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Gait Variability in Parkinson's Disease: Levodopa and Walking Direction

Mon S Bryant, PT, PhD^{1,2,3}, Diana H Rintala, PhD², Jyh-Gong Hou, MD, PhD⁴, Robert L Collins, PhD^{5,6}, and Elizabeth J Protas, PT, PhD³

¹Research Service, Michael E DeBakey Veterans Affairs Medical Center, Houston, TX

²Department of Physical Medicine and Rehabilitation, Baylor College of Medicine, Houston, TX

³Rehabilitation Sciences, University of Texas Medical Branch, Galveston, TX

⁴Lehigh Neurology, Lehigh Valley Health Network, Allentown, PA

⁵Neurology Care Line, Michael E DeBakey Veterans Affairs Medical Center, Houston, TX

⁶Department of Neurology, Baylor College of Medicine, Houston, TX

Abstract

Background—Levodopa treatment has been shown to improve gait spatio-temporal characteristics in both forward and backward walking. However, effect of levodopa on gait variability during backward walking compared to forward walking has not been reported.

Aims of Study—To study the effects of levodopa on gait variability of forward and backward walking in individuals with Parkinson's disease (PD).

Methods—Forty individuals with PD were studied. Their mean age was 68.70 ± 7.46 yr. The average time since diagnosis was 9.41 ± 5.72 yr. Gait variability was studied while 'OFF' and 'ON' levodopa when the participants walked forward and backward at their usual speed. Variability in step time, swing time, stride length, double support time and stride velocity were compared between medication condition and walking direction.

Results—Variability of step time, swing time, stride length and stride velocity decreased significantly during forward and backward walks ($p < .001$; $p < .001$; $p = .003$, $p = .001$, respectively) after levodopa administration. Variability of double support time was not changed after levodopa administration ($p = .054$).

Conclusions—Levodopa had positive effects on gait variability of forward and backward walking in individuals with PD. However, variability in double support time was not affected by the levodopa.

Keywords

Parkinson's disease; Gait Variability; Levodopa; Forward Walking; Backward Walking

Address all correspondence to Mon S Bryant, PT, PhD, Rehabilitation Research (153), 2002 Holcombe Blvd, Houston, TX 77030; Tel: 713-791-1414; Fax: 713-794-7623; ; Email: msbryant@bcm.edu

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Introduction

Gait disturbance in individuals with Parkinson's disease (PD) has been reported in both forward and backward directions, however, impairment in backward walking was more pronounced when compared to that of controls without PD (¹). Backward walking is difficult for individuals with PD who often lose their balance and fall as a result of moving in the backward direction (^{1, 2}). Gait patterns of both forward and backward walking in those with PD is characterized by slow speed, short stride lengths and increased cadence (^{1, 3}).

Gait dysfunction in PD also includes increased variability from stride to stride in various gait parameters (⁴). Increased stride-to-stride variability indicates inconsistency in stepping patterns and reduced postural control during walking (⁵). These characteristics indicated that the ability to maintain a steady gait rhythm is impaired in those with PD (⁶). Gait dysfunction and instability in both directions may predispose individuals with PD to fall. Body sway velocity was found to be associated with falls (⁷).

Levodopa treatment has been shown to improve gait spatio-temporal characteristics in both forward and backward walking, with a lesser extent of improvement in backward walking than the forward walking (⁸). These findings lead us to hypothesize that the effect of levodopa on gait variability might be different between the two walking directions. To our knowledge, the effect of levodopa on variability during backward walking has not been reported previously. In this study, the influence of levodopa on gait variability during forward and backward walking was studied.

Materials and methods

Forty community-dwelling individuals with PD (31 males, 9 females) who were able to stand and walk independently were studied (Table 1). Their PD diagnosis was confirmed by a movement disorder specialist. All participants reported that they had gait or balance impairment or had fallen. We included only participants who verbally reported that they experienced gait difficulties to ascertain that they had gait deficits and would likely demonstrate gait responses to levodopa medication for the purpose of the study. They were not allowed to use an assistive device during the test due to the potential gait modification effects from walking devices. The participants read and signed a consent form approved by the local institutional review boards prior to participation.

The walking test was performed while 'OFF' and 'ON' levodopa medication on the same day. For 'OFF' medication testing, the participants were tested in the morning after abstaining from all of their anti-parkinsonian medications overnight (12 hours). The Hoehn and Yahr staging scale (HY) and the Unified Parkinson's Disease Rating Scale (UPDRS) motor score were used to assess motor impairment. The participants were asked to walk forward and backward on a 5-m computerized mat to record their gait (GAITRite, CIR Systems Inc., Havertown, PA) at their self-selected, usual speed for two trials in each direction. The average of two trials would represent more reliable characterization of gait performance than one trial. The participants started walking a few steps before entering and

continued a few steps after leaving the carpet. The instruction was 'Walk on the mat at your comfortable speed'. After the walking test, they took all of their usual anti-parkinsonian medication and waited for approximately one hour for the medication to take effect. Once the participants reported that they felt 'ON,' they again were rated by a neurologist using the UPDRS motor section. The participants then repeated the walking tests for the 'ON' medication condition.

Variability in step time, swing time, double support time, stride length and stride velocity (coefficient of variation [CV]) were calculated using the following formula: % CV = (standard deviation ÷ mean) * 100.

Statistical Analysis

IBM SPSS version 22.0 was used for all analysis. Demographic data were descriptively summarized. Two-way repeated-measures analysis of variance (ANOVA) was used to assess the main effects of levodopa and walking direction on gait variability as well as interactions between the two factors. The significance level was set at $P < 0.05$.

