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PERSONAL VIEW

Gait quantification in multiple sclerosis: A single-centre experience of systematic evaluation

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Summary Gait disorders can be disabling in persons with multiple sclerosis (PMS). Different gait parameters have been used to evaluate gait disorders according to the International classification of functioning. Some authors have reported a direct relation between evaluations over short distances and long-term outcomes. This relationship is of interest for the purposes of clinical research, as it enables short-distance evaluations to be used as a primary endpoint for trials. However, these endpoints are not always particularly relevant for PMS, and furthermore, all evaluations do not present the same metrological characteristics, especially with regards to reproducibility. However, it is essential to have good reproducibility in order to be able to test the effect of a therapeutic strategy on walking parameters in PMS. Using a range of walk tests (timed 25-foot walk in different conditions, namely comfortable walking, fast walking and dual-task walking; the Timed Up and Go test; the 6 minute walk test) associated with neuromotor analysis of the lower limbs, we describe the advantages and limitations of gait evaluation in MS. Based on clinical experience accumulated over 4 years, we propose a minimum set of measurements to be used in clinical practice and also for research purposes.

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Introduction

Walking is among the most basic and ancient functions of the human species [33], and is strongly related to autonomy and quality of life in the population [19]. For this reason, walking is taken into account in the International classification of functioning, disability and health (ICF), which defines walking as ''moving along a surface on foot, step by step, so that one foot is always on the ground, such as when strolling, sauntering, walking forwards, backwards, or sideways''. The distance and speed are components of the ICF definition and are predictors of dependency in terms of the activities of daily living [52]. The ICF proposes evaluation of walking over short distances (10 meters) (d4500, activities and participation), with the possibility of analysing temporal and spatial parameters such as cadence and step length (b770, body functions), but also over long distances (2 or 6 minutes; d4501 activities and participation), with the possibility of analysing physiological parameters such as heart rate (b455, body functions).

Among the range of functions that are impaired in people with multiple sclerosis (PMS), walking is one of the most affected [29]. MS is a progressive neurological disease that frequently affects younger subjects [62]; walking is affected in up to 89%, as assessed by an Expanded Disability Status Scale (EDSS) score between 4.5 and 5 [31]. In certain patients, walking can even become impaired at the early stages of disease, with 22% of cases displaying an EDSS between 1 and 3.5 [11,34]. Gait disorders in MS can be of diverse origin [7], including neurological (cerebellar), sensory or motor impairments related to diffuse lesions of the central nervous system (CNS) [62]. Cognitive and visual impairment may also play a role [2]. In PMS, gait disorders are perceived to be the main source of disability [19], with far-reaching repercussions for the patient's quality of life [30].

Given that gait disorders can cause considerable limitations in PMS, it is of prime importance to offer regular evaluation of gait to these patients, to closely monitor disease progression, and assess the impact of the symptomatic treatments including rehabilitation. Since gait differs between patients according to their experience and the severity of disease [47], it cannot be studied with a single test alone. Therefore, we propose here a set of measurements that yield an overview of gait in PMS. This measurement set, which we have been using in clinical practice for more than 4 years in our centre, is designed to fulfil several functions, namely: routine implementation in clinical practice as a means of communication with PMS and their caregivers; as a teaching tool for students to learn a structured approach to evaluating gait disorders; and as a research tool, to follow disease progression in PMS and to allow evaluation of the effects of therapies with a view to improving management.

Choice of tests and implementation

We describe hereafter the chronological order of the tests performed, with the rationale for the choice of each test, and its relevance in this context.

Consultation with the physician (10 min)

An experienced neurologist consults with the patient to perform a clinical examination (e.g. any flares since last visit, changes in treatment, appearance of new complications, and so on), assess the EDSS and check that there are no contraindications to the scheduled evaluations [38].

Neuro-orthopedic work-up (45 min)

In view of the wide variability in the impairments and functional disorders that can affect ambulation in MS [7], analytic evaluation of the lower limbs is essential. This work-up is performed by an experienced physiotherapist. We chose to perform a complete neuro-orthopedic assessment of the lower limbs including range of motion of the joints, different types of sensation (epicritic and protopathic), spasticity (see example of neuro-orthopedic work-up in AppendixA). Finally, this work-up also includes anthropometric measures (height, weight, length of lower limbs, distance between the anterior superior iliac spines, ASIS) (see below) [32,43].

