Research report

Obstacle circumvention and eye coordination during walking to least and most affected side in people with Parkinson's disease

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ABSTRACT

Background: The mechanisms that contribute to gait asymmetry in people with Parkinson's disease (PD) are unclear, mainly during gait with greater environmental demand, such as when an obstacle is circumvented while walking.
Objective: The aim of this study was to investigate the effects of obstacle circumvention of the least and most affected side on motor and gaze behavior in people with PD under/without the effects of dopaminergic medication.
Methods: Fifteen people with PD and 15 matched-control individuals were instructed to walk along a pathway, at a self-selected velocity, and to circumvent an obstacle, avoiding contact with it. Each participant performed five trials for each side. Kinematic parameters, mediolateral and horizontal body clearance to the obstacle, strategy to circumvent the obstacle, and gaze behavior were calculated. Parameters were grouped according to the side that the obstacle was circumvented and compared by three-way ANOVAs.
Results: Both people with PD and the control group presented asymmetry to circumvent an obstacle during walking, however this was exacerbated in people with PD. Individuals with PD presented safe strategies (largest mediolateral and horizontal body clearance to the obstacle, "lead-out" strategy, and higher number and time of fixations on the obstacle) during obstacle circumvention for the least affected side compared to the most affected side. In addition, positive effects of dopaminergic medication on body clearance, spatial-temporal parameters, and gaze behavior were evidenced only when the obstacle was circumvented to the least affected side.
Conclusions: The obstacle circumvention to the most affected side is risky for people with PD.

1. Introduction

Obstacle circumvention is a more complex task than unobstructed walking. The former task requires that the individual detects the obstacle's position and edges, performs precise motor actions, and adjusts their movement around it, allowing adequate personal space (body clearance) at the point of moving past the obstacle to ensure safe navigation [1]. During obstacle circumvention, both people with Parkinson's disease (PD) and neurologically healthy individuals decrease step length and step velocity compared to unobstructed walking [2]. In addition, people with PD increase gait variability and duration of gaze fixations on the obstacle and ground when walking with obstacle circumvention, and reduce body clearance without effects from dopaminergic medication [2].

The planning and adjustments to circumvent an obstacle are according to the side of obstacle circumvention [3]. Previous studies have indicated that younger adults when performing circumvention of an obstacle during walking on the non-dominant side increase their personal space [3]. Preservation of body clearance to the obstacle is used as a control criterion by the locomotor system to plan motor adaptations, which is adjusted according to time required to acquire visual information and plan for upcoming hazards [3,4]. Circumvention of an obstacle to the non-dominant side seems to present slower information processing [5] that causes impairments (i.e. asymmetry) in the

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acquisition and use of visual information [6] to make motor adjustments during the task. These impairments may be exacerbated in people with PD [7] who present symptoms manifestation more severely on one side [10–12] of the body from early stage of the disease [13–18]. Asymmetrical degeneration of dopaminergic neurons in the substantia nigra [19], enlarged lateral ventricle contralateral to the more symptomatic side [20], and cognitive disruption often consistent with the symptomatic hemisphere [21] may explain the higher effects in most affected side in people with PD. In addition, dopaminergic treatment has been established to improve gait motor patterns for both side of the body [13,22], although levodopa has a greater effect on the most affected side [23,24]. However, no previous studies have investigated the effects of side to obstacle circumvention on body clearance to the obstacle, gait parameters and gaze behavior in people with PD.

The aim of this study was to investigate the effects on motor and visual behavior of obstacle circumvention during walking to the least and most affected side in people with PD, under and without the effects of dopaminergic medication. We analyzed the body clearance to the obstacle, circumvention strategy, spatial-temporal parameters, and gaze behavior during obstacle circumvention to both sides in people with PD and neurologically healthy individuals (control group). The hypotheses of this study were: i) people with PD would present safe strategies (increase body clearance, stride length and velocity and number of fixations on the obstacle) during obstacle circumvention to the side least affected by the disease compared to other side (most affected side) due to higher impairments presented in most affected side [13–18]; ii) dopaminergic medication would have a positive effect on body clearance, spatial-temporal adjustments and gaze behaviors (increase these parameters) for both sides during obstacle circumvention in people with PD, as indicated previously in a study with obstacle avoidance [22].

2. Materials and methods

2.1. Participants

Fifteen people with idiopathic PD and 15 matched-neurologically healthy individuals (control group) were selected to participate in the study. The participants with PD were referred to the current study by local neurologists. The diagnosis of the disease was performed by an expert neurologist according to the UK Brain Bank Criteria [27,28]. The groups were matched by age, gender, body weight, and height (Table 1).

The following exclusion criteria were established: disease stage above 3 on the Hoehn & Yahr scale [29,30], signs of dementia, a history of orthopedic or vision problems that would make it impossible to perform the experimental protocol. In addition, the inclusion criterion was the people with PD had to be taking PD medication. The study was approved by the local Ethics Committee (CAAE: 45435615.7.1001.5398). All participants gave their signed and written consent to all experimental procedures.

2.2. Experimental protocol

The individuals with PD performed the tasks in the OFF-medication state (after a minimum of 12 h withdrawal from PD medication), and then again 1 h after the participants had taken their dopaminergic medication (ON-medication state); if the individuals were taking dopaminergic agonist medication, they were evaluated after a minimum of 24 h withdrawal from medication. The control group performed the protocol only once.

2.3. Clinical evaluation

Participants with PD were evaluated by an expert researcher through anamneses (historical clinical, cognitive, and medication), the motor portion of the Unified Parkinson's Disease Rating Scale – UPDRS [31], and the H&Y (stage of disease). In addition, cognitive aspects were analyzed using the Mini Mental State Exam [32,33] in all participants.

In addition, for people with PD, motor UPDRS items 20, 21, 22, 23, 25, and 26 were used to assess appendicular asymmetry [14]. The most severely affected limb was determined by finding the difference between the scores for the right and left limbs in the aforementioned UPDRS items. Then, the values of this item-analysis were summed. When this calculation resulted in a positive value, the right limb was the most severely affected limb, but when negative values were obtained, this indicated that the left limb was more severely affected. For the control group, footedness was assessed by asking the participant to kick a ball at a target [21,23]. The limb used to kick the ball was considered as the dominant limb.

