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# Electromyographic profiles of gait prior to onset of freezing episodes in patients with Parkinson's disease

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## Summary

**Freezing in Parkinson's disease is a severe and disabling problem of unknown aetiology. The aim of this study was to analyse the temporal pattern and the magnitude of the electromyographic activity of the lower limb muscles just before freezing and to compare this with a voluntary stop and ongoing gait. We recruited 11 patients with a mean age of 64.8 years (SD 5.1) and a mean Unified Parkinson Disease Rating Scale (part III—off) score of 29 (SD 7.9). Within a standard 3D gait laboratory setting, surface electromyographic (EMG) data of the tibialis anterior (TA) and gastrocnemius (GS) muscles were collected using a portable EMG module. Patients in the off-phase of the medication cycle performed several trials of normal walking and voluntary stops or were exposed to freezing-provoking circumstances. Filtered EMG signals were rectified, smoothed and expressed as a percentage of the gait cycle. EMG onset was determined using a preset threshold, corrected after visual inspection. The magnitude of EMG was calculated by integrating EMG signals (iEMG) over (real) time. To control for the altered timing of activity, iEMG was also normalized for time ($iEMG_{normt}$). Analysis of variance of repeated measures analysis showed that significantly abnormal timing occurred in the TA and GS muscles with overall preserved reciprocity. Before freezing, TA swing activity already started prematurely during the pre-swing phase, whereas it was significantly shortened during the actual swing phase. For the GS muscle, a similar pattern of premature activation and termination was found during the stance phase before a freeze. GS activity also showed prolonged bursts of activity during the swing phase, not present during the normal and stop condition. Total iEMG activity of both TA and GS was significantly reduced during the pre-freezing gait cycles. However, when controlling for the altered duration of the bursts, the average $iEMG_{normt}$ increased, as did the peak EMG in TA. In GS, $iEMG_{normt}$ was not different in the three conditions. In conclusion, our data show that a consistent pattern of premature timing of TA and GS activity occurred before freezing, which was interpreted as a disturbance of central gait cycle timing. The total amount of EMG activity was reduced in both lower limb muscles due to the shortened time in which the muscles were active. In contrast to GS, activity in TA showed increased amplitudes of the EMG bursts, indicating a compensation strategy of pulling the leg into swing. The observed changes contribute to insufficient forward progression, deceleration and eventually a breakdown of movement.**

**Keywords**: akinesia; electromyography; freezing; gait; Parkinson's disease

**Abbreviations**: %GC = percentage of gait cycle; GS = gastrocnemius muscle; iEMG = integrated electromyographic activity; $iEMG_{normt}$ = integrated electromyographic activity normalized for time; MLR = mesencephalic locomotor region; PPN = pedunculopontine nucleus; %ST = percentage of the stance phase; %SW = percentage of the swing phase; TA = tibial anterior muscle; UPDRS = Unified Parkinson Disease Rating Scale

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## Introduction

Freezing of gait is a severely incapacitating problem in people with Parkinson's disease, in vascular parkinsonism and in multisystem neurodegenerative disease (Fahn, 1995; Giladi *et al.*, 1997). In Parkinson's disease, the prevalence of freezing increases with disease duration, occurring in up to 53% of the population after 5 years of illness (Giladi *et al.*, 2001*a*). The unpredictability of the freezing phenomenon makes it notoriously difficult to study experimentally.

Freezing manifests itself as an impairment of the initiation and termination of gait and as a sudden interruption of walking (Fahn, 1995). Usually, it occurs when subjects are exposed to specific tasks that require a shift of attention or a circumstantial or directional change (Giladi *et al.*, 2001*a*; Almeida *et al.*, 2003; Vaugoyeau *et al.*, 2003).

Study into the pathophysiological origins of freezing has focused mainly on initiation difficulties. These studies have shown that people with Parkinson's disease have reduced movement speed, step amplitudes and anticipatory postural shifts of the centre of mass in a forward and lateral direction in comparison with controls (Gantchev *et al.*, 1996; Burleigh-Jacobs *et al.*, 1997; Rosin *et al.*, 1997; Halliday *et al.*, 1998; Martin *et al.*, 2002; Vaugoyeau *et al.*, 2003). Patients also have decreased ground reaction forces and reduced tibialis anterior (TA) and gastrocnemius (GS) activity at the onset of gait (Gantchev *et al.*, 1996; Burleigh-Jacobs *et al.*, 1997; Halliday *et al.*, 1998). These changes have been observed in the absence of the classic inability to initiate stepping, and therefore may not explain actual freezing. In the rare cases when freezing did occur, a complete lack of the initiation of postural adjustments was found (Burleigh-Jacobs *et al.*, 1997).

Recent research on freezing of ongoing movement contradicts some of these initiation difficulties. Rather than delayed and slowed movements, a markedly reduced stride time or conversely an increased stepping frequency was found before freezing (Ueno *et al.*, 1993; Nieuwboer *et al.*, 2001; Yanagisawa *et al.*, 2001). Whether freezing of ongoing walking or at the onset of gait are distinct or similar features needs further clarification.

In our previous analysis on the spatiotemporal characteristics of three pre-freezing strides, we found both severely reduced stride length and markedly increased cadence (Nieuwboer *et al.*, 2001). The results emphasized a possible dyscontrol of the stepping rhythm inherent to freezing, as well as an inability to generate stride length. Giladi *et al.* (2001*b*), using a questionnaire-based enquiry, found that the occurrence of festination or hastening of stepping was highly related to freezing, and proposed that a common pathophysiological mechanism may be at play. Recently, Hausdorff *et al.* (2003) added to these findings that freezers have markedly impaired stride-to-stride control expressing itself as increased stride time variability already manifest during normal gait, a feature not present in non-freezers.

In the present study, we intended to investigate further the interplay between deficits of amplitude generation and the timing of movement by analysing the electromyographic (EMG) profiles of the gait cycles before freezing during ongoing gait.

In general, movement in Parkinson's disease is characterized by normally timed EMG bursts, but the amount of activity is underscaled relative to the desired movement parameters (Berardelli *et al.*, 2001). Mitoma *et al.* (2000) and Dietz *et al.* (1995) showed that these changes also applied to leg muscle activation during gait. GS activity was reduced in amplitude, and modulated less well to various walking conditions. In contrast, visual analysis of EMG profiles of freezing of gait showed highly abnormal traces of increased co-activation of the thigh flexors and extensors as well as of TA and GS muscles (Andrews, 1973). In another study, variable patterns of EMG activity were found in flexors and extensors of the leg, which largely contracted reciprocally and sometimes simultaneously, corresponding to whether or not trembling of the legs occurred during freezing (Ueno *et al.*, 1993). However, Yanagisawa *et al.* (2001) showed that the EMG patterns of leg muscles during freezing were different from those observed in resting and postural tremor during standing.

