Journal of the Neurological Sciences xxx (2015) xxx–xxx

Contents lists available at ScienceDirect

Journal of the Neurological Sciences

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

The "butterfly diagram": A gait marker for neurological and cerebellar impairment in people with multiple sclerosis☆·☆☆

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ARTICLE INFO

Article history:
Received 28 May 2015
Received in revised form 27 July 2015
Accepted 18 August 2015
Available online xxxx

Keywords:
Multiple sclerosis
Gait
Cerebellar impairment
Treadmill
Neurological disease
Gait variability

ABSTRACT

People with multiple sclerosis (PwMS) frequently experience walking and balance impairments. In our previous report, we demonstrated that spatio-temporal gait parameters, collected by the Zebris FDM-T instrumented treadmill (Zebris Medical GmbH, Germany), serve as valid markers of neurological impairment in the MS population. In the current study, we focused on a unique outcome statistic of the instrumented treadmill, the "butterfly" diagram which reflects the variability of the center of pressure trajectory during walking. Therefore, the aim of the study was to examine the relationship between parameters related to the gait butterfly diagram and the level of neurological impairment in PwMS. Specifically we examined whether the gait butterfly parameters can differentiate between MS patients with normal cerebellar function and those suffering from ataxia. Demographic, neurological and gait parameters were collected from 341 PwMS, 213 women, aged 42.3 (S.D. = 13.8). MS participants with ataxia demonstrated higher scores relating to the butterfly gait variability parameters compared to PwMS with normal or slightly abnormal cerebellar function. According to the results of the binary regression analysis, gait variability in the ant-post direction was found to explain 18.1% of the variance related to cerebellar function; $R^2 = 0.181$, $\chi^2_{(1)} = 67.852$, $P < 0.001$. Measurements derived from the butterfly diagram are proper estimators for important neurological functions in PwMS and should be considered in order to improve diagnosis and assessment of the MS population.

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1. Introduction

Multiple sclerosis (MS) is the most common progressive neurological disease [1] and the main cause of non-traumatic neurological disability in young adults [2]. Symptoms of MS are multifold and varied. They include visual disturbances, pyramidal signs (muscle weakness and spasticity), sensory dysfunction, incoordination, mobility difficulties and cognitive impairment [3]. People with MS (PwMS) frequently experience walking and balance impairment. Approximately 85% of PwMS report gait disturbances as their main complaint [4], and within 15 years of MS onset, up to 50% PwMS require walking assistance [5].

Walking and balance impairments are significant risk factors for falls [6]. Furthermore, PwMS with walking difficulties may fear falling, thus leading to activity curtailment, reduced participation, physical deconditioning and substantial reduction in quality of life [7]. Worth noting, any decline in mobility and function of PwMS dramatically increases the economic burden of the disease [8,9]. Therefore, gait assessment on a regular basis is essential for proper management of PwMS.

Measures of gait and balance in PwMS usually include clinically based tests (e.g., the 2-minute walk test, the Timed Up and Go test, the Timed 25-Foot Walk test) and laboratory based tests that are accessible in many medical settings. The latter option includes instrumented equipment, i.e. electronic walking mats, pressure insoles and posturography devices. The primary advantages of these tools are their ability to generate quantified values of gait and balance components, thus enabling exposure of subtle variations usually invisible to the naked eye. Moreover, early identification of walking and balance impairments, can promote intervention programs at a stage when patients will be able to benefit the most, focusing on decreasing accidental falls.

A common parameter collected by many of the instrumented devices is the center of pressure (CoP) movement [10,11]. Previous studies have demonstrated that CoP trajectory measurements during walking and standing relate to the clinical and radiological aspects of MS. In a series of papers published by Prosperini et al. [12–14], elevated trajectories of CoP during standing, were associated with falls, atrophy of the spinal cord, supratentorial associative white matter bundles and gray matter atrophy of the cerebellum in PwMS.

☆ Funding source: None.
☆☆ Conflict of interest: None.
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http://dx.doi.org/10.1016/j.jns.2015.08.028
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Please cite this article as: A. Kalron, L. Frid, The "butterfly diagram": A gait marker for neurological and cerebellar impairment in people with multiple sclerosis, J Neurol Sci (2015), http://dx.doi.org/10.1016/j.jns.2015.08.028

