gait

MS

walking

study

variables

kinematics

ability

flexion

due

extension

direct

proximal

mid-stance

climbing

challenging

flexor

disturbance

assessment

proximal

scores

minimally

minimal

progressive

results

significant

progression

confirmed

methods

Although

groups

small

also

addition

normal

effective

clearance

forefoot

scored

inadequate

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motor

motor

activity

disease

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et al.

inclusion

controls

cerebral

PSA

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PSA

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Gait patterns in patients with Multiple Sclerosis

J.C.E. Kempen
C.A.M. Doorenbosch
V. de Groot
D.L. Knol
H. Beckerman
ABSTRACT

Background
Limited walking ability is an important problem for patients with multiple sclerosis (MS). A better understanding of how gait impairments lead to limited walking ability may help to develop more targeted interventions. Although gait classifications are available in stroke and cerebral palsy, relevant knowledge in MS is scarce. The purpose of this study is to identify distinctive gait patterns in patients with MS, based on a combined evaluation of kinematics, gait features and muscle activity during walking.

Method
Eighty-one patients (including 51 women) participated, with an age range of 28-69 years and a median EDSS of 3.0 (range 1.0-7.0). Participants were recruited from the longitudinal study FuPro MS. All patients participated in a 2D video gait analysis, with concurrent measurement of surface electromyography (EMG) and ground reaction forces. A score chart, developed by an expert panel, was used to rate each gait analysis. A single rater performed the scoring. Latent class analysis (LCA) was used to identify gait classes.

Results
Latent class analysis of the 73 variables determined during gait analysis revealed that nine variables could distinguish classes. Three gait classes were defined, based on heel-rise in terminal-stance, push-off, clearance in initial swing, plantar flexion position mid-swing, pelvic rotation, arm-trunk movement, activity of the m. gastrocnemius in pre-swing, M-wave and the propulsive force. The EDSS score and gait speed worsened in ascending classes.

Conclusion
Based on a core set of nine variables measured with clinical gait analysis, patients with MS could be divided into three different gait classes. The gait variables of the core set were mainly related to push-off and clearance.
INTRODUCTION

In patients with multiple sclerosis (MS), motor deficits most commonly affect the lower extremities, leading to limitations in walking ability and daily activity.\(^1\) About 85% of the patients with MS indicate gait disturbances as the main complaint,\(^6,7\) which occur early in the MS disease course.\(^3\) Within 15 years of diagnosis, up on 50% of the patients require the assistance of a walking aid and 10% will be wheelchair dependent.\(^2\)

The course and progressive nature of MS implies that there will be changes in gait abnormalities over time. Since MS can affect diverse neurological systems, neurodegeneration might result in loss of muscle force, spasticity, impaired coordination and sensory impairment. Impairment in a single neurological system or in combination will contribute to a patient’s gait deviations and may result in a specific pattern of gait.\(^8\) A better understanding of the gait changes associated with disease progression is necessary to implement more targeted interventions and earlier clinical treatment. Categorising gait patterns could contribute to the development of such targeted treatments and may also facilitate clinical communication.\(^9,10\)

In stroke and cerebral palsy, gait analysis is a common method to plan and evaluate the treatment of gait disorders.\(^9-12\) According to Toro et al.,\(^9\) a gait ‘type’ can be defined when a group of patients display gait characteristics that are clinically identical in terms of aetiology, effect on gait and in the management of treatment. Patients with cerebral palsy are assigned to one of five gait patterns, mainly based on heel contact and knee position in mid-stance.\(^13\) Stroke patients have also been assigned to gait patterns based on kinematic variables during walking.\(^14\) Classifications in spastic hemiplegia and diplegia have a direct relevance in understanding the gait pattern and the treatment opportunities.\(^12\) It is therefore very plausible that the classification of gait patterns in MS patients would have considerable clinical utility.

