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HOME-BASED AEROBIC EXERCISE AMELIORATES SYMPTOMS IN PATIENTS WITH PARKINSON'S DISEASE

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ABSTRACT

Background: Rehabilitation for Parkinson's disease (PD) has not been found to be an effective intervention for primary impairments caused by dopaminergic cell degeneration, such as tremor or bradykinesia. Recent reports have indicated the efficacy of home exercise on ameliorating primary impairments. However, no studies have examined the effects of aerobic rehabilitation for managing primary impairments of PD.

This study aimed to examine the effects of a home-based aerobic exercise program on primary impairments in patients with PD.

Methods: This study was conducted by before-after design. The study enrolled 25 patients (male: 7, female: 18) with PD. The intervention involved self-directed aerobic exercise performed using a commercially available pedal exercise apparatus. The participants exercised at home for 20 minutes every day, for approximately four weeks. The variables measured were walking speed, stride length, leg muscle strength, and primary impairments of PD including the Unified Parkinson's Disease Rating Scale Part 3 (UPDRS3) score as well as the maximum distance, total path length, and movement speed in a finger tapping test.

Results: A significant improvement was found in the walking speed ($p<0.05$), UPDRS3 score ($p<0.01$), total path length ($p<0.01$).

Conclusions: The proposed home-based aerobic exercise program resulted in significant improvement in UPDRS3 scores, finger tapping test results, and ability to walk, suggesting that such an intervention can achieve recovery of primary impairments in PD patients.

The present findings indicate that home-based aerobic exercise therapy is effective for primary impairments of PD.

Keywords: Rehabilitation, Parkinson's disease, Aerobic exercise, Primary impairment, Neuroplasticity, Dopaminergic neuron.

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INTRODUCTION

Parkinson's disease (PD) is a progressive condition involving degeneration of dopaminergic cells. PD represents a major neurodegenerative disorder, ranking second in prevalence worldwide [1], and is predicted to become even more common in the future, as the population ages [2].

PD rehabilitation has been shown to be effective for the management of secondary impairments (e.g., disuse syndrome) caused by the primary impairments of PD that result directly from dopaminergic cell degeneration [3]. However, no such effect of rehabilitation has been sufficiently demonstrated for the primary impairments including tremor, bradykinesia, rigidity, or postural instability [4].

Meanwhile, many reports have confirmed the effects of exercise in animal models of PD, indicating that exercise has a regenerative and protective effect on dopaminergic cells [5-8]. In addition, recent reports indicate that aerobic exercise affects the neuroplasticity of dopaminergic neurons in patients with PD [9].

To date, home exercise therapy for patients with PD has been focused on muscle strengthening, walking practice, and balance practice, which have been reported to be effective for improving quality of life [10], reducing the rate of falls [11], and improving exercise performance [12]. However, there are few reports on the effect of home exercise therapy using aerobic exercise for primary impairments of PD.

Thus, the present study was performed with the objective of verifying the efficacy of aerobic exercise on the primary impairments of PD when patients perform the exercises in their own homes and manage exercise intensity by themselves.

METHODS

Study design

This study was conducted by before-after design.

Ethical considerations

The participants received explanations regarding the contents of the study both orally and in writing and afterward provided informed consent to participate in the study. The study has been approval of the ethics committee of Takasaki University of Health and Welfare (approval number. 2717). The study was also registered with the University Hospital Medical Information Network Center (trial registration number: UMIN0000208325).

Participants

45 patients with PD were considered for the study. The patients filled in a form regarding medical history, confirming that they were free of clinically significant another neurological disease, musculoskeletal disease, respiratory disease, cardiovascular disease, and major depression. All patients had independent ambulation and declared no history of falls. After applying the exclusion criteria, 25 patients were selected for the study. The baseline characteristics of the 25 patients are listed in Table 1. As an overview, the disease duration ranges from 2 to 20 years with a mean (9.0±4.9) years, disease severity was Hoehn & Yahr (H&Y) stage ranged from 1 to 3 with a mean (2.8±0.5).

