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Does freezing in Parkinson's disease change limb coordination?

A kinematic analysis

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Abstract The aim of this study was to analyse the kinematic characteristics of the strides before freezing and compare this with a voluntary stop and ongoing gait. Also, we investigated whether gait profiles were different as a function of the side of the body. Ten patients were included with a mean age of 64.8 years (SD 5.1). Within a Vicon 3D gait laboratory, patients performed several trials of normal walking and voluntary stops or were exposed to circumstances, which provoked freezing in the off-phase of the medication cycle. Spatiotemporal and key kinematic data of the four strides prior to freezing were compared between body sides and walking conditions using multiple regression models for repeated measures. Prior to freezing patients had severely decreased movement ranges in the sagittal plane (ranging between 31% and 61.5%), most notably in the ankle and hip joints. The general shape of movement remained in the pre-freezing profiles with largely intact dissociation of knee and hip movement in stance but reduced dissociation in

swing. Also present were reduced push-off movements in the ankle with fixed dorsiflexion, increased flexion in hip and knee and anterior tilt of the pelvis. During both voluntary (stopping) and involuntary deceleration (freezing), the body side with the last complete stride before the freeze, showed significantly smaller joint ranges ($p < .01$). Body side differences were larger than sequential deterioration of consecutive steps within each side. Freezing is distinct from normal deceleration of gait in that the reduction of propulsive movement is much greater. Despite hastening of steps, timing deficits did not affect overall movement shapes, except for the tendency to have a flexed walking pattern. The side of the body where gait terminated before freezing was in most cases the side of symptom-dominance, but not consistently so.

Key words Parkinson's disease · clinical features of freezing · gait analysis

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Introduction

The occurrence of freezing of gait is highly significant in the clinical evolution of Parkinson's disease (PD) as

it may be the cause of falling and loss of confidence [1, 2]. Freezing of gait manifests itself relatively independent from other symptoms of PD [3]. The phenomenon is frequently associated with festinating

movements of the legs [4], the presence of which is typical for the most common subtype of freezing [5]. Pharmacological intervention of the problem is not self-evident, possibly due to its non-dopaminergic origins [1, 6]. Deep brain stimulation has been reported to decrease the incidence of freezing during the *off*-period but not during *on* [7, 8]. Moreover, an increase of freezing symptoms was reported during a five-year follow-up study [9]. Rehabilitation strategies using auditory cueing techniques in the *on*-phase have also not shown effects on actual freezing episodes [10]. This may be due to low occurrence rates of freezing, reducing statistical power and the problematic outcome measures to evaluate freezing [11]. Also, cueing methods may need a specific approach adapted to the complex nature of freezing [12]. All these findings point to the urgent need to understand the underlying factors of freezing more fully.

Studies examining the mechanisms behind freezing as derived from movement analysis have shown that stride duration variability, which can be viewed as a parameter of gait rhythmicity and automaticity [13] is increased during normal gait in freezers when compared with non-freezers [14]. Previous study by our group [15] showed that the strides preceding freezing have a largely predictable spatiotemporal pattern, whereby an abnormally shortened gait cycle (increased stride frequency) and a reduced stride length seemed to interact with each other. This may point to a mechanism where rhythmic dyscontrol interferes with effective amplitude generation, leading to an involuntary movement breakdown. Electromyographical analysis of the lower limb muscles before freezing indicated early onset and shortened muscle activity consistent with a central timing deficit as a possible contributing factor [16, 17]. However, not all freezing episodes are characterised by deficient co-regulation of timing and amplitude of consecutive gait cycles and many other factors need to be considered. Recently, Plotnik and others [18] suggested that asymmetry of interlimb movement coordination may be involved in the pathogenesis of freezing. They found that normal gait was more asymmetric in terms of swing phase duration in freezers versus non-freezers. The hypothesis of asymmetry leading up to freezing is an attractive one, as many freezing episodes tend to occur during turning [5].

