Novel characterization of gait impairments in people with multiple sclerosis by means of the gait profile score

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1. Introduction

Multiple sclerosis (MS) is a chronic disease of the central nervous system (CNS) that affects a wide range of neurologic functions including cognition, vision, muscle strength and tone, coordination, sensation and balance. Individuals with MS often exhibit gait abnormalities (e.g. reduced walking speed, step length, cadence and increased step width [1]) and 35–60% of them are forced to use mobility aids 15 years after the onset [2,3]. Such impairment is one of the main determinants of neurological disability that produces a reduction in autonomy and quality of life and this justifies the huge efforts put into the development of physical therapies and rehabilitation programs necessary to improve, at least partly, some functionalities damaged by the progression of the disease [4]. The best approach to improving MS patients' quality of life is to prevent disability accumulation through the use of available "disease modifying drugs". However, the response to available drugs is not optimal in all MS patients and frequently an escalating approach, using more powerful but less safe drugs, will be needed to stop the disease.

Thus, it is very important to have available reliable and accurate techniques to assess the degree of deviation from a physiological gait pattern as well as to detect even slight changes in it consequent to pharmacological or rehabilitative treatment.

As in many neurological disorders, such evaluations are typically approached by direct observation of the clinician supported by a timed analysis (such as 10 m/25 ft walking test), functional scales (Ambulation Index, Rivermead Mobility Index etc.) and questionnaires [1,5]. Information derived from neurological evaluation is included in the "Expanded Disability Status Scale" (EDSS), the instrument most widely used to evaluate disability in MS, in both daily clinical practice and trials. The EDSS scale, despite being the gold standard for classifying MS impact severity, presents several critical points and an important inter- and intra-rater variability [6]. It is therefore essential to find new tools, complementary to the clinical scales, able to supply objective and quantitative data useful in supporting clinical assessment of the disability as well as its variations across time.

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In the last decade, limited attempts to objectively acquire quantitative data on gait alterations of MS patients have been performed using video analysis [7] computerized walkways[8–11], accelerometers [12, 13] and three-dimensional quantitative movement analyses based on optoelectronic stereophotogrammetry [14–19]. In particular, the latter technique, which is often referred to as gait analysis (GA) when gait is specifically investigated, is able to supply a very detailed and accurate representation of gait patterns through a combination of kinematic, kinetic and electromyographic (EMG) data.

Nevertheless, the use of GA in the clinical diagnostic routine for MS has been questioned as it requires highly specialized personnel (for both data acquisition and interpretation) and is expensive and time-consuming [1,8].

In particular, the large amount and complexity of available data, usually expressed in the form of kinematic and kinetic trends across the gait cycle for each articular district of interest (pelvis, hip, knee and foot) and EMG signals associated with muscular activation, make it difficult for physicians to easily assess the patient's status in a short time and with a single or reduced set of measures.

To overcome such difficulties and make GA at least partly suitable for clinical uses, researchers have attempted to define summary measures that should immediately give either an idea of gait quality or define the degree of deviation from a normal gait pattern. A detailed historical and technical overview of the several indexes proposed for this purpose can be found in a recent paper by Cimolin and Galli [20].

Among such indexes, the gait profile score (GPS [21]) has recently gained popularity. It represents a single index able to summarize the overall quality of an individual's gait on the basis of a set of kinematic measurements.

This approach has already been found reliable when tested on children and adults affected by cerebral palsy [21], Ehlers–Danlos syndrome [22] and a wide spectrum of orthopedic and neurologic pathologies [23]. Thus, GPS appears suitable for use in evaluating gait alteration associated with both neurological and non-neurological disorders, and has been found well correlated with clinicians' ratings of kinematic gait deviations [24]. However, to the authors' knowledge, no studies have yet been performed to assess the usefulness of such an approach in individuals affected by MS. Given the huge impact of this pathology on patients' mobility (and thus quality of life), it would be desirable to have available a summary measurement able to monitor the progression of the disease as well as to assess the effectiveness of pharmacological and rehabilitative treatments.

On the basis of the aforementioned considerations, this study intends: 1) to verify the feasibility of the use of GPS to characterize gait alterations in a sample of individuals affected by MS by comparing their GPS values with those of a control group of healthy subjects, 2) to investigate the existence of possible correlations between the Expanded Disability Status Scale (EDSS) and the GPS value, as well as with its distinct kinematic components and 3) to evaluate the potentiality of GPS as a complementary parameter in the follow-up of motor impairment in MS.

