Measuring Motor Fatigability in the Upper Limbs in Individuals With Neurologic Disorders

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SYSTEMATIC REVIEW

Measuring Motor Fatigability in the Upper Limbs in Individuals With Neurologic Disorders: A Systematic Review

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Abstract

Objective: To summarize the literature on definitions, assessment protocols, and outcome measures for motor fatigability in patients with neurologic problems and investigates the known clinimetric properties according to the COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN) criteria.

Data Sources: Two databases were consulted for studies published between January 2003 and November 2018 using the terms “motor fatigability,” “nervous system disease,” and “upper limb.”

Study Selection: Studies were included if they were (1) not older than 15 years; (2) written in English, German, or Dutch; (3) involved upper limbs of patients with neurologic disease; and (4) adequately described protocols using maximum voluntary contractions.

Data Extraction: Thirty-three studies were included, describing 14 definitions, 37 assessment protocols, and 9 outcome measures. The following data were obtained: (1) author and publication year; (2) aim; (3) fatigability definition; (4) sample characteristics; (5) fatigability protocol; (8) measurement system; and (9) outcome measure.

Data Synthesis: Protocols relating to body function level of the International Classification of Functioning (ICF) were most often performed in patients with multiple sclerosis (MS) including maximal or submaximal, isometric or concentric, and eccentric contractions of variable duration. For ICF activities level, most protocols included wheelchair-related tasks. Clinimetric properties were known in 2 included protocols. Test-retest reliability in patients with MS were moderate to excellent for the static fatigue index and moderate for the dynamic fatigue index.

Conclusions: Based on physiology, recommendations are made for protocols and outcome measures for motor fatigability at the ICF body function level. For the ICF activities level, too little is known to make sound statements on the use of protocols in populations with neurologic disease. Clinimetric properties should be further investigated for populations with neurologic problems.

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Fatigue is described as one of the most common symptoms in people with neurologic disorders and has a large influence on activities of daily living (ADL). Kluger et al1 developed a taxonomy for fatigue that distinguishes 2 main components: trait and state fatigue. While trait fatigue is defined as “a subjective lack of physical or mental energy perceived by the individual,” state fatigue (fatigability) is described as “fatigue dependent on the circumstances and fluctuating in time.” Within fatigability, 2 subcomponents can be distinguished: cognitive and motor. Motor fatigability can further be divided into a perceived and an objectively measurable part, the latter is called performance fatigability. Performance motor fatigability can be measured by quantifying the decline in 1 or more aspects of performance during prolonged task execution or comparing performance on a probe task before and immediately after prolonged performance of...
populations are available. In a recent review, Severijns et al.\textsuperscript{10} No data regarding test-retest reliability of this measure in other groups without neurologic conditions. In patients with MS, the prevalence of fatigue is reported to range between 40% and 80%.\textsuperscript{1} For patients with MS but also those with stroke, fatigue is reported to be a disabling symptom that impairs physical and social functioning and has a large influence on daily functioning such as carrying groceries.\textsuperscript{1,3} Motor fatigability in the upper limbs has also been shown to be associated with cognitive fatigue.\textsuperscript{14} However, research on this topic includes diverse outcomes resulting from different quantification methods and small sample sizes.\textsuperscript{5-7}

Most research on motor fatigability has focused on patients with MS. In these, the objective measure most often used is a test during which the patient performs a maximal contraction of hand grip, elbow flexion, or shoulder abduction for 30 seconds.\textsuperscript{8,9} Then, motor fatigability is quantified based on a ratio between the area under the curve (AUC) and the hypothetical area under the curve (HAUC) in the absence of fatigue. The test-retest reliability of this quantification for hand grip and elbow extension is moderate to excellent.\textsuperscript{8} However, the reliability of tests of shoulder abduction and elbow flexion still needs to be assessed in patients with MS. No data regarding test-retest reliability of this measure in other populations are available. In a recent review, Severijns et al.\textsuperscript{10} concluded that, even for MS, there is no criterion standard to assess motor fatigability because of the diversity of protocols and outcome measures and the limited information on clinimetric properties.

