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The Effect of An Exercise-Based Intervention to the Quality of Life of Patients Suffering From Parkinson's Disease: Prospective Study

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Abstract

Parkinson's disease is a progressive, degenerative neurological disorder associated to profound changes in the quality of life of its survivors. This study was designed to investigate the effectiveness of a 16-week program of exercise-based interventions aiming to [1] improve motor symptoms and [2] provide social integration of PD patients. To achieve this goal, we analyzed the scores recorded by the Parkinson's disease Quality of Life questionnaire (PDQL) before and after the intervention. Results revealed significant improvement in overall quality of life of our group of patients (p=0.002). The results also revealed significant improvements in scores recorded from two specific domains of the PDQL assessment tool; Parkinson Symptoms (p=0.002) and Social Functions (p=0.045). These findings are consistent with the hypothesis that the 16-week exercise-based protocol proposed was effective to promote improvement in measurements of mobility and social integration of PD patients.

Keywords: Parkinson's disease; Quality of life; Physical therapy; Posture; Balance; Exercise; PDQL

Introduction

Parkinson's disease (PD) is a complex and progressive neurodegenerative disorder associated to profound impact to the quality of life of its survivors [1]. This impact is mostly driven by the combination of a broad range of motor and non-motor symptoms that interfere negatively with the ability of these individuals to interact with the environment they live in. For example, as the motor impairments progress (tremor, rigidity, bradykinesia, inability to initiate movements, shuffling gait, and postural instability) non-motor symptoms also arise (psychological depression, insomnia, and dementia) contributing to lower levels of social interaction, isolation, and depression [2-4]. As an attempt to increase the quality of life and survival rates of PD patients, during the last decades there has been a considerable growth of interest regarding the development of multi-factorial clinical interventions aiming to improve their motor abilities; including those related postural instability.

Postural instability is one of the primary motor symptoms directly related to a reduction in survival rates of PD patients [4]. This relation is primarily founded by the inherently higher risk of falls [2,5,6] fractures [2,5] and mild traumatic brain injuries [7] accompanying postural instability. Therefore, enhancement of body balance is considered one of the key goals of exercise-based treatments for PD. In fact, postural stability is a pre-requisite for the execution of other important actions (such as walking) that will greatly define the level of independence of these patients. Previous studies have investigated the effectiveness of balance exercises and collectively they investigations suggest that balance training indeed reduce the number of falls and improve PD motor symptoms [8-13]. However; the superiority of any of the interventions reported cannot be inferred due to: discrepancies regarding the type of exercises implemented combination of exercise interventions with other therapies, duration, intensity, and the use of different outcome measures [4]. As a result, the current set of guidelines for developing programs of exercise-based interventions is still very broad, and further evidence is necessary to establish the effectiveness of customized programs.

Another aspect related to the adverse impact of PD to the quality of life of its survivors is related to the high prevalence of the neuropsychiatric symptoms [14,15]. According to previous reports, neuropsychiatric symptoms can affect up to 65% of the PD patients and anxiety and depression are the most common symptoms to affect this population [16,17]. These same symptoms are especially linked to behavioral changes associated to isolation, reduction of social functions, and consequent worsening levels of quality of life [15]. Therefore, another important aspect of the interventions aiming treatment of PD symptoms relates to the inclusion of patient's socialization. Specific literature focusing in the effectiveness of exercise-based physical therapy interventions to the non-motor symptoms of PD is scarce, but it is hypothesized that exercises (therapeutical or recreational) have the potential to break the deleterious cycle of a sedentary lifestyle considered as one of the factors related to increasing isolation of PD patients [18].

This study was designed to prospectively investigate the possible changes in the quality of life of PD patients submitted to a customized protocol based on [1] body balance training and [2] group interventions. Our main hypothesis is that this protocol would result in an increase of the levels of quality of life of these patients. We expected that improvements will occur in specific assessments of body mobility (motor symptoms) and social functions.

