Published in final edited form as:

Mov Disord. 2009 July 30; 24(10): 1481–1487. doi:10.1002/mds.22621.

Walking economy in people with Parkinson's disease

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Abstract

Gait dysfunction is an early problem identified by patients with Parkinson's disease (PD). Alterations in gait may result in an increase in the energy cost of walking (i.e., walking economy). The purpose of this study was to determine whether walking economy is atypical in patients with PD when compared with healthy controls. A secondary purpose was to evaluate the associations of age, sex, and level of disease severity with walking economy in patients with PD. The rate of oxygen consumption (VO_2) and other responses to treadmill walking were compared in 90 patients (64.4 ± 10.3 yr) and 44 controls (64.6 ± 7.3 yr) at several walking speeds. Pearson correlation coefficients (r) were calculated to determine relationships of age, sex, and disease state with walking economy in PD patients. Walking economy was significantly worse in PD patients than in controls at all speeds above 1.0 mph. Across all speeds, VO_2 was 6 to 10% higher in PD patients. Heart rate, minute ventilation, respiratory exchange ratio, and rating of perceived exertion were correspondingly elevated. No significant relationship of age, sex, or UPDRS score with VO_2

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was found for patients with PD. The findings suggest that the physiologic stress of daily physical activities is increased in patients with early to mid-stage PD, and this may contribute to the elevated level of fatigue that is characteristic of PD.

Keywords

energy expenditure; gait; Parkinson's disease; walking economy

INTRODUCTION

Gait dysfunction is a characteristic problem of Parkinson's disease (PD) and one of the earliest functional limitations identified by patients.¹ Changes in gait, such as decreased speed, decreased stride rate, and increased variability in stride length are evident in early stages of PD.^{2, 3} In addition, PD-related gait dysfunction is linked to perceived low quality of life.^{4, 5}

Walking economy, defined as the steady-state aerobic demand for a given submaximal speed of walking,⁶ is abnormal in some neurological and orthopedic disorders.⁷ Increased energy expenditure during walking (i.e., poor economy) has been linked to such conditions as stroke⁸, spinal cord injury⁹, amputation¹⁰, and cerebral palsy.¹¹ In men with PD, there was a trend for the energy cost of cycling to be increased relative to healthy age- and sex-matched controls.¹² The finding that energy expenditure was increased during cycling activity led us to the hypothesis that walking economy may also be impaired for patients with PD. If true, interventions targeted to improve economy would be indicated to limit patient fatigue during daily activity. However, to our knowledge, no studies have determined whether the energy cost of walking is increased in patients with PD. Therefore, the purpose of this study was to assess walking economy in patients with PD and healthy individuals of similar age and sex distribution. A secondary purpose was to evaluate the associations of age, sex, and level of disease severity with walking economy in patients with PD.

PATIENTS AND METHODS

Patients

The PD patients were participants in a randomized controlled trial of exercise training and functional ability. The current study was focused on walking economy at baseline, before the initiation of the exercise intervention. Healthy, women and men served as controls (HC). The Colorado Multiple Institutional Review Board approved the study, and volunteers provided written informed consent to participate.

PD patients were recruited through local neurology clinics, PD support groups, newspaper advertisements, churches, and word of mouth. Volunteers underwent screening via phone interview, personal interview, neurologist examination, blood testing, and a submaximal graded exercise stress test. Diagnosis of PD was verified by a neurologist using the UK Brain Bank criteria.¹³ Volunteers in stages 1.5 to 3 using the modified Hoehn and Yahr scale¹⁴ were enrolled. Patients were excluded if they had on-state freezing, uncontrolled hypertension, or limited exercise capacity based on musculoskeletal, neuromuscular (other than PD), or cardiovascular disorders.

Control subjects were recruited from the community through newspaper advertisements and word of mouth. Volunteers were recruited with the intent of having a group similar in age (50 to 80 years) and sex to the PD group. Volunteers were excluded if they had limited exercise capacity based on musculoskeletal, neuromuscular, or cardiovascular disorders.