In this study, we tested the hypothesis that Parkinson's disease patients have disturbed co-ordination of the GS and TA muscles prior to freezing, affecting both the timing and the magnitude of EMG activity. On the basis of our earlier findings and the literature so far, we assumed that we would find premature timing, increased overlap of muscle activity and decreased amplitudes of EMG activity. To control for possible changes of walking due to the normal process of deceleration, we compared: (i) the strides preceding freezing with (ii) normal strides and (iii) the strides occurring before a voluntary stop.

## Subjects and methods

### *Subjects*

In this study, 11 patients were included from a previous analysis on 14 subjects (Nieuwboer *et al.*, 2001). As we wanted to study the EMG changes leading up to freezing, the three patients who did not present actual freezing episodes (inability to continue walking) were excluded. Instead, these patients showed festinating gait when confronted with freezing-provoking circumstances, i.e. shuffling forward with small steps. Subjects were diagnosed as having idiopathic Parkinson's disease according to accepted research criteria (Ward and Gibb, 1990). They were referred for the study 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 co-morbidity affecting gait. Clinical testing was carried out by an experienced assessor (A.N.) before and after the walking tests in both the on and off phases, using the Unified Parkinson Disease Rating scale (UPDRS) (Fahn *et al.*, 1987) and the Hoehn & Yahr scale (Hoehn and Yahr, 1967). Subjects signed a

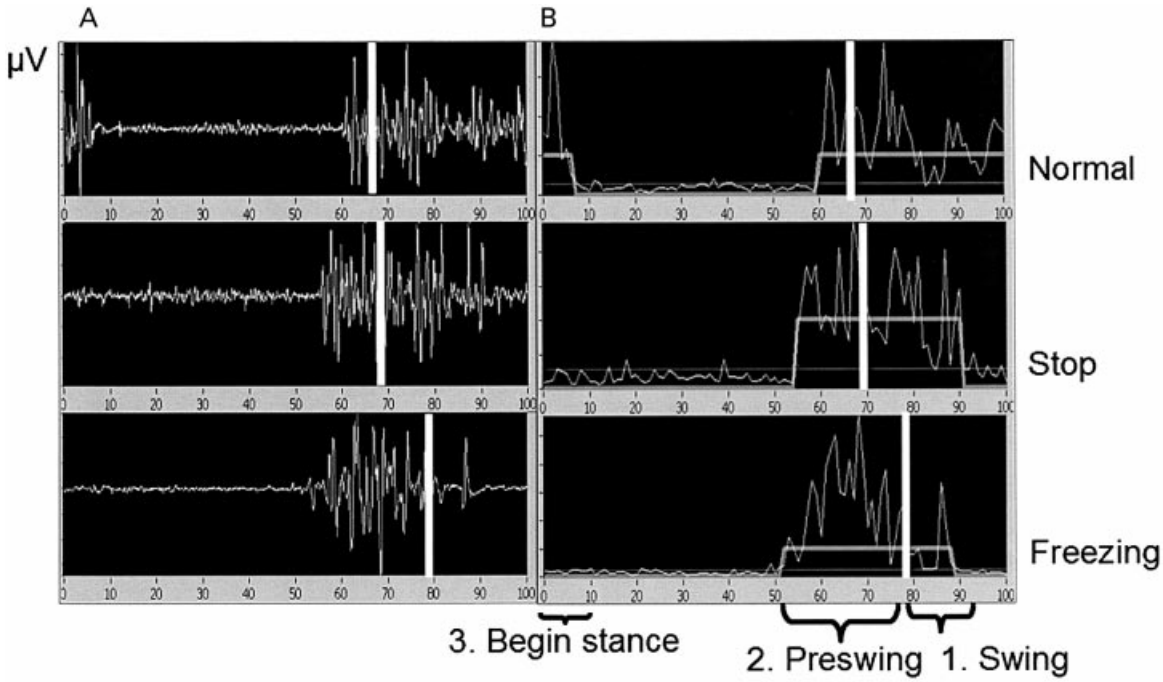


**Fig. 1** Example of the raw EMG activity (**A**) and of the linear envelope (**B**) in TA of one parkinsonian subject normalized as a percentage of the gait cycle. From the top to the bottom, the normal, stop and freezing conditions are represented. The white vertical lines are the beginning of toe-off or swing phase. The grey lines represent onset and termination of activity as determined by the threshold. Phases for analysis: 1, duration of swing activity; 2, duration and timing of pre-swing activity; and 3, duration of activity at the beginning of stance.

written consent form prior to participation in accordance with the Declaration of Helsinki. The study was approved by the local ethics committee (Commissie Medische Ethiek K.U.Leuven).

### *Procedure*

Gait analysis took place in the gait laboratory of the University Hospital in Leuven, Belgium, during the off phase, between 6 and 15 h after the last medication intake. Patients indicated on a visual representation whether they had reached the stable off period, using their normally experienced fluctuations as a point of reference. In this diagram, the off period was defined as the typical stable level of motor performance at the end of dose, when the action of medication is strongly decreased or absent. On was defined as the period in which the medication works well and as normal. A short clinical examination was carried out before and after gait analysis, based on the UPDRS motor section, assessing tremor (item 20), rigidity (item 22) and distal tapping (items 23, 25 and 26) to check the stability of the off condition. As reported earlier, comparing the scores using a Wilcoxon signed rank test revealed no significant differences within the off condition before and after testing (Nieuwboer *et al.*, 2001).

Subjects were instructed to walk on an 8-m trajectory at a comfortable speed for several trials. They were asked to perform voluntary stops (stop condition) or were made to freeze (freezing condition), the order of which was randomized 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), as described in detail elsewhere (Nieuwboer *et al.*, 2001). Patients were kept unaware of the need to freeze and were asked to walk normally through the obstacle course.

### *Materials*

Gait analysis was performed with a six-camera VICON data capturing system (370) (Oxford Metrics, Oxford, UK). This is a passive optical system sending and capturing infrared light, which enables accurate 3D gait registration 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. Surface EMG data of the lower leg muscles were collected bilaterally, using a portable integrated EMG module (16 channels K-Laboratory EMG system; The Netherlands). EMG signals were recorded with a sampling frequency of 2500 Hz using silver/silver pellet electrodes with a 0.5 cm active surface. Standard skin preparation techniques were used to reduce impedance. Two electrodes were placed 2 cm apart on the belly of each muscle in line with fibre direction. A ground electrode was attached to the subject's upper arm.