The present study aims to add a new perspective to the study of freezing, as it examines changes in the shape of movement in the lower limbs before a freezing episode, using our previous dataset comparing normal walking in the *off*-phase with voluntary (stopping) and involuntary deceleration (freezing). In this study, we addressed three hypotheses. Based on our previous findings [15] we

expected to see dramatic underscaling of movement just before freezing compared with normal walking and stopping. Based on the work of Plotnik and others [18], we expected that kinematic differences between body sides might be present particularly before freezing. Lastly, given the abnormality of the timing of EMG activity found in our earlier work [16] we also predicted altered intralimb coordination before freezing.

Methods

Subjects

Ten patients from a previous study on 11 subjects were included [16], as one patient had an incomplete kinematic dataset due to marker visibility problems, requiring too much interpolation of data points. Subjects were diagnosed as having idiopathic PD by a consultant neurologist. Patients were included if they had a recent history of regular freezing with a frequency of at least once a week and worsening during the *off* phase of the medication cycle. Subjects were excluded if their medical condition proved unstable due to acute neurological, orthopaedic or cardiovascular comorbidity affecting gait. Clinical testing was carried out before and after the walking tests in both the *on* and *off* phases, using the Unified Parkinson Disease Rating scale (UPDRS) [19] and the Hoehn & Yahr scale [20]. Symptom dominance was determined by recall of the first side to show signs of parkinsonism [21]. In addition, a UPDRS(III)-difference score was calculated as the absolute value of the left minus the right sided UPDRS-items 20, 21, 22, 23, 25, 26 in the *on* state [22]. Subjects signed a written consent form prior to participation in accordance with the Declaration of Helsinki. The study was approved by the local Ethics Committee.

Procedure

Gait analysis took place in the gait laboratory of the University Hospital Leuven (Belgium) during the *off* phase between 6 h and 15 h after the last medication intake. The procedure for checking the stability of the *off* period was described in an earlier report [15]. Subjects were instructed to walk on an eight-meter trajectory at a comfortable speed for several trials (normal). They were asked to perform voluntary stops (stop) or were made to freeze (freezing), the order of which was randomised to control for sequence effects. In the stop condition, patients stopped immediately at an auditory signal provided by the investigator. In the freezing condition patients were exposed to freezing provoking circumstances consisting of obstacles on the walkway with or without an additional cognitive task (serial number subtraction test). Patients were kept unaware of the need to freeze and were asked to walk normally through the obstacle course.

Apparatus

3D gait registration was performed with a six camera VICON data capturing system (370) (Oxford Metrics, United Kingdom) at a resolution of 50 Hz. Reflective markers (14 mm diameter) were placed on the anterior superior iliac spines, the sacrum, the mid-thighs, the lateral femur condyles, the mid-shanks, the lateral malleoli, the dorsal aspect of the foot between the second and third metatarsal heads, and on the calcaneus. Four analogue video

cameras were integrated into the system, aligned with the transversal, sagittal and coronal plane. Gait cycle events (toe off and initial foot contact) were defined manually, using Vicon Clinical Manager software (Oxford Metrics, Oxford, UK). This procedure proved to have a good inter-rater reliability between two independent observers, even in festinating gait (ICCs between 0.88 and 1). Prior to each analysis the measurement area was recalibrated. Ten repeated measures of a reference bar of 547 mm showed an accuracy of 0.36 mm as standard deviation for the measurement system.

■ Data processing and statistical analysis

Two normal gait trials and two successful stop and freezing trials were included for analysis. As reported earlier, freezing was very difficult to elicit [16]. Five patients froze 2 times, four did so 3 times and one patient froze 7 times. Freezing trials were included for analysis if an arrest of movement lasted longer than one second and if such an episode did not occur during a turn. The stop and freezing trials were matched for body side according to the last stride before termination of gait. Video recordings of the gait tests were used to select the valid trials on the basis of the following criteria: (1) freezing trials needed to show an actual freezing episode whereby patients were unable to continue walking (2) only freezes occurring without a directional change were considered and (3) stop trials were checked to be without signs of freezing and festination. Freezing was defined as yielding a sudden episode of involuntary cessation of gait often accompanied by trembling of the legs or festination. To obtain representative data for normal walking, the four middle strides of normal gait were used for analysis. The four consecutive strides closest to the freeze and the two strides before the stop were analysed. When comparing gait profiles in the three walking conditions, data of 8 normal strides (4 strides during 2 trials), 4 stop strides (2 strides during 2 trials) and 8 freezing strides (4 strides during 2 trials) were averaged. Two rather than 4 strides were compared to capture the stop data, as a "two-step" strategy was found to be most common in PD when stopping unexpectedly [23].