2. Methods

2.1. Subjects

Thirty-four patients suffering from relapsing–remitting MS (13 female, 21 male, mean age 46.6 ± 10.9 years) with an EDSS score of ≤ 6 (range 1.5–6, mean EDSS 3.5 ± 1.1) currently followed at the Multiple Sclerosis Centre of Cagliari (Sardinia, Italy) were enrolled in the study. The main criteria for inclusion were a diagnosis of MS according to the 2005 McDonald criteria [25], the ability to walk independently without any assisting devices (i.e. canes, crutches or walking frames) for at least 20 m and the absence of lower limb traumas able to affect gait. Neurological disability was evaluated for each patient by a neurologist expert in MS.

A control group (CG) of the same size, composed of healthy subjects free of any musculoskeletal disorder and gender- and age-matched (mean age 45.8 ± 12.3), was recruited after a public announcement. The main anthropometric features of the participants are shown in Table 1.

The ethics committee of the local Health Agency approved the study and all participants signed an informed consent agreeing to participate in the study.

2.2. Kinematic data collection and processing

Prior to the tests, a number of participants' anthropometric measures were collected. In particular, data on height, weight, anterior superior iliac spines (ASIS) distance, pelvis thickness, knee and ankle width, leg length (distance between ASIS and medial malleolus) were acquired using a digital scale, an ultrasonic height measurement device, a pelvimeter and a flexible meter. Then, 22 spherical retro-reflective passive markers (14 mm diameter) were placed on the skin of individuals' lower limbs and trunk at particular landmarks following the protocol described by Davis et al. [26].

The participants were asked to walk barefoot at a self-selected speed (which was recorded for each trial) in the most natural manner possible on a 10 m walkway for at least six times, allowing suitable rest times between the trials.

The acquisition of kinematics associated with the body segments of interest (trunk, pelvis, thigh, shank and foot) was performed using an optoelectronic system composed of eight Smart-D cameras (BTS Bioengineering, Italy) set at a frequency of 120 Hz.

The raw data were then processed with the dedicated software Smart Analyzer (BTS Bioengineering, Italy) to calculate the summary measure values for each limb (i.e. the gait profile score) as described below.

2.3. Gait profile score (GPS)

This summary measure of gait quality was recently proposed by Baker et al. [21] on the basis of the previously defined gait deviation index [27]. Basically, the GPS (expressed in degrees) represents the root mean square (RMS) difference between a patient's data and the mean value obtained from tests performed on the unaffected population calculated for a set of kinematic variables on the whole gait cycle [21]. In particular, the use of nine relevant variables, namely pelvic tilt, rotation and obliquity, hip flexion–extension, adduction–abduction and rotation, knee flexion–extension, ankle dorsiflexion and foot progression was suggested; the RMS difference referring to each of them is defined as the gait variable score (GVS).

Fig. 1 shows an example of GVS calculation referring to knee flexion–extension during the gait cycle for two MS patients characterized by different disability levels. As seen in the diagram, a more severe impairment leads to a greater distance between the patient's curve and that of the unaffected subject; correspondingly, the GVS score increases, thus indicating larger deviations from a hypothetical "normal" gait.

Table 1

Anthropometric features of the participants. Values are expressed as mean $\pm$ SD. The symbol * denotes a significant difference between MS and CG ($p < 0.05$).

	MS	CG	p-value
Participants # (M,F)	34 (21 M, 13 F)	34 (21 M, 13 F)	–
Age (years)	46.6 ± 10.9	45.8 ± 12.3	0.523
Body mass (kg)	66.5 ± 14.3	68.3 ± 12.9	0.578
Height (cm)	167.9 ± 6.9	166.6 ± 7.3	0.454
BMI (kg m^{-2})	23.4 ± 3.9	24.5 ± 3.9	0.250
Walking speed (s^{-2})	0.90 ± 0.28	1.35 ± 0.08	<0.001*
EDSS score	3.5 ± 1.1	–	–
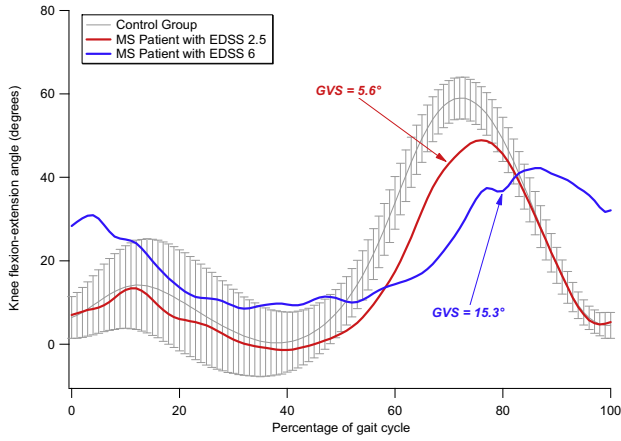
Fig. 1. Examples of GVS calculation for knee flexion–extension. The larger deviation from the physiological gait of the individual with higher EDSS results in a higher GVS value.