2.4. Obstacle circumvention during gait

The participants were instructed to walk along a pathway (approximately 8.5 m long by 3.5 m wide), at a self-selected velocity, and to circumvent an obstacle, avoiding contact with it. In addition, participants were instructed to return to the starting line. The obstacle was cylindrical (0.35 m diameter) and 1.30 m high [2]. The obstacle was positioned in the middle of the pathway, allowing a similar space on both sides (∼1.60 m) and 4 m from the starting point. In all trials, the participant was positioned lined up with the obstacle.

Each participant performed 5 circumventions for each side (10 trials in total). The participants were not instructed as to which side they needed to circumvent the obstacle. They chose the side until they had performed 5 trials for one side (e.g., right). Then, the researcher obstructed this side, necessitating that the participants circumvent the obstacle on the other side (e.g., left).

2.5. Data analysis

The kinematic parameters were recorded by an 8 cameras Vicon Motion System® (Bonita System Cameras) with a sample rate of 100 samples/s. Passive reflective markers were placed on the participants' skin at predefined landmarks according to the Plug-in-Gait Full Body model (Vicon) (left and right front and back head, 7th cervical vertebrae, 10th thoracic vertebrae, clavicle, sternum, middle of the right scapula, left and right shoulder, left and right upper arm, left and right elbow, left and right forearm, left and right wrist bar thumb and pinkie side, left and right fingers, left and right anterior and posterior superior iliac spine, mid-way between the posterior superior iliac spines, lateral epicondyle of the left and right knee, left and right lower lateral 1/3 surface of the thigh, left and right lateral malleolus, left and right lower lateral 1/3 of the shank, left and right second metatarsal head and left and right calcaneous) and four markers were placed on the obstacle. Data were filtered using a 5th order low-pass digital Butterworth filter (zero-lag) with a cutoff frequency of 6 Hz.

The data were recorded in two phases of obstacle circumvention: the approach phase − final stride before circumvention of the obstacle; and circumvention phase − stride during the obstacle circumvention (Fig. 1). Nexus software (Vicon) calculated the tridimensional center of mass (CoM) coordinates based on the tridimensional coordinates of the 39 markers, which defined a 15-segment model [34]. Following CoM coordinates, we calculated the mediolateral body clearance (largest mediolateral distance of the CoM to the obstacle during obstacle circumvention) [35,36] (solid arrow in Fig. 2C) and the horizontal body clearance (distance at which participants started to circumvent the obstacle. To calculated this parameter, first it was drawn an imaginary line between the CoM position where participant began the trial and the marker positioned centrally in the top of the obstacle. So, the begin of deviation was defined as five standard deviations of this line) (dashed arrow in Fig. 2C). In addition, the following spatial-temporal parameters of gait for each phase were calculated: stride length, stride

Table 1
Characteristics and clinical parameters of each participant in the control group and PD group. The last line of the table for the control group and PD group represents the means and standard deviations of each group in each parameter. FP − foot preference.

PD Group

	Sex	Age (years)	Body mass (kg)	Height (m)	H&Y OFF	H&Y ON	MMSE OFF (pts)	MMSE ON (pts)	UPDRS III OFF (pts)	UPDRS III ON (pts)	FP
1	M	61	82.20	1.70	2	2	30	30	26	25	R
2	F	64	70.00	1.60	2	2	28	29	22	17	R
3	F	54	86.00	1.52	2	2	30	29	25	23	R
4	M	61	50.30	1.63	2.5	2.5	29	30	47	39	R
5	F	74	48.00	1.41	3	3	20	21	60	48	R
6	F	74	64.80	1.61	1.5	1	26	26	26	16	R
7	F	64	85.70	1.55	1.5	1.5	30	28	26	24	R
8	F	52	70.70	1.49	2	2	27	30	41	32	R
9	M	80	79.30	1.70	2	2	28	27	35	24	R
10	F	63	47.30	1.58	1	1	27	27	16	15	R
11	M	75	61.50	1.67	2.5	2.5	25	25	39	33	R
12	F	84	67.00	1.60	3	3	28	28	25	24	R
13	M	58	98.00	1.69	2	1.5	30	30	23	19	R
14	F	53	80.00	1.60	2	1	26	30	18	11	R
15	F	63	51.10	1.60	2.5	2.5	29	30	32	21	R
Mean ± SD	5 M/10F	65.33	69.46	1.59	2.10	1.97	27.53	28.00	30.73	24.73	
		9.90	15.75	0.08	0.54	0.67	2.64	2.54	11.84	9.77	

Control Group

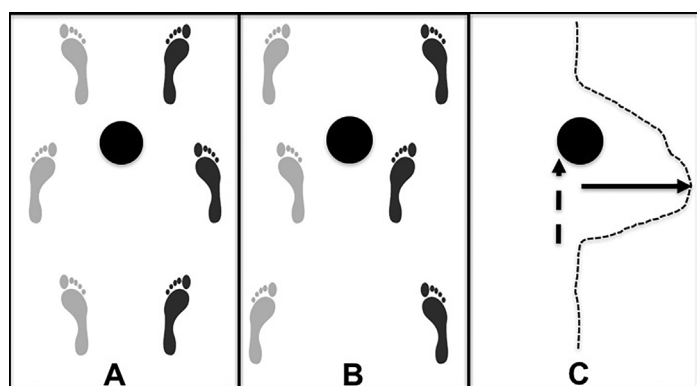|	Sex (M/F)	Age (years)	Body mass (kg)	Height (m)	MMSE (pts)	FP
1	F	74	63.50	1.53	29	R
2	F	56	57.50	1.57	26	R
3	M	67	76.50	1.67	29	R
4	M	74	74.00	1.68	27	R
5	F	65	62.90	1.65	29	R
6	M	67	64.70	1.69	27	R
7	F	62	80.30	1.59	27	R
8	F	71	67.60	1.57	27	R
9	F	65	76.50	1.55	27	R
10	F	65	75.40	1.54	24	R
11	M	77	62.30	1.62	28	R
12	F	77	77.80	1.57	27	R
13	M	69	88.00	1.75	28	L
14	F	73	51.00	1.52	29	R
15	F	66	59.00	1.56	25	R
Mean ± SD	5 M/10F	68.53	69.13	1.60	27.27	
		5.84	10.12	0.07	1.49	

width, stride duration, stride speed, and double support time (percentage of stride duration). The strategy chosen by the participants to circumvent the obstacle, "lead-out" (lead limb away from the obstacle during the crossing step) or "lead-in" (lead limb close to the obstacle during the crossing step) strategies, was also determined [35].

