Assessment of muscle strength and motor fatigue with a knee dynamometer in subjects with multiple sclerosis: a new fatigue index
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What is This?
Assessment of muscle strength and motor fatigue with a knee dynamometer in subjects with multiple sclerosis: a new fatigue index

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Objective: To measure muscle strength and motor fatigue with a knee dynamometer and to assess the intra-rater reliability of measurements for maximal isometric extensor and flexor torques and the reliability of a new fatigue index (Fl) in patients with mild to moderate multiple sclerosis (MS).

Design: Repeated assessments with one-week intervals.

Setting: The Masku Neurological Rehabilitation Centre, Masku, and the Social Insurance Institution, Research Department, Turku, Finland.

Subjects: Twenty-eight MS patients.

Outcome measures: Maximal isometric torque during 5 s and fatigue of knee flexors and extensors during isometric contractions of 30 s were assessed. A new Fl was established and compared with the two previously used indices (Fl1 and Fl2). All three indices are based on the calculated area under the force versus time curve (AUFC), with Fl1 using the 30-s recording time in its entirety and Fl2 omitting the initial 5 s in the calculation. In the new fatigue index (Fl3), the time point of maximum (TPM) torque achieved by the subject is used as the starting point in the calculation. The patient's subjective fatigue was measured by Fatigue Severity Scale (FSS).

Results: The intraclass correlation coefficient (ICC) was 0.97 in maximal isometric torque measurements. Fl3 showed good intra-rater reliability (ICC = 0.68–0.86). None of the fatigue indices correlated with FSS.

Conclusions: Maximal isometric torque and motor fatigue of knee flexor and extensor muscles can be reliably measured using a knee dynamometer in MS patients. The new Fl proved to be a reliable model for MS patients.

Introduction

Multiple sclerosis (MS) is a demyelinating disease of the central nervous system which results in interruptions of nervous connection. Weakness and fatigue are the two most common symptoms of the disease. Muscle strength of leg muscles in patients with MS is lower than that in healthy subjects.1,2 The concept motor fatigue denotes increased weakness with exercise or abnormal sense of tiredness experienced by MS patients.2–7 Fatigue in MS has been assessed either by questionnaires or by measuring the worsening of function during sustained activity. The latter

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method is considered more accurate since MS patients tend to use the word fatigue imprecisely.

Methods for measuring muscle strength include manual muscle testing, hand-held myometry, and isometric or isokinetic dynamometer recording. A conventional way to measure motor fatigue is to compare the maximal strength at the beginning and end of a 30-s sustained muscle contraction.\(^2,9\) However, it has been established that methods based on the area under the force versus time curve during the 30 s of sustained muscle contraction are more reliable in MS patients\(^2,9\); ICCs between the test–retest measurements for these fatigue indices varied between 0.64 and 0.96, and, for comparison, between 0.46 and 0.77 for the conventional method.\(^2,9\)

There are few studies of the reliability of motor fatigue and isometric torque measurements in MS patients, and additional research is needed to confirm the reliability of these methods. Such studies would be of importance in evaluating the effectiveness of physical training interventions or rehabilitation programmes.

The purpose of this study was to examine the intra-rater reliability of isometric torque measurements in maximal knee extension and flexion, as well as three fatigue indices in 28 ambulatory patients with mild to moderate MS. Further, the relationship between the subjective fatigue experienced by the MS patients and the motor fatigue indices was examined.

## Methods

### Subjects

Twenty-eight subjects with mild to moderate MS (mean Expanded Disability Scale Score (EDSS)\(^\text{10}\) 2.1 ± 1, range 0–5.0) participated in the study (Table 1). Subjects with MS were recruited among patients waiting for an inpatient rehabilitation course at the Masku Neurological Rehabilitation Centre, Masku, Finland. The disability of the patients was determined by a neurologist experienced in the use of the EDSS. Patients were selected on the basis of the following inclusion criteria: (1) age between 30 and 54 years, (2) confirmed MS diagnosis,\(^\text{11}\) (3) EDSS of 0.0–5.5, and (4) voluntary participation. Criteria for exclusion were the following: (1) any cardiovascular or musculoskeletal disorder possibly hindering the completion of measurements, (2) a relapse in MS ≤ one month before the study, (3) any other medical, psychological or other reason suggesting that the patient might not be able to complete the repeated measurements.