Figure 3 shows the stride selection before freezing, defining a freezing (FS) and a near-freezing side (N-FS). FS was the body side, which included the two completed strides nearest to the freeze, FR1 and FR3. N-FS was the body side that included the strides, which were completed one step before the freeze, FR2 and FR4. For one patient only the left side was included for data analysis due to marker visibility problems on the right. Spatiotemporal characteristics were calculated including gait speed, cadence, stride length, width and double and single support duration. Key kinematic parameters for pelvis, hip, knee and ankle in the sagittal plane were selected based on the routine protocol of the gait analysis laboratory of the Leuven University Hospital [24, 25]. Data were statistically analysed for the sagittal plane only, as no consistent trends were apparent in coronal and transverse planes. As a measure of intralimb coordination, we examined the timing differences of peak movements in hip and knee as a percentage of the gait cycle (%GC) using unpaired *t*-tests.

Regression models for repeated measures were used to compare the walking conditions, body sides and stride sequences, correcting for missing values. Either an unstructured or a more simplified covariance matrix was used with the Mixed Procedure in SAS (Statistical Analysis Software, version 8.2). In case of abnormally distributed residuals, statistical analysis was checked using data transformation techniques. No correction for multiple testing was carried out, but *p*-values are provided in full. Data are reported as estimated means (eMean), estimated mean differences (eMeanΔ) and standard errors (SE). Timing differences between peak movements in hip and knee are expressed as means and standard deviations.

Results

■ Subject characteristics

Participants included 5 men and 5 women with a mean age of 64.7 (± 5.6) years. Four patients were in Hoehn & Yahr III and six in stage IV during *off*. For more detailed clinical characteristics we refer to a previous report [15]. Table 1 shows that six patients had left and 4 right-sided disease dominance. However, UPDRS(III)-difference scores did not always coincide with the reported side of dominance. In 6 patients the dominantly affected leg was also the freezing side (see Fig. 3). In one case the symptom-dominant side as indicated by the UPDRS(III)-difference scores was the freezing side. One symmetrically affected patient froze alternately with both legs.

■ Effects of walking condition

The effects of the three walking conditions on the spatiotemporal characteristics are reported in Table 2. Spatiotemporal differences between pre-freezing and both normal and stop conditions were pronounced. Compared to the stop, pre-freezing stride lengths shortened dramatically with 58.4% ($P = 0.01$); cadence increased with 42.4% ($P < .0001$); and speed reduced with 41% ($P < .0001$). The within gait cycle phases were also significantly altered before freezing in comparison to both reference conditions. Compared to the stop, double support phase was increased with 9.8% ($P = 0.0002$) and single support duration decreased with 5.3% ($P = 0.0008$). No stride width differences were observed.

Figure 1 shows averaged kinematic profiles of the right and left leg in the three walking conditions in

Table 1 Clinical characteristics of study population

Subjects	Age (years)	H&Y on (off)	Dominant side	UPDRS (III) dif-score	Freezing side
1	64	II,5 (III)	L	2	R
2	67	III (IV)	L	3	L
3	69	II (III)	R	3	L
4	72	II (III)	L	7	L
5	60	II,5 (III)	L	2	L
6	65	II,5 (IV)	R	0	L + R
7	53	III (IV)	L	6	L
8	61	II (IV)	R	-3	L
9	70	II,5 (IV)	L	1	L
10	66	III (IV)	R	-2	R

H&Y = Hoehn & Yahr stages

L/R = left/right

Dominant side = body side at which first signs of parkinsonism appeared

UPDRS (III) dif-score = the absolute value of the left minus the right-sided items 20, 21, 22, 23, 25, 26

