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Neural Control of Movement

Is fatigue associated with balance in Parkinson's disease?

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Abstract - Background: Fatigue is a disabling symptom in the spectrum of Parkinson's disease (PD), affecting from 30% to 70% of the persons. Even though it is a common symptom, with negative repercussions for PD individuals, its correlation with balance is not established. **Aim:** The aims of this study were to verify the correlation between fatigue and balance in individuals with PD and to compare balance in individuals with PD that presents low fatigue or high fatigue. **Methods:** This study included 37 individuals with PD, who were divided into two groups: low fatigue (n = 25) and high fatigue (n = 12). Fatigue was evaluated using the Parkinson's disease Fatigue Scale and a force platform was used to assess four balance tasks: bipedal, tandem with eyes open/closed, and tandem with the dual-task, in three parameters: (1) 95% confidence ellipse area of the center of pressure (COP) (2) mean velocity (3) root mean square of COP. To verify the correlation between fatigue and balance, the Spearman rank-order correlation coefficient was assessed. Comparison of medians between the groups was analyzed using the Mann-Whitney test. **Results:** There was no significant correlation between fatigue and balance. There was no difference between the groups with low and high fatigue. **Conclusion:** This study's findings, together with those reported in the literature, suggest there is no correlation between fatigue and balance, and even though individuals with PD report fatigue or experience situations of fatigue, they do not present greater posture instability than individuals with PD who do not report fatigue.

Keywords: Parkinson's disease, signs and symptoms, rehabilitation.

Introduction

Fatigue is a common and disabling symptom in the spectrum of Parkinson's disease (PD), affecting from 30% to 70% of persons[1,2]. Fatigue is defined as a strong feeling of tiredness and exhaustion together with a lack of energy[3]. Even though fatigue has repercussions on the lives of those affected, its etiology is not fully understood and an efficacious treatment has not been established[4,5], so it still negatively impacts the lives of those with PD[6−10]. There is evidence relating fatigue to various non-motor symptoms of the disease[2], such as apathy and anxiety[2,11,12], excessive sleepiness[2,7,13−16], sleep disorders[7,12,17], autonomic dysfunctions[13], depression[7,12,16,18], and visual-spatial perceptions[4] perceperce. Findings reported in the literature concerning the association between fatigue and cognitive impairment diverge[2,4,19]. Foster et al. report such an association[20], while Siciliano et al. report an association between fatigue and anxiety, cognitive apathy, and sleepiness, rather than with cognitive impairment[2].

Even though there is a solid body of evidence associating fatigue with the other non-motor symptoms of PD previously mentioned, there is a lack of studies correlating fatigue with motor symptoms. It is known that individuals with PD experiencing fatigue, evaluated by Parkinson's fatigue Scale (PFS)[21], obtain higher scores in the motor domain of the Unified Parkinson's Disease Rating Scale (i.e., they experience greater impairment caused by the disease)[2], are more sedentary and have poorer functional capacity and physical function than those reporting less intense fatigue[22]. There is also evidence that individuals with PD are more likely to falls, present greater generalized physical fatigue, lower levels of energy and decreased productivity[23]. Additionally, studies show an association between physical fatigue and the risk of fall among healthy older people individuals[24]. On the other hand, the findings reported by Baer et al. show that balance did not deteriorate among individuals with PD when they underwent tests that provoked fatigue[25], suggesting fatigue does not negatively affect balance. Thus, the relationship between fatigue and postureral instability, one of the main factors triggering falls, is not clearly established.

Considering there is no consensus regarding association between fatigue and posture control, this study's objective was to assess a potential correlation between fatigue and posture control among individuals with PD, as well as to analyze the posture control of individuals under the category “low fatigue,” when compared to individuals under the “moderate to high fatigue” category. The hypothesis of this study is that individuals reporting fatigue would experience greater posture instability compared to individuals with low fatigue.

