Parkinson's Disease and Gait Asymmetry

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Abstract

Walking is considered symmetric in neurologically healthy individuals. However, asymmetry begins to occur with aging, and could be indicative of neurodegenerative diseases, such as Parkinson's disease (PD). The aim of this chapter is to discuss gait asymmetry in people with PD. Specifically, we present a general idea about unilateral signs/symptoms of PD and its influence on asymmetry and review the literature about unobstructed gait asymmetry in people with PD. Finally, we show the effects of obstacle crossing and auditory cues on gait asymmetry in people with PD. Previous studies have indicated that people with PD presented greater asymmetry in the temporal parameters compared to neurologically healthy older subjects. For obstacle crossing during walking, both people with PD and neurologically healthy older individuals demonstrated a higher symmetric index for step duration during obstacle

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crossing while walking compared to unobstructed walking. Therefore, obstacle avoidance increases gait asymmetry of neurologically healthy older individuals and people with PD. Auditory cues decreased asymmetry for step length, duration and velocity, and cadence in individuals with PD compared to neurologically healthy older individuals. However, only neurologically healthy older individuals demosntrated greater asymmetry in the trials with auditory cues for step length, duration and velocity, and cadence. Therefore, auditory cues seem to have no effects on gait asymmetry for unobstructed and obstacle walking in individuals with PD, and impair gait asymmetry in neurologically healthy older individuals during obstacle avoidance.

Keywords

Asymmetry • Walking • Parkinson's disease • Sidedness • Aging • Obstacle avoidance • Auditory cues

11.1 Introduction

The term asymmetry can mean both structural and functional left–right dissimilarities [1]. Asymmetry can be considered as differences in performance and motor control between sides. The concepts of symmetry and asymmetry are closely tied to function of the two hemispheres of the human brain. Despite having a preferred limb during tasks, walking is considered symmetric in neurologically healthy individuals [2]. However, asymmetry begins to occur with aging [2], and could be indicative of neurodegenerative diseases [3, 4], such as Parkinson's disease (PD). PD is characterized by a predominantly unilateral appearance of tremor, rigidity, and bradykinesia [5]. However, there is no obvious cause for the preferential unilateral neurodegenerative process [6].

The study of asymmetry in walking in people with PD may help in understanding the pathogenesis of the disease [6]. Clarifying what is responsible for motor asymmetry in PD is certainly important for understanding the cause of PD and its progression [7]. However, the motor control mechanisms of the limbs during walking are not well understood. The few studies that have analyzed asymmetry in gait evaluated tasks which presented little challenge, for example, walking without environmental demands (unobstructed walking). Challenging tasks, such as crossing an obstacle during walking, represent daily activities and can help in understanding the unilateral symptoms of PD. Therefore, in this chapter we discuss gait asymmetry in people with PD. Specifically, we present a general idea about unilateral signs/symptoms of PD and its influence on asymmetry and review the literature with regard to unobstructed gait asymmetry in people with PD. Finally, we show the effects of obstacle crossing and auditory cues on gait asymmetry in people with PD.

11.2 Parkinson's Disease and Unilateral Motor Impairment

PD is characterized by the dysfunction or death of neurons that produce dopamine. PD affects 0.3% of the general population, with the highest prevalence in individuals over 60 years old [8]. PD causes degeneration mainly in the substantia nigra of the basal ganglia that is located in the midbrain, causing several forms of motor impairment [9]. The reduced level of dopamine inhibits the thalamus cortical and brainstem motor systems, compromising other brain structures [10]. This degeneration affects the planning and execution of motor actions in people with PD, especially repetitive, simultaneous, and sequential movements [11].

The diagnosis of PD is generally detected through the characteristic signs and symptoms of the disease. The principal signs and symptoms of PD used for diagnosis are bradykinesia, akinesia, hypometry, resting tremors, and muscle stiffness [11]. In addition, the unilateral predominance of the disease is another important indicator for PD diagnosis [6, 7], which is related to asymmetry between the sides.