Freezing side (FS) = body side at which gait terminated just prior to freezing

Table 2 Effects of walking condition on spatiotemporal gait characteristics

Variables	Normal eMean $\pm$ SE	Stop eMean $\pm$ SE	Freeze eMean $\pm$ SE	P N-S	P N-F	P S-F
Cadence (step/min)	94.66 $\pm$ 3.22	104.64 $\pm$ 5.41	149.09 $\pm$ 9.78	0.006	<0.0001	<0.0001
Stride length (cm)	63.03 $\pm$ 7.47	42.55 $\pm$ 5.77	17.72 $\pm$ 2.03	0.0005	<0.0001	0.01
Stride width (cm)	16.45 $\pm$ 1.24	16.26 $\pm$ 1.27	16.91 $\pm$ 1.26	0.62	0.19	0.07
Gait speed (m/sec)	0.87 $\pm$ 0.12	0.61 $\pm$ 0.08	0.36 $\pm$ 0.05	0.006	<0.0001	<0.0001
Double support (%GC)	46.82 $\pm$ 5.06	45.24 $\pm$ 4.60	54.99 $\pm$ 6.40	0.37	0.0005	0.0002
Single support (%GC)	26.87 $\pm$ 2.44	28.79 $\pm$ 2.46	23.47 $\pm$ 3.38	0.09	0.03	0.0008

%GC = percentage of the gait cycle

eMean = estimated mean, SE = standard error

the sagittal plane. The three vertical lines indicate the three different moments of toe-off (beginning of swing phase). Toe-off occurred significantly later during freezing (78.64 $\pm$ 3.2%GC) than in the normal (73.6 $\pm$ 2.5%GC, $P = 0.0001$) and in the stop trials (74.3 $\pm$ 2.4%GC, $P = 0.001$), indicating a shortened swing phase before freezing.

Figure 1 and Table 3 show similar kinematic patterns in the stop and normal conditions, albeit with

overall reduced movement ranges in hip and knee inherent to stopping. During the stop the total range of motion in the pelvis was reduced by 20.3% ($P = 0.04$) and it was inclined to a more posterior tilted position, a result, which did not reach statistical significance.

Figure 1 and Table 3 illustrate throughout the four joints remarkable and significant reductions of movement in the freezing profiles compared with

Fig. 1 Averaged kinematic profiles (right and left) during normal gait (black line), voluntary stop (green line) and freezing (red line) in ankle (A), knee (B), hip (C) and pelvis (D). The three vertical lines indicate the beginning of swing phase each conditions. Gait cycle duration is expressed as a percentage (X-axis). Angular excursions are expressed in degrees (Y-axis). The red and black arrows in figure 2A highlight the push-off slopes in the freezing and normal condition. The black arrow in figure 2D denotes the direction of anterior pelvic tilt

Table 3 Effects of walking condition on key kinematic gait characteristics

Variables (degrees)	Normal eMean $\pm$ SE	Stop eMean $\pm$ SE	Freeze eMean $\pm$ SE	<i>P</i> N-S	<i>P</i> N-F	<i>P</i> S-F
<i>Ankle</i>						
ROM in swing	7.68 $\pm$ 0.99	6.89 $\pm$ 1.05	3.24 $\pm$ 0.62	0.41	<0.0001	<0.0001
ROM push-off*	13.04 $\pm$ 1.10	10.44 $\pm$ 1.29	5.01 $\pm$ 0.75	0.06	<0.0001	<0.0001
<i>Knee</i>						
ROM in stance	29.33 $\pm$ 2.70	25.44 $\pm$ 2.09	19.08 $\pm$ 2.08	0.04	<0.0001	<0.0001
Peak flexion swing	44.31 $\pm$ 2.50	39.81 $\pm$ 2.52	34.63 $\pm$ 2.21	0.02	<0.0001	0.002
Peak extension stance	5.99 $\pm$ 1.43	8.55 $\pm$ 1.39	12.20 $\pm$ 1.42	0.07	<0.0001	0.006
<i>Hip</i>						
ROM in stance	29.04 $\pm$ 2.11	23.96 $\pm$ 1.46	13.56 $\pm$ 1.12	0.009	<0.0001	<0.0001
Peak flexion swing	30.96 $\pm$ 1.93	26.21 $\pm$ 2.46	25.60 $\pm$ 1.44	0.002	<0.0001	0.6788
Peak extension stance	2.37 $\pm$ 1.54	5.09 $\pm$ 1.31	12.51 $\pm$ 0.99	0.06	<0.0001	<0.0001
<i>Pelvis</i>						
ROM	2.71 $\pm$ 0.24	2.16 $\pm$ 0.23	1.87 $\pm$ 0.19	0.04	0.0004	0.1789