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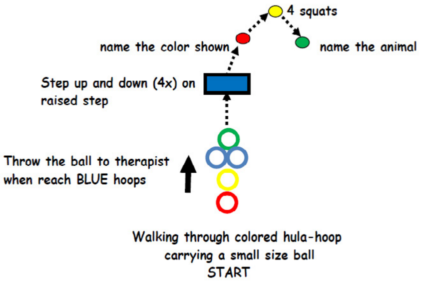
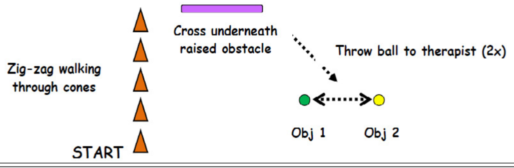
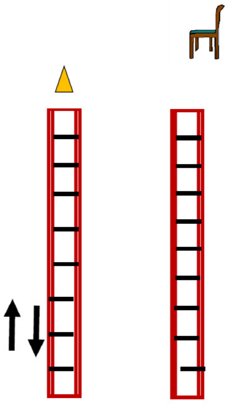
Interventions
Weeks 1-4 1) Balance training in Romberg position and enlarged base of support. Balance was trained with [1] eyes closed and opened [2] associated to trunk and upper extremities movements [3] associated to squatting. Emphasis was given on exploring the limits of body stability, anticipatory postural adjustments, and repetitions of exercises stable and unstable bases of support (foam, raised, step, trampoline). 2) Balance was also trained by walking through an obstacle course as follow: 
Weeks 5-8 1) Balance training in Tandem position and small base of support. Balance was trained with [1] eyes closed and opened [2] associated to trunk and upper extremities movements [3] associated to squatting. Emphasis was given on exploring the limits of body stability, anticipatory postural adjustments, and repetitions of exercises stable and unstable bases of support (foam, raised, step, trampoline). 2) Balance was also trained by walking through an obstacle course as follow: 
Weeks 9-12 1) Balance training in Romberg and Tandem position and enlarged base of support. Balance was trained with [1] eyes closed and opened [2] associated to trunk and upper extremities movements [3] associated to squatting. Emphasis was given on exploring the limits of body stability, anticipatory postural adjustments, and repetitions of exercises stable and unstable bases of support (foam, raised, step, trampoline 2) Balance was also trained by walking through an obstacle course as follows: 
Weeks 13-16 1) 2 exercises from previous series were used. Same exercises were also performed in UNIPEDAL stance 2) Balance was also trained by walking through combination of the obstacle courses already described.

Table 1: Description of protocol implemented along the 16 weeks interventional period.

Methods and Material

Participants

Thirteen adults (five females and eight males, 70.3 ± 5.9 years) participated voluntarily in this study. All participants were recruited from the same health care center (Neurologic Outpatient clinic at the General Hospital of the State University of Londrina, Londrina PR, Brazil). In order to study a group with similar clinical characteristics and developmental stages of PD, only patients complying with the following inclusion criteria were invited to participate: (1) ages above 50 years; (2) confirmed diagnosis of idiopathic PD within one year prior to the study; (3) undergoing similar and standard pharmacological treatment defined by the protocols of their treatment center, (4) PD classification of 1.5-3 accordingly to Hoehn and Yahr scale [19], (5) do not suffer from cardiovascular or musculoskeletal pathologies, (6) do not use any orthotic device associated to aid gait or balance control, (7) do not suffer from dementia (score 24 or higher on Mini-Mental State Examination –MMSE), (8) do not suffer of any other neurological disorders including those of central and peripheral nature. Prior to participation, all patients voluntarily gave their informed consent based on the procedures approved by the Institutional Review Board at The State University of Londrina and conformed to The Declaration of Helsinki (authorization #066/2011 in accordance with the Brazilian National Health Council and its resolution #196/96).

Procedures

All patients were submitted to a series of clinical assessments prior and after the implementation of the training protocol.

Clinical assessments

Geriatric depression scale (GDS): This assessment is composed by a 15-item questionnaire in which patients are asked to respond by answering yes or no about how they felt over a 3 weeks period prior to the date of the assessment. With scores ranging from 0-15, scores of 0-4 are considered normal; 5-8 indicate mild depression; 9-11 indicate moderate depression and 12-15 indicate severe depression [20,21]. We used this assessment to analyze the possible effects of the intervention protocol to depression symptoms.

Figure 1: Example of exercises being performed on the foam pad (Panel A), floor (Panel B), trampoline (Panel C), and raised step (Panel D).

Parkinson's disease quality of life (PDQL): This tool was used to measures the physical and emotional health of our group of patients. This scale is based on a set of 37 items divided into four categories: 1-parkinsonian symptoms (14 items), 2-systemic symptoms (7 items), 3-social functioning (7 items), and 4-emotional functioning (9 items). The scoring system ranges from 1 (Always) to 5 (Never) for each item. An overall score can be derived (185 points), with a higher score indicating better perceived quality of life. The PDQL is recognized for its high internal reliability (R=0.94) and is considered a valid measure of the quality of life of patients with Parkinson's disease [16,17].