Sidedness is used to differentiate PD from other neurodegenerative diseases [6]. More than half of people with PD present sidedness in motor impairment [12–16], commonly indicated by the Unified Parkinson's Disease Rating Scale [12, 17, 18]. The unilateral predominance of signs and symptoms affects patients in the early stages of the disease and may persist throughout the progression period of the disease—20–30 years [6, 19]. Previous studies have reported that impairment in the lower and upper limbs of people with PD occurs in accordance with the extent of brain damage in regions containing dopamine in each hemisphere [20–22]. Individuals with unilateral PD present significant differences in striatal uptake between sides, in both the caudate and putamen nuclei [23, 24]. In addition, the dominant hemisphere has a widespread distribution in the thalamus circuitry [25–27].

Structural, genetic, environmental, and toxic or metabolic mechanisms could explain this asymmetry in PD signs and symptoms [6]. However, two theories are most accepted to explain the unilateral signs and symptoms [6]. Before detailing the explanations, it is interesting to indicate that motor signs and symptoms emerge after the loss of about 50–70% of the nigral neurons [9, 10]. The first theory indicates that there are normal inborn differences in the numbers of nigral dopaminergic neurons. Consequently, from birth, the number of nigral neurons on one side may be lower than that on the other side. The degenerative process of the disease affects both sides equally, but the side with the primarily reduced number of neurons reaches the critical point of vulnerability earlier. The second theoretical possibility is that, for some reason, one substantia nigra is more vulnerable than the other, and once the degenerative process starts, accelerated cell death occurs first on that side (see reference [6] for more details).

11.3 Gait Asymmetry in People with Parkinson's Disease

Due to sidedness of motor impairments, people with PD present asymmetrical adjustments in walking. However, the mechanisms that cause gait asymmetry in people with PD are not well known. Gait asymmetries in PD reflect an asymmetrical depletion of dopamine in the substantia nigra [28, 29]. This results in asymmetrical deregulation of the striatum, leading to further asymmetrical dysfunction of multiple circuits involving the basal ganglia and cortical regions [30, 31].

Previous studies have indicated that people with PD presented greater asymmetry in the temporal parameters compared to neurologically healthy older subjects [4, 32–37]. Specifically, swing time and its variability are the most asymmetrical parameters in people with PD, which are related to freezing episodes, falls, and decreased executive function [4, 32–35]. However, step length [38] and ground reaction forces [32] seem to be symmetrical parameters in unobstructed walking for individuals with PD. Table 11.1 shows previous studies that investigated gait asymmetry in people with PD. It is important to indicate that the findings of these studies were from walking without environmental demand. The presence of an obstacle during walking could increase gait asymmetry due to the increased complexity of the task. In the next section we present our findings on the effects of obstacle avoidance on gait asymmetry in people with PD.

To mitigate the effects of the signs and symptoms, especially asymmetry, and to improve the quality of life of people with PD, some interventions are used. The most common is pharmacological treatment. Although pharmacological treatment is effective at improving motor performance in people with PD, it presents some side effects. Therefore, other interventions have also been used, such as the external cues paradigm [39, 40] to reduce asymmetry without side effects. Verbal external [41], visual [42], rhythmic [43, 44], and auditory [45–47] cues are conventionally used in PD treatment. Previous studies have indicated that auditory cues are most effective for people with PD [48, 49], which improve rhythmicity, walking speed, and step length [47, 50-52]. One possible explanation for the improvement in gait from auditory cues is that movement requires less effort and attention, which could facilitate walking [44]. However, the use of external cues, especially auditory cues, has not been sufficiently studied with respect to the effects on asymmetry in people with PD. It is possible, this intervention could decrease walking asymmetries in people with PD. The results of our study about the effects of auditory cues on gait asymmetry in unobstructed and with obstacle walking in people with PD are presented in the following sections.

