# Endurance Exercise Training to Improve Economy of Movement of People With Parkinson Disease: Three Case Reports

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## Background and Purpose

Even early in Parkinson disease (PD), individuals have reduced economy of movement. In this case report, the effects of endurance exercise training are examined on walking economy and other measures for 3 individuals in early and middle stages of PD.

## Patients

The patients were 1 woman and 2 men with PD, aged 52 to 72 years, classified at Hoehn and Yahr stages 2 to 2.5.

## Intervention

Each patient completed 4 months of supervised endurance exercise training and 12 months of home exercise, with monthly clinic follow-up sessions. Strategies were included to enhance adherence to exercise.

## Outcomes

The main outcome measure was economy of movement (rate of oxygen consumption during gait) measured at 4 treadmill speeds. Secondary outcome measures included the Unified Parkinson's Disease Rating Scale (UPDRS), Continuous-Scale Physical Functional Performance Test (CS-PFP), Functional Reach Test (FRT), and Functional Axial Rotation Test (FAR). Economy of movement improved for all 3 patients after 4 months of supervised exercise and remained above baseline at 16 months. Two patients also had scores that were above baseline for UPDRS total score, CS-PFP, FRT, and FAR, even at 16 months.

## Discussion and Conclusions

Evidence from these 3 individuals suggests that gains may occur with a treadmill training program that is coupled with specific strategies to enhance adherence to exercise.


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Parkinson disease (PD) is a potentially disabling condition resulting from degeneration of the substantia nigra with cardinal signs of rigidity, bradykinesia, tremor, and postural instability.[1–3] As the disease progresses, individuals with PD have increasing difficulties with walking, balance, and basic functional activities; eventually they may experience total disability.[2,3] People in the early to middle stages of PD can benefit from exercise interventions, with improvements reported for gait, flexibility, strength (force-generating capacity), and balance.[4–8] Relatively little evidence exists regarding endurance exercise training for people with PD. Yet endurance exercise training can be accomplished at a local health club or at home without equipment (eg, brisk walking) and with relatively little training. Even for people with significant bradykinesia, treadmill training can be used for cardiovascular endurance by increasing the treadmill grade to increase demand of the task. Therefore, it would be useful to understand the potential benefits for people with PD.

Endurance exercise training is of particular interest because of the mounting evidence that people with PD have altered cardiovascular function, compared with their counterparts who are healthy. Although maximal aerobic power in individuals with PD is similar to or only slightly lower than in age- and sex-matched individuals who are healthy, the attainment of peak aerobic power occurs at a significantly lower exercise level (eg, lower speed or grade on a treadmill test) in those with PD, indicating poor metabolic efficiency (ie, increased energy cost of the work performed).[9–11] Technically speaking, because "work" (ie, force × distance) cannot be measured during some forms of exercise, such as level treadmill walking, it is more appropriate to use the term "economy" in place of "efficiency" when assessing the energy cost of exercise. The general term "economy of movement" refers to the rate of energy expenditure during any motor task, whereas the term "walking economy" refers specifically to the rate of energy expenditure during walking. Data suggest that individuals with PD expend about 20% more energy than do their counterparts who are healthy during cycle ergometer or treadmill exercise,[10,12] suggesting poor economy of movement in general and poor walking economy specifically. Poor walking economy also has been documented in other disease states, including stroke.[13] To our knowledge, no data are yet available regarding the relationship of poor economy of movement to overall function of individuals with PD, although it can be hypothesized that the reduced economy of movement eventually could contribute to increased fatigue, typically reported by people with PD.[14]

It is not yet known whether endurance exercise training results in improved economy of movement for individuals with PD, although Macko and colleagues[13,15] demonstrated improved walking economy following a 6-month treadmill training program for individuals with chronic hemiparesis following a stroke. Whether a treadmill training program results in improvements beyond the cardiovascular system (eg, balance, overall functional ability) also is not known. Furthermore, it is important to establish whether adaptations to training can be sustained over time. This issue is of particular importance for people with PD, given the chronic, progressive nature of the disorder. For benefits to be sustainable, individuals must be able to carry out the conditioning program on their own, once they complete a supervised training program.

This article presents 3 case reports examining potential benefits of endurance exercise training. The 3 individuals were in the early to middle stages of PD. Specifically, the purposes of the case reports were: (1) to examine the effects of endurance exercise training on walking economy, (2) to examine the effects of endurance exercise training on specific symptoms of PD (ie, Uniform Parkinson's Disease Rating Scale [UPDRS] motor subscale score) and functional ability (eg, balance, overall functional capacity), and (3) to determine whether these individuals could maintain exercise-induced benefits over a 12-month period once they completed the supervised exercise program.

## Case Studies

### Background to the Case Studies

The 3 cases reported on here are from individuals who participated in a large randomized controlled trial (RCT), comparing 3 forms of exercise training for people in the early to middle stages of PD. Prior to presenting the 3 cases, some of the salient features of the RCT are summarized.

Participants in the RCT lived in the community and were able to ambulate without an assistive device. Participants were excluded if they had on-state freezing, uncontrolled hypertension, or exercise was limited by musculoskeletal, neuromuscular (other than PD), or cardiovascular disorders. The patients' neurologists were encouraged to keep antiparkinson medications stable unless there was significant worsening of function. All participants signed an informed consent statement prior to entering the RCT.