Table 1: Baseline characteristics of patients (n=25)

Age (years)	71.3±4.5
Sex	Male: 7 Female: 18
Disease duration (years)	9.0±4.9
H&Y stage	2.8±0.5 (I: 3 II: 4 III: 18)
Exercise count (number of times)	21.0±3.4
Continuous break of exercise (days)	1.8±0.8

H&Y: Hoehn & Yahr

Values are given as mean ± standard deviation

Exclusion criteria and an applicable number of patients:

1) Failure to participate in one of the two measurements (i.e., before and after intervention): n=8

2) Insufficient compliance (i.e., defined as performing the exercise for less than a half of the study duration): n=5

3) Cessation of intervention for four or more days in a row: n=1

4) Pain or other reason impeding participation: n=1

5) Change in PD medication during the intervention period: n=1

6) Partial loss of data: n=4

Intervention

The participants performed self-directed aerobic exercise at home, using a commercially available pedal exercise apparatus (TB-1316; NIHON MEDIX Co., Ltd., Chiba, Japan) (Figure 1), for 20 minutes a day for approximately four weeks. The patients were instructed to continue taking their medication during the course of the study. A target heart rate corresponding to 50% of the maximal oxygen uptake (VO2max) was calculated using the Fukuoka University equation (138-age/2) [13] so that the exercise intensity would be at a moderate level recommended for aerobic exercise. In addition, the exercise intensity was self-managed by the patient during the exercise by monitoring the pulse rate on a saturation monitor (OXi BOY S-121; X-Cardio Japan Co., Ltd., Shiga, Japan) and attempting to maintain the target pulse rate as much as possible.

Figure 1: Pedal exercise apparatus

During the exercise intervention, the participants kept daily records on (i) whether the exercise was performed, (ii) their physical condition during the exercise, and (iii) whether there were any changes to medications taken for PD.

Outcome measures

Two rounds of evaluation were performed, namely before and after the intervention. The evaluation times of both rounds were consistent, to exclude any differences in pharmaceutical effect related to when the medication was taken. The evaluations were performed to assess several key aspects of motor performance.

Walking ability assessment

Walking speed and stride was measured using a walking analyzer (Walk Way MW-1000; Anima Corp., Tokyo, Japan) with a 480-cm sheet-shaped sensor placed in the middle of a 10-m walking path. The participants were instructed to walk at a comfortable speed. Measurements were performed twice, and the average of the two measurements was recorded. Measurement items were walking speed, cadence, stride length.

Muscle strength assessment

Quadriceps muscle strength was measured using a handheld dynamometer (μTas F-1; Anima Corp.). Two measurements were taken for each side (left and right; total of four measurements), and the average of the two measurements for each side was retained, divided by body weight.

Assessment of primary PD impairments

(1) Comprehensive evaluation of PD status

The Unified Parkinson's Disease Rating Scale (UPDRS) [14] was used in the present study, as this comprehensive evaluation scale is used by researchers and physicians around the world. The study used only the 18 items in Part 3 of the UPDRS (UPDRS3), which cover motor function.

(2) Finger tapping test

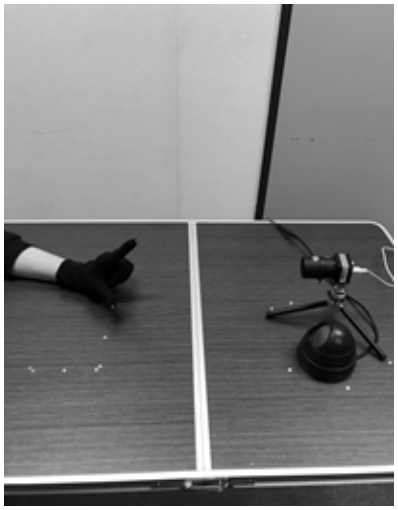

Figure 2: Finger tipping test

Patients wore black gloves with markers on the tip of the thumb and index fingers, and finger taps were recorded with a high-speed camera.