Gaze behavior was recorded by a mobile eye tracker (Mobile Eye-5 glasses, ASL, Bedford, MA, USA). The frequency of data acquisition was 60 Hz. The eye tracker system was calibrated using the nine-point calibration method. Participants fixated their gaze on nine points displayed in a 3 × 3 grid. Calibration was also checked periodically between trials. Gaze fixation was considered when the two times point of gaze standard deviation (95% confidence interval) was less than one
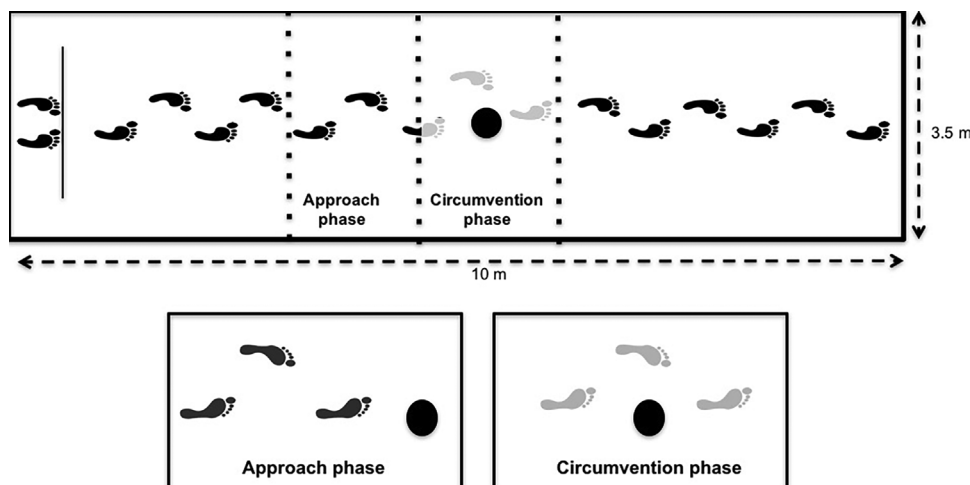
Fig. 1. Bird's eye view of the task when an individual performed obstacle circumvention to the left. The approach and circumvention phases are presented in the figure.

Fig. 2. A: Percentage of "lead-in" strategy according to side the obstacle was circumvented in people with PD under (ON) and without (OFF) the effects of dopaminergic medication. **B:** Percentage of "lead-out" strategy according to side the obstacle was circumvented in people with PD under and without the effects of dopaminergic medication. **C:** Means and standard deviations of mediolateral body clearance (solid arrow) and horizontal body clearance to the obstacle (dashed arrow) according to side the obstacle was circumvented in people with PD under and without the effects of dopaminergic medication. The values of variability (means and standard deviations) for each parameter are presented in brackets.

Horizontal distance (cm)

OFF	Least affected	146.87±27.96 (10.97±8.96)
	Most affected	142.33±26.84 (14.54±12.18)
ON	Least affected	154.40±24.61 (9.61±7.23)
	Most affected	140.47±25.30 (9.03±5.83)
CG	Dominant	158.93±16.94 (16.63±10.43)
	Non-dominant	145.93±13.86 (16.41±9.73)

"Lead-in" strategy (%)

OFF	Least affected	48.00
	Most affected	60.00
ON	Least affected	48.00
	Most affected	57.33
CG	Dominant	38.67
	Non-dominant	54.67

"Lead-out" strategy (%)

OFF	Least affected	52.00
	Most affected	40.00
ON	Least affected	52.00
	Most affected	42.67
CG	Dominant	61.33
	Non-dominant	45.33

Mediolateral body clearance (cm)

OFF	Least affected	43.51±9.00 (14.52±10.30)
	Most affected	42.26±14.18 (13.86±9.33)
ON	Least affected	49.31±8.38 (7.49±4.79)
	Most affected	45.79±9.45 (9.35±6.05)
CG	Dominant	47.59±5.50 (6.58±4.65)
	Non-dominant	46.55±6.74 (10.78±10.16)

degree of visual angle (horizontal and vertical) over 99 ms. We analyzed the following parameters: number of fixations (total number of fixations during the trial), mean duration of the fixations, and time of fixations (percentage of the travel time) [8]. In addition, gaze fixations were classified into four different areas of interest: ground (any location on the ground before, after or to the side of the obstacle), obstacle (any location on the obstacle), wall (any area on the wall at the end of the walkway), and random (any areas not included in the other three areas). Finally, we determined the percentage of trials in which there were no fixations on the obstacle (no area of interest to the obstacle).

The parameters were grouped considering the side that the obstacle was circumvented during the task: people with PD – most and least affected side (defined by UPDRS items); control group – dominant and non-dominant side. In addition, the variability of each parameter was calculated. First, the average and standard deviation of each parameter was calculated according to conditions for each participant. Then, the variability was calculated from the coefficient of variation [37].

2.6. Statistical analysis

The level of significance was set at 5% for all analyzes. For clinical parameters, paired sample student t-tests were employed to compare dopaminergic medication effects (OFF-medication state – without dopaminergic medication effects × ON-medication state – under effects of dopaminergic medication). Independent sample student t-tests were employed to compare cognitive status of the control group and people with PD under the effects of dopaminergic medication. The spatial-temporal parameters, mediolateral and horizontal body clearance to the obstacle, and gaze behavior, as well as the variability of these parameters, were compared by two-way ANOVAs (group: PD patients under effects of dopaminergic medication and control group X side: least affected/dominant side and most affected/non-dominant side), separately for the approach phase and the circumvention phase, with side as repeated measure. For areas of interest, the data were analyzed by three-way ANOVAs (group X side X area of interest: ground, wall, obstacle, and random), with side and area of interest as repeated measures. A separate analysis for people with PD was conducted with dopaminergic status in a within-subject design with ON and OFF medication state as the repeated-measure (dopaminergic status comparison). In addition, Tukey post hoc tests were carried out to identify

the significant differences when a significant main effect was found.

