's d coefficients. The effect size is classified as: small (d = 0.0-0.20), medium (d = 0.30-0.50) and large (d = 0.50-0.80).[38] Individuals identified as outliers (values superior to 3 standard deviations) were excluded from the statistical analysis.

The level of statistical significance adopted was $P \leq 0.05$. The analyses were performed using the statistical program (SPSS), version 24.0. Statistics were conducted with intention-to-treat analysis, for primary and secondary outcomes.

Results

Individuals characteristics

The flow diagram of the study is displayed in Figure 1. The baseline demographic and clinical characteristics of the participants are presented in Table 1. The homogeneity of the groups in the initial evaluation is

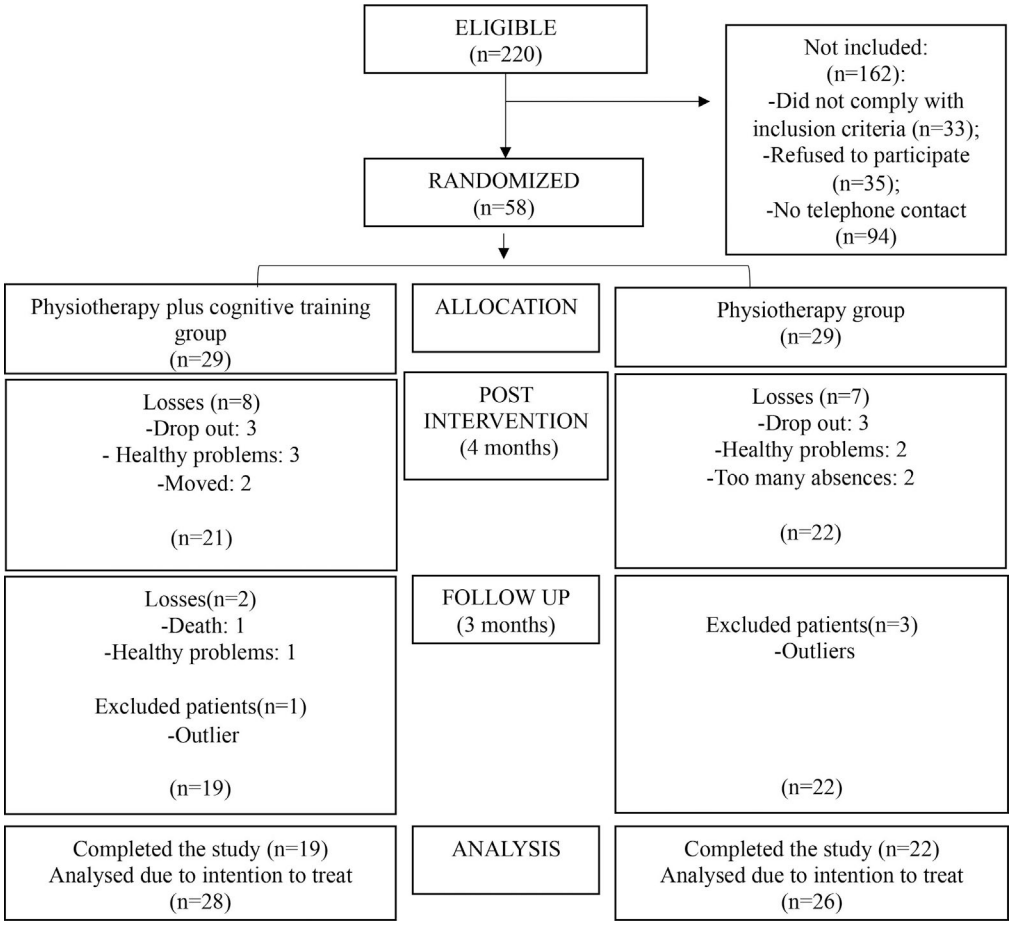


Figure 1 - Consort diagram. Flow diagram of the study.

observed, related to age, weight, height, body mass index (BMI), staging by the H&Y scale, UPDRS, MMSE, GDS and BESTest, PD duration, years of schooling and Levodopa daily equivalent dose. Regarding H&Y scale, the number of patients in each stage was for the PCG**:** 1,5=10; 2=2; 2,5=3; 3=13 and for the PG:1,5=6; 2=5; 2,5=5; 3=10.