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	Examine if freezing of gait is related to motor asymmetry in patients with de novo PD Assess the contribution of cognitive function to gait symmetry	Samples n = 24 (PD FOG+) H&Y = 3 (OFF); 2.7 (ON) n = 12 (PD FOG-) H&Y = 2.8 (OFF); 2.7 (ON) n = 35 (de novo PD) H&Y = 1-2, 5 n = 35 (de novo PD) H&Y = 1-2, 5 n = 22 (control group) H&Y = 2-3 n = 15 (older fallers) n = 15 (older fallers) n = 11 (control group)	Environment and condition Walk at their normal pace on level ground for a total of 80 m Walk on level ground (80 m) at self-selected usual walking speed Walk 25 m at comfortable pace under two walking and dual tasking (cognitive loading)	Main findings The group PD FOG+ showed larger asymmetry in ON and OFF state, compared to the group PD FOG- No correlation was found between asymmetry of clinical symptoms and gait asymmetry in de novo PD patients in temporal parameters (swing time), but not in ground reaction forces For both people with PD and older fallers: Gait asymmetry values were significantly higher during the usual walking condition in people with PD Gait asymmetry walked and performed a dual task compared to the usual walking condition Gait asymmetry was associated with gait speed and gait variability, but no correlations were found for PD motor symptoms
ssess symn atient ithou	Assess spatial step asymmetry during gait in patients with PD with and without freezing of gait	n = 12 (PD FOG+) H& Y = 2.4 n = 15 (PD FOG-) H& Y = 2.1 n = 15 (control group)	Walking 8 m overground at preferred speed and on treadmill at preferred speed	Step time asymmetry was larger in PD FOG- compared to control group during treadmill walking There were no differences in step length variation and asymmetry between PD FOG- and PD FOG+ UPDRS score was significantly associated with spatial step asymmetry

	Main findings	Significant correlation between gait asymmetry and FOGQ, between improvement in gait asymmetry and improvement in right stride length and improvement in FOGQ	Aging and PD significantly increased lowe limb joint asymmetry People with PD presented greater asymmetry than the control older adults
	Environment and condition	4-week rehabilitation treatment using a treadmill with auditory and visual cues	Walking on a split-belt treadmill for 5 min at preferred velocity
ontinued)	Samples	n = 30 (PD FOG+) $n = 30 (PD FOG-)$ $H& Y = 3$	n = 10 (DP group) n = 10 (control older adults) n = 20 (young adults)
	Purpose	Evaluate the relationship between gait asymmetry and freezing of gait and the effects of treadmill treatment on asymmetry	Investigate possible changes in coupling patterns, symmetry, complexity, and variability of lower extremity joints in gait of people with PD
Table 11.1 (continued)	Author	Frazzitta et al. [36]	Park et al. [37]

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FOG+ with freezing of gait, FOG- without freezing of gait, FOGQ freezing of gait questionnaire, ON under medication effects, OFF without medication effects, H&Y Hoehn and Yahr scale, UPDRS Unified Parkinson's Disease Rating Scale

11.4 Effects of Obstacle Avoidance on Gait Asymmetry in People with Parkinson's Disease

Unobstructed walking of individuals with PD is asymmetric. However, spatial parameters [38] and ground reaction forces [32] seem to be symmetric in unobstructed walking. Despite important findings about gait asymmetry in previous studies, analysis of asymmetry during complex gait tasks, such as obstacle crossing during gait, which are performed daily by this population [53], is neglected. Obstacle crossing during walking is one of the main factors leading to falling in people with PD [53–55]. Bilateral asymmetry reflects medial–lateral imbalance and instability and, hence, a predisposition to falls [33]. Previous researches has indicated that obstacle crossing during walking increases gait impairment in people with PD, mainly the hypometry and bradykinesia [53, 56–60], decreasing the toe clearance during obstacle crossing and changing the foot position in relation to the obstacle [53, 54, 61, 62]. Therefore, due to the increase in difficulty, complexity, and motor requirements during obstacle crossing for people with PD, asymmetry during this type of gait could be exacerbated.

