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Gait tests in multiple sclerosis: Reliability and cut-off values

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ABSTRACT

Background: Gait limitation is one of the most common disabilities in people with multiple sclerosis (MS). Several studies have used gait parameters to determine the effects of different therapies. However, few studies have determined their reproducibility, also the therapeutic effects could be overestimated.
Research question: To examine the reproducibility in gait measurements during short and long distances.
Methods: In this cross-sectional study we recruited a group of MS patients and compare it to a control group. The participants performed the following tests in a fixed order: a 25-foot walk at a comfortable speed, at a fast speed and during a dual task, a timed up-and-go test (TUG) and a six- minute walk test (6MWT). Two measurements were conducted a week apart. Systematic error was evaluated by the Student *t*-test, reliability by the intra-class correlation coefficients (ICC) and agreement by the minimum detectable change (MDC_{95}).
Results: A total of 58 people with MS and 19 healthy people were included. The absence of systematic error was only found for the fast speed condition. The reliability of the gait parameters had moderate to high ICC values (ICC > 0.7) except for the dual task cost (DTC) which was 0.45. The MDC_{95} was higher in people with MS compared to healthy people, and it was higher in people with MS for gait speeds in all conditions (> 34%). For the TUG and 6MWT, the MDC_{95} were 51.5% and 31.7% respectively. For people with MS the smallest MDC_{95} was found for the stance time for all conditions (6.8%), whereas the highest was found for the dual task cost (158.7%).
Significance: The MDC_{95} values were higher than the cut-off point based on the minimally important clinical difference (MICD) proposed in previous studies. Thus, the MDC_{95} should be used as a cut-off rather than MICD values.

1. Introduction

Gait limitation, defined as an activity limitation by the International Classification of Functioning Disability and Health, is one of the most common and disabling signs in people with multiple sclerosis (MS) [1,2], and 70% of them have reported gait limitations as the most serious problem [3].

Different parameters have been used to measure gait limitations in multiple sclerosis, including the timed 25-foot walk (T25FW), six-minute walk test (6MWT), spatio-temporal gait parameters measured with an instrumented walkway, or the timed up-and-go test (TUG) [4]. These different assessments can be performed using different conditions: a simple task, fast speed or dual task in which one gait is associated with a cognitive or other motor task [5].

Different approaches are possible for studying walking and changes in gait. The minimally important clinical difference (MICD) is one method and is defined as the smallest difference in an outcome of interest that is perceived as beneficial and non-trivial by patients and clinicians and can enhance patient management [6]. For people with MS, changes from baseline in the T25FW around 17.2%–20% are generally considered as clinically meaningful [7–12].

In order to determine meaningful clinical parameters as described above, it is also important to determine the amount of error in the evaluation procedures. To do so involves looking at reproducibility, an umbrella term that involves reliability and agreement [13]. Reliability is defined as the ability of a measurement to differentiate between participants, usually measured by intraclass correlation (ICC) tests. Agreement is defined as the ability of a measurement to assess to what extent scores or ratings are identical when the phenomenon studied does not change. Agreement is often measured by standard error of measurement (SEM) and minimum detectable change (MDC) [13,14]. Ideally, an MICD difference should be close to these reproducibility

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measurements to ensure that the phenomenon and any changes can be detected by the measurement method chosen by the evaluator.

With regard to MS, few studies have first focused on determining reproducibility and there are inconsistencies in the designs of these. First, the time between evaluations varied from one hour [15] to six months [16]. The relatively recent emergence of treatments with rapid action (14 days) on gait parameters in the MS population [17] required the study of reliability over an equivalent period. This has been done in one study [18], and in this study only 3 tests were used (T25WT fast condition, TUG and 6MWT. There is a striking absence of research reporting reproducibility for different gait parameters using dual tasks for patients with MS. To our knowledge only one study has used dual task assessment [15] and for a small number of gait parameters.