To participate in the RCT, each individual completed a series of screening procedures. Idiopathic PD was verified by a neurologist, using UK Brain Bank criteria,[16] and individuals

**Table 1.**
Characteristics of the 3 Patients

| | Patient 1 | Patient 2 | Patient 3 |
|---|---|---|---|
| Age (y) | 60 | 72 | 52 |
| Sex | Male | Male | Female |
| Body mass index (kg/$m^2$) | 27.7 | 25.1 | 14.1 |
| Baseline UPDRS[a] total score | 41 | 27 | 17 |
| Baseline Hoehn and Yahr score | 2 | 2 | 2.5 |
| Premorbid conditions | Arthritis of the right hip | None | Livedo reticularis, bilateral lower extremities |
| Maximum tolerable treadmill speed (mph) | 3.0 | 2.5 | 3.5 |

[a] UPDRS=Unified Parkinson's Disease Rating Scale.

were referred back to their neurologist if it was determined that they were not optimally treated. To establish that participants could exercise safely in an endurance exercise program, screening tests included a physical examination, assessment of blood chemistries, and a graded exercise stress test with monitoring of blood pressure and 12-lead electrocardiographic (ECG) activity. The exercise test involved walking on a treadmill at the fastest tolerable walking pace with a 2% increase in grade every 2 minutes. Heart rate (HR) and ECG activity were monitored continuously, and blood pressure and rate of perceived exertion (RPE) were recorded at the end of each 2-minute stage. The test continued until: (1) HR reached 85% of the age-predicted maximum HR (HRmax), (2) gait became festinating and unsafe, (3) volitional exhaustion occurred, or (4) the test was stopped by the administering physician due to abnormal ECG or blood pressure responses. Once participants in the RCT completed these steps, they were eligible to participate in the endurance exercise training program.

Data for the RCT were collected by trained raters, blinded to the exercise program of the participants. Thus, the raters were unaware that the 3 patients in this case report were receiving endurance exercise training. Measurements were obtained for each individual at the same time of day, and each person was asked to take medications for PD at the same time of day for each test session.

The intervention for participants in the aerobic arm of the study included a 4-month supervised endurance exercise program and a 12-month follow-up period, during which the 3 patients were instructed to exercise at home, with one monthly supervised exercise session in the laboratory. Outcomes were assessed at baseline and at 4, 10, and 16 months.

The three individuals in this case report were chosen from the first 22 participants who entered the RCT. They were 3 of the first 6 graduates of the aerobic arm of the study and were selected because the research assistants who worked with them reported that they were highly adherent to their exercise program and to documenting their exercise.

## Patients

The 3 patients (2 men, 1 woman) were in early to middle stages of PD and ranged in age from 52 to 72 years (Tab. 1). Patient 1 had a baseline UPDRS total score of 41. His maximum treadmill speed was 3 mph. Patient 2 was moderately affected by PD according to his baseline UPDRS total score of 27. His gait was most affected of the 3 patients, with a maximum tolerable treadmill speed at baseline of only 2.5 mph. Patient 3 was the least affected by PD at baseline, as indicated by her baseline UPDRS total score of 17 and her ability to walk on the treadmill at 3.5 mph.

## Test and Measures

Tests and measures for the RCT were chosen based on the hypotheses of that investigation. For the purposes of this case report, economy of movement is considered the primary outcome measure and all other measures are considered secondary.

Tests and measures were administered on 2 separate sessions. During the first session, PD was rated using the UPDRS and modified Hoehn and Yahr scale (H&Y).[17] The UPDRS is considered the gold standard for quantifying signs and symptoms of PD, with reports of test-retest reliability.[18,19] The modified H&Y (used to determine stage of PD) is part of the UPDRS. Overall physical functional capacity was determined next using the Continuous-Scale Physical Functional Performance Test (CS-PFP).[20,21] This test consists of 16 tasks, performed serially, as fast as is comfortably possible for the individual. A total score and subscale scores are obtained and range from 0 to 100. Reliability and validity have been established for older adults without specific disorders[20,22] and for individuals with PD.[21] Responsiveness has been established for community-dwelling adults without specific disorders.[23] Task performance then was determined using established protocols for the following measures[24–26]: Functional Reach Test (FRT), Functional Axial Rotation Test (FAR), and 360-degree turn in a standing position. Interrater reliability is good (intraclass correlation coefficient=.70–.89) for these measures with individuals who have PD.[27] Six-minute walk distance was measured as part of the CS-PFP and is reported separately as well.

During a second test session, economy of movement was determined by having the patients walk on a treadmill at 4 speeds in 0.5-mph increments.[28] The maximum speed for this test was based on each patient's fastest tolerable speed during the graded exercise test. A heart rate monitor was worn throughout the test, and rate of perceived exertion (RPE) scores were obtained during each walking stage. The first stage consisted of a resting measurement for 5 minutes while sitting in a chair. The patient then walked for 5 minutes at each of 4 different speeds, beginning with the slowest speed. Oxygen consumption ($\dot{V}O_2$) was measured during the last 2 minutes of each stage by having the individual breath into a tube connected to an automated indirect calorimeter system (TruMax 2400 metabolic cart*). This system uses exhaled oxygen and carbon dioxide to compute the amount of oxygen utilized during walking.

## Adherence to Exercise

Before beginning the endurance exercise training, the patients participated in an introductory session to assist them to develop exercise adherence habits. This session included exploration of the individual's beliefs about exercise, expectations regarding participation in the exercise program, and possible concerns regarding ability to exercise regularly.[29,30] Each patient received and was oriented to a booklet that included information regarding benefits of and barriers to exercise.[31] The booklet included monthly documentation sheets on which the patients were instructed to record observed benefits, barriers, illnesses, falls, or changes of PD medications. The booklet also contained monthly exercise calendars in which they were instructed to record the mode of exercise and time spent exercising on each day that they exercised. Although instructed to do so, these 3 patients did not systematically record their HR for months 5 through 16 during daily exercise in these booklets. Calendars were reviewed on a monthly basis, and summary data were recorded for each patient.