We investigated the influence of obstacle crossing on gait asymmetry in individuals with PD and neurologically healthy older individuals (control group) (Table 11.2). Participants performed five trials of unobstructed gait and ten trials of obstacle crossing during gait (five trials of crossing with each leg) at a self-selected speed. Both people with PD and neurologically healthy older individuals (control group) demonstrated a higher symmetric index [63–65] for step duration during obstacle crossing while walking compared to unobstructed walking. Obstacle crossing increased step duration of both crossing step limbs compared to step duration in unobstructed walking and increased step duration of the step with the most affected (people with PD)/non-dominant (control group) limb compared to the step with the least affected/dominant limb. Our findings confirmed the idea that obstacle crossing increased gait asymmetry compared to unobstructed walking.

Obstacle crossing requires that individuals perform adjustments during walking, necessitating rapid planning and execution of adaptive movements [66], which seems to exacerbate gait asymmetry. Obstacle avoidance involves complex circuitry, such as the parietal and motor cortex, the lateral cerebellum, and pontine gray nuclei [66], which appears to be more susceptible to sudden interference. For example, obstacle avoidance is characterized by reduced velocity, shortened step length, and larger step width [53, 55, 57, 67, 68], which needs a more conservative and cautious strategy. The combination of consciously controlled walking with deliberate obstacle avoidance may well outweigh the available resources, causing these adjustments and increasing gait asymmetry. Older people already present deficits in the circuitry indicated below, mainly in peripheral structures [69], which could cause gait asymmetry during complex locomotion. These structures are more impaired in PD, affecting the basal ganglia and requiring greater compensatory involvement from other parts of the brain during walking [70]. In addition, individuals with PD present a progressive difference in striatal uptake between the cerebral hemispheres in both the caudate and putamen nuclei and in the

Table 11.2Meanscrossing in individua	and standard deviatic als with PD and neuro	Table 11.2 Means and standard deviations of the walking parameters and symmetric index [63–65] on unobstructed walking and walking with obstacle crossing in individuals with PD and neurologically healthy older individuals	neters and symmetric individuals	ndex [63-65] on uno	bstructed walking and w	alking with obstacle
	People with PD			Neurologically healthy older individuals	hy older individuals	
	Least/dominant limb	Most/non-dominant limb	Symmetric index (%)	Least/dominant limb	Most/non-dominant limb	Symmetric index (%)
Unobstructed walking	ng					
Step length (cm)	57.96 ± 6.77	59.0 ± 7.10	2.30 ± 2.09	63.57 ± 4.25	62.88 ± 5.84	1.94 ± 2.02
Step duration (s)	0.54 ± 0.06	0.54 ± 0.05	1.23 ± 0.77	0.50 ± 0.05	0.51 ± 0.05	1.07 ± 0.86
Step width (cm)	10.55 ± 3.51	11.00 ± 3.62	6.39 ± 6.84	10.53 ± 2.24	10.86 ± 2.87	3.82 ± 3.10
Step velocity (cm/s)	108.57 ± 18.62	110.69 ± 20.33	2.60 ± 1.96	126.16 ± 1085	123.27 ± 11.97	1.89 ± 1.80
Double support (%)	24.61 ± 2.91	26.10 ± 1.82	4.33 ± 4.74	23.28 ± 2.05	24.44 ± 1.88	2.95 ± 2.69
Obstacle walking						
Step length (cm)	63.42 ± 6.06	64.14 ± 6.73	1.88 ± 1.45	65.23 ± 6.9	65.9 ± 6.43	2.11 ± 1.75
Step duration (s)	0.74 ± 0.09	0.75 ± 0.08	2.30 ± 1.67	0.65 ± 0.07	0.68 ± 0.07	2.52 ± 1.84
Step width (cm)	10.63 ± 1.89	11.21 ± 2.13	5.94 ± 5.80	13.08 ± 4.69	13.10 ± 3.77	7.57 ± 5.85
Step velocity (cm/s)	87.01 ± 13.8	87.14 ± 15.98	2.20 ± 1.55	101.71 ± 11.7	98.96 ± 13.78	2.77 ± 1.60
Double support (%)	15.9 ± 2.40	16.42 ± 2.18	2.96 ± 3.59	15.21 ± 2.43	15.94 ± 1.90	5.10 ± 4.10

