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Progression of postural control and gait deficits in Parkinson's disease and freezing of gait: A longitudinal study

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ABSTRACT

Background and aims: The relationship between impaired postural control and freezing of gait (FOG) in Parkinson's disease (PD) is still unclear. Our aim was to identify if postural control deficits and gait dysfunction progress differently in freezers compared to non-freezers and whether this relates to FOG development.

Methods: 76 PD patients, classified as freezer (n = 17) or non-freezer (n = 59), and 24 controls underwent a gait and postural control assessments at baseline and after 12 months follow-up. Non-freezers who developed FOG during the study period were categorized as FOG converters (n = 5). Gait was analyzed during walking at self-preferred pace. Postural control was assessed using the Mini-BESTest and its sub-categories: sensory orientation, anticipatory, reactive and dynamic postural control.

Results: Mini-BESTest scores were lower in PD compared to controls ($p < 0.001$), and in freezers compared to non-freezers ($p = 0.02$). PD has worse anticipatory ($p = 0.01$), reactive ($p = 0.02$) and dynamic postural control ($p = 0.003$) compared to controls. Freezers scored lower on dynamic postural control compared to non-freezers ($p = 0.02$). There were no baseline differences between converters and non-converters. Decline in postural control was worse in PD compared to controls ($p = 0.02$) as shown by a greater decrease in the total Mini-BESTest score. Similar patterns were found in freezers ($p = 0.006$), who also showed more decline in anticipatory ($p < 0.001$) and dynamic postural control ($p = 0.02$) compared to non-freezers. FOG converters had a greater decline in the total Mini-BESTest ($p = 0.005$) and dynamic postural control scores ($p = 0.04$) compared to non-converters. Gait outcomes showed no significant differences in any of the analyses.

Conclusion: FOG is associated with more severe decline in postural control, which can be detected by the clinical Mini-BESTest.

1. Introduction

Impaired postural control and gait are important contributors to reduced mobility in patients with Parkinson's disease (PD) [1]. Postural control dysfunction impacts on quality of life in PD as it is one of the major causes of increased fall risk [2]. Recurrent falls are an even larger concern in patients with freezing of gait (FOG) [2,3]. FOG is defined as a brief, episodic absence or marked reduction of forward progression of the feet despite the intention to walk [4]. Although several studies have suggested that impaired postural control and falls are two related phenomena (for review: [2]), the relationship between postural control and FOG is currently still unclear.

Postural control requires several mechanisms to align the body with respect to gravity, the support surface and visual surroundings and is aimed to stabilize the COM of the body relative to its base of support [1]. According to a recently proposed multi-component framework, these control systems comprise postural sway during sensory manipulations in quiet stance, reactive postural control,

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anticipatory postural adjustments (APAs) and dynamic balance [1]. These mechanisms have been investigated in PD in general, but studies in the context of FOG are scarce and showed contradictory results. Two of these studies found altered postural sway parameters indicating a lower adaptability of postural sway in freezers compared to non-freezers [5,6]. A recent study from Schlenstedt et al. (2015) showed a posterior shift in the center of pressure in freezers compared to non-freezers, which was hypothesized to generate inadequate forward movement progression during gait initiation, thereby contributing to FOG [7]. However, the same study found no alterations in sway properties of the center of pressure, corroborating our earlier findings of comparable sway parameters in freezers and non-freezers, even when sensory input was compromised [8]. We also examined APAs during a voluntary weight-shifting paradigm demonstrating poorer directional control in freezers compared to non-freezers. Deficient APA's have been consistently reported in freezers [9–11] and are suggested to have a close relationship to FOG due to the observation that knee trembling prior to a freezing episode represents decoupling between APAs and the selection of the appropriate motor program at gait initiation [10]. Moreover, high-frequency knee trembling is currently used to identify freezing episodes [12].