Intervention protocol

A series of 32 physical therapy group sessions were distributed over a 16 weeks period (2 sessions per week) between the pre- and post-clinical assessment. Each session had duration of 90 minutes and comprised of interventions of increasingly difficult as the weeks progressed. During the 16 weeks, patients were submitted to balance training while standing on stable or unstable surfaces. Two stable surfaces were used, and they were: [1] the floor and [2] a step raised 15cm from the floor. Two unstable surfaces were used and they were: [1] a medium density foam pad (dimensions 65cm x 35cm x 10cm *LxWxH*) and [2] a 90cm diam. trampoline.

The implemented training protocol was based on the execution of dual tasks where patients were required to balance their bodies while executing secondary movements of the trunk, upper extremities, or combined to walking on a simple obstacle course. During exercises performed on the obstacle course, patients were also asked to execute other tasks such as catching or throwing a ball, naming animals and colors provided by the therapist.

Changes in the configuration of the body's base of support were also used as variations of exercises performed on the step, foam pads, and trampoline. More specifically, exercises were performed while keeping either the feet parallel to each other or in tandem position. Distances between the feet were also varied as weeks progressed. Low amplitudes jumps, handling of objects away from the trunk, and changes in body direction were also introduced as part of the progression. A more detailed description of the exercises used in this protocol is provided on Table 1. Ten repetitions were performed for each exercise, and trained personnel were available to provide safety for the patients. Figure 1 shows actual pictures taken of exercises being performed on the foam pad (Panel A), floor (Panel B), trampoline (Panel C), and raised step (Panel D).

Data processing

Scores obtained from clinical assessments were compiled and analyzed by the IBM SPSS statistics software suite (version 20, IBM® SPSS®). Due to our small sample size (n=13), comparisons of scores obtained before and after the intervention protocol were performed by series of non-parametric tests (Wilcoxon signed-rank test for related data) with levels of significance kept at 5% (α = 0.05) for all analyses performed. A non-parametric approach was taken due to the lower number of observations (n<30) recorded for this prospective study.

Results

Due to subtle changes observed between some the pre- and post-intervention scores, descriptive statistics are presented in two formats: [1] averages and standard deviation (Table 1) and [2] medians and quartiles (Figure 2).

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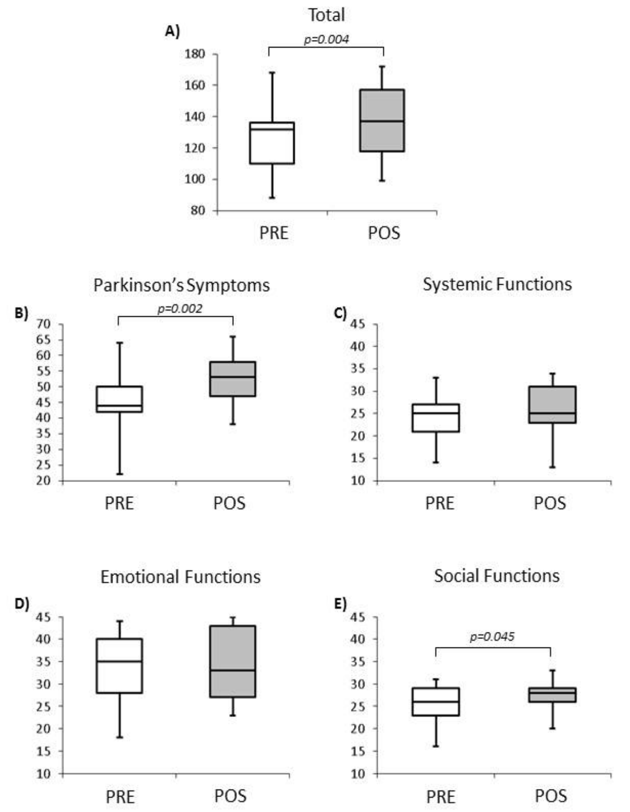


Figure 2: Box-plots of scores obtained across all participants before and after the implementation of interventional protocol (white and gray bars, respectively). Panel A shows the added scores (Total score) from each of the four domains. Panels B-E shows the scores obtained separately from each of the four domains (Parkinson's symptoms, Systemic functions, Emotional functions, and Social functions, respectively).

In general, all patients tolerated well the interventions implemented. The patients between interventions reported no complaints of fatigue or pain. In fact, patients reported a general positive change in their mood. This change was captured by a sensible decrease in the scores obtained by the Geriatric Depression Scale (GDS) before and after the protocol. Averages and standard deviations across patients for this variable were 5.2 ± 2.54 and 4.3 ± 2.46 prior and after the application of the protocol, respectively. Even though the recorded reduction was relatively small (approximately 0.9 points) our group of patients changed their general status regarding the depression symptoms from mild depression to normal (no-depression).