The GPS summarizes the overall quality of gait kinematics by combining the nine GVS values according to the following relationship:

$$GPS = \sqrt{\frac{1}{N}\sum_{i=1}^{N} GVS_i^2} \qquad (1)$$

Higher GPS values indicate a larger deviation from a physiological gait pattern.

2.4. Statistical analysis

Differences in the GVS and GPS scores induced by the pathology were assessed using two-way multivariate analyses of variance (MANOVA) performed using the IBM SPSS Statistics v.20 software (IBM, Armonk, NY, USA). The independent variables were the individual's status (MS or CG) and limb (right, left), and the ten dependent variables were the nine GVS scores and the GPS index. The level of significance was set at $p = 0.05$ and effect sizes were assessed using the eta-squared coefficient (η^2). Follow-up analyses were conducted using one-way ANOVAs for each dependent variable, by setting the level of significance at $p = 0.005$ (0.05/10) after a Bonferroni adjustment for multiple comparisons.

The relationship between GVS/GPS, EDSS scores and walking speed was assessed by means of the Pearson product moment correlation analysis. The level of significance was set at $p = 0.05$ also in this case.

3. Results

Table 2 shows the results for the GPS and GVS values calculated for MS and CG. MANOVA revealed a significant influence of MS on gait kinematics [$F_{(10,123)} = 15.79$, $p < 0.001$, Wilks $\lambda = 0.44$, $\eta^2 = 0.56$] but not of limb or status per limb interaction.

The follow-up, carried out by means of two-way ANOVA (status × limb) on GPS and GVS variables detected significant effects of status for GPS ($p < 0.001$) and all the GVS kinematic variables ($p < 0.001$) except pelvic obliquity, hip adduction-abduction and foot progression.

Significant positive correlations were also found between the EDSS score, GPS and five GVS kinematic variables (Table 3), namely pelvic tilt, rotation and obliquity, hip and knee flexion–extension. In particular, the highest correlation was found between EDSS and the GPS index ($r = 0.63$, $p < 0.001$), thus indicating that individuals with higher EDSS scores, who are characterized by a more severe walking impairment, had higher GPS values.

A low (albeit significant) negative correlation was found between walking speed and GPS ($r = -0.43$, $p < 0.001$) while speed was moderately correlated with the EDSS score ($r = -0.60$, $p < 0.001$).

4. Discussion

The findings of the present study strengthen the idea that GA is a test that provides reliable quantitative data on gait pattern and may support the clinician in assessing functional limitations on walking, which are a typical determinant in disability of individuals with MS. In particular, our data confirm the initial hypothesis that significant differences exist in terms of lower limb kinematics between individuals with MS and healthy subjects. Moreover, to easily summarize these alterations, GPS represents an immediate and clear way of understanding the difference in gait pattern with respect to the healthy population, and thus may help in establishing the level of functional limitation. In this way, the clinician can assess the current impairment of the patient and monitor the disease progression as well as the treatment outcome, whether pharmacological or rehabilitative. The existence of a moderate positive correlation between the GPS and EDSS scores indicates that such a measure is able to identify the progressive motor impairment associated with increasing disability as evaluated by clinicians.

A direct comparison of our data with the results of previous studies carried out using similar techniques can be made by considering the single GVS values associated with hip, knee and ankle joint kinematics, given that these are the most frequently investigated districts in characterizing gait patterns of MS patients.

Features commonly encountered in gait patterns of people with MS and detected using GA include increased hip flexion and reduced knee flexion–extension [14,16,28] as well as reduced plantar flexion [14,17]

Table 2
Comparison between GPS and GVS values in individuals with MS (MS) and healthy controls (CG). Values are expressed as mean ± SD. The symbol * denotes a significant difference between MS and CG after Bonferroni correction.