cortical–basal ganglia–thalamic circuitry [25–27], which cause gait asymmetry and seem to increase during challenging tasks. Therefore, obstacle avoidance increases gait asymmetry in neurologically healthy older individuals and people with PD.

11.5 Influence of Auditory Cues on Gait Asymmetry during Obstacle Avoidance

Previous studies have indicated that auditory cues are the most effective cues for people with PD [48, 49]. Auditory cues are external stimuli associated with the initiation and ongoing facilitation of a movement [40], which improves rhythmicity, walking speed, and step length [47, 50–52]. Due to auditory cues that influence the neural circuitry regulating gait, Brodie and collaborator [73] indicated that symmetry matched auditory cues compensated the unsteady gait in the majority people with PD, but did not interfere in gait asymmetry. Despite this, the authors suggest that during challenging walking task, such as turning or obstacle crossing, auditory cues could decrease gait asymmetry.

Our group investigated the influence of auditory cue on gait asymmetry during obstacle avoidance in people with PD and neurologically healthy older individuals. Participants performed five trials of unobstructed gait and ten trials of obstacle crossing during gait (five trials of crossing with each leg) with and without auditory cues. First, the individuals performed the trials without auditory cues. For the auditory cue trials, the cue (controlled by a metronome) was customized for each individual according to the cadence determined by three trials performed prior to starting the experiment.

People with PD and neurologically healthy older individuals presented different behaviors for gait asymmetry when auditory cues were provided (Table 11.3). Individuals with PD demonstrated lesser asymmetry for step length, duration and velocity, and cadence than neurological healthy older individuals when auditory cues were offered. For individuals with PD, auditory cues in unobstructed walking decreased step velocity asymmetry. Only neurologically healthy older individuals showed greater asymmetry in the trials with auditory cues for step length, duration and velocity, and cadence. In addition, the control group demonstrated greater asymmetry for stride velocity with auditory cues in obstacle crossing compared to unobstructed walking. Finally, neurologically healthy older individuals increased gait asymmetry (step length, velocity, and cadence) during obstacle crossing with auditory cues compared to without auditory cues.

Auditory cues had no effects on gait asymmetry for unobstructed and obstacle walking in individuals with PD. Only step velocity in unobstructed walking improved gait asymmetry with auditory cues. The findings corroborate with Brodie and collaborators [73] who did not find an influence of auditory cues on gait asymmetry. This finding could be interpreted as asymmetry in morphology, musculature, and joints related to aging than directly through mechanisms related to the diagnosis of PD [73]. However, although auditory cues influence the neural circuitry regulating gait [43, 46], improving automatic movement [71, 72] and