During each monthly session, the patients set their own goals for the coming month with regard to the number of days that they anticipated being able to exercise and the amount of time for each session. Before setting goals, the exercise trainer reviewed the booklet with each patient, helping the patient to explore any concerns about ability to exercise 5 to 7 times per week. The patient and exercise trainer then reviewed the booklet each month thereafter, set new goals for exercise, and developed strategies to overcome any perceived barriers to exercise. During these monthly review sessions, the trainer encouraged the patient to find ways to increase exercise frequency, as needed.

## Supervised Exercise Training (Months 1–4)

Patients exercised at a clinical exercise research laboratory containing a wide variety of exercise options (eg, treadmills, bicycles, elliptical trainers). They were encouraged to complete most of their exercise training on the treadmill, because this is the most functionally relevant training option.

During the introductory session, the patients were instructed that they should initially exercise at a moderate intensity (ie, 60%–70% of HRmax), with a goal of progressing to more vigorous exercise (ie, 70%-85% of HRmax) for the next 16 months. They were shown how to monitor and reach their target HR while exercising, either using an HR monitor or by counting their pulse. They were shown how to record their HR during each exercise session in a log kept at the exercise facility. They also were oriented to the exercise equipment in the exercise facility (eg, operation of the treadmills, elliptical trainers). Finally, during the initial exercise sessions, the exercise trainer supervised the patient to ensure that he or she was able to walk on a treadmill safely without assistance. The patient was instructed to use the handrails, as needed, for support. No other external support was provided.

During months 1 to 4 of the program, patients exercised 3 times per week for 40 minutes under the guidance of an exercise professional. They were encouraged to exercise on their own at home on other days. The treadmill training speed or grade was increased gradually during the program to achieve the target HR. At the end of 4 months, the patients were encouraged to exercise 5 to 7

* ParvoMedics, 8152 South 1715 East, Sandy, UT 84093.

**Table 2.**
Exercise Mode, Frequency, Intensity, and Duration for the 3 Patients

| | Patient 1 | Patient 2 | Patient 3 |
|---|---|---|---|
| Months 1–4 | | | |
| Modes of exercise | Treadmill, bicycle, rowing | Treadmill, elliptical, rowing | Treadmill, bicycle |
| Average percentage of age-predicted maximum heart rate | 67 | 73 | 80 |
| Average days of exercise per week | 2.8 | 2.9 | 2.9 |
| Average exercise time per week (min) | 122.8 | 111.2 | 129.7 |
| Months 5–16 | | | |
| Modes of exercise | Walking over ground and on treadmill | Walking over ground outside; working out at the study exercise facility (walking on treadmill and rowing) | Walking on treadmill at a local gym |
| Average days of exercise per week | 6.5 over ground; 0.7 on treadmill | 3 | 2.7 |
| Average exercise time or distance per week[a] | 23.04 km (14.4 miles) per week over ground; 0.67 day per week on treadmill for 21.4 min per week | 92.5 min at study exercise facility; 2.56 km (1.6 miles) per week over ground walking outside | 140.5 min per week at local gym |

[a] Patients were not consistent in recording different modes of exercise.

times per week on their own at home or in a local gym.

### Home Exercise Program (Months 5–16)

After 4 months of supervised exercise, the timing was tapered to 2 sessions per week for 2 weeks and then to 1 session per week for 2 weeks. Thereafter, the patients came to the exercise facility for supervised exercise once a month, where their progress was monitored, problems with adherence were addressed, and any questions were answered by the research staff. The patients documented day, time, and mode of exercise in the calendars in their exercise booklets.

## Outcomes

Data for outcome measures were obtained on completion of the first 4 months of supervised exercise, at 10 months (6 months after completion of the supervised exercise program), and at 16 months (1 year after completion of the supervised exercise program). Exercise calendars were used to determine frequency of exercise each week for months 5 to 16.

Patient 1 exercised at an average of 67% of HRmax during the first 4 months and had an average walking frequency of 2.8 days per week (Tab. 2). At the end of the 4-month training period, this patient was walking at 3.2 mph with a 5% grade. At 4 months, his walking economy had improved at all speeds (less oxygen consumed), and his 6-minute walk distance had increased by 17.0%.

Over the next 12 months, patient 1 exercised an average of 6.5 days per week, walking an average of 23.04 km (14.4 miles) per week. In addition, this individual worked out at a local recreation center, averaging 0.7 day per week on a treadmill for an average of 21.4 minutes per week. Walking economy for all except one data point continued to move in the direction of the predicted economy through 16 months, although walking economy remained above the level of energy expenditure predicted[32] for a person of his age (referred to as "predicted energy expenditure") (Fig. 1). Commensurate with the decreased level of energy expenditure during walking, his HR response to exercise also decreased in response to exercise training (Fig. 1). His 6-minute walk distance was greater than baseline by 17.0% at 16 months (Tab. 3).

