Parkinsonism and Related Disorders 25 (2016) 72–77

Contents lists available at ScienceDirect

Parkinsonism and Related Disorders

journal homepage: www.elsevier.com/locate/parkreldis

Postural sensory correlates of freezing of gait in Parkinson's disease

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ARTICLE INFO

Article history:
Received 7 December 2015
Received in revised form
27 January 2016
Accepted 1 February 2016

Keywords:
Parkinson's disease
Freezing of gait
Postural sensory deficits
Vestibular impairment

ABSTRACT

Introduction: To elucidate the unique patterns of postural sensory deficits contributing to freezing of gait (FOG) in patients with Parkinson's disease (PD) and to identify postural sensory modalities that correlate with FOG severity.

Methods: Twenty-five PD patients with FOG, 22 PD patients without FOG, and 26 age-matched controls were evaluated using a sensory organization test and clinical measures including the Unified Parkinson's Disease Rating Scale motor score, Montreal Cognitive Assessment, Frontal Assessment Battery, Activities-specific Balance Confidence, Beck Anxiety Inventory, Beck Depression Inventory, and Berg Balance Scale. Multivariable logistic regression analysis was performed for posturographic parameters and possible confounders to determine postural sensory contributors to FOG. We also correlated FOG severity, measured using a New Freezing of Gait Questionnaire, with posturographic parameters.

Results: PD patients with FOG showed worse postural sensory processing compared with those without FOG. In particular, the inability to use the vestibular information (odds ratio [OR] 1.447; 95% confidential interval [CI]: 1.120, 1.869) and poor control over the perturbed somatosensory inputs (OR 2.904; 95% CI: 1.028, 8.202) significantly contributed to FOG. Among PD patients with FOG, FOG severity was correlated with higher reliance on visual information ($\rho = -0.432$, $p = 0.039$).

Conclusions: Postural sensory deficits involving specific sensory modalities are strongly associated with FOG. Quantitative measurement of postural sensory deficits in PD patients with FOG may provide a better understanding of pathomechanisms of FOG and increase the efficacy of sensory cueing strategies for alleviating FOG, by more accurately identifying suitable patients for rehabilitative therapies.

1. Introduction

Freezing of gait (FOG) is characterized by an episodic inability to generate effective stepping despite intention to walk [1]. It is a devastating condition in patients with Parkinson's disease (PD), as it causes falls and diminishes mobility and quality of life [1]. Several factors, including disease severity, cognitive dysfunction, attention deficits, emotional state, and postural instability, are associated with FOG, reflecting its complex pathomechanism [1–3].

PD patients with FOG also exhibit deficits in sensory processing [4–6]. During normal locomotion, sensory signals from visual, vestibular, and somatosensory systems are integrated via central neural networks and provide real-time information used as references for cognitive, emotional, and automatic locomotor processes [7]. Accordingly, the inability to integrate postural sensory inputs may contribute to the generation of FOG [7]. Indeed, FOG can be provoked under sensory conflicting situations in which balance is challenged [1] and also alleviated by various sensory cues [1,8,9]. However, little is known about how postural sensory deficits are implicated to pathomechanisms of FOG.

We aimed to characterize postural sensory deficits in PD patients with FOG and to determine specific patterns of postural sensory deficits that contribute to FOG. Quantitative

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http://dx.doi.org/10.1016/j.parkreldis.2016.02.004
1353-8020/

posturographic measures were compared between PD patients with and without FOG using a sensory organization test (SOT). We also identified postural sensory modalities associated with the severity of FOG.

2. Methods

2.1. Subjects

We recruited 47 patients with idiopathic PD and 26 age-matched healthy controls through the Movement Disorders Clinic of Samsung Medical Center. A diagnosis of idiopathic PD was made by a specialist experienced in movement disorders (J.W.C) based on UK Parkinson's Disease Society Brain Bank criteria. All patients were taking levodopa in combination with dopamine agonist and experienced levodopa-related motor fluctuations. Subjects were excluded if they could not safely stand unaided, or had a history of falls in the last 12 months, dementia, visual disturbances, clinical signs of disorders affecting proprioception, musculoskeletal problems, orthostatic hypotension, or neurosurgical interventions. Subjects were also excluded if they had a history or clinical signs of vestibular diseases, including the presence of spontaneous or head-shaking nystagmus or corrective saccades during head impulse testing. Motor disability was assessed using the Unified Parkinson's Disease Rating Scale motor score (UPDRS-III). For clinical balance measurement, we used the Berg Balance Scale (BBS), a 56-point scale in which lower scores indicate worse balance [10]. Global cognitive and executive functions were tested using Montreal Cognitive Assessment (MOCA) and Frontal Assessment Battery (FAB), respectively. The New Freezing of Gait Questionnaire (NFOGQ) was used to evaluate the presence and severity of FOG [11]. The Activities-specific Balance Confidence (ABC) scale (0–100%) was used to estimate fear of falling (FOF) by measuring confidence in maintaining balance while performing various ambulatory activities [10,12]. Lower scores indicate greater FOF. All subjects completed the Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI). Clinical and neurological examinations and posturography were performed during the morning off-medication, at least 12 h after withholding anti-parkinsonian medications.