Methods

Participants

This is a cross-sectional study, conducted at Universidade Estadual de Londrina (UEL), carried out from April to September 2017, in the Center for Research and Postgraduate Studies in Rehabilitation Sciences of UEL, Londrina, Paraná, Brazil. The study was approved by the Institutional Review Board of the of the State University of Londrina/ (Report 2.289.247). Individuals with idiopathic PD from the Neurology Clinic at the *Hospital das Clinicas* from UEL were screened for inclusion. Individuals were included if they met the following inclusion criteria: PD according to the London Brain Bank's criteria[26]; classified as stages 1.5 to 3 (mild to moderate), according to the modified Hoehn & Yahr scale[27]; who were able to walk independently. Participants were excluded if they presented other forms of parkinsonism or other neurological or musculoskeletal conditions.

Measurements

The evaluation procedures were conducted in the Center for Research and Postgraduate Studies in Rehabilitation Sciences of the UEL. All procedures were conducted by the same investigator, experienced in movement disorders, in the same environment and at the same time of day to ensure uniformity, and when the medication was in the “on” phase (one hour after the last administration of medication). On the first day, the demographic data were collected, and the following evaluations were carried out: 1) Unified Parkinson´s Disease Rating Scale (UPDRS)[28]; 2) Mini Mental State Examination (MMSE)[29] and Geriatric Depression Scale (GDS)[30,31]. On the second day, the evaluation of fatigue was initially performed, followed by the evaluation of the balance.

Assessment of fatigue

Fatigue was measured using the Brazilian version of Parkinson's Fatigue Scale (PFS)[21,32]. The scale evaluates the presence of fatigue and its impact in activities of daily living. The PFS contains 16 items and is self-administered. The cut-off point was: “low fatigue” = PFS < 3.3 points and “moderate to high fatigue” = PFS > 3.3 points[21,32]. This cut-off point was stablished by Brown et. al, with a sensitivity of 84.7% and a specificity of 82.1%[21].

Assessment of balance

A force platform (BIOMEC400 - EMG System do Brasil, São Paulo) was used to assess four balance tasks: 1) Bipedal position for 30 s (feet parallel, with a distance of 10 cm between the heels); 2) Tandem condition (one foot in front of the other, with a distance of 5 cm between the hallux of the foot behind and the heel of the front foot) with open eyes (OE) for 30 s; 3) Tandem condition with closed eyes (CE) for 30 s; 4) Tandem condition with OE associated with a dual task (DT): attending the word-color Stroop test while maintaining the position in the platform, for 30 s[33,34]. In the Stroop test, the participant identifies the color of the word shown instead of the actual word, as quickly as possible. The colors could be congruent (color of the word shown is same as the word), incongruent (color of the word shown is different than the word)[35]. The test was performed using a banner attached to the wall at the front (2 m) and the participant should name the colors concurrently with the platform test. The same examiner conducted all the trials. The individuals stood quietly on the force plate for two trials with one-minute rest between trials. The average value was retained for subsequent analysis.

All tests were performed without any shoes on. The individuals were instructed to look straight ahead with their head upright and their arms resting at their sides, while maintaining balance. Each subject was instructed by the examiner to: “stand upright, with your arms resting at your sides, without moving or speaking until you get further instructions”. To prevent falls or injury during the testing, an examiner stood close to each participant throughout all the experimental tasks. Stabilographic analysis of COP data led to the calculation of three balance parameters: (1) 95% confidence ellipse area of COP (ACOP in cm^2); (2) mean velocity (MVeloc in cm/s); (3) Root Mean Square (RMS) of COP sway (RMS in cm)[36].

Statistical analysis

All statistical analysis were performed with SPSS statistical software (version 20.0 for Windows). The level of significance was set at 5% for all analyses. Descriptive data were presented as means and standard deviations or as medians and interquartile ranges, according to the normality distribution, analyzed using the Shapiro-Wilk test. It was found a non-normal distribution for fatigue and balance variables. To verify the correlation between fatigue and balance parameters, the Spearman rank order correlation coefficient was assessed for non-parametric data, considering all participants. Comparison of medians between the groups of participants with low fatigue (PFS < 3.3 points) versus moderate to high fatigue scores (PFS ≥ 3.3 points) were analyzed using the Mann-Whitney test.

