Oxygen Cost of Overground Walking On vs. Off Medication in Individuals with Mild to Moderate Parkinson's Disease

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Abstract

Background

Parkinson disease (PD) is a neurodegenerative disease that results in gait disturbances impacting mobility. A consequence of gait impairments experienced is increased metabolic cost of walking (COW) or worse walking economy. People with PD demonstrate a higher metabolic COW compared to controls. Because the primary pharmacological approach to treating symptoms of PD is dopaminergic medications, the purpose of this study is to determine the effect of dopaminergic medications on metabolic COW and spatiotemporal parameters of gait in people with PD when walking overground.

Methods

Individuals with PD H&Y Stage 2-3 were recruited to participate in a single testing session. Participants completed a 6-Minute Walk Test (6MWT) under two conditions; OFF and ON medication. Walking capacity and metabolic energy expenditure were measured with a COSMED device under each condition.

Results

Individuals demonstrated no significant difference between oxygen COW, spatiotemporal measures of gait, or endurance when comparing ON versus OFF dopaminergic medication.

Discussion

These findings suggest that providers should not rely on medication alone to address quality and efficiency of gait among individuals with PD. Instead, these results highlight the importance of incorporating aerobic exercise and gait training to enhance spatiotemporal parameters of gait and walking economy.

Introduction

Parkinson disease (PD) is a common neurodegenerative disease that results in gait disturbances which significantly impact the individual's functional mobility and independence. Common motor symptoms associated with PD include bradykinesia (slowed movement), hypokinesia (small amplitude movement), rigidity, tremor, and postural instability, all of which can contribute to gait deficits. For example, bradykinesia may contribute to decreased gait speed whereas hypokinesia results in shorter stride lengths, and decreased arm swing. Further, rigidity may contribute to reduced trunk and limb movements, and appear as asymmetry of the upper and lower extremities. [1, 2, 3] These gait impairments are common characteristics of PD and are even present early in the disease progression.[2]

The primary pharmacological approach to treating these symptoms of PD includes the use of dopaminergic medications, which aim to increase dopamine levels in the brain. This medication has a mixed effect regarding the alleviation of gait disturbances commonly experienced by individuals with PD.[4] Dopaminergic medication may be particularly effective in addressing symptoms such as bradykinesia, rigidity, and tremors.[4,5] Consequently, such medication appears to enhance various spatiotemporal aspects of gait (e.g., step length, gait speed) in people with PD by increasing the movement amplitude of the legs, trunk, and arms.[4,5]

A consequence of gait impairments experienced by people with PD is increased metabolic (i.e., oxygen) cost of walking or worse walking economy.[8] Consistent with evidence from other clinical populations with gait disturbances,[9,10] people with mild-to-moderate PD demonstrate a higher metabolic cost of walking during overground walking compared to healthy controls.[8] Increased metabolic cost of walking reduces walking capacity and increases feelings of

fatigue.[12] Because metabolic cost of walking has been associated with spatiotemporal gait impairment,[13] it is not surprising that people with PD exhibit increased oxygen cost of walking. Given that dopaminergic medication can improve spatiotemporal parameters, it is possible that such medication may also influence the metabolic cost of walking.

Unfortunately, there is limited understanding regarding the potential effect of dopaminergic medication on walking economy in people with PD. Prior work either measured metabolic cost without changing medication or changed medication without looking at metabolic cost.[4,5,8] More recent evidence, however, suggests that dopaminergic medication may not influence metabolic cost of walking when walking at a constant speed on a treadmill.[11] However, treadmill walking does not accurately reflect real-world conditions due to participants being unable to modulate their gait speed over time. By allowing participants to self-select and manipulate their gait speed, we may expect additional spatiotemporal changes that may not have occurred during treadmill walking that could impact metabolic cost and increase ecological validity.