Walking Economy

Walking economy was determined by measuring rate of oxygen consumption (VO_2) by indirect calorimetry (TruMax 2400, ParvoMedics, Sandy, UT) at rest and during treadmill walking at 4 speeds (more in some PD patients), separated by 0.5 mph increments; the range of walking speeds among participants was 0.8 to 4.0 mph. After a 5-minute sitting rest period, participants walked for 5 minutes at each of the 4 speeds. For PD patients, the selected speeds were based on the maximum walking speed obtained during the -screening graded exercise test; participants were advanced to additional stages if they felt capable of walking faster. For the HC group, maximum walking speed ranged from 2.5 to 3.5 mph, based on individual preference.

Treadmill belt speed was timed near the midpoint of each stage to verify walking speed. Measurements of VO_2 , rate of carbon dioxide production (VCO_2), minute ventilation (VE), and respiratory exchange ratio (RER) were recorded every 30 s and averaged across the last 2 minutes of each stage. Heart rate (HR) was measured using an electronic heart rate monitor (Polar Electro Inc., Lake Success, NY) and averaged across the last 2 minutes of each stage. Participants provided a rating of perceived exertion (RPE)¹⁵, using a scale posted in front of the treadmill, at the end of each walking stage.

Factors Associated with Walking Economy

Age, sex, and level of disease severity were examined as potential covariates of walking economy in the PD group. Score on the Unified Parkinson's Disease Rating Scale (UPDRS)¹⁴ 16 (total of Parts I, II, and III) served as the measure of disease severity. The UPDRS was performed by the same trained tester in all participants within one week of the walking economy test.

Statistical Analyses

Because plots of outcome variables suggested normal distributions, no transformations were applied. Baseline characteristics of the two groups were compared by 2-group *t* tests or likelihood ratio chi square tests for independent proportions, as appropriate. A general linear mixed model approach¹⁷ was used to model VO_2 curves over time for the two groups. A general linear mixed model with an unstructured covariance matrix and pre-planned contrasts at each stage was used to compare HC and PD patients on VO_2 , HR, RER, VE, VE/VO_2 , and RPE. Tukey's adjustment was made for multiple comparisons across stage, with level of significance set at $\alpha = 0.05$. Pearson correlations were used to compare age and UPDRS score (PD patients only) with VO_2 at 2.5 mph for PD patients and healthy controls separately; this speed was selected for its relevance to the question of interest. Sex differences were compared using a 2-group *t* test. General linear mixed models were used to estimate the association of the pre-determined covariates (age, sex, and UPDRS score) on VO_2 over all walking stages.

RESULTS

Baseline Characteristics

PD patients and controls were comparable in age, sex distribution, and anthropometric measures (Table 1). Resting HR, VE, and VE/VO_2 were significantly higher in PD patients than in controls. The duration of disease in PD patients was 4.8 ± 4.1 years (mean $\pm$ SD). The Hoehn & Yahr and UPDRS score averages were 2.3 ± 0.4 and 33.6 ± 14.4 , respectively.

Walking Economy

As expected, VO_2 increased linearly with increasing walking speed in both groups (Figure 1). However, PD patients had a steeper increase in VO_2 than controls across all walking speeds (estimated slope $\pm$ SE; 3.32 ± 0.07 versus 2.77 ± 0.09 , $p < 0.001$). Even when walking speed was restricted to 1 to 3.5 mph (the range of speeds for which data were available on control subjects), PD patients had a steeper increase in VO_2 (3.37 ± 0.12 versus 2.90 ± 0.16 , $p=0.02$).

Because VO_2 curves were not purely linear, a general linear mixed model approach suggested by Cnaan et al.¹⁷ was used to model the curves. Using this approach, resting VO_2 was the same for the two groups, but VO_2 was higher in PD patients than in controls at all walking speeds equal to and greater than 1.5 mph (Table 2).

