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Gait variability in multiple sclerosis: a better falls predictor than EDSS in patients with low disability

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Abstract This longitudinal study aims to compare the role of stride time variability (STV) and EDSS for predicting falls in 50 patients with multiple sclerosis with low disability. 21.7 % developed falls (follow-up: 22 months). STV (IRR: 1.73, 95 % CI: 1.23–2.41, $p = 0.001$) and EDSS (IRR: 2.29, 95 % CI: 1.35–3.90, $p = 0.002$) were associated with the number of falls. Adding STV to EDSS improves the predictive power of the model from 21 to 26 %, but not adding EDSS to STV.

Keywords Gait disorders · Falls · Disability · Longitudinal study · Multiple sclerosis

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Introduction

Falls are common in patients with multiple sclerosis (MS), with more than 50 % of patients reporting injurious falls over 6 months, representing a major source of disability (Peterson et al. 2008). Gait disorders and disability, assessed by the expanded disability status scale (EDSS) constitute the main fall predictors in patients with MS (Gunn et al. 2013); however, the fall risk peaks at EDSS levels of 4.0 and 6.0 (Nilsagard et al. 2015), suggesting that other falls predictors would be more accurate in patients with low disability. Fluctuation of gait parameters (i.e. gait variability), especially stride time variability, predicts falls in aging (Verghese et al. 2009) and in patients with white matter disease of vascular origin (Srikanth et al. 2009). If the interest of quantifying gait variability has been demonstrated in patients with MS with low disability (Sosnoff et al. 2012), the predictive value of stride time variability for predicting falls in patients with MS has interestingly never been specifically studied.

To address these knowledge gaps, we conducted a longitudinal study on patients with MS with low disability to evaluate the role of stride time variability to predict incidental falls. While gait variability, especially stride time variability, has been considered as an appropriate marker of the neural control of gait (Hausdorff 2005) and that the EDSS becomes an interesting falls predictor in patients with significant disability (Nilsagard et al. 2015), but not in low disabled patients, we hypothesized that stride time variability will predict number of falls better than the EDSS in patients with low disability. With the considerable development of gait analysis systems, establishing falls predictors based on gait parameters in patients with MS with low disability will improve the clinical practice, especially the fall's prevention strategy.

Methods

Participants

Fifty outpatients with relapsing-remitting MS [age 41.0 ± 10.0 years; 60 % female, EDSS (median and interquartile range) 2.0 (1.0)] diagnosed according to the revised McDonald criteria (Polman et al. 2005) were recruited in this longitudinal study. The study procedures have been previously described (Allali et al. 2012). Briefly, exclusion criteria were: acute medical illness in the past month, neurological and psychiatric diseases except MS, orthopedic or rheumatologic condition affecting walking, and the use of a walking aid. Following a structured screening interview, all consecutive patients contacted from May 2010 to August 2014, who fulfilled the inclusion criteria and who accepted to participate to the research protocol were included in this analysis. All patients were stable (without any MS relapse in the last 2 months) and have been taking the same treatment for at least 3 months. Patients presenting any falls in the follow-up period (mean follow-up time: 22.2 ± 13.9 months) were considered as fallers. The Geneva University Hospitals Committee on Human Research approved the research protocol, and informed consent was obtained from all participants.

Gait evaluation

The participants walked at their usual self-selected walking speed on a distance of 10 m. Spatio-temporal gait parameters were recorded by an optoelectronic system (Vicon Mx3+, Vicon Peak) synchronized with footswitches (Aurion Zerowire). Stride time variability were calculated by the formula and expressed in percentage: stride time variability = (standard deviation of stride time/mean value of stride time) × 100.

Falls

A fall was defined as unintentionally coming down to the floor or lower level not due to a major intrinsic or extrinsic event. At baseline, retrospective falls were recorded if the presence of any falls in the previous 12 months. Then, incident falls were systematically assessed during our annual in-house visit or by telephone if the patients were not able to complete their visit.

Statistics

Descriptive statistics were calculated and compared fallers and non-fallers. The associations between number of falls (dependent variable), and stride time variability and EDSS (independent variables) were examined using a multivariate binomial negative regression analyses (adjusted for follow-up time). Two missing values of EDSS were imputed by a multiple linear regression adjusted for sex, age, being a faller and having a history of falls. To assess differences among the three models' predictive powers [(1) stride time variability, (2) EDSS, (3) stride time variability and EDSS], we used the likelihood ratio test (LR test). All statistics were performed using the Stata Statistical Software, version 13.1 and $p < 0.05$ was considered significant for all analyses.

