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DEMYELINATING DISORDERS (J. BERNARD & M. CAMERON, SECTION EDITORS)

Assessment and Measurement of Spasticity in MS: State of the Evidence

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Abstract

Purpose of Review The purpose of this review is to familiarize the reader with assessments and measurement of spasticity in people with multiple sclerosis (MS). Spasticity affects 60–84% of people with MS, worsening as disability worsens and impacting activity, participation, and quality of life. Spasticity manifests in many ways, including spasms, resistance to passive stretch, pain, and perception of tightness, and can affect muscles throughout the body, making assessment and quantification of spasticity challenging but important. Assessment tools include those quantified by clinicians, instrumentation, and patients.

Recent Findings Most tools for measuring spasticity are based on clinician scoring, were developed many years ago, and have undergone minimal recent advances. More recent developments are patient-reported outcome measures for spasticity, including the Numeric Rating Scale for Spasticity (NRS-S) and the disease-specific Multiple Sclerosis Spasticity Scale-88 (MSSS), and, most recently, imaging through elastography.

Summary MS-related spasticity is common and often disabling. There are various spasticity measurement tools available, each with advantages and limitations. Newer tools are likely to be developed as our understanding of spasticity in MS grows.

Keywords Multiple sclerosis · Spasticity · Measurement · Assessment · Outcomes

Introduction

Multiple sclerosis (MS) is a common and often disabling disease of the central nervous system (CNS) that affects approximately 2.5 million people worldwide and over 900,000 people in the USA [1]. People with MS (PwMS) experience a wide range of symptoms including spasticity, weakness, pain, numbness and tingling, cognitive dysfunction, fatigue, and depression.

Spasticity is an involuntary stimulus to muscle tissue to contract or shorten as part of the upper motor neuron syndrome. Spasticity occurs in 60–84% of PwMS, contributing to disability by causing gait disorders, falls, fatigue, spasms, sleep disturbance, pain, and potentially hastening the time to wheelchair dependence. Increased disability and dependence can then lead to social isolation and depression, cardiovascular disease, muscle fibrosis and joint contracture with secondary skin breakdown, infection, and death [2–7]. In a quality of life survey of people with MS and spasticity, 20% of participants rated their quality of life as worse than death because of their spasticity [8].

Spasticity in MS is thought to result from demyelination and/or axonal degeneration in descending inhibitory CNS motor tracts (corticospinal, medial reticulospinal, lateral vestibular, and dorsal reticulospinal tracts) causing disinhibition of muscle contraction [9, 10]. Spasticity is classically defined as "a motor disorder characterized by a velocity dependent increase in tonic stretch reflexes (muscle tone) with exaggerated tendon jerks, resulting from hyperexcitability of the stretch reflex, as one component of the upper motor neuron syndrome [11]." Spasticity differs from rigidity because rigidity lacks velocity dependence. Other definitions of spasticity have also been proposed. A more recent, patient-centered description of spasticity for use in MS is "unusual tightening of muscles that feels like leg stiffness, jumping of the legs, a

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repetitive bouncing of the foot, muscle cramping in the legs or arms, the legs going out tight and straight or drawing up [2]."

In PwMS, spasticity may vary across days and through the day. Spasticity also fluctuates with changes in temperature, fatigue, and activity. Spasticity may affect different muscles, depending on the location and size of MS lesions. MS spasticity worsens with longer disease duration and greater gait disability and may also worsen with relapses or progression of the disease, treatments for the disease process, treatment for other symptoms, infections, injuries or wounds, temperature extremes, stress, tight clothing, other medical problems or symptoms, and other noxious stimuli. As spasticity worsens, quality of life worsens and healthcare utilization increases.

Progress in the management of the disease course of MS has improved substantially in the last several decades, with over a dozen approved MS disease-modifying treatments (DMT). Unfortunately, none of the DMTs completely stops or reverses the disease process, and none specifically treats the symptoms of MS. Symptom management continues to rely primarily on medications, used on- and off-label, for specific symptoms as well as on the skills of allied health professionals such as rehabilitation therapists (physical, occupational, and speech therapists) and psychologists. Treatment of MS spasticity generally relies on a combination of medications, physical therapy, and exercise. A survey of PwMS and spasticity found that 78% reported taking one medication for spasticity and 46% reported taking two or more medications for spasticity [2]. Stretching of affected muscles is considered the cornerstone of spasticity management from onset of first symptoms [3].