ROM = range of motion

eMean = estimated mean, SE = standard error

*Push-off is defined as the period between peak dorsiflexion and toe-off

normal and stop conditions. Overall, ankle ranges during freezing showed an almost fixed dorsiflexion with complete loss of heel strike at initial contact. Compared to normal gait, ankle movements reduced by 57.8% ($P < .0001$) in swing phase and 61.5% ($P < .0001$) during the push-off phase of stance, defined as occurring between maximal dorsiflexion and toe-off. Severely abnormal push-off before freezing was further illustrated by the flat slope of ankle plantar flexion in this phase, indicated by the arrows in Fig. 1A. Flattening of joint angle excursions was also apparent in hip and knee joints before freezing, a pattern, which showed statistical significance when compared with both reference conditions. Range of motion reductions in the hip varied from 53.3% ($P < .0001$) compared to normal gait and 43.4% compared to the stop ($P < .0001$); in the knee from 34.9% ($P < .0001$) and 25% ($P < .0001$), respectively. The hip and knee joints also remained significantly more in flexion before freezing as peak extension values in stance were greater (12.2° in the knee; and 12.5° in the hip) than in the normal and stop (5.99° and 8.55° in the knee; and 2.37° and 5.9° in the hip). Pelvic tilting range of motion was significantly reduced before freezing but only in comparison to normal gait (31%, $P = 0.0004$). Moreover, Fig. 2D shows that particularly in contrast to the voluntary stop the pelvis was tilted in a more anterior direction.

■ Differences between body sides

Analysis of the differences between freezing (FS) and near-freezing body sides (N-FS) was based on matching the last right or left completed stride before freezing with the same left or right strides before stopping and ongoing gait. No significant spatiotem-

poral differences between body sides were found in normal walking and freezing, indicating symmetrical gait. However, before the stop stride length (-0.23 ± 0.05 ; $P = 0.0002$) and gait speed (-0.18 ± 0.04 cm/sec; $P < .0001$) differences indicated greater reduction of movement in the FS compared to the N-FS.

Figure 2 A, B, C, D show the averaged profiles of the last four strides before freezing. The vertical line indicates the averaged moments of toe-off at the beginning of swing phase (78.6%GC). No difference was found between toe-off and thus in the relative duration of swing phase at the FS ($78.34 \pm 3.0\%$ GC) and at the N-FS ($78.93 \pm 3.5\%$ GC). Figure 2 illustrates that the shape of the last stride before freezing, the solid black line, is predicted best by the preceding stride on the FS (dotted black line). On the contrary, the strides of the N-FS in red have greater amplitudes and follow a more normal shape than those of the FS. The plantar flexion slope during push-off was somewhat preserved in the N-FS and completely absent in the FS. These profiles suggest that body side is more predictive of freezing than the sequential deterioration seen in consecutive strides.

Key kinematic variables displayed in Table 4 confirm that differences between body sides were most pronounced during the stop condition. Ankle range of motion was significantly reduced in the FS in swing and in the push-off phase. Peak knee and hip flexion during swing were significantly smaller in the FS.

Some significant kinematic differences between body sides in knee and hip were also present in the freezing condition. Peak knee and hip flexion during swing were significantly smaller in the FS, including an overall decreased hip range of motion ($3.47^\circ \pm 1.34$, $P = 0.01$). No kinematic differences between body sides were present in the normal condition.

Fig. 2 Averaged kinematic profiles of the last four strides before freezing in ankle (A), knee (B), hip (C) and pelvis (D). Black solid line indicates the last stride before the freeze (FR1). Black dotted line indicates the preceding stride at the same body side (FR3). Red solid line indicates the one but last stride before the freeze (FR2). Red dotted line indicates the preceding stride at the same body side (FR4). Gait cycle duration is expressed as percentage (X-axis). Angular excursions are expressed in degrees (Y-axis)

Near freezing side (N-FS)

Fig. 3 Stride selection for data analysis. Grey shapes indicate the sequence of two strides (FR1 and FR3) just before freezing (freezing side, FS). The black shapes indicate the two strides (FR2 and FR4) of the near-freezing side (N-FS) where gait terminated one step before freezing

■ Differences within body sides (FR1 versus FR3 and FR2 versus FR4)

The spatiotemporal and kinematic changes within each body side were also analysed to explore the possibility of progressive movement reduction in the

strides prior to freezing. No significant differences between spatiotemporal or kinematic characteristics were observed in the N-FS regarding stride FR2 versus FR4. However, in the FS a significant reduction of stride length ($P = 0.001$) and gait speed ($P = 0.001$) was found in FR1 compared to FR3. Sequential stride analysis in the FS revealed no differences between kinematic variables.