Results

Demographic and disease characteristics

Thirty-seven participants were enrolled in the study, 25 with low fatigue (mean age 65.64 years (10.94); 19 males) and 12 with moderate to high fatigue (mean age 64.92 years (10.78); 4 males). 51.72% of the study participants considered fatigue as one of their three worst and most disabling symptoms. In addition, 32.43% of the sample had moderate to high fatigue (PFS > 3.3 points). The presence of depressive symptoms was clinically low in both groups (GDS < 5 points), and the subjects did not present cognitive dysfunction (MMSE > 24 points). There was no difference between low fatigue and high fatigue groups regarding demographic data. See Table 1 for a summary of demographic and disease characteristics.

Correlation between fatigue and balance

The results from the correlation analyses between fatigue and balance parameters showed that fatigue, measured by the PFS, is not correlated with balance parameters. This result is presented in Table 2.

Comparison of balance parameters between low fatigue versus high fatigue groups

When comparing participants with low (PFS < 3.3 points) and moderate to high fatigue (PFS > 3.3 points) scores, there were no statistically differences between the groups, considering the balance parameters. These results are presented in the Tables 3, 4 and 5.

Table 1 - Demographic and disease characteristics.

Variable	Parkinson Fatigue Scale (PFS)		
	Low Fatigue PFS < 3.3 (points) (n = 25)	**High Fatigue PFS > 3.3 (points) (n = 12)**	**p**
Age mean (years)	65.64 (10.94)	64.92 (10.78)	0.85
BMI (points)	26.96 (4.73)	26.66 (5.93)	0.87
Years of diagnosis (years)	6.68 (4.8)	6.17 (4.72)	0.76
HY (points)	2.06 (0.48)	2.33 (0.57)	0.14
MMSE (points)	27.16 (3.17)	26.22 (3.52)	0.47
GDS (points)	3.72 (2.92)	4.41 (3.11)	0.51
UPDRS - ADL (points)	9.84 (5.58)	12.08 (5.72)	0.26
UPDRS - MOTOR (points)	19.96 (9.28)	23.00 (11.16)	0.38
UPDRS - TOTAL (points)	29.80 (13.15)	35.08 (14.52)	0.27

BMI = Body mass index; HY = Modified Hoehn & Yahr Scale; MMSE = Mini Mental State Examination; GDS = Geriatric Depression Scale; UPDRS = Unified Parkinson's Disease Rating Scale; ADL = Activities of Daily Living; PFS = Parkinson's Fatigue Scale.

Table 2 - Correlation between balance parameters and Parkinson Fatigue Scale.

	Parkinson Fatigue Scale (PFS)				
	R	**p**		**R**	**p**
ACOP-Bipodal (cm^2)	−0.04	0.812	ACOP-Tandem CE	0.08	0.628
ACOP-Tandem OE (cm^2)	0.07	0.641	ACOP-Tandem DT	−0.09	0.571
MVelocAP-Bipodal (cm/s)	0.12	0.472	MVelocML-Bipodal	0.17	0.304
MVelocAP-Tandem OE (cm/s)	0.08	0.634	MVelocML-Tandem OE	0.12	0.447
MVelocAP-Tandem CE (cm/s)	0.06	0.705	MVelocML-Tandem CE	0.08	0.621
MVelocAP-Tandem DT (cm/s)	0.09	0.559	MVelocML-Tandem DT	0.16	0.338
RMSAP-Bipodal (cm)	0.03	0.829	RMSML-Bipodal	−0.12	0.471
RMSAP-Tandem OE (cm)	0.02	0.894	RMSML-Tandem OE	0.05	0.752
RMSAP-Tandem CE (cm)	0.02	0.902	RMSML-Tandem CE	0.06	0.686
RMSAP-Tandem DT (cm)	0.16	0.339	RMSML-Tandem DT	−0.02	0.881

ACOP = 95% confidence ellipse area of COP (cm^2); MVeloc = mean velocity (cm/s); RMS = root mean Square of COP sway (cm); AP = antero-posterior; ML = medio-lateral; OE = open eyes; CE = closed eyes; DT = dual task; PFS = Parkinson's Fatigue Scale (points).