The study was approved by the Ethical Committee of the South-Western Finland District of Health Care. All subjects gave their written informed consent for the participation in the study.

### Measurements

The isometric torque during 5 s and fatigue of knee flexors and extensors during isometric contractions of 30 s were measured by using a knee muscle dynamometer (Ab HUR\(^\text{®}\), Oy, Kokkola, Finland). The dynamometer uses a hydraulically powered lever arm that measures the isometric

### Table 1 Baseline characteristics of the MS patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>MS patients (n = 28)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender female/male (n)</td>
<td>16/12</td>
</tr>
<tr>
<td>Age, years (mean ± SD)</td>
<td>44 ± 7</td>
</tr>
<tr>
<td>Height, cm (mean ± SD)</td>
<td>171 ± 9</td>
</tr>
<tr>
<td>Weight, kg (mean ± SD)</td>
<td>76 ± 15</td>
</tr>
<tr>
<td>Employed (n)</td>
<td>12</td>
</tr>
<tr>
<td>Unemployed, retired or on sick-leave (n)</td>
<td>16</td>
</tr>
</tbody>
</table>
| Physical activity at leisure (n)\(^a\)        | Little: 6, Some: 16, Plent: 6 | 4
| Present sports activity (n)                   | 21                   |
| Previous sports activity (n)                  | 23                   |
| Years since the diagnosis, mean ± SD (range)  | 4.0 ± 5 (0–20)       |
| Relapsing-remitting course (n)                | 24                   |
| Primary/Secondary progressive course (n)      | 4                    |
| EDSS, mean ± SD (range)                       | 2.1 ± 1.0 (0–5)      |
| Subjective fatigue, FSS (mean ± SD)          | 4.8 ± 1.4            |
| Right knee extensor torque, Nm (mean ± SD)   | 133 ± 52             |
| Left knee extensor torque, Nm (mean ± SD)    | 121 ± 52             |
| Right knee flexor torque, Nm (mean ± SD)     | 77 ± 28              |
| Left knee flexor torque, Nm (mean ± SD)      | 71 ± 25              |

EDSS, Expanded Disability Status Scale; FSS, Fatigue Severity Scale

\(^a\) The amount of self-reported physical leisure activity (including gardening, household, sports activities etc.) on a three-point scale: plenty, some, little.
contraction of knee extensor and flexor muscles. The measurement was repeated after seven days. The repeated measurements were performed at the same time of day and the measurement protocol was always the same. Two investigators, both with two years’ experience in the use of the dynamometer, conducted all the tests.

**Measurement of maximal 5-s isometric knee extension and flexion torque (Nm)**

The subject sat on a chair with their hands on the handles on each side. In extension, the knee angle was 140° (180° refers to full extension) and the hip angle 110°, while in flexion the knee angle was 120° and the hip angle 110°. The subject was instructed to exert maximal extension and flexion torque and to maintain it for 5 s. Two attempts were measured for both legs with 2 min of rest between. The measurements always started with the right leg and extension.

The maximal isometric knee extension and flexion torque was recorded as the mean value of 1 s (200 Hz).

**The measurement of fatigue in 30-s sustained knee extension and flexion**

Seated as described above, the subject was instructed to exert maximal extension and flexion torque and to maintain it for 30 s. The torque signal was recorded on a computer for the subsequent calculation of the fatigue index (FI).

The measurement was performed once for each leg, starting with the right leg and with at least 2 min of rest between the attempts.