Considering the limitations of previous research, further reproducibility studies for gait measurements in patients with MS are necessary. Therefore, the aims of this study were to establish reproducibility in terms of reliability and agreement using ICC and MDC over a one- week period of time for different locomotion conditions in this population.

2. Methods

2.1. Study design

This cross-sectional study is derived from FAMPISEP (NCT02849782). Patients were recruited in Besancon (France) area between April 2014 and May 2016. They were evaluated two times one week apart before beginning drug treatment (Fampridine) [19] (Fig. 1).

2.2. Participants

The inclusion criteria were: (i) a multiple sclerosis diagnosis according to the modified McDonald criteria [20]; (ii) an Expanded Disability Status Scale (EDSS) status between 4.0 and 6.5; and (iii) the ability to walk for a period of six minutes. The exclusion criteria were: (i) worsening multiple sclerosis symptoms during the previous 60 days; and (ii) immunotherapy change in the previous 60 days. Healthy volunteers who were similar in terms of sex, age, height, weight and body mass index to the patient group participated in this study as a control group.

This protocol was governed by French legislation concerning interventional biomedical research and was submitted to the local ethics committee (#13/405). The study was approved by the French Health Products Safety Agency (#2013-A002305-56). Written informed consent was obtained from all participants of this study.

2.3. Measurements

Gait evaluation was carried out in a dedicated room at a controlled temperature (approximately 22 °C) using a 6.10 m GaitRite™ system (CIR Systems Inc) pressure sensitive walkway. Participants were asked to walk a 25-foot (7.62 m) distance which was delineated by two photocell barriers (Microgate Polifemo, Italy) [21]. They began and stopped walking two meters away from the 25-foot area. The GaitRite system was positioned in the middle of the barriers.

After appropriate instructions and familiarisation, participants were asked to perform three gait tasks: walking at a self-selected comfortable speed [22], walking at their maximum speed [23] and walking at a self-selected comfortable speed with a mental-tracking task [24], which was a dual-task recommended for people with MS [25]. The mental-tracking task consisted of serial subtractions of seven to be performed as accurately as possible [26]. As described in previous studies, the number seven was chosen because it did not involve auditory-pace synchronisation [27,28]. The cognitive function was evaluated by the symbol digit modalities tests (SDMT) [29].

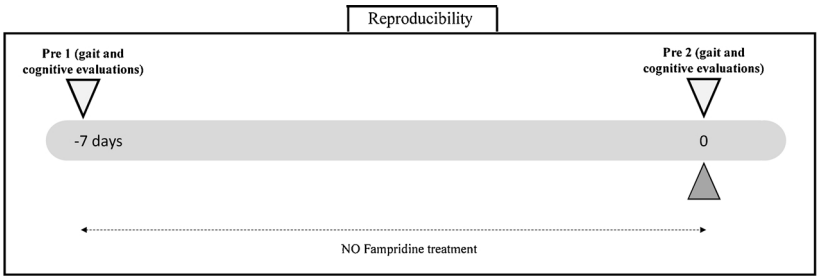
Ten gait cycles for each task were used for further analysis [30] and at least a five-minute rest period was allowed between tasks. Moreover, the dual task cost (%), which refers to the ratio between comfortable speed with a mental-tracking task and comfortable speed, was calculated for the dual task condition [31].

For the TUG test, a chair, 47 cm in height, with armrest and backrest was used. Participants were 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 [32]. The TUG was performed twice. A third trial was performed if a difference of 10% was found between the first two trials. The mean value calculated from the two closest trials was used.

The 6MWT assessed the submaximal level of functional capacity. It was adapted from the recommendations of the American Thoracic Society [33]. The 6MWT instructions were read to the participants before each walk. Participants walked around a 24-meter circuit. They were allowed to have rests if necessary and words of encouragement were spoken every 30 s. The distance walked in 6 min was measured.