Gait evaluation (45 min)

Gait is evaluated in a dedicated room by a biomechanical engineer. Measurements during the different walking conditions are recorded using simple instruments such as a GaitRite walkway and video recording. The room temperature is controlled and maintained at around 23 °C, in order to limit the impact of high temperatures on the locomotor capacities of the patient [61].

Video analysis

Full-body analysis from the front, back and side enables qualitative evaluation of gait disorders (stance, position of trunk, arms etc). The qualitative analysis is recorded in a secure database allowing simultaneous visualization of the videos by one or several evaluators. The analysis is described using a standardized procedure (adapted from the Edinburgh Visual Gait Score [55]) and makes it possible to interpret the observed disorders together with the neuro-orthopedic work-up (see above).

General considerations about walking conditions

For the walking conditions, we chose to perform tests in several different conditions. The so-called ''short-distance'' tests are performed based on the timed 25-foot walk (T25FW) (equivalent to 7.62 meters). This test forms part of the battery of tests used to evaluate walking speed over a short distance (10 meters, 30 meters). It was initially developed as one of the three components of the multiple sclerosis functional composite (MSFC). From a static start, the patient is instructed to walk as quickly and as safely as possible along the 25-foot course. Assistive devices (e.g canes or crutches) can be used. This test is associated, independently of the other components of the MSFC (nine hold peg test and paced auditory serial addition test), with EDSS, with a stronger relation observed for patients with severe disability and for those with progressive forms of disease [35]. Usually, the only parameter recorded in this test is the time taken to cover the 25-foot course. The test is commonly associated with an instrumental measure, notably using equipment such as a GAITRite™ walkway [44]. We chose this latter approach to simplify data recording and to increase the number of available parameters for analysis (e.g. cadence, step length, step asymmetry, step width etc.). Different authors have proposed different conditions for the walkway test, with variations in the starting instructions (static vs. dynamic start), or in the speed (comfortable vs. maximal safe speed) [25]. Furthermore, gait can be analyzed either barefoot or while wearing shoes. For all the walking conditions described below, the start and finish is 2 meters outside the measurement zone in order to limit the effect of acceleration and deceleration. Variables are calculated from a minimum of 14 gait cycles for each task [37]. A rest period of at least five minutes is allowed between tasks.

Comfortable, barefoot walking

In the first test, we ask patients to walk barefoot, to enable us to better identify primary gait problems, and to record the plantar footprints with the instrumental walkway. In all the subsequent assessments, the patients wear their usual footwear.

Comfortable walking speed (CWS)

The impact on gait of footwear has not been extensively studied. One study in children showed an increase in step length when wearing shoes [51]. Adults are generally more accustomed to walking with shoes. A comfortable walking condition is natural and intuitive, although less reproducible than fast walking [17]; this nonetheless appears to us to be a good means of communication with the patient and carers concerning his/her walking abilities. Furthermore, comfortable walking is considered to be one of the best predictors of dependency, risk of hospitalization, need for rehabilitation, ambulation category [19] and life expectancy in elderly persons [60].

Fast walking speed (FWS)

We also record the fast walking speed (FWS) for its metrological properties [8], especially its reproducibility in measuring therapeutic effects [17]. In addition, the ratio between FWS and CWS, known as the walking speed reserve (WSR), is an important indicator, as it reflects an individual's ability to increase their walking speed on demand whilst performing daily living activities, such as when attempting to catch a bus/train or crossing the street when the traffic light suddenly begins to change. People may also need to ambulate quickly indoors, such as running to answer a ringing phone and/or the doorbell, or shutting off the cooker when the timer buzzes [36]. Walking speed reserve (WSR) is defined as the extent of increase from CWS to FWS [36].