A small number of studies have previously described gait patterns in patients with MS, with a focus on spatiotemporal parameters and differences to healthy controls.\(^1,4,15\) MS patients walk with a lower gait speed, shorter stride length and a more prolonged double support phase than healthy controls. However, these global spatiotemporal parameters do not reflect potential
changes at the hip, knee and ankle joint or describe the quality of gait.\textsuperscript{[6,16]} A more complete gait assessment will therefore be achieved by including the kinematics of the lower extremities.\textsuperscript{[6]} Several studies have measured both spatiotemporal parameters and kinematics,\textsuperscript{[2,6,17,18]} and they all found significantly smaller ranges of motion in the lower limb joints in patients with MS, compared to healthy controls. Kelleher et al.\textsuperscript{[2]} divided MS patients into good ambulatory and reduced ambulatory groups, but no significant differences in either spatiotemporal parameters or kinematics were found. A limitation, in regard to the interpretation of gait analysis, is that small differences in joint angles do not reveal the quality of walking.

Herbert et al.\textsuperscript{[19]} suggested an observational approach to evaluate gait features, combining several biomechanical variables during gait. Scoring gait features, such as push off and clearance, will be beneficial for the categorisation of gait in MS patients and a more complete gait analysis could be achieved with additional muscle coordination parameters derived from electromyography (EMG) and reaction force. In addition, 2D gait analysis to evaluate these gait features and qualitatively assess kinematics is easy to use in clinical practice and the interpretation of the results is more straightforward.

The purpose of this study was to explore whether distinct gait patterns in patients with MS could be identified, based on the combined assessment of kinematics, gait features and muscle activity during walking, which are assumed as clinically relevant items.

**METHODS**

**Participants**

The data in this study were obtained from patients who participated in a longitudinal study on outcome measurement and functional prognosis in early MS.\textsuperscript{[20]} An inception cohort of 156 recently diagnosed patients (within the previous 6 months), aged 16-59 years, was recruited between 1998 and 2000. For the measurement at 10 years post-diagnosis, 137 patients from the original cohort were approached, of whom 109 agreed to participate.
The measurements at 10 years were supplemented with additional physical tests that focused on walking ability. To complete these tests, patients had to be able to walk 10 meters without assistance from another person. A total of 81 patients completed the supplementary walking tests, as fifteen patients were not able to complete all measurements and 13 patients decided not to travel to the outpatient clinic.

The Medical Ethics Committee of the VU University Medical Center granted approval for this study.

**Measurements**

**Gait analysis**

All patients performed a 2D clinical gait analysis in which they were asked to walk barefoot over a 10 meter walkway at a comfortable walking speed and when possible, without a walking aid. Two high-speed video cameras recorded in the sagittal and frontal planes (sample frequency 50Hz; Basler Pilot piA640-210gc GigE, Basler, Germany), while synchronized electromyography (EMG) recorded signals from five muscles of each leg. Gait speed was monitored for each trial.

**Electromyography**

Electromyography activity was recorded (sample frequency 1000Hz; bandwidth of 20-1500 Hz; Aurion, Milan, Italia). After standard skin preparation, electrodes (Tyco Healthcare Nederland b.v., Zaltbommel, The Netherlands; Ag-AgCl; lead-off area 1 cm²; inter-electrode distance 2.5 cm) were placed longitudinally over the muscle bellies of the m. rectus femoris, m.semitendinosus, m. tibialis anterior, the medial and lateral m. gastrocnemius and the m. soleus.[21]

**Ground reaction force**

The vertical and fore-after components of the ground reaction force (GRF) were recorded with a built-in force plate at a sample frequency of 1000Hz.
(AMTI, OR6-5-1000, Watertown, Massachusetts, USA), synchronously with the video analysis. From the signals, the magnitude, direction and point of application of the GRF were calculated. Trials were repeated until a successful force plate strike for each foot was recorded.

**Descriptive variables**

The Expanded Disability Status Scale (EDSS) was used to indicate the severity of MS.\(^{[22]}\) Scores on the EDSS range from 0-10.