### *Data analysis*

Three consecutive normal gait trials were included for analysis. For the stop and freezing conditions it was possible to select two successful trials in most cases. The video recordings were used to select the valid trials on the basis of the following criteria: (i) freezing

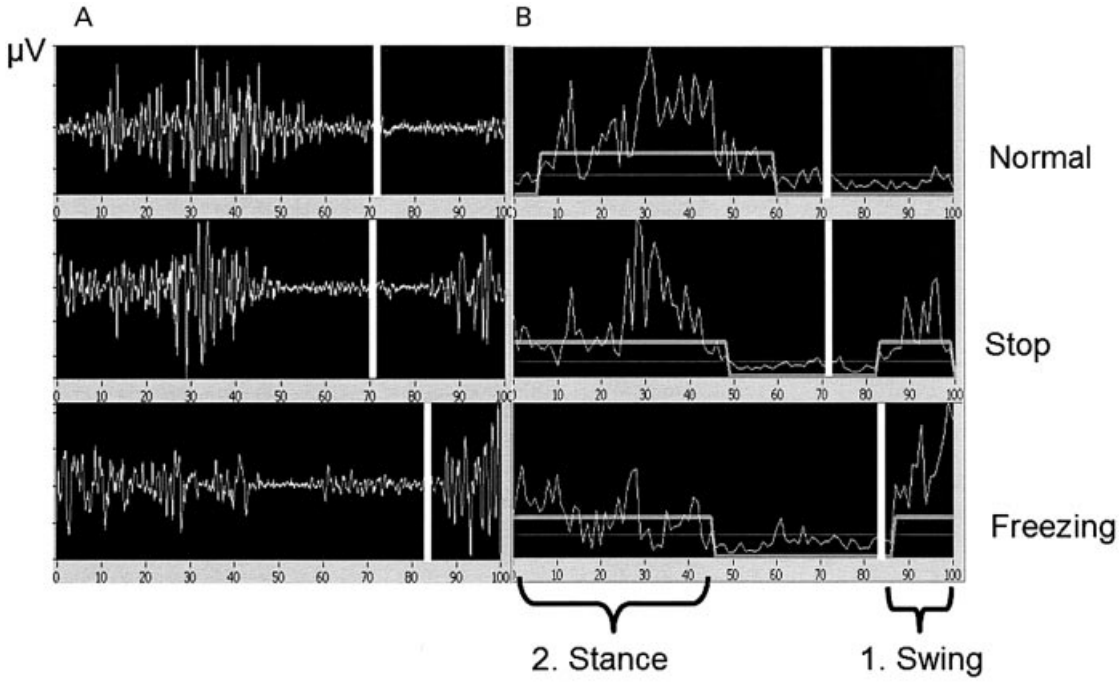


**Fig. 2** Example of the raw EMG activity (**A**) and of the linear envelope (**B**) in GS of one parkinsonian subject, normalized as a percentage of the gait cycle. From the top to the bottom, the normal, stop and freezing conditions are represented. The white vertical lines are the beginning of toe-off or swing phase. Phases for analysis: 1, duration of swing activity; and 2, duration and timing of stance activity.



trials needed to show an actual freezing episode whereby patients were unable to continue walking; (ii) only freezes occurring without a directional change were considered; and (iii) 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 three middle strides of the normal gait trials were used for analysis. The three consecutive strides closest to the freeze and one or two complete strides before stopping were analysed, excluding the final incomplete step. Two experienced testers also rated the clinical features of the selected freezing trials using the videotapes on the basis of consensus. The freezing episodes were characterized according to the situation in which they occurred (subtypes) and the motion of the legs before and during freezing (manifestation) as defined by Schaafsma *et al.* (2003). Furthermore, the alterations of the foot strike pattern and posture were recorded before freezing for comparison with normal off gait as well as the provocation strategy to elicit freezing.

Spatiotemporal profiles for both feet, including cadence expressed as the number of steps per minute, were calculated with Vicon Clinical Manager software 1997 (Oxford Metrics). Initial and terminal foot contacts were determined manually as markers for the gait cycles. Previously, we reported that the inter-tester reliability of this procedure for both normal and festinating gait on ten Parkinson's disease patients was highly satisfactory (Nieuwboer *et al.*, 2001).

Data from the TA and GS were considered for analysis. The raw and processed EMG data were normalized as a percentage of the gait cycle duration (see Fig. 1A). The EMG signals were high-pass filtered with a cut-off frequency at 20 Hz (18 dB/oct, Butterworth implementation). Amplification (100) took place at input impedance of >100 Ω (Common Mode Rejection Ratio >115 dB measured at 50 Hz). The processed signals were then rectified (full rectification) and subsequently low-pass filtered (25 Hz). Transformation into a linear envelope was carried out using custom-made software in Labview. Each trace was checked for cross-talk and artefacts. Continuous EMG traces defined as showing activity for 90% of the gait cycle or more (Perry, 1992) were excluded from the statistical analysis as no clear phasic pattern could be determined.

Onset and duration of bursts of activity were determined with an adjustable threshold, set by a computer algorithm based on a percentage of three averaged peaks of activity subtracted by the mean background activity. Pilot analysis of the data revealed that presetting the threshold level at 9% gave overall good agreement with visual determination of onset. However, based on the recommendations by Hodges and Bui (1996) computer-derived onset times were visually verified on both the raw and processed traces and threshold levels adjusted when necessary. Threshold values were recorded and statistically analysed retrospectively.

For the temporal analysis we identified specific phases of activity for both muscles (see Figs 1 and 2). Figure 1 shows that it was relevant to determine the duration and onset of the TA pre-swing and swing activity separately, as the former occurred in the stance phase and showed clear abnormalities. To normalize for differences in gait cycle, and swing and stance phase durations, time intervals were calculated as a percentage of the gait cycle (%GC), or swing (%SW) and stance (%ST) phase.

The following variables were identified for the GS muscle: (i) total duration of activity within the gait cycle (%GC); (ii) duration of stance phase activity (%ST); (iii) duration of swing phase activity (%SW); (iv) onset of stance phase activity (%ST); and (v) termination of stance phase activity (%ST).

**Table 1** *Patient demographics*

| Patient | Age (years) | Sex | Duration (years) | H & Y [on (off)] | UPDRS (III) [on (off)] | Medication | Daily dose (mg) |
|---|---|---|---|---|---|---|---|
| 1 | 64 | F | 12 | II.5 (III) | 18 (30) | Dopamine | 350 |
| | | | | | | Pergolide | 1 |
| | | | | | | Amantadine | 100 |
| 2 | 67 | F | 23 | III (IV) | 22 (29) | Dopamine | 575 |
| | | | | | | Pergolide | 3 |
| | | | | | | Orfenadrine | 50 |
| 3 | 69 | F | 7 | II (III) | 12 (26) | Dopamine | 600 |
| | | | | | | Sinemet | 600 |
| | | | | | | Amantadine | 100 |
| 4 | 66 | M | 9 | III (IV) | 18 (31) | Dopamine | 900 |
| | | | | | | Bromocriptine | 30 |
| | | | | | | Orfenadrine | 50 |
| 5 | 72 | F | 5 | II (III) | 10 (13) | Dopamine | 300 |
| | | | | | | Pergolide | 0.75 |
| 6 | 60 | M | 23 | II.5 (III) | 11 (22) | Dopamine | 600 |
| | | | | | | Pergolide | 3 |
| | | | | | | Selegeline | 5 |
| 7 | 65 | M | 15 | II.5 (IV) | 21 (27) | Dopamine | 425 |
| | | | | | | Bromocriptine | 15 |
| 8 | 53 | M | 22 | III (IV) | 22 (47) | Dopamine | 500 |
| | | | | | | Pergolide | 3 |
| 9 | 61 | F | 14 | II (IV) | 15 (29) | Dopamine | 600 |
| | | | | | | Selegeline | 10 |
| | | | | | | Amantadine | 200 |
| 10 | 70 | M | 9 | II.5 (IV) | 15 (33) | Dopamine | 1150 |
| | | | | | | Bromocriptine | 30 |
| 11 | 66 | M | 10 | III (IV) | 13 (34) | Dopamine | 900 |
| | | | | | | Bromocriptine | 30 |

H & Y = Hoehn & Yahr stages; UPDRS (III) = Part III of the Unified Parkinson Disease Rating Scale.