Primary outcome

The primary outcome of this study was balance, evaluated by the BESTest. Data from BESTest had non normal distribution. For the intergroup comparison, analyzed by Mann-Whitney test, (between PCG and PG) (Table 2), the difference of means (variation between two moments - Δ) was calculated between: post-pre, follow-up-pre and follow-up-post. It was indicated a statistic significant difference only when compared the mean difference (Δ) in the moments post-pre, between the groups, in favor of PCG, in section stability in gait (VI) (P=0.024). There was no intergroup difference in the other balance domains.

In the intra-group analysis, analyzed by Friedman test, (pre vs. post; pre vs. follow up and post vs. follow up - time effect) (Table 3; Graphs 1 and 2), there were significant differences for PCG in the domains: I-biomechanical constraints [pre vs. post (ES = 0.20) and pre vs. follow-up (ES = 0.30)]; III-anticipatory postural adjustments [pre vs. post (ES = 0.29) and pre vs. follow-up (ES = 0.32)]; VI-stability in gait [pre vs. post (ES = 0.24) and pre vs. follow-up (ES = 0.05)] and in the total score [pre vs. post (ES = 0.27) and pre vs. follow-up (ES = 0.26)]. For PG, there was a difference in the domain V-sensory orientation [pre vs. post (ES = 0.32) and pre vs. follow-up (ES = 0.41)].

Secondary outcome

The second outcome of this study was the evaluation of the signs and symptoms of PD through UPDRS. The results, analyzed by ANOVAs, concerning the intergroup and intragroup comparisons in UPDRS are described in Table 4. There was no intergroup difference and no time X group interaction was verified. Significant differences were observed for PCG when considering the time effect in ADLs domain [pre vs. post (ES = -0.33) and pre vs. follow-up (ES = -0.34)], motor domain [pre vs. post (ES = -0.31)] and the total score [pre vs. post (ES =

Table 1 - Subjects characteristics – baseline.

	PCG (n=28)	PG (n=26)	P value
Gender (M/F)	10 (35.7%) /18 (64.3%)	12 (46.2%) /14 (53.8%)	0.43
Age (years)	67.11±8.14	64.33±7.77	0.21
Weight (kg)	75.01±15.68	75.03±13.72	0.99
Height (m)	1.66±0.09	1.64±0.09	0.45
BMI (kg/m^2)	27.06±5.25	27.80±4.67	0.59
H&Y stage	2.5[1.5-3.0]	2.5[2.0-3.0]	0.21
UPDRS (ADL score)	10.58 ± 4.21	11.54 ± 4.70	0.20
UPDRS (motor score)	24 ± 9.07	22.87 ± 8.90	0.78
UPDRS (total score)	34.58 ± 12.20	34.41 ± 12.16	0.77
BesTest (% total)	80.71 ± 10.44	82.50 ± 10.44	0.54
MMSE (score) GDS	28(26-29.25)	27(26-29)	0.53
GDS	3.0[1.25-6.75]	3.5[2.0-5.75]	0.57
PD duration (years)	4.5(2-9.25)	6(2-7)	0.93
Years of schooling (years)	12(7.75-16)	9(4-16)	0.48
Daily levodopa equivalent dosage (mg)	500(400-775)	500(332.50-832.50)	0.81

Data presented as mean values ± standard deviation; M= male; F= female; kg= kilogram; m=meters; BMI= Body Mass Index; H&Y= Modified Hoehn & Yahr scale; UPDRS= Unified Parkinson's Disease Rating Scale; ADL: activities of daily living; BesTest= Balance Evaluation Systems Test; MMSE: Mini-Mental State Examination; PD= Parkinson`s disease; mg= milligram; PCG= physiotherapy plus cognitive training group; PG= physiotherapy group; P<0,05 = no significant differences between groups.

-0.34)]. In PG, a significant difference was observed in the total score [pre vs. post (ES = -0.35)].

