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EFFECTS OF LEVODOPA ON FORWARD AND BACKWARD GAIT PATTERNS IN PERSONS WITH PARKINSON'S DISEASE

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Abstract

Introduction—Backward walking is difficult for persons with Parkinson's disease (PD). It is unknown how levodopa influences backward gait patterns, especially when compared to forward gait patterns.

Purpose—Investigate the effects of levodopa on forward and backward gait patterns in individuals with PD.

Design—A repeated measures design was used.

Methods—The sample consisted of 21 individuals with PD (15 males, 6 females). Their mean age was 70.24 ± 8.69 yr. The average time since diagnosis was 11.81 ± 5.49 years. The median of the Hoehn and Yahr stage while 'ON' medication was 2.57. Gait patterns during forward and backward walking at a self-selected comfortable speed were recorded before and after taking levodopa on the same day.

Results—Levodopa significantly increased gait speed and stride length and decreased the percent of the gait cycle (%GC) spent in double support. Gait speed and stride length were greater and the %GC spent in double support was less during forward walking compared with backward walking. Cadence was not changed by levodopa or walking direction.

Conclusions—Levodopa improved gait characteristics during backward walking in a manner similar to that during forward walking in persons with PD.

Keywords

Parkinson's disease; Gait; Levodopa; Backward walking; Forward walking

1. Introduction

Backward walking is often used to perform many activities in daily living, such as when backing out of closets or away from the kitchen sink or dresser. We also use stepping back

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rather than turning around in some tight and dangerous situations (e.g. avoiding oncoming objects such as approaching vehicles or a running dog, or to allow someone to pass in a narrow hallway). Backward walking may be particularly difficult for persons with Parkinson's disease (PD) who often lose their balance and fall as a result of moving or being perturbed in the backward direction [19,7,5].

Forward gait characteristics in persons with PD have been studied extensively over the past two decades. Recently, Hackney and Earhart reported both forward and backward gait patterns in persons with PD while on anti-parkinsonian medication compared to age-matched controls [5]. In forward walking, people with PD had significantly shorter strides, spent a lower percentage of time in swing phase, and had a higher percentage of time in stance phase than controls [15]. In backward walking, those with PD showed significantly slower gait speeds with shorter strides, a lower percentage of time in swing phase, a greater percentage of time in double support and stance phase, and lower functional ambulation profiles compared with the controls. These results clearly demonstrated that persons with PD had impairment in both forward and backward walking, however, impairment in backward walking was more pronounced when compared to that of the controls [5].

It has been shown that levodopa change gait patterns in persons with PD during forward walking [11,9,10]. Since the biomechanics of backward walking are almost a simple reversal of those of forward walking [20], it is reasonable to hypothesize that levodopa might also modify gait patterns while walking backward. However, no information was found in the literature regarding how levodopa influence backward gait. Therefore, in this study, our aim was to investigate the effects of levodopa on backward gait patterns and compare them to the effects on forward gait patterns in individuals with PD. We hypothesized that the effect of levodopa on gait patterns during backward walking would be similar to its effects during forward walking. Based on previous findings, we also hypothesized that gait patterns would significantly differ between forward and backward walking.

2. Methods

2.1 Subjects

Twenty-one subjects with PD were recruited from PD support groups and movement disorders clinics in XXX, XX. On average they were 70.24 ± 8.69 years old and had been diagnosed with PD an average of 11.81 ± 5.49 years prior to study entry. The median of the Hoehn and Yahr (HY) stage while 'ON' medication was 2.57. Five participants were in stage 2, eight were in stage 2.5, and eight were in stage 3. The mean Unified Parkinson's Disease Rating Scale (UPDRS) motor score while 'OFF' medication was 32.91 ± 9.61 and while 'ON' medication was 20.62 ± 7.05. They all reported either balance impairment or falls as a result of PD. Nineteen subjects (90%) experienced freezing of gait (FOG), indicated by a score ≥ 1 on item 14 (freezing) of the UPDRS. None of the subjects had a history of brain surgery or deep brain stimulation for PD. All subjects were able to walk independently in both 'OFF' and 'ON' medication states without freezing episodes and had no evidence of dementia. All subjects were receiving dopamine treatment (carbidopa/levodopa or carbidopa/levodopa/entacapone). The amount of levodopa taken by the subjects ranged from 100 to 300 mg (mean = 152.38 mg). Additional medications included pramipexole in eight subjects, amantadine hydrochloride (Amantadine) in nine, Azilect (rasagiline) in two, ropinirole in five, entacapone in five, selegiline in four, and trihexyphenidylin in one. Eleven subjects had dyskinesia after they took their medication.

