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Research Article

Relationship between Amount of Exercise and Fatigue in People with Parkinson's Disease

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Abstract

Fatigue is one of the most debilitating symptoms in Parkinson's disease (PD). It has been identified as an unmet need by the PD community due to limited understanding of fatigue. Fatigue likely not only limits patient's participation in activity but also hinders patients' compliance in therapy. Accumulating evidence suggests that exercise may be effective in management of PD-fatigue. The objective of this study was to examine the relationship between exercise and fatigue in individuals with PD. Further, the impact of depression and disease history on fatigue was also investigated. This was an observational, cross-sectional study. One hundred and thirty-one (131) patients participated in this survey research by filling in the Parkinson's Fatigue Scale (PFS) and providing information about their weekly exercise duration, history of PD, and with or without a clinical depression. Pearson correlation analysis was applied to examine the relationship between weekly exercise duration expressed in 1/minute and PFS score. T-tests were performed to compare fatigue between participants with and without clinical depression as well as between participants at early and advanced stages of PD. A significant correlation was observed between the inversed weekly exercise duration (1/minute) and fatigue ($r = 0.267$; $P = 0.02$). Less fatigue was associated with increased physical activity. Further, a significant difference was found in fatigue level between patients with and without depression ($P = 0.02$). There was no difference in fatigue between the early and the advanced stages of PD groups ($P = 0.23$). The findings of this study support that an adequate amount of exercise and physical activity may be an effective approach to managing PD-fatigue and improving quality of life in individuals with PD.

Keywords: *Parkinson's Disease; Fatigue; Physical Activity; Exercise; Association*

Abbreviations

ICC: Intra-Class Correlation Coefficient; PD: Parkinson's Disease; PFS: Parkinson Fatigue Scale

Introduction

Parkinson's disease (PD) is a chronic, progressive neurodegenerative disease that is characterized by bradykinesia, rigidity, tremor and postural instability. In recent years, there has been an increasing recognition of nonmotor symptoms associated with PD [1,2]. Fatigue is a common, severe and debilitating nonmotor symptom in PD [2-4]. It is estimated that disabling fatigue affects more than 50% of patients with PD [5-12]. Research has consistently shown that fatigue has a significantly negative impact on patients' quality of life and is one of the major contributors to poor patient outcomes [7,8,11,13]. Fatigue was also found to have an independent effect on health-related quality of life [13]. Although fatigue appears to be correlated with depression, it remains unrelieved even though depression improves, thus

suggesting that fatigue may not simply be an outcome of depression [12,14,15]. Fatigue can be broadly defined and operationalized as a state of extreme tiredness, weakness, or exhaustion [16,17]. Further, fatigue is consistently described as subjective fatigue and objective fatigability. The former refers to subjective perception and experiences of being tired or exhaustion while the latter is an objective measure of how quickly an individual gets tired and is observable on any prolonged and/or intensive task [16]. In this article, fatigue refers to "subjective fatigue" given that the level of fatigue was reported by each participant.

Like many other nonmotor symptoms, fatigue may antedate the development of motor symptoms by several months or longer and occurs throughout every stage of PD [18]. It is pivotal to identify fatigue early and to treat it timely as fatigue likely both limits patients' ability to participate in therapy and hinders patients' compliance in rehabilitation as observed in persons experiencing fatigue due to multiple sclerosis [19,20]. Thus, it is important for clinicians to be aware of this important topic. Since fatigue was initially recognized as a common and debilitating symptom in PD some 20 years ago, little progress has been made about its etiology or treatment [12,21]. In 2013 World Parkinson Congress, fatigue was voted as the leading symptom in need of research by patients with PD [21]. Treatment of PD-fatigue is among the unmet needs in clinical management of Parkinson's disease [22].

There is a lack of effective medication regime for PD-related fatigue which has equivocal responses to dopamine-replacement therapy [7,8]. Dopaminergic medication such as Levodopa and rasagiline may have an effect on fatigue, but none of the above is specifically used to treat fatigue in individuals with PD [9].