Despite the benefits of dopaminergic medication on spatiotemporal parameters of gait, and its potential effect on metabolic cost, the prolonged use of dopaminergic medication is associated with motor complications such as dyskinesia.[6] Dyskinesia is characterized by involuntary, purposeless, and irregular movements and is observed in approximately 30% of people with PD after five years of continuous medication use.[7,8] The increased muscle activity induced with dyskinesia may exaggerate energy expenditure and thus metabolic cost of walking. Consequently, any improvements in metabolic cost observed due to dopaminergic-induced

improvements in spatiotemporal parameters may be mitigated by excessive muscle activity from dyskinesias.

The purpose of the current study is to determine the effect of dopaminergic medications on metabolic cost and gait in people with PD when walking overground. Given that dopaminergic medication positively impacts spatiotemporal parameters of gait in people with PD, we hypothesize that dopaminergic medication will have a beneficial impact on spatiotemporal parameters of gait; therefore, people with PD will exhibit more efficient gait that decreases oxygen consumption.[4,5,8]Additionally, we hypothesize that oxygen consumption will increase in people with PD who exhibit medication induced dyskinesia due to the presence of increased muscle activity.[6,7]

Methods

Participants

We recruited individuals with idiopathic Parkinson disease Hoehn and Yahr Stage 2-3 to participate in a single testing session. Participants were recruited from local physical therapy clinics, local PD support groups, and neurologic clinics. Potential participants were included if they self-reported the ability to ambulate uninterrupted for 10 minutes without therapist assistance, exhibited deficits in gait (e.g., shuffling, shortened strides, freezing, bradykinesia, etc.) based on observational gait analysis, Movement Disorders Society - Unified Parkinson Disease Rating Scale (MDS-UPDRS-III) item 10 $\geq$1 and <3, taking stable doses of orally-administered dopaminergic medication, and age 50-80 years old. Potential participants were excluded if they were receiving concurrent physical therapy, have undergone deep brain

stimulation surgery, cannot walk without therapist assistance, exhibit uncontrolled cardiorespiratory/metabolic disease, or have other neurologic disorders or orthopedic injury that may affect gait. All participants were receiving dopaminergic medication (carbidopa/levodopa). The study was approved by a University Institutional Review Board. Data were collected during a single visit on the University of North Carolina at Chapel Hill campus and all participants signed an informed consent before participating.

Procedure

In this cross-sectional study design, participants completed two conditions of overground walking to measure walking capacity and metabolic energy expenditure. The first condition was performed OFF medication for at least 12 hours. The second condition was then performed 1 hour after taking medication (ON meds).[5] For each condition, participants completed a 6-Minute Walk Test (6MWT) in a 6 ft wide hallway with tape marks 100 feet apart on the floor away to demarcate turns. Participants were instructed to walk as far as possible in 6 minutes and were told when each minute had elapsed. A 14' x 2' GaitRite mat (CIR, Haverford, PA) was placed ~10ft from the starting point, so participants walked over the GaitRite during each pass. During the 6MWT, we measured participant's VO2 and VCO2 inspired using a portable metabolic cart (K5, Cosmed). The system was calibrated according to Cosmed standards. The participants were fitted with the Cosmed mask and air exchange was measured at rest for 5 minutes while sitting in a standard chair. Prior to testing, all participants completed demographic information, medication information, Hoehn and Yahr scale, and the Unified Parkinson's Disease Rating Scale (UPDRS).

Data Management

6MWT distance was calculated using a measuring wheel and total distance was reported in feet. A ratio of the distance walked in the last minute to the distance walked in the first minute was calculated to determine the participants' "endurance index". This endurance index represents how the individual changed speed during the 6MWT. Spatiotemporal measures of gait, including step width, stride length, cadence, and gait speed were collected from each pass over the GaitRite mat during the 6MWT, and averaged for representative values. Net mass-specific oxygen consumption during activity was based on steady-state oxygen use during the last two minutes of the 6MWT. Net oxygen consumption was normalized to gait speed to calculate oxygen cost of walking for each participant. O_2 cost of walking represents the amount of oxygen consumed per kilogram of body weight per distance traveled (mL/kg/m).