The finger tapping test, which is also part of the UPDRS3, was used to evaluate motor symptoms. Conventionally, the finger tapping test is scored by measuring the number of times the thumb and index finger can be opened and closed in during a five-second interval, and by performing additional observations during the exercise. However, the present study used a special device equipped with finger-tapping video analysis software (S-15079; Takei Scientific Instruments Co., Ltd., Niigata, Japan) to analyze the motion of markers attached to the tips of the fingers, which allows to quantitatively measure the finger opening/closing speed and the motion path. The participants were requested to perform the move as quickly and as exaggeratedly as possible. The variables measured were as follows: (i) the average of the greatest opening distance between the thumb and index finger on the left and right sides during the fifth finger tap from the beginning, hereafter referred to as the maximum distance, calculated by the formula: (right maximum distance + left maximum distance) / 2; (ii) the average total path length of the thumb and index fingers on the left and right sides, hereafter referred to as the total path length, calculated by the formula: (right thumb total path length + right index finger total path length + left thumb total path length + left index finger total path length) / 4; and (iii) the average movement speed of the thumb and index finger on the left and right sides, hereafter referred to as the movement speed, calculated by the formula: (right thumb movement speed + right index finger movement speed + left thumb movement speed + left index finger movement speed) / 4.

Statistical analysis

The t-test was used to compare walking ability, leg muscle strength, and finger tapping test scores obtained before and after the intervention. The Wilcoxon signed-rank test was used to compare UPDRS3 scores, before and after the intervention. SPSS® for windows® (Statistics 17.0, IBM, USA) was used to perform all analyses, and the statistical significance threshold was set at 5%.

RESULTS

Intervention outcomes

Table 2: Outcomes of result (n=25)

	Walking ability				
	Speed (cm/sec)	Cadence (step/min)	Stride (cm)	Leg strength (N)	UP-DRS3 score
Before intervention	85.8±28.4	112.0±10.4	90.3±27.0	149.5±53.9	9.6±6.6
After intervention	90.6±30.1	115.1±14.4	93.0±27.7	156.5±69.4	3.1±2.9
p-value	< 0.05	0.42	0.21	0.49	0.00

	Finger tapping test		
	Maximum distance (mm)	Total path length (mm)	Movement speed (mm/sec)
Before intervention	533.4± 171.3	115.2± 28.4	175.2± 73.0
After intervention	604.1± 133.7	119.8± 21.2	182.8± 59.5
p-value	< 0.01	0.33	0.47

UPDRS3: Unified Parkinson's Disease Rating Scale Part 3

Maximum distance = (right maximum distance + left maximum distance) / 2

Total path length = (right thumb total path length + right index finger total path length + left thumb total path length + left index finger total path length) / 4

Movement speed = (right thumb movement speed + right index finger movement speed + left thumb movement speed + left index finger movement speed) / 4

Values are given as mean ± standard deviation

Among the variables reflecting walking function, speed was found to have increased significantly after the intervention. Although cadence and stride length tended towards increase, the difference was not significant. Leg muscle strength exhibited an upward trend, but no significant difference was found. The UPDRS3 score was found to have improved significantly after the intervention.

Among the variables reflecting finger tapping test, the total path length was found to have increased significantly after the intervention. Although maximum distance and movement speed tended towards increase, the difference was not significant.

DISCUSSION

The home-based aerobic exercise program developed and assessed in the present study confirmed the improvement of not only UPDRS3 scores but also results of the finger tapping test, which involved parts of the body that was not the object of the intervention. In addition, while there was no significant change in leg muscle strength, a significant improvement in stride length was observed, suggesting that the intervention achieved recovery of primary impairments of PD.

Currently, the main therapeutic strategy for PD is drug treatment with levodopa, which is known to cause motor complications when used long term. On the other hand, exercise therapy can proceed without causing motor complications. Moreover, therapy by self-directed exercise leads to a reduction in medical expenses. In this context, the results of the study show the importance of rehabilitation using aerobic exercise and suggest the feasibility of altering the treatment concept for PD.