**Data analysis**

A score form was composed based on the literature,\(^{[11]}\) of which most kinematic items correspond to the reliable and validated Edinburgh Gait Scale,\(^{[23]}\) and in cooperation with both clinical and gait analysis experts. The score form consisted of three parts: kinematic, EMG and GRF. The chosen items were based on the prerequisites of gait defined by Gage,\(^{[11]}\) and all items had to be able to be scored from the 2D video analysis. Video and data analysis was done in the MoXie Viewer.\(^{[24]}\)

**Kinematics**

Kinematics were evaluated according to the list of items shown in Table 6.1a. Each item was scored as normal or by its deviation from normal.\(^{[11,25]}\) Push-off comprised the following kinematic parameters, absent heel-rise in terminal-stance, no clearance in initial swing and a lack of properly timed m. gastrocnemius activity in pre-swing.

**Electromyography**

The EMG signals were processed offline (low pass filter 2\(^{nd}\) order Butterworth, unidirectional at 2 Hz) to obtain smoothed rectified EMG envelopes (SR-EMG). For each gait phase, timing of muscle activity was scored as normal or aberrant compared to the muscle activity patterns of healthy individuals (see Table 6.1b).\(^{[11,25]}\) The scoring was done by visual inspection of the SR-EMG-signals.
## Table 6.1a Kinematic variables included in the latent class analyses

<table>
<thead>
<tr>
<th>Gait Phase</th>
<th>Item</th>
<th>Normal</th>
<th>Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial Contact</td>
<td>heel contact</td>
<td>heel</td>
<td>low heel(^a) toe</td>
</tr>
<tr>
<td>Loading Response</td>
<td>foot contact (LR)</td>
<td>total foot</td>
<td>no total foot</td>
</tr>
<tr>
<td></td>
<td>knee movement</td>
<td>flexion</td>
<td>no movement extension</td>
</tr>
<tr>
<td>Mid Stance</td>
<td>foot contact</td>
<td>total foot</td>
<td>early heellrise</td>
</tr>
<tr>
<td></td>
<td>translation tibia</td>
<td>translation</td>
<td>no translation flexion</td>
</tr>
<tr>
<td></td>
<td>knee movement</td>
<td>extension</td>
<td>hyper extension</td>
</tr>
<tr>
<td></td>
<td>hip movement</td>
<td>move to</td>
<td>flexion</td>
</tr>
<tr>
<td></td>
<td>position pelvic</td>
<td>neutral obliquity</td>
<td>contralateral drop</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>contralateral lift</td>
</tr>
<tr>
<td>Terminal Stance</td>
<td>heelrise</td>
<td>heelrise</td>
<td>early heelrise</td>
</tr>
<tr>
<td></td>
<td>knee extension</td>
<td>extension</td>
<td>flexion</td>
</tr>
<tr>
<td></td>
<td>hip extension</td>
<td>extension</td>
<td>flexion</td>
</tr>
<tr>
<td>Pre Swing</td>
<td>plantair flexion movement ankle</td>
<td>plantair</td>
<td>neutral</td>
</tr>
<tr>
<td></td>
<td>fast knee/hip flexion</td>
<td>flexion</td>
<td>dorsal flexion</td>
</tr>
<tr>
<td></td>
<td>active push-off(^b)</td>
<td>adequate</td>
<td>not adequate</td>
</tr>
<tr>
<td>Initial Swing/Mid Swing</td>
<td>clearance (ISw)</td>
<td>normal move to neutral/dorsal flexion</td>
<td>no clearance move to plantair flexion</td>
</tr>
<tr>
<td></td>
<td>ankle position</td>
<td>neutral</td>
<td>no movement</td>
</tr>
<tr>
<td></td>
<td>clearance (MSw)</td>
<td>normal</td>
<td>no clearance</td>
</tr>
<tr>
<td>Terminal Swing</td>
<td>positioning foot</td>
<td>dorsal flexion/inversion</td>
<td>neutral/eversion plantair flexion</td>
</tr>
<tr>
<td></td>
<td>extension knee</td>
<td>full extension</td>
<td>towards extension flexion</td>
</tr>
<tr>
<td></td>
<td>rotation pelvic</td>
<td>internal rotation</td>
<td>no rotation external rotation</td>
</tr>
<tr>
<td></td>
<td>arm-trunk movements</td>
<td>normal</td>
<td>less movements extra movements</td>
</tr>
</tbody>
</table>