The analyses described above were conducted using total exercise VO_2 . The results remained the same when the analyses were conducted using the net increase in VO_2 attributable to walking (i.e., VO_2 at each stage minus resting VO_2). Commensurate with the higher VO_2 values during walking, other exercise responses (i.e., HR, V_E/VO_2 , RER, and RPE) also tended to be higher in PD patients than in controls (Table 2).

Factors Associated with Walking Economy

Among PD patients, neither age nor UPDRS was correlated with VO_2 at 2.5 mph; VO_2 was not significantly different by sex. Women in the HC group had lower VO_2 values than men (10.8 ± 0.7 vs. 11.9 ± 1.6 , $p=0.003$); there was no significant correlation between age and VO_2 among controls. Table 3 presents the associations of each covariate with VO_2 based on the general linear mixed model for the PD patients.

DISCUSSION

The major finding of this study was that walking economy was worse in PD patients than in healthy control subjects. The higher VO_2 during walking in PD patients was not explained by differences in resting VO_2 . Commensurate with elevated VO_2 during walking, PD patients also tended to have higher HR, V_E/VO_2 , RER, and RPE responses to exercise than control subjects.

The possibility that energy cost of movement may be adversely influenced by PD has received little attention. Protas and colleagues¹² studied 8 men with PD and 7 healthy men during lower-extremity cycling exercise. There were no significant differences in peak aerobic power ($\text{VO}_{2\text{max}}$) between the groups, but PD patients achieved $\text{VO}_{2\text{max}}$ at significantly lower power outputs than control subjects. Although the investigators did not provide statistical comparisons of VO_2 during submaximal cycling, graphic illustrations of data suggested submaximal VO_2 was approximately 15–25% higher in PD patients than in controls. That observation is consistent with an adverse effect of PD on economy of movement. In a follow-up study, Protas and colleagues¹⁸ confirmed their previous observation that men with PD achieved the same $\text{VO}_{2\text{max}}$ as healthy men, but at a lower power output. However, in a small group ($N=7$) of female patients, responses were not different from those of control subjects.

To our knowledge, the current study was the first to determine whether walking economy is adversely affected by PD. Our finding that VO_2 during walking was higher in both female and male PD patients than in controls across a range of submaximal walking speeds was consistent with the previous observations that men with PD achieved the same VO_2 peak level as controls at a lower power output.^{12, 18} During walking, PD patients expended from 6 to 10% more energy than control participants, with increasing disparity at faster walking

speeds. Thus, patients with PD increase energy expenditure more for a given increase in walking speed than do healthy adults.

Difficulty with walking is experienced by most people with PD.³ Alterations in walking performance, such as increased stride length variability and reduced gait speed, are common even in early stages of the disease.² 19 The poor gait economy we observed may result from a culmination of changes related to the cardinal PD motor symptoms of tremor, rigidity, hypokinesia, and postural instability. These characteristic motor impairments are present early in the disease process and progress rapidly.²⁰ It is possible that early changes in motor symptoms are reflected by worsened gait economy even when gait function is not dramatically altered.

Tremor, which is most prominent during rest in people with PD, may influence walking economy for people in early stages of PD. The lack of difference in VO_2 at rest between the PD and HC groups in the current study suggests that tremor did not contribute to the observed differences in the energy cost of walking. However, tremor has been shown in other studies to contribute to increased resting energy expenditure as the disease progresses. Investigations of people with advanced PD symptoms have demonstrated increased resting energy expenditure.²¹ 22 For example, Markus and colleagues²² reported resting energy expenditure levels 22% greater in individuals with PD (Hoehn & Yahr scores of 3–4; $N=11$) than control participants. Although data regarding tremor were not presented, energy expenditure was significantly higher when patients were off antiparkinsonian medications. The participants in our study were in relatively early stages of PD and on medication at the time of testing. It is possible that the differences we observed in walking economy between PD patients and controls become even greater with disease progression as a result of tremor.