The following variables were identified for the TA muscle: (i) total duration of activity within the gait cycle (%GC); (ii) duration of pre-swing activity (%ST); (iii) duration of swing phase activity (%SW); (iv) onset of pre-swing activity (%ST); and (v) duration of activity at the beginning of stance (%ST).

For analysis of the amplitude of the EMG data we integrated the signals (iEMG) over time (μV*s) during the total duration of the gait cycle or the duration of stance (GS) and pre-swing and swing (TA) activity (not normalized as a %GC). Hereafter, iEMG data were normalized for time by dividing by the duration of the phases of activity indicated as $iEMG_{normt}$ (μV).

For the GS the following parameters were analysed: (i) total iEMG and $iEMG_{normt}$ for the full duration of the gait cycle; and (ii) EMG and $iEMG_{normt}$ for the activity during the stance phase.

For the TA the following parameters were analysed: (i) total iEMG and $iEMG_{normt}$ for the full duration of the gait cycle; and (ii) iEMG and $iEMG_{normt}$ for the activity during the pre-swing and swing phase.

Peak EMG represented an average of the three highest peaks of the linear envelope calculated for both TA and GS.

### *Statistical analysis*

For statistical analysis we averaged the data of multiple trials and multiple strides for the normal walks only. The selected stop and freezing strides were analysed separately within the same statistical model. As few differences were observed between consecutive strides, we only report on the joined results, with some exceptions. An analysis of variance (ANOVA) of repeated measures was used to analyse the difference between conditions. A paired Student's *t*-test tested the differences between the TA and GS muscle. In the case of not normally distributed data, statistical analysis was repeated after logarithmic transformation.

To take into account missing values, the SAS procedure PROC MIXED (version 6.12) was used. In accordance with this statistical model, data are expressed in estimated mean values (β) and standard errors (SE). Considering the explorative nature of the study, Bonferroni correction was not carried out. $P$ values $<0.05$ were considered as statistically significant. The influence of provocation strategy on the EMG changes was examined using the Kruskal–Wallis test.

## Results

### *Subjects*

Patients' demographics are shown in Table 1. The group consisted of five women and six men with an average age of 64.8 (±5.1) years and mean disease duration of 13.5 (±6.5) years. During the off-phase seven patients were in Hoehn & Yahr stage IV and four in stage III. The mean score of the UPDRS (part III) was 29 (±7.9) in off and 16 (±4.2) in on.

**Table 2** *Clinical manifestation of freezing trials*

| Patient | Subtype | Number of F episodes, provocation strategy used | Leg motion | Foot strike | Posture |
|---|---|---|---|---|---|
| 1 | Turn hesitation (without directional change) | F = 2, obstacles | Festination | Flat-footed >N | Flexed (N + F) |
| 2 | Hesitation tight quarters | F = 2, obstacles + cogn. task | Slow shuffles, trembling in place | Heel strike = N | Flexed (N + F) |
| 3 | Hesitation tight quarters | F = 2, obstacles + cogn. task | Festination, trembling in place | Flat-footed >N | Flexed (N + F), flexion > just before F |
| 4 | – | F = 2, obstacles + cogn. task | – | – | – |
| 5 | Turn hesitation (without directional change) | F = 2, obstacles | Festination | Flat-footed >N | Flexed (N + F) |
| 6 | Hesitation tight quarters | F = 2, obstacles | Festination | Flat-footed >N | Normal (N + F) |
| 7 | Hesitation tight quarters | F = 2, obstacles | Festination | Flat-footed >N | Normal (N + F), falling |
| 8 | Open space | F = 1, spontaneous | Festination, feet stuck to floor | Flat-footed >N | Flexed (N + F), falling |
| 9 | Open space | F = 2, spontaneous | Festination | Flat-footed >N | Flexed (N + F), flexion > just before F |
| 10 | Hesitation tight quarters | F = 2, obstacles | Festination, trembling in place | Flat-footed >N, toe-strike last step before F | Flexed (N + F) |
| 11 | Hesitation tight quarters | F = 2, obstacles | Festination, trembling in place | Flat-footed >N | Flexed (N + F), falling |

N = the normal condition (off); F = freezing; cogn. = cognitive. Subtypes of freezing and leg motion based on Schaafsma *et al.* (2003). Patient 4: no video available, but written records of provocation strategy.

**Table 3** *Gait cycle characteristics of the normal, stop and freezing strides*

| | Normal [β (SE)] | Stop [β (SE)] | Freezing [β (SE)] | *P* (N – F) | *P* (S – F) |
|---|---|---|---|---|---|
| Gait cycle (s) | 1.25 (0.06) | 1.11 (0.08) | 0.81 (0.07) | 0.0001* | 0.0001* |
| Stance phase (s) | 0.93 (0.07) | 0.87 (0.08) | 0.67 (0.07) | 0.0001* | 0.0003* |
| Swing phase (s) | 0.31 (0.03) | 0.33 (0.03) | 0.17 (0.03) | 0.0001* | 0.0001* |
| Stance phase (%GC) | 74.20 (2.4) | 71.55 (2.13) | 79.35 (3.0) | 0.02* | 0.0002* |
| Swing phase (%GC) | 25.80 (2.4) | 28.45 (2.1) | 20.65 (3.0) | 0.01* | 0.0002* |

*$P < 0.05$; %GC = percentage of the gait cycle; β = estimated mean; SE = standard error; N = normal (off); S = stop; F = freezing.

## *Video assessments*

Table 2 summarizes the variable clinical pattern of the freezing episodes and the provocation strategies used as analysed from the video data (10 out of 11 available). Two patients had freezing in open space (spontaneous). Six patients froze when approaching obstacles, two of them before making a turn. In three patients, freezing was provoked when passing through obstacles, while verbally performing an additional cognitive task. Leg motion before or during freezing was mostly characterized by festination ($n$ = 9), sometimes accompanied by trembling of the legs during freezing ($n$ = 3). One patient showed the typical pattern of the feet being suddenly stuck to floor and one patient had slow shuffling before freezing rather than festination. Except for one patient, who had a heel strike similar to that in the normal (off) condition, most patients ($n$ = 9) showed an increase of flat-footed stepping before freezing. Only one patient showed the highly abnormal toe strike pattern during the last step before freezing. Although most patients showed marked flexed posture during both the normal gait and the freezing condition ($n$ = 8), no increase of flexion was observed before freezing except in two patients. Three patients fell forward during freezing, but these events fell outside the boundaries of the EMG analysis, which concerned the pre-freezing strides only.