2.4. Procedure

Disability was ascertained using the Self-Report Expanded Disability Status Scale (SR-EDSS) [34]. The disease course was determined by the Lublin and Reingold classification [35]. The gait was evaluated (single evaluator) as described in the section above (2.2) on 2 occasions, with an interval of a week between each one. The evaluation was done on the same day of the week, but not systematically at the same time of day. All the measurements were administered in a fixed order (T25FW at three conditions, comfortable speed, fast speed and dual task; TUG; 6MWT). The use of a participant's assistive device was allowed and worn at each session. All the gait parameters were caring out with the GAITRite system (velocity, cadence, stride length, stride time, stance



Pre 1: first visit before fampridine treatment, Pre 2: second visit before fampridine treatment, Post 1: first visit after fampridine treatment, Post 2: second visit after fampridine treatment.
The only two first evaluations were used for this study.

Fig. 1. Study design.
Pre 1: first visit before fampridine treatment, Pre 2: second visit before fampridine treatment. Post 1: first visit after fampridine treatment, Post 2: second visit after fampridine treatment.
The only two first evaluations were used for this study.

time, double support time, base of support and toe in/out).

2.5. Statistical analysis

We first evaluated if the variables were normally distributed using Kolmogorov-Smirnov and Lilliefors tests for normally. Because all variables were normally distributed, the mean and standard deviation (SD) were used in the analysis. All trials for an individual were averaged, then the average trial values for each individual were compared between the two days. The MS and healthy groups were compared in terms of sex distribution, age, body mass, size and body mass index using a Chi-square and independent Student *t*-tests. A systematic error between test and retest evaluations was evaluated using the Student *t*-test. The level of significance was set at 0.05. The variance components were estimated with the gait outcome values as dependent parameters and people and evaluations as random factors, using the restricted maximum likelihood method [13]. Reliability was assessed afterwards using the calculation of ICC with a 2-way random effects model [13].

Estimated values of 0.6–0.80, 0.80–1 and close to 1 were considered to have moderate but still acceptable, good and strong reliability, respectively [36]. The SEM and MDC_{95} values, expressed in the unit of measurement, describe the amount of change required to indicate real change for a group of individuals or at an individual level, respectively. The SEM and MDC_{95} were calculated using the formulae below: [13]

$$SEM = \sqrt{\sigma^2_{eval} + \sigma^2_{residual}}$$

$$MDC = 1.96 \times \sqrt{2} \times SEM$$

Both SEM and MDC were also expressed as a percentage of the mean (i.e., SEM% and MDC_{95}%), to facilitate comparisons between parameters. Data management and analyses were performed using Statistica version 10 (StatSoft. USA).

3. Results

3.1. Participant characteristics

Fifty-eight patients with MS and 19 healthy volunteers were included. The demographic characteristics of participants are provided in Table 1. There was no significant difference in age, gender or body mass index between the people with MS and the control group. For the people with MS, the mean (SD) EDSS and disease duration were 5.2 (1.1) and 14.0 (10) years respectively. The majority of these patients were in the progressive phase of the disease (80%).

3.2. Gait in short distances

A systematic error was found in most parameters due to an improvement in gait parameters after the first test, especially for comfortable speed and dual task conditions (Tables 2 and 4). Systematic error was not found in most parameters in the fast speed condition (Table 3). The reliability of the gait parameters (ICC) was moderate to strong under all conditions in the two populations (people with MS: 0.81–0.98, controls: 0.77–0.99), but on average the patient group had a higher score than the control group. As far as agreement was concerned, for the MDC_{95}% of gait speed values were over 34% for people with MS and over 21% for controls. In spatio-temporal parameters, patients had higher values than the controls in most parameters (SEM and MDC values were below 15% and 40% for the patient group and 10% and 29% for controls, respectively). These relative cut-off values are higher in people with MS than in controls, as the absolute values of MDC_{95} (patients between 0.28 and 0.38, controls between 0.32 and 0.54) were frequently lower for people with MS than controls.