Dual task walking (DTW)

PMS frequently present cognitive impairment [39]. For this reason, we choose to evaluate dual task walking (DTW). Indeed, it has been shown that DTW reduces walking speed by 6 to 27% [64]. For the cognitive task to be performed, we choose counting serial sevens aloud. As described in previous studies, the number seven was chosen because it does not involve auditory-pace synchronization [12]. The ratio between DT performance and single-task walking enables the calculation of a useful indicator known as the dual task cost (DTC), which is calculated as: DTC= (single-task−DT)/single-task $\times$ 100 [5]. The DTC corresponds to the ''cost'' of the cognitive task on walking ability. In PMW, this cost has been reported to range from 5.6% to 34.4% [42]. The interference between cognitive and motor tasks has important repercussions in daily life, and is known to be related to the risk of falls [27]. For the purposes of our evaluations, the starting number for the serial sevens counting is different at each trial. The replies are noted to verify that the task is performed correctly. CWS, FWS and speed during DTW are measured.

Dynamic balance test

The timed up and go (TUG) test is a quantitative evaluation of walking, transferring ability (from sitting to standing and vice-versa) and turning around [53]. Initially developed for use in elderly people, it has since been widely used in PMS [17]. In PMS, there is a strong correlation between the 10m-walk test and EDSS score > 4 (r = 0.85), but the correlation is weaker in persons with less severe disability (EDSS $\leq$ 4, r = 0.70) [48]. The TUG was not retained in the recently proposed measurement set of outcome measures for adults with neurologic conditions undergoing rehabilitation [46], given the lack of reliability data in acute neurological conditions. The role of this test in a chronic disease such as MS is, however, well established, where it has been shown to have a smallest real ratio (i.e. smallest percentage difference required to detect a genuine change) ranging from −24% to +31% [48]. For the evaluations performed in our center, a chair, 47 cm in height, with an armrest and a backrest is used. Participants are instructed to get up from the chair, walk three meters, turn around a cone and come back and sit down on the chair as quickly as possible, whilst ensuring their safety [48]. The TUG is performed twice. A third trial is performed if a difference of 10% is found between the first two trials. The mean value calculated from the two trials with the closest values is used.

Submaximal exercise test

The 6-minute walk test (6MWT) is a recording of the distance covered over a period of 6 minutes. The initial test was modified for use among PMS to allow for rest periods [22], and this is the version that we choose to use in our practice. The 6MWT is strongly correlated with overall measures of disability, including EDSS (r = 0.73, P < 0.001) and MSFC (r = 0.72, P < 0.0001), and with a patient-reported measure of walking, the 12-Item Multiple Sclerosis Walking Scale (MSWS-12; r = 0.81, P < 0.001) [22]. Evaluation of the test's reproducibility showed a standard measurement error comprised between 27.5 and 32 meters [40,41,52]. However, compared to the T25FW (included in the MSFC), the 6MWT is a better indicator of walking endurance [22]. Although the 2-minute walk test has been shown to correlate very strongly with the 6-minute test [21,57], we choose to use the 6MWT to enable assessment of the instantaneous speed during the test each time the patient walks over the GAITRite™ walkway [28]. The change in gait velocity over the course of the test is related to the severity of the walking impairment [16,22]. In our centre, the 6MWT is adapted from the recommendations of the American Thoracic Society [4]. The instructions for the test are read to the participants before each walk, and participants walk around a 24-meter circuit.

Perceived exertion

The Borg scale gives the patient's perception of the level of exertion required, and of the heart rate during exercise [10]. It provides an estimate of physiological functions (ICF: b455) without a need for direct measurement. Although the Borg scale has not been widely used among PMS [26], we decided to use this scale in our evaluations during the 6MWT, given the importance of establishing the patient's perception of their own physical condition. Patients rate their perceived exertion on the Borg scale at three timepoints, namely the 2nd, 4th and 6th minutes.

Second medical consultation (15 min)

At this second consultation, based on the preliminary results (only spatio-temporal parameters), the physician is able to outline some initial recommendations for follow-up and treatment of the PMS.

How the data are used

In our experience, performing all these tests, along with a full neuro-orthopedic work-up, requires the patient to be on site for 2 hours: 1 hour for the neuro-orthopedic work-up, and 1 hour for the gait tests and consultations. The whole procedure requires three staff members working within a multi-disciplinary team, namely a neurologist, a physiotherapist and a biomechanical engineer, who then come together to discuss the patient's results and propose a therapeutic plan. This meeting lasts about 30 minutes. Medical students also participate in the meetings, to learn about diagnostic and therapeutic approaches on the basis of systematic evaluation.