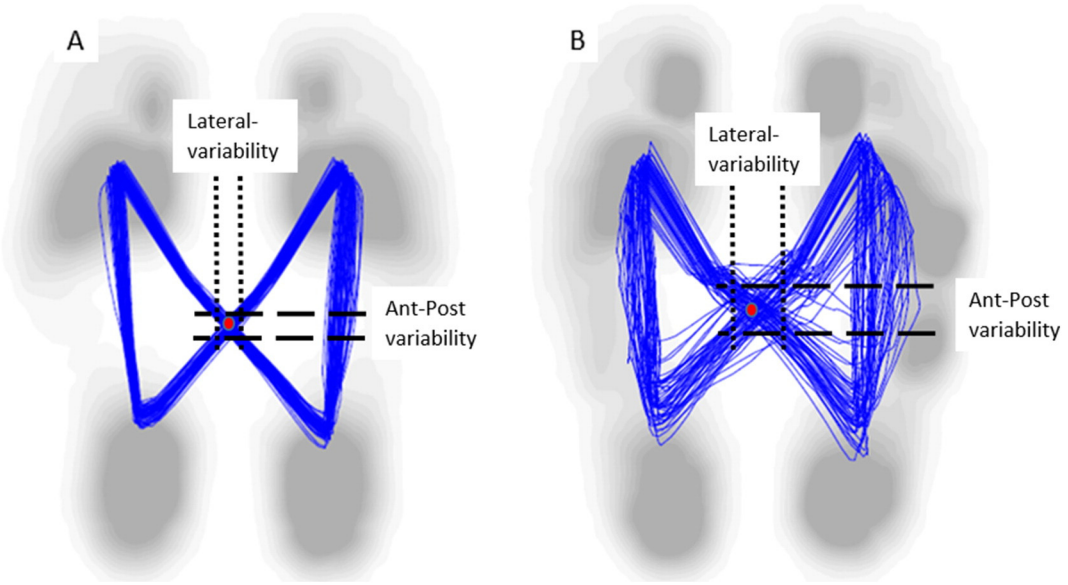


Fig. 1. Title: A butterfly diagram derived from the instrumented treadmill. Legend: Gait variability parameters derived from the butterfly diagram. Red dot indicates the intersection point of the center of pressure trajectory during walking. Dashed lines represent CoP variability in A-P and lateral directions. (A) Healthy person. (B) Person with MS (EDSS = 4.0).

During the last decade, instrumented treadmills have been introduced for gait and balance measurements. Recently, the Zebris instrumented treadmill (Zebris Medical GmbH, Germany) was found to be a valid and reliable measuring instrument for gait and balance performance [15,16]. An advantage of this device is that it measures walking over relatively long distances, possibly reflecting the fatigue component common in PwMS. In our previous report, we demonstrated that spatiotemporal gait parameters, collected by the instrumented treadmill, serve as valid markers of neurological impairment in the MS population [17].

In the current study, we focused on a unique outcome statistic of the instrumented treadmill, the "butterfly" diagram, also named the cyclogram (Fig. 1). This diagram, detailed in the method section, reflects the repeated movement of the CoP during ambulation on a treadmill, capturing in a single frame many gait characteristics essential for efficient walking. For example, the diagram represents gait variability, stride width, single/double support and symmetry in terms of weight shifting between the legs.

From a clinical standpoint, simplified graphs such as the butterfly diagram are easier to use compared to long detailed tables, especially in MS clinical settings where each medical practitioner is busy managing many patients in a relatively short time frame. Moreover, neurologists and physical therapists may view this diagram as beneficial in estimating important neurological characteristics of PwMS, such as the EDSS score and cerebellar involvement. However, to date, information regarding the relationship between the butterfly diagram characteristics and the neurological condition of PwMS are still lacking.

Therefore, our aim was to examine the relationship between parameters related to the gait butterfly diagram and the level of neurological impairment in PwMS. We also focused on cerebellar function by examining whether the gait butterfly parameters can differentiate between MS patients with normal cerebellar function and those suffering from ataxia. We hypothesized that a positive correlation exists between the butterfly gait variability parameters, level of neurological impairment and impaired cerebellar function.

2. Methods

2.1. Study participants

This study was an observational cross-sectional study comprising 341 PwMS, 213 women and 128 men, aged 42.3 (S.D. = 13.8) from the Multiple Sclerosis Center, Sheba Medical Center, Tel-Hashomer, Israel. Inclusion criteria included: (1) a neurologist-confirmed diagnosis of definite MS according to the revised McDonald criteria [18]; (2) <7.0 on the Expanded Disability Status Scale (EDSS) [19], equivalent to the ability to walk at least 20 m without resting; and (3) relapse-free

Table 1
Descriptive statistics.

	Mean (S.D.)			
	Very mild (EDSS = 0–2.5)	Mild (EDSS = 3–4)	Moderate (EDSS = 4.5–5.5)	Severe (EDSS = 6.0–6.5)
Number of patients (n = 341)	185	89	40	27
Age; years	37.8 (13.7)	47.6 (12.6)	46.8 (10.2)	48.5 (12.4)
Female	122	50	24	17
Male	63	39	16	10
Disease duration; years	4.0 (6.3)	8.1 (6.6)	7.6 (8.0)	9.8 (7.6)
Type of MS; RR/PP/SP	183/1/1	81/7/1	37/2/1	23/1/3
Mean EDSS	1.4 (0.9)	3.7 (0.4)	4.8 (0.4)	6.1 (0.2)
Cerebellar	0.4 (0.6)	1.5 (1.0)	2.1 (0.8)	2.0 (1.2)
Pyramidal	0.8 (0.8)	2.5 (0.8)	2.7 (0.9)	3.3 (0.6)
Sensory	0.5 (0.8)	1.2 (1.1)	1.4 (1.2)	1.6 (1.2)

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Table 2
Butterfly diagram parameters according to cerebellar function scores.

Cerebellar function score	Number of patients	Mean (S.D.)		
		Ant-Post variability (mm)	Lateral variability (mm)	Lateral asymmetry (mm)
0 (Normal)	164	6.52 (5.25)	12.90 (12.18)	7.90 (12.22)
1 (Abnormal)	46	6.54 (3.96)	14.33 (11.85)	8.22 (7.85)
2 (Mild ataxia)	95	11.17 (5.36)	24.45 (14.37)	10.59 (8.70)
3 (Moderate ataxia)	36	13.66 (6.78)	25.43 (13.69)	12.69 (12.04)
F, P-value, η^2		28.67, $P < 0.001$, 0.204	21.35, $P < 0.001$, 0.160	2.66, $P = 0.048$, 0.023

for at least 30 days prior to testing. Exclusion criteria included: (1) orthopedic disorders that could negatively affect mobility; (2) major depression or cognitive decline preventing walking on a treadmill; (3) pregnancy; (4) blurred vision; (5) cardiovascular disorders; (6) respiratory disorders; (7) or taking steroids or fampridine. The study was approved by the Sheba Institutional Review Board.

