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Oxygen cost of over-ground walking in persons with mild-to-moderate Parkinson's disease

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Abstract

Background—Oxygen (O₂) cost of walking is a physiological marker of walking dysfunction and reflects the amount of O₂ consumed per kilogram of body weight per unit distance walked. The onset of walking dysfunction (i.e., reduced walking speed and shorter stride length) is commonly observed in Parkinson's disease (PD), even in the early stages of the disease. However, the O₂ cost of walking has not been assessed in persons with PD.

Research question—Does O₂ cost of walking differ between persons with PD and controls matched by age and sex?

Methods—The sample included 31 persons with mild-to-moderate PD (Hoehn and Yahr stages 2–3) and 31 age- and sex-matched controls in this cross-sectional study. O₂ consumption (VO₂) was measured using a portable indirect calorimetry system during a 6-minute period of over-ground walking at a normal comfortable speed, and the O₂ cost of walking was calculated based on the ratio of net relative VO₂ (ml·kg⁻¹·min⁻¹) and speed (m·min⁻¹).

Results—There were no differences in resting VO₂, steady-state VO₂, and over-ground walking speed between persons with PD and controls ($p>0.05$). There was a significant difference in the O₂ cost of walking between persons with PD and healthy controls ($p<0.01$) such that persons with PD

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had a higher O_2 cost of walking. The mean(SD) O_2 cost of walking for persons with PD was $0.179(0.038) \text{ ml}\cdot\text{kg}^{-1}\cdot\text{m}^{-1}$, and the O_2 cost of walking for healthy controls was $0.153(0.024) \text{ ml}\cdot\text{kg}^{-1}\cdot\text{m}^{-1}$.

Significance—Persons with PD demonstrated a higher O_2 cost of walking compared with controls, and this may reflect worse walking economy in PD. The possibility of worse walking economy under free-living conditions may result in reduced community ambulation and participation.

Keywords

Parkinson's disease; energy expenditure; walking; rehabilitation

Parkinson's disease (PD) is a neurodegenerative disease of the central nervous system with an estimated prevalence of 1 million adults in the United States [1]. One hallmark feature of this disease involves declines in mobility. The onset of walking dysfunction, in particular, is a common manifestation of PD that is present even in the early stages of the disease (i.e., Hoehn and Yahr stages 2–3) [2].

One relatively unstudied manifestation of walking dysfunction in PD is the oxygen (O_2) cost of walking. The O_2 cost of walking is an indicator of walking economy and reflects the amount of oxygen consumed (VO_2) per kilogram of body weight per unit distance traveled [3]. The O_2 cost of walking is an important metric of walking dysfunction, as it is a physiological marker associated with pathological gait abnormalities and other manifestations of neurological diseases [3]. Based on previous research in multiple sclerosis, the O_2 cost of walking is associated with neurological disability, inactivity, and fatigue [4,5]; we would expect similar associations in PD. The O_2 cost of walking is further associated with body composition, health and well-being [6]. Overall, this supports the examination of O_2 cost of walking in persons with PD who have mild-to-moderate disability.

We located two studies that compared O_2 cost of walking between persons with PD and controls. One study reported no significant difference between persons with PD and controls in O_2 cost of walking during over-ground walking [7]. However, the controls were matched by age, but not sex, and the study included a small sample for examining group differences in O_2 cost of walking. Another study reported higher O_2 cost of walking, or worse walking economy, in persons with PD than age- and sex-matched controls across increasing treadmill speeds [8]. However, the study did not assess O_2 cost of over-ground walking performed during normal comfortable walking speed. This is important, given that over-ground walking might involve different gait mechanics than treadmill walking, and self-selected, normal pacing more closely reflects walking economy during everyday, free-living walking [4,9].

The present study examined the O_2 cost of over-ground walking at self-selected speed in persons with PD and controls. The study further examined the possible associations among O_2 cost of walking, stride length, and cadence in persons with PD based on observations of associations in multiple sclerosis [10]. We expected slower walking speeds, but higher VO_2 , in persons with PD compared with controls, and that such differences would result in elevated O_2 cost of walking in persons with PD compared with controls. We further

hypothesized that persons with PD who had worse gait alterations would demonstrate a higher O_2 cost of walking based on previous research [11].