Adverse effects

No adverse effects were reported throughout the treatment in both groups.

Discussion

The results of our study confirm that physiotherapy plus cognitive training (PCG) is not superior, for the outcome balance, compared to the isolated motor physiotherapy (PG). Considering the time effect, both interventions showed benefits on balance, motor signs and symptoms of PD and activities of daily living. In the evaluation after the follow-up, improvement in the activities of daily living and balance were maintained in the PCG after the three months of follow-up. Whereas, in PG, only the improvement in balance was maintained.

Our choice to add cognitive training to motor physical therapy was based on the fact that balance is multimodal and requires the integration of several systems (neuromuscular, cognitive, perceptual, sensory, environment, among others)[7]. So it is considered proactive, adaptive and based on prior experiences[35,39–41], which made us think that cognitive training could positively impact this outcome. In the consolidation of this idea, associations have been reported between postural instability/gait disorders with global cognitive function, executive function (working memory and processing speed) and phonemic[11,42,43]. Regarding the best treatment indication,

Table 2 - Intergroup comparasion of balance outcome according to BESTest.

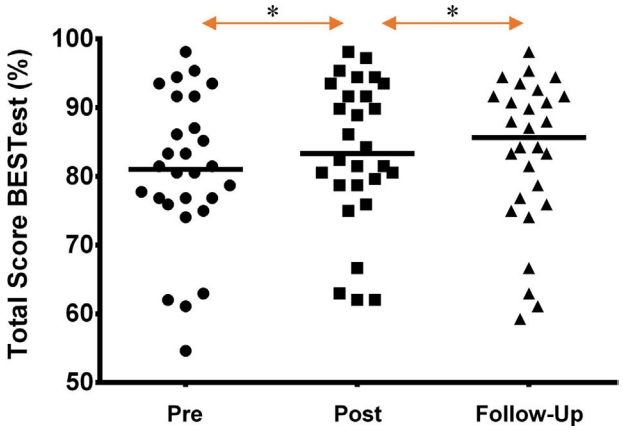
	Δ Post - pre			Δ Follow up – pre			Δ Follow up - post		
	PCG	PG	P	PCG	PG	P	PCG	PG	P
BESTest subsections score (0 - 100%)									
Section I	4.52 (-1.10;10.15)	1.28 (-3.65;6.21)	0.13	5.95 (-1.02;12.92)	0.51 (-5.57;6.60)	0,.28	1.42 (-3.80; 6.66)	-0.76 (-5.66;4.12)	0.67
Section II	3.13 (-1.09;7.35)	1.64 (-1.06; 4.36)	0.97	4.25 (0.15; 8.34)	0.36 (-2.3; 3.08)	0.24	1.11 (-2.44; 4.68)	-1.28 (-4.52; 1.96)	0.35
Section III	4.36 (-0.37; 9.10)	4.06 (0.32; 7.79)	0.85	5.35 (0.61; 10.10)	0.21 (-4.15; 4.58)	0.22	0.99 (-0.86; 2.85)	-3.84 (-9.07; 1.37)	0.06
Section IV	0.00 (-5; 5.01)	0.42 (-5.75; 6.61)	0.96	0.39 (-4.84; 5.63)	3.42 (-1.45; 8.29)	0.53	0.39 (-3.01; 3.81)	2.99 (-1.27; 7.26)	0.30
Section V	0.95 (-0.20; 2.11)	2.30 (0.03; 4.58)	0.41	-0.23 (-1.72; 1.25)	2.05 (0.07; 4.03)	0.07	-1.19 (-2.42; 0.03)	-0.25 (-2.33; 1.82)	0.19
Section VI	3.41 (0.13; 6.70)	-1.16 (-4.97; 2.64)	0.02*	0.18 (-3.23; 3.60)	-1.68 (-5.93; 2.56)	0.45	-3.23 (-6.41; -0.05)	-0.52 (-4.21; 3.16)	0.26
BESTest total score (0 - 100%)	2.74 (0.33; 5.15)	1.48 (-0.69; 3.67)	0.17	2.61 (0.10; 5.12)	0.82 (-2.05; 3.70)	0.37	-0.13 (-1.54; 1.28)	-0.66 (-2.63; 1.30)	0.49

Data presented as mean and confidence interval values. **Δ=** difference of means between post-pre, follow up-pre and follow up-post; BESTest= Balance Evaluation Systems Test; Section I= Biomechanical constraints; Section II= Stability limits/Verticality; Section III= Anticipatory postural adjustments; Section IV= Postural responses; Section V= Sensory orientation; Section VI= Stability in gait; PCG= physiotherapy plus cognitive training group; PG= physiotherapy group. *P≤0,05 (intergroup comparasion): post-pre.