## *Gait cycle changes*

Very similar results were obtained for the right and left legs. Therefore, we will report on the left side only, except in cases where differences were found. Table 3 gives the results of the gait cycle characteristics in the freezing, stop and normal conditions. It shows that just before freezing, the gait cycle duration became significantly shorter than during normal off

**Table 4** *Temporal characteristics of tibial anterior activity for the normal, stop and freezing strides*

| EMG activity in TA | Normal (off) [β (SE)] | Stop [β (SE)] | Freezing [β (SE)] | *P* (N – F) | *P* (S – F) |
|---|---|---|---|---|---|
| Total duration (%GC) | 46.59 (2.6) | 42.29 (8.9) | 36.66 (5.4) | 0.004* | 0.31 |
| Onset pre-swing (%ST) | 79.49 (1.8) | 82.61 (4.8) | 72.59 (3.8) | 0.03* | 0.0003* |
| Duration pre-swing (%ST) | 18.34 (1.5) | 16.57 (4.7) | 25.83 (3.9) | 0.02* | 0.008* |
| Duration swing (%SW) | 67.06 (7.0) | 72.69 (9.3) | 38.77 (8.1) | 0.002* | 0.0001* |
| Duration begin stance (%ST) | 19.74 (3.4) | 11.63 (5.1) | 8.21 (5.0) | 0.0002* | 0.38 |

*$P < 0.05$; %GC = percentage of the gait cycle; %ST = percentage of stance phase; %SW = percentage of swing phase; β= estimated mean; SE = standard error; N = normal (off); S = stop; F = freezing.

**Table 5** *Temporal characteristics of gastrocnemius activity for the normal, stop and freezing strides*

| EMG activity in GS | Normal (off) [β (SE)] | Stop [β (SE)] | Freezing [β (SE)] | *P* (N – F) | *P* (S – F) |
|---|---|---|---|---|---|
| Total duration (%GC) | 50.02 (2.4) | 49.68 (5.4) | 55.62 (5.3) | 0.09 | 0.29 |
| Duration stance (%ST) | 62.21 (3.2) | 67.16 (3.7) | 57.95 (5.1) | 0.33 | 0.02* |
| Onset stance (%ST) | 11.51 (2.9) | 8.42 (3.1) | 5.40 (3.3) | 0.007* | 0.01* |
| Termination stance (%ST) | 76.94 (2.4) | 84.33 (6.6) | 65.85 (7.7) | 0.035* | 0.0002* |
| Duration swing (%SW) | 12.58 (4.9) | 22.20 (9.6) | 44.28 (9.9) | 0.003* | 0.03* |

*$P < 0.05$; %GC = percentage of the gait cycle; %ST = percentage of stance phase; %SW = percentage of swing phase; β= estimated mean; SE = standard error; N = normal (off); S = stop; F = freezing.



gait and before the voluntary stop, indicating a reduction of 35.2% and 27%, respectively. The gait cycle also shortened before a voluntary stop, with 11.2% in comparison with normal walking, but this change was not significant ($P$ = 0.09). Within the gait cycle, a significantly shorter swing phase and elongated stance phase was noted just before freezing in comparison with the other conditions.

## *EMG data*

A total of 634 EMG profiles were analysed for the right and the left side together. Large differences were observed in the number of continuous EMG traces found in the GS and TA muscles, which were subsequently excluded from the analysis. In GS this was 14.5% of the total number of traces observed for this muscle, whereas in TA this was 0.95%. Three patients showed no continuous traces. Continuous traces occurred in all three conditions, 33.3% in the normal, 20.3% in the stop and 46.4% in the freezing condition. Comparing the magnitude of the background activity of the EMG profiles revealed no significant changes between the normal, stop and freezing conditions within both muscles. Statistical analysis of the adaptations of the 9% threshold value for onset determination revealed no significant changes between the two muscles, as the mean threshold value for TA was 9.5% (±1.3) and for GS was 9.4% (±1.3). Similarly, non-significant differences were found when comparing the threshold values between experimental conditions.

## *Temporal changes of TA activity*

Total duration of TA EMG activity during the entire gait cycle was 9.9% shorter ($P$ = 0.004) before freezing compared with normal off gait (Table 4). However, this shortening was not significantly different from the stop condition.

Looking at the specific phases of TA activity, a striking result was that the onset of pre-swing activity occurred prematurely before freezing at 72.6% (±3.8) of the stance phase. When analysing the duration of pre-swing activity, Table 4 shows that before freezing it took 25.8% (±3.9) of stance phase compared with 16.6% (±4.7) in the voluntary stop ($P$ = 0.008) and 18.3% (±1.3) in normal off gait ($P$ = 0.02). The results also showed that swing phase traces were significantly shorter before a freeze, lasting 38.7% (±8.1). Before the stop and in normal off gait it took 67.1% (±7.0) and 72.7% (±9.3) of swing phase, respectively (Table 4). Making a comparison between the three pre-freezing strides, a significantly increased elongation of pre-swing activity could be observed from the stride furthest from the freeze (24.1 ± 3.3%) to the one closest to it (28 ± 3.9%) ($P$ = 0.02). Hence, it seemed that TA activity was progressively initiated too early before freezing, whereby the activity shifted from the swing into stance phase. TA activity at the beginning of stance, at loading response, was significantly shorter in the freezing condition (8.2 ± 5%) compared with normal gait (19.7 ± 3.4%) ($P$ = 0.0002). However, a similar pattern of reduced activity at the onset of stance was also found in the stop condition (11.6 ± 5.1%) ($P$ = 0.02). No other significant differences were observed between the normal and the

**Table 6** *Magnitude of EMG activity of tibialis anterior and gastrocnemius for the normal, stop and freezing strides for the left side*

| EMG activity | Normal (off) [β (SE)] | Stop [β (SE)] | Freezing [β (SE)] | *P* (N – F) | *P* (S – F) |
|---|---|---|---|---|---|
| *Tibialis anterior* | | | | | |
| Total iEMG (μV*s) | 1792.1 (272) | 671.5 (108.6) | 390.7 (57.5) | 0.0001* | 0.03* |
| iEMG swing + presw (μV*s) | 1217 (189.5) | 560 (87) | 316.5 (38) | 0.0002* | 0.003* |
| Total $iEMG_{normt}$ (μV) | 481.9 (42.7) | 490.9 (50.6) | 691.8 (56.1) | 0.002* | 0.003* |
| Peak EMG (μV) | 3027.3 (191) | 2948.3 (228) | 3328.8 (156) | 0.05* | 0.05* |
| $iEMG_{normt}$ swing + presw (μV) | 498 (54.3) | 542.2 (71) | 743.5 (60.3) | 0.0002* | 0.008* |
| *Gastrocnemius* | | | | | |
| Total iEMG (μV*s) | 598.9 (118.8) | 364.1 (85) | 124.5 (27.5) | 0.0007* | 0.004* |
| iEMG stance (μV*s) | 535.3 (106.8) | 304 (80) | 87.3 (13.7) | 0.0007* | 0.01* |
| Total $iEMG_{normt}$ (μV) | 182.2 (33.6) | 178.8 (42.1) | 178 (26.2) | 0.85 | 0.98 |
| Peak EMG (μV) | 1595.7 (247.4) | 1735.8 (308) | 1473.4 (241) | 0.35 | 0.44 |
| $iEMG_{normt}$ stance (μV) | 180.9 (32.1) | 206.6 (38.3) | 172 (21.5) | 0.69 | 0.2 |

*$P < 0.05$; β = estimated mean; SE = standard error; N = normal (off); S = stop; F = freezing.

voluntary stop condition. Figure 1 shows the EMG pattern of one subject (subject 6 in Table 2), which illustrates that unlike the group results, no activity was present at loading response in the stop and freezing conditions. The normal double peaked activation of TA was preserved in the normal condition, was reduced before normal stopping and showed a single burst only before freezing with peak activity occurring in pre-swing phase.