\(^a\) Low heel: all foot contacts without clear heel or toe contact
\(^b\) Push-off: combination of absent heel-rise in terminal-stance, no clearance in initial swing and a lack of properly timed m. gastrocnemius activity in pre-swing

Abbreviations: LR: loading response; ISw: initial swing; MSw: mid-swing
**Table 6.1b** EMG variables included in the latent class analyses

<table>
<thead>
<tr>
<th>Gait Phase</th>
<th>Item</th>
<th>Normal</th>
<th>Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial Contact</td>
<td>m. hamstring</td>
<td>active</td>
<td>no activity</td>
</tr>
<tr>
<td>Loading Response</td>
<td>m. hamstring</td>
<td>active</td>
<td>no activity</td>
</tr>
<tr>
<td></td>
<td>m. rectus femoris</td>
<td>active</td>
<td>no activity</td>
</tr>
<tr>
<td></td>
<td>m. tibialis anterior</td>
<td>active</td>
<td>no activity</td>
</tr>
<tr>
<td>Mid Stance</td>
<td>m. soleus</td>
<td>no activity</td>
<td>active</td>
</tr>
<tr>
<td></td>
<td>m. gastrocnemius</td>
<td>no activity</td>
<td>active</td>
</tr>
<tr>
<td>Terminal Stance</td>
<td>m. soleus</td>
<td>active (peak)</td>
<td>no activity</td>
</tr>
<tr>
<td></td>
<td>m. gastrocnemius</td>
<td>active (peak)</td>
<td>no activity</td>
</tr>
<tr>
<td>Pre Swing</td>
<td>m. soleus</td>
<td>active (peak)</td>
<td>no activity</td>
</tr>
<tr>
<td></td>
<td>m. gastrocnemius</td>
<td>active (peak)</td>
<td>no activity</td>
</tr>
<tr>
<td>Initial Swing</td>
<td>m. rectus femoris</td>
<td>active</td>
<td>no activity</td>
</tr>
<tr>
<td>Initial Swing/Mid Swing/</td>
<td>m. tibialis anterior</td>
<td>active</td>
<td>no activity</td>
</tr>
<tr>
<td>Terminal Swing</td>
<td>m. soleus</td>
<td>no activity</td>
<td>active</td>
</tr>
<tr>
<td></td>
<td>m. gastrocnemius</td>
<td>no activity</td>
<td>active</td>
</tr>
<tr>
<td>Terminal Swing</td>
<td>m. hamstring</td>
<td>activity</td>
<td>no activity</td>
</tr>
</tbody>
</table>

Abbreviation: m: muscle

**Table 6.1c** Force plate variables included in the latent class analyses

<table>
<thead>
<tr>
<th>Gait phase</th>
<th>Item</th>
<th>Normal</th>
<th>Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole gait cycle</td>
<td>z-vector force</td>
<td>M-wave</td>
<td>no pattern</td>
</tr>
<tr>
<td>Pre Swing</td>
<td>y-vector force</td>
<td>Mean propulsive force [N]</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviation: N: Newton
Ground reaction force

The fore-after component of the GRF was used to determine the magnitude of the push-off force. The amount of push-off force (in Newton) was scored. The typical M-wave, the vertical component of the GRF, was scored as present (normal) or absent (abnormal) (see Table 6.1c).

Statistical analyses

The demographics of the study population were analyzed with descriptive statistics using the Statistical Package for the Social Sciences (SPSS, version 18.0 for Windows).