Although tremor is most common at rest, rigidity, hypokinesia, and postural instability are directly involved during movement. Key predictors of walking economy, such as stride spatiotemporal parameters²³, can be influenced by these factors. It has been noted that altered regulation of step length is the fundamental deficit in gait hypokinesia²⁴ and reductions in step length occur at early stages of PD.¹⁹ Alterations in stride length are known to influence walking economy in healthy individuals.²³ Because gait analyses were not performed in the current study, the associations of abnormal gait patterns with walking economy could not be assessed.

Postural instability of PD has been related to increased muscle co-activation.²⁵ Dimitrova and colleagues²⁵ demonstrated that PD patients (Hoehn & Yahr scores 2.8 ± 0.3) had greater magnitudes of muscle activity during tasks challenging postural stability than healthy control subjects. It has been suggested that increased co-activation of agonist and antagonist muscle groups occurs with aging and can lead to poor walking economy in older adults.²⁶ Thus, it is possible that the increased level of co-activation in people with PD adversely affects walking economy.

A problem related to rigidity and hypokinesia for people with PD is pulmonary dysfunction.²⁷ 28 PD progression is characterized by decreased upper airway and chest wall compliance.²⁷ In addition, respiratory muscle strength in people with PD has been shown to be significantly less than in age-matched controls.²⁹ For the PD group, V_E/VO_2 tended to be higher than in controls during walking, indicating excess ventilation relative to the level of energy expenditure. It is not clear why ventilation during exercise would be increased in PD patients, but the additional energy required to support higher ventilatory rates could have contributed to the higher VO_2 levels during walking in PD patients. However, the differences in V_E of only 5–6 L/min would likely have had only a minimal impact on VO_2 (~ 0.1 mL/min/kg).³⁰ It has also been shown that pulmonary dysfunction in PD results in

ventilatory inefficiency (i.e., greater respiratory muscle energy expenditure).²⁸ Thus, factors such as decreased airway and chest wall compliance could increase the work of breathing, thereby increasing the total energy cost of walking.

Along with the factors listed above, other PD-related physiologic impairments may contribute to poor walking economy, including altered mitochondrial and autonomic nervous system functions. Mitochondrial energy production in the substantia nigra is known to be impaired in people with PD.³¹ If mitochondrial dysfunction is also present in skeletal muscles, which is currently not clearly understood,³² a link to energy expenditure during walking is possible. In addition, autonomic dysfunction^{33, 34} and, specifically, cardiac sympathetic denervation³⁵ is present in patients with PD. Changes in cardiovascular responses to exercise have been linked to functional consequences such as shortness of breath and tendency to fatigue during activity.³⁴ Such changes in breathing and level of fatigue may be related to the poor walking economy observed in this study.

Evaluation of age, sex, and level of disease severity in relation to walking economy in patients with PD revealed no significant associations. Based on the PD-related movement disorders discussed above, it was expected that walking economy would be associated with disease severity. However, the expected relationship between UPDRS score, an indicator of disease severity, and VO_2 was not statistically significant. Homogeneity of the PD group (restricted to Hoehn and Yahr scale scores of 1.5–3) may have limited the ability to assess this association. In addition, the relatively narrow age range of participants in the study may have limited the ability to assess the influence of age on walking economy.

Limitations

When interpreting the results of this study, several limitations must be considered. The study was designed to determine whether walking economy is atypical in patients with PD, not to identify underlying mechanisms. Further research will be necessary to understand the role of such factors as rigidity, muscle co-activation, ventilatory dysfunction, muscle mitochondrial function, and autonomic function.