Parkinson's disease Quality of Life (PDQL)

Table 2 describes averages and standard deviations across participants for all four domains of symptoms captured by the PDQL assessment tool. Note the increase in average values for all domains and, consequently, resulting in a higher total score recorded after the protocol (from 126.92 pre-treatment to 139.77 points post-treatment). This overall effect was confirmed by a significant increase in the total scores (p=0.004). Scores recorded from two domains also reached significance, and they were Parkinson's symptoms (p=0.002) and Social function (p=0.045). Figure 2 shows the box plots of these scores obtained before (white bars) and after (gray bars) the execution of the protocol.

It is also important to note that within all four domains we observed a broad range of changes in pre- and post-intervention scores. For example, within the Parkinson's symptoms domain we observed relative differences in scores ranging from 4.00 to 62.50% (Table 1, % Diff column). This finding indicates that even though the overall effect of the protocol was positive, some symptoms responded more positively to the intervention than others.

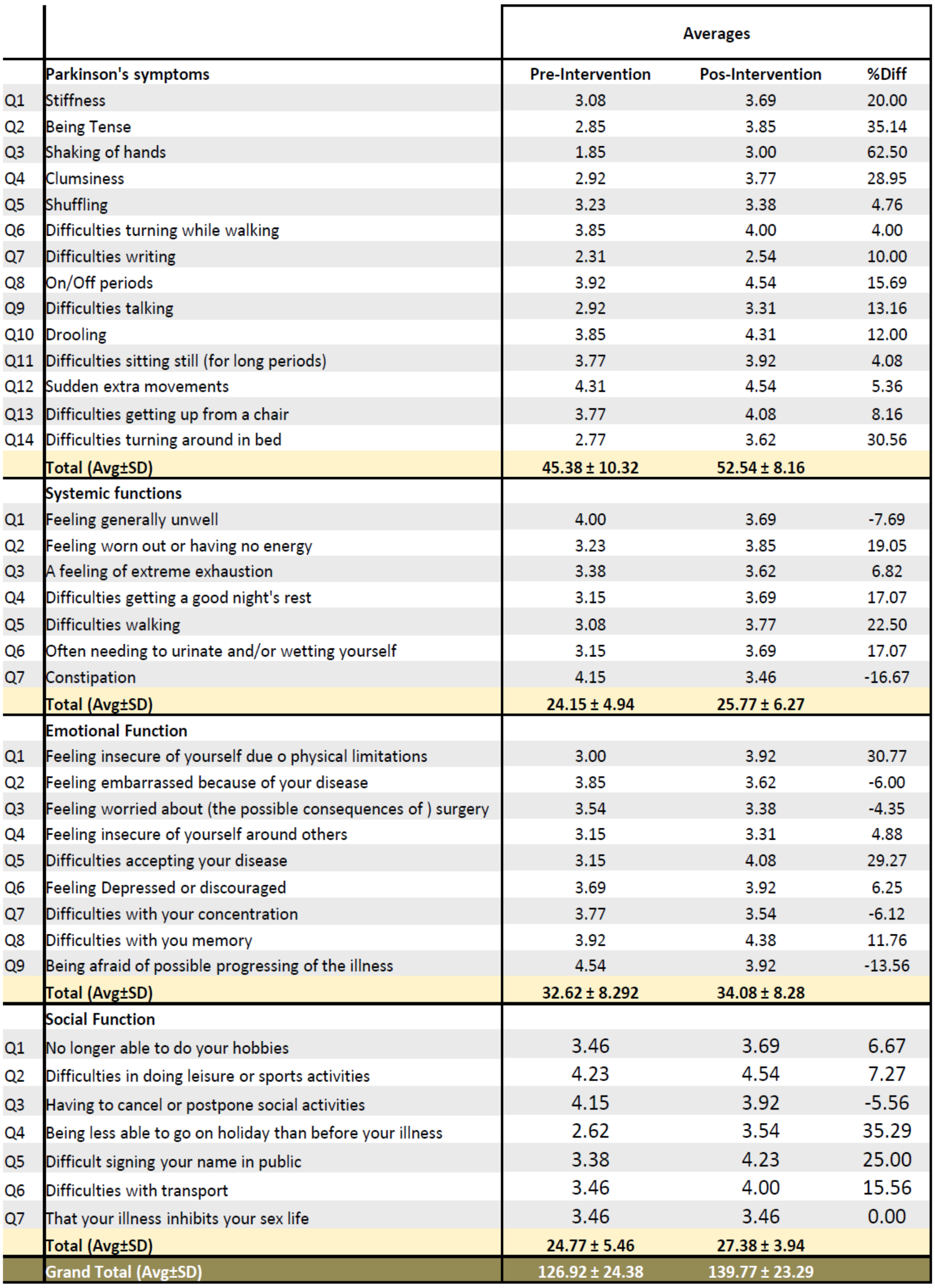
Discussion

This study was designed as a prospective study aiming to provide initial results related to the effectiveness of an exercise-based protocol to the improvement of motor and non-motor symptoms of PD. In general lines, the protocol proposed here promoted enhancement of 30 scores (81% of all 37 possible scores) distributed across all four domains of life quality measured by the PDQL assessment tool. This increase ultimately resulted in a significant improvement of the total scores obtained after the intervention (from 126.92 pre-treatment to 139.77 points post-treatment). This finding allows us to conclude that the protocol was effective to improve the quality of life of our group of patients; confirming our main hypothesis.

This finding is in agreement with several previous studies suggesting that the exercise-based balance training indeed improve aspects of life quality of PD patients [22]. For example, Pompeu et al. [22] recently reported that a customized protocol of balance training based on virtual reality (Microsoft Kinect, Microsoft$^{®}$) was able to improve aspects of quality of life of PD patients (measured by PDQ-39). These authors reported that the positive results produced by their protocol were not restricted to quality of life assessment tools but were able to improve clinical measures such as the 6-minute walk test, balance evaluation system test, and dynamic gait index. In addition, an extensive review made by Tomlinson et al. [23,24] corroborates with these observations by describing improvements in a variety of physical symptoms including walking speed, functional mobility, postural instability, and agility. Collectively, these reports are suggestive of a general positive effect that therapeutical exercises have in the quality of life of these patients.