Mplus (version 6.1) was used for latent class analysis (LCA). The latent class model consists of 54 dichotomous, 17 categorical and 2 continuous variables (Table 6.1a–c). The latent classes are defined by the criterion of conditional independence. This means that within each latent class, each variable is statistically independent of every other variable. Maximum likelihood (ML) estimation was used to fit the latent class model to the dataset, and was repeated with 1500 different starting values to achieve a global maximum.

In order to determine the number of latent classes, we started by assessing one class and added an extra class stepwise until no further improvement in fit occurred. The model fit is estimated by fit indices, that is, Akaike information criterion (AIC) and Bayesian information criterion (BIC). Smaller values represent a more optimal balance of model fit and parsimony. Both AIC and BIC correct for the number of parameters in relation to the maximum possible number of parameters. Besides these two criteria, the model interpretability is an important factor in evaluating the model.

With the Bayes theorem, patients are assigned to one of the latent classes by calculating the posterior probability of patient membership in each class (person orientation), which tends to be the largest when the homogeneity within a latent class and the latent class separation are both strong. The class membership of patients gives an impression whether the formed classes are clinically useful. A variable was chosen as a variable distinctive between the classes when the probability of the same score (normal or aberrant) within
a class was 60% (homogeneity) and when the other class(es) had a higher probability of the contrary score (heterogeneity).

To evaluate the clinical relevance of the classes, additional analyses were carried out (SPSS, version 18.0 for Windows). EDSS and gait speed were used as indicative variables. A one-way ANOVA was performed to determine whether the means were significantly different between the classes. The Bonferroni post hoc test was performed in cases with a significant difference. Significance level was set at 0.05.

**RESULTS**

**Participants**

The 81 participants who visited the VU University Medical Center had a mean age 47.1 years (range 28-69), median EDSS was 3.0 (range 1.0-7.0), mean gait speed was 1.15 ms\(^{-1}\) (range 0.26 - 1.66) and there were 51 women and 30 men.

During the gait analysis, two participants used a single cane and four needed a walker. Force plate data were missing for the four participants who required a walker. EMG was missing for one participant.

**Latent Class Analysis**

The results of the iterative process to find the best fitting model are shown in table 6.2. Based on the model fit parameters, in combination with the model interpretability, it was decided that 3 was the optimal number of classes.

A core set of nine variables satisfied the conditions of within-class homogeneity and between-class heterogeneity: heel-rise terminal-stance, the push off, clearance initial swing, plantar flexion ankle mid-swing, pelvic rotation, arm-trunk movements, activity gastrocnemius pre-swing, the M-wave and the mean propulsive force. Table 6.3 shows the probability of an aberrant score for these variables in for each class. Figure 6.1 shows a typical example for each class.
Table 6.2 Model fit indices Latent Class Analyses

<table>
<thead>
<tr>
<th></th>
<th>Maximum Log Likelihood</th>
<th>Parameters</th>
<th>AIC</th>
<th>BIC</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 class</td>
<td>-3236.170</td>
<td>92</td>
<td>6656.339</td>
<td>6876.629</td>
</tr>
<tr>
<td>2 classes</td>
<td>-2647.309</td>
<td>185</td>
<td>5664.619</td>
<td>6107.592</td>
</tr>
<tr>
<td>3 classes</td>
<td>-2518.620</td>
<td>278</td>
<td>5593.239</td>
<td>6258.896</td>
</tr>
<tr>
<td>4 classes</td>
<td>-2441.940</td>
<td>371</td>
<td>5625.880</td>
<td>6514.220</td>
</tr>
</tbody>
</table>

Abbreviations: AIC: Aikake information criterion; BIC: Bayesian information criterion

Figure 6.1 Typical examples of the three gait classes in MS
The video stills show the clinical picture of the three classes (rows) from the position of the left leg. Each column corresponds to a variable of the core set, i.e. heel-rise in terminal-stance, clearance in initial swing and ankle angle in mid-swing. Patients in class 1 show a normal gait pattern. All three variables have a probability of 1.000. Patients in class 2 also show heel-rise, clearance and a sufficient ankle angle but less convincing compared with class 1 (probabilities respectively 1.000, 0.750, 0.583). The bottom row show characteristics of a class 3 patient with no heel-rise in terminal-stance (probability 0.714), no clearance (probability 0.786) and plantar flexion of the ankle in mid-swing (probability 0.857).
Gait patterns