Assessment of MS-Related Spasticity

The signs and symptoms of MS-associated spasticity are varied and can include muscle spasms, myoclonic jerks, increased resistance to passive movement, clonus, cocontraction, stiffness, heaviness, pain, sleep disturbance, fatigue, weakness, poor motor control, incoordination, loss of dexterity, and slowed movements. Spasticity in MS can affect the vocal cords, bladder, trunk, and upper extremities, but generally affects the lower extremities most and earliest.

This tremendous range of signs and symptoms has long made spasticity assessment and measurement challenging, but accurate measurement is essential for developing and evaluating the efficacy of potential therapies. In 1997, Nance referenced articles from as early as 1951 and 1981 and stated that "difficulty in quantitating spasticity clinically has limited evaluation of prospective therapies [12]." Historically, the severity of spasticity has primarily been assessed with clinician assessed scales with few gradations. There have been attempts to provide more precise grading of these scales with instrumentation, but these approaches are not widely used or well validated. More recently, there has been a growing interest in, and growing supportive evidence for, using both short and long patient-reported outcomes (PROs) to assess spasticity in MS. In this paper, we review the commonly used clinician and patient-reported measures of spasticity and select instrumented approaches studied in PwMS.

Clinical Measures of Spasticity

The most common clinical assessment of spasticity in MS is as a component of the standard neurological examination. More focused clinical scales for measuring spasticity include the Ashworth Scale and the Modified Ashworth Scale, the Tardieu Scale and Modified Tardieu Scales, and the pendulum test.

A clinical evaluation always begins with a complete history, including information on frequency, severity, location and duration of spasticity, the effect on sleep and daily activities and of medications tried, and then a physical examination. The components of the neurological examination related to spasticity in PwMS generally include assessment of tone, stretch reflexes, the Babinski test and walking, and evaluating range of motion, strength, functional activity, and the presence of other pathological reflexes. Assessment of tone involves the clinician passively moving the patient's joints slowly and quickly and rating the degree of resistance felt to rapid stretch, typically as increased or decreased relative to a presumed normal. Stretch reflexes are also tested, and the response is rated on a 0 to 4 scale, with 0 reflecting no response/no muscle tone, 1 reflecting that there is a response but this response is less than normal or hyporeflexia, 2 reflecting normal response, 3 reflecting increased or brisk response to the stimulus or hyperreflexia, and 4 reflecting sustained clonus or overflow of the response to other muscles. Some clinicians also evaluate the stretch reflex in the large muscle groups of knee extensors or elbow extensors during the clinical neurological examination with a pendulum test in which the extremity is supported over the examiner's arm while the examiner's hand drops the lower part of the limb and assesses the speed of the limb dropping and/or freedom of motion including oscillations back and forth. The Babinski test is also performed to evaluate for disinhibition of motor reflexes, again looking for the normal response of downgoing toes, an abnormal disinhibited response of upgoing toes, or an indeterminate or neutral response with no clear up or down motion of the toes in response to the stimulus. Finally, clinicians observe walking and assess for the presence of spasticity by looking for typical features such as toe walking or scissoring gait.

The Ashworth Scale (AS) and the Modified Ashworth Scale (MAS) are the most common assessments of spasticity used clinically by physical and occupational therapists and the most common assessments used in research studies [13, 14]. These scales are similar to the assessment of tone in the neurological examination, although, in contrast to the neurological examination which scores muscle tone as decreased or increased, the AS