3. Results

3.1. Clinical parameters

The characteristics of both the PD and control groups and clinical features of the PD group under and without the effects of dopaminergic medication are presented in Table 1. The groups presented no significant differences in cognitive aspects ($t_{14} = 1.36$, p = 0.34). In addition, there were dopaminergic medication effects in UPDRS-motor, in which people with PD presented the lowest score (improvement in UPDRS-motor) under the effects of dopaminergic medication ($t_{14} = 5.75$, p ≪ 0.001). There were no effects of dopaminergic medication on H&Y ($t_{14} = 1.74$, p = 0.11) or cognitive aspects ($t_{14} = -1.20$, p = 0.25).

3.2. Obstacle circumvention strategy, body clearance, and spatial-temporal parameters

There was not a preferred side (most/non-dominant or least/dominant side) to circumvent the obstacle for both groups. For control group, five participants, two participants and eight participants performed the first five obstacle circumvention to, respectively, dominant side, non-dominant side and randomly (i.e. two for one side and for the another side). For people with PD, two participants performed the first five obstacle circumvention to least affected side (five participants in OFF-medication state), one participant performed the first five obstacle circumvention to most affected side (two participants in OFF-medication state) and twelve participants performed the first five trials randomly (eight participants in OFF-medication state).

Regarding obstacle circumvention strategies, people with PD used the "lead-in" strategy more when they performed obstacle circumvention to the most affected side while the control group used the "lead-in" strategy and "lead-out" strategy more when they performed obstacle circumvention to the dominant side and non-dominant side, respectively (Fig. 2).

Both groups increased the horizontal body clearance to the obstacle (beginning the obstacle circumvention) when they performed obstacle circumvention to the least affected/dominant side ($F_{1,28} = 14.89$,

Table 2

Means and standard deviations of spatial-temporal parameters according to side the obstacle was circumvented and group. The first part of the table presents parameters for the approach phase and the second part presents parameters for the circumvention phase. The values of variability (means and standard deviations) for each parameter are presented in brackets.

Phase	Parameter	Group DP OFF-medication state		Group DP ON-medication state		Control group	
		Circumvention to least affected side	Circumvention to most affected side	Circumvention to least affected side	Circumvention to most affected side	Circumvention to dominant side	Circumvention to non-dominant side
Approach phase	Stride length (cm)	86.60 ± 15.60 (7.06 ± 3.70)	25.87 ± 37.92 (31.01 ± 36.58)	91.69 ± 15.83 (6.92 ± 3.17)	25.98 ± 26.75 (30.17 ± 24.52)	109.94 ± 12.94 (7.67 ± 4.70)	106.90 ± 16.31 (5.54 ± 4.57)
	Stride width (cm)	20.08 ± 5.85 (32.58 ± 21.68)	18.69 ± 9.46 (15.95 ± 8.40)	19.65 ± 4.47 (36.67 ± 22.97)	19.05 ± 10.24 (16.56 ± 9.25)	15.18 ± 7.76 (30.73 ± 24.75)	18.09 ± 4.93 (17.51 ± 10.66)
	Stride duration (s)	1.08 ± 0.13 (3.99 ± 2.28)	1.91 ± 1.39 (1.72 ± 1.29)	1.08 ± 0.09 (4.76 ± 2.92)	2.14 ± 1.40 (1.87 ± 1.25)	1.07 ± 0.11 (3.42 ± 1.80)	1.09 ± 0.11 (3.59 ± 1.61)
	Stride speed (cm/s)	81.46 ± 16.31 (8.63 ± 5.42)	25.75 ± 35.09 (30.59 ± 33.61)	85.23 ± 15.43 (8.28 ± 3.30)	25.14 ± 24.33 (28.68 ± 22.47)	105.11 ± 21.41 (7.57 ± 4.82)	100.30 ± 22.61 (6.47 ± 3.90)
	Double support duration (%)	38.76 ± 5.50 (8.12 ± 5.02)	11.95 ± 14.67 (13.58 ± 14.24)	38.31 ± 5.54 (11.98 ± 10.37)	13.38 ± 9.41 (14.34 ± 8.85)	39.98 ± 2.71 (5.88 ± 4.43)	40.52 ± 3.86 (4.94 ± 2.47)
Circumvention phase	Stride length (cm)	79.66 ± 12.17 (9.56 ± 5.81)	24.36 ± 36.92 (29.69 ± 35.44)	91.36 ± 14.22 (9.99 ± 3.64)	26.10 ± 25.97 (29.77 ± 24.15)	111.97 ± 14.16 (5.44 ± 2.51)	106.43 ± 13.43 (5.58 ± 3.02)
	Stride width (cm)	19.35 ± 5.37 (23.24 ± 13.18)	15.57 ± 7.28 (14.61 ± 6.81)	17.86 ± 4.53 (27.94 ± 7.62)	13.86 ± 7.64 (12.37 ± 7.09)	16.94 ± 6.11 (23.89 ± 8.51)	19.09 ± 5.53 (23.32 ± 14.17)
	Stride duration (s)	1.08 ± 0.11 (4.63 ± 2.69)	2.35 ± 1.84 (2.20 ± 1.79)	1.08 ± 0.10 (4.78 ± 2.25)	2.37 ± 1.44 (2.02 ± 1.20)	1.1 ± 0.12 (3.67 ± 2.07)	1.09 ± 0.10 (5.51 ± 2.57)
	Stride speed (cm/s)	74.64 ± 13.84 (9.78 ± 6.62)	24.06 ± 33.72 (28.91 ± 32.20)	85.33 ± 13.84 (11.17 ± 4.96)	25.06 ± 23.74 (28.30 ± 22.10)	103.39 ± 16.74 (6.48 ± 2.78)	98.63 ± 16.46 (7.89 ± 3.46)
	Double support duration (%)	38.68 ± 5.32 (10.84 ± 6.48)	13.29 ± 13.85 (14.67 ± 13.41)	37.72 ± 6.73 (14.28 ± 8.28)	13.95 ± 8.92 (14.51 ± 8.65)	39.51 ± 3.45 (7.36 ± 5.95)	39.95 ± 4.38 (8.78 ± 5.14)