With regard to secondary outcome measures, his UPDRS total score decreased by 6 points over the first 4 months and continued to decrease for the next 12 months. His motor score was 29.5 at baseline and 17 at month 16. During the first 4 months, his physical functional capacity (CS-PFP score) increased by

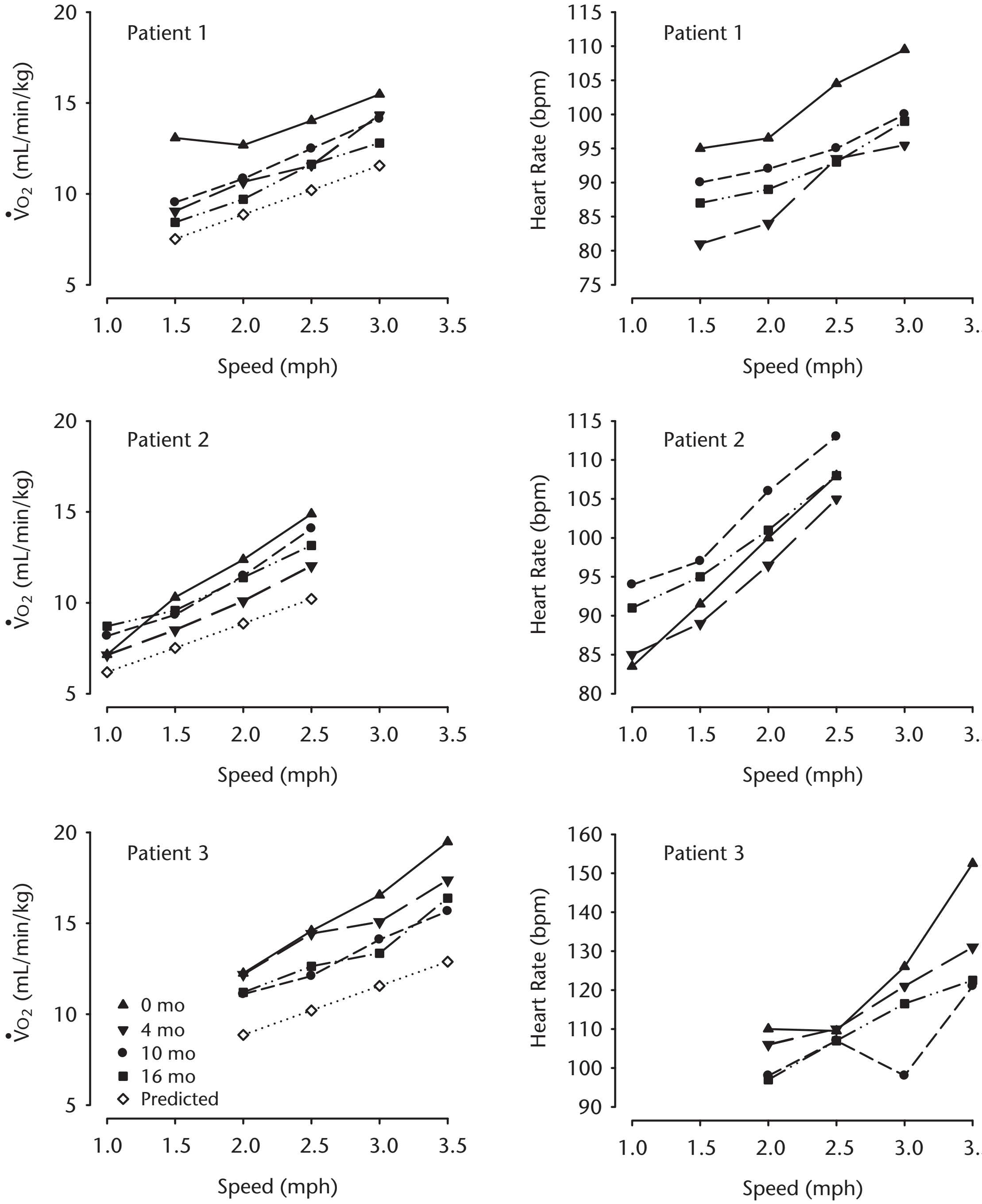


**Figure 1.**
Oxygen consumption ($\dot{V}O_2$) and heart rate at 4 speeds for 3 patients. Predicted rate of $\dot{V}O_2$ is from the *American College of Sports Medicine: Guidelines for Exercise Testing and Prescription.*[32]

49% and was still above baseline at 16 months. His forward functional reach increased by 25.9% at 4 months and remained above baseline at 16 months. His right lateral reach increased but his left lateral reach decreased during this time period. His FAR scores increased to the right (16.1%) and left (20.1%) (Tab. 3, Fig. 2). Number of steps to complete the 360-degree turn did not change appreciably over the 16 months.

Patient 2 averaged 2.9 days of exercise per week at an average of 73% of HRmax for the first 4 months of supervised training (Tab. 2). At the end of the 4-month supervised training period, he was walking at

**Table 3.**
Outcome Measures for Patient 1[a]

| Measure | Baseline | 4 mo | 10 mo | 16 mo |
|---|---|---|---|---|
| UPDRS | | | | |
| Total (0–106) | 41 | 35 | 27 | 26 |
| Motor (0–52) | 29.5 | 23.5 | 19.5 | 17 |
| ADL (0–48) | 7.5 | 10.5 | 6.5 | 8.0 |
| Mental (0–16) | 4 | 1 | 1 | 1 |
| CS-PFP (0–100 for each score) | | | | |
| Total | 49 | 73 | 69 | 66 |
| Upper-body strength | 58 | 79 | 69 | 69 |
| Upper-body flexibility | 58 | 71 | 64 | 80 |
| Lower-body strength | 47 | 73 | 70 | 59 |
| Balance/coordination | 44 | 68 | 66 | 60 |
| Endurance | 48 | 75 | 70 | 69 |
| RPE | 12 | 12 | 13 | 12 |
| FRT (in) | | | | |
| Forward | 10.8 | 13.6 | 13.5 | 14.7 |
| Right | 9.7 | 11.5 | 11.8 | 11.8 |
| Left | 8.2 | 7.7 | 7.0 | 7.7 |
| FAR (°) | | | | |
| Right | 77.5 | 90 | 87.5 | 87.5 |
| Left | 75.0 | 92.5 | 95.0 | 102.5 |
| 6-min walk distance (m) | 537.2 | 628.6 | 603.3 | 629.8 |
| Timed "Up & Go" Test (s) | 10.19 | 8.02 | 10.20 | 9.37 |
| 360° turn | | | | |
| Right, seconds | 4.1 | 4.0 | 4.5 | 4.2 |
| Right, steps | 7 | 7 | 7 | 7 |
| Left, seconds | 4.2 | 3.7 | 4.2 | 4.1 |
| Left, steps | 7.5 | 6.5 | 6 | 6 |
| Levodopa equivalent (mg) | 667 | 667 | 967 | 967 |

[a] UPDRS=Unified Parkinson's Disease Rating Scale, ADL=activities-of-daily-living subscale, CS-PFP=Continuous-Scale Physical Functional Performance Test, RPE=rate of perceived exertion, FRT=Functional Reach Test, FAR=Functional Axial Rotation Test.