2.2. Gait assessment

Gait parameters were obtained using the Zebris FDM-T Treadmill (Zebris1 Medical GmbH, Germany) fitted with an electronic mat of 10,240 miniature force sensors, each approximately 0.85 cm × 0.85 cm, embedded underneath the belt. The treadmill's contact surface measures 150 cm × 50 cm and its speed can be adjusted from 0.2 and 22 km/h at intervals of 0.1 km/h. When the subject stands/walks on the treadmill, the force exerted by his feet (the so-called reactive-normal force in directions x, y and z) is recorded by the sensors at a sampling rate of 120 Hz. Due to the high density of the sensors, the foot is mapped at a high resolution to facilitate even subtle changes in force distribution. Timing can also be monitored. Dedicated software integrates the force signals and provides 2-D/3-D graphic representation of major spatiotemporal parameters during gait.

In 2013, Wearing et al. reported high levels of between- and within-day reliability in healthy people for the majority of spatiotemporal gait parameters recorded by the Zebris treadmill system during walking, with coefficients of variation typically below 5% and 7%, respectively [16].

Prior to the measurement phase, all participants actively participated in an adaptation-familiarization trial in order to establish each individual's level of speed. Starting at a fixed speed of 0.5 km/h, the belt speed was increased by 0.3 km/h every 15 s in a stepwise manner. Once the participant informed the tester of the speed that best characterized his/her normal walking pace, that was determined as his/her comfort speed. Following this adaptation phase, each participant was instructed to walk barefoot on the treadmill for one consecutive minute at his/her comfort speed. Individuals who constantly used foot assistive devices for walking were allowed to perform the walking trial together with their ambulatory device. For those patients who regularly used a unilateral walking cane, we allowed them to perform the walking trial while gripping the treadmill's handrail on the same side as the cane. Patients with bilateral walking devices were excluded from the study.

Gait assessment was performed at the Center of Advanced Technologies in Rehabilitation, Sheba Medical Center. Measurements were calculated by an experienced physical therapist specialized in neurological rehabilitation.

2.3. The butterfly diagram (Cyclogram)

The treadmill's dedicated software generates a graphic pattern termed the 'butterfly', which represents a continuous trace of the CoP trajectory during walking (Fig. 1).

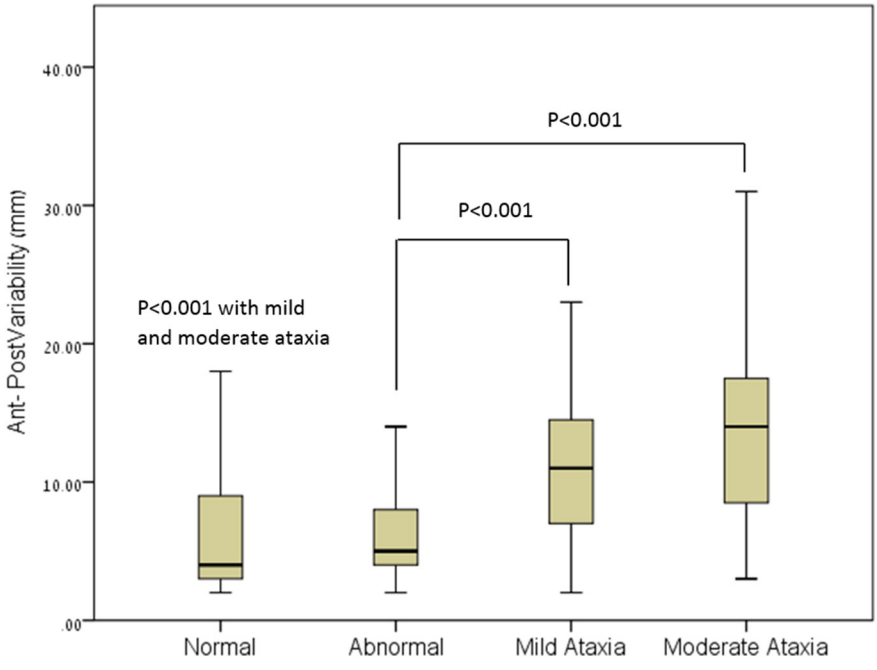


Fig. 2. Gait variability in the ant-post plane according to the cerebellar function level.