In conclusion, research on upper limb motor fatigability in patients with neurologic conditions presents with diverse outcomes that may be due to small sample sizes and a diverse use of motor fatigability protocols. It is, therefore, important to provide an overview of this literature. Also, clinimetric properties of protocols used to measure upper limb motor fatigability need to be investigated. This systematic review aims (1) to provide a systematic overview of used definitions, protocols, and outcome measures used for quantifying motor fatigability in the upper limbs of neurological populations and (2) to summarize clinimetric properties of these outcome measures according to the COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN) criteria.\textsuperscript{11}

### Methods

#### Data sources and search

Two databases (PubMed and Web of Science) were searched using a combination of (MeSH) terms and keywords: “muscle fatigue,” “muscular fatigue,” “fatigue, muscular,” “motor fatigue,” “fatigue resistance,” “fatigability,” “muscle endurance,” “neurovascular system disease,” “multiple sclerosis,” “cerebral palsy,” “hemiplegia,” “traumatic brain injury,” “upper extremity,” “upper limb,” “extremity, upper,” “arm,” and “hand.” The initial search was done in January 2018 and updated in November 2018.

#### Study selection

Studies were selected based on title and abstract by 2 independent reviewers. Studies were divided equally among 5 reviewers (J.V., P.H., L.M., M.M., L.B.). The selection was based on 4 criteria: (1) written in English, German, or Dutch; (2) published in the last 15 years; (3) included persons with neurologic disorders; and (4) fatigability measured in the upper limb(s). Reviews, interventional studies on the effectiveness of medication, conference papers, meeting reports, and letters were excluded. After exclusions based on title and abstract, the studies were divided among the 5 reviewers (J.V., P.H., L.M., M.M., L.B.), and each again screened by 2 reviewers with the following additional inclusion criteria: (1) fatigability protocol and calculations adequately explained and (2) motor fatigability based on voluntary muscle contraction. Studies based on electrical stimulation were excluded. In case of disagreement between 2 reviewers in each of the previously mentioned steps, consensus was reached by consulting a third reviewer (E.R.). Reference lists of included papers were checked for further relevant articles.

#### Quality assessment

To assess the quality of the included studies, 3 different checklists were used. For cohort studies and case-control studies, the Newcastle-Ottawa scale (NOS) was used. This scale rates studies based on 8 items categorized in 3 domains: (1) selection of study groups (3 stars); (2) comparability of the groups (2 stars); and (3) ascertainment of either the exposure or the outcome of interest (3 stars). Stars are awarded based on each item, and a total of 9 stars can be awarded.\textsuperscript{12}

To assess randomized studies, a risk of bias (RoB) tool was used. The tool assesses 16 items categorized in 5 domains: (1) randomization; (2) deviations from intended interventions; (3) missing outcome data; (4) measurement of outcome; and (5) selection of reported results.\textsuperscript{13} For each category, RoB is assessed as “low,” “some concerns,” or “high,” after which an overall RoB is assessed.

To assess nonrandomized studies, a tool for RoB in non-randomized studies (ROBINS-I) was used. Here, studies were assessed on 7 domains: (1) bias due to confounding; (2) bias in selection of participants in the study; (3) bias in classification of interventions; (4) bias due to deviation from intended intervention;
(5) bias due to missing data; (6) bias due to measurement of outcomes; and (7) bias due to selection of reported results.14

For each included study, the relevant checklist was filled out independently by 2 reviewers (L.B., E.R.), after which the reviewers checked for any differences. In case of disagreement, a third reviewer (K.K.) was consulted.

Data extraction

The following data were extracted from the included studies: (1) author and publication year; (2) study aim; (3) fatigability definition; (4) sample characteristics; (5) fatigability protocol; (6) measurement system; and (7) outcome measure. Studies reporting protocols for a single muscle group or limb during nonfunctional activities were classified as referring to the ICF body function level. Studies reporting muscle fatigue during the performance of functional activities were classified as relating to the ICF activities level.