Results

Clinical characteristics of the 50 patients with MS compared the 13 fallers (21.7 %) and the 37 non-fallers (Table 1). The fallers reported more retrospective falls (46 versus 5 %, $p = 0.002$) and were more disabled (EDSS (median and interquartile range) 2.50 (2.50) versus 1.84 (1.00), $p = 0.004$) than the non-fallers. The observation

Table 1 Clinical characteristics and gait performances of prospective fallers and non-fallers multiple sclerosis patients ($n = 50$)

	Fallers ($n = 13$)	Non-fallers ($n = 37$)	p value*
Age, mean ± SD (years)	43.14 ± 13.17	40.60 ± 8.83	0.682
Female, n (%)	8 (27)	22 (59)	1.000
Education, mean ± SD (years)	13.69 ± 3.25	14.69 ± 2.84	0.100
Observation time, mean ± SD (months)	32.03 ± 13.40	18.69 ± 12.50	**0.001**
History of fall, n (%)	6 (46)	2 (5)	**0.002**
EDSS (/10), median (interquartile range)	2.50 (2.50)	1.84 (1.00)	**0.004**

Values are mean ± standard deviation or n (%)

EDSS Expanded Disability Status Scale

* Comparison based on Mann–Whitney test or Fisher exact test as appropriate. Significant p value (<0.05) are bolded

Table 2 Binomial negative regression showing the association between prospective fallers and non-fallers multiple sclerosis patients (dependent variable) and stride time variability, and EDSS (independent variables), adjusted for follow-up time

	Model 1				Model 2				Model 3			
	IRR	95 % CI	*p* value	Pseudo R^2	IRR	95 % CI	*p* value	Pseudo R^2	IRR	95 % CI	*p* value	Pseudo R^2
				0.24				0.21				0.26
Stride time variability	1.73	1.23–2.41	**0.001**						1.51	1.07–2.12	**0.018**	
EDSS					2.29	1.35–3.90	**0.002**		1.56	0.91–2.65	0.104	

IRR incidence-rate ratio, *EDSS* expanded disability status scale

Significant *p* value ($p < 0.05$) are bolded

time differed between fallers and non-fallers, with an increased time for the fallers group (32.03 ± 12.40 versus 18.69 ± 12.50 months, $p = 0.002$). A total of 45 falls was reported in the fallers group.

Mean gait speed was 1.10 ± 0.24 m/s for fallers and 1.26 ± 0.22 m/s for non-fallers ($p = 0.053$) and the stride time variability was increased (i.e. worse performance) in fallers compared to non-fallers (3.49 ± 2.83 versus 1.83 ± 1.14 % for non-fallers; $p = 0.015$). Stride time variability (incidence-rate ratio (IRR) 1.73, 95 % CI 1.23–2.41, $p = 0.001$) and EDSS (IRR 2.29, 95 % CI 1.35–3.90, $p = 0.002$) were associated individually with the number of falls (Model 1 and 2; Table 2). However, in the fully adjusted model (Model 3), only stride time variability, but not EDSS, was associated with the number of falls (IRR 1.19, 95 % CI 1.10–1.29, $p < 0.001$). The LR test between Model 3 and 2 was significant ($p = 0.017$), but not between Model 3 and 1 ($p = 0.105$), indicating that adding stride time variability to EDSS improves the predictive power of the model from 21 to 26 %, but adding EDSS to stride time variability does not improve the predictive power of the model (24 versus 26 %).

Discussion

The findings showed that prospective fallers presented more disturbed stride time variability than non-fallers. Worse variability (i.e. increase) of stride time and EDSS were associated individually with the number of falls of patients with MS with low disability. However, the predictive power of stride time variability was significantly superior to EDSS to predict falls.

Gait variability reflects the stride-to-stride fluctuation in walking and increased stride time variability has been associated with neurological conditions affecting the central nervous systems, including patients with MS with low disability (Sosnoff et al. 2012). Increased gait variability (i.e. stride time) reflecting gait instability represents a more sensitive marker for falls than average measures of gait, as suggested by studies conducted in aging or in neurodegenerative conditions (Hausdorff et al. 1997), and has been associated with white matter lesions in older adults (Rosano et al. 2007). Furthermore, a common pathway has been suggested between white matter integrity and gait variability to explain falls in aging (Srikanth et al. 2009). Although the pathophysiological mechanisms affecting the white matter differ between MS and aging, the contribution of white matter integrity seems to be crucial for explaining the relationship between gait variability and falls.

With the recent developments in motion analysis (Behrens et al. 2014; Sosnoff et al. 2012), the use of quantitative gait and balance parameters to evaluate patients follow-up or response to pharmacological (Allali et al. 2014) or rehabilitation (Brichetto et al. 2013; Gandolfi et al. 2015) therapies will contribute to a better clinical management of MS patients.