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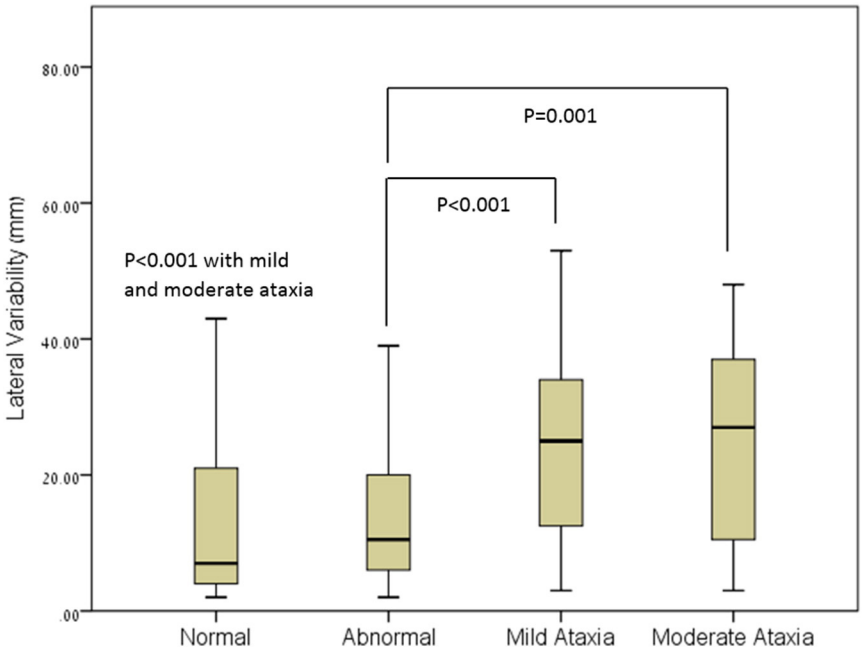


Fig. 3. Gait variability in the lateral plane according to the cerebellar function level.

The following set of parameters is automatically derived from the butterfly:

1) Anterior/posterior variability (mm): defined as the standard deviation of the intersection point in the anterior/posterior direction; 'zero' is equivalent to constant strides while walking on the treadmill.
2) Lateral variability (mm): defined as the standard deviation of the intersection point in the lateral direction. Similarly as the ant/post variability parameter, 'zero' is equivalent to constant strides in terms of width between the legs.
3) Lateral symmetry (mm): left/right shift of the intersection point; 'zero position' is equivalent to perfect symmetry.

2.4. EDSS and cerebellar function

Since the establishment of the MS Center, an electronic record-keeping system has documented the patients' demographic, clinical and imaging data. This system is updated by the Center's medical staff during each patient visit to the clinic. Every 6 months, a complete neurological examination is performed and an EDSS score is assigned and recorded.

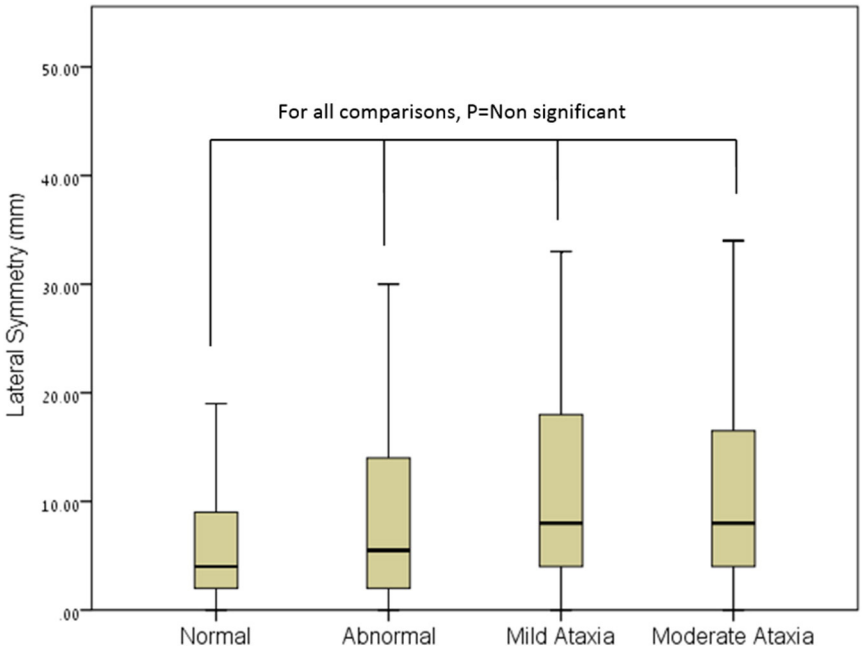


Fig. 4. Gait symmetry score according to the cerebellar function level.

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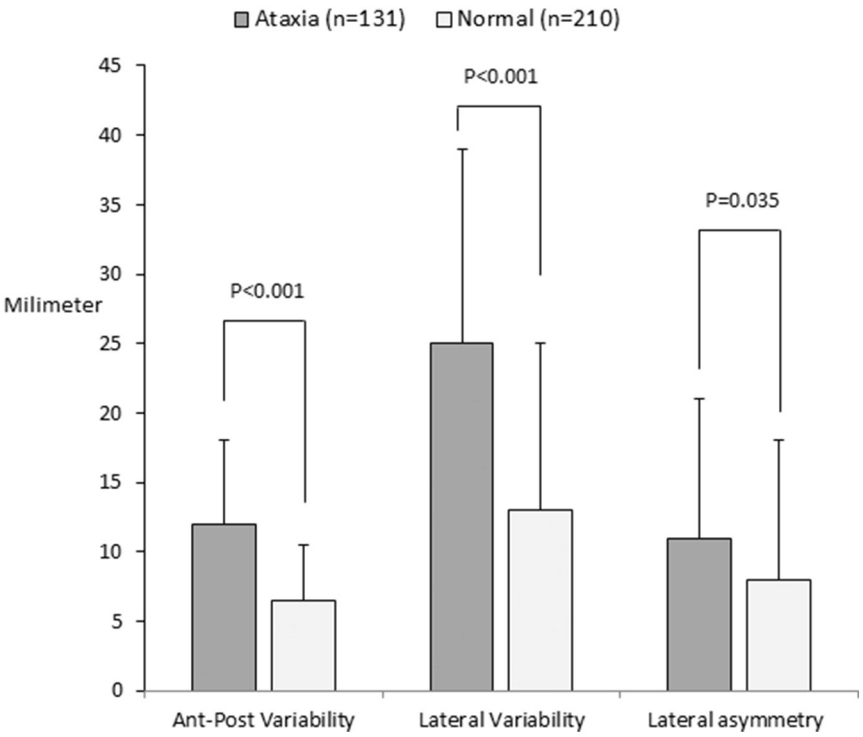


Fig. 5. Butterfly gait parameters according to cerebellar function groups.

