The effect of fatigue on balance performance in Parkinson’s disease

Herb Karpatkin *, Suzanne Babyar, Emily Gayeski, Leesha Meredith, Emily Polster, Penina Sheer, David Schroeder

Hunter College, United States of America

ABSTRACT

Introduction: Balance loss and falls are a common and multifactorial finding in persons with Parkinson’s Disease (pwPD). Objective fatigability is thought to contribute to falls in other neurologic conditions, but its impact on balance in pwPD is not known. The two-fold purpose of this study was to: 1) establish that a 6-minute walk (6MWFast) is a stimulus to subjective fatigue for pwPD; and, 2) determine if the Mini Balance Evaluation Systems Test (MBT) is sensitive to change that was induced by a fatiguing condition.

Methods: Using a randomized crossover design, 19 research participants performed a Mini Balance Evaluation Systems Test (MBT) before and after either a ‘fast’ 6-minute walk (6MWFast) to induce fatigue or a 6-minute rest.

Results: VASF scores increased after the 6MWFast. Total MBT scores in research participants with Modified Hoehn and Yahr (H&Y) scores of 3.0 and above differed significantly before and after the ‘fast’ 6-minute walk (p = .007, n = 9) while participants with H&Y scores of 1.5 to 2.5 (p = .084, n = 10) did not, suggesting that more disabled pwPD were more likely to experience fatigability that interfered with balance.

Conclusions: A 6MWFast is a sufficient stimulus to induce subjective fatigue in pwPD and to decrease total MBT scores for more disabled pwPD. Balance evaluations should occur when pwPD are in fatigue and unfatigued states to determine whether fatigue has an impact on balance performance.

1. Introduction

Parkinson’s disease (PD) is a neurodegenerative disorder characterized by idiopathic destruction of the substantia nigra [1], affecting approximately 1% of people over the age of 60 in industrialized countries [2]. Persons with PD (pwPD) experience progressive loss of gait and balance [3,4]. Falls in pwPD can be potentially catastrophic, resulting in prolonged and costly hospitalization and rehabilitation [5]. Evaluation of falls risk in pwPD should lead to appropriate interventions needed to address specific findings [4]. Clinicians recognize that falls risk may have motor and non-motor aspects. Fatigue is a well-known non-motor aspect of falls risk which is poorly understood, possibly because it is not captured in standard balance assessment tools. Although fatigue has been shown to be a factor in falls in other progressive neurologic diseases such as multiple sclerosis (MS) [6], its impact on balance and falls in pwPD has not been well examined.

Over 50% of pwPD reported fatigue [7] as one of their most distressing symptoms. Those who reported fatigue had greater difficulties with physical functioning, [8] thus indicating that fatigue is a multifactorial concept. Kluger et al. [9] described fatigue in neurologic illness as a construct that consisted of subjective feelings of fatigue and objective observations of fatigability. Subjective fatigue and objective fatigability are not mutually exclusive because they can exist in persons with neurologic disorders at the same time [10]. Subjective fatigue encompasses feelings of tiredness, exhaustion, lethargy, and lassitude as measured using self-report measures [11]. Objective fatigability, refers to measurable worsening of physical performance over time [12]. Appendix 1 displays the different dimensions of fatigue seen in neurologic disorders and typical means of measuring baseline levels and change during rehabilitation. In MS, objective fatigability has been reported in measurements of both gait [13] and balance [14]. Although subjective fatigue has been examined in pwPD, objective fatigability has received little attention.

Lindholm et al. [15] used only self-report measures to demonstrate that pwPD experiencing subjective fatigue fell more frequently than those without fatigue. Bryant et al. [8] noted that physical fatigue was higher in PD fallers than non-fallers, but similarly used only self-report measures. Baer et al. [16] did not find evidence of fatigability in balance testing in PD following an induced fatigue load via treadmill walking; however, the authors acknowledged that treadmill walking, although a proper stimulus to fatigue, may have resulted in greater ambulation symmetry and stability leading to improved balance [17].