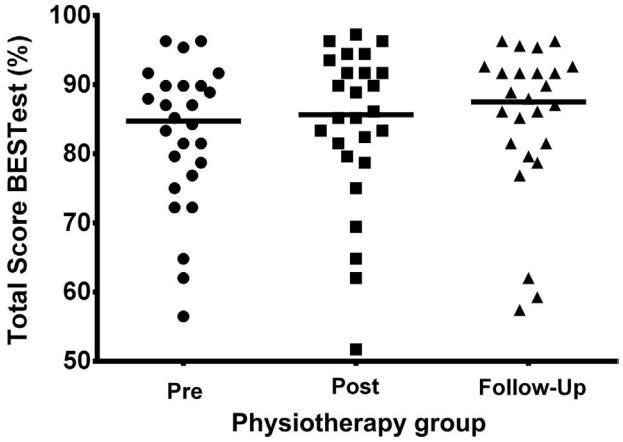
Table 3 - Intragroup comparasion of balance outcome according to BESTest.

		Time			
		Pre	Post	Follow up	P value
BESTest subsection score (0 - 100%)					
Section I	**PCG**	66.66 (54.99-86.66)	73.33 (60-80)*	73.33 (66.66-86.66)#	0.02
	PG	76.66 (46.66-84.99)	80 (60-91.66)	80 (60-86.66)	0.93
Section II	**PCG**	83.33 (71.42-90.47)	85.71 (76.19-95.23)	85.71 (76.19-94.04)	0.30
	PG	85.71 (71.42-89.28)	85.71 (76.19-94.04)	85.71 (76.19-90.47)	0.41
Section III	**PCG**	80.55 (73.60-94.44)	88.88 (73.60-98.61)*	88.88 (73.60-94.44) #	0.04
	PG	88.88 (73.60-98.61)	94.44 (77.77-100)	94.44 (73.60-100)	0.10
Section IV	**PCG**	88.88 (77.77-100)	88.88 (79.16-100)	94.44 (77.77-100)	0.89
	PG	88.88 (77.77-100)	88.88 (77.77-100)	97.22 (77.77-100)	0.37
Section V	**PCG**	100 (94.99-100)	100 (100-100)	100 (94.99-100)	0.13
	PG	96.66 (93.33-100)	100 (93.33-100)*	100 (100-100) #	0.03
Section VI	**PCG**	80.95 (71.42-85.71)	85.71 (64.28-90.47)*	83.33 (61.90-89.28) #	0.05
	PG	83.33 (71.42-89.28)	83.33 (71.42-85.71)	80.95 (71.42-90.47)	0.53
BesTest total score (0 - 100%)	**PCG**	81.01 (76.85-90.27)	83.32 (78.93-93.51)*	86.10 (73.31-92.35) #	0.05
	PG	84.71 (77.31-89.81)	85.64 (80.08-91.66)	87.49 (80.08-91.66)	0.60

Data presented as median and interquartile range. BESTest= Balance Evaluation Systems Test; Section I= Biomechanical constraints; Section II= Stability limits/Verticality; Section III= Anticipatory postural adjustments; Section IV= Postural responses; Section V= Sensory orientation; Section VI= Stability in gait; PCG= physiotherapy plus cognitive training group; PG= physiotherapy group. *P≤0,05 (intragroup comparasion): pre *versus* post comparasion; # P≤0,05 (intragroup comparasion): pre *versus* follow up comparasion.