Including a quantitative measure of gait in this longitudinal cohort assessing the predictors of fall in patients with MS constitutes the main strength of this study. However, the relatively small sample size and the approach for assessing incidental falls (clinical interview instead of calendar) represent both limitations of this study. The faller group presented a longer follow-up time than the non-faller group. Although we adjusted the multivariate binomial negative regression analyses for follow-up time, we cannot exclude the presence of other confounding variables.

In conclusion, the findings suggest that stride time variability represents a clinical potential predictor of falls in patients with MS with low disability that is more appropriate than the EDSS. The measure of gait variability should be included in observational and interventional studies focusing on falls prevention in MS.

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Compliance with ethical standards

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Conflict of interest The authors declare that they have no conflict of interest.

References

Allali G, Laidet M, Assal F, Beauchet O, Chofflon M, Armand S, Lalive PH (2012) Adapted timed up and go: a rapid clinical test to assess gait and cognition in multiple sclerosis. Eur Neurol 67(2):116–120. doi:10.1159/000334394

Allali G, Laidet M, Assal F, Chofflon M, Armand S, Lalive PH (2014) Dual-task assessment in natalizumab-treated multiple sclerosis patients. Eur Neurol 71(5–6):247–251. doi:10.1159/000357217

Behrens J, Pfuller C, Mansow-Model S, Otte K, Paul F, Brandt AU (2014) Using perceptive computing in multiple sclerosis—the Short Maximum Speed Walk test. J Neuroeng Rehabil 11:89. doi:10.1186/1743-0003-11-89

Brichetto G, Spallarossa P, de Carvalho ML, Battaglia MA (2013) The effect of Nintendo(R) Wii(R) on balance in people with multiple sclerosis: a pilot randomized control study. Multiple Scler 19(9):1219–1221. doi:10.1177/1352458512472747

Gandolfi M, Munari D, Geroin C, Gajofatto A, Benedetti MD, Midiri A, Carla F, Picelli A, Waldner A, Smania N (2015) Sensory integration balance training in patients with multiple sclerosis: a randomized, controlled trial. Mult Scler 21(11):1453–1462. doi:10.1177/1352458514562438

Gunn H, Creanor S, Haas B, Marsden J, Freeman J (2013) Risk factors for falls in multiple sclerosis: an observational study. Mult Scler 19(14):1913–1922. doi:10.1177/1352458513488233

Hausdorff JM (2005) Gait variability: methods, modeling and meaning. J Neuroeng Rehabil 2:19. doi:10.1186/1743-0003-2-19

Hausdorff JM, Edelberg HK, Mitchell SL, Goldberger AL, Wei JY (1997) Increased gait unsteadiness in community-dwelling elderly fallers. Arch Phys Med Rehabil 78(3):278–283

Nilsagard Y, Gunn H, Freeman J, Hoang P, Lord S, Mazumder R, Cameron M (2015) Falls in people with MS—an individual data meta-analysis from studies from Australia, Sweden, United Kingdom and the United States. Mult Scler 21(1):92–100. doi:10.1177/1352458514538884

Peterson EW, Cho CC, von Koch L, Finlayson ML (2008) Injurious falls among middle aged and older adults with multiple sclerosis. Arch Phys Med Rehabil 89(6):1031–1037. doi:10.1016/j.apmr.2007.10.043

Polman CH, Reingold SC, Edan G, Filippi M, Hartung HP, Kappos L, Lublin FD, Metz LM, McFarland HF, O'Connor PW, Sandberg-Wollheim M, Thompson AJ, Weinshenker BG, Wolinsky JS (2005) Diagnostic criteria for multiple sclerosis: 2005 revisions to the "McDonald Criteria". Ann Neurol 58(6):840–846. doi:10.1002/ana.20703

Rosano C, Brach J, Studenski S, Longstreth WT Jr, Newman AB (2007) Gait variability is associated with subclinical brain vascular abnormalities in high-functioning older adults. Neuroepidemiology 29(3–4):193–200. doi:10.1159/000111582

Sosnoff JJ, Sandroff BM, Motl RW (2012) Quantifying gait abnormalities in persons with multiple sclerosis with minimal disability. Gait Posture 36(1):154–156. doi:10.1016/j.gaitpost.2011.11.027

Srikanth V, Beare R, Blizzard L, Phan T, Stapleton J, Chen J, Callisaya M, Martin K, Reutens D (2009) Cerebral white matter lesions, gait, and the risk of incident falls: a prospective population-based study. Stroke 40(1):175–180. doi:10.1161/STROKEAHA.108.524355

Verghese J, Holtzer R, Lipton RB, Wang C (2009) Quantitative gait markers and incident fall risk in older adults. J Gerontol Ser A Biol Sci Med Sci 64(8):896–901. doi:10.1093/gerona/glp033