The lowest MDC was found for stance time in both populations (patients between 6.1% at comfortable speed and 7.5% in dual task; controls between 3.2% at comfortable speed and 5.0% at fast speed). The highest MDC was found for the dual task cost (MDC_{95}% = 158.7% for the group with MS and 244.7% for the control group) (Table 4).

3.3. TUG and 6MWT

Concerning TUG, a systematic error was observed due to an improvement in the people with MS, but not in the controls (Table 5). Reliability was good to strong (ICC = 0.87 for controls and 0.97 for patients). Agreement values were higher in people with MS compared to controls in absolute values (MDC_{95} = 7.9 s for patients and 1.1 s for controls) as well as in percentage (MDC_{95}% = 51.5 for patients and 22.5 for controls). For the 6MWT, the systematic error was found in both populations. The ICC was moderate (0.79 for controls) to strong (0.98 for patients). Agreement values were higher in people in MS than in controls (MDC_{95}% values were 31.7% for patients and 22.1% for controls).

4. Discussion

Gait limitation is an important consequence of multiple sclerosis that impacts patients' quality of life [37]. Several parameters can be used to evaluate gait limitation for people with MS. One important concept is to evaluate the reproducibility of gait parameters before interventional programs to assess the extent to which error measurements and interventions affect the results. Repetition of pre-intervention evaluations has only been done in a very few studies [17,19], with no reproducibility assessment. Moreover, reproducibility using the set

Table 1
Demographic data and multiple sclerosis/control-related characteristics of participants att baseline.

			PwMS (n = 58)	Ref (n = 19)	p-value
Gender (female/male)		n/n	37/21	9/10	0.2762
Age (years)		Mean (SD)	50.7 (11.9)	46.6 (8.6)	0.1702
Body mass (kg)		Mean (SD)	75.6 (17.1)	71.9 (13.3)	0.3793
Size (m)		Mean (SD)	1.7 (0.1)	1.7 (0.1)	0.0800
BMI (kg m^{-2})		Mean (SD)	26.9 (5.6)	24.3 (3.1)	0.0613
SDMT (symbols/90 s)		Mean (SD)	33.4 (11.6)	52.0 (13.1)	< 0.0000
Disease duration (years)		Mean (SD)	14.1 (9.9)	NA	NA
EDSS (4–6.5)		Mean (SD)	5.2 (1.1)	NA	NA
MS Type	**SP n (%)**	n(%)	26 (45)	NA	NA
	PP n (%)	n(%)	20 (35)	NA	NA
	RR n (%)	n(%)	12 (20)	NA	NA

SD: standard deviation; PwMS: People with Multiple Sclerosis; EDSS: Expanded Disabilty Status Scale; MS: Multiple Sclerosis; SP: Secondary Progressive; PP: Primary Progressive; RR: Remittent Regressive; NA: not applicable.

Table 2
Gait parameters in the T25FW comfortable speed condition.