	People with PD		Neurologically healthy older individuals	
Symmetric index (%)	Without auditory cues	With auditory cues	Without auditory cues	With auditory cues
Unobstructed walking				
Step length	2.30 ± 2.09	1.60 ± 1.50	1.94 ± 2.02	1.93 ± 1.16
Step duration	1.23 ± 0.77	1.17 ± 0.70	1.07 ± 0.86	1.05 ± 0.67
Step width	6.39 ± 6.84	3.60 ± 3.17	3.82 ± 3.10	3.63 ± 3.50
Step velocity	2.60 ± 1.96	1.50 ± 1.19	1.95 ± 1.72	2.29 ± 1.30
Cadence	1.24 ± 0.77	1.17 ± 0.72	1.06 ± 0.87	1.03 ± 0.67
Double support	4.33 ± 4.74	3.49 ± 2.48	2.50 ± 2.41	2.76 ± 4.35
Obstacle walking				
Step length	1.88 ± 1.45	2.34 ± 1.36	2.28 ± 1.69	5.74 ± 3.91
Step duration	2.30 ± 1.67	2.43 ± 2.97	1.96 ± 0.68	7.44 ± 4.80
Step width	5.94 ± 5.80	7.60 ± 5.24	7.57 ± 5.85	15.36 ± 16.18
Step velocity	2.20 ± 1.55	3.18 ± 2.50	2.48 ± 1.53	10.53 ± 6.86
Cadence	2.30 ± 1.66	2.47 ± 3.01	1.98 ± 0.64	7.47 ± 4.70
Double support	2.96 ± 3.59	3.34 ± 3.99	5.20 ± 4.72	7.62 ± 3.85

 Table 11.3
 Means and standard deviations of the walking parameters and symmetric index [63–65] without and with auditory cues in people with PD and neurologically healthy older individuals

decreasing asymmetry, when individuals with PD cross an obstacle, auditory cues did not improve, but did not impair, gait asymmetry. The findings seem to indicate that people with PD do not use auditory cues, or that obstacle avoidance impairs the benefit of auditory stimuli in gait asymmetry. An important aspect to analyze in future studies is if people with PD are able to synchronize their steps (heel contact) with auditory cues. It is possible that the higher demands of this task prevent adequate the use adequately of the auditory information.

More surprising were the results for neurologically healthy older individuals. The combination of obstacle avoidance and auditory cues increased gait asymmetry. Auditory cues seem to disrupt the gait pattern of neurologically healthy older individuals, which increases gait variability [39]. Possibly the combination of auditory cues and obstacle crossing increases the robustness of the task, increasing gait pattern disruption. Auditory cues seem to interfere with well-learned movement patterns in people without basal ganglia deficits, which perturbs the functioning of internal mechanisms [73]. Therefore, the use of auditory cues for neurologically healthy older individuals during obstacle avoidance seems not to be recommended.

11.6 Final Remarks

Neurologically healthy older individuals seem to start presenting asymmetry in gait, probably caused by aging effects. However, gait asymmetry is exacerbated in people with PD due to the effects of the disease that generate unilateral motor

degradation. Several studies have found greater unobstructed gait asymmetry in individuals with PD, especially for temporal gait parameters. However, little is known about gait asymmetry during obstacle avoidance in both people with PD and neurologically healthy older individuals.

Obstacle avoidance seems to increase gait asymmetry in both people with PD and neurologically healthy older individuals. Differently from unobstructed gait, the effects of aging seem to increase gait asymmetry in complex walking, independent of the effects of PD. Older people already present deficits in brain circuitry, which are more impaired in people with PD, increasing gait asymmetry during obstacle avoidance. Older individuals, and particularly people with PD, are especially impaired to switching in motor tasks, requiring subjects to make corrective steps instead of walking straight [66], predominantly during challenging walking tasks. It is possible that the basal ganglia are important for set-dependent adaptation of movement patterns for changes in condition, indicating that individuals have inflexible control [74], which is aggravated by sensory and perceptual deficits such as in people with PD [75].

Auditory cues seem to have no effects on gait asymmetry for unobstructed and obstacle walking in individuals with PD, but they impair gait asymmetry in neurologically healthy older individuals during obstacle avoidance. Possibly the combination of auditory cues and obstacle crossing disrupted the gait pattern in neurologically health older individuals, increasing gait asymmetry. In addition, individuals with PD were not able to use auditory cues to improve gait asymmetry during obstacle avoidance. This task seems to be a complex movement for people with PD that demands more movement coordination and attention, impairing the use of auditory stimulus.

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