3.1 mph with a 9% grade and reported that he exercised 2.9 days per week. His walking economy improved at 3 speeds (Fig. 1).

After the first 4 months, patient 2 chose to continue to exercise at the exercise facility, where he walked on the treadmill 3 days per week for an average of 92.5 minutes per week. In addition, he walked outside an average of 1 day per week (average of 2.56 km [1.6 miles] per week). At the end of 16 months, his walking economy continued to be more economical than at baseline. Despite the slightly reduced level of energy expenditure during walking in response to exercise training, his HR response to exercise tended to be elevated rather than reduced. His 6-minute walk distance was only 556 m at baseline, increased 16.2% at 4 months, and returned to baseline by 16 months.

With regard to secondary outcome measures, patient 2's UPDRS total score increased to 43.5 over 16 months (an increase of 16.5 points,

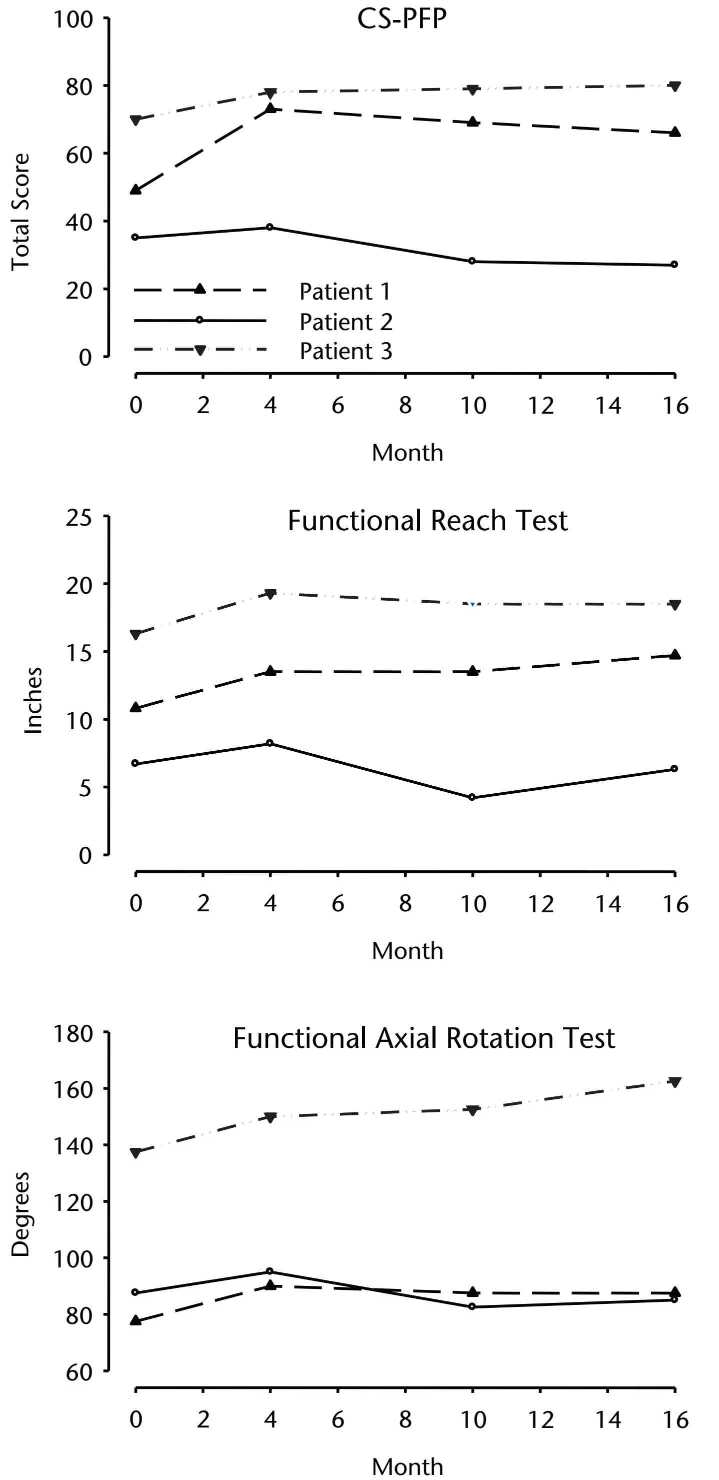


**Figure 2.**
Performance measures for the 3 patients: Continuous-Scale Physical Functional Performance Test (CS-PFP), Functional Reach Test, and Functional Axial Rotation Test.

suggesting that his disease progressed over the course of 16 months (Tab. 4, Fig. 2). During the first 4 months, his physical functional capacity (CS-PFP score) increased by 8.6%. His FRT score improved by 22.4% at 4 months but declined again over the next year, and his FAR score improved by 8.6% to the right but declined by 5.6% to the left (Tab. 4, Fig. 2). It is noteworthy that steps during the 360-degree turn decreased from 13 steps to the right at baseline to 6.5 steps at 4 months and were still below baseline (9.5 steps) at 16 months.