Patients were assigned to PD patients with FOG (PD-FOG) if they experienced FOG at least once during the past month based on NFOGQ item 1, and one or more FOG episodes were provoked and detected by two experienced movement specialists (Y.E.H. and J.W.C.) during experiments. FOG was elicited using a turning-in-place task in which patients were asked to make tight and rapid 360° turns to the left or right for 2 min, immediately before posturography assessment [13,14]. All PD-FOG showed worse freezing during the off-medication state, and no PD patients without FOG (PD-noFOG) reported either self-assessed or experimentally provoked FOG episodes. PD-FOG and PD-noFOG were matched for age and off Hoehn and Yahr stage, which ranged from 2 to 3.

Written informed consent was obtained from each subject and the study protocol was approved by the Institutional Review Board of Samsung Medical Center.

2.2. Posturography

Postural sensory deficits were assessed using the SOT protocol of a computerized dynamic posturography system (EquiTest®; NeuroCom International, Clackamas, OR, USA) [15], which was equipped with a force plate enclosed by a visual surround. During the SOT, subjects stood on the force plate from which the position of their center of pressure was recorded at a sampling rate of 100 Hz. Digitized center of pressure data were automatically converted into center of gravity sway and analyzed using an arithmetic algorithm provided by the EquiTest® system. The force plate and visual surround were fixed or programmed to revolve in reference to subject's sways in an anterior-posterior direction. By manipulating fixed/sway-referenced and eye open/closed conditions, visual and/or somatosensory inputs were distorted or eliminated. The SOT protocol consisted of six conditions (Fig. 1A). Static balance measures were obtained from condition 1 in which all sensory sources were available. In conditions 2 and 3, visual inputs were absent and distorted, respectively. In the last three conditions, somatosensory inputs were distorted, while visual inputs were available (condition 4), absent (condition 5), or inaccurate (condition 6).

All participants were outfitted with a safety harness and stood barefoot at a standardized stance width based on their body height. They were instructed to remain as still as possible in an upright posture during each condition, which was composed of three repeated 20-s trials. A fall was noted when subjects swayed beyond their limit of stability, requiring a corrective step or assistance.

2.3. Balance measurements

To assess postural stability, an equilibrium score was obtained from each SOT trial, by comparing the maximum angle of center of gravity sway in an anterior-posterior direction with the theoretical limit of stability which was assumed to be 12.5° (Fig. 1B) [15]. Equilibrium scores ranged from 0% to 100%, with higher scores indicating better ability to maintain balance and 0% indicating a fall. Averaged equilibrium scores of three trials (ESs) from each SOT condition were used to assess postural stability.

Sensory ratios (SRs) were calculated to measure the contribution of each sensory input to postural balance [15]. The ability to use somatosensory information (SR-SOM), visual information (SR-VIS), and vestibular information (SR-VEST) were estimated as ratios between the ES of condition 2 (ES2) and ES of condition 1 (ES1), between the ES of condition 4 (ES4) and ES1, and between the ES of condition 5 (ES5) and ES1, respectively. Lower SRs indicated a poorer ability to use relevant sensory information to maintain balance. Visual preference (SR-VISPREF) was defined as a ratio of the sum of the ES of condition 3 (ES3) and the ES of condition 6 (ES6) to the sum of ES2 and ES5. Lower SR-VISPREFs indicated higher dependency on visual information, even if inaccurate. The ability to manage distorted somatosensory inputs (SR-MANSOM) was calculated by dividing the sum of ESs from sway-referenced plate conditions (ES4 + ES5 + ES6) by that from fixed plate conditions (ES1 + ES2 + ES3) [16,17].

2.4. Statistical analysis

To assess overall differences between groups in demographic, clinical, and posturographic variables, Kruskal–Wallis or Man–Whitney U tests, where appropriate, were performed for continuous data, as normal distributions could not be assumed for most variables. Significant main effects of group were further examined by post hoc analysis with Tukey's tests using ranked data. χ^2-tests were used to analyze categorical data. To identify postural sensory modalities contributing to FOG, we conducted a multivariable multinomial logistic regression analysis for all SR values with adjustment for clinical variables that differed between groups with $p < 0.2$. Variance inflation factors (VIFs) were estimated for each variable entering the multivariable model. Variables with a VIF ≥ 10 were considered to have a high level of multi-collinearity and omitted from the model. VIFs of remaining variables were recalculated to ensure an independent association with FOG. To investigate correlations between the severity of FOG and each postural sensory modality, Spearman partial correlations were performed