Statistical Analysis

All analyses were performed using SPSS version 28 (IBM). Given the small sample size, we opted to use non-parametric statistics. For our primary analysis, we performed a Mann-Whitney U test to compare oxygen cost of walking ON versus OFF medication. For a secondary analysis, Mann-Whitney U tests were performed to compare spatiotemporal parameters of gait including stride length, gait speed, cadence, and step width between conditions. A Mann-Whitney U test was performed to compare endurance index between conditions. Further, a Mann-Whitney U test was used to compare total distance traveled during the 6MWT ON versus OFF medication for each subject. The alpha level was set to 0.05.

We conducted Spearman correlational analyses for spatiotemporal parameters of gait and oxygen cost of walking. Specifically, we evaluated potential relationships between the change in cost of walking between OFF and ON conditions with the change in spatiotemporal gait parameters. Values for correlation coefficients were interpreted as small (0.1), moderate (0.3), and large (0.5) and significance level was set to 0.05.

Results

Descriptive characteristics of participants (n=8) are presented in Table 1. Participants had a mean disease duration of 4.57 years and a mean MDS-UPDRS score of 24.8 which is considered mild-to-moderate disability severity.

Table 1 Demographic Characteristics

Subject	Height	Weight	Chronicity	HY	MDS UPDRS
1	5'9	145	9 years	2	21
2	5'3	100	4 years	2	36
3	5'8	180	Not Reported	2	26
4	6'1	230	5 years	2	21
5	5'7	203	2 years	2	28
6	5'6	130	3 years	2	22
7	5'7	113	2 years	2	20
8	5'8	212	7 years	1	Not Reported

Effect of medication on oxygen cost

Individuals demonstrated no significant difference between oxygen cost of walking ON versus OFF medications when walking overground with the ability to self-select gait speed ($p = 0.575$).

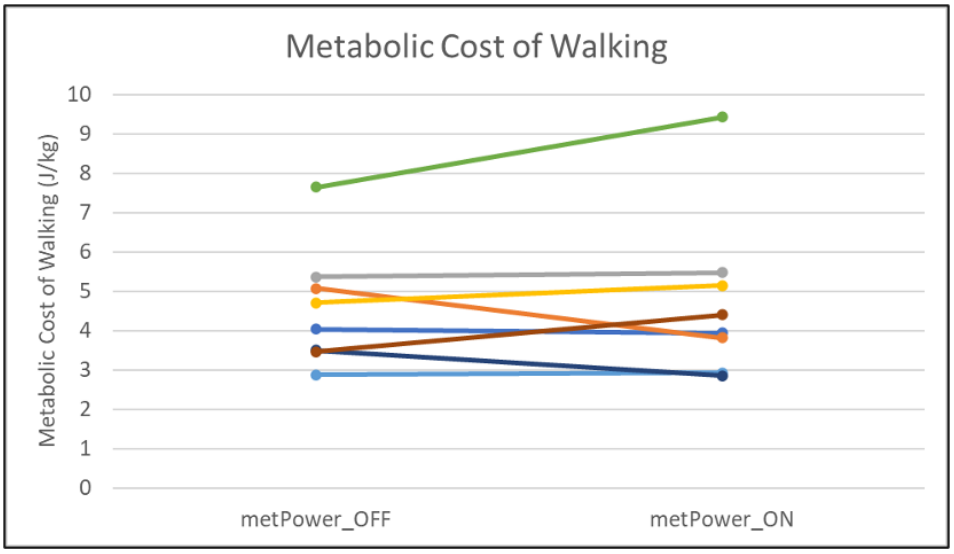

Figure 1: Changes in metabolic cost of walking OFF versus ON medication for each participant.