■ Intralimb coordination

As for changes in the pattern of movement before freezing, largely similar movement shapes were apparent even during the severely flattened curves of the pre-freezing strides (Fig. 2). Figure 4 presents the analysis of the difference in peak hip and knee movement timing as a measure of hip-knee dissociation. Significant dissociation of peak hip and knee extension in stance were present in all three conditions ($P < 0.001$), indicating preserved intralimb coordination of hip and knee movement. However, in relation to the beginning of swing phase, peak hip

Table 4 Key kinematic differences between the freezing and near-freezing body sides

Variables (degrees)	Normal FS-N-FS		Stop FS-N-FS		Freeze FS-N-FS	
	eMeanΔ ± SE	P	eMeanΔ ± SE	P	eMeanΔ ± SE	P
<i>Ankle</i>						
ROM in swing	0.94 ± 1.31	0.48	-2.81 ± 1.25	0.03	-1.17 ± 0.79	0.14
ROM push-off*	0.22 ± 1.58	0.89	-9.92 ± 1.80	0.04	-1.38 ± 1.02	0.18
<i>Knee</i>						
ROM in stance	0.51 ± 2.47	0.84	-2.43 ± 2.04	0.25	-1.49 ± 1.71	0.39
Peak flexion swing	-2.24 ± 2.35	0.35	-7.73 ± 2.15	0.002	-3.92 ± 1.75	0.03
Peak extension stance	-0.66 ± 2.09	0.76	-3.00 ± 1.97	0.14	-1.40 ± 1.83	0.45
<i>Hip</i>						
ROM in stance	-3.57 ± 2.12	0.10	-3.92 ± 2.24	0.09	-3.47 ± 1.34	0.01
Peak flexion swing	-2.96 ± 1.65	0.09	-8.34 ± 1.76	<0.0001	-2.22 ± 0.94	0.02
Peak extension stance	0.47 ± 1.85	0.80	0.96 ± -2.06	0.65	1.26 ± 1.26	0.32
<i>Pelvis</i>						
ROM	-0.16 ± 0.38	0.67	0.35 ± 0.35	0.92	-0.28 ± 0.25	0.27

eMeanΔ = estimated mean difference between the freezing side (FS) minus the near-freezing side (N-FS)

SE = standard error

*Push-off is defined as the period between peak dorsiflexion and toe-off

ROM = Range of motion

Fig. 4 Significant dissociations (indicated by *) between mean peak extension timing in hip (black) and knee (grey) during stance phase and between mean peak flexion timing in hip (white) and knee (dots) during swing phase in normal, stop and freeze. Error bars indicate standard deviations

extension occurred earlier in freezing by 8.2%GC ($P < .0001$) compared to normal walking and 7.3%GC compared to stopping ($P < .0001$).

In swing phase, the timing of peak flexion movements in the normal and stop condition differed significantly. In contrast, dissociation of peak hip and knee flexion was not significant before freezing ($93.4 \pm 2.6\%$ GC in the hip; $83.6 \pm 0.8\%$ GC in the knee, $P = 0.31$). In relation to the beginning of swing phase, peak hip flexion occurred 10.1%GC ($P < .0001$) earlier in freezing compared to the normal and 6.4%GC ($P = 0.0002$) compared to the stop condition. Peak knee flexion was 1.7%GC earlier ($P = 0.001$) in relation to toe-off when compared to normal gait only.