Takakusaki (2009) [15] considers that motor impairment in PD is related to dysfunction in a coordinated regulatory mechanism, caused by an abnormality in the dopaminergic system with respect to the function of the basal ganglia. To date, rehabilitation for PD has had the objective of improving secondary impairments, focusing on balance practice, muscle strengthening practice, and walking practice according to disease stage. No adequate interventions have been developed aiming towards an improvement in the dopaminergic system. However, in recent years, there have been numerous studies on the effect of exercise in animal models of PD, reporting restoration and protection of dopaminergic cells. The underlying mechanism for this effect has been reported to involve several aspects, namely: a reduction in oxidative stress in the corpus striatum [6]; the action of the brain-derived neurotrophic factor (BDNF) [5]; an increase in the levels of glycogen synthase kinase 3β, which is related to synaptic plasticity; and a recovery in the levels of extracellular signal-regulated kinases [7]. In PD patients, regular aerobic exercise has been reported to increase BDNF levels [16], and a positron emission tomography test of dopamine D2 receptor binding ability reportedly found D2 receptor upregulation after exercise [9]. Ridgel et al. (2012) [17] reported that exercise using an electric bicycle ameliorated tremors and bradykinesia, which are primary impairments of PD. Meanwhile, Shulman et al. (2013) [18] performed a high-intensity and low-intensity sustained treadmill walking experiment, reporting that, although VO2max improved in both groups, no UPDRS score improvement was found. Thus, the effect of aerobic exercise in PD patients has remained unclear.

The present study indicated an increase in stride length, an improvement in UPDRS3 score, and an increase in the maximum distance and total path in the finger tapping test following a four-week home-based aerobic exercise program. Since the pedaling exercise used as the intervention in this study primarily involves the muscles of the legs, it is expected that increased leg muscle strength would result in improved performance. However, the results indicated no significant change in leg muscle strength, suggesting that the improvement in stride length is related to improvement in primary impairments of PD. Importantly, a significant increase was found in the maximum distance and total path length in the finger tapping test, even though the fingers were not involved in the exercise intervention. When interpreting the finger tapping test results according to the standard UPDRS, reduced movement speed and amplitude are considered to indicate an exacerbation of symptoms. For this reason, Shima et al. (2008) [19] suggested that the finger tapping test could be used as an indicator of the se-

verity of PD symptoms. The aerobic exercise intervention used in the present study seems to have an effect similar to those observed in prior studies, in that it was effective against problems in the dopaminergic system, which are the cause of primary impairments in PD.

With respect to the validity of the intervention applied in the present study, Herman et al. (2007) [20] reported that exercise intervention involving six weeks of treadmill training in PD patients with an H and Y stage of 3 or less resulted in an improvement in relevant scores such as those of PD Questionnaire-39, UPDRS3, and walking speed. However, PD is a condition that involves a very high rate of falls [21], which is particularly high in patients with an H&Y stage of 3, at which point impairment of the postural reflex begins to manifest [22]. In the present study, the exercise involved pedaling from a seated position and thus can be considered a method that is easier to implement in the home setting because, unlike exercising using bulky equipment such as the treadmill, it involves minimal risk of falling or equipment-related injury. Therefore, the information that aerobic exercise is effective against the primary impairments of PD, as well as the protocol of the home-based exercise program is useful for developing self-directed rehabilitation programs for PD.

The main limitations of this study contain the less number of participants and the lack of a control group. In addition, certain aspects relevant to PD were not considered, including constipation [23], which is caused by decreased digestive activity resulting from autonomous nervous system impairment [24,25] and which diminishes the absorption of drugs, potentially decreasing their therapeutic effect. Therefore, it is possible that the present observations regarding the improvement in primary impairments also reflected increased digestive activity (and therefore better drug absorption) as a result of the exercise. Future studies should confirm the effect of exercise using positron emission tomography and blood test data.

CONCLUSION

This study aimed to determine the efficacy of home-based aerobic exercise for ameliorating primary impairments in patients with PD. The present findings indicated that a four-week program involving exercises using a pedal exercise machine was effective for improving primary impairments of PD. The present study thus suggests not only that aerobic exercise is effective for managing the primary impairments of PD, but also that self-directed, home-based exercise therapy is sufficient for improving symptoms related to primary impairments of PD. Demonstrating the recovery of primary impairments by aerobic exercise may change the concept of rehabilitation for PD and lead to more beneficial therapeutic effects in PD patients. Furthermore, achieving such recovery via self-directed exercise would lead to a reduction in medical expenses.

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