2.2 Equipment and Measures

The HY and the UPDRS motor subscale were used to assess the severity of the disease and the degree of impairment [6,4]. All subjects were rated during “OFF” and “ON” medication states by a neurologist who was blinded to the hypotheses of the study.

The GAITRite system (GAITRite, CIR Systems Inc., Havertown, PA), is a 3-m, instrumented walkway containing an array of 6 sensor pads encapsulated in a roll-up carpet with an active area 61 cm wide by 366 cm long. While the subject walks, the system continuously scans the sensors to detect pressures, and transfers the information to the connected computer for calculating gait characteristics [3]. Measurement of gait speed, cadence, symmetry, stride length, and other characteristics are recorded and stored on the computer by the system. Gait speed is reported as cm/sec. Cadence is the number of steps/minute. Stride length is the length (in centimeters) of two consecutive footfalls of the same extremity. Percentage of the gait cycle (%GC) spent in double support is the sum of the time elapsed between the first contact of the current footfall and the last contact of the previous footfall and the time elapsed between the last contact of the current footfall and the first contact of the next footfall divided by the total time of the gait cycle.

2.3 Experimental procedures

All subjects read and signed a consent form approved by the local institutional review boards prior to participation. Participants were asked to walk forward and backward before and after taking medication on the same day. For ‘OFF’ medication testing, the subjects were tested in the morning after abstaining from their medications overnight. The wash-out period was at least 12 hours in the ‘OFF’ medication state. The subject’s ‘OFF’ medication state was rated with the UPDRS Motor section III by a neurologist prior to performing the walking test. After completing forward and backward walking tests, the subject took his or her morning dose of medications and waited for the medications to take effect. Once the subject reported that he/she felt ‘ON’, which was approximately 45 minutes to one hour, the same neurologist rated the subject again on the UPDRS motor section. Then, the subject walked forward and backward again following the same procedure as in the off-medication condition.

In both the ‘OFF’ and ‘ON’ conditions, subjects were instructed to walk forward and backward at their self-selected comfortable speed on the GAITRite mat. The oral instruction was “Walk at your comfortable speed”. The instruction was given only before the subject started walking. No instruction was given after the subject started walking in order to prevent any influence of verbal cueing on gait performance. The subject walked twice in each direction and the average of the two trials for each direction was used in data analysis. Variables of interest were gait speed, cadence, stride length, and %GC spent in double support. All subjects wore a gait belt and were guarded by a research assistant to prevent falls. The research assistant walked alongside and slightly behind the subject and was ready to hold the gait belt if a fall was about to happen.

2.4 Statistical analysis

Demographic data were descriptively summarized. Analyses were performed by using SPSS version 18.0. Two-way repeated-measures analysis of variance (ANOVA) was used to assess the main effects of levodopa and walking direction on gait characteristics as well as any interactions between the variables. The significance level was set at $P < 0.05$.

3. Results

Gait characteristics are displayed in Table 1. Levodopa increased gait speed ($F(1, 20) = 15.98$) and stride length ($F(1, 20) = 15.61$) and decreased %GC spent in double support ($F(1, 20) = 8.75$). No significant main effect of levodopa on cadence was found ($F(1, 20) = 1.29$) while walking forward or backward.