Although these studies provided insights into some of the important individual components of freezing-related postural instability, to date, there is no consensus on which aspects of this multicomponent process are most affected in FOG. Previous studies investigated this matter in a cross-sectional manner, making it difficult to pinpoint specific mechanism contributing to FOG. Therefore, the current study applied an integrated and longitudinal approach to clarify whether and how different postural control aspects underpin FOG. The Mini-BESTest is a clinical test, which includes sub-scores of anticipatory and reactive postural control, sensory orientation and dynamic postural control. It was recently shown to be able to detect balance decline in PD after 6 and 12 months follow-up [13] and was indicated by a recent study from Duncan et al. (2015) [14] to be the preferred tool for clinically assessing postural control deficits associated with FOG in mild to moderate PD. The same research group also demonstrated the Mini-BESTest to be a more sensitive predictor of falls in PD (sensitivity = 0.75; specificity = 0.79) in comparison with gait speed (sensitivity = 0.67; specificity = 0.72) [15]. Although previous studies suggested that gait impairment is already present in de novo and early PD [16], a recent progression study could only detect subtle changes in gait speed, step length and swing time after 18 months follow-up in PD compared to controls [17].

Therefore, this study aimed to evaluate if decline in postural control and gait performance are related to FOG and its development. For this purpose, we compared Mini-BESTest scores between freezers and non-freezers cross-sectionally and investigated the progression after 12 months follow-up. In addition, we examined the relationship with the development of FOG by comparing the same outcome measures in non-freezers who converted to freezers during the follow-up period with those who did not. We also investigated the sub-scores of the Mini-BESTest to identify which aspects of postural control dysfunction were most FOG-related.

2. Methods

2.1. Subjects

Seventy-six PD patients and 24 healthy age-matched controls were recruited for this study (for details, see Supplementary Materials). Patients were included if they were diagnosed with PD according to the UK Brain bank criteria and if they had a Hoehn and Yahr (H&Y) stage between 1 and 3 while 'off' medication. Exclusion criteria were a Mini-Mental State Examination (MMSE) score < 24 and presence of neurological comorbidities. The New freezing of gait questionnaire (NFOG-Q) or FOG occurrence in the lab was used to classify patients as freezers (FOG) (n = 17) or non-freezers (NFOG) (n = 59). Disease severity was measured by Movement Disorder Society Unified Parkinson's Disease Rating Scale III (MDS-UPDRS) and H&Y staging while 'off' medication. Disease duration was expressed as the number of years since onset of the first motor symptom. The study was approved by the local ethics committee of the University Hospitals Leuven and all subjects gave written informed consent prior to participation.

2.2. Test protocol

Subjects underwent a postural control and gait assessment at baseline and after 12 months follow-up. All tests were performed in the practically defined 'off' state. Five PD patients and 4 controls only underwent baseline assessment because they were recruited as part of another cross-sectional study which included the same balance assessments. In addition, 4 PD patients dropped out during the follow-up period due to personal reasons or development of comorbidity. This led to a final sample size of 67 PD patients (11 FOG and 56 NFOG) and 20 controls for the longitudinal analysis.

2.3. Postural control assessment

Postural control was assessed using the mini-BESTest [18], which is derived from the BESTest. It consists of 14 items with scores ranging between 0 and 2. The anticipatory postural control part (part 1: 3 items) it tests the ability to prepare for voluntary center of mass (COM) movements. The reactive postural control (part: 3 items) probes the involuntary postural responses when postural support is suddenly withdrawn. The sensory orientation sub-score assesses postural control when sensory information is compromised (part 3: 3 items). Finally, dynamic postural control tests CoM stability in challenging gait conditions such as speed changes and dual-tasking (part 4: 5 items). Outcome measures were scores of the 4 sub-domains and the total score ranging between 0 and 28. In addition, we collected fall data via fall diaries [19] during the 12 month follow-up period. Subjects were contacted monthly to go over their fall history. If one or more falls occurred during this 12 month follow-up, participants were considered to be fallers. One patient and 4 healthy controls did not fill-out their diaries regularly and were excluded from the falls data analysis.

2.4. Gait assessment

Gait analysis was performed using the VICON 3D motion analysis system (©Vicon Motion Systems Ltd.; Oxford Metrics, UK) as previously described [20]. Gait speed, swing time and step length were chosen as outcomes as they were recently shown to be significantly declined after 18 month follow-up in the context of the 'Incidence of Cognitive Impairment in Cohorts with Longitudinal Evaluation–Parkinson Disease' (ICICLE-PD) study [17]. We also included variability measures of swing time and step length as they proved important markers of FOG [21] and falling [22].

2.5. Statistical analyses

Descriptive statistics were compared between groups using unpaired T-tests for continuous variables and chi-squared tests for non-continuous variables. Paired T-tests were used to evaluate within group differences in PD and controls between baseline follow-up. Outcome measures for the baseline postural control and

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