	GPS and GVS scores				
		MS	CG	Status effect p-value	Limb effect p-value
GVS	GPS	9.12 ± 2.28	5.67 ± 1.07	<0.001*	0.734
	Pelvic tilt	7.16 ± 5.33	3.32 ± 2.00	<0.001*	0.970
	Pelvic rotation	4.83 ± 2.45	3.42 ± 1.43	<0.001*	0.359
	Pelvic obliquity	3.10 ± 1.47	2.65 ± 1.80	0.113	0.733
	Hip flexion–extension	13.75 ± 6.78	6.29 ± 2.53	<0.001*	0.973
	Hip abduction–adduction	4.58 ± 2.87	3.66 ± 1.66	0.025	0.676
	Hip rotation	11.75 ± 5.67	8.67 ± 3.90	<0.001*	0.106
	Knee flexion–extension	11.37 ± 4.46	6.90 ± 2.07	<0.001*	0.408
	Ankle dorsi- and plantar-flexion	6.60 ± 2.48	4.90 ± 1.83	<0.001*	0.337
	Foot progression	7.38 ± 3.61	6.30 ± 4.32	0.120	0.406

Table 3
Pearson product moment correlation coefficient between EDSS scale values and GPS/GVS values. The symbol * denotes statistical significance ($p < 0.05$).

	Parameter	r	p-value
EDSS vs.	GPS	0.63	<0.001*
	Pelvic tilt	0.54	<0.001*
	Pelvic rotation	0.41	<0.001*
	Pelvic obliquity	0.30	0.012*
	Hip flexion–extension	0.55	<0.001*
	Hip abduction–adduction	−0.01	0.960
	Hip rotation	0.20	0.105
	Knee flexion–extension	0.41	0.001*
	Ankle dorsi- and plantar-flexion	−0.01	0.923
	Foot progression	0.09	0.458

and reduced angular range, joint torque and joint power at hip, knee and ankle [18]. Such alterations in gait mechanics are mainly due to pyramidal distribution weakness, spasticity, reduced proprioception and changes in motor integration [29].

However, a certain degree of heterogeneity in the (few) available data on gait kinematics of individuals with MS must be acknowledged, as most previous studies focus on the attempt to detect early signs of abnormalities when the disability is low or even absent (i.e. EDSS in the range of 1–2.5) [7,14,17] while in one case EDSS values are not even reported, the mobility impairment being described only in terms of level of spasticity and ambulation index [16].

Some similarities with the present study in terms of mobility impairment of the analyzed sample can be found in the research performed by Rodgers et al. [28] who investigated gait patterns in a cohort of 18 patients with EDSS in the range of 1–6.5 and reported a reduced range of motion in knee and hip flexion–extension.

Consistent with these findings, the GVS scores calculated in our sample of individuals with MS for knee and hip flexion–extension appear practically doubled with respect to controls, thus indicating large deviations from a physiological gait. In particular, most of the individuals with MS tested exhibit inadequate extension or excessive hip flexion, which in most cases (approximately 2/3 of the sample) are similar for both limbs. This fact results in an alteration of stability during the weight acceptance phase and modifies posture so that trunk forward lean and excessive knee flexion occur.

Alterations in knee kinematics were found in most of the individuals with MS tested, either in the form of excessive or inadequate flexion–extension. This reflects on the associated GVS score which, even in this case as found for the hip, is approximately double with respect to what was calculated for the healthy controls. Such impairments are likely due to a deficit in strength of the knee extensors muscles, which was found to be linked to walking capacity [30], especially in individuals with moderate disability (EDSS 4.5–6.5).

Finally, ankle dorsi- and plantar-flexion appears significantly altered in MS patients, but the magnitude of changes in GVS is lower with respect to what was observed for hip and knee joints, as the increase is only +30% when compared with healthy controls. From a detailed analysis of patients' kinematic data related to ankle, we observed a common trend consisting of a lack of dorsi-flexion in the stance phase followed by an excess of plantar-flexion in the swing phase. This is likely due to weakness of the tibialis anterior muscle and/or spasticity of the gastrocnemius which typically results in foot drop, a gait alteration commonly encountered in people with MS [31].

The general reliability of the approach also appears to be confirmed by the GPS values found for the group of healthy controls (mean 5.7°, median 5.4°) which are in fairly good agreement with those reported in previous studies in children (median 5.2° in Baker et al. [21]) and adults (mean 4.6° in Celletti et al. [22], median 4.8° in Schweizer et al. [23]).

Our results also suggest that, given the degree of correlation found between the GPS and the EDSS scores, the former may represent a

useful objective quantitative measure of mobility impairment potentially suitable for clinical purposes. These findings are consistent with previous observations on gait features in individuals with MS, although this represents the first attempt to correlate EDSS with a single summary measure of gait kinematics.