Results

Main effect: Influence of levodopa on gait variability

Levodopa decreased variability in step time ($F(1,39) = 17.08$, $P < .001$), swing time ($F(1,39) = 18.14$; $P < .001$), stride length ($F(1, 39) = 9.83$; $P = .003$) and stride velocity ($F(1, 39) = 13.75$, $P = .001$) while walking forward or backward. No significant main effect of levodopa on variability in double support time was found ($F(1, 39) = 3.95$, $P = .054$) while walking forward or backward.

Main effect: Influence of walking direction on gait variability

Compared with backward walking, variability was lower during forward walking, for step time ($F(1,39) = 85.97$, $P < .001$), swing time ($F(1,39) = 105.23$, $P < .001$), double support time ($F(1,39) = 58.18$, $P < .001$), stride length ($F(1,39) = 167.79$, $P < .001$) and stride velocity ($F(1,39) = 125.50$, $P < .001$).

Interaction of levodopa and walking direction on gait variability

There was no significant interaction between walking direction and medication state on the variability of step time ($F(1,39) = 3.92$, $P = .055$), swing time ($F(1,39) = 3.56$, $P = .067$), double support time ($F(1,39) = .223$, $P = .640$), stride length ($F(1,39) = .908$, $P = .347$), or stride velocity ($F(1,39) = .618$, $P = .436$) (Tables 2). Levodopa did not influence gait variability differently when walking in one direction versus the other.

Discussion

Based on our literature search, this is the first study to report the influence of levodopa on gait variability during both forward and backward walking in individuals with PD. This study demonstrated new findings. First, backward walking demonstrated more variability than did forward walking during both 'OFF' and 'ON' medication states. Second, our results

demonstrated that the variability of most gait parameters improved with levodopa regardless of walking direction. Third, all gait variability measures were improved with medication except for double limb support time variability.

Previous investigators have reported evidence to support the independence of certain gait characteristics from dopamine, suggesting that impaired gait in PD has a complex pathophysiology, with spatial parameters responding more favorably to dopamine than temporal parameters (⁹). Our results showed that the variability in double limb support time was not different after taking levodopa medication, whereas the other variability parameters decreased. Such findings demonstrated that both spatial and temporal components of gait variability responded to levodopa and did not support the hypothesis that temporal variability parameters are dopamine independent.

Dopamine did not have more influence on variability in one walking direction compared to the other as supported by the lack of interaction between medication state and walking direction. This finding could be reasonably expected because the biomechanics of backward walking are almost a simple reversal of those of forward walking (¹⁰).

Double support time has been considered an important indicator of abnormal balance control in healthy, older adults and those with cerebellar dysfunction, as well as those with basal ganglia pathology (⁴). It is an alternative measure of variability that reflects balance control mechanisms contributing to the dynamic act of walking (¹¹). Balance deficits and postural instability in individuals with PD are known to be dopamine resistant (^{12, 13}). This might explain the finding that there was no effect of levodopa on variability in double support time. Impaired proprioception in PD has been attributed to abnormal processing of proprioceptive signals in the basal ganglia, which may be an important factor contributing to postural control deficits (¹⁴). The influence of dopamine on gait variability appeared to be selective and did not improve postural instability in this population.

In PD rehabilitation, walking backward is often used in clinical practice. Knowledge of changes in gait variability from levodopa can be helpful to clinicians. The results demonstrated that the medication decreased gait variability. Therefore, at the end of the dose, greater variability of both forward and backward walking can be expected, thus clinicians should be more cautious when providing the rehabilitation. In addition, PD patients had more gait instability during backward walking than during forward walking as indicated by higher values of variation.

There are some limitations to the current study. Seventy-eight percent of the study sample was male, which might limit the generalizability of the findings to females. Only two trials for each walking direction were performed. More trials might yield different variability estimates but would be subject to a potential practice effect. Walking tests were performed without assistive devices. The gait variability might be different when walking with devices.

Conclusion

In summary, individuals with PD demonstrated greater gait variability when they walked backward compared to forward. Clinicians should be aware that levodopa, a standard

medication for patients with PD, improved several parameters of gait variability when walking in both directions, but had no influence on variability in double support time.

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Table 1
Subject Characteristics

	PD (N=40)
Gender	Male 31 (77.5%); Female 9
Age	68.70 ± 7.46
Year since diagnosis of PD	9.41 ± 5.72
HY Stage('ON meds')	HY 1.5 (N = 2) HY 2 (N = 10) HY 2.5 (N = 16) HY 3 (N = 12)
UPDRS 'OFF meds'	30.50 ± 12.35
UPDRS 'ON meds'	20.13 ± 7.57
Daily Levodopa equivalent dose (mg) (15, 16)	801.55 ± 484.58

Table 2
The effects of levodopa and walking direction on gait variability in individuals with PD (N = 40, 31 males, 9 females)

Gait Variability	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	OFF Mean ± SD	ON Mean ± SD			
Step time	4.91 ± 1.90	3.81 ± 1.45	10.13 ± 4.54	7.58 ± 2.68	< .001	< .001	.055
Swing time	6.48 ± 3.19	5.28 ± 2.81	13.34 ± 5.45	10.52 ± 3.93	< .001	< .001	.067
Double support time	7.09 ± 2.82	5.79 ± 2.66	11.18 ± 3.65	10.27 ± 4.28	.054	< .001	.640
Stride length	4.51 ± 2.65	3.53 ± 2.07	13.11 ± 5.25	11.34 ± 4.48	.003	< .001	.347
Stride velocity	4.94 ± 2.13	3.83 ± 1.93	11.89 ± 4.88	10.24 ± 4.34	.001	< .001	.436

^aTwo-way repeated-measures ANOVA.