**Fatigue indices**

Fatigue index FI₁ (Figure 1a) was developed by Djaldetti et al.⁹ for knee extensors. The test–retest reliability of that index was evaluated by using ICC for repeated measurements, and Schwid et al.² have reported a coefficient of 0.75 in a study with MS subjects. The calculation is based on the area under the force-time (force giving the moment (Nm)) curve (AUFC) for the entire contraction period from 0 to 30 s. The AUFC during 30 s is divided by the hypothetical AUFC that would be obtained if the patient sustained maximal initial force during the whole 30 s.

\[
FI₁ = 100\% \times [1 - \left( AUFC_{0-30}/(F_{max, 0-5} \times 30) \right)]
\]

Fatigue index FI₂ (Figure 1b) is a modified model of FI₁ in which the first 5 s, when the torque generation is increasing toward a peak, are omitted in the FI calculation. The ICC of FI₂ for knee extensors was 0.83 in MS patients.² The AUFC for the period 5–30 s of the sustained contraction is divided by the hypothetical AUFC.
that would be obtained if the patient sustained the maximal force achieved during the first 5 s throughout the period from 5 to 30 s.

\[
F_{I2} = 100\% \times \left[1 - \left(\frac{\text{AUFC}_{5-30}}{(F_{\text{max}}, 0-5 \times 25)}\right)\right]
\]

Fatigue index \(F_{I3}\) (Figure 1c) is introduced in this study. The highest mean value of 1 s during the period from 0 to 5 s was chosen for the time point of maximum value of the muscle torque (TPM). The TPM serves as the starting point for the AUFC calculation. The AUFC from this point to the end of the contraction (30 s) is divided by the hypothetical AUFC that would be obtained if the patient sustained the same maximal force until the end of the 30 s.

\[
F_{I3} = 100\% \times \left[1 - \left(\frac{\text{AUFC}_{\text{TPM-30}}}{(F_{\text{max}}, 0-5} \times (\text{TPM-30}))\right)\right]
\]

**Fatigue Severity Scale (FSS)**

To assess subjective fatigue, the MS patients completed the nine-item self-report questionnaire developed and validated by Krupp *et al.* A high internal consistency was demonstrated by a Cronbach’s alpha of 0.88. Test–retest analysis between two time points, separated by 5 to 33 weeks, showed no statistically significant differences in a group of clinically stable patients with MS or systemic lupus erythematosus (SLE).

**Statistical analysis**

Intraclass correlation coefficients (ICC) of the mean torque value in extension and flexion for both legs together were calculated by random effects model to test the reproducibility (excellent >0.75, good =0.4–0.75). Reliability within the motor fatigue indices and the difference between them were assessed by repeated analysis of variance. The Bland–Altman method was used to determine the limits of agreement with 95% CIs between \(F_{I1}, F_{I2}\) and \(F_{I3}\). Spearman’s correlation coefficients were calculated between maximal isometric torques, fatigue indices and FSS. SAS software version 8.2 (SAS Institute, Cary, NC, USA) was used for all calculations.

**Results**

**Reproducibility of measurements**

The mean maximal isometric knee muscle torque during the first measurement session is presented in Table 1. The intra-rater reproducibility was \(r = 0.97\) in both isometric knee extension and flexion torque measurements.

The fatigue indices (\(F_{I1}, F_{I2}\) and \(F_{I3}\)) of the first measurement are presented in Table 2. The motor fatigue test–retest force versus time curves are visualized in Figure 2.

In motor fatigue measurements, the highest test–retest reliability coefficients in MS patients were observed for the indices \(F_{I1}\) and \(F_{I3}\) (Table 3). The reliability coefficients were >0.75 in knee flexion for all fatigue indices, while in extension the reliability was <0.75 for all indices. There were no statistically significant differences in the repeatability between the indices in MS patients (\(p = 0.99\) in extension and \(p = 0.77\) in flexion) (i.e., no time x index interaction was observed). However, the fatigue index levels of the indices \(F_{I1}\) and \(F_{I3}\) were significantly higher than those of \(F_{I2}\) (all \(p < 0.0001\)).