Compared with walking forward, gait speed was slower ($F(1, 20) = 146.87$), stride length was shorter ($F(1, 20) = 149.12$), and %GC spent in double support was greater when walking backward ($F(1, 20) = 32.28$). There was no significant main effect of walking direction on cadence ($F(1, 20) = 1.54$).

There was no significant interaction between medication status and walking direction on gait speed, cadence, stride length, or %GC spent in double support. These results indicate that levodopa did not influence gait characteristics differently when walking in different directions.

The percentage of change in these gait parameters from the 'OFF' to the 'ON' condition was not different between forward and backward walking (Table 1).

4. Discussion

Our study is the first to report the influence of levodopa on both forward and backward gait patterns in persons with PD. Levodopa is known to improve gait and mobility in persons with PD [8]. However, the benefit of levodopa on backward walking has not been reported previously.

We studied the changes in gait patterns when subjects walked forward and backward before and after taking levodopa. This compliments a recent report by Hackney and Earhart who compared forward and backward gait patterns of persons with PD to those of age-matched controls. They found that both groups walked slower and with a wider base of support when walking backward compared with walking forward. Furthermore, as noted in the introduction, persons with PD were at a disadvantage on several gait characteristics compared with the controls when walking backward. Our sample showed more deficits in gait speed, cadence, and stride length while walking both forward and backward while on medication than those reported by Hackney and Earhart [5]. These differences might be related to the fact that our subjects had more severe PD, on average, compared to those in their study. The range of HY stage from our sample was 2–3 (mean = 2.57), whereas the subjects of Hackney and Earhart ranged from 0.5 – 3 (mean = 2.05).

Our results showed that levodopa improved gait patterns in persons with PD when walking both forward and backward. Improvement was reflected by increased gait speed, increased stride length and decreased %GC spent in double support after the levodopa took effect. Changes in gait speed, cadence, and stride length during backward walking after taking levodopa were greater than those during forward walking, while the percentage of change in double support time was greater during forward walking (Table 1). However, none of the differences in the percentage of change were significant.

Similar findings were reported earlier for forward walking. Nieuwboer and colleagues reported a pronounced increase in stride length and gait speed in three patients with PD when they were in the 'ON' phase of the medication cycle [16]. Moore et al. studied the dynamic, quantitative response of locomotion to levodopa administration in patients with fluctuating PD and reported that walking speed correlated with changes in mean stride length, whereas cadence did not [9]. As in the present study, cadence has been previously

reported to be dopa-resistant by other investigators [1,18,8]. It is still unknown why this temporal characteristic of gait is not responsive to levodopa.

Laboratory studies have suggested that preferred cadence of over-ground human walking is approximately 120 steps/min [14]. The average cadence of normal speed walking in healthy men and women at age 70–79 were 114 and 121 step/min, respectively [17]. From our data, cadence during both forward and backward walking while 'OFF' and 'ON' medication was within this range (111 to 121 steps/min, Table 1). This could explain why cadence did not change significantly after taking levodopa because the subjects were already walking within the normal preferred range of usual walking, thus leaving little room for improvement.

Lubik et al. reported that gait velocity and step length of patients with PD treated with either levodopa or subthalamic nucleus stimulation (SNS) were greatly improved, with more improvement demonstrated by the levodopa group. Cadence was not improved by levodopa, SNS, or a combination of both treatments [8]. Morris et al. reported that persons with PD used cadence modification as a compensatory mechanism for the reduced step length [12]. Levodopa improved stride length significantly in both forward and backward walking in the current study. It was possible that modification in stride length was preferred to the modification of cadence, especially when the cadence was already within the optimal range of usual walking. Results from Morris et al. demonstrated that patients with PD have the capacity to walk at a faster speed with larger steps and normal timing [12]. An inability to generate an appropriate stride length appears to be the fundamental problem underlying gait hypokinesia (slowness) in persons with PD [13].

Elders without PD demonstrated a lower %GC spent in double support compared to persons with PD during both forward and backward walking [5]. A decrease in double support time while on medication during forward walking was reported earlier by Bowes and colleagues [2]. Our results showed that the %GC spent in double support decreased after taking levodopa for both forward and backward walking. This suggests that levodopa improved gait patterns in persons with PD and moved them toward more normal values.