Discussion

The hypothesis that dramatic reduction of movement excursions would be present before freezing was confirmed by the results of this study. Pre-freezing range of movement was overall reduced between 31% and 61.6% in the lower limb joints compared to normal gait without medication. This reduction was only between 13% and 20.3% when the same patients were stopping voluntarily. Previous study comparing the kinematic profiles of normal *off-gait* in PD with healthy controls found reductions of between 0.03% and 30.3% particularly when walking without cues [26]. These findings were interpreted as a motor set deficit. Hypokinesia is, according to this view, the core motor problem in PD, caused by a central programming mismatch between cortically selected movement amplitude and basal ganglia maintenance mechanisms [26]. Prior to freezing this problem seems to be episodically exacerbated, possibly provoked by circumstances when the reliance on basal ganglia control is increased, i.e. when gait needs to be adapted or attention is distracted.

The present study highlighted that the shape of movement was roughly preserved even before freezing, with the exception of a few abnormalities not present in the normal and stop profiles. Ankle movement was fixed in dorsiflexion, which may partly be explained by the general tendency to increased flexion in hip and knees before freezing and decreased stride length. In older and younger adults push-off and hip extension are the main determinants of stride length [27]. Although freezing is experienced by patients as 'the feet getting stuck to the floor' or as an

inability to actively initiate swing phase, the kinematic profiles emphasize the lack of push-off and increased lower limb flexion as a 'passive' explanation for the lack of forward progression. At initial foot contact, eccentric contraction of TA normally provides shock absorption and deceleration of the body's inertia. The kinematic data showed hardly any heel strike at initial contact before freezing. This abnormality explains the lack of tibial activity found at the beginning of stance prior to freezing [16] and points to possible fall risk due to reduced foot clearance.

Pelvic tilting excursions were reduced and fixed in an anterior direction before freezing. Before the voluntary stop the pelvis tended to be tilted backwards compared with ongoing gait. Reclining the trunk in a posterior direction was found to be a normal preparatory postural strategy for slowing down in healthy controls [28]. The anterior pelvic tilt observed before freezing possibly indicates a lack of anticipatory postural adaptation, hence increasing the risk of falling forward before freezing [29]. Alternatively, it could be that tilting the pelvis backwards was less needed because of poor push-off and reduced forward momentum preceding the freezing episode.

With regards to intralimb coordination, our results do not support movement-timing abnormalities in stance as peak extension in hip and knee revealed intact dissociation of movement. However, in the swing phase timing of peak hip and knee flexion had a smaller time gap. Also, there was evidence of early peak movement timing in relation to the beginning of swing phase, which could be explained by the general tendency for hastening and the delayed onset of swing phase. This is consistent with the increased double support phases found and the increased flexion in all joints before freezing, indicating strategies to lower the centre of gravity possibly as an adjustment to potential loss of stability. However, increasing stride width was apparently not used as a compensatory strategy, which is in line with previous reports that in PD stride width is not different from controls [30] and narrows as the disease progresses [31].

Previous work pointed to a disturbed timing component as a possible mechanisms underlying freezing, as stride duration variability was increased during normal gait in freezers when compared with non-freezers [14]. The regulation of gait cycle timing was also found to be attention demanding as it worsened during secondary task performance, an indication that its normal automatic regulation is reduced in PD [13]. Iansek and co-workers [32] proposed that the basal ganglia are involved in running each component of a movement sequence in a timely manner. In patients suffering from freezing and festination, they demonstrated the occurrence of smaller and smaller steps during walking, called a

sequence effect. However, this sequence effect manifested itself in a variable fashion across patients and conditions and may be present in non-freezers. As freezing is an episodic phenomenon, gait cycle timing dysregulation may temporarily be exacerbated. Insufficient time to generate movement in conjunction with the motor set deficits mentioned earlier [26], may explain the pronounced amplitude changes leading up to freezing underscored by this study. Why these problems come to the fore in freezers and not in non-freezers in this episodic fashion needs further investigation.