Patient 3 averaged 2.9 days of exercise per week at 80% of HRmax for the first 4 months of supervised exercise (Tab. 2). At the end of the 4-month training period, she was walking at 3.9 mph with a 9% grade, and her walking economy had increased at 2 speeds.

For the next 12 months, patient 3 reported that she exercised an average of 2.7 days per week, averaging 140.5 minutes per week on a treadmill at a local gym. Her walking economy showed further gains at all speeds at 10 months and was better than baseline at all speeds through 16 months. Like patient 1 and in contrast to patient 2, her improvement in walking speed was accompanied by a decrease in the HR response to exercise. Her 6-minute walk distance increased by 15.3% over the 16 months.

Patient 3 showed little change in UPDRS scores over the 16 months of the exercise program. During the supervised training period (months 1–4), this individual's physical functional capacity (CS-PFP score) and forward functional reach improved and at 16 months were still better than at baseline (Tab. 5, Fig. 2). In contrast, lateral reach to the left declined over this period. Her FAR score improved to the right but declined to the left over the 16-month

**Table 4.**
Outcome Measures for Patient 2[a]

| Measure | Baseline | 4 mo | 10 mo | 16 mo |
|---|---|---|---|---|
| UPDRS | | | | |
| Total (0–106) | 27 | 32 | 45 | 43.5 |
| Motor (0–52) | 22.5 | 30.5 | 35.5 | 32 |
| ADL (0–48) | 4.5 | 1.5 | 9.5 | 9.5 |
| Mental (0–16) | 2 | 2.5 | 2.5 | 3 |
| CS-PFP (0–100 for each score) | | | | |
| Total | 35 | 38 | 28 | 27 |
| Upper-body strength | 43 | 51 | 41 | 38 |
| Upper-body flexibility | 34 | 54 | 37 | 42 |
| Lower-body strength | 21 | 29 | 16 | 17 |
| Balance/coordination | 34 | 33 | 26 | 25 |
| Endurance | 39 | 39 | 29 | 26 |
| RPE | 11 | – – –[b] | 13 | 13 |
| FRT (in) | | | | |
| Forward | 6.7 | 8.2 | 4.2 | 6.3 |
| Right | 4.0 | 4.3 | 5.5 | 5.3 |
| Left | 5.2 | 5.7 | 4.8 | 3.3 |
| FAR (°) | | | | |
| Right | 87.5 | 95 | 82.5 | 85 |
| Left | 100 | 87.5 | 80 | 80 |
| 6-min walk distance (m) | 556.6 | 646.6 | 569.3 | 540.6 |
| Timed "Up & Go" Test (s) | 9.56 | 8.77 | 12.31 | 10.36 |
| 360° turn | | | | |
| Right, seconds | 5.1 | 4.1 | 7.2 | 4.0 |
| Right, steps | 13 | 6.5 | 8.5 | 9.5 |
| Left, seconds | 5.7 | 4.4 | 8.7 | 4.7 |
| Left, steps | 14 | 7 | 9 | 11.5 |
| Levodopa equivalent (mg) | 325 | 325 | 325 | 550 |

[a] UPDRS=Unified Parkinson's Disease Rating Scale, ADL=activities-of-daily-living subscale, CS-PFP=Continuous-Scale Physical Functional Performance Test, RPE=rate of perceived exertion, FRT=Functional Reach Test, FAR=Functional Axial Rotation Test.
[b] Missing data.

period. Her number of steps to complete the 360-degree turn were relatively unchanged over the 16 months.

## Discussion

Clinicians who treat individuals with PD are required to make decisions regarding the best approach to intervention, yet the guidelines for making those decisions remain elusive. To date, no definitive studies have identified the most important aspects of exercise for people with PD. A small number of RCTs have been reported on a few approaches to exercise for people with PD,[4–6] none of which included aerobic conditioning exercises. Bergen and colleagues[33] reported on 4 individuals with whom they used a 16-week treadmill program for endurance exercise training. The patients were all at H&Y stage 2. They ranged in age from 47 to 67 years. Four individuals of comparable age and stage of PD served as controls. Peak $\dot{V}O_2$ scores showed a significant group × time effect, with 32% improvement for the exercisers and a 10% decrease for the control group. However, no studies have reported on the potential benefits of endurance exercise

**Table 5.**
Outcome Measures for Patient 3[a]

| Measure | Baseline | 4 mo | 10 mo | 16 mo |
|---|---|---|---|---|
| UPDRS | | | | |
| Total (0–106) | 17 | 13 | 16.5 | 15.5 |
| Motor (0–52) | 15.5 | 8 | 11.5 | 8.5 |
| ADL (0–48) | 1.5 | 4 | 4 | 5 |
| Mental (0–16) | 0 | 1 | 1 | 2 |
| CS-PFP (0–100 for each score) | | | | |
| Total | 70 | 78 | 79 | 80 |
| Upper-body strength | 60 | 63 | 68 | 66 |
| Upper-body flexibility | 82 | 86 | 84 | 86 |
| Lower-body strength | 63 | 71 | 75 | 75 |
| Balance/coordination | 72 | 83 | 81 | 84 |
| Endurance | 75 | 84 | 84 | 87 |
| RPE | 11 | 12 | 12 | 14 |
| FRT (in) | | | | |
| Forward | 16.3 | 19.3 | 18.5 | 18.5 |
| Right | 9.3 | 13.5 | 12.7 | 13.8 |
| Left | 10.0 | 11.3 | 9.8 | 9.5 |
| FAR (°) | | | | |
| Right | 137.5 | 150.0 | 152.5 | 162.5 |
| Left | 132.5 | 130.0 | 117.5 | 127.5 |
| 6-min walk distance (m) | 599 | 629.2 | 675 | 665.9 |
| Timed "Up & Go" Test (s) | 8.61 | 8.38 | 7.24 | 8.05 |
| 360° turn | | | | |
| Right, seconds | 2.8 | 2.7 | 2.7 | 2.5 |
| Right, steps | 6.0 | 6.5 | 5.5 | 5.0 |
| Left, seconds | 2.9 | 2.7 | 2.6 | 2.5 |
| Left, steps | 5.5 | 5.0 | 6.0 | 5.5 |
| Levodopa equivalent (mg) | 600 | 600 | 600 | 600 |