The protocol presented here was elaborated specifically to promote improvements of motor symptoms and increase socialization of PD patients. Our rationale in concentrate our efforts in balance training exercises arises from the principle that body balancing is a pre-requirement for the execution tasks that are directly related to the independence of the individual (such as walking, stand-up, sit-down, reach for objects during standing-up). In fact, previous studies have provided evidence that balance exercises can improve balance control on PD patients and therefore reduce the number of falls affecting this population [3,9,25]. For example, Smania et al. [9] reported a significant improvement on postural stability resulting from a series of 21 intervention sessions aiming to decrease the deleterious effect of PD to body balance. This same randomized control trial a large number of PD patients (n=64) where only those submitted to the balance specific interventions were able to improve their postural stability. Other studies have also suggested that the effectiveness of balance-oriented interventions can be enhanced when other training modalities are incorporated to the treatment [3,25]. The neural mechanisms related to this improvement are yet not known.

As expected, the majority of the physical symptoms recorded by the PDQL questionnaire suffered a positive effect of our interventions. However, it is evident that some symptoms were more sensitive to the effects of the protocol than others. This observation is corroborated by the large range of relative positive changes recorded between pre- and post-scores across questions (4%-62.50%). One may note that several



		Averages		
	Parkinson's symptoms	**Pre-Intervention**	**Pos-Intervention**	**%Diff**
Q1	Stiffness	3.08	3.69	20.00
Q2	Being Tense	2.85	3.85	35.14
Q3	Shaking of hands	1.85	3.00	62.50
Q4	Clumsiness	2.92	3.77	28.95
Q5	Shuffling	3.23	3.38	4.76
Q6	Difficulties turning while walking	3.85	4.00	4.00
Q7	Difficulties writing	2.31	2.54	10.00
Q8	On/Off periods	3.92	4.54	15.69
Q9	Difficulties talking	2.92	3.31	13.16
Q10	Drooling	3.85	4.31	12.00
Q11	Difficulties sitting still (for long periods)	3.77	3.92	4.08
Q12	Sudden extra movements	4.31	4.54	5.36
Q13	Difficulties getting up from a chair	3.77	4.08	8.16
Q14	Difficulties turning around in bed	2.77	3.62	30.56
	Total (Avg±SD)	**45.38 ± 10.32**	**52.54 ± 8.16**	
	Systemic functions			
Q1	Feeling generally unwell	4.00	3.69	-7.69
Q2	Feeling worn out or having no energy	3.23	3.85	19.05
Q3	A feeling of extreme exhaustion	3.38	3.62	6.82
Q4	Difficulties getting a good night's rest	3.15	3.69	17.07
Q5	Difficulties walking	3.08	3.77	22.50
Q6	Often needing to urinate and/or wetting yourself	3.15	3.69	17.07
Q7	Constipation	4.15	3.46	-16.67
	Total (Avg±SD)	**24.15 ± 4.94**	**25.77 ± 6.27**	
	Emotional Function			
Q1	Feeling insecure of yourself due o physical limitations	3.00	3.92	30.77
Q2	Feeling embarrassed because of your disease	3.85	3.62	-6.00
Q3	Feeling worried about (the possible consequences of) surgery	3.54	3.38	-4.35
Q4	Feeling insecure of yourself around others	3.15	3.31	4.88
Q5	Difficulties accepting your disease	3.15	4.08	29.27
Q6	Feeling Depressed or discouraged	3.69	3.92	6.25
Q7	Difficulties with your concentration	3.77	3.54	-6.12
Q8	Difficulties with you memory	3.92	4.38	11.76
Q9	Being afraid of possible progressing of the illness	4.54	3.92	-13.56
	Total (Avg±SD)	**32.62 ± 8.292**	**34.08 ± 8.28**	
	Social Function			
Q1	No longer able to do your hobbies	3.46	3.69	6.67
Q2	Difficulties in doing leisure or sports activities	4.23	4.54	7.27
Q3	Having to cancel or postpone social activities	4.15	3.92	-5.56
Q4	Being less able to go on holiday than before your illness	2.62	3.54	35.29
Q5	Difficult signing your name in public	3.38	4.23	25.00
Q6	Difficulties with transport	3.46	4.00	15.56
Q7	That your illness inhibits your sex life	3.46	3.46	0.00
	Total (Avg±SD)	**24.77 ± 5.46**	**27.38 ± 3.94**	
	Grand Total (Avg±SD)	**126.92 ± 24.38**	**139.77 ± 23.29**	

