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TURNING AND UNILATERAL CUEING IN PARKINSON'S DISEASE PATIENTS WITH AND WITHOUT FREEZING OF GAIT

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Abstract—Background: Freezing of gait (FOG) is one of the most disabling symptoms in Parkinson's disease (PD), and cueing has been reported to improve FOG during straight-line walking. Studies on how cueing affects FOG during turning are lacking. Given the asymmetrical nature of turning and the asymmetrical disease expression, we aimed to gain a new perspective on how unilateral cueing may alleviate FOG. Objective: To explore disease dominance and turning side as contributing factors to turning problems and FOG and to investigate the effect of unilateral cueing. Methods: In the first study, 13 PD patients with FOG (freezers) and 13 without FOG (nonfreezers) turned toward their disease-dominant and nondominant side (off medication). During the second study, 16 freezers and 14 nonfreezers turned with and without a unilateral auditory cue at −10% of preferred cadence. Total number of steps, turn duration, cadence, and FOG episodes were measured using VICON. Results: Cadence, but not FOG frequency, was higher when turning toward the disease-dominant side. FOG started more frequently (64.9%) on the inner side of the turning cycle. Unilateral cueing seemed to prevent FOG in most patients, irrespective of the side at which the cue was offered. A carryover effect was found for cadence during turning, but the effect on FOG disappeared when the cue was removed. Conclusions: The occurrence of FOG is not influenced by turning toward the disease-dominant or nondominant side, which is confirmed by the fact that it does not make a difference at which side unilateral cueing is applied. Cueing reduces FOG during turning, but these effects disappear dramatically after cue removal. This raises further questions as to the influence of training on cue dependency and on the feasibility of either continuous application of cues or using cognitive strategies as an alternative. © 2012 IBRO. Published by Elsevier Ltd. All rights reserved.

Key words: turning, freezing of gait, cueing, Parkinson's disease, asymmetry.

Freezing of gait (FOG) is one of the most disabling symptoms in Parkinson's disease (PD) and is often characterized by the degradation of normal gait into episodes of small steps at a high frequency leading to an involuntary halt (Iansek et al., 2006). FOG provokes frequent falling (Giladi et al., 2001; Michalowska et al., 2005) with a higher percentage of fractures (especially hip fractures) (Genever et al., 2005), which has a significant impact on quality of life, depression, and anxiety (Rahman et al., 2008).

At the moment, pharmacological interventions are only partially effective to reduce FOG (Schaafsma et al., 2003; Giladi, 2008), and subthalamic nucleus stimulation (STN-DBS) has a positive influence on FOG during off medication, but seems to have less impact on dopamine-resistant FOG. FOG might, in some cases, be an adverse effect of STN-DBS (Ferraye et al., 2008).

Many studies highlighted an immediate beneficial effect of cueing on straight-line gait in PD (Rubinstein et al., 2002). However, this effect is less clear during turning and in patients with FOG (Willems et al., 2007). Turning seems a strong trigger for FOG. Freezing occurs most frequently during turning (Schaafsma et al., 2003), and no less than 86% of all PD patients with turning difficulties report frequent freezing and falling (Stack et al., 2006).

In healthy subjects, Courtine and Schieppati (2003a) described separate functions for the inner and outer leg during turning. Although the step length and swing velocity of the inner leg decreases in combination with an increase of stance phase duration during turning, the outer leg continues the ongoing movement and decreases the stance phase duration, inducing asymmetry (Courtine and Schieppati, 2003b).

In addition to the asymmetry of turning, PD itself also has an asymmetric symptom distribution (Djaldetti et al., 2006). The disorder usually displays a unilateral onset, and the symptom distribution remains highly asymmetrical throughout the disease in approximately 85% of the patients (Yust-Katz et al., 2008). A connection between turning preference and side of disease dominance has been suggested by a previous study (Bracha et al., 1987), which found that hemi-PD patients turned spontaneously toward the nonaffected side, thus keeping the most affected leg at the outer side of the turning cycle.

Our previous work pointed to the fact that freezing may also be influenced by disease asymmetry because FOG (Nieuwboer et al., 2007a) as well as upper limb freezing (Vercruysse et al., 2011) started most frequently at the

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Abbreviations: COM, center of mass; DT, dual task; FOG, freezing of gait; FRs, freezers; H&Y, Hoehn and Yahr; IQR, interquartile ranges; MMSE, Mini-Mental State Examination; NFOGQ, New Freezing of Gait Questionnaire; nFRs, nonfreezers; PD, Parkinson's disease; UPDRS, Unified Parkinson Disease Rating Scale.

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most affected (i.e. disease-dominant) side. However, this was not explicitly tested in these studies. Therefore, we will first examine the influence of disease dominance on turning and freezing by requiring participants to make turns toward their disease-dominant and their nondominant side. Taking into account that the inner side of the turn is characterized by smaller step length, we expect that turning toward the disease-dominant side will induce more turning difficulties than turning toward the other side and therefore provoke more FOG. Moreover, we suspect that freezing is also influenced by the asymmetry of turning itself, and that FOG will start more often on the inner side of the turn, that is, the side with the smallest step length, longer stance duration, and slowest velocity.

