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SPLIT-BELT LOCOMOTION IN PARKINSON'S DISEASE WITH AND WITHOUT FREEZING OF GAIT

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Abstract—*Background:* Parkinson's disease (PD) patients have an increased gait asymmetry and variability, which is most pronounced in patients with freezing of gait (FOG). We examined if stride time variability and deficits in interlimb coordination between the upper and lower limbs would increase during split-belt locomotion in PD, and particularly so in patients with FOG.
Methods: **Fourteen PD patients (seven with FOG, matched for disease severity with the seven non-freezers) and 10 healthy controls walked on a treadmill with split belts at different speeds (2 versus 3 km/h). Gait was recorded by means of a video motion analysis system. Outcome measures were stride length asymmetry and variability, stride time asymmetry and variability, ipsilateral and contralateral interlimb coordination, and phase coordination index.**
Results: **Both PD subjects and controls were able to adapt to split-belt walking by modulating their stride length. However, freezers showed a larger increase in stride time asymmetry and stride time variability due to split-belt walking compared to non-freezers. Furthermore, contralateral interlimb coordination improved in control subjects during split-belt walking, but not in PD patients (freezers and non-freezers). Phase coordination index did not change differently across the three groups.**
Conclusions: **The ability to walk under split-belt conditions was preserved in PD. Non-freezers and controls compensated for the experimentally increased stride length asymmetry by decreasing their stride time asymmetry. This ability was lost in freezers, who in fact *increased* their stride time asymmetry during split-belt walking. As a result, stride time variability also increased in freezers. These findings support the hypothesis that FOG is related to gait asymmetries and to gait timing deficits.**

Key words: freezing of gait, gait asymmetry, gait variability, Parkinson's disease, split-belt locomotion, treadmill.

INTRODUCTION

Patients with Parkinson's disease (PD) are easily recognized by their shuffling gait with small slow steps (Morris et al., 2001). Less obviously, the parkinsonian gait is also highly variable in its spatial and temporal characteristics (Morris et al., 1994; Almeida et al., 2007), with subtle asymmetries between both legs (Plotnik et al., 2007). The variability and asymmetry of gait timing are particularly pronounced in PD patients who manifest episodes of freezing of gait (FOG), even in between FOG episodes (Hausdorff et al., 2003; Plotnik et al., 2005). Additionally, the adaptive coordination of interlimb movements between the upper and lower limbs appears to be defective in PD (Winogrodzka et al., 2005; Carpinella et al., 2007; Crenna et al., 2008; Nanhoe-Mahabier et al., 2011). Furthermore, intralimb coordination between the legs is known to be worse in PD patients, and especially in patients who manifest FOG (Plotnik et al., 2008; Fasano et al., 2011; Peterson et al., 2012).

A treadmill with a split belt – allowing both legs to move independently at different speeds – can be used to artificially generate (additional) asymmetry between the legs during walking. An earlier study using a split-belt treadmill for PD patients showed that patients were able to adapt intralimb coordination (between both legs) to split-belt walking (Dietz et al., 1995). Split-belt walking also affects arm movements, but this has only been studied in healthy controls (McFadyen et al., 2012).

In this study, we examined whether split-belt walking would not only provoke gait asymmetry, but also increase the stride-to-stride variability. Second, we investigated whether split-belt locomotion provokes deficits in interlimb coordination between the arms and legs. We studied differences between PD patients and control subjects. We reasoned that the intrinsic gait asymmetry and defective interlimb coordination that are characteristic of PD would make patients extra vulnerable to an externally imposed asymmetry between both legs. Since gait asymmetry and gait variability are more pronounced in PD patients with FOG, we

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Abbreviations: ANCOVA, analysis of covariance; ANOVA, analysis of variance; FOG, freezing of gait; PCI, phase coordination index; PD, Parkinson's disease.

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additionally hypothesized that these patients would experience more difficulties during split-belt walking. Therefore, we also examined if the split-belt influences gait in PD patients with FOG ('freezers') differently compared to matched patients without FOG ('non-freezers').

EXPERIMENTAL PROCEDURES

Subjects

We included 14 PD patients (seven with subjective FOG), diagnosed according to the UK Brain Bank criteria (Hughes et al., 1992) and 10 age- and gender-matched healthy control subjects. Patients were excluded if they had cognitive impairments (Mini Mental State Examination < 25 or Frontal Assessment Battery < 12), other causes for gait disorders (neurological, musculoskeletal, visual, vestibular), major psychiatric disorders, severe co-morbidity (e.g. cancer), or were unable to walk independently on the treadmill for 10 consecutive minutes. The study was approved by our local ethics committee and all patients gave written informed consent according to the Declaration of Helsinki prior to participation.