Spatiotemporal

When comparing spatiotemporal measures of gait (gait speed, stride length, cadence, and step width) ON vs OFF medications, no significant differences were found ($p = 0.123$ for gait speed, $p = 0.674$ for stride length, $p = 0.161$ for cadence, and $p = 0.161$ for step width).

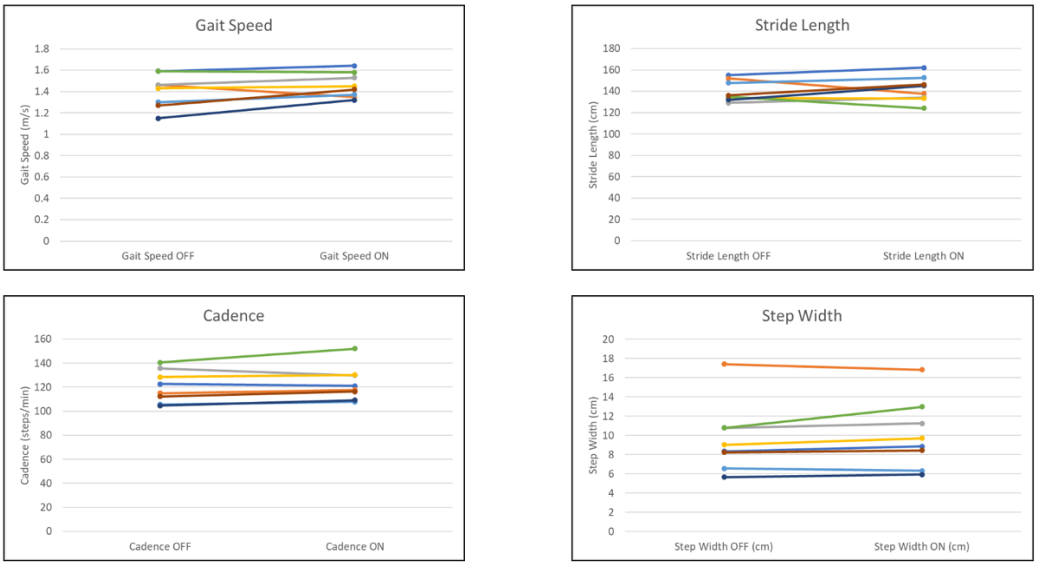

Figure 2: Changes in spatiotemporal gait parameters OFF versus ON medication in each participant.

Endurance

Endurance was measured by total distance traveled during the 6MWT and endurance index. There was no significant difference in total distance traveled during the 6MWT ON versus OFF medication ($p = 0.161$). Additionally, there was no significant difference between endurance index ON versus OFF medication ($p = 0.123$).

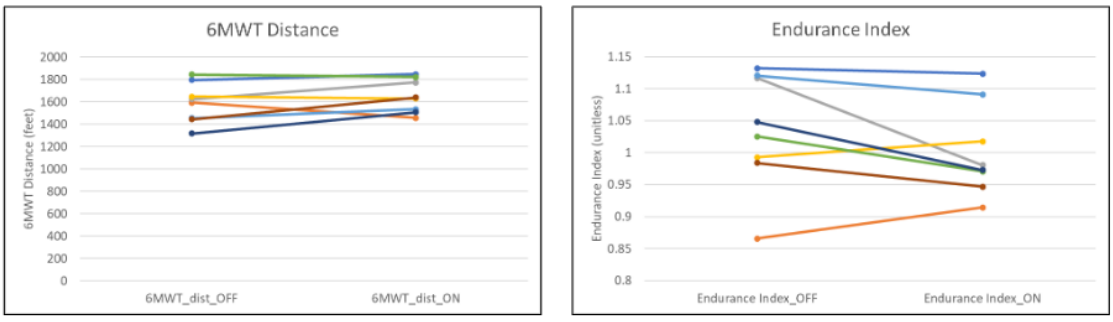

Figure 3: Changes in total 6MWT distance and endurance index OFF versus ON medication in each participant.