Table 3 - Comparison of ACOP between low-fatigue *versus* high-fatigue groups.

ACOP (cm^2)	**Parkinson Fatigue Scale (PFS)**		
	Low Fatigue PFS < 3.3 (points) (n = 25)	**High Fatigue PFS > 3.3 (points) (n = 12)**	**p**
Bipedal	0.69 [0.24-7.79]	0.98 [0.53-1.56]	0.18
Tandem OE	2.17 [0.71-9.21]	2.61 [1.11-8]	0.24
Tandem CE	2.96 [0.81-11.44]	3.03 [1.39-9.10]	0.68
Tandem DT	2.23 [0.67-6.49]	1.93 [0.78-8.32]	0.39

ACOP = 95% confidence ellipse area of COP (cm^2); OE = open eyes; CE = closed eyes; DT = dual task; PFS = Parkinson's Fatigue Scale (points). Variables are shown by median and interquartile ranges.

Table 4 - Comparison of MVeloc AP and ML between low-fatigue *versus* high-fatigue groups.

MVeloc AP (cm/s)	**Parkinson Fatigue Scale (PFS)**		
	Low Fatigue PFS < 3.3 (points) (n = 25)	**High Fatigue PFS > 3.3 (points) (n = 12)**	**p**
Bipedal	1.69 [0.93-2.82]	1.94 [1.10-4.35]	0.13
Tandem OE	2.03 [0.95-5.08]	2.24 [1.24-4.52]	0.32
Tandem CE	2.42 [0.58-6.55]	2.66 [1.40-4.69]	0.41
Tandem DT	1.88 [1.11-4.29]	2.53 [1.26-4.64]	0.16
MVeloc ML (cm/s)			
Bipedal	1.62 [0.87-2.87]	1.70 [1.12-3.57]	0.17
Tandem OE	1.83 [1.16-3.03]	1.96 [1.55-3.65]	0.18
Tandem CE	1.99 [1.35-3.88]	2.33 [1.73-3.70]	0.32
Tandem DT	1.91 [1.17-2.93]	2.19 [1.42-4.07]	0.09

MVeloc = mean velocity (cm/s); AP = antero-posterior; ML = medio-lateral; OE = open eyes; CE = closed eyes; DT = dual task; PFS = Parkinson's Fatigue Scale (points). Variables are shown by median and interquartile ranges.

Table 5 - Comparison of RMS AP and ML between low-fatigue *versus* high-fatigue groups.

RMS AP (cm)	**Parkinson Fatigue Scale (PFS)**		
	Low Fatigue PFS < 3.3 (points) (n = 25)	**High Fatigue PFS > 3.3 (points) (n = 12)**	**p**
Bipedal	1.38 [0.78-4.70]	1.70 [0.94-3.01]	0.51
Tandem OE	2.52 [0.99-6.46]	2.69 [1.66-4.47]	0.34
Tandem CE	3.31 [1.34-6.26]	3.18 [1.74-5.59]	0.96
Tandem DT	2.48 [1.15-4.79]	2.34 [1.42-5.29]	0.76
RMS ML (cm)			
Bipedal	1.40 [0.51-3.02]	1.68 [0.70-2.99]	0.93
Tandem OE	2.10 [1.04-4.75]	2.43 [1.23-3.99]	0.26
Tandem CE	2.48 [1.42-4.01]	2.56 [1.39-5.51]	0.66
Tandem DT	2.04 [1.05-2.97]	2.04 [1.12-4.25]	0.91

RMS = root mean Square of COP sway (cm); AP = antero-posterior; ML = medio-lateral; OE = open eyes; CE = closed eyes; DT = dual task; PFS = Parkinson's Fatigue Scale (points). Variables are shown by median and interquartile ranges.