$p \ll 0.001$) (Fig. 2). In addition, people with PD presented lower variability in horizontal body clearance to the obstacle than the control group for obstacle circumvention to the least affected/dominant side ($F_{1,28} = 7.61$, $p \ll 0.01$). With respect to mediolateral body clearance to the obstacle, people with PD increased the clearance to the obstacle ($p \ll 0.008$) when they performed obstacle circumvention to the least affected side compared to obstacle circumvention to the most affected side (group*side interaction − $F_{1,28} = 4.95$, $p \ll 0.004$). The control group did not present significant differences between sides for mediolateral body clearance, however they increased variability of mediolateral body clearance ($p \ll 0.04$) for non-dominant obstacle circumvention compared to dominant obstacle circumvention (group*side interaction − $F_{1,28} = 3.42$, $p \ll 0.02$).

People with PD presented slower stride velocity (approach phase − $F_{1,28} = 6.08$, $p \ll 0.02$; circumvention phase − $F_{1,28} = 8.07$, $p \ll 0.008$), shorter stride length (approach phase − $F_{1,28} = 10.01$, $p \ll 0.004$; circumvention phase − $F_{1,28} = 12.70$, $p \ll 0.001$), and higher variability of double support time (approach phase − $F_{1,28} = 6.71$, $p \ll 0.01$; circumvention phase − $F_{1,28} = 5.39$, $p \ll 0.02$) in both the approach and circumvention phases than the control group (Table 2). Specifically for the approach phase, people with PD increased stride width ($F_{1,28} = 8.08$, $p \ll 0.008$) and variability of this parameter ($F_{1,28} = 5.47$, $p \ll 0.02$) compared to the control group. In addition, when the individuals performed the obstacle circumvention to the most affected/non-dominant side, people with PD increased variability of stride width ($p \ll 0.03$) compared to the control group in the approach phase (group*side interaction − $F_{1,28} = 10.33$, $p \ll 0.003$). For the circumvention phase, people with PD increased variability of stride length ($F_{1,28} = 7.63$, $p \ll 0.01$) and velocity ($F_{1,28} = 3.88$, $p \ll 0.05$) compared to the control group. In addition, when individuals performed obstacle circumvention to the least affected/dominant side, people with PD increased variability of stride length ($p \ll 0.001$), velocity ($p \ll 0.003$), and double support time ($p \ll 0.01$) compared to the control group (group*side interaction: stride length − $F_{1,28} = 3.53$, $p \ll 0.05$; stride velocity − $F_{1,28} = 7.16$, $p \ll 0.01$; double support time − $F_{1,28} = 3.59$, $p \ll 0.05$). People with PD also increased variability of stride length ($p \ll 0.01$) and velocity ($p \ll 0.01$) when they performed obstacle circumvention to the least affected side compared to the most affected side, while the control group reduced variability of stride duration ($p \ll 0.05$) when they circumvented the obstacle to the dominant side compared to non-dominant side (group*side interaction: variability of stride duration − $F_{1,28} = 3.67$, $p \ll 0.05$). Finally, the control group was faster (increased stride velocity) in both phases (approach phase − $p \ll 0.01$; circumvention phase − $p \ll 0.05$) when they performed obstacle circumvention to the dominant side compared to the non-dominant side.

3.3. Gaze behavior and area of interest

People with PD presented higher variability of time of fixations ($F_{1,28} = 4.22$, $p \ll 0.04$) compared to the control group (Table 3). In addition, when individuals performed obstacle circumvention to the least affected/dominant side, they increased variability of mean duration of fixations ($F_{1,28} = 5.35$, $p \ll 0.02$). Post hoc analysis of group*side interaction (mean duration of fixation − $F_{1,28} = 4.82$, $p \ll 0.03$; variability of time of fixations − $F_{1,28} = 10.98$, $p \ll 0.003$) indicated that when the obstacle circumvention was performed to the most affected/non-dominant side, people with PD increased the mean duration of fixation ($p \ll 0.04$) and variability of time of fixations ($p \ll 0.03$) compared to the control group. In addition, the control group presented higher time of fixations ($p \ll 0.04$) when they circumvented the obstacle to the dominant side (group*side interaction − $F_{1,28} = 4.82$, $p \ll 0.03$).

In general, for area of interest, individuals presented a higher number of fixations ($F_{1,28} = 36.52$, $p \ll 0.001$) and time of fixations ($F_{1,28} = 43.56$, $p \ll 0.001$) on the ground compared to other areas of

interest (obstacle, wall, and random areas) (Table 3). The number of fixations ($p \ll 0.001$) and time of fixations ($p \ll 0.001$) on the obstacle was higher than on the wall and random. In addition, the mean duration of fixations ($F_{1,28} = 9.13$, $p \ll 0.001$) on the obstacle and ground was higher than random. When individuals performed obstacle circumvention to the most affected/non-dominant side, they decreased the number of fixations ($p \ll 0.002$) and time of fixations ($p \ll 0.004$) on the obstacle, and increased the number of fixations ($p \ll 0.002$), time of fixations ($p \ll 0.002$), and mean duration of fixations ($p \ll 0.01$) on the ground compared to obstacle circumvention to the least affected/dominant side (side*area interaction − number of fixations: $F_{1,28} = 13.56$, $p \ll 0.001$; mean duration of fixations: $F_{1,28} = 6.31$, $p \ll 0.001$; time of fixations: $F_{1,28} = 13.24$, $p \ll 0.001$). Furthermore, when obstacle circumvention was performed to the most affected/non-dominant side, they performed a higher number of fixations ($p \ll 0.001$) and time of fixations ($p \ll 0.001$) on the ground than the other three areas of interest, while when obstacle circumvention was performed to the least affected/dominant side, they performed the same number of fixations ($p \ll 0.001$) and time of fixations ($p \ll 0.001$) on the obstacle and ground, but both higher than on the wall and random.