[a] UPDRS=Unified Parkinson's Disease Rating Scale, ADL=activities-of-daily-living subscale, CS-PFP=Continuous-Scale Physical Functional Performance Test, RPE=rate of perceived exertion, FRT=Functional Reach Test, FAR=Functional Axial Rotation Test.

training to improve economy of movement, and none have investigated 16-month responses.

The 3 cases reported on here also suggest that it is possible for people with mild or moderate PD to benefit from an endurance exercise program. Furthermore, the changes were not restricted to economy of movement, but extended to motor features of parkinsonism, physical functional capacity, balance, and flexibility. Perhaps most importantly, findings from these cases suggest that it may be possible to retain exercise benefits or even continue to improve for up to 1 year after a supervised exercise training program by performing home-based exercise with monthly follow-up to check on the adherence to the exercise program and performance of exercise and to provide encouragement.

The approach to adherence to exercise, coupled with monthly appointments with the exercise trainer, may have played a key role in the ability of these 3 individuals to develop consistent exercise habits. Important aspects of this approach to adherence include the following:

(1) adherence was addressed from the beginning of the program, (2) the patients set goals each month regarding how much they would exercise, when, and where, and (3) training was supervised for 4 months, then supervision was tapered for 1 month, and monthly clinic appointments continued for the remainder of the 16 months to provide encouragement and accountability. Possibly, a similar strategy should be used when working with all patients who have a chronic, progressive neurological disorder that responds to exercise.

Reduced economy of movement, seen at baseline in our 3 patients, is consistent with a previous report by Protas and colleagues.[10] These authors reported that, over a range of submaximal cycling intensities, rates of energy expenditure were approximately 20% higher in individuals with PD than in people of comparable age and sex who were healthy. To our knowledge, the data from the 3 cases reported here are the first to suggest that it may be possible to improve economy of movement of individuals with PD. All 3 patients had better economy of movement (as evidenced by lower rates of $\dot{V}O_2$) at 4 months, and all 3 patients still had better economy of movement even after 16 months. The 6-minute walk distance was greater for all 3 patients at 4 months and remained above baseline through the 1-year follow-up in 2 patients.

These findings should be considered in context of the observation that walking economy is typically normal in sedentary adults who are healthy.[34,35] Furthermore, in contrast to these individuals with PD, walking economy in sedentary adults who are healthy does not change in response to endurance exercise training,[36,37] although a decrease in the HR response to exercise is an expected adaptation.

Although all 3 patients approached the predicted level of $\dot{V}O_2$ in response to exercise training, none reached the predicted levels.[32] A number of factors that can influence walking economy have been identified[38]: (1) resting energy expenditure, (2) efficiency of mitochondrial energy production via oxidative phosphorylation, (3) energy cost of ventilation, and (4) mechanical muscle contraction efficiency, which may be influenced by such factors as muscle fiber type and multisegment movement coordination. In our patients, resting energy expenditure while sitting decreased slightly during the intervention period. However, the decrease in resting energy expenditure accounted for only 15% to 30% of the decrease in walking energy expenditure in response to exercise training. For example, the average increase in energy expenditure above the resting value during walking at 2.5 mph for all 3 patients was 10.7 mL/min/kg at baseline, 9.4 mL/min/kg at 4 months, and 8.9 mL/min/kg at 16 months. Thus, factors other than resting energy expenditure that influence walking economy appear to be changed in response to endurance exercise training in individuals with PD.

It is not known whether the poor economy of walking in individuals with PD is a result of decreased efficiency of energy production by oxidative phosphorylation. Mitochondrial complex I dysfunction has been observed in the substantia nigra pars compacta of individuals with parkinsonism.[39] Whether mitochondrial dysfunction also is present in the skeletal muscle of individuals with parkinsonism remains controversial.[40] If mitochondrial dysfunction does occur in muscle, further research will be necessary to confirm whether the defect results in decreased energy efficiency and whether this improves in response to endurance exercise training.

Finally, the effects of PD on cost of ventilation and multisegmental movement coordination also should be considered. In this regard, there is a high prevalence of mostly asymptomatic airway obstructive and restrictive pulmonary dysfunction, as well as weakness of muscles of respiration, even among people in relatively early stages of PD.[41–44] Yet to be addressed is whether these compromises relate to the energy cost of walking.

For 2 of the 3 patients, UPDRS total and motor subscale scores were lower (better) than baseline after 4 months of supervised exercise, and scores were still lower than baseline even after 16 months. These findings are consistent with a report of Miyai and colleagues,[45] who observed a nonsignificant trend toward modestly lower UPDRS total scores following body-weight–supported treadmill training (33.3±2.9 at baseline and 27.8±3.2 at 1 month, with worsening scores thereafter). Data of Jankovic and Kapadia[46] predict about a 1.8-point increase (worsening) in UPDRS total score over 16 months. Therefore, the sustained improvements of the magnitudes observed in our 3 patients are of great interest. A recent article[47] suggests a minimal clinically important difference of 5 points for the UPDRS motor subscale and 2 points for the activities-of-daily-living (ADL) subscale. If one accepts these parameters, the differences seen in the motor subscale score for patient 1 and the ADL subscale score for patient 3 easily meet the criteria for clinical relevance. Given the 16-month duration of the exercise program, these changes are particularly relevant, especially in light of the expected *worsening* in scores over that time period.