The influence of treadmill compared to overground walking on economy of people with PD is not known. For healthy individuals, kinematic and kinetic measures walking overground compared to on a treadmill are similar.³⁶ However, it is known that people with PD walk with less temporal variability on a treadmill compared to overground.³⁷ If stride variability is related to poor walking economy, the measurement of economy on a treadmill may underestimate the magnitude of the impairment during community walking for people with PD.

Upper extremity activity during economy testing was not controlled in this study. Both HC and PD patients were allowed to use treadmill handrails for support, although they were encouraged to touch the rails only lightly. Frenkel-Toledo and colleagues²³ have previously examined the influence of upper extremity support during overground walking for patients with PD. They found that patients with PD walk with slightly shorter stride lengths, but similar stride variability when comparing upper extremity use (using a walker) to no support. Future examination of controlled upper extremity support will be needed to determine if this is a relatively greater factor for economy of treadmill walking in people with PD compared to healthy individuals.

Finally, among PD patients, 14% were using negative chronotropic medications and 11% were using angiotensin converting enzyme inhibitors. Use of cardiac-related medications by HC subjects was not determined. Martin and colleagues³⁸ examined a group of hypertensive men and demonstrated no difference between placebo and treatment groups in submaximal

VO₂ after short term use of beta-blocker medications. However, there is evidence that long term use of such medications may influence metabolic responses during walking.^{39, 40} For example; Witte and colleagues⁴⁰ studied individuals with congestive heart failure and found 12 months of beta-blocker usage to be linked to decreased submaximal VO₂ during treadmill walking. In our study, differences in walking economy between groups may have been minimized if more PD patients than controls were using negative chronotropic medications. Future research should account for the influence of cardiac medications.

Clinical Implications

The major finding of this study was that patients with PD have poor walking economy when compared to similarly aged healthy adults. Although maximal aerobic power (VO₂max) was not measured, previous studies have demonstrated that VO₂max is normal in patients with PD.^{12, 18} If true, the impairment in walking economy means that relative intensity of walking (i.e., percent of VO₂max) is higher for PD patients than for controls and could contribute to excess fatigue. Our findings suggest a need for targeted interventions to improve walking economy and decrease PD-related movement dysfunction. The clinical importance of movement economy in PD is indirectly supported by several studies demonstrating aerobic exercise benefit for people with PD.^{5, 41-45} Building from this study, future work should evaluate mechanisms related to poorer walking economy and the response of walking economy to various interventions.

Acknowledgments

Financial Disclosure: We acknowledge the financial support of NIH (Protocol: # 1 R01 HD043770) for this study.

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Figure 1.
Relationship between rate of oxygen consumption (VO_2) and speed of treadmill walking. Values below the graph indicate the number of participants from each group who walked at each speed. VO_2 , rate of oxygen consumption; PD, Parkinson's disease.

Table 1

Baseline and resting metabolic characteristics of healthy controls (HC) and patients with Parkinson's disease (PD)

Variable	HC (N = 44)	PD (N = 90)	<i>p</i> -value
Age (years)	64.6 ± 7.3	64.4 ± 10.3	0.9174
Sex (% male)	24/44 (54.6%)	60/90 (66.7%)	0.1731
Height (cm)	171.9 ± 10.1	173.2 ± 9.3	0.4860
Body mass (kg)	77.2 ± 12.9	79.6 ± 16.1	0.3790
VO ₂ (mL/min/kg)	3.5 ± 0.5	3.5 ± 0.7	0.9662
Heart rate (beat/min)	68 ± 10	73 ± 11	0.0049
RER	0.85 ± 0.10	0.86 ± 0.11	0.6737
VE (L/min)	10.4 ± 2.7	11.8 ± 2.8	0.0083
VE/VO ₂	32.3 ± 6.0	36.2 ± 8.0	0.0045

Data are mean ± SD, except for sex.