4.1 Limitations

There are some limitations of the study to be addressed. Our sample consisted of individuals with diagnosed idiopathic PD and reported either balance impairment or falls as a result of PD. Their gait patterns might be different from persons with PD who do not have balance impairment or who have never had problems with falling due to the disease. Persons with balance or falling problems may be more likely to automatically modify their backward gait patterns.

The design of the study necessitated us to measure gait first when the subjects were off medication and second while on medication. We measured gait when they had not had levodopa for approximately 12 hours to assure the off-state testing. We could not have done the testing on the same day if we had measured them while on medication first. Because of this design, there may have been some practice effect during the 'ON' condition. However, the effect should have occurred equally on forward and backward walking.

The amount of levodopa taken by the subjects was not controlled because the subjects took their usual type and dosage of their medications. The unequal amount of levodopa might influence gait changes to different degrees. The medications were the combination of levodopa and adjunct medications. However, we assumed that each subject was at their best motor response to the medications because they were individually prescribed and tailored by their own neurologist. Locomotor response of the levodopa alone in comparison to its combination with adjunct medications is not known. Food intake was not monitored in this

study and might contribute to disparities in protein content between subjects, which may delay absorption and reduce cerebral intake. This variation might affect gait improvement in each individual.

Fatigue might have occurred from travelling to the laboratory in the morning without the medication and having possibly endured impaired mobility and physical discomfort from PD. However, we minimized this effect by providing rest periods whenever requested.

4.2 Clinical implications

Some individuals may encounter difficulties in taking several consecutive steps backward. While walking backward, fear of falling may also prevent them from making sufficiently large steps or lifting their feet off of the walking surface. Walking backward may be a novel task for some people, especially elderly persons with PD. Therefore, the ability to test backward walking may be limited in certain patients.

Clinicians should be aware that some (e.g., speed, stride length, and %GC) but not all aspects of gait (e.g., cadence) are improved by levodopa in persons with PD. This suggests that clinical assessments of gait should be conducted at similar times in the medication cycle in order to assure comparability of the measures. Likewise, other interventions need to be explored if the aim of treatment is to change the cadence of gait in individuals with PD. Finally, backward walking might be a valuable clinical tool for gait assessment in individuals with PD.

5. Conclusion

Levodopa produced similar improvements in gait speed, stride length, and %GC spent in double support when persons with PD walked either forward or backward, but had no significant effect on cadence in either direction.

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Table 1

The effects of levodopa and walking direction on gait patterns in persons with PD (N = 21, 15 males, 6 females)

Gait Parameters	Forward Walking		Backward Walking		P-Value [a] (OFF vs. ON)	P-Value [a] (Forward vs. Backward)	P-Value [a] (Interactions)
	OFF Mean ± SD	ON Mean ± SD (% Change)*	OFF Mean ± SD	ON Mean ± SD (% Change)*			
Gait Speed (cm/sec)	84.14 ± 24.39	101.28 ± 18.71 (20.37%)	46.16 ± 20.08	58.71 ± 21.75 (27.19%)	.001	<. 001	.203
Cadence (steps/min)	111.78 ± 9.31	114.02 ± 11.33 (2%)	116.87 ± 30.21	121.56 ± 20.82 (4.01%)	.269	.229	.576
Stride Length (cm)	91.11 ± 26.09	108.45 ± 23.86 (19.03%)	48.21 ± 17.87	60.12 ± 24.01 (24.70%)	.001	<. 001	.145
Double support (%GC)	34.54 ± 8.85	30.99 ± 5.57 (−10.28%)	41.95 ± 8.60	38.87 ± 9.87 (−7.34%)	.008	<. 001	.701

% GC = percentage of gait cycle spent in double support.

[a]Two-way repeated-measures ANOVA; Based on estimated marginal means.

*% Change compared to before levodopa.