Evidence accumulates suggesting that non-pharmacologic treatments such as exercise and physical activity are potentially beneficial and effective in management of PD fatigue [9,23-25]. Abrantes., *et al*. [26] reported a strong association between fatigue and physical activity levels and suggested that increasing leisure-time physical activity in patients with PD may be an effective non-motor pharmacologic approach to decreasing neuropsychiatric symptoms and improving the quality of life in these patients. A recent systematic review based on the available evidence has shown that the exercise programs are effective in decreasing fatigue [27]. Studies of this review examined and found effectiveness of various types of exercise interventions including but not limited to Argentine tango and continuous training of aerobic walking [28,29].

Despite emerging evidence on the effectiveness of exercise intervention in treatment of PD-fatigue, little is known about a possible association between exercise and fatigue in individuals with PD. Earlier studies examined an association of fatigue with physical activity [25,26]. The terms, exercise and physical activity, are interchangeably used in this report as distinction was not specifically surveyed in this context. In general, exercise refers to planned, structured, and repetitive movement to improve or maintain components of physical fitness whereas physical activity refers to body movement that is produced by the contraction of skeletal muscles and increases energy expenditure.

Objective of the Study

The primary objective of this study was to examine the relationship between the amount of exercise and fatigue in individuals with PD. The secondary objective was to investigate the impact of depression and disease history on the level of fatigue by stratifying patients with PD into sub-groups according to depression (clinically depressed or non-depressed) and disease history (early or advanced stage), respectively.

Methods

Participants

One hundred and thirty-one (131) volunteers with PD participated in this survey research. The participants' age ranged from 50.5 to 87.2 years old, with an average age of 68.3 (SD = 8.2) years. The disease history had a mean of 6.7 (SD = 4.8) years, ranging from 0.3 to 21.3 years. Inclusion criteria were (1) having a diagnosis of PD and (2) being physically active or participating in a structured exercise regime. Exclusion criterion included cognitive impairments that might prevent individuals from understanding and answering questions in the survey. The study protocol was approved by the Institutional Review Board of the University where this study was conducted. Consent to participation was obtained from each respondent who completed at least one section of the survey. The beginning of the survey described the purpose of the study, the guarantee of anonymity of individual responses and the approximate amount of time needed to complete the survey and stated that participation was voluntary.

Study design and procedures

This research utilized an observational, cross-sectional design. The survey consisted of two sections: (1) the Parkinson fatigue scale (PFS) and (2) clinical demographic data. The PFS is an instrument specifically designed to measure fatigue in PD and related disorders [17] and encompasses the physical aspects of fatigue and their impact on patients' daily function. Information on clinical characteristics of the participants included age, gender, month/year of clinical diagnosis of PD, three most debilitating symptoms, weekly exercise duration, types of exercises performed, and presence/absence of a clinical diagnosis of depression including the time of receiving the diagnosis if applicable.

The survey was sent to the prospective participants through the Parkinson Foundation Heartland via email with an embedded link to the online software (Qualtrics, Provo, UT) where the survey was available for completion. Parkinson Foundation Heartland serves patients with PD and their families within a few different states. The survey was open for 30 days.

Outcome measures

Primary outcomes of this study were the Parkinson's fatigue scale (PFS) and weekly exercise duration. The PFS is a 16-item self-report questionnaire completed on the basis of the patient's feelings, perceptions and experiences of the preceding month. Participants were asked to rate each item with respect to their fatigue level on a scale from one (i.e. "strongly disagree") to five ("strongly agree"). According to the original study [17] an average score of 2.95 indicates that the patient has experienced fatigue, with a sensitivity of 81.0% and specificity of 85.7%, whereas a higher score of 3.30 identifies those perceiving fatigue to be a problem with a sensitivity of 84.7% and specificity of 82.1%. The PFS-16 has been shown to have an excellent test-retest reliability with an intra-class correlation coefficient (ICC) score of 0.83 and excellent internal consistency (Cronbach's $\alpha = 0.98$) [17]. Participants were also asked to provide the average number of minutes per week on exercise and physical activity over the preceding month.