Table 2: Averages across participants for all PDQL questions on each of the four domains studied before and after the interventional protocol (Pre- Pos-intervention columns, respectively). Averages across participants of the percentage of change in scores obtained before and after the interventional protocol is also presented (*%Diff* column).

scores with higher relative changes are not directly related to main features of posture control. For example, symptoms such as shaking of hands, auto-perceived clumsiness, difficult signing your name in public and difficulties writing scored either better or comparatively to those abilities requiring postural stability control such as difficulties walking, difficulties getting up from a chair, and difficulties in doing leisure or sports activities. It is also important to emphasize that some of these larger relative changes in scores were related to improvement of dyskinesia-related symptoms.

In fact, we expected an improvement of dyskinesia-related symptoms, but not as pronounced as the results recorded. This finding compel us to interpret that the exercise-based interventions proposed here had its effect to basic neural mechanisms involved to the regulation of human motor actions. This interpretation is corroborated by current evidence indicating that physical activity can attenuate motor impairments related to PD, including dyskinesia [26-30]. Dyskinesia is a complication from dopamine replacement therapy characterized by involuntary movements and lack of coordination. Park et al. [31] studied the effects of dopaminergic replacement to aspects of hand control in PD patients. More specifically, these authors applied the idea of synergies and the framework of the uncontrolled manifold hypothesis to explore the effects of dopamine replacement therapy on finger interaction and coordination in patients with early-stage PD. Their results demonstrated a significant improvement of finger coordination within 24 hours of dopamine replacement withdraws. Accordingly to Heumann et al. [30], the effects induced by dopamine replacement therapy are widespread in the brain, however, the striatum, the most dopamine receptor-rich area, is where the major neurochemical and functional changes that underlie dyskinesia take place.

Interventions seeking to ameliorate dyskinesia symptoms include deep brain stimulation [32], pharmacological [30], exercise-based therapies [33], and surgical procedures [34]. Due to its several advantages, exercise-based therapies are currently gaining importance as a primary intervention in early-stages of development of PD. Even though we can cite its relative simplicity and lower costs of implementation as its primary advantages, exercise-based interventions seems to not impact the positive effects of dopamine replacements [30,35,36] and yet have positive cardio-vascular effects [37]. In addition, exercise-based therapies have the potential to counteract depression and anxiety related symptoms [19,38-40]. These neuropsychiatric symptoms are not exclusively present in late stages of PD development and can precede motor symptoms on early development stages [41,42]. Currently, the number of investigations addressing the effectiveness of exercise-based interventions to the control of neuropsychiatric is scarce and, most of the information available is based on investigations of healthy aging patients [10].

Our result revealed improvements on non-motor symptoms, including those of neuropsychiatric origin. The subtle changes to results recorded by the Geriatric Depression Scale reinforce this observation. It is important to emphasize that we can only speculate about the mechanisms of these changes that can originate from; [1] neurophysiological changes induced by the exercises; [2] approximation of other patients suffering from the same condition and exhibiting similar symptoms; or [6] a combination of both factors. Based on our interaction with our patients we are inclined to accept the third hypothesis. During the 16 weeks of implementation of the protocol, we experienced the creation of a certain bond among the patients and a gradual change on the acceptance of their condition. These changes were also perceived regarding their acceptance of physical activity that increased along the 16-weeks of the protocol. Due to the prospective nature of this study, this question remains and we expect to follow-up with studies designed to test this very same hypothesis. Based on these initial results we also expect to extend our investigations by including more patients and neurophysiological measurements to advance our understanding of PD movement disorders.