In particular, Sosnoff et al. [9] found moderate to strong correlations between EDSS, the functional ambulatory profile (FAP) score supplied by the electronic GAITRite® system and spatio-temporal parameters such as gait velocity, single and double support times and base of support width, while Huisinga et al. [18] detected significant correlations of EDSS with joint angles, torques and power. Socie and Sonsoff [11] observed a similar degree of correlations between EDSS and walking velocity, step length, time and width and with gait variability parameters.

Our data integrate the aforementioned observations and contribute to outlining an experimental framework in which spatio-temporal parameters of gait (widely assessed in MS patients) and kinematic variables are objectively acquired and summarized in a fashion that makes the routine clinical use of such techniques appear feasible. This would effectively support the clinician's observations, not only to have a better representation of the patient's state, but also to verify more accurately the outcomes of pharmacological and rehabilitative treatments.

Some limitations of this study must be acknowledged. Firstly, the range of the disability that characterizes the participants is quite large, and thus it was not possible to verify the sensitivity of the GPS measure when minimal impairments associated with low EDSS (e.g. <2.5) are to be assessed. Baker et al. [32] established that in the case of children who exhibited gait alterations consequent to orthopedic or neurologic diseases, the minimal clinically important difference (MCID) in GPS is 1.6°. In the case of MS it would be important not only to define MCID values for GPS to identify a clinically meaningful impairment but also, possibly, to define a value (or range of values) to be coupled with EDSS scores.

Moreover, it must be considered that GPS/GVS represent in a synthetic way the gait alterations and they may be suitable for comparison between quantitative data of gait and clinical data such as EDSS evaluations. On analyzing the value of these indexes, it is clear that the higher the values of GPS/GVS the more impaired the patient's gait. In any case, these indexes have some limits to be taken into consideration. First of all, they are based only on kinematic variables (i.e. angle kinematics), neglecting spatio-temporal values as well as kinetic values. Moreover, their values do not take into consideration the type of alterations (i.e. the same values of knee GVS may indicate either a flexed or a hyperextended knee) or the timing in the gait cycle of some kinematic parameters (i.e. timing of maximal flexion of the knee). Thus, these parameters can quantify how far a patient's gait pattern is from that of a healthy person (GPS) and which joints are particularly involved in such an alteration (GVS), but they need to be supported by the gait analysis graphs for a better comprehension of the patient's gait pattern.

Finally, it must be considered that individuals with MS are characterized by reduced walking speed, [1] as also confirmed by the present study; this might represent a confounding factor in the GPS analysis, as in previous studies mixed evidences of significant and non-significant correlations between walking speed and gait kinematic parameters were reported [33,34]. Even though the correlation between the GPS score and walking speed was found low in the present study, further investigations are needed to fully clarify the influence of walking speed on the joint kinematics considered for GPS calculation in the specific case of individuals with MS.

5. Conclusions

The present study proposes a novel approach to quantitative assessment of gait alterations from a kinematic point of view in individuals affected by MS. Using three-dimensional quantitative GA, summary measures (GPS/GVS) calculated on the basis of a number of relevant kinematic variables referring to pelvis, hip, knee and ankle joints were

calculated and a comparison between individuals with MS and healthy controls was made. The results show significant differences in terms of GPS between the two groups as the result of significant differences in five out of nine GVS values. Moreover, the GPS value appears moderately correlated with the severity of the disability (expressed in terms of EDSS value), thus suggesting that such a measure is suitable for representing gait deviations from physiological patterns in MS. These factors can assign GPS the role of a complementary, adjunctive measure in clinical trials with respect to the well-established walking performance scales and timed tests. The GPS may be useful in monitoring the progression of the disease, in planning specific treatments on an individual basis, as well as providing ease in assessing outcomes of either pharmacological or physical therapies because it gives global and specific quantitative and qualitative information on the basis of objective and reliable measurements.

Future developments of the study include further validation by testing larger samples, specific investigations on homogeneous classes of disability (e.g. mild, moderate and severe) and possibly the establishment of a GPS scale corresponding to disability levels as defined by the EDSS scale. Also, given the substantial irrelevance of some of the kinematic variables currently used in calculating GPS, a custom index specific for the MS pathology could be defined with a subset of the 9 classical GVS scores to achieve better sensitivity in the evaluation of MS patients.

Conflicts of interest

The authors report no conflicts of interest.

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