Methods

Participants

Persons with PD were recruited through support groups, local clinics, and community events through the distribution of flyers. The inclusion criteria for persons with PD were the following: (1) diagnosis of idiopathic PD, defined as the presence of bradykinesia and rigidity and/or resting tremor; (2) age 50–74 years; (3) Hoehn and Yahr stage 2–3; and (4) ability to walk independently without the use of an assistive device. Persons with PD were assessed when they had taken their medications for symptom management (i.e., levodopa). Persons with PD were excluded from the study if they (1) were not responsive to dopaminergic medications or (2) had motor impairments due to neuroleptic medication or multiple strokes.

The controls were recruited from community events through distribution of flyers and word-of-mouth and met the following additional inclusion criteria: (1) age 50–74 years; (2) apparently healthy characterized by the absence of major cardiovascular, neuromuscular, and/or pulmonary disease; and (3) ability to walk independently without an assistive device. We matched persons with PD and controls by age (within 5 years) and sex based on previous research in multiple sclerosis [4]. Persons with PD and controls were excluded from the study based on the presence of any medication or medical condition that is known to influence metabolism (e.g., diabetes).

Measures

O_2 cost of walking was measured by a portable indirect calorimetry system (OXYCON Mobile) that was calibrated based on the manufacturer's recommendations before all testing sessions. The device is accurate when calibrated before data collection, and the measurement of VO_2 should be no different in PD than any other population [12,13]. We calculated the O_2 cost of walking based on the ratio of net relative O_2 consumption (VO_2 ; $ml \cdot kg^{-1} \cdot min^{-1}$) and speed ($m \cdot min^{-1}$) [3]. We measured VO_2 during a 5-minute period of seated rest and then as 30-second averages throughout the 6-minute walking bout. Participants were instructed to perform one 6-minute bout of over-ground walking with a normal comfortable pace. We measured net steady-state VO_2 as the difference between average VO_2 during the last three minutes of the 6-minute bout and average resting VO_2 . Steady-state VO_2 was determined from the last three minutes of the 6-minute walk when the differences in VO_2 varied less than $3 ml \cdot kg^{-1} \cdot min^{-1}$, based on criteria from previous research on oxygen kinetics [3,4,10]. Walking speed was calculated by dividing the distance walked in meters over the 6-minute period by 6, and we expressed walking speed as $m \cdot min^{-1}$. To measure distance accurately, one member of the research team used a distance-measuring wheel (Stanley MW50, New Briton) when following directly behind the participant during the walking bout. The O_2 cost of walking was then expressed as $ml \cdot kg^{-1} \cdot m^{-1}$ by dividing net steady-state VO_2 by walking speed (steady-state VO_2 –resting VO_2)/speed).

Demographic and clinical information included age, sex, height, and weight. Body mass index was calculated based on height and weight. Participants with PD provided the number diagnosed with PD. The Hoehn and Yahr scale was used to assess the stage of PD. Motor symptoms were assessed using the Movement Disorder Society version of the Motor Examination of the Unified Parkinson's Disease Scale Rating (MDS-UPDRS ME) [14]. Both assessments were administered by two research team members who completed the UPDRS training.

We computed stride length and cadence using the manual recordings of strides taken during the 6-minute walking bout. Manual counting using a hand-tally device is commonly included as a criterion compared against other methods of recording steps, as it is considered an accurate and direct measure of steps taken [15]. We ensured accuracy through extensive training of the personnel and began data collection only when all personnel could accurately count steps with 99% accuracy during practice sessions of over-ground walking. We further had one person whose entire role during the protocol involved counting steps using the hand-tally counter. Stride length was calculated based on distance in meters divided by number of stride counts and expressed in meters per stride. Cadence was calculated by multiplying manually counted strides by 2 to obtain steps, and then dividing this value by 6 (i.e., length of time of the walking bout) and expressed as $\text{steps} \cdot \text{min}^{-1}$ [16].