Clinimetric properties

The COSMIN protocol was used, this being a 4-point rating scale (excellent, good, fair, poor) recommended for the use in systematic reviews of clinimetric properties. The checklist contains 9 boxes, each describing 1 measurement property (internal consistency, reliability, measurement error, content validity, structural validity, hypothesis testing, cross-cultural validity, criterion validity, and responsiveness). Each box contains between 5 and 18 items explaining how each specific clinimetric property should be assessed. For each measurement protocol, an additional manual literature search was done to identify clinimetric studies on patients with a neurologic disorder. Also, first authors of included studies were contacted to enquire whether there were any nonpublished data on clinimetric properties. The COSMIN checklist was filled out by 2 independent reviewers (L.B., E.R.).

Results

Study selection

A total of 568 studies were found, of which 520 remained after deduplication, of which 33 papers were included (fig 1).

Quality of the included studies

A total of 28 studies were rated with the NOS, 1 case-control study,15 and 27 cohort studies.5-10,16-36 Scores ranged from 0-7 stars. Five studies received 7 stars23,24,27 and 2 studies received no stars.6,7 Most problems with the quality of the studies were due to
Results of the RoB rating indicated that only 1 study had an overall low RoB, with the only issue being with the selection of the participants in the study.37 The results indicated an overall serious RoB in 1 study and a moderate RoB in 2 studies.38,39 Most problems originated from the selection of the participants, handling of missing data, and the measurement of the outcomes (supplemental table S3, available online only at http://www.archives-pmr.org/).

### Data extraction and study aims

The aims of the included studies were varied. In most of the studies (21 studies out of 33) the aim was to investigate the

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### Table 1

<table>
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<th>Authors</th>
<th>Diagnosis</th>
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<th>Mean Age (y) ± SD</th>
<th>Included Patients</th>
<th>Diagnosis</th>
<th>No.</th>
<th>Mean Age (y) ± SD</th>
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Note: A hyphen (-) indicates not specified.

Abbreviations: CMT1A, Charcot-Marie-Tooth type 1A; CTS, carpal tunnel syndrome; GBS, Guillain-Barre´ syndrome; HC, healthy control; MG, myasthenia gravis; NMD, neuromuscular disease; TOS, thoracic outlet syndrome.

* Indicates units are in months.
occurrence of motor fatigability in different populations with neurologic conditions\textsuperscript{5-9,15,18-22,24,27,29-36} (table 1).

**Fatigability definitions**

Fourteen different definitions for fatigability were reported. Most described a decrease in force or power or a decrease in performance. Others referred to an increase in effort during fatigue\textsuperscript{8} (table 2).

Twelve definitions related to the ICF body function level as they described a decrease in muscle force or power.\textsuperscript{5,8-10,16,18,22,24,25,27,29,31-33,35} Only 2 definitions also referred to the ICF activities level, as they described a decrease in performance of a functional task, next to a decrease in mechanical output.\textsuperscript{17,26} In 14 studies, no definition for motor fatigability was provided.

**Subject populations**

In total, 712 subjects were included in the studies, ranging from 6-60 subjects per study. In 11 studies, subjects with MS were included,\textsuperscript{8-10,15-17,21,29,31-33,35} 6 studies included children with CP,\textsuperscript{5,18,20,34,36,39} and 5 studies included subjects with SCI\textsuperscript{15,28,37,38,40} (see table 1).

**Motor fatigability protocols**

Thirty-seven different fatigability protocols were described in the 33 included studies. For the ICF body function level, a total of 31 protocols were used, 23 involving sustained isometric contractions, and 8 involving repeated concentric and eccentric contractions (fig 2). For the ICF activity level, 6 different protocols were described, consisting of tasks such as throwing a ball, propelling a
wheelchair, and playing a video game. Detailed information on all protocols can be found in supplemental table S4 (available online only at http://www.archives-pmr.org/).

Protocols for the ICF body function level

The protocols for the ICF body function level were categorized according to muscle and muscle groups and the intensity and duration of the activities.