Conclusions

We found that the 16-week exercise-based protocol aiming the improvement of body balance control in patients with PD was successful to increase the levels of life quality of the patients studied.

References

1. Caviness JN (2014) Pathophysiology of Parkinson's disease behavior--a view from the network. Parkinsonism Relat Disord 20 Suppl 1: S39-43.
2. Kerr GK, Worringham CJ, Cole MH, Lacherez PF, Wood JM, et al. (2010) Predictors of future falls in Parkinson disease. Neurology 75: 116-124.
3. Hinnell C, Hurt CS, Landau S, Brown RG, Samuel M; PROMS-PD Study Group (2012) Nonmotor versus motor symptoms: how much do they matter to health status in Parkinson's disease? Mov Disord 27: 236-241.
4. van der Kolk NM, King LA (2013) Effects of exercise on mobility in people with Parkinson's disease. Mov Disord 28: 1587-1596.
5. Schaafsma JD, Giladi N, Balash Y, Bartels AL, Gurevich T, et al. (2003) Gait dynamics in Parkinson's disease: relationship to Parkinsonian features, falls and response to levodopa. J Neurol Sci 212: 47-53.
6. Lo RY, Tanner CM, Albers KB, Leimpeter AD, Fross RD, et al. (2009) Clinical features in early Parkinson disease and survival. Arch Neurol 66: 1353-1358.
7. Boyé ND, Mattace-Raso FU, Van der Velde N, Lieshout EM, De Vries OJ, et al. (2014) Circumstances leading to injurious falls in older men and women in the Netherlands. Injury 45: 1224-1230.
8. Antony PM, Diederich NJ, Krüger R, Balling R (2013) The hallmarks of Parkinson's disease. FEBS J 280: 5981-5993.
9. Hirsch MA, Dulin M, Iyer SS, Hammond FM (2009) Exercise for management and treatment of Parkinson disease. Am Fam Physician 79: 1043.
10. Hirsch MA, Toole T, Maitland CG, Rider RA (2003) The effects of balance training and high-intensity resistance training on persons with idiopathic Parkinson's disease. Arch Phys Med Rehabil 84: 1109-1117.
11. Ashburn A, Fazakarley L, Ballinger C, Pickering R, McLellan LD, et al. (2007) A randomised controlled trial of a home based exercise programme to reduce the risk of falling among people with Parkinson's disease. J Neurol Neurosurg Psychiatry 78: 678-684.
12. Allen NE, Canning CG, Sherrington C, Lord SR, Latt MD, et al. (2010) The effects of an exercise program on fall risk factors in people with Parkinson's disease: a randomized controlled trial. Mov Disord 25: 1217-1225.
13. Smania N, Corato E, Tinazzi M, Stanzani C, Fiaschi A, et al. (2010) Effect of balance training on postural instability in patients with idiopathic Parkinson's disease. Neurorehabil Neural Repair 24: 826-834.
14. Fernandez HH (2012) Updates in the medical management of Parkinson disease. Cleve Clin J Med 79: 28-35.
15. Sagna A, Gallo JJ, Pontone GM (2014) Systematic review of factors associated with depression and anxiety disorders among older adults with Parkinson's disease. Parkinsonism Relat Disord 20: 708-715.
16. Pontone GM, Williams JR, Anderson KE, Chase G, Goldstein SA, et al. (2009) Prevalence of anxiety disorders and anxiety subtypes in patients with Parkinson's disease. Mov Disord 24: 1333-1338.
17. Leentjens AF, Dujardin K, Marsh L, Martinez-Martin P, Richard IH, et al. (2011) Symptomatology and markers of anxiety disorders in Parkinson's disease: a cross-sectional study. Mov Disord 26: 484-492.
18. Speelman AD, van Nimwegen M, Borm GF, Bloem BR, Munneke M (2011) Monitoring of walking in Parkinson's disease: validation of an ambulatory activity monitor. Parkinsonism Relat Disord 17: 402-404.
19. Hoehn MM, Yahr MD (1967) Parkinsonism: onset, progression and mortality. Neurology17:427-442.
20. Johnco C, Knight A, Tadic D, Wuthrich VM (2014) Psychometric properties of the Geriatric Anxiety Inventory (GAI) and its short-form (GAI-SF) in a clinical and non-clinical sample of older adults. Int Psychogeriatr .
21. Sunwoo MK, Hong JY, Lee JE, Lee HS, Lee PH, et al. (2014) Depression and voice handicap in Parkinson disease. J Neurol Sci .
22. Pompeu JE, Arduini LA, Botelho AR, Fonseca MB, Pompeu SM, et al. (2014) Feasibility, safety and outcomes of playing Kinect Adventures!â„¢ for people with Parkinson's disease: a pilot study. Physiotherapy 100: 162-168.
23. Tomlinson CL, Patel S, Meek C, Herd CP, Clarke CE et al. (2012) Physiotherapy versus placebo or no intervention in Parkinson's disease. Cochrane database of Systematic Reviews: doi 002/14651858.CD002817.pub4.