To visualize the reliability of \(F_{I3}\), the individual patient data for the two time points are presented.
Figure 2  Mean values for torque (Nm) versus time (s) during the 30-s fatigue measurements 1 and 2 in (a) knee extension and (b) knee flexion for male and female MS patients. Plotted with 1-s intervals to the end of the 30-s recording.

for knee flexor muscles (Figure 3a) and for knee extensor muscles (Figure 3b).

The limits of agreement (CIs) were 1.49 (-1.82, 4.80) and 21.74 (18.43, 25.06) between Fl3 and Fl2, and -2.57 (-3.25, -1.88) and 1.63 (0.95, 2.32)

Table 3 Intra-rater reliability coefficients (ICC) of fatigue indices Fl1, Fl2 and Fl3

<table>
<thead>
<tr>
<th></th>
<th>Fatigue index (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ICC</td>
</tr>
<tr>
<td><strong>Knee extensors</strong></td>
<td></td>
</tr>
<tr>
<td>Fl1</td>
<td>0.70</td>
</tr>
<tr>
<td>Fl2</td>
<td>0.68</td>
</tr>
<tr>
<td>Fl3</td>
<td>0.68</td>
</tr>
<tr>
<td><strong>Knee flexors</strong></td>
<td></td>
</tr>
<tr>
<td>Fl1</td>
<td>0.85</td>
</tr>
<tr>
<td>Fl2</td>
<td>0.81</td>
</tr>
<tr>
<td>Fl3</td>
<td>0.86</td>
</tr>
</tbody>
</table>

Reliability is calculated as the mean reliability of knee extensors and flexors (both legs) in MS patients (n=28).

between Fl3 and Fl1 in extension. The corresponding figures in flexion were 3.21 (0.49, 5.92) and 19.50 (16.78, 22.21) between Fl3 and Fl2, and -2.86 (-3.50, -2.21) and 1.08 (0.44, 1.73) between Fl3 and Fl1.

Significant positive correlation between the average and difference of Fl3 and Fl1 in flexion (r=0.47, p=0.01) and extension (r=0.43, p=0.02) was observed in MS patients. The positive correlation means that Fl3 tends to yield larger values than Fl1 at high fatigability, and the contrary is true at low fatigability.

Correlation between maximal torque (the 5-s maximal isometric torque measurement) and fatigue indices (the 30-s static fatigue measurement)

Fl2 correlated with the maximal isometric flexion torque: high maximal torque (Nm) was associated with high fatigability (%) (Table 4).
corresponding coefficients for knee extension were 0.26, 0.17 and −0.04. The relationship between FI3 and the FSS score is visualized in Figure 4.

Discussion

Isometric torque

The excellent test–retest reliability of the measurement of maximal isometric torque confirms that knee muscle strength can be reliably measured with a fixed knee dynamometer in patients with MS. The result of our study is supported by similar results of Schwid et al.2

Fatigue

The measurement of static fatigue was highly reproducible for all three indices. The indices FI1 and FI2 were also found to be highly reliable in the test–retest evaluation in a study of Schwid et al.,2 while in the same study the dynamic fatigue index showed poor reliability in repeated measures in MS patients (ICC 0.44). The conventional and simplest method to analyse the rate of fatigue is to compare the maximal torque at the beginning and at the end of the contraction.2,8 While suitable for examining the linearly increasing fatigue in hand muscles (m. adductor pollicis),15 this method could not be used in our study, because the fatigability of knee muscles does not show consistent linear increase. For knee muscles (slower contracting, postural and more fatigue resistant) it takes a longer time to reach the peak torque than for hand muscles (faster, more fatigable),16 and after reaching the peak, the fatigability is faster and the decline of the slope sharper for hand muscles.