Muscle and muscle groups

Different tests were used to assess motor fatigability with isometric contractions (see supplemental table S4). Ten protocols used grip strength contractions, 8,21-25,27,34-36,39 5 elbow flexion contractions, 6,7,26 and 2 elbow extension contractions. 38 Contractions of index finger abduction, shoulder abduction and flexion, and contractions of the trapezius muscle were each used in 1 protocol. 5,9,40

Eight protocols used repeated concentric and eccentric contractions. These tasks consisted of repeated hand grip contractions, 8,9,16,17,21,25, small finger abduction, 41,17,25,27,35-36,39-40,36-38 shoulder flexion, and repeated shoulder flexion and extension movements. 30

Intensity of muscle contractions

Twenty-three protocols used isometric muscle contractions. Of these, 14 used a maximal isometric contraction 5,8,9,16,17,21,25,34-36,39 and 9 used submaximal isometric contractions with intensities ranging from 10%–80% of maximal contractions 5,8,9,16,17,21,25,34-36,39 (see fig 2). Eight protocols used repeated contractions to investigate motor fatigability. 5,6,7,16,17,21,25,34-38 Of these, 5 used maximal contractions 5,8,9,16,17,21,25,34-38 and 3 used submaximal contractions 5,6,7,16,17,21,25,34-38 (see supplemental table S4).

Task duration

In the protocols that used an isometric task, the most common timeframe for measurement was between 8.3 seconds and 3 minutes. 6,7,16,17,21,25,34-36,39 Five protocols used exercise “until task failure” 5,6,7,16,17,21,25,34-38 (see fig 2).

In 8 repeated contraction protocols, 7 different numbers of repetitions were used. Fifteen repetitions were used in 2 protocols 5,8,16,17,25, all other numbers of repetitions (5, 10, 18, 23, 25, 30, 60, and until task failure) were each used only in 1 protocol. 9,20,21,30 The duration per contraction ranged from 1-7 seconds per repetition (see fig 2).

Protocols for ICF activities level

For the ICF activities level, 6 different protocols were identified. One protocol consisted of a serious gaming task during which participants played a game 5 times for 3 minutes per trial. 29 The goal of the game was to collect as many points as possible by painting penguins with the matching color using a HapticMaster robot with their affected arm. 29

In 2 protocols, participants were asked to first propel a wheelchair at their own pace for 5 minutes and then at a speed of 1 m per second for 5 minutes. 15 In 2 protocols, arm crank
ergometry was used, asking participants to propel their arms as fast as possible against a predetermined load for 30 seconds. In 1 protocol, subjects had to hold a wheelchair in position while a predetermined load pulled the wheelchair back. The load was set at 60% of maximum possible load.

One protocol used throwing a ball. Here, participants first had to throw a ball 3 times, as fast as possible, and then throw 72 times aiming at a target.

Motor fatigability outcomes

Of all 37 protocols quantifying motor fatigability, the outcome measures could be divided into 3 categories: strength-based outcomes; electromyography-based outcomes; and task-specific outcomes (see supplemental table S4).

Strength-based outcomes

Twenty-five protocols used different calculations of strength as an outcome measure for fatigability. In general, 3 different methods were used: percentage of change in maximum voluntary contraction (MVC) force; static fatigue index (SFI); and a dynamic fatigue index (DFI). The SFI is a fatigue calculation based on the AUC of a force-time curve, divided by a HAUC, mimicking a situation where strength would have been sustained at maximum level during the trial. Four slightly different calculations have been described in the literature. SFI1 is based on the AUC divided by the HAUC for the entire 30 seconds of the trial; SFI2 is based on dividing the AUC of only the last 25 seconds by the peak strength (Fmax) within the first 5 seconds (Tmax0-5) multiplied by 25; SFI3 is based on AUC after the peak strength within the first 5 seconds (Tmax0-5) divided by the HAUC from Tmax0-5 onward; SFI4 is different from SFI3 in that Tmax is determined not within the first 5 seconds, but within the first 10 seconds of a 30-second trial. The 4 different equations for SFI are described:

\[ \text{SFI1} = 100\% \times \frac{\text{AUC}_{0-30}}{\text{HAUC}_{0-30}} \]

\[ \text{SFI2} = 100\% \times \frac{\text{AUC}_{5-30}}{\text{F}_{\text{max}0-5} \times 25} \]

\[ \text{SFI3} = 100\% \times \frac{\text{AUC}_{\text{Tmax}0-5}}{\text{HAUC}_{\text{Tmax}0-5}} \]

\[ \text{SFI4} = 100\% \times \frac{\text{AUC}_{\text{Tmax}0-10}}{\text{HAUC}_{\text{Tmax}0-10}} \]

The DFI is a ratio calculated by dividing the last 3 (MVC2) dynamic hand grip trials by the first 3 (MVC1) trials, as described by Schwidd et al. The DFI is calculated as follows:

\[ \text{DFI} = 100\% \times \frac{\text{MVC2}}{\text{MVC1}} \]

Electromyography-based outcomes

Thirteen protocols used secondary outcomes consisting of different parameters of surface electromyography during both isometric sustained and repeated contractions, but also during the penguin painting task, throwing a ball, and while propelling a wheelchair. Here, root mean square was used in 7 protocols, mean frequency in 6 protocols, and median frequency in 5 protocols, while the amplitude, co-contraction ratio, and muscle fiber conduction velocity were used once each (see supplemental table S4).

Task-specific outcomes

Task-specific outcomes for the quantification of motor fatigability consisted of the time-to-fatigue (7 protocols), the difference between a target value and the actual force produced while squeezing a grip force device (1 protocol), differences in wheelchair kinematics at the beginning and end of a fatiguing exercise (3 protocols), game scores (1 protocol), and ball speed and target hitting rate by throwing a ball (2 protocols) (see supplemental table S4).

Clinimetric properties

Of all 41 outcome measures, only 1 study reported on the clinimetric properties of the SFI1-SFI3 and the DFI (supplemental table S4, available online only at http://www.archives-pmr.org/). For the SFI and DFI, only test-retest reliability measures were reported in subjects with MS, which indicated intraclass correlation coefficient (ICC) values of between 0.46 (SFI1) and 0.96 (SFI3) for handgrip and 0.64 (SFI2) and 0.77 (SFI1) for elbow flexion. This resulted in a poor COSMIN score for test-retest reliability. The DFI resulted in an ICC value of 0.44 (COSMIN score: poor). Also, correlations between SFI1-SFI3 and DFI were reported, resulting in a low and nonsignificant correlation coefficient (r = 0.07; P > 0.05), indicating a low validity.

Discussion

This systematic review summarizes the definitions, measurement protocols, and outcome measures on upper limb motor fatigability in populations with neurologic disease. Furthermore, we investigated the clinimetric properties of the protocols described. Thirty-three studies were included, with 15 different fatigability definitions and 37 different motor fatigability protocols. This large variety in the definitions, upper limb protocols, and outcome measures used with subjects with neurologic conditions hinders direct comparisons between different studies. Furthermore, virtually nothing is known about the clinimetric properties of the outcome measures used.

Fatigability definitions

In the taxonomy for fatigue, Kluger et al introduced a definition for motor fatigability, which was also incorporated in the study of Severijns et al. They defined motor fatigability as “an exercise-induced reduction in the ability of muscles to produce force or power, regardless of whether a task can be sustained.” In order to achieve consensus and because this definition specifies the outcome measure (ie, force or power, and measures motor fatigability objectively), it is suggested that future research incorporates this definition for motor fatigability.