## *Temporal changes of GS activity*

In contrast to the TA muscle, total duration of GS activity during the gait cycle was not different between conditions (Table 5), although a trend could be observed towards longer lasting EMG activity before freezing ($P = 0.09$). Examining the pattern within the different phases of the gait cycle, the duration of stance activity showed a shortening before freezing in comparison with the stop condition only. Between-stride differences prior to freezing showed a progressively shorter stance activity in the stride closest to the freeze (42.4 ± 4.2%) compared with the second one away from the freeze (50.2 ± 3.4%), for the right leg only. This trend was near significant ($P = 0.06$) (not shown in Table 5).

We also found a clear alteration of both onset and termination of activation of the GS muscle pointing again to a premature timing before freezing, as summarized in Table 5. Descriptions of GS activity in healthy young and older people indicate that the main GS burst occurs during terminal stance (30–50%GC) lasting into pre-swing (50–60%GC), with peak activity at ~50 (Winter and Yack, 1987; Perry, 1992; Judge *et al.*, 1996). In this study, the GS bursts started on average at 8.7% of the gait cycle and lasted up to 58.1%. Figure 2 shows that, in the example subject the peak of the GS burst occurred at the beginning of terminal stance (30–50%GC) in the normal condition and was mildly earlier during the stop. Before freezing, no peak activity was present during the stance phase. Instead, it seemed to occur during swing phase.

Group results (Table 5) also show that GS activity in swing phase was significantly prolonged just before freezing, taking up 44.3% (±9.9). Before the stop and in normal off gait this was 22.2% (±9.6) and 12.6% (±4.9), respectively. Figure 2 suggests that this pattern of prolonged swing activity may be due to early activation of GS already starting in swing. It also shows that some swing activity was present before the stop. Group results confirm that both in normal gait and before the stop GS was active for short periods of time. Overall, no statistical differences were found between the normal and the stop condition.

## *Additional analyses on both muscles*

Considering the prolonged duration of TA activity at the beginning of stance (Table 4) and the premature onset of the GS burst in stance (Table 5), analysis of overlap during the stance phase revealed mild co-activation between the muscles in the freezing condition at loading response. However, this overlap was not significantly different from the other conditions. To analyse whether the provocation strategy to elicit freezing influenced the pattern of results, the difference scores between the normal and the freezing condition were analysed in both muscles. This analysis revealed no significant differences between provocation conditions, except for the duration of TA swing activity ($P = 0.04$). This result was highly influenced by one patient, who showed a different manifestation of freezing, namely a slow shuffling rather than a festinating pattern, and therefore had increased rather than a shortened swing activity.

## *Magnitude changes of TA and GS activity*

As noted in Table 6, total iEMG activity of TA was significantly reduced during the pre-freezing gait cycles (390.7 ± 57.5 μV*s) compared with the normal (1792.1 ± 57.5 μV*s) ($P = 0.0001$) and pre-stop strides (671.5 ± 108.6

μV*s) ($P = 0.03$). This reduction was similar during the swing and pre-swing phases taken together.

When normalizing for time, a different pattern was found. The magnitude of average $iEMG_{normt}$ was higher in the freezing (691.8 ± 56.1 μV) than in the normal (481.9 ± 42.7 μV) ($P = 0.002$) and stop (490.9 ± 50.6 μV) condition ($P = 0.003$). This finding was confirmed by the significantly increased levels of peak EMG and increased $iEMG_{normt}$ during swing and pre-swing before freezing.

Comparing stride-to-stride differences of TA activity, a progressive increase of swing and pre-swing activity was found from the stride furthest from the freeze (655.2 ± 57.3 μV) to the one closest to it (815.1 ± 71.1 μV) ($P = 0.02$).

Table 6 indicates a similar pattern of significantly reduced total iEMG activity during the entire gait cycle in the GS muscle (124.5 ± 27.5 μV*s) compared with normal (598.9 ± 118.8 μV*s) ($P = 0.0007$) and pre-stop gait (364.1 ± 85.5 μV*s) ($P = 0.004$). Also, during stance phase an important decrease of activity before freezing was found. When normalizing for time, no significant differences were seen in the levels of $iEMG_{normt}$ during the entire gait cycle, in stance, or in the peaks of EMG activity between the different walking conditions.

Provocation strategy to elicit freezing did not influence the magnitude changes seen before freezing in both muscles.

## Discussion

The aim of this study was to determine the contribution of abnormal leg muscle activation to the pathophysiology of freezing in patients with Parkinson's disease. Analysis of the EMG changes prior to freezing highlighted that disturbed temporal co-ordination of GS and TA activity took place with preserved reciprocity but premature activity in both muscles. EMG amplitudes were normal in GS but increased in TA when controlling for the altered temporal profiles of the bursts.

As in our previous analysis, we found a dramatically shortened gait cycle before freezing by an average of 35% pointing to festinating steps at freezing onset (Nieuwboer *et al.*, 2001). The present study extends these results by showing that within the gait cycle also, altered timing occurred. In the normal condition, stance phase was already abnormally long, lasting 74.2% of the gait cycle as compared with 63% in normal reference data (Judge *et al.*, 1996). Before freezing, stance phase was even further prolonged and swing phase reduced by ~5%. These results concur with the lengthened postural preparation phase (stance) of stepping found in freezers compared with healthy controls during gait initiation tasks (Gantchev *et al.*, 1996; Vaugoyeau *et al.*, 2003). These changes were suggested to reflect a deficit of the coordination between whole-body postural control requirements and step triggering, a coupling normally ensured on the basis of proprioceptive information processing. As we found reduced instead of prolonged gait cycles before freezing as opposed to before step initiation, postural adjustment may have come under increased pressure, posing additional difficulties in freezing of ongoing gait.