The EDSS, an accepted method of quantifying disability in PwMS consists of an eight-function system scale monitoring motor, sensory, cerebellar, brain stem, visual, bowel and bladder, pyramidal and other functions. Each domain is graded from 0 = no disability to 5 or 6 = maximal disability [19]. According to the score achieved from each functional system, an integrated score between 0 = normal examination and 10 = death from MS is derived. Scores ranging from 1.0 to 4.5 indicate patients who are fully ambulatory without aid; 5.0 to 7.5 reveal moderate to severe impairment in ambulation and 8.0 to 9.5 refer to PwMS essentially restricted to bed.

In the present study, we divided the study cohort into four subgroups based on their EDSS score: very mild (EDSS 0–2.5), mild (EDSS 3.0–4.0), moderate (EDSS 4.5–5.5) and severe (EDSS 6.0–6.5). We also specifically investigated the cerebellar function domain. Subjects were divided according to the cerebellar functional system score: 0 = normal, 1 = abnormal signs without disability, 2 = mild ataxia and/or moderate station ataxia (Romberg) and/or tandem walking not possible, 3 = moderate limb ataxia and/or moderate or severe gait/truncal ataxia, 4 = severe gait/truncal ataxia and severe ataxia in three or four limbs and 5 = unable to perform coordinated movements due to ataxia.

2.5. Statistical analysis

Descriptive statistics determined the demographic and clinical characteristics of the study participants according to their level of neurological impairment. Butterfly parameters of gait data were normally distributed according to the Kolmogorov–Smirnov test. Differences in butterfly gait parameters between PwMS subgroups were determined using the multivariate analysis of variance (MANOVA) test. The Bonferroni test enabled paired multiple comparisons between EDSS subgroups (very mild, mild, moderate, severe) and cerebellar subgroups (0–4).

The relationship between the EDSS, cerebellar function score and the butterfly gait parameters were measured by Spearman's rank-order correlation coefficient tests. Correlation coefficients which were ≤0.35 are generally considered low or weak correlations, 0.36 to 0.67 are considered modest or moderate, 0.68 to 0.89 strong or high correlations and r coefficients ≥0.90 are considered very high correlations.

Evaluation of potential predictors for cerebellar function status (i.e. the dependent variable) was calculated by a stepwise binary regression analysis. For this purpose, cerebellar function was classified into two main categories: non/slight disability (cerebellar function grade <2) and mild/moderate disability (cerebellar function grade ≥2).

Butterfly parameters of gait were entered into the model as covariates. At each subsequent step, the regression equations comprised those variables reaching specific thresholds of F and P values (for variable inclusion, F ≥ 1 and P ≤ 0.05; for exclusion, F < 1 and P > 0.05). Moreover, if a butterfly gait variable was found significant according to the ordinal regression analysis, a receiver operating characteristic (ROC) curve was performed in an attempt to determine an optimal classification model.

Table 3
Butterfly diagram parameters according to EDSS subgroups.

EDSS score	Number of patients	Mean (S.D.)		
		Ant-post variability (mm)	Lateral variability (mm)	Lateral asymmetry (mm)
Very mild (0–2.5)	185	5.92 (4.40)	11.67 (11.12)	7.25 (11.27)
Mild (3.0–4.0)	89	10.52 (5.71)	22.85 (15.21)	10.91 (10.01)
Moderate (4.5–5.5)	40	12.98 (5.01)	27.55 (9.76)	12.20 (9.18)
Severe (6.0–6.5)	27	13.52 (7.41)	25.85 (14.59)	12.26 (10.57)
F, P-value, η^2		39.15, P < 0.001, 0.258	31.66, P < 0.001, 0.220	4.60, P = 0.004, 0.039

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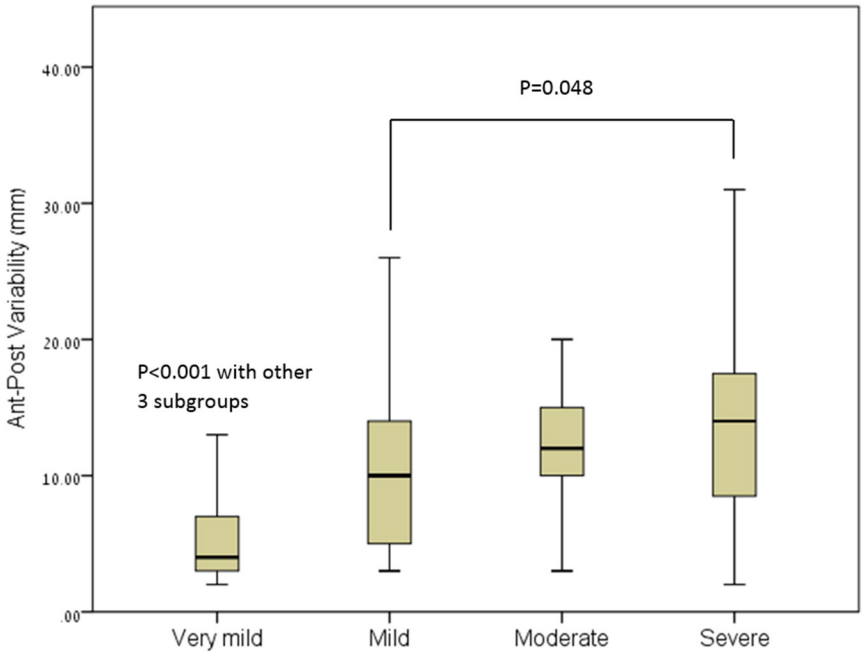