		Session 1 Mean (SD)	Session 2 Mean (SD)	Diff %	*p-value*	ICC (95%CI)	SEM	MDC_{95}	SEM %	MDC_{95} %
Velocity ($m\,s^{-1}$)	PwMS	0.8 (0.4)	0.8 (0.4)	7.7	**0.0029**	0.96 [0.91–0.98]	0.1	0.3	13.9	38.7
	Control	1.5 (0.2)	1.6 (0.2)	8.4	**0.0001**	0.79 [0.27–0.93]	0.1	0.3	7.6	21.0
Cadence (steps. min^{-1})	PwMS	86.7 (24.2)	89.8 (23.9)	3.6	**0.0007**	0.98 [0.95–0.99]	5.1	14.1	5.8	16.0
	Control	116.9 (8.1)	120.9 (7.5)	3.4	**0.0001**	0.88 [0.43–0.96]	3.7	10.2	3.1	8.6
Stride length (m)	PwMS	1.0 (0.3)	1.0 (0.3)	4.3	**0.0021**	0.96 [0.93–0.98]	0.1	0.2	7.5	20.9
	Control	1.5 (0.1)	1.6 (0.1)	4.8	**0.0004**	0.85 [0.49–0.95]	0.1	0.2	4.6	12.8
Stride time (s)	PwMS	1.6 (0.7)	1.5 (0.6)	−5.4	**0.0048**	0.92 [0.86–0.96]	0.2	0.4	10.5	29.2
	Control	1.0 (0.1)	1.00 (0.1)	−3.4	**0.0002**	0.87 [0.44–0.96]	0.0	0.1	3.3	9.3
Stance time (%)	PwMS	68.8 (5.9)	68.0 (23.9)	−1.2	**0.0000**	0.95 [0.92–0.97]	1.5	4.2	2.2	6.1
	Control	61.5 (1.2)	60.8 (1.2)	−1.1	**0.0008**	0.80 [0.44–0.92]	0.7	2.0	1.2	3.2
Double support time (%)	PwMS	37.9 (12.0)	36.1 (11.0)	−4.6	**0.0005**	0.81 [0.69–0.89]	2.8	7.8	7.6	21.1
	Control	23.2 (2.4)	21.8 (2.3)	−6.0	**0.0008**	0.77 [0.40–0.91]	1.4	4.0	6.4	17.7
Base of support (m)	PwMS	0.1 (0.1)	0.1 (0.1)	0.3	0.8747	0.96 [0.94–0.98]	0.0	0.1	11.2	31.1
	Control	0.1 (0.0)	0.1 (0.0)	6.4	0.0862	0.86 [0.65–0.94]	0.0	0.0	3.7	10.1
Toe in/out (°)	PwMS	8.6 (6.4)	9.1 (6.7)	4.7	0.3115	0.94 [0.91–0.97]	2.2	6.0	24.6	68.1
	Control	6.33.0)	6.1 (3.1)	−2.4	0.3715	0.99 [0.97–1.00]	0.5	1.4	8.1	22.4

T25FW: timed 25-foot walk; PwMS: People with Multiple Sclerosis; SD: standard deviation; Diff: difference between session 1 and session2; ICC: intraclass correlation; SEM: standard error of measurement; MDC_{95}: minimal detectable change; SEM%: standard error of measurement expressed as a percentage; MDC_{95}%: minimal detectable change expressed as a percentage.

Table 3
Gait parameters in the T25FW fast speed condition.

		Session 1 Mean (SD)	Session 2 Mean (SD)	Diff %	*p-value*	ICC (95%CI)	SEM	MDC_{95}	SEM %	MDC_{95} %
Velocity ($m\,s^{-1}$)	PwMS	1.1 (0.5)	1.11 (0.5)	1.8	0.4692	0.96 [0.93–0.98]	0.1	0.4	12.6	34.9
	Control	2.3 (0.3)	2.31 (0.5)	−1.6	0.5697	0.88 [0.69–0.95]	0.2	0.5	8.3	23.1
Cadence (steps. min^{-1})	PwMS	106.5 (28.5)	107.74 (28.2)	1.1	0.4943	0.95 [0.91–0.97]	8.9	24.6	8.3	23.0
	Control	151.8 (14.8)	150.11 (18.3)	−1.1	0.4846	0.90 [0.73–0.96]	7.3	20.4	4.9	13.5
Stride length (m)	PwMS	1.2 (0.3)	1.18 (0.3)	0.6	0.6238	0.98 [0.96–0.99]	0.1	0.2	6.1	16.9
	Control	1.9 (0.2)	1.83 (0.2)	−1.0	0.5114	0.88 [0.70–0.95]	0.1	0.2	4.7	13.0
Stride time (s)	PwMS	1.3 (0.5)	1.22 (0.4)	−2.4	0.2868	0.95 [0.92–0.97]	0.1	0.4	11.3	31.3
	Control	0.8 (0.1)	0.81 (0.1)	1.9	0.3107	0.86 [0.65–0.95]	0.0	0.1	5.5	15.2
Stance time (%)	PwMS	65.7 (5.4)	65.57 (5.6)	−0.2	0.7074	0.96 [0.92–0.98]	1.6	4.4	2.4	6.7
	Control	57.6 (2.1)	57.58 (2.8)	0.1	0.9373	0.91 [0.76–0.96]	1.0	2.9	1.8	5.0
Double support time (%)	PwMS	31.9 (10.8)	31.32 (11.1)	−1.7	0.3819	0.96 [0.93k0.98]	3.2	8.8	10.0	27.7
	Control	15.4 (4.3)	15.47 (5.1)	0.4	0.9146	0.93 [0.81–0.97]	1.8	4.9	11.4	31.7
Base of support (m)	PwMS	0.1 (0.1)	0.13 (0.1)	−2.8	0.3003	0.93 [0.89–0.96]	0.0	0.1	13.8	38.3
	Control	0.1 (0.0)	0.11 (0.0)	7.7	**0.0017**	0.79 [0.22–0.93]	0.0	0.0	8.4	23.2