Correlations

When determining the relationship between changes in oxygen cost of walking and changes in spatiotemporal parameters of gait ON versus OFF medication, we found that no spatiotemporal parameters were associated with the change in cost of walking between conditions. However, we noted that an increase in gait speed between conditions was strongly associated to an increase in stride length ($r = 0.922$, $p = 0.001$).

Correlations

			COWDiff	GaitSpeedDiff	StrideLength Diff	CadenceDiff	StepWidthDiff
Spearman's rho	COWDiff	Correlation Coefficient	1.000	-.012	-.071	.190	.595
		Sig. (2-tailed)	.	.978	.867	.651	.120
		N	8	8	8	8	8
	GaitSpeedDiff	Correlation Coefficient	-.012	1.000	.922**	.036	-.204
		Sig. (2-tailed)	.978	.	.001	.933	.629
		N	8	8	8	8	8
	StrideLengthDiff	Correlation Coefficient	-.071	.922**	1.000	-.024	-.048
		Sig. (2-tailed)	.867	.001	.	.955	.911
		N	8	8	8	8	8
	CadenceDiff	Correlation Coefficient	.190	.036	-.024	1.000	-.024
		Sig. (2-tailed)	.651	.933	.955	.	.955
		N	8	8	8	8	8
	StepWidthDiff	Correlation Coefficient	.595	-.204	-.048	-.024	1.000
		Sig. (2-tailed)	.120	.629	.911	.955	.
		N	8	8	8	8	8

**. Correlation is significant at the 0.01 level (2-tailed).

Figure 4. Correlation between Changes in Oxygen Cost of Walking and Changes in Spatiotemporal Parameters of Gait