Fig. 6. Gait variability in the ant-post plane according to the EDSS subgroups.

All analyses were performed using IBM SPSS statistics software (Version 21.0 for Windows, SPSS Inc. NY, USA). All reported P-values were two-tailed. The level of significance was set at $P < 0.05$.

3. Results

The individuals' characteristics and neurological assessment scores are summarized in Table 1.

3.1. Butterfly gait parameters, cerebellar function and the EDSS

Participants with ataxia (a functional score of 2 or 3) demonstrated higher scores relating to gait variability in both the ant-post and lateral directions compared to patients with normal or slightly abnormal cerebellar function (a functional score of 0 and 1). An ~90% increase was observed between patients with a slightly abnormal cerebellar condition (functional score of 1) to those with mild ataxia (cerebellar function 2). Non-significant differences in gait variability were demonstrated between cerebellar functional level 0 to 1 and between functional levels 2 to 3. In terms of gait asymmetry, no differences were found between cerebellar function conditions. Table 2 and Figs. 2–4 identify the relationship between the gait butterfly scores and cerebellar function level. Fig. 5 presents gait butterfly parameters according to the two cerebellar function groups.

In terms of the EDSS, participants classified with a very mild disability level demonstrated a decreased gait variability (in both the ant-post

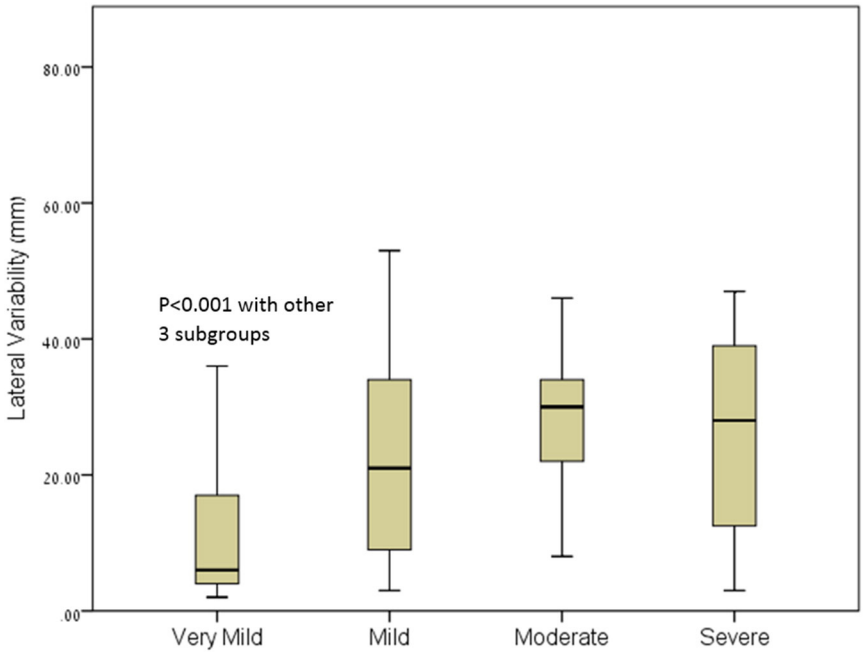


Fig. 7. Gait variability in the lateral plane according to the EDSS subgroups.

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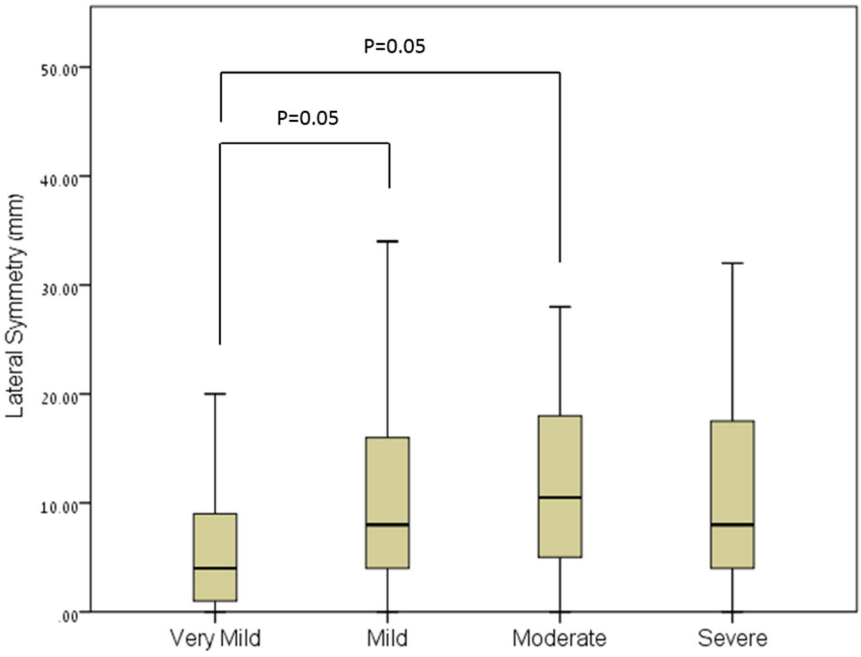