Discussion

Our findings show no correlation between fatigue and posture control, and also no significant differences were found between individuals classified under the "low fatigue" and "high fatigue" categories, in terms of the three balance parameters assessed: ACOP; MVeloc and RMS AP and ML.

The study correlating fatigue and posture control parameters reports no significant correlation between the outcomes. To the best of our knowledge, this is the first study addressing the relationship between these factors. So far, correlations between fatigue and anxiety, cognitive apathy and day-time sleepiness[2,17], severity of the disease (according to the Modified Hoehn Yahr Scale), PD's motor signs and symptoms, loss of interest in routine tasks, difficulty concentrating, difficulty falling asleep at night[17] and visual-spatial skills[4] have been addressed. This study shows a need for studies addressing the relationship between fatigue and PD's motor symptoms, especially balance, so that the impact of fatigue on PD's motor symptoms is clarified. Studies using regression analyses to verify how fatigue is associated with balance and other motor symptoms are encouraged by this study's authors.

Additionally, no difference was found when posture control was compared between the low fatigue and high fatigue groups. The initial hypothesis was that individuals reporting fatigue would experience greater posture instability; the results, however, do not confirm this. This could be explained by the fact that there are evidence supporting fatigue as a non-motor symptom in PD[37]. Also, such an outcome may be due to the way fatigue was assessed, that is, using a subjective instrument that exclusively relies on the individuals' perceptions. Additionally, the participants did not experience fatigue at the time balance was assessed. The secondary objective was to compare posture control between a group of individuals reporting fatigue and a group of individuals who did not report fatigue in their daily lives. That is, the participants had to identify fatigue as a factor that interfered in their routine tasks rather than after a test that provoked fatigue. Santos et. al. compared the gait of individuals with PD and healthy individuals before and after a fatiguing condition was introduced and verified that both groups presented changes in their gait after the situation that generated fatigue, suggesting fatigue negatively affects the gait of individuals. Note that the authors did not analyze data concerning balance[38].

Baer et. al. addressed the balance and gaits of individuals with PD at two points in time: before and after a fatiguing condition was introduced[25] and verified that individuals with PD, who experienced a fatiguing condition, did not demonstrate significant decrements in anticipatory balance responses, adaptive balance responses, sensory organization, dynamic gait, or gait characteristics. These results corroborate the finding that fatigue does not influence posture control among individuals with PD.

Integration of motor stimuli and cognitive, emotional, limbic and motivational information portrays one of the main functions of the basal ganglia[39]. Changes in the balance of neurotransmitters (especially serotoninergic ones) in this region, as occurs in PD, would be responsible for compromising this integration[39,40]. Considering that posture control and motor planning are compromised among individuals with PD, individuals can use compensatory strategies (increasing attention and cognitive demands) to successfully perform a given motor task [41]. In normal situations, a lack of motivation may affect one's sensation of fatigue. In a test situation, however, there is a cognitive and limbic stimulus resulting from the individuals' desire to perform properly a task that is presented to them; that is, a desire to obtain success may overcome one's sensation of fatigue so that an individual may still perform well in a test[18,39]. Moreover, there is evidence that reward systems, which may be activated when in the face of a task, impact one's perception of fatigue[42-44], and also that the caudate nucleus is associated with motivation and reward[45,46], though these specific mechanisms have not been clearly shown to exist in PD yet[47]. Therefore, our proposition is that, in an attempt for a individual to achieve his/her goal of maintaining a given posture for a period of time that is determined in a test, s/he may use attention and conscious mechanisms for a previously automatic task to be effectively performed[48]. This is a very interesting idea because, even when individuals experience high levels of fatigue, they may positively manage fatigue and effectively respond to treatments intended to improve posture instability. Even though fatigue is considered one of the most disabling symptoms of PD, its relationship to balance is not fully understood. This study's findings, together with those reported in the literature[25], suggest there is no correlation between fatigue and balance, and even though individuals with PD report fatigue or experience situations of fatigue, they do not present greater posture instability than individuals with PD who do not report fatigue. Even though there is no clearly defined definition, etiology and classification, fatigue is mostly considered a non-motor symptom of PD. Fatigue can be classified as central, physical, cognitive, peripheral fatigue or a combination of different mechanisms[1]. Despite a perception that fatigue can be subjective, individuals with PD reporting high levels of fatigue present atrophic dorsal striatum (specifically in the caudate nucleus) and insula, while their healthy counterparts reporting high levels of fatigue, matched according to age, do not present this change, which shows that fatigue is a component of the physiology of PD[47].