and MAS only score tone as normal or increased. Both the AS and the MAS are scored on a 0–4 scale; the difference between the two scales is that the MAS has an additional score of 1+, between 1 and 2. For the AS and MAS, the examiner moves a joint quickly and rates the resistance from 0 to 4, with 0 reflects no increase in tone, 1 reflects slight increase in tone with a catch in the muscle near the end of the range of motion but resistance does not continue and full range of motion is present, 2 reflects a marked increase in tone but the joint is easily moved, 3 reflects considerable increase in tone making movement difficult but full range of motion is still obtained, and 4 reflects the limb being rigid and likely includes the presence of contractures. The 1+ added in the MAS reflects a slight increase in tone with a catch followed by resistance throughout the remaining range of motion at the joint being tested. The AS and MAS are recommended for use in people with stroke and traumatic brain injury, but, even though the original Ashworth Scale was first described in PwMS, both are unable to be recommended in PwMS because they do not have established validity and reliability in this population. Additional concerns with the AS and MAS in any population include the requirement for adequate training and standardized technique to ensure interrater reliability; reliability differs between muscles; they only measure resistance to passive movement, which is only one aspect of spasticity and not a comprehensive assessment; they do not compare resistance at fast and slow velocities to isolate the velocity dependent component of resistance, and they are likely influenced by noncontractile soft tissue properties, persistent muscle activity, intrinsic joint stiffness, and by stretch reflex responses. In addition, ambiguous wording and lack of standardized procedures limit comparison and reliability [15].

The Tardieu Scale (TS) and its various modifications (MTS) assess muscle response to stretch at given velocities and take into account resistance to passive movement at both slow and fast speeds. The subject is positioned supine to test spasticity in the lower extremities. Each joint is passively moved at three different velocities: V1 = as slow as possible, V2 = the speed of the limb falling against gravity, and V3 = moving the limb as fast as possible. Spasticity is rated based on the quality of resistance to this motion and the angle where this resistance occurs. The quality of resistance is scored on a 0–4 scale (or 5 depending on the version used). Zero reflects no resistance to passive motion and 4 reflects infatigable clonus lasting more than 10 s. Two angles are noted: R1 (the angle where a catch or clonus is found during V3) and R2 (the full passive range of motion at V1). R1 is then subtracted from R2 to represent the dynamic tone component of the muscle as opposed to resistance from passive components [16]. The TS/MTS is mostly used for rating spasticity in children with cerebral palsy (CP) and, although rarely used in adults, has been validated in people with stroke, but there has been little study in MS. There is one recent study evaluating the intrarater reliability of the MTS in the hip adductors, knee extensors, and ankle plantar flexors of 30 PwMS. In this study, a physical therapist examiner inexperienced with this test examined each subject twice at least 7 days apart. The researchers found moderate to good agreement for the rating of resistance quality (kappa = 0.72), but only poor to good intrarater reliability for R1 and R2 angles (ICC agreement 0.45–0.83) and the smallest detectable change for all the components across the muscle groups was unacceptably large (range 14.6–55.6). The authors concluded that these results did not support good intrarater reliability for the MTS when assessing lower limb muscle spasticity in PwMS by a physical therapist with no previous experience in the scale and with limited training [17•]. Although the TS and MTS do distinguish between resistance at slow and fast velocities, they also, like the AS and MAS, have the following shortcomings: they require substantial training and experience, only measure passive resistance, and reliability and validity in MS are not proven.

The pendulum test assesses spasticity by visually assessing a muscle's response to sudden stretch imposed by gravity and the resulting oscillations between flexion and extension. The pendulum test is most often applied to the knee extensor muscles (the quadriceps) but can also be applied to other larger joints such as the elbow. To perform the pendulum test on the knee extensors, the patient is placed in a half-lying or supine position, with their knee at the edge of the examination table. The examiner lifts the patient's leg and then allows the leg to drop and swing freely, rating the freedom and ease of movement; however, there is no accepted scale. Both legs can be tested simultaneously, if the patient is appropriately positioned, allowing direct comparison between legs [18].

Instrumented Measures of Spasticity

The TS and the pendulum test have been instrumented with the goal of improving the precision, objectivity, reliability, and validity of these spasticity measures. In addition, several other instrumented approaches have been reported, using electromyography, ultrasound imaging, and isokinetic dynamometry; however, access to the equipment and necessary expertise to perform and interpret these tests limit their evaluation and widespread adoption.

An instrumented version of the TS was developed and evaluated in children with CP but has not been tested in PwMS. The instrumented TS integrates biomechanical (joint angle and torque) and electrophysiological (surface electromyography) signals during manually performed low- and high-velocity passive stretches. In evaluating this approach for testing the medial hamstrings and gastrocnemius in children with CP, investigators found moderately high reliability for both muscle groups, moderate correlation with the MAS for both muscle groups, and good correlation to the MTS for the hamstrings [19]. In addition, in a study evaluating this instrumented TS in 31 children with spasticity from CP being treated with botulinum toxin injections, investigators

concluded that the instrumented TS was more responsive than both the AS and TS clinical scales and is therefore a promising approach for evaluating treatment response [20]. Further study is needed to determine if an instrumented TS is valid and reliable in PwMS with spasticity.

