

Title

Identification of gait patterns among patients with parkinsonism based on normalized gait obtained using multiple regression models

Affiliations

Flora Ferreira (PhD), Algoritmi Center, University of Minho and ESTG, Polytechnic of Porto

Carlos Fernandes (BSc), Algoritmi Center, University of Minho

Miguel Gago (MD, PhD), Neurology Service, Hospital Senhora da Oliveira and ICVS, School of Medicine, University of Minho

Nuno Sousa (MD, PhD), ICVS, School of Medicine, University of Minho

Wolfram Erlhagen (PhD), Center of Mathematics, University of Minho

Estela Bicho (PhD), Algoritmi Center, University of Minho

Corresponding author: Flora Ferreira, flora.ferreira@gmail.com

Keywords: Multiple regression models, clustering, gait analysis

Abstract (4000 a 6000 characters, including spaces):

Introduction: Parkinsonism is a syndrome manifested by the presence of slow movements (bradykinesia) with either resting tremor, muscle rigidity, impairment of gait or postural instability. The most common cause of parkinsonism is idiopathic Parkinson's disease (IPD), a neurodegenerative disorder of the central nervous system (CNS) that affects motor skills of the body, typically asymmetrically, with progressive impairment of gait. In contrast, Vascular Parkinsonism (VaP) is secondary to vascular CNS lesions, typically characterized by lower body parkinsonism with early and rapid impairment of gait and postural control. Still, there is substantial clinical heterogeneity in both diseases, leading to significant clinical diagnostic overlap. There are few instrumental biomarkers helping physicians in ameliorating diagnostic accuracy when VaP is suspected [1]. There has been growing evidence showing gait assessment as a complementary clinical tool in the differential diagnosis and management of parkinsonian disorders [2, 3]. However, differentiation studies between VaP and IPD based on gait data and, even more, studies that explore the existence of different homogeneous subgroups of patients with parkinsonism according to gait pattern are scarce. Gait measurements of a subject are affected by his physical properties including sex, age, height, and weight, as well as by walking speed or stride length [2, 3]. In [2] and more recently in [4], a multiple regression (MR) normalization method was employed on spatiotemporal gait data to minimize the effect of between-subject physical differences. Comparing to other methods, such as dimensionless equations and detrending method, MR revealed better results on reducing the interference of subject-specific physical properties and its gait variables, thereby improving differentiation of parkinsonian gait from healthy controls [2]. This study aims to identify subgroups of patients with parkinsonism (VaP and IPD) with similar foot clearance and spatiotemporal gait characteristics, after applying MR normalization.

Methods: Gait measurements of 15 VaP patients, 15 IPD patients, and 15 age-matched healthy controls were collected using foot-worn inertial sensors while the subjects walked a 60-meter

continuous course at a self-selected walking speed. The gait variables considered in this study are stride length, stride time, cadence, maximum heel, maximum toe early swing, minimum toe, and maximum toe late swing. Using the control dataset, different multiple regression models were found for each gait variable considering different combinations of the independent variables (age, sex, weight, height, and speed or stride length). Each gait variable is normalized by dividing the original value by the value estimated according to the best MR model selected based on adjusted R-square and Akaike's information criterion (AIC) values. (for more detail, see [2]). First, we sought to assess the accuracy of the two clustering methods (k-means and hierarchical clustering) in assigning the patients to their correct clusters using: 1) raw gait measures; 2) gait measures normalized using the MR approach. Cluster analysis was performed on data of the 30 patients and the number of clusters was predefined as 2. Then, the method with higher accuracy as used to perform unsupervised cluster analysis, where the number of clusters was identified by the elbow method. Before performing the clustering analysis, a principal component analysis (PCA) was applied to data 1) and 2) in order to reduce the dimensionality and allow graphical representation of clustering result. According to Kaiser's criterion, the principal components with a corresponding eigenvalue greater than 1 were retained.

Results: The first two principal components accounted 79.87% and 75.93% of the total variability were retained, using data 1) and 2) respectively. The higher accuracy (about 67.86%) was found for the hierarchical method based on the first principal components obtained from the gait measures normalized using the MR approach. Hierarchical clustering was then performed using the normalized gait data. The number of clusters is set at 3. Cluster 1 is represented majority by IPD (11 IPD and 3 VaP). The patients of this cluster correspond to the group with higher stride time and lower cadence. Cluster 2 covered 1 IPD and 7 VaP with lower stride length, stride time, and foot elevation and higher cadence. Cluster 3 with 3 IPD and 5 VaP correspond to the group of patients with higher stride length and foot elevation. While most of the IPD patients are grouped in cluster 1, most VaP patients are distributed among 2 clusters revealing a higher heterogeneity in VaP patients.

Discussion and conclusions: These first results reveal that the identification of subgroups through clustering analysis based on gait measures normalized using the MR approach may be useful on the detection of gait biomarkers among patients with parkinsonism, improving personalized medicine.

Acknowledgements This work was partially supported by the projects NORTE-01-0145-FEDER-000026(DeM-Deus Ex Machina) financed by NORTE2020 and FEDER, and FP7 NETT project.

References

- [1] Mostile G, Nicoletti A, Zappia M. Vascular Parkinsonism: Still Looking for a Diagnosis. *Frontiers in neurology*. 2018;9:411.
- [2] Wahid F, Begg R, Lythgo N, Hass CJ, Halgamuge S, Ackland DC. A multiple regression approach to normalization of spatiotemporal gait features. *Journal of applied biomechanics*. 2016 Apr;32(2):128-39.

[3] Alcock L, Galna B, Perkins R, Lord S, Rochester L. Step length determines minimum toe clearance in older adults and people with Parkinson's disease. *Journal of biomechanics*. 2018 Apr 11;71:30-6.

[4] Mikos V, Yen SC, Tay A, Heng CH, Chung CL, Liew SH, Tan DM, Au WL. Regression analysis of gait parameters and mobility measures in a healthy cohort for subject-specific normative values. *PloS one*. 2018 Jun 18;13(6):e0199215.

ACCEPTED EXTENDED ABSTRACT