Journal of Statistics on Health Decision

EXTENDED ABSTRACT

P25

The effect of levodopa medication on stride time variability in patients with Parkinsonism

Flora Ferreira[1], Carlos Fernandes[2], José Braga[2], Estela Bicho[2], Wolfram Erlhagen[1], Miguel F. Gago[3,4]

[1] Center of Mathematics, University of Minho,
[2] Center Algoritmi, University of Minho,
[3] Neurology Services, Hospital Senhora da Oliveira,
[4] ICVS, School of Medicine, University of Minho

Introduction

Stride time variability, as measured by the coefficient of variation (CV), is considered as a marker to evaluate of Idiopathic Parkinson's disease (IPD) progression [1], and to predict the risk of fall [2]. Typically, patients with IPD show higher stride time variability compared to healthy age-matched subjects and this variability is significantly reduced in response to levodopa [3]. While it is unanimous the benefit of levodopa in gait variability on patients with IPD, in patients with vascular Parkinsonism (VaP) is still unclear. Although patients with VaP are less responsive to levodopa compared to IPD previous study [4] shows that levodopa had some positive effects on gait variability in VaP patients.

Objective

This study aims to evaluate the effect of levodopa medication on stride time variability in VaP patients compared to IPD patients.

Methods

The participants of this study were recruited from the Movement Disorder outpatient consultations of a local Portuguese hospital. The values of stride time and speed in each gait cycle were obtained by wearing foot-worn inertial sensors (Physilog®, Gait Up, Switzerland) while the subjects walked a 60-meter continuous course (a 30 meters corridor with one turn) at a self-selected walking. Fifteen IPD patients (age range of 67-83 years) and 15 VaP patients (age range of 73-90 years) were assessed in two states: before (Off medication), and one hour after (On medication) the acute administration of a suprathreshold (1.5 times the usual) levodopa dose. The exclusion criteria for all patients were: the presence of resting tremor, moderate-severe dementia (CDR > 2), musculoskeletal disease, and overt clinical progression since diagnosis (Hoehn-Yahr > 3). The local hospital ethics committee approved the study protocol, submitted by ICVS/UM and Center Algoritmi/UM. Written consent was obtained from all subjects or their guardians.

Stride-time variability is affected by subject physical properties including height and age, as well as by walking speed [5]. Therefore, the variable stride time has been normalized for age, height, and speed using a multiple regression (MR) normalization approach according to Wahid et al.'s method [6]. The model's coefficients are estimated using a control data of thirty-four healthy subjects (age range of 20-85 years and height range of 1.53-1.89 meters) (see [7] for more details). The MR model is then used to normalize each stride (gait cycle) according to the respective stride' speed and subject physical properties. Then the coefficient of variation was determined based on the normalized stride time series. Since data were not normally distributed, based on the Shapiro-Wilk test, a non-parametric Aligned Rank Transform (ART) ANOVA [8] test was performed to investigate both the main effects and the interaction effect between group (IPD and VaP) and state (Off medication and On medication). To compare the differences between the two states within each group of patients a non-parametric Wilcoxon Signed-Rank test was also performed. The type I error was set to 5%. Statistical analysis was performed by R software using 'ARTool' package.

Keywords:
Stride variability, Levodopa, Parkinsonian disorders

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

First published: 23 OCT 2020

Results

The ART ANOVA test result showed no significant interaction between group and state ($F_{1,28} = 0.61, p = 0.440$). There were significant main effects for both group ($F_{1,28} = 6.44, p = 0.017$) and state ($F_{1,28} = 5.20, p = 0.031$). The Wilcoxon Signed-Rank test showed that stride time variability was significantly lower in the On medication state than in the Off medication for the IDP group ($Z = 2.73, p = 0.004$). The differences between the two states in VaP patients were not significantly different ($Z = 0.47, p = 0.670$).

Discussion and Conclusion

In line with previous studies [3,4] levodopa medication significantly reduced stride time variability in IPD patients. Some reduction of variability is also observed in VaP patients albeit with a lower magnitude when compared to IPD, reinforcing the hypothesis that some VaP patients are likely to benefit from levodopa [4]. Additionally, the results reveal that stride time variability may be a good biomarker to differentiate IPD versus VaP, as well as to support the individualized decision of levodopa dose.

Acknowledgments

The work received financial support from the FCT – Fundação para a Ciência e Tecnologia within the R&D Units Project Scope: UIDB/00319/2020 and UIDB/00013/2020.

References

1. Hausdorff, J. M. Gait dynamics in Parkinson's disease: common and distinct behavior among stride length, gait variability, and fractal-like scaling. Chaos: An Interdisciplinary Journal of Nonlinear Science, 2009;19(2), 026113. https://doi.org/10.1063/1.3147408
2. Hoskovcová, M., Dušek, P., Sieger, T., Brožová, H., Zárubová, K., Bezdíček, O. et al. Predicting falls in Parkinson disease: What is the value of instrumented testing in OFF medication state?. PloS one, 2015;10(10):e0139849. https://doi.org/10.1371/journal.pone.0139849
3. Bryant, M. S., Rintala, D. H., Hou, J. G., Charness, A. L., Fernandez, A. L., Collins, R. L., et al. Gait variability in Parkinson's disease: influence of walking speed and dopaminergic treatment. Neurological research, 2011;33(9):959-964. https://doi.org/10.1179/1743132811Y.0000000044
4. Ferreira, F., Gago, M.F., Bicho, E., Carvalho, C., Mollaei, N., Rodrigues, L., et al. Gait stride-to-stride variability and foot clearance pattern analysis in Idiopathic Parkinson's Disease and Vascular Parkinsonism. Journal of biomechanics, 2019;92:98-104. https://doi.org/10.1016/j.jbiomech.2019.05.039
5. M Beauchet, O., Annweiler, C., Lecordroch, Y., Allali, G., Dubost, V., Herrmann, F. R., & Kressig, R. W. Walking speed-related changes in stride time variability: effects of decreased speed. Journal of neuroengineering and rehabilitation, 2009;6(1):32. https://doi.org/10.1186/1743-0003-6-32
6. Wahid, F., Begg, R., Lythgo, N., Hass, C.J., Halgamuge, S. and Ackland, D.C. A multiple regression approach to normalization of spatiotemporal gait features. Journal of applied biomechanics, 2016;32(2):128-139. https://doi.org/10.1123/jab.2015-0035
7. Fernandes, C., Ferreira, F., Gago, M., Azevedo, O., Sousa, N., Erlhagen, W. and Bicho, E. Gait classification of patients with Fabry's disease based on normalized gait features obtained using multiple regression models. In 2019 IEEE International Conference on Bioinformatics and Biomedicine (BIBM) (pp. 2288-2295). IEEE. https://doi.org/10.1109/BIBM47256.2019.8983241
8. J.O. Wobbrock, L. Findlater, D. Gergle, J.J. Higgins, "The aligned rank transform for nonparametric factorial analyses using only ANOVA procedures", Proc. SIGCHI Conf. Human Factors Comput. Syst., pp. 143-146, May 2011. https://doi.org/10.1145/1978942.1978963