Graph 1 - Intragroup comparison of balance outcome according to BESTest total score for Physiotherapy plus Cognitive Training Group. Comparison intragroup between the three moments: pre, post and follow up (after 3 months); BESTest- Balance Evaluation Systems Test (total score); * P < 0.05.



Graph 2 - Intragroup comparison of balance outcome according to BESTest total score for Physiotherapy Group. Comparison intragroup between the three moments: pre, post and follow up (after 3 months); BESTest- Balance Evaluation Systems Test (total score).

however, the results available in the literature still remain divergent: they point to beneficial effects for balance either in essentially motor therapies or in cognitive-motor therapies, both in individuals with PD and in healthy elderly individuals[14,17,31,37,44,45].

We can mention some studies performed in individuals with PD, using motor interventions similar to the one used in this study, such as the clinical trial conducted by Santos et al.[31], aiming to compare the effectiveness of two essentially motor therapeutic programs for the outcome balance (resistance exercises versus exercises with an emphasis on postural control components)[31]. In the same sense, Conradsson and colleagues performed a clinical trial comparing the intervention group (specific and balance-challenging exercises) and the control group (instructed to maintain their routine activities)[14]. In both

Table 4 - Data on UPDRS.

		Pre	Post	Follow up	P time	P group	P interaction
Domain II (score)	**PCG**	10.58 ± 4.21	9.16 ± 4.15*	9.12 ± 3.99#	0.004	0.507	0.95
	PG	11.54 ± 4.70	10.04 ± 4.91	9.83 ± 5.39			
Domain III (score)	**PCG**	24 ± 9.07	21.16 ± 8.97*	21.29 ± 10.46	0.025	0.905	0.35
	PG	22.87 ± 8.90	20.04 ± 7.76	22.54 ± 10.19			
Total (score)	**PCG**	34.58 ± 12.20	30.33 ± 12.06*	30.41 ± 12.92	0.009	0.894	0.55
	PG	34.41 ± 12.16	30.08 ± 11.77*	32.37 ± 14.51			

Data presented as mean values ± standard deviations. UPDRS= Unified Parkinson's Disease Rating Scale; Domain II= ADL: activities of daily living; Domain III= Motor exam; PCG= physiotherapy plus cognitive training group; PG= physiotherapy group; *P≤0,05, pre versus post; #P≤0,05, pre versus follow up.

studies, balance improved in the groups that were trained with specific postural control exercises (essentially motor treatment). On the other hand, Pompeu et al.[17], aiming to associate cognitive and motor training, performed a clinical trial comparing two interventions: control group (30 minutes of global physiotherapy exercises + 30 minutes of balance training) and intervention group (30 minutes of global physiotherapy exercises + 30 minutes of cognitive-motor activities using Nintendo Wii Fit). As a result, both groups achieved improvements in the ADL domain of UPDRS, balance (Berg scale), one-leg stance time and cognition (Montreal scale)[17] In our study, we found similar results, with improvements in both PCG and PG in the outcomes balance, and ADL domain of UPDRS.

Our hypothesis that the addition of cognitive to motor training would be more effective than isolated motor training was not confirmed. In the functional evaluation of balance, there was only a statistical difference between groups when comparing the subsection VI – stability of gait, however, the confidence interval values showed too much variation. Concerning the time effect, our results showed that: 1) there were improvements in PCG, in sections biomechanical restrictions, anticipatory postural adjustments, stability in gait and total score while, in PG, there was improvement only in the sensory orientation domain of the BESTest; 2) for both groups, balance improvement was maintained at the follow-up. There was an improvement for both groups regarding balance, however, the time effect sizes were small for all the outcomes. When comparing the studies available in the literature that also used the BESTest as an assesment instrument, with a methodological design similar to ours, we could observe high scores for the individuals included in our study at pre-intervention (superior to 80% for all sections except for section biomechanical constraints, with a score of 66.66% PCG and 76.66% PG), which may have minimized the detection of improvement of the individuals in response to the treatment. For example: Hagovská et al.[45] also performed cognitive-motor training compared to isolated balance training in elderly with mild cognitive impairment. They observed improvement in all domains of BESTest for the cognitive-motor group, but the pre-treatment domain scores in the experimental group were lower than those found in our sample: 55% in section biomechanical constraints; 82% in section stability limits/verticality; 61% in section anticipatory postural adjustments; 89% in section postural responses; 78% in section sensory orientation; 70% in section stability in gait; 73% in the total score[45]. Two other studies that also used the BESTest, but in people with PD, obtained similar results to those described by Hagovská, with a total score at pre-intervention, for the experimental groups, of 76.6% in the study by Wong-Yu and 74.1% in the Pompeu study[37,46]. The participants' characteristics in the aforementioned studies were very similar to our individuals (age, time since diagnosis, HY, UPDRS). The occurrence of high initial scores in our population can be attributed to the fact that these individuals belong to an outpatient clinic specializing in PD treatment and some of the participants have already undergone prior treatments.