Although subjective fatigue has been noted in pwPD, the question of whether they experience fatigability that impacts their mobility and falls risk is not known. For this to occur, an appropriate means of both inducing fatigue and measuring its impact on falls risk must be determined. We tested an assumption that pwPD would experience fatigue by walking as fast as possible for 6 min (6MWFast). We based this assumption upon prior research with persons with MS where the 6 MW was an adequate stimulus to fatigue [13,14]. Upon establishing that the 6MWFast induced fatigue, the
second research question about whether the MBT is sensitive to change induced by a fatiguing condition can be answered. The two-fold purpose of this study was to: 1) establish that a 6-minute walk (6MWFast) is a stimulus to subjective fatigue for pwPD; and, 2) determine if the Mini Balance Evaluation Systems Test (MBT) is sensitive to change that was induced by a fatiguing condition. The MBT quantifies balance performance during functional tasks and scores on its subtests may guide interventions specifically related to specific deficits. Knowledge of how fatigue influences these subtest scores may further assist clinicians in designing appropriate interventions to ameliorate falls risk. Our aim was to establish the link between constructs of fatigue and balance that may serve as a basis for future clinical research studying the impact of methods to ameliorate fatigue on balance and falls risk on pwPD.

2. Methods

2.1. Participants

Research participants between the ages of 18–79 were recruited from local PD exercise groups. Inclusion criteria were: a definite diagnosis of PD, the self-determined ability to walk continuously for 6 min (with or without an assistive device), and the ability to read, understand, and sign an informed consent written in English. Exclusion criteria were any cardio-pulmonary, orthopedic, or non-Parkinson’s neurological co-morbidities that would prevent participation in the study. Participants provided demographic and medical history data via a questionnaire for age, sex, years since diagnosis, use of medication, use of any assistive device, and disease severity as measured by Modified Hoehn and Yahr Scale (H&Y) score. The baseline measures collected included the Parkinson’s Disease Fatigue Scale (PFS-16) [18] and Parkinson’s Disease Quality of Life Scale (PDQ-39) [19]. This project was approved by the Human Research Protection Program of Hunter College The City University of New York.

2.2. Measurement of fatigue and balance

A randomized crossover design examined each participant twice, once in a fatigued condition and once in a non-fatigued condition. The Visual Analog Scale of Fatigue (VASF) measured subjective fatigue. The VASF is a quick self-report measure used to quantify subjective perceptions of fatigue during a particular task by marking a 100 mm line with 0 mm representing no fatigue and 100 mm representing maximum fatigue. One can calculate immediate effect of a task on subjective fatigue by subtracting the immediate pre-test measure from the immediate post-test measure designated by each research participant. This ability to measure immediate effects of a task makes the VASF a better option than other self-report measures like the PFS-16 which measure the generalized state of fatigue specifically with persons with PD. Although it has not been studied in PD, the VASF has been found to be more sensitive than other self-report fatigue measures for measuring fatigue in other neurodegenerative diseases [20].

Balance was measured with MBT, a 14-item test that measures balance in 4 domains: anticipatory balance, reactive postural control, sensory orientation, and dynamic gait. Its validity and reliability in PD has been established [21,22]. A 6-minute walk, performed as fast as possible, was used to induce fatigue. Subjects were asked to walk as fast as possible, for 6 min while being guarded by an examiner, and were told they could stop at any time. Distance measured in minute 6 that was less than the distance measured in minute 1 was considered an indicator of fatigability. The 6 MW has been shown to be a means of inducing both subjective fatigue [23] and objective fatigability [13] in MS.

2.3. Procedures

On day 1 of testing, research participants were randomized into one of 2 conditions, fatigued or unfatigued. The research participants then completed the protocol for the randomly selected first condition. One week later, the research participants were crossed over to complete the protocol for the other condition. The fatigued condition consisted of the research participant performing the MBT, immediately followed by the 6MWFast, immediately followed by another MBT. VASF was collected 4 times: immediately before and after the first MBT (VASF1 and VASF2), immediately after the 6MWFast (VASF3) and immediately after the second MBT (VASF4). Research participants undergoing the unfatigued condition performed the identical protocol but with a 6-minute seated rest rather than a 6MWFast, with VASF3 being collected immediately after the 6-minute rest. A schematic of the protocol is presented in Appendix 2.