If FOG is dependent on disease dominance or the turning side, cueing one specific body side during turning may alleviate these difficulties and prevent FOG. Therefore, the second study raises the question whether cueing can reduce FOG during turning. We will examine the effect of a unilateral auditory cue (i.e. cueing each stride instead of each separate step) applied to either the disease-dominant or the nondominant side and to the inner or outer side of the turn. Hence, these studies will provide valuable clinical information for physiotherapists on which leg to emphasize when applying cueing or other rehabilitation strategies during turning.

STUDY 1

Methods of study 1

Participants. Twenty-six patients diagnosed with PD stage II or III of Hoehn and Yahr (1967) (H&Y) were recruited in the Movement Disorders Clinic of the University Hospital Leuven. The study was approved by the local ethics committee, and all participants gave written informed consent. Participants were included if (1) they were able to walk 10 m repeatedly during the off phase, and if (2) no dementia as measured by the Mini-Mental State Examination (MMSE$>$24) (Folstein et al., 1975), (3) no deep brain stimulation, and (4) no comorbidity limiting gait were present. As the study examined the importance of disease dominance on turning and FOG, participants with a complete symmetrical symptom distribution according to the Unified Parkinson Disease Rating Scale motor part (UPDRS III) (Movement Disorder Society, 2003) were also excluded. The participants with and without FOG were divided according to the first item of the revised New Freezing of Gait Questionnaire (NFOGQ) (Nieuwboer et al., 2009b). Freezers (FRs) were defined as participants who had experienced freezing at least once during the past month (NFOGQ item 1$\geq$1). One participant was classified in the nonfreezer (nFR) group, but froze during our test protocol. Therefore, he was reallocated to the freezer group. The two patient groups (13 FRs and 13 nFRs) were matched for disease duration and disease severity based on H&Y stage and the UPDRS III administered in OFF.

Test protocol. Participants were tested in practically defined off state, that is, in the morning, 12–15 h after the last anti-Parkinson medication intake. Side of disease dominance (worst disease severity) was calculated for each participant as the difference of the left and right scores on items 20–26 and item 31 of the UPDRS during off (i.e. UPDRS difference) (Uitti et al., 2005). A negative value categorized a participant as being right dominant, whereas a positive score indicated left dominance. The degree of disease asymmetry was defined as the absolute value of the UPDRS difference and used as a descriptive parameter for comparing groups.

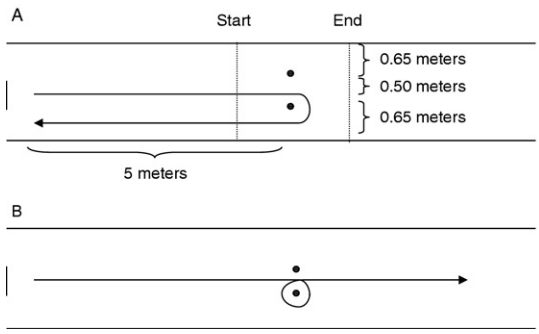

Fig. 1. Walkway. Two retroreflective markers (●) were placed in the middle of the walkway. Data collection started one meter in front (START) and stopped one meter after the markers (END). (A) Trajectory during 180° turning. (B) Trajectory during 360° turning.

The protocol required participants to walk along a walkway of 5 m between two retroreflective markers placed 0.5 m away from each other, as previously described (Spildooren et al., 2010) (Fig. 1). The small and unobtrusive markers were positioned so that no impression of space limitation for turning was induced. Participants were therefore discouraged to enlarge their turning cycle and encouraged to standardize turning performance. Participants were asked to perform a 180° and 360° turn toward their disease-dominant and nondominant side in a random order, within blocks of trials with and without a verbal cognitive dual task (the color classification task) (Bowen et al., 2001; Canning et al., 2006), which were counterbalanced (see Spildooren et al., 2010). The dual task (DT) and 360° turning were included to induce FOG as much as possible and therefore only used for the evaluation of FOG episodes and not the spatiotemporal characteristics. Every condition was performed three times. Resting periods were provided at regular intervals to avoid fatigue.

Apparatus. An eight camera VICON data capturing system (Vicon Motion Systems, Workstation 612, Oxford Metrics, Oxford, UK) was set up around a 10-meter walkway. Thirty-one retroreflective markers of 14 mm in diameter were located on the anatomical bony landmarks according to the standardized procedure of the gait laboratory (full body plug-in-gait marker configuration). Polygon software was used for the visualization of FOG episodes.

Data processing. The data processing started from the first initial foot one meter in front of the reflective markers placed on the floor, till the first initial foot contact one meter after the markers. This meant that during the turning conditions, the data largely represented the actual turning action, including the straight-line steps just before and after the turn within the spatial confines of two meters (Spildooren et al., 2010). This method ensured an equal walking distance for each participant during the turning trajectories.

The following dependent parameters were obtained to describe differences in turning behavior to the left and right side:

(1) Total number of steps, total turn duration, and cadence (steps/min) were calculated between the start and the endpoint of turning toward the disease-dominant and nondominant side separately.
(2) Number of freezing episodes when turning to the left and right side: *FOG* was defined according to the recently published definition as an episode of inability to generate effective stepping often leading to a halt (Giladi and Nieuwboer, 2008) based on visual analysis of the 3D images of the whole body skeleton in polygon. Both periods with a complete halt as well as severely disrupted motion (a nearly