Procedure

The study procedure was approved by the University Institutional Review Board. All data were collected in the laboratory on a single visit, and all participants provided written informed consent. Participants provided demographic and clinical information, and then completed the Physical Activity Readiness Questionnaire [17] and underwent a measure of resting blood pressure for identifying additional contraindications for engaging in exercise. Participants with PD underwent the Hoehn and Yahr scale and the MDS-UPDRS ME. Height and weight were measured using a standard scale and stadiometer. The participants were then fitted with the portable metabolic system and had a 5-minute rest for the measurement of resting metabolic rate. The participants then completed the 6-minute walking bout at normal comfortable pace.

Statistical Analysis

All analyses were performed using SPSS, version 25.0. Descriptive statistics are presented as mean(SD), unless otherwise stated. We conducted a 2×12 mixed-factor ANOVA on VO_2 across the 12, 30-second time points between groups (PD and controls). We further conducted independent samples *t*-test for walking speed, stride length, cadence, distance, resting VO_2 , steady-state VO_2 , and O_2 cost of walking between groups. Effect sizes estimates based on Cohen's *d* were delineated as small, medium, and large based on 0.2, 0.5, and 0.8, respectively [18]. We lastly conducted Pearson product-moment correlations among O_2 cost of walking, stride length, and cadence. Values for correlation coefficients were interpreted as small, moderate, and large based on 0.1, 0.3, and 0.5, respectively [18].

Results

Descriptive characteristics of the sample with PD ($n=31$), and controls ($n=31$) are presented in Table 1. There were no differences between groups in age, sex, height, and weight. The persons with PD had a mean disease duration of 6.5(5.2) years and a median(interquartile range) MDS-UPDRS ME score of 21(28); this value is considered as mild-to-moderate disability severity [19].

The VO_2 values per 30-second interval over the 6-minute walking bout in the samples with PD and controls are depicted in Figure 1. Both groups demonstrated a steep increase in VO_2 when starting the walking bout, and then achieved and maintained steady-state VO_2 in the last three minutes of the bout. The two-way mixed-factor ANOVA indicated a significant main effect of time on VO_2 ($F=152.1, p<0.01, \eta_p^2=0.72$), but no main effect of group ($F=1.2, p>0.05, \eta_p^2=0.02$) or interaction of

The values of walking speed, distance, resting and steady-state VO_2 , and O_2 cost of walking for the subsamples of PD and controls and the effect sizes are provided in Table 2. There were no significant differences in walking speed, distance walked, and resting or steady-state VO_2 between groups ($p>0.05$). There was a significant and large ($p<0.01, d=0.79$) difference in the O_2 cost of walking between groups, such that persons with PD had a higher O_2 cost of walking than controls.

The values of gait parameters for the overall sample and the subsamples and the effect sizes are provided in Table 2. There was a significant and moderate ($p<0.05, d=0.64$) difference in stride length between groups, such that persons with PD had a shorter stride length. The bivariate correlations between gait parameters and O_2 cost of walking in the overall sample and the subsamples are provided in Table 3. In the sample with PD, stride length ($r=-0.40, p<0.05$), but not cadence ($r=-0.08, p>0.05$), was associated with O_2 cost of walking, whereas neither stride length ($r=-0.07, p>0.05$) nor cadence ($r=-0.34, p>0.05$) were associated with O_2 cost of walking in the controls.

Discussion

The study examined the O_2 cost of walking of over-ground walking at normal comfortable pace between persons with PD and controls. Our results indicated no significant differences in walking speed and distance walked between the two groups; however, there was a trend, such that persons with PD had a slower walking speed and walked a shorter distance than controls. Of note, persons with PD had taken symptom-managing medications such as levodopa. Importantly, persons with PD demonstrated a higher O_2 cost of walking than controls; this reflects worse walking economy in PD. Stride length, but not cadence, was associated with O_2 cost of walking in persons with PD. Overall, these findings suggest that persons with PD may have worse walking economy under free-living conditions than controls, and this might be associated with PD-related reductions in stride length (i.e., gait abnormalities).