2.4. Data analysis

Descriptive statistics summarized demographics, characteristics, and experimental variables. To determine if the MBT induced subjective fatigue, non-parametric Friedman tests were chosen to for within-subject determination if VASF changed throughout the protocol. Post hoc Wilcoxon Signed Rank Tests examined specific within-subjects comparisons before and after each MBT and within conditions. Wilcoxon Signed Rank test made a within-subjects comparison of distance (m) covered in minute 1 of the 6MWFast to minute 6 distance. Post hoc between-group analyses were conducted to compare Group 1 (Modified Hoehn and Yahr Score = 1.5 to 2.5) and Group 2 (Modified Hoehn and Yahr Score = 3) using Mann-Whitney U Tests.

3. Results

3.1. Demographics

Nineteen pwPD participated in the study (8 female; 11 male). Table 1 illustrates demographic characteristics. One participant used a cane or rolling walker during ambulation. One participant wore an ankle-foot orthosis for walking. The remainder (n = 17) reported that they did not use assistive devices. Post hoc groups based on Modified Hoehn and Yahr scores 1.5–2.5 (Group 1, 6 female, 4 male) and 3 (Group 2; 2 female, 7 male) are included in Table 1.

3.2. Mini balance evaluation systems test

Table 2 displays mean (SD) subscale and total scores for the Mini BEST before and after the fatigue and rest conditions. Friedman Tests for within-subjects comparison of all 4 conditions (before/after, rest/fatigue) failed to show statistical significance for any of the subscales or for the total scores. Post hoc analysis with Wilcoxon Signed Rank Tests for within-subject differences.

Table 1

| Age | Mean | SD | Minimum | Maximum |
|-----|------|----|---------|---------|
| Group 1 | 62.7 | 9.2 | 38 | 76 |
| Group 2 | 64.9 | 6.3 | 59 | 76 |
| Disease duration (y) | Group 1 | 6.6 | 5.2 | 0.5 | 18 |
| Group 2 | 6.7 | 6.3 | 0.5 | 18 |
| PDQ-39 (out of 100) | Group 1 | 37.0 | 16.4 | 9 | 69 |
| Group 2 | 32.7 | 16.8 | 9 | 63 |
| PFS-16 (out of 80) | Group 1 | 43.6 | 16.5 | 16 | 65 |
| Group 2 | 38.6 | 18.3 | 16 | 65 |
| Modified Hoehn & Yahr staging score | Group 1 | 49.1 | 13.0 | 29 | 64 |
| n (%) | 2.0 | 2.0 (10.5%) | 3.0 | 3 (15.8%) |
| Modified Hoehn & Yahr staging score | Group 2 | 1.5 | 5 (26.3%) | 3.0 | 9 (47.4%) |

PDQ-39 = Parkinson’s Disease Quality of Life; PFS-16 = Parkinson’s Disease Fatigue Scale – 16)
comparisons of MBT subscales and total scores before and after each condition (Table 2) also failed to show statistical significance. Post hoc analysis revealed that research participants could be grouped by H&Y scores: 1.5–2.5 (Group 1) and 3.0 (Group 2). The Bonferroni correction for multiple comparisons should be applied in interpreting these post hoc findings (p < .0125, 4 comparisons). Research participants in Group 2 (n = 9) had the largest increase in VASF before and after MBT testing at the start and end of the 6-minute walk (z = 10.0, p = .004). In contrast, prior to and after the rest condition, Wilcoxon Signed Rank tests did not differ in VASF scores before and after administration of the MBT. In Group 2 research participants (H = 3) exhibited this increase in VASF before and after MBT testing for the fatigue condition (z = −2.699, p = .007) and Dynamic Gait (z = −2.558, p = .011) subscale scores after the ‘fast’ 6-min walk. In contrast, Group 1 (n = 10) total MBT and subscales were not changed after the 6MWFast.