VO₂, resting oxygen consumption; RER, respiratory exchange ration; VE, pulmonary minute ventilation; VE/VO₂, ventilatory equivalent

Table 2

Between group comparison at each speed from repeated measures analysis of primary and secondary outcome variables*

Variable	Gait Speed (mph)	HC	PD	<i>p</i> -value [†]
VO ₂ (ml/min/kg)	1.0	8.1 ± 0.3	8.6 ± 0.2	0.1551
	1.5	9.1 ± 0.3	9.8 ± 0.2	0.0266
	2.0	10.0 ± 0.3	11.0 ± 0.2	0.0011
	2.5	11.4 ± 0.3	12.4 ± 0.2	0.0037
	3.0	13.2 ± 0.3	14.4 ± 0.2	0.0036
	3.5	15.3 ± 0.4	16.7 ± 0.3	0.0061
Heart Rate (beats/min)	1.0	80 ± 2	86 ± 1	0.0176
	1.5	82 ± 2	89 ± 1	0.0129
	2.0	85 ± 2	92 ± 1	0.0036
	2.5	90 ± 2	98 ± 1	0.0013
	3.0	98 ± 2	104 ± 2	0.0218
	3.5	106 ± 3	115 ± 2	0.0088
RER	1.0	0.77 ± 0.01	0.79 ± 0.01	0.1614
	1.5	0.82 ± 0.01	0.83 ± 0.01	0.3779
	2.0	0.83 ± 0.01	0.86 ± 0.01	0.0318
	2.5	0.85 ± 0.01	0.88 ± 0.01	0.0033
	3.0	0.87 ± 0.01	0.90 ± 0.01	0.0052
	3.5	0.89 ± 0.01	0.93 ± 0.01	0.0005
VE (L/min)	1.0	17.8 ± 0.9	21.1 ± 0.7	0.0045
	1.5	21.1 ± 0.9	24.1 ± 0.6	0.0065
	2.0	22.8 ± 1.0	27.0 ± 0.7	0.0006
	2.5	26.1 ± 1.1	31.0 ± 0.8	0.0005
	3.0	30.3 ± 1.5	36.8 ± 0.9	0.0002
	3.5	35.7 ± 1.8	43.5 ± 1.2	0.0005
VE/VO ₂	1.0	24.3 ± 0.7	26.3 ± 0.5	0.0201
	1.5	25.2 ± 0.6	26.5 ± 0.4	0.0956

Variable	Gait Speed (mph)	HC	PD	<i>p</i> -value [†]
	2.0	25.0 ± 0.6	26.6 ± 0.4	0.0253
	2.5	24.9 ± 0.6	26.6 ± 0.3	0.0141
	3.0	25.0 ± 0.6	27.0 ± 0.4	0.0059
	3.5	25.5 ± 0.6	27.6 ± 0.4	0.0050
RPE	1.0	0.8 ± 0.2	0.8 ± 0.2	0.9565
	1.5	1.1 ± 0.2	1.4 ± 0.1	0.1893
	2.0	1.5 ± 0.2	2.0 ± 0.1	0.0359
	2.5	2.0 ± 0.2	2.7 ± 0.2	0.0112
	3.0	2.5 ± 0.3	3.5 ± 0.2	0.0022
	3.5	3.4 ± 0.3	4.4 ± 0.2	0.0013

* Data shown are means ± SD unless otherwise stated.

[†]The *p*-values reflect Tukey's adjustment for multiple comparisons across stage. VO₂, rate of oxygen consumption; RER, respiratory exchange ratio; VE, minute ventilation; VE/VO₂, ventilatory equivalent ratio for oxygen; RPE, rating of perceived exertion.

Table 3Regression of VO₂/kg on age, sex, UPDRS score controlling for stage (speed) in a linear mixed model

Effect	β estimate	SE	<i>p</i> -value
Age	0.03	0.02	0.13
Female	0.46	0.37	0.22
UPDRS	0.02	0.01	0.14
Stage	3.68	0.05	<.0001

UPDRS, Unified Parkinson's Disease Rating Scale.