Study limitations

There are some limitations for this study: the sample is reduced, so the research is susceptible to a type II error; fatigue was assessed by a valid, but subjective instrument; only static balance was evaluated; participants were limited to PD 1.5-3 H&Y.

Conclusion

Our findings suggest that there is no correlation between fatigue and balance, and that individuals with moderate to high fatigue do not present worse balance impairments, as compared with individuals with low fatigue.

References

1. Chong R, Albor L, Wakade C, Morgan J. The dimensionality of fatigue in Parkinson's disease. J Transl Med. 2018;16:192. doi
2. Siciliano M, Trojano L, De Micco R, De Mase A, Garramone F, Russo A, et al. Motor, behavioural, and cognitive correlates of fatigue in early, de novo Parkinson disease patients. Parkinsonism Relat Disord. 2017;45:63-8. doi
3. Berardelli A, Conte A, Fabbrini G, Bologna M, Latorre A, Rocchi L, et al. Pathophysiology of pain and fatigue in Parkinson's disease. Parkinsonism Relat Disord. 2012;18:S226-8. doi
4. Kluger BM, Pedersen KF, Tysnes OB, Ongre SO, Øygarden B, Herlofson K. Is fatigue associated with cognitive dysfunction in early Parkinson's disease? Parkinsonism Relat Disord. 2017;37:87-91. doi
5. Franssen M, Winward C, Collett J, Wade D, Dawes H. Interventions for fatigue in Parkinson's disease: a systematic review and meta-analysis. Mov Disord. 2014;29(13):1675-8. doi
6. Dogan VB, Koksal A, Dirican A, Baybas S, Dirican A, Dogan GB. Independent effect of fatigue on health-related quality of life in patients with idiopathic Parkinson's disease. Neurol Sci. 2015;36(12):2221-6. doi
7. Stocchi F, Abbruzzese G, Ceravolo R, Cortelli P, D' Amelio M, De Pandis MF, et al. Prevalence of fatigue in Parkinson disease and its clinical correlates. Neurology. 2014;83 (3):215-20. doi
8. Elbers RG, Van Wegen EEH, Verhoef J, Kwakkel G. Impact of fatigue on health-related quality of life in patients with Parkinson's disease: a prospective study. Clin Rehabil. 2014;28(3):300-11. doi
9. Miwa H, Miwa T. Fatigue in patients with Parkinson's disease: impact on quality of life. Intern Med. 2011;50 (15):1553-8. doi
10. Havlikova E, Rosenberger J, Nagyova I, Dubayova Z, Gdovinova JP, Van Dijk JW, et al. Impact of fatigue on quality of life in patients with Parkinson's disease. Eur J Neurol. 2008;15(5):475-80. doi
11. Sáez-Francàs N, Hernández-Vara J, Roso MC, Martín JA, Brugué MC. The association of apathy with central fatigue perception in patients with Parkinson's disease. Behav Neurosci. 2013;127(2):237-44. doi
12. Metta V, Logishetty K, Martinez-Martin P, Gage HM, Schartau PES, Kaluarachchi TK, et al. The possible clinical predictors of fatigue in parkinson's disease: a study of 135 patients as part of international nonmotor scale validation project. Parkinsons Dis. 2011;2011:125271. doi
13. Chou KL, Gilman S, Bohnen NI. Association between autonomic dysfunction and fatigue in Parkinson disease. J Neurol Sci. 2017;377:190-2. doi
14. Valko PO, Waldvogel D, Weller M, Bassetti CL, Held U, Baumann CR. Fatigue and excessive daytime sleepiness in idiopathic Parkinson's disease differently correlate with motor symptoms, depression and dopaminergic treatment. Eur J Neurol. 2010;17(12):1428-36. doi