T25FW: timed 25-foot walk; PwMS: People with Multiple Sclerosis; SD: standard deviation; Diff: difference between session 1 and session2; ICC: intraclass correlation; SEM: standard error of measurement; MDC_{95}: minimal detectable change; SEM%: standard error of measurement expressed as a percentage; MDC_{95}%: minimal detectable change expressed as a percentage.

of spatio-temporal parameters has been reported in only one study to our knowledge [38].

Our study aimed to provide more accurate results by evaluating reliability and agreement in various gait conditions and parameters for the same study and in a targeted population of people with MS who could benefit from a specific treatment to improve gait problems (i.e. EDSS between 4.0 and 6.5). Therefore, there was no unique gait parameter to assess gait improvement in these patients. This study could help to determine different cut-off values for different gait tests.

A systematic error due to improvement may be explained by a learning effect by participants in gait assessments. Systematic errors were found in most conditions except the fast walking condition. Our study is in line with previous studies [15,18,38]. However, concerning TUG and 6MWT, our study was not in accordance with a previous study [18]. In our study, the systematic errors have been taken into account for the reproducibility assessments. However those errors remains very small in relation to the magnitude of the phenomenon observed so its influence remains low on the final result of ICC.

The measurements were highly reliable over a one-week period in most of the parameters, with the ICC estimate exceeding 0.77 except for the dual task cost in the group with MS (ICC: 0.45). These results satisfied the criteria for acceptable reliability in the subsamples [39]. This complements previous studies [15,16,18,32,38,40]. As shown before [15], reliability was better in the group with MS than in the control population. Indeed, unlike the group with MS, the spatio-temporal parameters of healthy participants are close to each other, so it is more difficult to discriminate them. Furthermore, the results from healthy people must be viewed with caution because of the large confidence intervals.

The changes in gait speed can be interpreted from different points of view. Based on the variability of mean scores over consecutive walks, a change of 20% has generally been accepted as an MICD [8,11,12]. These results should be interpreted with caution, because in most cases, the level of clinical improvement is smaller than that which could be measured in equivalent experimental conditions. In the present study, the MDC_{95}% in patients with MS was over 30% for short distances (comfortable speed = 38.7%, fast speed = 34.9%, dual task = 39.6%) and these values are in agreement with previous studies [15,16,32,41]. Similarly, for the 6MWT, the SEM was 31.1 m, in accordance with previous results [16,18] and the MDC_{95}% was 31.7%, which was higher than a previous finding (20%) [16] but in line with another study (31%) [18]. In a research context, we suggest using MDC which are higher than MICD in order to have scientifically valid responses of therapeutic effects. Absolute values or percentage of MDC can both be used according to the clinical sense that would be done.