Class 1
Terminal-stance
Heel-rise at contralateral IC

Class 2
Initial Swing
Clearance

Class 3
Mid-swing
Ankle angle
### Table 6.3 The core set of nine gait variables defining gait patterns in patients with MS

<table>
<thead>
<tr>
<th>Kinematics</th>
<th>Class 1 (N=55, 68%)</th>
<th>Class 2 (N=12, 15%)</th>
<th>Class 3 (N=14, 17%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Left</td>
<td>Right</td>
<td>Left</td>
</tr>
<tr>
<td>1. heelrise (terminal-stance)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>normal</td>
<td>0.982</td>
<td>1.000</td>
<td>1.000</td>
</tr>
<tr>
<td>early heelrise</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
</tr>
<tr>
<td>no heelrise</td>
<td>0.018</td>
<td>0.000</td>
<td>0.000</td>
</tr>
<tr>
<td>2. push-off</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>adequate</td>
<td>1.000</td>
<td>1.000</td>
<td>0.500</td>
</tr>
<tr>
<td>no adequate</td>
<td>0.000</td>
<td>0.000</td>
<td>0.500</td>
</tr>
<tr>
<td>3. clearance (initial swing)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>yes</td>
<td>1.000</td>
<td>1.000</td>
<td>0.750</td>
</tr>
<tr>
<td>no</td>
<td>0.000</td>
<td>0.000</td>
<td>0.250</td>
</tr>
<tr>
<td>4. postion ankle (mid-swing)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>neutral/dorsal flexion</td>
<td>0.964</td>
<td>0.945</td>
<td>0.583</td>
</tr>
<tr>
<td>plantarflexion</td>
<td>0.036</td>
<td>0.055</td>
<td>0.417</td>
</tr>
<tr>
<td>5. pelvic rotation (terminal-swing)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>normal</td>
<td>0.891</td>
<td>0.873</td>
<td>0.500</td>
</tr>
<tr>
<td>no rotation</td>
<td>0.109</td>
<td>0.127</td>
<td>0.500</td>
</tr>
<tr>
<td>external rotation</td>
<td>0.000</td>
<td>0.000</td>
<td>0.000</td>
</tr>
</tbody>
</table>
Table 6.3 (continued) The core set of nine gait variables defining gait patterns in patients with MS

<table>
<thead>
<tr>
<th>6. arm trunk movement</th>
<th>Class 1 (N=55, 68%)</th>
<th>Class 2 (N=12, 15%)</th>
<th>Class 3 (N=14, 17%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Left</td>
<td>Right</td>
<td>Left</td>
</tr>
<tr>
<td>normal</td>
<td>0.818</td>
<td>0.083</td>
<td>0.071</td>
</tr>
<tr>
<td>less movements</td>
<td>0.182</td>
<td>0.750</td>
<td>0.643</td>
</tr>
<tr>
<td>extra movements</td>
<td>0.000</td>
<td>0.167</td>
<td>0.286</td>
</tr>
</tbody>
</table>

EMG

<table>
<thead>
<tr>
<th>7. m. gastrocnemius (pre-swing)</th>
<th>Class 1 (N=55, 68%)</th>
<th>Class 2 (N=12, 15%)</th>
<th>Class 3 (N=14, 17%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>activity</td>
<td>0.852</td>
<td>0.963</td>
<td>0.917</td>
</tr>
<tr>
<td>no activity</td>
<td>0.148</td>
<td>0.037</td>
<td>0.083</td>
</tr>
</tbody>
</table>

Force plate

<table>
<thead>
<tr>
<th>8. M-wave</th>
<th>Class 1 (N=55, 68%)</th>
<th>Class 2 (N=12, 15%)</th>
<th>Class 3 (N=14, 17%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>M-wave</td>
<td>1.000</td>
<td>0.964</td>
<td>0.600</td>
</tr>
<tr>
<td>no pattern</td>
<td>0.000</td>
<td>0.036</td>
<td>0.400</td>
</tr>
</tbody>
</table>

Abbreviations: N: Newton
Terminal-stance, initial swing and mid-swing are presented, since these are the gait phases where, according to the core set, the classes are most distinctive from each other.