15. Chung S, Bohnen NI, Albin RL, Frey KA, Müller MLTM, Chervin RD. Insomnia and sleepiness in Parkinson disease: associations with symptoms and comorbidities. J Clin Sleep Med. 2013;9(11):1131-7. doi
16. Skorvanek M, Nagyova I, Rosenberger J, Saeedian RG, Groothoff JW, Gdovinova Z, et al. Clinical determinants of primary and secondary fatigue in patients with Parkinson's disease. J Neurol. 2013;260(6):1554-61. doi
17. Solla P, Cannas A, Mulas CS, Perra S, Corona A, Bassareo PP, et al. Association between fatigue and other motor and non-motor symptoms in Parkinson's disease patients. J Neurol. 2014;261(2):382-91.
18. Friedman JH, Brown RG, Comella C, Garber CE, Krupp LB, Lou J, et al. Fatigue in Parkinson's disease: a review. Mov Disord. 2007;22(3):297-308. doi
19. Goldman JG, Stebbins GT, Leung V, Tilley BC, Goetz CG. Relationships among cognitive impairment, sleep, and fatigue in Parkinson's disease using the MDS-UPDRS. Park Relat Disord. 2014;20(11):1135-9. doi
20. Foster ER, Golden L, Duncan RP, Earhart GM. Community-based argentine tango dance program is associated with increased activity participation among individuals with parkinson's disease. Arch Phys Med Rehabil. 2013;94(2):240-9. doi
21. Brown RG, Dittner A, Findley L, Wessely SC. The Parkinson fatigue scale. Park Relat Disord. 2005;11(1):49-55. doi
22. Garber CE, Friedman JH. Effects of fatigue on physical activity and function in patients with Parkinson's disease. Neurology. 2003;60(7):1119-24. doi
23. Bryant MS, Rintala DH, Hou JG, Rivas SP, Fernandez AL, Lai EC, et al. The relation of falls to fatigue, depression and daytime sleepiness in Parkinson's disease. Eur Neurol. 2012;67(6):326-30. doi
24. Helbostad JL, Leirfall S, Moe-Nilssen R, Sletvold O. Older persons. J Am Geriatr Soc. 2007;62(9):1010-5. doi
25. Baer M, Klemetson B, Scott D, Murtishaw AS, Navalta JW, Kinney JW, et al. Effects of fatigue on balance in individuals with Parkinson disease: influence of medication and brain-derived neurotrophic factor genotype. J Neurol Phys Ther. 2018;42(2):61-71. doi
26. Hughes AJ, Daniel SE, Kilford L, Lees AJ. Accuracy of clinical diagnosis of idiopathic Parkinson's disease: a clinico-pathological study of 100 cases. Journal of neurology, Neurosurgery & Psychiatry. 1992;55(3):181-4. doi
27. Hoehn MM, Yahr MD. Parkinsonism: onset, progression, and mortality. Neurology. 1967;17(5):427-42. doi
28. Fahn S, Elton R. Unified rating scale for Parkinson's disease. Recent Developments in Parkinson's Disease. 1987;2:153-63.
29. Folstein MF, Susan E, McHugh RM. Mini-mental state: a practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res. 1975;12:189-98.
30. Yesavage JA, Brink TL, Rose TL, Lum O, Huang V, Adey M, et al. Development and validation of a geriatric depression screening scale: a preliminary report. J Psychiatr Res. 1982;17(1):37-49. doi
31. Lopez FV, Split M, Filoteo JV, Litvan I, Moore RC, Pirogovsky-Turk E, et al. Does the geriatric depression scale measure depression in parkinson's disease? Int J Geriatr Psychiatry. 2018;33(12):1662-70. doi