24. Tomlinson CL, Patel S, Meek C, Herd CP, Clarke CE, et al. (2012) Physiotherapy intervention in Parkinson's disease: systematic review and meta-analysis. BMJ 345: e5004.
25. Falvo MJ, Schilling BK, Earhart GM (2008) Parkinson's disease and resistive exercise: rationale, review, and recommendations. Mov Disord 23: 1-11.
26. Goulart F, Pereira LX (2005) Uso de escalas para avaliação da doença de Parkinson em fisioterapia. Fisioter Pesqui 11: 65-69.
27. de Boer AG, Wijker W, Speelman JD, de Haes JC (1996) Quality of life in patients with Parkinson's disease: development of a questionnaire. J Neurol Neurosurg Psychiatry 61: 70-74.
28. Campos M, de Rezende CH, Farnese Vda C, da Silva CH, Morales NM, et al. (2011) Translation, Cross-Cultural Adaptation, and Validation of the Parkinson's Disease Quality of Life Questionnaire (PDQL), the "PDQL-BR", into Brazilian Portuguese. ISRN Neurol 2011: 954787.
29. Hackney ME, Earhart GM (2009) Backward walking in Parkinson's disease. Mov Disord 24: 218-223.
30. Frazzitta G, Pezzoli G, Bertotti G, Maestri R (2013) Asymmetry and freezing of gait in parkinsonian patients. J Neurol 260: 71-76.
31. Heumann R, Moratalla R, Herrero MT, Chakrabarty K, Drucker-Colín R, et al. (2014) Dyskinesia in Parkinson's disease: mechanisms and current non-pharmacological interventions. J Neurochem 130: 472-489.
32. Park J, Lewis MM, Huang X, Latash ML (2014) Dopaminergic modulation of motor coordinaton in Parkinson's disease. Parkinsonism Relat Disord 20: 64-68.
33. Monteiro A, Andrade C, Rosas MJ, Linhares P, Massano J, et al. (2014) Deep brain stimulation of the subthalamic nucleus in advanced Parkinson's disease: five year follow-up at a Portuguese center. Rev Neurol 58: 433-439.
34. King LA, Horak FB (2009) Delaying mobility disability in people with Parkinson disease using a sensorimotor agility exercise program. Phys Ther 89: 384-393.
35. Munhoz RP, Cerasa A, Okun MS (2014) Surgical treatment of dyskinesia in Parkinson's disease. Front Neurol 5: 65.
36. Goetz CG, Thelen JA, MacLeod CM, Carvey PM, Bartley EA, et al. (1993) Blood levodopa levels and unified Parkinson's disease rating scale function: with and without exercise. Neurology 43: 1040-1042.
37. Reuter I, Harder S, Engelhardt M, Baas H (2000) The effect of exercise on pharmacokinetics and pharmacodynamics of levodopa. Mov Disord 15: 862-868.
38. Shulman LM, Katzel LI, Ivey FM, Sorkin JD, Favors K, et al. (2013) Randomized clinical trial of 3 types of physical exercise for patients with Parkinson disease. JAMA Neurol 70: 183-190.
39. Reid KJ, Baron KG, Lu B, Naylor E, Wolfe L, et al. (2010) Aerobic exercise improves self-reported sleep and quality of life in older adults with insomnia. Sleep Med 11: 934-940.
40. Bridle C, Spanjers K, Patel S, Atherton NM, Lamb SE (2012) Effect of exercise on depression severity in older people: systematic review and meta-analysis of randomised controlled trials. Br J Psychiatry 201: 180-185.
41. Khoo TK, Burn DJ (2009) Non-motor symptoms may herald Parkinson's disease. Practitioner 253: 19-24.
42. Khoo TK, Yarnall AJ, Duncan GW, Coleman S, O'Brien JT, et al. (2013) The spectrum of nonmotor symptoms in early Parkinson disease. Neurology 80: 276-281.