From the 30 EMG variables, only the non-activity of the m. gastrocnemius in pre-swing fulfilled the conditions of within-class homogeneity and between-class heterogeneity. In all classes, the patients had a high probability for pre-activity of the m. soleus and m. gastrocnemius in mid-stance (data not shown).

The force plate data showed the same course as the kinematic data. The probability of a normal M-wave decreased with each successive class. The same applies for the propulsive force, which significantly declined from class 1 to class 3.

### Clinical interpretation

In table 6.4, the median EDSS and mean gait speed are shown to confirm the clinical relevance of the classes. The median EDSS increased, whereas gait speed decreased, in the classes with reduced walking ability. The Bonferroni post hoc test showed a significant difference between the 3 classes for both variables (p<0.01).

**Table 6.4 Patients characteristics for each gait class**

<table>
<thead>
<tr>
<th></th>
<th>Class 1</th>
<th>Class 2</th>
<th>Class 3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>EDSS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>median</td>
<td>2.5</td>
<td>4.0</td>
<td>6.0</td>
</tr>
<tr>
<td>range</td>
<td>1.0 - 5.0</td>
<td>2.5 - 6.5</td>
<td>3.0 - 7.0</td>
</tr>
<tr>
<td><strong>Gait speed [ms⁻¹]</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>1.31 (0.145)</td>
<td>0.98 (0.177)</td>
<td>0.51 (0.196)</td>
</tr>
<tr>
<td>range</td>
<td>0.95 - 1.66</td>
<td>0.75 - 1.28</td>
<td>0.26 - 0.88</td>
</tr>
</tbody>
</table>

Abbreviations: SD: standard deviation
**DISCUSSION**

The aim of this study was to identify distinct gait patterns in patients with MS in order to facilitate targeted treatment for patients with walking disorders. The results showed that three classes could be defined based on a small set of combined kinematic and electromyographic variables.

From 73 variables determined in the gait analysis (39 kinematics, 30 EMG and 4 force plate), a core-set (Table 6.3) of nine variables satisfied all conditions required to distinguish between the three classes. A sensitivity analysis, with fewer variables in the LCA, confirmed that the set of nine variables is sufficient to achieve the same distinctive gait patterns (results not shown). This core set of variables can be easily observed with video analysis and enables a clinically relevant classification of patients with MS, related to the progressive course of the disease. The classes identify MS patients as good walkers (class 1), minimally impaired walkers (class 2) and moderately impaired walkers (class 3).

The results of our study show that the classes are based on a deterioration of the core set of nine gait variables. Kelleher et al.\(^2\) also expected to find degenerative gait patterns as a consequence of disease progression, but could not confirm this. These authors clustered MS patients *a priori* as good or impaired walkers, based on the Hauser Ambulation Index (HAI), but no significant differences in kinematics were found between these two groups. A functional score such as the HAI is apparently too aspecific and not directly related to the deviations in kinematics during walking.