Gait in PMS is a part of the definition laid down by the ICF, and it is therefore logical to investigate gait disorders using the components of this classification. The challenge lies in achieving a suitable compromise between recording a maximum of data, and clinical feasibility. Indeed, on the one hand, it is necessary to perform an evaluation that is sufficiently complete to give a valid overview of the gait of the PMS, but on the other hand, it should not be so complicated as to be impractical in routine practice. The set of tests proposed here give an extensive overview of the walking capacity of PMS, while the shared experiences from professionals from different disciplines during the meetings is informative and beneficial for the management of PMS patients [20].

This type of multimodal assessment is applied in other disciplines, such as geriatric medicine [15,45,58], which encounters similar complexities to those of patients with neurological conditions such as MS.

The measurement set described here meets two predefined objectives, namely clinical evaluation and research. Regarding the clinical evaluation, this measurement set enables us to present the results in a manner that is intelligible and meaningful for MS patients and their physicians, especially colleagues in rehabilitation facilities in the region. Furthermore, in view of the current public health policy aimed at regrouping hospital services across the national territory through the use of telemedicine and centralized long-term follow-up for chronic diseases, improved communication between healthcare providers is of particular importance. For example, CWS is presented using a graph taken from the study by Bohannon et al. [9], showing the position of the patient in relation to the general population of the same sex and age. In this way, any progress achieved after rehabilitation programmes, can easily be visualized if the patient's curve moves closer to the normative curve (Fig. 1). Rehabilitation objectives can also be set on the basis of the curves. Beyond this specific evaluation, other measures are also presented graphically, comparing results from different timepoints, and thus enabling visualization of the course of disease progression.

The measurement set presented here is also implemented in the framework of a wider series of evaluations performed for the FAMPISEP study (NCT02849782), which aims to investigate the efficacy of fampridine on more diverse functions than just walking as evaluated by a short test. Fampridine is a potassium channel blocker that improves nerve conduction through demyelinated fibres in the central nervous system. It was initially validated to improve walking speed in the T25FW in PMS [24]. To ensure accurate interpretation of the data using repeated tests, in the research context, we determined the reproducibility of the T25FW, 6MWT and TUG performed twice at 7 days' interval [17], and determined the thresholds of minimal detectable change (MDC) [16]. Using the MDC makes it possible to avoid systematic error, and detect improvements with greater accuracy in patients under treatment. We showed, for example, that for a 6MWT in a patient with MS with an EDSS between 4.0 and 6.5, the MDC is 86.1 meters, or 31.7%. The threshold can be applied as an absolute value or as a percentage, depending on how one chooses to consider an ''improvement'' in walking [17].

In our unit, all these tests are performed in a dedicated room, with simple measurement instruments. However, not all wards or departments dealing with PMS have the possibility of all these resources. Alternative solutions exist for such cases. For example, the T25FW can be performed using a simple stopwatch and sufficient space [18]. The different walking conditions are relatively easy to implement and require neither specific equipment nor additional personnel. The TUG can also be performed in a small space; all that is required is a chair. The 6MWT can also be performed as long as there is sufficient space available, such as a hall or gymnasium, a rehab room or even a long corridor. The only caveat