Table 4
Gait parameters in the T25FW dual task condition.

		Session 1 Mean (SD)	Session 2 Mean (SD)	Diff %	*p-value*	ICC (95%CI)	SEM	MDC_{95}	SEM %	MDC_{95} %
Velocity ($m\,s^{-1}$)	PwMS	0.6 (0.3)	0.7 (0.4)	10.3	**0.0000**	0.96 [0.90–0.98]	0.1	0.3	14.3	39.6
	Control	1.3 (0.2)	1.5 (0.2)	10.7	**0.0021**	0.83 [0.36–0.94]	0.1	0.4	9.4	25.9
Cadence (steps. min^{-1})	PwMS	80.1 (24.0)	84.6 (24.0)	5.5	**0.0000**	0.97 [0.92–0.99]	5.6	15.5	6.8	18.8
	Control	113.3 (11.3)	118.0 (9.6)	4.1	**0.0001**	0.86 [0.57–0.95]	5.2	14.3	4.5	12.4
Stride length (m)	PwMS	1.0 (0.3)	1.0 (0.3)	4.5	**0.0012**	0.97 [0.93–0.98]	0.1	0.2	7.2	19.9
	Control	1.4 (0.2)	1.5 (02)	6.4	**0.0085**	0.87 [0.43–0.96]	0.1	0.2	5.6	15.6
Stride time (s)	PwMS	1.7 (1.0)	1.6 (0.7)	−7.8	**0.0003**	0.97 [0.94–0.98]	0.2	0.6	12.5	34.5
	Control	1.1 (0.1)	1.0 (0.1)	−4.3	**0.0000**	0.81 [0.49–0.93]	0.1	0.2	5.5	15.3
Stance time (%)	PwMS	69.4 (6.9)	68.8 (6.2)	−0.9	0.0892	0.96 [0.93–0.98]	1.9	5.2	2.7	7.5
	Control	62.3 (1.2)	61.4 (1.3)	−1.3	**0.0000**	0.83 [0.23–0.95]	0.8	2.1	1.2	3.4
Double support time (%)	PwMS	39.5 (13.3)	37.8 (12.1)	−4.3	**0.0018**	0.97 [0.94–0.98]	3.0	8.3	7.7	21.4
	Control	24.6 (2.5)	23.0 (2.6)	−6.5	0.5320	0.82 [0.31–0.94]	1.5	4.2	6.4	17.6
Base of support (m)	PwMS	0.1 (0.1)	0.1 (0.1)	−2.6	0.0855	0.98 [0.96–0.99]	0.0	0.0	8.2	22.6
	Control	0.1 (0.0)	0.1 (0.0)	2.1	**0.0001**	0.92 [0.80–0.97]	0.0	0.0	9.7	26.8
Toe in/out (°)	PwMS	8.6 (6.9)	9.3 (7.2)	7.8	**0.0244**	0.97 [0.95–0.98]	1.6	4.3	17.4	49.9
	Control	6.3 (3.4)	6.0 (3.6)	−5.6	**0.0000**	0.98 [0.96–0.99]	0.6	1.7	10.0	29.2
DTC (%)	PwMS	14.0 (13.3)	11.8 (13.2)	−15.5	0.1173	0.45 [0.06–0.67]	7 .4	20.5	57.3	158.7
	Control	8.4 (10.3)	6.1 (11.5)	−28.3	**0.0001**	0.83 [0.58–0.93]	5.9	16.3	81.1	224.7

T25FW: timed 25-foot walk; PwMS: People with Multiple Sclerosis; SD: standard deviation; Diff: difference between session 1 and session2; ICC: intraclass correlation; SEM: standard error of measurement; MDC_{95}: minimal detectable change; DTC: dual task cost; SEM%: standard error of measurement expressed as a percentage; MDC_{95}%: minimal detectable change expressed as a percentage.

Table 5
Gait parameters in TUG and 6MWT.