Specifically, people with PD presented a higher number of fixations ($p \ll 0.001$) and time of fixations ($p \ll 0.002$) on the obstacle than the control group (group*area interaction – number of fixations: $F_{1,28} = 5.01$, $p \ll 0.02$; time of fixations: $F_{1,28} = 7.78$, $p \ll 0.003$). In addition, people with PD increased the number of fixations ($p \ll 0.001$), mean duration of fixations ($p \ll 0.04$), and time of fixations ($p \ll 0.001$) on the obstacle when performing obstacle circumvention to the least affected limb compared to the control group when circumventing the obstacle to the dominant side (group*side*area interaction – number of fixations: $F_{1,28} = 17.20$, $p \ll 0.001$; mean duration of fixations: $F_{1,28} = 4.29$, $p \ll 0.01$; time of fixations: $F_{1,28} = 24.56$, $p \ll 0.001$). For the other side (most affected and non-dominant side), people with PD increased the mean duration of fixations ($p \ll 0.002$) on the ground compared to the control group. Furthermore, when people with PD circumvented the obstacle to the most affected side, they decreased the number of fixations ($p \ll 0.001$) and time of fixations ($p \ll 0.001$) on the obstacle and increased the number of fixations ($p \ll 0.001$), mean duration of fixations ($p \ll 0.001$), and time of fixations ($p \ll 0.001$) on the ground; they did not fixate the obstacle in 62.66% of trials when circumventing the obstacle to the most affected side (for least affected side only 9.3% of trials). In contrast, the control group presented similarity in this variable for both sides of obstacle circumvention (dominant side – 62.66% of trials; non-dominant side – 48% of trials).

3.4. ON-medication state vs OFF-medication state

People with PD increased the use of a "lead-in" strategy when performing obstacle circumvention to the most affected side, independent of the effects (both under and without) of dopaminergic medication (Fig. 2). However, they used a similar number of "lead-in" and "lead-out" strategies when performing obstacle circumvention to the least affected side, independent of the effects of dopaminergic medication. In addition, the lack of dopaminergic medication increased the variability of mediolateral body clearance ($F_{1,28} = 5.78$, $p \ll 0.02$), especially when circumventing the obstacle to the least affected side (dopaminergic status*side interaction − $F_{1,28} = 5.74$, $p \ll 0.02$) (Fig. 2). Furthermore, under the effects of dopaminergic medication, people with PD began ($p \ll 0.04$) the obstacle circumvention earlier (horizontal body clearance) than when they performed obstacle circumvention to the least affected side compared to the most affected side (medication*side interaction − $F_{1,28} = 3.84$, $p \ll 0.05$).

There were no effects of dopaminergic medication, side or interaction between factors for spatial-temporal parameters of obstacle circumvention during the approach phase (Table 2). During the obstacle circumvention phase, the lack of dopaminergic medication decreased stride length ($p \ll 0.02$) and velocity ($p \ll 0.04$) when circumventing

the obstacle to the least affected side − compared to the ON-dopaminergic medication state (medication*side interaction − stride length: $F_{1,28} = 3.97$, $p \ll 0.05$; stride velocity: $F_{1,28} = 4.47$, $p \ll 0.04$).Furthermore, when the people with PD, without the effects of dopaminergic medication, performed obstacle circumvention to the most affected side, they increased stride length ($p \ll 0.006$) and velocity ($p \ll 0.02$) compared to the least affected side. However, dopaminergic medication increased the variability of stride length ($p \ll 0.05$) and velocity ($p \ll 0.03$) when people with PD circumvented the obstacle to the least affected side compared to the most affected side (medication*side interaction − stride length: $F_{1,28} = 4.77$, $p \ll 0.03$; stride velocity: $F_{1,28} = 5.20$, $p \ll 0.03$).

There were no effects of dopaminergic medication, side or interaction between factors for gaze behavior (Table 3). However, for areas of interest, the lack of dopaminergic medication decreased the number of fixations ($p \ll 0.006$) and time of fixations ($p \ll 0.009$) on the obstacle and increased the mean duration of fixations ($p \ll 0.02$) on the ground (medication*area interaction − number of fixations: $F_{1,28} = 4.62$, $p \ll 0.03$; time of fixations: $F_{1,28} = 5.82$, $p \ll 0.01$; mean duration of fixations: $F_{1,28} = 5.79$, $p \ll 0.02$). In addition, the lack of dopaminergic medication increased the number of fixations ($p \ll 0.002$), mean duration of fixations ($p \ll 0.003$), and time of fixations ($p \ll 0.001$) on the ground, and reduced the number of fixations ($p \ll 0.001$) and time of fixations ($p \ll 0.001$) on the obstacle when the obstacle was circumvented to the least affected side − compared to under the effects of dopaminergic medication (medication*side*area interaction − number of fixations: $F_{1,28} = 18.50$, $p \ll 0.001$; mean duration of fixations: $F_{1,28} = 3.27$, $p \ll 0.02$; time of fixations: $F_{1,28} = 24.26$, $p \ll 0.001$). In addition, the mean duration of fixations on the obstacle decreased ($p \ll 0.04$) when they performed obstacle circumvention to the most affected side compared to the least affected side without the effects of dopaminergic medication. Dopaminergic medication increased the number of fixations ($p \ll 0.001$), mean duration of fixations ($p \ll 0.001$), and time of fixations ($p \ll 0.001$) on the ground and decreased the number of fixations ($p \ll 0.001$) and time of fixations ($p \ll 0.001$) on the obstacle when people with PD performed obstacle circumvention to the most affected limb compared to obstacle circumvention to the least affected limb. Finally, people with PD without the effects of dopaminergic medication did not fixate the obstacle in 41.33% and 48% of trials when circumventing the obstacle to the least and most affected sides, respectively. The percentage was greater for the least affected side and lower for the most affected side compared to under the effects of dopaminergic medication (see end of Section 3.3).