Although current theories of motor control emphasize that training should be task specific,[48] these 3 individuals demonstrated changes in performance beyond economy of movement. At the end of the 4-month supervised exercise program, all 3 patients demonstrated greater scores than at baseline for physical functional capacity (measured by CS-PFP), FRT, and FAR. Even at 16 months, 2 of the 3 patients also performed better than at baseline on the CS-PFP, FRT, and FAR. These findings are remarkable, considering the fact that the exercise program consisted of only endurance exercise training (mainly on a treadmill or outdoors) and did not include any exercises specifically targeting balance or trunk flexibility. The changes in FRT scores are consistent with the report of Protas and colleagues[49] that gait and step training reduces falls in people who are in H&Y stages 2 and 3.

The third patient declined in performance over the 16 months. It is noteworthy that this patient's disease worsened substantially during the 16 months, as evidenced by increases in both UPDRS total and motor subscale scores (16.5 and 9.5 points, respectively). Given the increase in his UPDRS scores, this individual's physical functional capacity, balance, and task performance might have been expected to decline over the 16-month period, yet they remained relatively stable. In addition, this individual's gait was festinating at baseline; by 4 months, he required many fewer steps to turn, and he continued to be able to turn better at 10 and 16 months. Possibly, this finding is related to the immediate effects of gait training noted by Frenkel-Toledo and colleagues.[50]

One observation that should be considered is that the patients had better CS-PFP scores, but worse scores on the UPDRS ADL subscale. Possibly, these individuals had a greater capacity than they utilized during routine daily activity. An alternate explanation for the discrepancy is that the UPDRS ADL subscale includes 8/13 items related to functions such as eating, swallowing, fine motor control, and tremor, none of which would be expected to respond to aerobic conditioning exercises. These items were the main source of decline for patients 1 and 3. Patient 2, whose UPDRS scores suggested progressing disease, had equal decline for the related and nonrelated items of the ADL subscale.

One of the strengths of the training program is that strategies were in place from the beginning of the supervised exercise program to assist the patients to develop exercise habits. This may be a critical factor in the ability of these individuals to maintain gains and improve over the 16 months of the exercise program.

The case format, including several different patients, has the advantage of illustrating the very different responses of these 3 individuals. On the surface, patient 1 appeared to benefit most from this approach to exercise. Patient 2 showed functional decline during the 16 months, and patient 3 was in very good condition at the start of the exercise program and did not have as much room for improvement as the other 2 individuals. However, it is difficult to draw any conclusions regarding the benefits for the 3 patients for the following reason: We cannot know what would have happened to these individuals had they not participated in the program. Possibly, patient 2 would have experienced much faster functional decline and would have been at H&Y stage 4 (functionally dependent) had he not participated in the aerobic program. Similarly, it is possible that patient 3 would have begun to show functional decline as well. Indeed, there is some evidence from animal studies[51,52] suggesting that exercise may play a neuroprotective role for individuals with PD. Without large, definitive studies, it is not possible to speculate on the long-term benefits of endurance exercise training for individuals at different levels of dysfunction associated with PD.

Several limitations should be considered when interpreting these data. Most importantly, these are simply case descriptions. Changes in these 3 individuals could have been due to a variety of factors. Possibly, the improvements represent improvements in test performance, although the tests were 4 to 6 months apart, which argues against this interpretation. Possibly, the changes noted were due to usual day-to-day variation for these 3 patients, although it should be noted that the trends in the repeated measures were fairly consistent in the direction of improvement for patients 1 and 3. Furthermore, it is unknown to what extent these findings will generalize to other individuals in the early and middle stages of PD. These 3 individuals were in early to middle stages of PD and highly motivated, which may have contributed to their reported adherence, even after completing the supervised part of the program.

We cannot determine whether these 3 individuals exercised at their target heart rates from months 5 to 16. Each patient was instructed in monitoring HR and in increasing speed or grade as necessary to stay in the target range. However, the 3 individuals were not adherent in recording their HR during each exercise session.

Finally, patient 1, who showed the greatest differences across all measures, also had an increase in levodopa during the study. Possibly, the increased levodopa equivalent accounted for the observed scores for this individual. A number of factors argue against this being the only cause of the observed changes.

First, this individual demonstrated changes suggestive of improvement across many measures at 4 months, prior to the change in levodopa. Second, all of the patients were assessed at entry to the exercise program for optimal treatment; the expected change in UPDRS score is about a 1.8-point *increase* (indicating decline in function) as opposed to the observed 15-point *decrease* observed for patient 1. It is unlikely that the 15-point decrease in UPDRS score was solely due to medication changes. Finally, the third individual showed similar (although less dramatic) decreases across the 16 months of the exercise program, without any change in levodopa equivalent during the 16 months.

In summary, these 3 cases suggest that aerobic conditioning may be beneficial for individuals with mild to moderate PD. Outcomes emphasize the potential importance of examining aerobic conditioning exercises in a clinical trial as well as the importance of determining the characteristics of individuals with PD that predict good outcomes from this type of exercise. Outcomes also suggest some areas of study to better understand the mechanisms underlying the reduced economy of movement of individuals who have PD. At this time, clinicians have relatively limited information from which to determine the best approach to exercise for people in the early to middle stages of PD. Although outcomes from case series are necessarily limited, clinicians can take into consideration information from these 3 individuals as they develop exercise programs for specific patients who have PD.

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