Fig. 8. Gait symmetry score according to the EDSS subgroups.

and lateral planes) compared to all other EDSS subgroups (mild, moderate, severe). In a similar context, mildly impaired PwMS exhibited lower gait variability in the ant-post direction compared to the severe group. Non-significant values were observed in terms of gait variability between the moderate and severe groups. Furthermore, the asymmetry parameter did not differentiate between the EDSS subgroups. Table 3 and Figs. 6–8 identify the relationship between the gait butterfly scores and the EDSS subgroups.

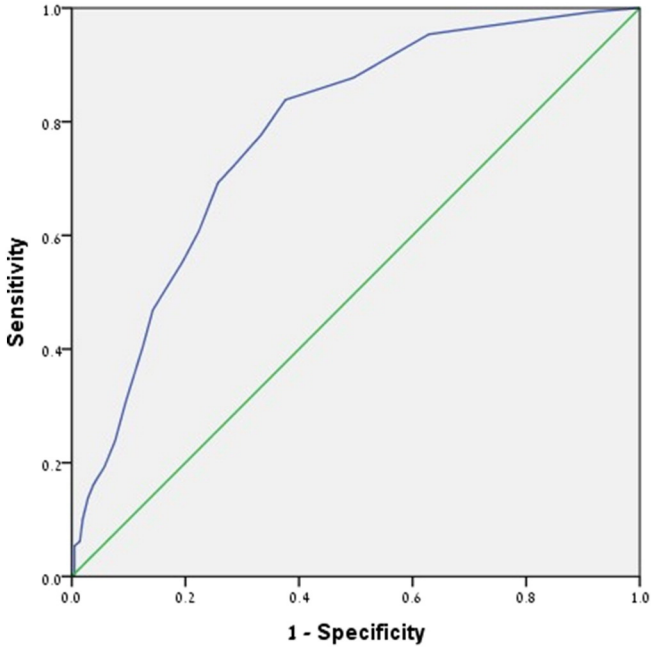


Fig. 9. Receiver-operating characteristics curve for gait variability in the ant-post direction.

3.2. Spearman's rho correlation analysis

Butterfly gait parameters positively correlated with the EDSS and cerebellar function scores. The strongest correlations were observed in terms of the ant-post variability parameter, 0.516 ($P < 0.001$) and 0.431 ($P < 0.001$), respectively. Correlation coefficient scores between gait variability in the lateral plane with the EDSS and cerebellar function were slightly weaker, 0.477 ($P < 0.001$) and 0.381 ($P < 0.001$), respectively. These findings indicate that in PwMS, gait variability is positively related with a higher neurological impairment level and reduced cerebellar function. Weaker scores were demonstrated in terms of the symmetry parameter. Correlation between the symmetry gait parameter to the EDSS score was 0.241 ($P < 0.001$) and 0.147 ($P = 0.007$) with the cerebellar function level. The current study's correlation results are similar to those presented in our previous report of 87 PwMS [17].

3.3. Binary regression analysis for detection of cerebellar function

As noted earlier, cerebellar function was classified into two main categories: non/slight disability (cerebellar function grade <2) (n = 210) and mild/moderate disability (cerebellar function grade ≥2) (n = 131). According to the results of the binary regression analysis, gait variability in the ant-post direction was found to explain 18.1% of the variance related to the cerebellar function group; $R^2 = 0.181$, $\chi^2_{(1)} = 67.852$, $P < 0.001$. The lateral variability and lateral symmetry gait parameters were not included in the equation. Consequently, a ROC curve based on the best performing single predictor, variability in the ant-post direction, was executed (Fig. 9). The area under the curve c-statistic was 0.778 (95% CI, 0.728–0.827), indicating a good overall predictive ability. Using the least distance and Youden index methods, the optimal cut-off point was set at 5.5 with a sensitivity and specificity of 83.8% and 62.4%, respectively.

4. Discussion

The aim of the present investigation was to examine the relationship between the level of neurological impairment and cerebellar function in

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PwMS to gait parameters derived from a butterfly diagram, a novel presentation of the CoP movement during walking. We found that variability of the CoP movement during gait, especially in the anterior-posterior direction, is associated with the level of cerebellar impairment in PwMS. According to the binary regression model, variability of the CoP intersection point in the ant-post direction was found to explain 18.1% of the variance related to ataxia in the MS study sample.

Previous investigations performed in the elderly and other neurological populations have shown that gait variability is related to a slower walking speed, increased falls, fear of falling [20–22], subclinical brain vascular abnormalities [23] higher energetic costs [24] and reduced motor control [25,26]. Regarding the MS population, previous reports have clearly shown that PwMS have greater gait variability, demonstrated in short [27,28] and long distance walks [29]. Moreover, increased gait variability has clinical significance in PwMS. Motl et al. (2011) demonstrated that recurrent fallers (i.e. 1 + falls/year) with MS exhibit greater variability of spatial footfall placement than nonfallers with MS [30].