4. Discussion

The aim of this study was to investigate the effects on body clearance, spatial-temporal adjustments, and gaze behavior of obstacle circumvention to the least and most affected side in people with PD, under and without the effects of dopaminergic medication, and compare these effects with neurologically healthy individuals. People with PD and the control group presented similar strategies to circumvent an obstacle (both used "lead-in" and "lead-out" strategies, began obstacle circumvention at a similar horizontal body clearance to the obstacle, and had similar mediolateral body clearance from the obstacle), which corroborated with our previous study [2]. However, the groups performed different spatial-temporal and gaze adjustments to circumvent the obstacle. People with PD reduced gait velocity and stride length during the approach and circumvention phases, which may be due to hypometric movements and bradykinesia caused by PD [7,9]. This strategy suggests an increased time to acquire information on the environment [38], mainly the obstacle. People with PD were more gaze obstacle-dependent (they increased the number and time of fixations on the obstacle). Vitório and collaborators [39] demonstrated that environmental constraints, such as postural threat, increase the dependence of people with PD on dynamic visual information during

locomotion. Sensory and perceptual deficits caused by PD [40–42] are the main explanation for this gaze behavior during obstacle circumvention. Basal ganglia damage may be associated with sensory and perceptual deficits [43,44] as well as right hemisphere damage, which is responsible for visuospatial processing [45]. On the other hand, reduced gait velocity and stride length increases instability during walking [46–48]. To deal with this unstable gait, people with PD increased the basis of support (stride width) during the approach phase. In addition, the greater variability in stride width and double support time could be an attempt by the system to seek stability. Despite this, a large variability (besides stride width and double support time, people with PD increased variability of stride length and velocity during the approach phase), may suggest impairment in both mechanisms that regulate gait rhythm and the central pattern generator and those that regulate balance [49] and sequential and rhythmic movements caused by lesions in the posterior part of the putamen [42,50]. The greater variability in people with PD could be interpreted, from a pathophysiology aspect, as a deficit in the basal ganglia internal rhythmicity [51,52].

4.1. Strategies of people with PD to deal with asymmetry when circumventing the obstacle

Our most important finding was that people with PD presented asymmetry when circumventing the obstacle, which confirmed our first hypothesis. People with PD presented safe strategies (greater mediolateral and horizontal body clearance to the obstacle, "lead-out" strategy, and higher number and time of fixations on the obstacle) during obstacle circumvention to the least affected side compared to the most affected side, which seems to indicate asymmetric motor and gaze behavior to circumvent an obstacle. However, neurologically healthy individuals also presented asymmetric behavior, although lower than people with PD, in the obstacle circumvention strategy, body clearance, spatial-temporal, and gaze strategies, which seems to indicate that asymmetric behavior during obstacle circumvention begins in neurologically healthy individuals and is exacerbated in people with PD. A previous study [3] related asymmetric behavior during obstacle circumvention in younger and older adults. The explanation for this asymmetric behavior is that visual-spatial information is processed faster when obstacle circumvention is performed to the dominant side due to the greater cortical representation and salience of this side [53].

People with PD performed a risky strategy when circumventing an obstacle to the most affected side. They began the obstacle circumvention closer to the obstacle (shorter horizontal body clearance), used a "lead-in" strategy and smaller mediolateral body clearance compared to when the obstacle was circumvented to the least affected side. In addition, they increased the number and time of fixations on the ground and decreased these parameters on the obstacle when circumventing the obstacle to the most affected side. These findings reinforce the risky strategy, which can increase the chances of making contact with the obstacle. Obstacle circumvention to the most affected side seemed to increase the need to guarantee the accuracy and precision of foot placement and the path to obstacle circumvention. To deal with this need is the reduced gait velocity during approach and circumvention phases during obstacle circumvention to the most affected side, which increased the time to plan the foot position and to place the foot precisely [48,54]. Due to the proprioceptive [43] and working memory [55] deficits usually observed in people with PD, they are more dependent on the availability of visual information in an on-line mode to fine tune the accuracy of foot placement [8]. Therefore, asymmetric control of the basal ganglia seems to be evidenced due to the fact that the brain side that controls the most affected limb seems to present worse striatal uptake in both the caudate and putamen nuclei [56,57] and reduced distribution throughout the cortical-basal ganglia-thalamic circuitry [58,59]. In addition, the deficits in circumventing the obstacle to the most affected side were not only in the motor system, but also in

the sensorial system. We can speculate that degeneration in the most affected brain side also occurred in perceptual brain areas. Previous studies have also indicated that veering is side affected to PD-dependent [60,61]. Perceptual/sensorial asymmetry is a characteristic in the earliest stages of the disease [54,59,62,63], which seems to be manifested depending on the basal ganglia-cortical loops activated by the visual and motor demands of the task [62]. Finally, obstacle circumvention to the most affected side decreased the variability of stride length and velocity. This strategy seems to indicate a greater robustness of the motor system that can be explained by the difficulty of people with PD to perform adjustments during challenging tasks due to impairments in the basal ganglia, decreasing motor flexibility − action reprogramming [37], which seems to be a worse strategy if an adaptation is necessary during the task [22].