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**Protocols and outcome measures**

**Body function level**

The protocols included in this systematic review were very diverse and investigated motor fatigability at different levels of the ICF model. Thirty-one protocols relating to the ICF body function level were identified, using muscle contractions and strength tests to induce motor fatigability. The tests at body function level in the included protocols varied between maximal and submaximal contractions in an isometric and repeated approach with a duration of between 8.3 seconds and 3 minutes or until task failure. Based on the physiological principles of the alactic, anaerobic energy supply system, when using maximal voluntary contractions time to failure is to be expected within 30 seconds.\(^{[43]}\) This means that protocols lasting longer than this timeframe do not add anything to our understanding of motor fatigability.\(^{[5]}\) This is in accordance with our finding that protocols in which a maximal contraction is used for 30 seconds, are able to discriminate between different neurologic conditions, and can distinguish between patients and controls without neurologic conditions.\(^{[5,23]}\) Submaximal contractions, when both the alactic and lactic anaerobic energy supply systems are utilized, a timeframe of up to 90 seconds is appropriate. Therefore, it is recommended that, when using maximal contractions, a fatigability protocol should last up to 30 seconds whereas a submaximal protocol should last up to 90 seconds.\(^{[5,23,43]}\)

The protocols included a variety of different outcome measures mainly focusing on strength decline, such as the SFI calculated as the AUC,\(^{[8,10,25,27,34,39]}\) a percentage decline,\(^{[6,7,16,17,21,23,24,31,33]}\) or electromyography measures comparing strength with motor unit recruitment.\(^{[5-7,9,10,18,23,26,28,29,34,36,38]}\) Using the SFI in a 30-second maximum voluntary isometric contraction in subjects with MS, motor fatigability has been studied quite extensively. This method for quantifying motor fatigability has been shown to have a poor-to-excellent test-retest reliability (ICC, 0.46-0.96) in this population. However, the clinimetric properties have not been tested in other populations.\(^{[12]}\) Furthermore, the DFI has been used in the same population to quantify a strength decline using 15 repeated MVC within 30 seconds. This method has been shown to have a poor test-retest reliability (ICC, 0.44) and needs to be optimized before being tested and used in other patient populations.\(^{[44]}\) However, the protocol does show promise in patients with MS since it was able to discriminate between subjects with MS and controls without MS.\(^{[42]}\)

In the protocols identified, different muscles and muscle groups were tested, including grip strength, wrist and elbow extension, and wrist and elbow flexion, along with shoulder flexion and abduction. When deciding what muscle or muscle group to investigate, one should consider which of these are most relevant to daily life in the specific patient population. In people with MS, motor fatigability has already been investigated using index finger abduction, grip strength, elbow flexion, and shoulder abduction.\(^{[10]}\) Using the SFI, it was shown that there were significant correlations between both the SFI during elbow flexion and shoulder abduction and the Manual Ability Measure-36, indicating a relation between fatigability in proximal muscles and the use of upper limbs in everyday life. However, no significant correlation was found between the SFI of hand grip and index finger abduction and any of the perceived fatigue scales.\(^{[10]}\) This indicates that in this population motor fatigability in proximal muscle groups may be more relevant to investigate than distal ones. Also in patients who are wheelchair-bound due to SCI, it may be more relevant to investigate motor fatigability in proximal muscles, or muscle groups related to wheelchair use. Fay et al\(^{[15]}\) have investigated the differences in wheelchair dynamics between people with MS, patients with SCI, and people without disabilities. They concluded that the population of people with MS lost a larger percentage of power per push after fatigue indicating higher motor fatigability in this population than with patients with SCI and people without disabilities.\(^{[15]}\) However, patients with SCI also show more motor fatigability than controls without neurologic problems, which indicates the need to investigate fatigue in the proximal muscles of these patient populations.

In children with CP, Lemmens et al\(^{[44]}\) identified key tasks in the ADL. They then identified key components per task and concluded that for cutting meat, the key component was pushing, pulling, or shoving of the dominant hand, and holding and fixating for the assisting hand. This indicates that for the affected hand distal muscle strength and motor fatigability may have a larger effect on ADL than, for example, proximal arm strength. Klingels et al\(^{[45]}\) had already concluded that distal muscle strength (wrist strength and grip strength) explained up to 76% of variance in bimanual performance. However, in children with CP, virtually nothing is known about distal motor fatigability and its effect on bimanual performance and ADL.\(^{[45]}\)

Also, there are no studies comparing fatigability in different upper limb muscle groups in this population.