### 3.3. Visual analog scale of fatigue

Table 3 shows VASF mean (SD) values before and after MBT testing, prior to and after each 6-minute condition. Wilcoxon Signed Ranks Tests showed worse subjective fatigue after the ‘fast’ 6-minute walk (z = −3.725, p < .001) and no change in subjective fatigue after the 6-minute rest (z = 1.0). Wilcoxon Signed Rank Tests (Table 3) established if the MBT induced subjective fatigue at initial assessment (between VASF1 and VASF2) and after the 6-minute condition (between VASF2 and VASF3) on a within-subject basis. Prior to and after the fatigue condition, research participants did not differ in VASF scores before and after administration of the MBT. In contrast, prior to and after the rest condition, Wilcoxon Signed Rank tests showed increases in VASF before and after MBT testing for the fatigue condition (z = −2.699, p = .007) and Dynamic Gait (z = −2.558, p = .011) subscale scores after the ‘fast’ 6-min walk. In contrast, Group 1 (n = 10) total MBT and subscales were not changed after the 6MWFast.

### 3.4. 6-minute walk distances

Table 4 shows that the mean (SD) distances (m) covered in minute 1 and in minute 6 of the 6MWFast. Wilcoxon Signed Rank Tests revealed that these distances were not statistically different (z = −0.724, p = .469) on a within-subject basis. Post hoc between-subject analysis of groups did not demonstrate a difference in 1 and 6-min comparisons for either group.

### 4. Discussion

We hypothesized that the 6MWFast would result in increased fatigue, which would result in reduced scores on the MBT. Our results showed that the 6MWFast significantly increased subjective perceptions of fatigue in pWPD. MBT scores did not differ before and after each 6-minute condition for the whole sample. Post hoc analysis of persons grouped by H&Y scores, showed that Dynamic Gait subscores and Total MBT scores decreased in the subset of research participants with modified H&Y scores of 3. These findings suggest that the 6MWFast was an adequate stimulus for subjective fatigue but detectable objective fatigue (and perhaps, related falls risk) via the MBT may be related to degree of disability.
The 6MWFast raised VASF scores (Table 3) in comparison to the 6-minute rest, indicating that the physical effort of the 6MWFast increased subjective feelings of fatigue. This supports our assumption that the 6MWFast was a sufficient stimulus to subjective fatigue. We also expected that distances covered in the first minute would be greater than those from the 6th minute, however, this potential indicator of objective fatigue was not established. The 6 MW has been used to illustrate fatigability in other neurologic conditions where this potential indicator of objective fatigue was not established. The 6 MW slower over the course of a 6-minute walk [13]. In the current study, some fatigue is prominent. Persons with MS have been found to walk progressively impaired which occurs in PD because the pathophysiology of these diseases is markedly different. Although the fatigability in both conditions are probably multifactorial, much of the fatigability in MS is directly related to CNS demyelination, while the mechanism for fatigue in PD is not known.

Neither 6-minute condition appeared to influence MBT scores for the whole sample. However, when research participants were grouped in less disabled (H&Y = 1.5 to 2.5) and more disabled (H&Y = 3), post hoc analysis showed that the more disabled group had a significant within-subjects decrease in mean total MBT scores (20.33 to 17.22, p = .008). This is consistent with the classification of Modified Hoehn and Yahr whereby 3 represents mild to moderate bilateral symptoms and postural instability despite independence in activities of daily living [24]. Interestingly, VASF scores before and after the MBT testing during the rest condition indicated that the MBT caused subjective fatigue. This appears to be driven by Group 2 participants who indicated increased fatigue after the first and second MBT testing in the rest condition and after the first MBT testing in the fatigue condition. More study is needed to determine why this phenomenon was not observed after the 6-minute walk for patients with H&Y scores of 3. In contrast to Baer et al. [16] who did not find fatigability for pwPD, the current study indicated that vigorous walking may produce subjective fatigue and objective fatigue in persons with Modified Hoehn and Yahr scores of 3 whereby they are physically independent but demonstrate some postural instability. When comparing pwPD to healthy adults, Lou, et al. [25] noted that patients with PD experience more self-reported physical fatigue and subjective fatigue using the Multidimensional Fatigue Inventory (MFI). Consistent with this study, they observed that physical fatigue did not correlate to subjective fatigue in pwPD. Lou et al. [25] also found that self-reports of physical fatigue via MFI scores did not correlate to Modified Hoehn and Yahr Staging Scores. The current study shows that objective measures of performance, like the total MBT and Dynamic Gait subscale, can capture physical fatigue for pwPD who have mild to moderate bilateral symptoms and postural instability (H&Y = 3). Future research should focus on pwPD with a wide range of modified H&Y scores and a concomitant falls risk profile. Future research might also include a ‘fast’ 12-minute walk to increase the likelihood of fatigue for pwPD with less disability.