4.2. No effect of dopaminergic medication during obstacle circumvention to the most affected side

The second main important finding of our study was that dopaminergic medication presented no effects on motor or perceptual systems for obstacle circumvention to the most affected side. Therefore, our second hypothesis was only confirmed when people with PD performed obstacle circumvention to the least affected side, which presented positive effects from dopaminergic medication on mediolateral body clearance (reduced variability), spatial-temporal parameters (greater stride length during circumvention phase), and gaze behavior (higher number and longer fixations on the obstacle). However, our analysis did not reveal effects from dopaminergic medication when obstacle circumvention was performed to the most affected side. These results suggest that effects from dopaminergic medication were dependent on the side that people with PD performed obstacle circumvention. No symmetrical action of dopaminergic medication can explain our findings [23,64]. Previous studies have demonstrated that there are differences in cerebral activity between the most and least affected sides and that levodopa has a preferential effect on brain activations in task-relevant brain areas [21]. The least affected side might have preferentially responded to levodopa because the nigrostriatal dopaminergic terminals of that side were less degenerated [64]. These findings corroborate with our previous study that found PD medication improved postural control asymmetry in people with PD in the early stage of disease, but not in the moderate stage, during challenging postural tasks [26]. Asymmetrical degeneration of dopaminergic neurons in the substantia nigra, such as contralateral lateral ventricle is enlarged to the most symptomatic side and hypoactivity in motor regions is higher in the most affected side, underlying symptom asymmetry in PD [18,19]. The advanced brain impairment due to PD presents a greater response with shorter duration resulting in waxing and waning between medication doses, and eventually, abrupt changes in response as if turned on and off by a switch [65,66] which results in delayed onset to the most affected side compared with the least affected side [66]. In addition, no effects from dopaminergic medication during obstacle circumvention to the most affected side occurred in the perceptual system, which seems to indicate that dopaminergic circuits within the basal ganglia may not be responsible for perceptual deficits, corroborating with previous studies [41,67,68]. Therefore, obstacle circumvention to the most affected side is risky task, which could have a contact with the obstacle in people with PD without the effects of dopaminergic medication.

In conclusion, both people with PD and neurologically healthy individuals presented asymmetric behavior between sides when circumventing the obstacle, however, this asymmetry was exacerbated in the former. People with PD performed worse motor and perceptual strategies during obstacle circumvention to the most affected side compared to the least affected side. In addition, dopaminergic medication had no effects on motor or perceptual systems for obstacle circumvention to the most affected side. The effects from dopaminergic medication occurred only when obstacle circumvention was performed

Table 3

Means and standard deviations of gaze behavior according to side that obstacle was circumvented and group. The first part of the table presents general gaze behavior during obstacle circumvention to the least affected/dominant and most affected/non-dominant side in people with PD (under and without the effects of dopaminergic medication) and the control group. The values of variability (means and standard deviations) for each parameter are presented in brackets. The second part of the table presents gaze behavior according to areas of interest.

	Group DP OFF		Group DP ON		Control group	
	Circumvention to least affected side	Circumvention to most affected side	Circumvention to least affected side	Circumvention to most affected side	Circumvention to dominant side	Circumvention to non-dominant side
Number of fixations	12.31 ± 7.8-5 (39.05 ± 34-.66)	11.60 ± 7.9-8 (40.39 ± 43-.23)	9.56 ± 7.11 (33.78 ± 15-.72)	10.38 ± 6.2-4 (27.09 ± 16-.23)	8.02 ± 3.81 (32.66 ± 19-.90)	8.17 ± 3.9-9 (39.04 ± - 25.78)
Mean duration of fixations (s)	0.24 ± 0.13 (20.76 ± 13-.68)	0.24 ± 0.17 (22.28 ± 15-.77)	0.19 ± 0.09 (24.88 ± 13-.04)	0.20 ± 0.10 (20.14 ± 12-.34)	0.16 ± 0.02 (21.29 ± 11-.67)	0.15 ± 0.-02 (16.13 ± - 7.46)
Time of fixations (%)	31.42 ± 17.-00 (6.96 ± 9.1-1)	29.31 ± 18.-05 (8.22 ± 12.-86)	27.64 ± 16.-53 (4.97 ± 5.2-8)	29.67 ± 14.-81 (4.82 ± 4.4-8)	28.49 ± 13.-52 (1.76 ± 1.7-2)	25.44 ± 1.-3.43 (2.57 ± 2-.64)
Area of Interest						
Ground						
Number of fixations	42.13 ± 38.-90	37.73 ± 33.-34	5.94 ± 7.83	38.27 ± 36.-41	30.28 ± 17.-69	28.00 ± 1-6.23
Mean duration of fixations (s)	0.16 ± 0.02	0.16 ± 0.02	0.10 ± 0.07	0.16 ± 0.02	0.16 ± 0.02	0.14 ± 0.-02
Time of fixations (%)	21.77 ± 15.-98	18.74 ± 15.-02	3.39 ± 4.67	21.72 ± 15.-07	21.50 ± 13.-57	17.71 ± 1-0.89
Obstacle						
Number of fixations	8.67 ± 7.86	9.60 ± 10.8-5	32.44 ± 21.-24	6.67 ± 9.01	5.94 ± 8.56	7.56 ± 7.-78
Mean duration of fixations (s)	0.18 ± 0.07	0.13 ± 0.08	0.15 ± 0.02	0.12 ± 0.08	0.12 ± 0.07	0.14 ± 0.-06
Time of fixations (%)	5.30 ± 5.88	5.50 ± 6.73	18.86 ± 11.-37	4.55 ± 6.49	3.87 ± 5.04	5.40 ± 5.-72
Wall						
Number of fixations	1.67 ± 2.23	2.93 ± 8.19	11.81 ± 11.-02	0.80 ± 2.08	2.07 ± 3.24	1.29 ± 2.-05
Mean duration of fixations (s)	0.08 ± 0.10	0.05 ± 0.07	0.15 ± 0.06	0.04 ± 0.06	0.12 ± 0.19	0.08 ± 0.-11
Time of fixations (%)	0.78 ± 1.30	0.40 ± 0.92	7.28 ± 6.80	0.52 ± 1.54	1.47 ± 2.00	0.88v1.33
Random						
Number of fixations	6.27 ± 10.9-2	6.20 ± 9.30	0.44 ± 0.89	1.53 ± 1.96	1.21 ± 1.15	2.00 ± 2.-42
Mean duration of fixations (s)	0.08 ± 0.08	0.12 ± 0.08	0.04 ± 0.07	0.10 ± 0.09	0.09 ± 0.08	0.09 ± 0.-08
Time of fixations (%)	2.90 ± 4.37	2.68 ± 3.19	0.32 ± 0.68	0.80 ± 1.00	0.84 ± 0.85	1.39 ± 1.-66

to the least affected side. Therefore, obstacle circumvention to the most affected side is risky for people with PD, mainly without the effects of dopaminergic medication. Future studies should investigate the relationship between side preference and side (most) affected by the disease to advance discussions about degeneration of the brain.

Conflict of interests

The authors have no conflict of interest to report.

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