Secondary outcomes included diagnosis of clinical depression and disease duration. Disease duration was calculated based on the time when the diagnosis was made. Participants were stratified into two groups: early-stage PD and advanced-stage PD. The former group refers to those with a disease history of equal to or less than (≤) five years and the latter a disease history of greater than (>) five years [30]. Participants were also asked to report if they were diagnosed with clinical depression, which is a common non-motor symptom in PD and potentially associated with fatigue [9,17,25,26,31].

Statistical analyses

A Pearson correlation analysis was performed to quantify the relationship between fatigue and level of physical activity and/or exer-

cise in those who not only responded to the PFS tool but also provided weekly duration on physical activity. The severity of fatigue was assessed using the mean value of PFS-16 and the level of physical activity was denoted by an inverse of the weekly duration in minute (i.e. 1/minute). The inverse function was used for the latter variable because of its liner relationship with fatigue. In addition, t-tests were performed to determine whether there was any difference in fatigue between participants with and without clinical depression as well as between participants at the early and the advanced stages of PD, respectively. Statistical significance was set at a level of 0.05.

Results and Discussion

One hundred and thirty-one (131) individuals with PD responded to the survey. Of the 131 participants, 104 completed the PFS tool and 71 completed the entire section of the questionnaire including both the PFS and the questionnaire items of the Part II. Of those that completed the PFS tool, 67.6% experienced fatigue (i.e. scored 2.95) and 60% had problems due to fatigue (scored 3.30).

The Pearson correlation coefficient revealed a statistically significant with a fair degree of correlation between the inversed physical activity level and fatigue (r = 0.32; P = 0.02), suggesting an association of the more severe fatigue with the lower level of physical activity, and of the less fatigue with the higher activity level in 71 participants (Figure 1).

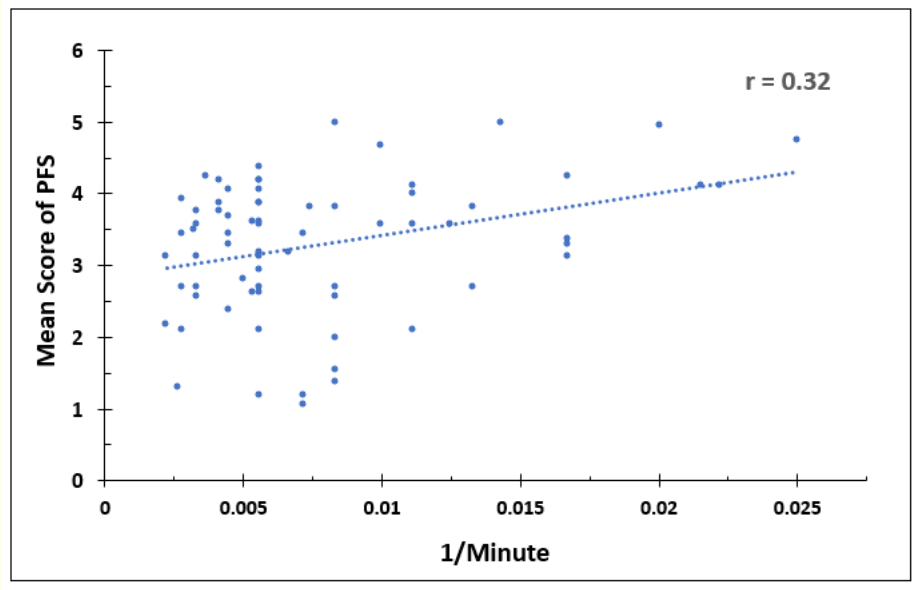

Figure 1: *Scatter plot of mean scores of PFS and the inverse of weekly excised minutes in 70 patients with PD. The Pearson correlation analysis revealed a significant correlation between the two variables (r = 0.32, P = 0.02).*

Further, 29 participants indicated a medical diagnosis of clinical depression, while 45 reported with no such a diagnosis. The mean fatigue level in those with depression was found to be 3.65 ± 0.80. Participants without depression had an average fatigue level of 3.14 ± 0.99. Figure 2 shows that patients who were clinically depressed experienced a significantly more severe fatigue than those who were not (P = 0.02).