The results of our study should be interpreted with caution. As previously mentioned, our subjects had relatively mild impairments due to the disease. It is possible that, with more severely impaired pwPD, different findings may have been obtained. Similarly, our subject pool was relatively

Table 4

| Table 4 | Mean (SD) Distances (m) Walked in Minute 1 and Minute 6 of the 6-Minute Walk and Results of Wilcoxon Signed Rank Tests Comparing Minute 1 to Minute 6 (n = 19) and for Hoehn and Yahr Group 1 (1.5 to 2.5; n = 10) and Group 2 (3.0; n = 9). |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
|                 | Mean | SD   | Minimum | Maximum | p               |                 |
| Minute 1 distance (m) | 80.9 | 21.6 | 11.8 | 106.7 | .469            |
| Group 1          | 79.9 | 27.6 | 11.8 | 106.7 | .799            |
| Group 2          | 82.1 | 13.8 | 58.9 | 98.6  | .214            |
| Minute 6 distance (m) | 82.1 | 10.1 | 56.5 | 97.1  | .971            |
| Group 1          | 84.7 | 9.1  | 72.8 | 97.1  | .971            |
| Group 2          | 79.1 | 10.7 | 56.5 | 92.3  | .971            |
young and was relatively newly diagnosed. It is possible that with greater age and accumulated disability, greater fatigability might have been seen. By the same token, it may be that with a more provocative measure than the 6MWFast may be needed to provoke objective fatigability.

4.1. Clinical implications

Our study is one of the first to suggest that objective fatigability and subjective fatigability occur in pwPD. Studies with larger sample sizes are warranted to further explore if objective fatigability may be a factor in the balance loss and falls of pwPD with greater disability. The VASF was an effective tool to record change in subjective fatigue, therefore, clinicians working with pwPD should consider using this tool when interpreting findings from gait and balance testing. Based on evidence found in this study, a 30 to 45-minute physical therapy or exercise session in which a pwPD practices ambulation and balance exercises, may cause a significant change in subjective fatigue level, regardless of H&Y score, and on objective fatigability if their H&Y scores are 3 or above. Simple monitoring with the VASF throughout treatment may help gauge whether such fatigue may influence their falls risk when pwPD return home after an exercise session. Because falls in pwPD are more likely to occur during a fatigued state, clinicians should consider performing falls risk assessments on patients in both fatigued and non-fatigued conditions.

The findings of this study also suggest that balance scores in persons with PD may be different when they are tested in a fatigued as opposed to a non-fatigued condition. Perhaps a threshold Modified Hoehn and Yahr score exists whereby the role of fatigue in balance testing should be considered.

In conclusion, this study provides evidence that subjective fatigue can be induced with a 6MWFast. Balance testing with the MBT may be a measure of objective fatigability but a threshold H&Y score may exist whereby balance decreases with fatigue. Clinicians should both understand and maintain a constant awareness of the state of fatigue of pwPD, perhaps by a systematic review and meta-analysis, J. Psychiar. Res. 100 (2017) 1–7, https://doi.org/10.1016/j.jpsychires.2017.06.017.

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4.2. Conclusions

The 6MWFast may be needed to provoke objective fatigability. Clinicians should both understand and maintain a constant awareness of the state of fatigue of pwPD, perhaps by a systematic review and meta-analysis, J. Psychiar. Res. 100 (2017) 1–7, https://doi.org/10.1016/j.jpsychires.2017.06.017.

Conflicts of interest

None.

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[21] Doctor David Schroeder was involved in data collection and manuscript preparation.

[22] Doctor Emily Polster was involved in data collection and manuscript preparation.

[23] Doctor Leesha Meredith was involved in data collection and manuscript preparation.

[24] Doctor David Schroeder was involved in data collection and manuscript preparation.

[25] This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of competing interest

None.