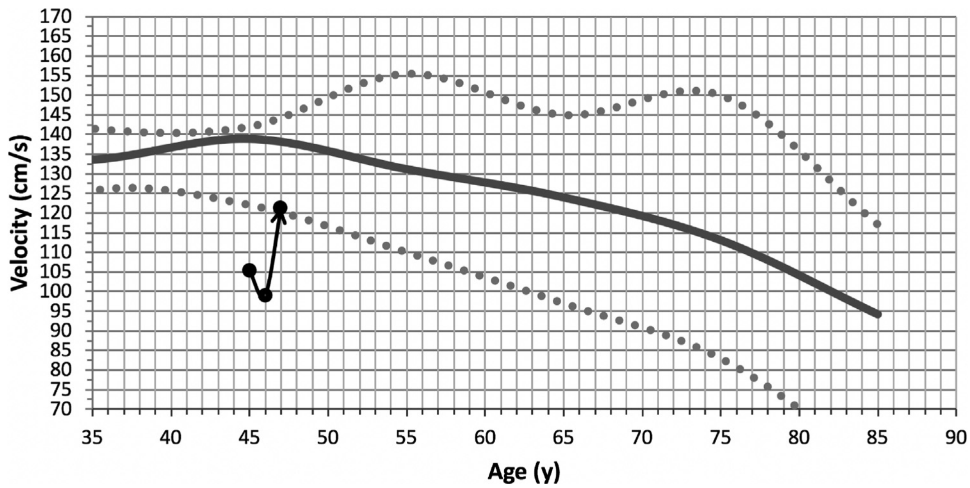

Figure 1 Example of results of gait evaluation. This patient was evaluated three times (dark points and arrows). These results are given in reference to normative curve (from Bohannon et al. [9]).

is that the space should be cleared of other uses during the test, to avoid interference related to the presence or movement within the test space of other persons not involved in the test.

Perspectives

The EDSS is used to classify MS patients and monitor changes over time, based on the importance of walking as an indicator of disability. However, the psychometric qualities of the EDSS remain debated. The Disability Status Scale (DSS), subsequently modified in 1983 as the EDSS, has been subject to some controversy since its low inter- and intra-rater reliability levels are a source of concern [3,13,23,49,50,54,59,63]. Other instruments are garnering increasing interest to achieve improved psychometric properties, such as the streamlined EDSS (sEDSS). Adapted from the initial EDSS, the principle for revision in the sEDSS was to remove weaker items and those that diverged the most between evaluators. These include assessment of pyramidal signs (motor signs from the pyramidal functional system (FS)); findings that do not necessarily impact disability or function in isolation, such as disc pallor (from the visual FS); requiring two muscles to be affected to consider a limb as being weak; and bowel symptoms. However, the sEDSS remains to be validated in patients with an EDSS > 6.0, and for patients with progressive disease [6]. Similarly, the Neurostatus e-Scoring (NESC) system was developed to further improve the reliability and internal consistency of EDSS assessments. It is an electronic data capture, analysis and management system that makes it possible to capture the results of neurological examination, including Neurostatus subscores, FS scores, AS and final EDSS step, with a touchscreen-based tablet device (iPad™). It provides algorithm-based real-time feedback on potential inconsistencies [13].

While acknowledging the need to reach a compromise between the capacity to perform several motor tests in PMS, and their feasibility, there are other useful evaluations that could also be included in the measurement set, such as static balance, for example. This is an important exam because static balance is a prerequisite for ambulation. The TUG provides an evaluation of balance, but only dynamic balance. That being said, the evaluation of turning using the TUG has been shown to be an important marker of balance confidence and walking limitation in PMS [1]. Among specific balance tests, the Berg Balance Scale (BBS) has been shown to have excellent metrological properties with a high grade of recommendation [46], and could be easily integrated into our proposed measurement set.

While we have previously reported preliminary investigations [56], our evaluations are nonetheless performed in laboratory conditions, and walking is therefore not measured in real-life conditions. Gait in real-life activity could be measured with the aid of actimeters [56] or other on-board or smart devices. Indeed, according to the ICF, the concept of capacity (as assessed in a ''uniform'' or ''standard'' environment) and performance (how the individual performs in real-life situations) are complementary, and together determine the level of limitation or restriction. In addition, gait measurement both provides additional information and serves to monitor EDSS. Indeed, while the assessment of walking distance with the EDSS by a neurologist is more accurate than the patient's own perception, it nonetheless remains less accurate than Global Positioning System (GPS) evaluation as measured using smart devices [14].

Conclusion

The measurement set proposed here is intended to enable multimodal evaluation of gait in persons with MS. The tests chosen for inclusion in this set have been shown to have excellent psychometric properties and are recommended for gait evaluation in patients with neurological disorders. Our experience shows that this measurement set is feasible in an acceptable length of time for PMS, and is compatible both with clinical evaluation in routine practice, and with research objectives in a gait laboratory.

Disclosure of interest

The authors declare that they have no competing interest.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.neucli.2019.01.004.

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