The cerebellum rather than the basal ganglia has traditionally been assigned to being the specific system for movement timing. Recently, the basal ganglia were indeed shown to play only a minimal role in sequence timing during repetitive upper limb tasks [33]. Pope et al. [34] investigated the combined force and time control in rhythm production in PD, whereby force control may be interpreted as a measure of achieving accurate amplitudes. While this study confirmed the overall preserved timing of movement sequencing, it also showed that when specific timing requirements were brought to bear on force production, performance was compromised. Hence, the basal ganglia may have a role during the co-regulation of force and timing of movement, especially when movement changes are required. It appears that freezing exemplifies a disruption of the co-regulation of timing and amplitude [15, 32], no doubt brought on and magnified by multiple factors such as motor and postural adaptations [1] and visual/spatial deficits interacting with perception of the environment [35]. In addition, mental aspects [36] of emotional as well as cognitive origin and of which attention is possibly the most crucial factor [32, 37], are considered contributory to lowering the threshold for the occurrence of freezing.

There were some differences between spatiotemporal and kinematic profiles when comparing the freezing side (FS) with the near-freezing side (N-FS) of the body in both the stop and freezing conditions, which were matched for FS and N-FS body sides. The fact that these differences were more pronounced during the voluntary stop, may reflect the consecutive nature of the analysis, which defined the FS to contain the last two completed strides before the stop or freeze in one body side. In general, PD patients are braking with less modulation of muscular activity of the stance limb during unplanned stops than controls, leading to at least two-step stopping strategies [23]. Previous study also points to differences between "lead" and "trail" limb muscle activation during voluntary stopping in normal controls and PD [38]. This inherent asymmetry in limb function may explain why the normal stop showed a more pro-

nounced reduction of movement of the freezing limb than during actual freezing. It could either mean more inadequate braking of the freezing side before freezing, hence less clear differences between body sides or it means that the reductions of movement were going on for longer not requiring such fierce braking in one leg. The present findings support this latter hypothesis as severe reductions of movement in the four strides leading up to the freeze were shown.

Plotnik et al. [18] showed that freezers as opposed to non-freezers had more asymmetry of gait coordination as measured by ratios of left and right swing times. The present study does not seem to add to the hypothesis of asymmetry being a possible causal factor of freezing, as spatiotemporal and kinematic differences between body sides did not increase before freezing. It also does not contradict previous findings as the present outcomes address a different set of dependent variables not representing gait coordination and are based on a consecutive analysis of gait cycles.

Within both sides, no sequence effects were shown in the kinematic data before freezing. Consecutive strides did show a progressive decline of stride length and speed in the freezing side only, as was found by Iansek et al. [32]. However, between body side differences overshadowed those witnessed within body sides. Different behaviour of body sides and sequence effects within body side may be predictive of freezing but may equally be explained by normal stopping. Future study needs to address the contribution of body side and sequence effects to the aetiology of freezing in controls, freezers and non-freezers particularly in continuous walking tasks such as turning.

Plotnik et al. [18] found that asymmetry of gait timing was independent of disease symptom asymmetry. The present data show that in 7 patients the freezing side coincided with the symptom-dominant side, which in one case was only defined by the UPDRS(III)-difference scores. One symmetrical patient froze with both sides. These data suggest a prepon-

derance for the symptom-dominant side to be involved in freezing but also show that this was not consistently so. The discrepancies between self-reported and measured symptom-dominance illustrate the problem of defining the extent of asymmetric disease, which can be different with disease progression and across the three cardinal symptoms of PD [21, 22]. Future research on a larger sample needs to address the relation of symptom dominance with freezing, taking into account that the definition of disease dominance may require sign-specific considerations. Also, the freezing side in this study was defined by the completed stride pattern before freezing. Future analysis of the incomplete steps preceding freezing, excluded from this analysis due to its variable pattern, may highlight whether freezing is preceded by difficulties to complete a swing or a stance phase.

Previous gait analysis comparing PD during the *on*-phase with age-matched controls revealed that abnormalities in the kinetics of gait were much more manifest than in the kinematics [25]. Lack of kinetic data limits a firm interpretation of the kinematic profiles in this study. The problem of evoking FOG episodes in a laboratory environment and performing gait analysis *off* medication precludes obtaining reliable force plate measures. Despite these limitations, we can conclude that marked reductions of amplitude precede freezing particularly in the ankle joint. Intralimb analysis shows that coordination difficulties do not occur before freezing, apart from the movement abnormalities inherent to hastening, increased flexion and postural adaptation. Interlimb analysis suggests the existence of a freezing side showing progressive reduction of stride amplitudes, but further study is needed to distinguish this pattern from asymmetry inherent to normal deceleration.

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