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WALKING PATTERNS IN PARKINSON'S DISEASE WITH AND WITHOUT FREEZING OF GAIT

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Abstract—The pathophysiology underlying freezing of gait (FOG) in Parkinson's disease remains incompletely understood. Patients with FOG ("freezers") have a higher temporal variability and asymmetry of strides compared to patients without FOG ("non-freezers"). We aimed to extend this view, by assessing spatial variability and asymmetry of steps and interlimb coordination between the upper and lower limbs during gait. Twelve freezers, 15 non-freezers, and 15 age-matched controls were instructed to walk overground and on a treadmill. Kinematic data were recorded with a motion analysis system. Both freezers and non-freezers showed an increased spatial variability of leg movements compared to controls. In addition, both patient groups had a deficit in interlimb coordination, not only between ipsilateral arms and legs, but also between diagonally positioned limbs. The only difference between freezers and non-freezers was a decreased step length during treadmill walking. We conclude that parkinsonian gait—regardless of FOG—is irregular, not only in the legs, but also with respect to interlimb coordination between the arms and legs. FOG is reflected by abnormal treadmill walking, presumably because this provides a greater challenge to the defective supraspinal control than overground walking, hampering the ability of freezers to increase their stride length when necessary. © 2011 Published by Elsevier Ltd on behalf of IBRO.

Key words: central pattern generator, freezing of gait, gait disorders, interlimb coordination, Parkinson's disease.

Gait disturbances are among the most disabling features of Parkinson's disease (PD) (Morris et al., 2001). Approximately 30%–60% of PD patients suffer from freezing of gait (FOG), an episodic gait disorder during which patients suddenly become unable to start walking or to continue moving forward (Schaafsma et al., 2003). FOG impairs quality of life, mobility and independence, and can lead to falls (Moore et al., 2007).

Several studies that investigated the pathophysiology of FOG focused on the coordination of leg movements. The results showed differences in temporal stride regulation between PD patients with FOG ("freezers") and patients without FOG ("non-freezers"). Even outside actual FOG episodes, freezers showed a markedly increased stride-to-stride variability (Hausdorff et al., 2003) and a higher asymmetry of gait, defined as larger differences between left and right swing times (Plotnik et al., 2005, 2008). Additionally, it has been shown that freezing like episodes, so-called motor blocks, can occur in the upper limbs during voluntary hand movements, such as tapping (Ziv et al., 1999) or a bimanual rhythmic task (Nieuwboer et al., 2009b).

Arm swing is integrated into locomotion via tight coordination between the upper and lower limbs (interlimb coordination) by specialized neural circuits in the spinal cord that can produce self-sustained patterns of behavior (central pattern generators, CPGs) (Dietz et al., 2001; Dietz, 2002; Zehr and Duysens, 2004). In PD, the adaptive coordination of interlimb movements during walking appears defective, both when walking speed is varied (Dietz et al., 1995; Winogrodzka et al., 2005) or kept constant (Carpinella et al., 2007; Crenna et al., 2008). During gait there is a basic difference between arm and leg movements, as leg movements involve load regulation, that is input from load receptors provide afferent input to the leg muscles for appropriate activation (Dietz, 2003). A decreased load sensitivity has been suggested as a cause for gait disorders in PD; a deficit in the processing of load related input may lead to reduced leg extensor activation during the stance phase of gait (Dietz and Duysens, 2000). Several etiologies have been suggested for FOG (Okuma, 2006). In this experiment, we will focus on two of these explanations: defects in coordination of leg movements and an altered load regulation. If FOG is mainly a disorder of load regulation, then no major interlimb coordination difference is expected between freezers and non-freezers. Conversely, if FOG is actually the ultimate manifestation of a severe segmental coordination problem, then interlimb coordination deficits should be amplified in freezers.

To address this question, we studied leg movements (spatial and temporal parameters) and interlimb coordination between the upper and lower limbs during gait in PD patients with and without FOG, and in healthy controls. We

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Abbreviations: CPGs, central pattern generators; CV, coefficient of variation; FOG, freezing of gait; H&Y, Hoehn & Yahr; NFOG-Q, new FOG questionnaire; PD, Parkinson's disease; UPDRS, Unified Parkinson's Disease Rating Scale.