In the present study, reliability was high for FI1 and FI3 in MS patients. However, FI3 offers several advantages in comparison with the previously used indices FI19 and FI2.2

FI3 is based on the calculation of the fatigue index from the exact TPM (time point of maximum), while FI1 includes the initial 5 s, when the subject is still increasing the force. The period with increasing force should not be included in the fatigability calculations. At high fatigability FI3 tends to give larger values than FI1, which is caused by the different cut-off points in calculating the indices FI1 and FI3, (area A in Figure 1a is included in the index calculation in FI1).

Figure 3 Individual patient data on fatigue index FI3 at measurement time 1 (F3_1) and 2 (F3_2) for (a) knee flexor and (b) knee extensor muscles, with identity line.

Correlation between FI1, FI2, FI3 and FSS

At baseline measurements, the correlation coefficient between knee flexion FI1 and FSS was 0.23 (ns), between FI2 and FSS 0.17 (ns) and between FI3 and FSS it was −0.004 (ns).
Table 4 Spearman correlations between isometric torque (Nm) and fatigue indices (F11, F12 and F13) in the first measurements on the right side and during the 30-s fatigue test in MS patients (n = 28)

<table>
<thead>
<tr>
<th>Fatigue index</th>
<th>Extensor torque (Nm)</th>
<th>Flexor torque (Nm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>F11</td>
<td>-0.23</td>
<td>0.21</td>
</tr>
<tr>
<td>F12</td>
<td>-0.15</td>
<td>0.43*</td>
</tr>
<tr>
<td>F13</td>
<td>-0.22</td>
<td>0.21</td>
</tr>
</tbody>
</table>

*p < 0.05.

In F12, the initial time period of 5 s is omitted. Figure 2 shows that MS patients usually reach the TPM earlier than at 5 s (approximately within 2–3 s). In F12, the fatigue index calculation starts at a time point when the decline in torque has already started and probably continued for a few seconds. Consequently, this results in far too low values. The index calculation used in F12 also unnecessarily shortens the time period (30 s), and as shown in Figure 2, subjects succeed in maintaining the muscle force at a relatively high level until the end of the measurement. The distortion of this index is probably more pronounced if the subject achieves maximum force very fast and the decline in force is also rapid. In this case, the calculated fatigue index is misleading, and a lot of valuable information is hidden during the period of 0–5 s.

We found correlations between the maximal 5 s isometric flexion torque measurement and F12. The correlation indicates that those with high isometric torque values showed high fatigability. Earlier, Schwid et al.2 did not find any correlation between weakness and fatigue, while Djaldetti et al.9 did. The origin of fatigue and weakness and their interaction remain unsettled.2,7,17–20 In our study, motor fatigue had no correlation with subjective fatigue, which is in line with the results of Sharma et al.,17 indicating that fatigue has both peripheral and central components. The reason for the lack of any correlations between the fatigue indices (F11, F12 and F13) and FSS may be that they measure different things (i.e., motor fatigue and generalized fatigue, respectively). Further, it has been argued that the FSS scale is a measure of fatigue quality rather than fatigue severity, although the internal consistency, test–retest reliability and responsiveness of FSS have been established.7

A limitation in our study was the fact that the MS patients were not severely affected by the disease. Also, the study sample should have been larger than 28 subjects. Although 30 s may be a sufficient time for sustained muscle contraction in more disabled MS patients, the time could have been longer, perhaps 45 s, for this patient sample (mean EDSS 2.1). This would have made the test more sensitive in measuring motor fatigue.

Clinical messages

- Maximal isometric strength of knee muscles can be reliably measured in MS patients with a fixed knee extensor dynamometer.
- A new fatigue index is reliable for the assessment of motor fatigue of knee muscles in MS patients.
The new fatigue index, FI3, is highly reproducible and accurate in fatigue measurements. It offers a useful tool for detecting motor dysfunction in MS. Hopefully, the measurement method presented here is of use in planning and following up the rehabilitation for patients with MS. However, additional studies are necessary to develop more accurate and sensitive methods for measuring fatigue.

Acknowledgements
This study was supported by a grant from the Social Insurance Institution of Finland.

References