		Session 1 Mean (SD)	Session 2 Mean (SD)	Diff %	*p-value*	ICC (95%CI)	SEM	$MDC_{95\%}$	SEM %	$MDC_{95\ \%}$%
TUG (s)	PwMS	15.9 (13.0)	14.7 (11.3)	−7.9	**0.0151**	0.97 [0.95–0.98]	2.8	7.9	18.6	51.5
	Control	4.9 (0.9)	4.7 (0.7)	−3.1	0.2400	0.87 [0.67–0.95]	0.4	1.1	8.1	22.5
6MWT (m)	PwMS	262.1 (139 .3)	281.5 (143.2)	7.4	**0.0012**	0.98 [0.95–0.99]	31.01	86.1	11.4	31.7
	Control	655.5 (81.1)	705.8 (91.1)	7.7	**0.0020**	0.79 [0.22–0.93]	54.3	150.6	8.0	22.1

PwMS: People with Multiple Sclerosis; SD: standard deviation; Diff: difference between session 1 and session2; ICC: intraclass correlation; SEM: standard error of measurement; MDC_{95}: minimal detectable change, SEM%: standard error of measurement expressed as a percentage; MDC_{95}%: minimal detectable change expressed as a percentage.

The dual task is a clinically relevant outcome for people with MS, taking into account gait and cognitive disabilities [42]. The dual task cost, which indicates the extent of gait limitation due to the concomitance of cognitive involvement has been proposed as an outcome to evaluate interventions on walking [43]. However, if the dual task expressed in terms of gait speed is in line with simple task speed measurements (MDC_{95}% = 39.6%), the dual task cost requires a very great improvement to be detectable (MDC_{95}% = 158.7% for people with MS and 224.7% for controls).

For clinical interpretations, it is also important that the absolute values of the parameters are taken into account. The MDC_{95}% was substantially lower in the control group than in the patient group in most conditions, whereas absolute values were higher. This is due to the gait speed. In patients with a slow gait, a minimal modification will have a major impact on MDC_{95}%, exceeding these cut-off values. In the same way, a small improvement in the absolute value will appear artificially big, expressed as a percentage. It may be useful to take the absolute values and relate them to the ability to carry out daily activities, that is, considering the effect of the improvement on daily activities (for example, an improvement in gait speed allowing the participant to safely cross the road before traffic lights turn green) [44].

The study has some limitations. Same-day clinical fluctuations are often reported by people with MS. However, no study has been conducted to investigate these fluctuations in terms of gait. To avoid increasing variability due to this, it would be preferable to evaluate people systematically at the same time of day. This was not possible as it was too complex to organize. In addition, same-day clinical fluctuations are often reported by people with MS. However, fatigue but not gait measurements were affected by the time of day of the evaluations [45]. Indeed, this aspect should be take into account for future studies.

Only two evaluations were performed to evaluate reproducibility. For example, to obtain acceptable reliability in centre of pressure measurements, an average of three to five trials was proposed [46]. However, the increased number of measurements in a short period in the same population could lead to fatigue and limit the feasibility of the study.

5. Conclusions

Determining reproducibility is necessary in research to interpret gait changes after therapeutic interventions. In this study, reproducibility in several gait conditions and parameters was in line with previous studies in most of the parameters studied. Previous results of MICD should be interpreted with caution, because in most cases, the level of clinical improvement (i.e, 20%) is lower than the range in which an equivalent experimental set could be measured (Fig. 1).

In our study, the mean MDC_{95} for all conditions and parameters was 39.3% for patients and 22.9% for controls. These results must be tested in a therapeutic condition capable of improving the spatio-temporal parameters of gait.

Authorship statements

Decavel P. MD, PhD: funding, data acquisition, data analysis, protocol development, manuscript writing.

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Sagawa Jr Y. PhD: protocol development, data acquisition, data analysis, statistics, manuscript writing.

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Appendix A. Supplementary data

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