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Table 1. Subject characteristics

	Freezers	Non-freezers	Controls	Group* differences
N	12	15	15	NS
Age	60.5±7.9	60.2±9.2	57.9±7.3	NS
Female (%)	29%	30%	40%	NS
MMSE	29.3±1.0	29.1±1.2	29.4±0.6	NS
FAB	16.0±2.0	15.7±2.1	17.3±1.0	NS
Disease duration	9.6±3.6	7.7±4.5	—	NS
H&Y[a]	2.4±0.3	2.1±0.3	—	NS
UPDRS (Part III)[a]	35.4±8.9	30.6±7.0	—	NS
NFOG-Q score (max. 24)	11.6±5.3	0.0±0.0	—	<0.001

Data reflect means±SE. N, number of subjects; NS, not significant; MMSE, Mini Mental State Exam; FAB, Frontal Assessment Battery; UPDRS, Unified Parkinson's Disease Rating Scale; H&Y, Hoehn & Yahr; NFOG-Q, New Freezing Of Gait Questionnaire.
[a] UPDRS and H&Y score were determined in off medication state.
* Significance was assessed by a univariate ANOVA ($P<0.01$).

examined overground walking and also treadmill walking, as this requires a more complex supraspinal control (Regnaux et al., 2006).

EXPERIMENTAL PROCEDURES

Subjects

We recruited 27 PD patients, diagnosed according to the UK Brain Bank criteria (Hughes et al., 1992), and 15 age-matched controls (Table 1). All participants were free from other neurological, visual, vestibular or muscular limb deficits that would influence their gait. Other exclusion criteria were cognitive disturbances (Mini Mental State Examination<25 or Frontal Assessment Battery<12), psychiatric pathology or severe co-morbidity. All subjects gave written informed consent according to the Declaration of Helsinki prior to participation. The study was approved by the local ethics committee. Patients were recorded in an OFF-state, after at least 12 h withdrawal of dopaminergic medication.

Assessment of FOG

All patients completed a FOG provocation trajectory in off medication state (Snijders et al., 2008), which involved rising from a chair, gait initiation, 360° and 540° turns to both sides, passing between narrowly placed barriers, and gait termination. This was done thrice: at preferred speed, as rapidly as possible, and in combination with a cognitive dual task (counting back from 100 with steps of seven). If any FOG episode was observed during this gait trajectory, the patient was defined as a freezer. However, since FOG is difficult to elicit in a research setting (Snijders et al., 2008), all patients additionally completed the new FOG questionnaire (NFOG-Q) (Nieuwboer et al., 2009a). As a part of this questionnaire a video with examples of typical FOG episodes was shown, to ensure that patients understood what was meant by a FOG episode. Subsequently, if they answered "yes" to the first question of the NFOG-Q ("Have you experienced FOG episodes during the past month?"), they were also defined as a freezer. Twelve patients were thus defined as having "off" period FOG (all with subjective FOG according to the NFOG-Q, and seven (58.3%) with additional FOG episodes during the gait trajectory).

There were no differences in age, gender, and cognitive scores between the three groups (Table 1). In addition, Hoehn & Yahr (H&Y) stage, Unified Parkinson's Disease Rating Scale (UPDRS) score and disease duration were not significantly different between freezers and non-freezers (Table 1). None of the PD patients showed any freezing episodes during the formal experiment (consisting only of straight walking).

Gait analysis

To analyze overground gait, participants walked across an 8-meter walkway. Six trials while walking at preferred speed were recorded. Spatiotemporal data were collected for each trial, using a 6-camera VICON® motion analysis system (Oxford Metrics, UK) with reflective markers placed according to the standard VICON® Plug-in-Gait marker set.

Subsequently, subjects were instructed to walk on a treadmill at their preferred speed. Treadmill speed was increased or decreased until a comfortable walking speed, indicated by the subject, was reached. After that, treadmill speed remained constant during the experiment. Before recording, subjects were familiarized with treadmill walking for approximately 10 min. Then, spatiotemporal data were collected during one min of walking, in the same way as described above. We always performed the overground protocol first to avoid possible short-term treadmill training effects. We did not inform the subjects about the aims of the study and we instructed them to walk as naturally as possible, without any "tricks" they could have learned from their physiotherapist to improve gait or arm swing. During the experiment we did not observe any remarkable gait patterns.

Outcome measures

We measured gait variables during the two conditions. Outcome measures were amplitude, variation, and asymmetry of step length (spatial) and step time (temporal). Step length was defined as the distance traversed between heel strike of one foot and the consecutive heel strike of the contralateral foot. Step time was calculated as the time elapsed between sequential left and right heel strikes. Spatial variation was calculated as the coefficient of variation (CV) of all step lengths in one trial, while temporal variation was the CV of all step times. These outcome measures were determined for the most affected side in patients (highest UPDRS score) and for the non-dominant side in controls. Spatial asymmetry between left and right step length was calculated using the following formula: $\frac{\text{max } amplitude - \text{min } amplitude}{\text{max } amplitude} \cdot 100\%$, where "max *amplitude*" represents the largest step length among mean left and right step lengths, and "min *amplitude*" represents the smallest step length. Temporal asymmetry was calculated in the same way for step time. Additionally, we calculated the phase coordination index as the duration of one step divided by the duration of one stride, a measure of bilateral coordination in producing left–right stepping phases (Plotnik et al., 2007).