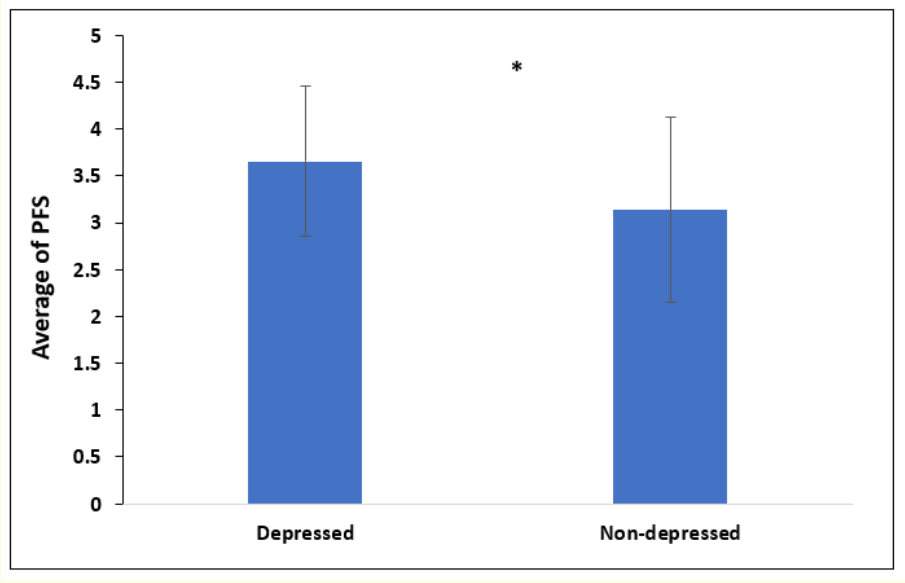

Figure 2: *Comparison of mean PFS between 29 patients with depression (3.65 ± 0.80) and 45 patients without depression (3.14 ± 0.99). There was a significant difference in fatigue between the two sub-groups (P = 0.02).*

A comparison was also made regarding fatigue scores between patients with an early diagnosis of PD and patients with more advanced PD based on a 5-year disease history as threshold. Forty-three patients indicated an early diagnosis with a mean fatigue level of 3.16 ± 0.98 and 35 had longer disease history with an average fatigue level of 3.51 ± 0.91 (Figure 3). There was no significant difference in fatigue between the early and the advanced PD groups (P = 0.23).

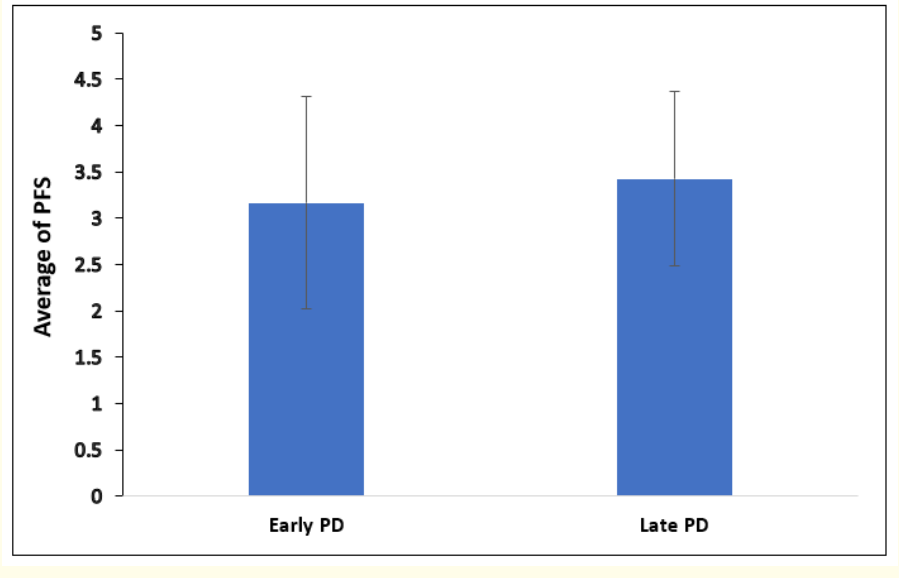

Figure 3: *Averaged PFS fatigue scores compared between 43 patients with early PD (3.16 ± 0.98) and 35 patients with advanced PD (3.51 ± 0.91) based on a 5-year cut-off. The PFS fatigue score was higher in the advanced group than that of the early PD group. There was not a significant difference between the two groups (P = 0.23).*

The main finding of this study showed a significant correlation between the amount of physical activity and degree of fatigue in PD. Outcomes of secondary objective revealed that there was an influence of depression on fatigue whereas fatigue was independent of the length of PD.