These results indicated that persons with PD and controls have similar metabolic rates while resting and walking at normal comfortable pace, consistent with previous research using

similar preparations for measuring VO_2 [7,8]. For example, one study reported no difference in resting VO_2 between persons with PD and controls [8]; the resting VO_2 for persons with PD and controls in our sample were $3.5(0.9)$ and $3.5(0.7) \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ (i.e., one metabolic equivalent of rest is $3.5 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$), respectively. Another study reported no difference in values of steady-state VO_2 from the last two minutes of a 5-minute over-ground walking bout at normal comfortable pace between persons with PD and controls [7]. Our sample of persons with PD and controls demonstrated values of 11.1 and $10.1 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$, respectively. To that end, it is not surprising that our analyses did not identify a statistically significant difference in VO_2 between groups when walking over-ground at normal comfortable pace, as aerobic capacity of persons with mild-to-moderate PD may not differ significantly from controls until the later or more severe stages of PD [20,21].

This study is the one of the few that examined the O_2 cost of walking between persons with PD and controls. To date, we are aware of two studies that examined the O_2 cost of treadmill and over-ground walking in persons with PD and controls. One study reported significantly higher values of VO_2 during treadmill walking at fast speeds in persons with PD compared with age- and sex-matched controls; this suggests worse walking economy in those with PD compared with controls when walking at increasingly faster speeds on the treadmill [8]. Another study reported that persons with PD and age-matched controls demonstrated similar values of O_2 cost of over-ground walking [7], whereas our sample with PD demonstrated a significantly higher value of O_2 cost of walking compared with age- and sex-matched controls. However, the aforementioned study was underpowered and did not match controls with persons with PD by sex. Although VO_2 and comfortable walking speed did not significantly differ between the groups, the significant difference in O_2 cost of walking might be driven by the combined slight increase in VO_2 and slower walking speed in persons with PD and other factors. Factors that may contribute toward higher O_2 cost of walking include gait impairments, as these may interfere with several walking-related daily activities, particularly as the disease transitions from Hoehn and Yahr stage 2 to 3 [2]. Of note, the $0.03 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{m}^{-1}$ difference in O_2 cost of walking between persons with PD and controls is consistent with previous studies, wherein there was a significant difference in O_2 cost of walking (i.e., $0.02 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{m}^{-1}$) between persons with multiple sclerosis and controls [4]. The higher O_2 cost of walking in persons with multiple sclerosis who had minimal disability was associated with worse disability status, gait impairments, daily inactivity, and more severe fatigue [4,5]. Overall, our study extends the previous research in that persons with PD demonstrate worse walking economy during free-living over-ground walking at normal comfortable pace. This underscores the importance of examining possible modifiable correlates of elevated O_2 cost of walking that may inform the design of interventions as an approach for reducing the O_2 cost of walking in PD, as worse walking economy may possibly lead to significant declines in physical activity levels or reduced community participation [6].

Our results indicated that persons with PD demonstrated a shorter stride length when compared with controls. There further was a non-significant trend ($p=0.11$), such that persons with PD further demonstrated a faster cadence than controls. This is consistent with previous research, in that persons with PD often demonstrate altered gait, particularly stride length, even early in the onset of the disease from hypokinesia [11,22]. We have extended

this research by examining the relationship among O₂ cost of walking, stride length, and cadence during walking at normal comfortable speed. If persons with PD were to walk at the same speed as controls, persons with PD may demonstrate reduced step length and faster cadence. Our results indicated a significant association between O₂ cost of walking and stride length and a nearly significant association between O₂ cost of walking and cadence when walking at normal comfortable speed; however, this relationship was not present in controls, suggesting that despite the non-significant difference in VO₂ and walking speed, gait parameters, specifically stride length, might explain this difference in values of O₂ cost of walking. This suggests that persons with PD who have shorter stride length (i.e., worse gait parameters) demonstrate higher values of O₂ cost of walking. This supports the concept that O₂ cost of walking, a physiological marker of walking dysfunction, reflects gait abnormalities in persons with neurological diseases [3]. This might further suggest that interventions should target abnormalities in stride length as an approach for reducing O₂ cost of walking in PD.