Study protocol

Subjects walked on a customized motor-driven split-belt treadmill (Bonte Zwolle BV, The Netherlands), wearing a safety harness to prevent falling. They were instructed to walk with one foot on each belt of the treadmill, while the speed of the treadmill was manipulated on both sides. Participants were asked to walk as stable as they could with the speeds provided by the treadmill. No particular instruction was given to the subject concerning their hand or arm movements during gait. Furthermore, no information on belt speed was provided to the subjects. All patients were examined during the OFF medication state, after overnight withdrawal of dopaminergic medication for at least 12 h.

All subjects started with the baseline condition at a velocity of 2 km/h on both belts of the treadmill. Subsequently, a split-belt condition with a speed of 2 km/h on one side and 3 km/h on the other side was applied. All subjects executed this split-belt condition twice in random order: once with the fast belt speed on the side of the least affected leg, and once with the fast belt speed on the side of the most affected leg. For controls the non-dominant side was referred to as the most affected side. In between the split-belt conditions subjects walked with equal speeds on both sides. We used fixed belt speeds instead of self-paced walking velocity to standardize the difference between the two sides. The duration of each trial was 2 min. Spatiotemporal data were collected for each trial, using a 6-camera Vicon® motion analysis system (Oxford Metrics, UK) at a sampling rate of 100 Hz. Reflective markers were placed on the shoes of the subject on the lateral malleoli, heels, and big toes, and on the hands below the head of the second metacarpal (dorsum of the hand).

Outcome measures

The first 30 s of each condition were not taken into account for further analysis, as the first 12–15 strides are generally needed to adapt to the treadmill (Prokop et al., 1995). Moreover, from previous studies on split-belt walking it appears that most of this adaptation occurs within these first 30 s, even in elderly subjects (Vasudevan and Bastian, 2010; Bruijn et al., 2012). We used at least 10 consecutive strides of each condition for further analysis. Strides during which the hands were tied (for example a hand on the face or both hands tied at the back) were excluded from the analysis. Outcome measures were calculated using MatLab (version 7.1).

We computed stride length asymmetry with the following formula: $\frac{\max \textit{stride length} - \min \textit{stride length}}{\max \textit{stride length}} \cdot 100\%$. Stride time asymmetry was determined similarly. Stride length variability and stride time variability were calculated as the coefficient of variation (CV) of stride length and stride time respectively. Interlimb coordination between the upper and the lower limbs was defined as the synchronization between arm swing and steps as described previously in (Nanhoe-Mahabier et al., 2011). Ipsilateral interlimb coordination was calculated as the delay in time between heel strike of the foot and maximal backward arm swing of the ipsilateral arm. Contralateral interlimb coordination was determined as the delay in time between heel strike of the foot and maximal forward arm swing of the contralateral arm. Interlimb coordination was expressed as a percentage of gait cycle time. Additionally, we calculated the phase coordination index (PCI), which was previously described as a measure for bilateral coordination between the legs (Plotnik et al., 2007).

Statistical analysis

Statistical analysis was performed using SPSS for Windows (version 18.0). Skewed data were normalized by means of log-transformation. For all outcome measures, there was no difference between the two split-belt conditions (most affected versus less affected leg on the 3 km/h belt), as assessed by Student's *t*-test for each subject group. We therefore merged the split-belt conditions into one split-belt condition, with 33% difference in velocity between the two belts (2 km/h versus 3 km/h). Additionally, for the variability and interlimb coordination outcome measures, we averaged the values of the most affected and least affected leg into one variable, since there were no significant differences between both legs. For gait asymmetry and phase coordination index outcomes, differences between the most and less affected leg were already incorporated in the calculation, so averaging sides was not necessary.

We analyzed if changes in stride asymmetry, stride variability, and interlimb coordination during split-belt walking compared to baseline walking were different between groups. For this purpose, we conducted an analysis of covariance (ANCOVA) with the variable during the split-belt condition as a dependent variable, 'group' as a fixed factor, and the variable during the baseline condition as a covariate. We performed this analysis twice: once comparing healthy controls with PD patients, and once comparing freezers with non-freezers. Level of significance (α) was set at $P = 0.01$ to correct for multiple comparisons.

RESULTS

Subjects

Clinical details are described in Table 1. Seven patients had subjective FOG according to the new FOG questionnaire (Nieuwboer et al., 2009). Five of these patients additionally showed objective freezing episodes while walking along a specific gait trajectory to provoke FOG (ascertained by an experienced movement disorders neurologist). Therefore, the freezers group consisted of five 'definite' freezers and two 'probable' freezers (Mahabier et al., 2010). In our analyses we did not distinguish between these two subgroups of freezers. There were no differences in disease severity and disease duration between freezers and