Turning to the EMG data, the present results of continued reciprocal activity before freezing are in line with those from Ueno *et al.* (1993) and Yanagisawa *et al.* (2001). However, sometimes co-activation due to continuous activity was reported in the lower limb muscles by the previous authors and Andrews (1973). What is not clear from these reports is whether this co-activation occurred before or during freezing. In this study we encountered continuous traces within the three strides before the freeze, which were excluded from statistical analysis because of their highly abnormal pattern. Although continuous traces were more frequent before freezing, they were also present during normal (off) gait and stopping. Three patients did not show any continuous EMG activity but did freeze. Therefore, abnormal co-activation may be indicative of the severity of the walking difficulty in the off phase of the medication cycle in patients with a tendency to freeze, rather than a causal factor of freezing.

Based on normal reference data, normal double-peaked activity in TA starts at pre-swing (50–60%GC) and peaks at the onset of toe-off to dorsiflex the foot for toe clearance (Winter and Yack, 1987; Perry, 1992). A second peak occurs at loading response (0–10%GC), enabling normal foot placement. In the present study this pattern was roughly preserved during the normal condition and mildly premature in the stop condition. Before freezing, peak TA activity shifted dramatically from the swing to the pre-swing phase of stance, resulting in reduced activity during the actual swing phase. A decreased and sometimes absent second peak of activity at loading response was found, which may explain the abnormal foot placement observed during freezing characterized by an absence of heel strike (Ueno *et al.*, 1993).

The main burst of GS activity in healthy older people lasts from terminal stance (30–50%GC) to pre-swing (50–60%GC), and is absent in swing (Perry, 1992; Judge *et al.*, 1996). Peak activity is developed at ~50%, which is presumed to accelerate the body forward. In this study we found premature and relatively prolonged activity of GS already present in the normal and the stop condition. In contrast to normal reference data, GS was also active for short periods in swing phase. It is possible that these changes were caused by the generally more flexed posture present in the three conditions, as was revealed by the video analysis. Owing to increased flexion throughout the body, the ground reaction force in midstance may have been situated more in front of the ankles, creating an external momentum and eliciting early GS activity to counteract this force. Significant exacerbation of early GS activity was found before freezing, with activity seemingly starting in swing phase. Video analysis showed that only two patients had enhanced flexed posture just before freezing. Therefore, an increase of postural abnormalities before freezing cannot fully explain this premature activity. The shift of GS activity towards early stance and even late swing phase may partly explain the inadequate propulsion

and reduced vertical ground reaction forces to propel the body forward in freezers (Ueno *et al.*, 1993).

Premature activity patterns were found systematically in both muscles and happened in the same direction within the gait cycle. We interpret this finding as a disordered central timing mechanism of muscle activation before freezing. Although premature timing as such was not found in previous studies, Hausdorff *et al.* (2003) also suggested that a central gait timing disorder was connected with the aetiology of freezing. They found markedly increased stride-to-stride variability in the normal gait of freezers, and hypothesized that this could be viewed as a risk factor for a transient gait abnormality to occur such as freezing.

The central timing mechanisms of gait may well be controlled by brainstem, cerebellar and spinal regions with overriding control by the frontal motor cortices (Morris *et al.*, 2001). Recent work suggests that dysfunction of the pedunculopontine nucleus (PPN) and the mesencephalic locomotor region (MLR) plays an important role in the aetiology of gait disturbance in Parkinson's disease, although this is at present largely based on non-primate research (Pahapill and Lozano, 2000; Takakusaki *et al.*, 2003). Major efferent projections from the globus pallidus, subthalamic nucleus and particularly substantia nigra (pars reticulata) enter the PPN and MLR. The functional role of the basal ganglia–brainstem system is thought to be inhibitory, controlling the automatic processes of regulation of muscle tone and rhythmic limb alteration during locomotion. Excessive inhibition of the MLR as a result of disturbed basal ganglia output and a decrease in cortical excitation of the brainstem may elicit gait failure (Takakusaki *et al.*, 2003). Signals from the MLR and PPN also activate central pattern generators in the spinal cord, mainly through the reticulospinal tracts (Pahapill and Lozano, 2000). PPN neurons may act as pace-setters for their target neurons. It is assumed that central pattern generators determine the rhythm of the bursts of motoneurons during locomotion, which is then modulated by afferent proprioceptive input (MacKay-Lyons, 2002; Dietz, 2003). Although impaired supraspinal control may contribute to freezing, it does not explain the altered timing of gait, which looks as if the central pattern generation is providing faulty information rather than is being suppressed.

We hypothesized *a priori* that the magnitude of the EMG signals would be reduced before freezing. The present results show that both muscles generated less activity throughout the gait cycle due to the reduced duration of the EMG bursts. After normalizing for time, levels of GS activity were similar throughout conditions and increased in TA before freezing. Earlier studies of EMG profiles during normal walking and gait initiation in Parkinson's disease reported a tendency of reduced or normal TA and diminished GS activity compared with healthy controls (Dietz *et al.*, 1995; Gantchev *et al.*, 1996; Halliday *et al.*, 1998; Mitoma *et al.*, 2000).

It is difficult to disentangle whether the magnitude changes of TA activity are at the root of the freezing problem or happen as a compensatory mechanism. Morris *et al.* (2001) speculated that the basal ganglia fail to regulate the motor gain of sequential movements, resulting in an overall scaling down of movement and fail to deliver the normal internal cue to string together submovements in a sequence. When processed by faulty feedback loops, movement becomes progressively smaller such as seen in festination. According to this line of thinking, it would have been more logical to have found a gradual reduction of EMG amplitude in both muscles before freezing. The unexpected increase of activity in TA may, therefore, be interpreted as compensatory rather than as primary. Altered timing of the EMG bursts and the following cascade of events leading to reduced forward acceleration and reduced gravitational energy for swing may have triggered this compensatory TA activity. Against the background of faulty timing inherent to freezing, in which swing activity shifts towards the stance phase and *vice versa*, this compensation may be ineffective and movement eventually stops. The fact that enlarged TA peaks are being generated in a shortened gait cycle may also pose problems in Parkinson's disease. Lack of energizing of muscle activity and slower rates of force production have been shown to partially explain the characteristic slowness of movement (Berardelli *et al.*, 2001). In the steps leading up to freezing, compensatory peaks of TA activity may have been generated in an attempt to generate swing up to the point of saturating the motor system and an eventual inability to initiate toe-off.

This study took place after withdrawal of medication to facilitate the occurrence of freezing. Therefore, the present analysis constitutes a comparison between freezing and ongoing (off) gait rather than 'normal' gait, and applies to off-freezing only. The off state may have affected the EMG patterns throughout the conditions. Background activity between the phasic bursts was relatively high in this study. According to Hodges and Bui (1996), levels of background activity will influence EMG onset determination, which needs to be taken into account when interpreting the results of the present study. However, no differences in background activity levels and threshold values for onset determination were found between conditions.

Video analysis of foot strike revealed more flat-footed gait before freezing in comparison with the normal condition. A highly abnormal pattern of foot strike, like walking on toes, was only detected in one step. Manual definition of the gait cycle was previously found to be a reproducible procedure in both pre-freezing and normal stepping (Nieuwboer *et al.*, 2001).