In conclusion, for motor fatigability protocols relating to the ICF body function level, the test should be short (between 30-90s depending on the intensity of the activities), standardized (isometric or repeated) and performed in muscles and muscle groups relevant for the specific patient population. However, more research is needed to optimize methods for quantifying motor fatigability and to investigating reliability and validity in different populations.

**Activity level**

Six different protocols were found relating to the ICF activity level. Tasks consisted of propelling a wheelchair,\(^{[15,19,28]}\) playing a boccia game,\(^{[3]}\) or playing a serious game.\(^{[29]}\) Too little is known about the protocols relating to ICF activity level to be able to recommend which to use for each neurologic population. We recommend researchers to first investigate which tasks are relevant for ADL in each population with neurologic conditions before trying to measure or quantify motor fatigability in these activities.

**Study limitations**

The aim of this systematic review was to investigate protocols for motor fatigability based on voluntary contractions. This resulted in the exclusion of studies that used electrical stimulation techniques to induce motor fatigability. This may have limited the scope of the review since protocols that used a combination of voluntary activation and electrical stimulation were excluded.

The quality of the included studies ranged from poor to moderate, but this did not affect the quality of this review because most quality issues related to participant recruitment and reporting of the results. These parameters were not of interest in this review because only the content of the protocols for motor fatigability was investigated. The review did not aim to gain more insight into the phenomenon of motor fatigability in different populations with neurologic or the effect of fatigability on ADL.

Lastly, this review found that very limited literature is available on clinimetric properties of motor fatigability protocols in populations with neurologic conditions. In 13 protocols, significant differences were found between a patient population and a control.
group without neurologic problems in terms of motor fatigability.\textsuperscript{7,10,15,20,22,25,27,28,30,33,35,36} We, therefore, hypothesize that there may be protocols that have the potential to discriminate between a patient population and a control group without neurologic deficits. However, future research should further investigate clinimetric properties such as reliability, validity, and responsiveness to change and establish norm values for populations to enable a better understanding of motor fatigability in different populations with neurologic deficits.

**Future research**

Miller et al\textsuperscript{46} have stressed the importance of therapeutic interventions for decreasing fatigue and depression to increase functional status and quality of life in patients with MS. Because it is also important to evaluate the effectiveness of treatments, there is a need for a reliable protocol to quantify motor fatigability. Moreover, Severijns et al\textsuperscript{47} states that that protocols for clinical use should be feasible, quick, easy to interpret, and reliable. None of the included protocols comply with these demands, highlighting the need for further research.

Moreover, in this systematic review, because of the large heterogeneity of the included definitions, protocols, and outcome measures, and based on the fact that there is very limited knowledge of the psychometric properties of the known protocols and outcome measures, we want to emphasize the importance of more research in this field. More specifically, we suggest that future research should focus on investigating the psychometric properties of motor fatigability protocols in patients with neurologic conditions and that these should be specific to each patient population.

**Conclusions**

This systematic review has summarized current literature in the light of a definition of motor fatigability, examining protocols used to investigate motor fatigability in different populations with neurologic deficits. However, it has also revealed the gap in knowledge on motor fatigability in these populations. Because of the large variety in definitions, upper limb protocols, and outcome measures used in these populations, direct comparisons between studies were not possible. However, based on physiological fundamentals, recommendations were made on how to investigate motor fatigability from the perspective of the ICF body function level. To do this, research protocols for motor fatigability should be optimized in order to correspond better with the needs of the patient population. Furthermore, more attention should be paid to investigating the psychometric properties of the protocols. At the ICF activities level, too little is known to make a sound statement on the use of protocols with these populations. Lastly, clinimetric properties of the protocols used to examine motor fatigability should be investigated for different populations with neurologic conditions.

**Keywords**

Neurological rehabilitation; Rehabilitation; Upper limb

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