The three distinct classes seem to be based on a progressive insufficiency of the push-off. Reduced push-off was determined from a combination of absent heel-rise in terminal-stance, no clearance in initial swing and a lack of properly timed m. gastrocnemius activity in pre-swing. The mean propulsive force component supported the observation of reduced push-off. In clinical practice, reduced push-off is commonly associated with kinematic changes of the more proximal joints, e.g. a decreased knee extension in terminal-swing and an increased hip flexion in pre-swing.\(^{27}\) A small increase in hip flexion is sufficient to achieve greater power in the hip joint, and this is a
common strategy to compensate for reduced push-off ability.\cite{2,18} In the present study, such small differences in joint angles were not measured, as a three dimensional (3D) gait analysis would have been required. Insufficient knee extension in terminal swing is a result of reduced acceleration of the leg in swing.\cite{28} Although knee extension in swing did not fully meet the criteria for inclusion in the core set, the latent class analysis showed an increased probability of an aberrant score in classes with impaired walkers (probability of knee flexion in terminal-swing: class 1: 16%; class 2: 58%; class 3: 57%).

The discrepancies found in kinematics could not all be explained by the deviations found in the EMG variables. For example, the persistent plantar flexion of the ankle during swing is inconsistent with the normal pattern of the m. tibialis anterior, which could be due to weakness of this muscle. However, in the present study EMG signals could not estimate individual muscle forces. Furthermore, despite early activity of the m. gastrocnemius and the m. soleus in mid-stance, a late heel-rise was found in the minimally impaired and moderately impaired walkers. Benedetti et al.\cite{18} found similar discrepancies between EMG abnormalities and the expected alterations of gait kinematics. They concluded that this early activation of the calf muscle might represent a primary gait disturbance, rather than a compensatory gait disturbance, since early activation of the calf muscles is observed with higher speeds during normal walking.\cite{29}

An advantage of the scoring method used in our study is that, gait features, e.g. push-off and clearance, were also scored, which are direct indicators for targeted treatment, such as orthoses or physical therapy. Although, 2D gait analysis is beneficial in clinical practice, the reliability of this method is often discussed.\cite{16,30} Based on the clinical relevance of our gait classes the used method is sufficient. The outcome of our scoring method corresponds with the gait speeds in the observed classifications, i.e. a higher walking class is related to lower gait speed. This agrees with findings often seen in patients with a reduced walking ability.\cite{31} Furthermore, the differences in EDSS scores between the classes also confirmed the deterioration in walking ability with this scoring method.
With regard to implications for clinical practice, our study shows that the gait patterns of MS patients can be classified by scoring a core set of nine variables. This classification seems useful for monitoring and evaluating patients with MS, as it reflects the degenerative course of the disease. Furthermore, since reduced push-off ability is one of the main causes of reduced walking ability, it will be a challenge to investigate whether treatment options, such as ankle-foot orthoses, are also effective in the MS population.

**Limitations**

Although 81 gait analyses to characterize gait patterns in MS patients gives a robust indication, several limitations should be considered. The study population consisted principally of participants with minimally to moderately impaired walking ability according to the EDSS, and most were classified in Class 1. Therefore, the number of patients in Classes 2 and 3, both impaired walkers, was relatively small and prevented subgroup analyses. These small amount of severe impaired patients and the fact that our patient group consists of patients with combined EDSS domains, made it unable to distinguish possible differences in gait parameters in EDSS domains, such as pyramidal and cerebellar. In addition, since the clinical gait analyses were conducted in a safe environment, barefoot, and without a walking aid where possible, translation of the results to daily activities will require further monitoring and evaluation.

**Recommendations for future research**

A priority of future research is to test the reliability and validity of the score form used in this study. Analogous to the gait classifications in cerebral palsy, another important line of investigation will be to determine whether ‘typical’ patterns can be recognized in patients with severe walking problems. To achieve this, more subjects need to be included. Furthermore, the proposed core set of variables should be evaluated in rehabilitation medicine.
CONCLUSION

This study showed a first step in the development of distinctive gait patterns in patients with MS. Based on a core set of nine variables measured with clinical gait analysis, patients with MS could be divided into three different gait classes. The gait variables of the core set were mainly related to the gait features push-off and clearance. This small set of kinematic variables, identified the gait classes, which coincided with the neurodegenerative pattern of the disease MS. These results indicate that there is potential for the use of gait classes in patients with MS, and important steps regarding reliability and validity have to be taken before clinical implementation is possible.
REFERENCES