There are important limitations of this study. One limitation is the inclusion of persons with PD at Hoehn and Yahr stages of 2–3, limiting the generalizability of our results and may not be representative of the general population of persons with PD. Another limitation is that these observations were made in persons with PD who had taken a dose of medications for symptom management, as persons on “off” periods may elicit a different response during testing. Future research may examine how the O₂ cost of walking may differ between periods of “on” and “off” medications. A potential avenue may involve examining the slope of VO₂ before onset of steady-state kinetics, as a steeper slope of VO₂ may indicate worse walking economy through mechanisms such as inefficient metabolic systems in PD. One limitation is the lack of a guideline for minimal clinically important difference in values for the O₂ cost of walking, and this would be an important direction for future research for determining the amount of difference that may have clinical relevance in the lives of persons with PD. Another limitation of the study is that we did not examine other modifiable correlates or possible consequences (i.e., physical inactivity) of the O₂ cost of walking. One promising avenue for research is to identify the domains of physical fitness (i.e., aerobic capacity, muscular strength, balance) that may be associated with elevated O₂ cost of walking in persons with PD. This may inform the design of exercise programs to reduce the elevated O₂ cost of walking in PD for managing possible consequences.

The present study indicated that persons with PD demonstrated higher O₂ cost of over-ground walking and shorter stride length than controls. The findings of this study highlight the importance of considering O₂ cost of walking as a physiological indicator of walking economy for persons with PD. Our observations also suggest developing interventions that target stride length as an approach to reduce the O₂ cost of walking for improving walking economy in PD.

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Highlights

- Persons with Parkinson's disease had a higher oxygen cost of walking than controls.
- Stride length, but not cadence, was associated with oxygen cost of walking.
- This highlights developing exercise programs to reduce the oxygen cost of walking.
- Interventions may target increasing stride length to improve walking economy.

Figure 1.

Oxygen consumption over the six-minute over-ground walking bout in 31 persons with Parkinson's disease and 31 controls. $\text{VO}_2 = \text{O}_2$ consumption.

Table 1.

Descriptive characteristics of the subsamples of Parkinson's disease (n=31) and healthy controls (n=31).

Characteristic	Parkinson's disease	Controls	<i>p</i> -value
Age (years)	64.3 (6.3)	63.3 (6.9)	0.55
Sex (M:F)	19:12	19:12	1.00
Height (cm)	170.4 (8.5)	173.8 (9.2)	0.12
Weight (kg)	79.9 (16.5)	80.3 (15.7)	0.65
Body mass index	27.5 (4.9)	26.4 (3.3)	0.32
Disease duration (years)	6.5 (5.2)	N/A	N/A
MDS-UPDRS ME	21 (28)	N/A	N/A

Note: MDS-UPDRS ME = Movement Disorder Society-Unified Parkinson's Disease Rating Scale Motor Examination. Data are presented as mean (SD), ratios, and percentages. Only MDS-UPDRS ME is presented as median (interquartile range).

Table 2.

Descriptive statistics for walking speed, stride length, cadence, resting and steady-state VO_2 , and O_2 cost of walking for the subsamples of Parkinson's disease (n=31) and healthy controls (n=31).

Variable	Parkinson's disease	Controls	Cohen's <i>d</i>
Walking speed ($\text{m}\cdot\text{min}^{-1}$)	62.8 (9.4)	66.9 (10.4)	0.41
Stride length (m)	1.20 (0.17)	1.30 (0.14)	0.64
Cadence ($\text{steps}\cdot\text{min}^{-1}$)	104.7 (8.8)	102.9 (8.0)	0.21
Distance (m)	376.9 (56.6)	401.3 (62.6)	0.41
Resting VO_2 ($\text{ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$)	3.5 (0.9)	3.5 (0.7)	0.00
Steady-state VO_2 ($\text{ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$)	11.1 (2.4)	10.2 (1.8)	0.42
O_2 cost ($\text{ml}\cdot\text{kg}^{-1}\cdot\text{m}^{-1}$)	0.178 (0.038)	0.153 (0.024)	0.79

Note: VO_2 = Oxygen consumption. Data are presented as mean (SD).

Table 3.

Bivariate correlations among O₂ cost of walking, stride length, and cadence in the subsamples of Parkinson's disease (n=31) and controls (n=31).

Variable	Parkinson's disease	Controls
Stride length	−0.40 *	−0.07
Cadence	−0.08	−0.34

Note: * indicates $p < 0.05$.