In our study, the only domain that differed from the standard described above was sensory orientation, which presented the highest scores found (median of 100% for PCG and 96.66% for PG). Significant improvement in this domain was found only in PG, although the initial score was high (96.6%). In the attempt to understand this fact, a qualitative analysis of the initial data of the study was carried out in both groups, where we found that: at the starting point of the study, 46% of PG versus 75% of PCG reached a score of 100%, leaving PG more prone to treatment responsiveness, although there was no statistically significant difference between the groups at baseline.

Our secondary outcome was UPDRS. It was observed that there was no difference or interaction effects between the groups. In the time effect, it was revealed improvements for PCG in ADLs and motor domains, and total score when the pre- and post-intervention moments were compared, with improvement in the follow-up of the sample for ADLs domain. The maintenance of the improvement in ADL's after the follow-up clarifies that, possibly, the of motor and cognitive stimuli has improved the capacity to retain and transfer the use of information[47], with positive repercussions for functional independence[48–50].

In the PG, improvements in the total UPDRS score were also verified when the moments before and after the intervention were compared. In addition, both groups presented clinical improvement, as a relevant clinical improvement is stipulated as a difference of 3.5 points between the post and pre-treatment.[51] In our case, this was established by the decrease of 4.25 points for the PCG and 4.33 points for the PG in the total UPDRS score.

As strengths of our study, we can highlight: 1) the proposed clinical trial is original in the literature in individuals with PD, 2) the innovation in the therapeutic approach, complementing motor training with cognitive training, 3) the length of the intervention (32 sessions), 3) the follow-up of the population, 4) the characteristics of the intervention program: direct, supervised, low cost and with wide clinical applicability.

Some limitations of this study should be considered: the balance evaluation method, despite being a valid instrument, is not the gold standard to ensure the absence of measurement bias; our results cannot be generalized for individuals with more advanced staging, as individuals were only included in the mild to moderate stages of the disease and without cognitive deficits; individuals without balance impairment (H&Y 1.5-2.5) were included, which could limit the improvements; investigation about which training delivers better effect on cognition should be done considering other groups (control, cognitive, motor and cognitive-motor groups); cognition was evaluated only by the MMSE.

Several aspects related to balance and postural control in PD need to be better investigated. For example, were the number of sessions or the weekly frequency established in this study sufficient to change the motor patterns negatively influenced by PD in the balance of these individuals? Would the use of measures such as the force platform converge with the results found? This study points to the need for a larger number of researches investigating multimodal programs combining motor and cognitive stimuli in order to test the benefits its therapeutic benefits in individuals with PD. These results entail implications for the prescription of exercises in rehabilitation programs when the goal of treatment is balance in individuals with PD, considering the broad clinical applicability and low cost of the proposed treatment.

Conclusions

Physiotherapy plus cognitive training treatment was not superior to motor treatment in individuals with PD. Both groups showed improvement regarding motor symptoms and balance when the time effect was considered. In the evaluation after the follow-up, improvements in activities of daily living and balance were maintained in PCG after the three months of follow-up whereas, in PG, only the improvement in balance was maintained.

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Corresponding author

Marcelle Brandão Terra Av. Robert Koch, 60, Vila Operária, CEP: 86038-350 Londrina, PR, Brasil.
E-mail: celleterra@gmail.com.

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