Various trials have attempted to determine potential factors for the increase in gait variability among the elderly and neurological populations. Possible explanations include altered neural control, reduced muscle function, poor postural control, cardiovascular changes, heart fluctuations, cognitive impairments and mental health [31]. However, the majority of these factors haven't been confirmed in the MS population.

The current study findings shed some light on this in terms of factors associated with gait variability. According to our results, ataxia is partly associated with increased gait variability in PwMS. Subjects with mild and moderate ataxia revealed approximately twice as much gait variability compared to subjects with normal or slight cerebellar dysfunction.

Ataxia is characterized by hypermetric and dysmetric movements and is one of the most disabling symptoms in PwMS. Severe ataxia can interfere with balance, as well as transfer and ambulatory activities [32], therefore, it is very logical and seemingly clinically evident that cerebellar ataxia was associated with gait variability in our study group. However, based on the notion that controlling gait involves numerous neural processes and coordination of the trunk and limbs, ataxia is most likely not a single individual mechanism contributing to gait variability, but rather a combination of deficits, hence, additional research is needed to uncover other potential factors for this gait phenomenon in PwMS.

From a clinical standpoint, existing evidence demonstrates that goal directed physical rehabilitation programs can improve walking and balance capabilities, specifically in PwMS suffering from cerebellar ataxia. Rehabilitation program options include virtual reality, biofeedback, treadmill exercises with supported bodyweight and torso weighting [33]. For example, in 26 outpatients with ataxic MS, neuromuscular rehabilitation provided significant improvements in balance and gait parameters, as well as in pendular movements and dysdiadochokinesia [34], therefore, early detection of ataxia in MS individuals may be helpful.

We believe that addressing patients with mild ataxia can lead to better outcomes compared to treatment begun at the moderate and severe level. Treatment may be provided by simply providing guidance on how to properly manage gait ataxia and/or by goal directed exercises. Many practitioners in the MS field believe that early treatment may prevent the perils related to ataxia, such as an increased risk of falls. Accordingly, our results offer a relatively easy method of detecting MS candidates for ataxia rehabilitation. Moreover, we suggest that medical professionals include the butterfly diagram gait variability parameters as an assessment marker to monitor the efficacy of such interventions. However, we are aware that longitudinal RCT are required in order to prove these assumptions.

In contrast with gait variability, gait symmetry was not correlated to level of cerebellar function. The exact contribution of asymmetrical CoP distribution on cerebellar function, balance and falls is indeterminate in different neurological pathologies, including stroke patients [35]. We speculate that PwMS may have favored an asymmetrical position for reasons of safety and motor control. By increasing the somatosensory input on the relatively stronger limb, this walking strategy could be viewed as a way of maintaining a relatively stable and constant gait pattern. MS rehabilitation professionals should be made aware of this observation. Although a strategy directed at improving gait symmetry is important in order to reduce muscular disuse and prevent increased joint degeneration, this approach may not be relevant in cases of gait ataxia.

In line with our discussion on gait variability in PwMS, we find it important to state that currently there is no gold standard to quantify gait variability. Generally, gait variability is quantified using distributional metrics, such as standard deviation and coefficient of variation of kinematic and spatiotemporal gait parameters [31]. Other nonlinear metrics, such as trended fluctuation analysis and approximate entropy, have been used to examine the temporal sequential structure of gait variability (i.e. the time-evolving structure of variability) [36]. Since different metrics quantify different aspects of gait variability and operate on different timescales, there is a possibility that gait variability measured while walking on a treadmill, is somewhat different compared to gait variability measured during over ground walking, although, Hoogkamer et al. (2015) recently reported that gait variability measured by an instrumented treadmill provided sensitive metrics in mildly ataxic cerebellar patients [37]. Yet, in order to clarify this issue, future studies comparing measures of gait variability measured during ambulation on a treadmill and over ground walking in PwMS, are needed. Another future investigation can examine the relationship between gait variability measures derived from the butterfly diagram and the variability of major spatio-temporal parameters of gait while walking on a treadmill (e.g. step/stride length variability, stance/swing period variability).

It is worth noting that while the Zebris treadmill has numerous clinical advantages, the financial and spatial requirements for the system may preclude this device from being a rehabilitation aid in several medical centers and in MS patients treated in the community and/or restricted to their home. However, there is a possibility that simpler gait measurement systems, such as footswitches, will create parameters resembling the butterfly diagram parameters, though, dedicated software is needed to generate this data.

5. Conclusion

The butterfly diagram is a simple and easy graph to interpret. The diagram captures a wide variety of gait characteristics. In the present study, we demonstrated that parameters derived from the butterfly diagram, suggest the existence of ataxia in PwMS. Moreover, variability of the CoP movement was found to be a gross estimator of the level of neurological impairment, represented by the EDSS in the study sample. We suggest neurologists, physical therapist and related medical staff to consider employing the butterfly diagram in order to improve diagnosis and assessment of the MS population. Hopefully, our new measure will aid in reducing the effects of ataxia/gait variability in MS and ultimately serve to modify factors related to falls in PwMS, a key outcome of daily life.

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Please cite this article as: A. Kalron, L. Frid, The “butterfly diagram”: A gait marker for neurological and cerebellar impairment in people with multiple sclerosis, J Neurol Sci (2015), http://dx.doi.org/10.1016/j.jns.2015.08.028

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Please cite this article as: A. Kalron, L. Frid, The "butterfly diagram": A gait marker for neurological and cerebellar impairment in people with multiple sclerosis, J Neurol Sci (2015), http://dx.doi.org/10.1016/j.jns.2015.08.028