Although different circumstances were used to provoke freezing, a similar motor pattern was observed of festinating leg motion prior to freezing, except in one patient who had a slow shuffling pattern. The present findings may thus apply to a festinating type of freezing only and must not be generalized to all clinical manifestations of the phenomenon.

In conclusion, this study found abnormal co-ordination of TA and GS activity at the onset of freezing, which was more pronounced with regards to the timing rather than the magnitude of the EMG traces. The findings probably reflect

a mixture of the primary deficit of freezing and compensatory processes. The current study suggests that a central deficit of the timing of stepping is fundamental to freezing. As a result, compensatory activity may fail to be effective or no longer be delivered, challenging the capacity to quickly generate peak muscle activity. Future work needs to concentrate on integrated data sets, combining EMG data (including proximal muscles) force measures and kinematic data, leading to a full understanding of the biomechanical factors relating to freezing.

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### References

Almeida QJ, Wishart LR, Lee TD. Disruptive influences of a cued voluntary shift on coordinated movement in Parkinson's disease. Neuropsychologia 2003; 41: 442–52.

Andrews C. Influence of dystonia on the response to long term L-dopa therapy in Parkinson's disease. J Neurol Neurosurg Psychiatry 1973; 36: 630–6.

Berardelli A, Rothwell JC, Thompson PD, Hallett M. Pathophysiology of bradykinesia in Parkinson's disease. Brain 2001; 124: 2131–46.

Burleigh-Jacobs A, Horak FB, Nutt JG, Obeso JA. Step initiation in Parkinson's disease: influence of levodopa and external sensory triggers. Mov Disord 1997; 12: 206–15.

Dietz V. Spinal cord pattern generators for locomotion. Clin Neurophysiol 2003; 114: 1379–89.

Dietz V, Zijlstra W, Prokop T, Berger W. Leg muscle activation during gait in Parkinson's disease: adaptation and interlimb coordination. Electroencephalogr Clin Neurophysiol 1995; 97: 408–15.

Fahn S. The freezing phenomenon in Parkinsonism. Adv Neurol 1995; 67: 53–63.

Fahn S, Elton RL. Unified Parkinson's Disease Rating Scale. In: Fahn S, Marsden CD, Calne DB, Goldstein M, editors. Recent developments in Parkinson's disease, Vol. II. Florham Park (NJ): MacMillan Healthcare Information; 1987. p. 153–63.

Gantchev N, Viallet F, Aurenty R, Massion J. Impairment of posturo-kinetic co-ordination during initiation of forward oriented stepping movements in parkinsonian patients. Electroencephalogr Clin Neurophysiol 1996; 101: 110–20.

Giladi N, Kao R, Fahn S. Freezing phenomenon in patients with parkinsonian syndromes. Mov Disord 1997; 12: 302–5.

Giladi N, Treves TA, Simon ES, Shabtai H, Orlov Y, Kandinov B, et al. Freezing of gait in patients with advanced Parkinson's disease. J Neural Transm 2001a; 108: 53–61.

Giladi N, Shabtai H, Rozenberg E, Shabtai E. Gait festination in Parkinson's disease. Parkinsonism Relat Disord 2001b; 7: 135–8.

Halliday SE, Winter DA, Frank JS, Patla AE, Prince F. The initiation of gait in young, elderly, and Parkinson's disease subjects. Gait Posture 1998; 8: 8–14.

Hausdorff JM, Schaafsma JD, Balash Y, Bartels AL, Gurevich T, Giladi N. Impaired regulation of stride variability in Parkinson's disease subjects with freezing of gait. Exp Brain Res 2003; 149: 187–94.

Hodges PW, Bui BH. A comparison of computer-based methods for the determination of onset of muscle contraction using electromyography. Electroencephalogr Clin Neurophysiol 1996; 101: 511–9.

Hoehn MM, Yahr MD. Parkinsonism: onset, progression and mortality. Neurology 1967; 17: 427–42.

Horak FB, Frank J, Nutt J. Effects of dopamine on postural control in parkinsonian subjects: scaling, set, and tone. J Neurophysiol 1996; 75: 2380–96.

Judge JO, Ounpuu S, Davis RB. Effects of age on the biomechanics and physiology of gait. Clin Geriatr Med 1996; 12: 659–78.

MacKay-Lyons M. Central pattern generation of locomotion: a review of the evidence. Phys Ther 2002; 82: 69–83.

Martin M, Shinberg M, Kuchibhatla M, Ray L, Carollo JJ, Schenkman ML. Gait initiation in community-dwelling adults with Parkinson's disease: comparison with older and younger adults without the disease. Phys Ther 2002; 82: 566–77.

Mitoma H, Hayashi R, Yanagisawa N, Tsukagoshi H. Characteristics of parkinsonian and ataxic gaits: a study using surface electromyograms, angular displacements and floor reaction forces. J Neurol Sci 2000; 174: 22–39.

Morris ME, Huxham FE, McGinley J, Iansek R. Gait disorders and gait rehabilitation in Parkinson's disease. Adv Neurol 2001; 87: 347–61.

Nieuwboer A, Dom R, De Weerdt W, Desloovere K, Fieuws S, Broens-Kaucsik E. Abnormalities of the spatiotemporal characteristics of gait at the onset of freezing in Parkinson's disease. Mov Disord 2001; 16: 1066–75.

Pahapill PA, Lozano AM. The pedunculopontine nucleus and Parkinson's disease. Brain 2000; 123: 1767–83.

Perry J. Gait analysis: normal and pathological function. Thorofare (NJ): SLACK; 1992. p. 397.

Rosin R, Topka H, Dichgans J. Gait initiation in Parkinson's disease. Mov Disord 1997; 12: 682–90.

Schaafsma JD, Balash Y, Gurevich T, Bartels AL, Hausdorff JM, Giladi N. Characterization of freezing of gait subtypes and the response of each to levodopa in Parkinson's disease. Eur J Neurol 2003; 10: 391–8.

Takakusaki K, Habaguchi T, Ohtinata-Sugimoto J, Saitoh K, Sakamoto T. Basal ganglia efferents to the brainstem centers controlling postural muscle tone and locomotion: a new concept for understanding motor disorders in basal ganglia dysfunction. Neuroscience 2003; 119: 293–308.

Ueno E, Yanagisawa N, Takami M. Gait disorders in parkinsonism: a study with floor reaction forces and EMG. Adv Neurol 1993; 60: 414–8.

Vaugoyeau M, Viallet F, Mesure S, Massion J. Coordination of axial rotation and step execution: deficits in Parkinson's disease. Gait Posture 2003; 18: 150–7.

Ward CD, Gibb WR. Research diagnostic criteria for Parkinson's disease. Adv Neurol 1990; 53: 245–9.

Winter DA, Yack HJ. EMG profiles during normal human walking: stride-to-stride and inter-subject variability. Electroencephalogr Clin Neurophysiol 1987; 67: 402–11.

Yanagisawa N, Hayashi R, Mitoma H. Pathophysiology of frozen gait in parkinsonism. Adv Neurol 2001; 87: 199–207.