Fatigue is a prevalent symptom experienced by more than half of patients with PD [6-12]. In the current study, 67.6% reported experiencing fatigue, and 60% showed perceiving fatigue as a problem among 104 participants who completed the PFS tool. The result of fatigue prevalence is in consistent with that reported in the previous studies. The authors of the PFS tool found higher percentages of fatigue prevalence, with 86.6% experiencing fatigue and 61.3% perceiving fatigue to be problematic [17].

Many motor symptoms in individuals with PD have been effectively treated by physical activity and exercise programs including aerobic endurance, balance, muscle strength and functional ability [32-34]. For example, aerobic conditioning provided the most consistent long-term benefits and improvements in motor abilities given that long-term adherence might be relatively easier with the aerobic exercise. It was noted that benefits were found in other types of exercise (flexibility, balance, and functional) although the effects did not last as long, possibly due to non-adherence [32]. It has been suggested that reduced levels of movement efficiency can contribute to the non-motor symptoms e.g. fatigue [32]. The presence of fatigue severely impacts quality of life and reduces compliance to exercise programs and other physical activities [33].

As described in the Introduction, fatigue in PD is in an urgent need of research [21]. Current study aimed to examine whether there was an association of the amount of exercise and physical activity with the degree of fatigue in individuals with PD. The finding obtained from this study demonstrated that the greater duration of weekly exercise is correlated with the lower level of PD-fatigue, suggesting an association of the more physical activity with the less fatigue. Secondary aspects examined in this study included the effects of depression on fatigue levels and length of PD diagnosis. A significant difference was found in fatigue levels when comparing individuals who were medically diagnosed with depression to those who were not. This finding could indicate that fatigue is associated with non-motor symptoms, such as depression, in individuals with PD, which is in agreement with other literature [9,17]. In analyses of the relationship between fatigue levels and the length of disease, no significant difference was found regardless of a cutoff of three years or five years between "early" and "advanced" stages of PD. This observation supported that non-motor symptoms such as fatigue preceded motor symptoms, and thus may be biomarkers of a pre-motor or preclinical stage of PD [35,36]. Since fatigue may occur at an early stage of the disease and can reduce patients' adherence to therapy, a priority should be given to treatment of fatigue before it becomes a more chronic problem.

Limitation of the Study

Limitations are present in this study. Data were gathered through an online questionnaire, which did not allow for volunteers to obtain clarification on inquired information. All participants did not complete every part of the questionnaire or the entire PFS tool, resulting in missing information from some participants whose available data had to be discarded during the analyses. Additionally, this study utilized an observational or correlational design which is non-experimental in nature, and thus cannot establish a cause-and-effect relationship between PD-fatigue and exercise.

Conclusion

In conclusion, the findings of the study suggested that exercise can serve as an effective tool for combating PD-related fatigue. This paper addresses a subject of tremendous importance that fatigue may negatively impact mobility and adherence of physical therapy in people with Parkinson's disease. The amount of research on these topics is lacking, despite the debilitating impact of fatigue in patients with PD. To guide clinical practice, future research should be directed to examine the effectiveness of exercise, such as the amount of and the type of the exercise, on reducing fatigue and improving participation and quality of life in individuals with PD. Research utilizing mixed

methods of quantitative and qualitative paradigms is warranted to increase our understanding of fatigue that is a complex and multifaceted phenomenon, due to the subjective nature of fatigue and the challenge of measuring fatigue. Thus, it is important for clinicians to be aware of this important topic.

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Conflict of Interest

There is no financial or conflict of interest to declare.

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