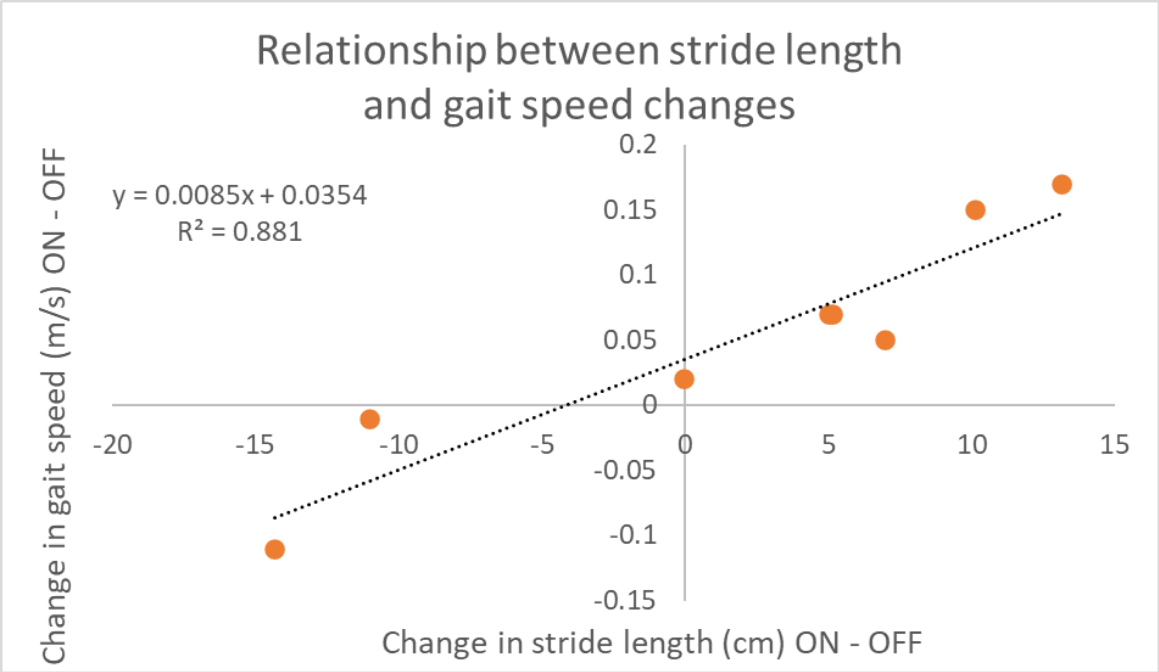

Figure 5: Correlation Between Change in Stride Length and Change in Gait Speed

Table 2: Difference in Outcomes ON vs. OFF Medication

	OFF Meds	ON meds	P-value
Oxygen Cost of Walking/Metabolic Power	Median = 4.37 IQR = 1.82	Median = 4.17 IQR = 2.24	P = 0.575
Total distance during 6MWT	Median = 1,609.5 IQR = 311	Median = 1,635 IQR = 297	P = 0.161
Gait Speed	Median = 1.45 IQR = 0.28	Median = 1.44 IQR = 0.21	P = 0.123
Stride Length	Median = 135.66 IQR = 18.57	Median = 141.40 IQR = 17.40	P = 0.674
Cadence	Median = 118.76 IQR = 26.49	Median =119.36 IQR = 19.28	P = 0.161
Step Width	Median = 8.68 IQR = 3.79	Median = 9.28 IQR = 5.69	P = 0.161
Endurance Index	Median = 1.04 IQR = 0.13	Median = 0.98 IQR = 0.10	P = 0.123

Discussion

This study examined oxygen cost of walking ON versus OFF medication during overground walking in people with mild-to-moderate PD. Our results suggest oxygen cost of walking is not significantly different ON versus OFF medication in people with PD. These results do not support our hypothesis that dopaminergic medication would have a beneficial impact on spatiotemporal parameters of gait and consequently decrease oxygen consumption. This is likely explained by the fact that participants' spatiotemporal gait parameters did not significantly change ON versus OFF medication. In the short-term, dopaminergic medication was not effective in improving spatiotemporal gait parameters during overground walking nor was it effective in improving walking efficiency.

Oxygen cost of walking can be improved in two ways 1) by using less oxygen when traveling the same distance, and 2) by traveling a further distance with the same amount of oxygen used. In this study, participants did not use less oxygen or travel further total distances ON versus OFF medication. This study is one of the few that has investigated the impact of dopaminergic medication on walking economy in people with PD. Although some literature suggests dopaminergic medication can impact spatiotemporal parameters of gait,[4,5] this study adds to the body of knowledge that dopaminergic medication may not consistently impact spatiotemporal gait measures in the short-term.[14, 15]

There are important assumptions and limitations of this study. One assumption is that participants were optimally medicated for their PD. Another assumption is that the one-hour time we allotted between ingesting medication and testing was adequate for the medication to take effect. The primary limitation of this study was the small sample size (n = 8) which limits the

generalizability of results. Because of the small sample size, our results may not be representative of the entire population of people with PD. Additionally, given the majority of the participants in the study were H&Y 2, there is a possibility that these subjects were not impaired enough to demonstrate a significant difference in presentation ON versus OFF medication.

Another limitation is the researchers' lack of ability to standardize and objectively measure dyskinesias in participants. Due to this limitation, we were unable to completely address our secondary hypothesis that an increase in dyskinesia would result in increased oxygen consumption. If we were able to objectively measure dyskinesias, then we may have seen a relationship between why some participants improved oxygen cost of walking and some participants had decreased oxygen cost of walking when ON dopaminergic medication.

Overall, metabolic cost of walking has significant implications for participation in meaningful and daily activities. Individuals with neurological conditions such as PD have decreased oxygen cost of walking compared to healthy controls[8] which has significant repercussions for participation due to fatigue and increased energy requirements.[12] The present findings suggest that physical therapists and physicians should not rely on medication alone to provide improvements in quality of gait and walking economy in ambulatory individuals with PD. It is important to note these findings do not mean the cost of walking cannot change. However, these results highlight the importance of aerobic exercise and gait training to improve spatiotemporal parameters of gait which ultimately leads to improved walking economy overtime.[16]

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