32. Kummer A, Scalzo P, Cardoso F, Teixeira AL. Evaluation of fatigue in Parkinson's disease using the Brazilian version of Parkinson's fatigue scale. Acta Neurol Scand. 2011;123 (2):130-6. doi
33. Santos SM, Da Silva RA, Terra MB, Almeida IA, De Melo LB, Ferraz HB. Balance versus resistance training on postural control in patients with Parkinson's disease: a randomized controlled trial. Eur J Phys Rehabil Med. 2017;53 (2):173-83. doi
34. Terra MB, Da Silva RA, Bueno MEB, Ferraz HB, Smaili SM. Center of pressure-based balance evaluation in individuals with Parkinson's disease: a reliability study. Physiother Theory Pract. 2020;36(7):826-33. doi
35. Garcia IQ, Pessoa IA, Monteiro B, Daniel F, Lemos L, Espírito-Santo H. Propriedades psicométricas da versão Torga do Teste Stroop. Rev Port Investig Comport e Soc. 2016;2(2):55-64. doi
36. Da Silva RA, Bilodeau M, Parreira RB, Teixeira DC, Amorim CF. Age-related differences in time-limit performance and force platform-based balance measures during one-leg stance. J Electromyogr Kinesiol. 2013;23(3):634-9. doi
37. Fabbrini G, Latorre A, Suppa A, Bloise M, Frontoni M, Berardelli A. Fatigue in Parkinson's disease: motor or nonmotor symptom? Park Relat Disord. 2013;19(2):148-52. doi
38. Santos PCR, Gobbi LTB, Orcioli-Silva D, Simieli L, van Dieën JH, Barbieri FA. Effects of leg muscle fatigue on gait in patients with Parkinson's disease and controls with high and low levels of daily physical activity. Gait Posture. 2016;47:86-91. doi
39. Pavese N, Metta V, Bose SK, Chaudhuri KR, Brooks DJ. Fatigue in Parkinson's disease is linked to striatal and limbic serotonergic dysfunction. Brain. 2010;133(11):3434-43. doi
40. Nassif DV, Pereira JS. Fatigue in Parkinson's disease: concepts and clinical approach. Psychogeriatrics. 2018;18 (2):143-50. doi
41. Peterson DS, Horak FB. Neural control of walking in people with Parkinsonism. Physiology. 2016;31(2):95-107. doi
42. Boksem MAS, Tops M. Mental fatigue: costs and benefits. Brain Res Rev. 2008;59(1):125-39. doi
43. Pardini M, Krueger F, Raymont V, Grafman J. Ventromedial prefrontal cortex modulates fatigue after penetrating traumatic brain injury. Neurology. 2010;74(9):749-54. doi
44. Dobryakova E, Deluca J, Genova HM, Wylie GR. Neural correlates of cognitive fatigue: cortico-striatal circuitry and effort-reward imbalance. J Int Neuropsychol Soc. 2013;19 (8):849-53. doi
45. Aupperle RL, Melrose AJ, Francisco A, Paulus MP, Stein MB. Neural substrates of approach-avoidance conflict. Hum Brain Mapp. 2015;36(2):449-62. doi
46. Yamada H, Matsumoto N, Kimura M. Tonically active neurons in the primate caudate nucleus and putamen differentially encode instructed motivational outcomes of action. The Journal of Neuroscience. 2004;24(14):3500-10. doi
47. Kluger BM, Zhao Q, Tanner JJ, Schwab NA, Levy SA, Burke SE, et al. Structural brain correlates of fatigue in older adults with and without Parkinson's disease. NeuroImage Clin. 2019;22:101730. doi
48. Schoneburg B, Mancini M, Horak F, Nutt JG. Framework for understanding balance dysfunction in Parkinson's disease. Mov Disord. 2013;28(11):1474-82. doi

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