A standardized version of the pendulum test, with subsequent instrumented quantification from videotapes, was developed in healthy adults and was subsequently used in studies demonstrating the efficacy of tizanidine for spasticity in people with spinal cord injury (SCI) and then in PwMS. For this version of the pendulum test, the subject is positioned lying or half-lying on a table with their trunk and thighs supported and their lower legs hanging freely. Proximal stabilization of the trunk may be applied to minimize motion overflow that may mask the effect at the joint of interest. Reflective markers are adhered approximating the joint axes of the lower extremity. The leg is then dropped from the horizontal by an examiner, and the foot is allowed to oscillate freely until finally coming to rest. The test is videotaped to allow for blinded computerized motion analysis of the angular displacement, velocity, and acceleration response of knee flexion and extension. When used in people with SCI, this video-based version of the pendulum test demonstrated significant correlation with the AS and, when used in PwMS, showed a dose response to the medication similar to that found with the AS [12, 21, 22].

In addition to instrumentation of clinical tests, the Hofmann's reflex or H-reflex, as measured by electromyography (EMG), has been used to assess spasticity in PwMS. The H-reflex measures the threshold spinal reflex reaction in muscles after electrical stimulation of the peripheral nerve, believed to be indicative of alpha motor neuron excitability. People with spasticity have increased alpha motor neuron excitability and increased H-reflex amplitude and following M-response, thus allowing measurement of the H-reflex, the M-response, and the H/M ratio. The H/M ratio, as measured from the soleus muscle by stimulating the tibial nerve in the popliteal fossa, has been used as an outcome in a trial of repetitive transcranial magnetic stimulation for spasticity in MS and a trial examining the association between spasticity and postural control in MS [23, 24]. Although this approach seems to provide precision and is reported to be a reliable electrophysiologic measure of stretch reflex, it is subject to errors in estimation of maximal waveforms, only measures the stretch reflex in a single muscle, has not been found to correlate strongly with clinical scales (e.g., AS/MAS), and requires specialized equipment, skill, time, and expertise to perform.

The most recently described approach to evaluating spasticity in PwMS is real-time ultrasound muscle elastography. This approach, first used in the detection of malignant tumors, examines the mechanical elastic properties of tissues. To evaluate spasticity, muscle elasticity is rated on a 5-point scale called the Muscle Elastography MS Scale (MEMSs). MEMSs 1 indicates that muscle fibers have normal elasticity and are homogeneously distributed. MEMSs 2 indicates that muscle fibers have normal elasticity in the central part while superior and inferior parts are characterized by fibers with lower elasticity. MEMSs 3 indicates that muscle fibers with low elasticity are present peripherally. MEMSs 4 indicates that muscle fibers with low elasticity are present in almost all the muscle. MEMSs 5 indicates that muscle fibers have the lowest grade of elasticity. In 110 PwMS, MEMSs scores correlated strongly with AS score (Pearson's $r = 0.9162$, $p < 0.0001$). In addition, in 55 PwMS and spasticity treated with tetrahydrocannabinol:cannabidiol oral mucosal spray, 65% of responders (those with ≥ 20% improvement in numeric rating scale (NRS) for spasticity (see below for description of this patient-reported outcome)) improved on the NRS by 1.87 points ($p < 0.0001$) and on the MEMSs by 1.97 points ($p < 0.0001$). Nonresponders also showed a significant reduction on the MEMSs (0.8 points, $p < 0.002$) which the authors interpret as suggesting that real-time elastography may be a more sensitive measure of spasticity in MS, but which could also indicate poor specificity of this measure [25•].

A number of other instrumented versions of clinical spasticity tests have been developed, but none of these has been evaluated in PwMS and none has sufficient validation to clearly be recommended in other conditions [26]. In addition, some authors have used isokinetic dynamometers and EMG to assess muscle activation during stretching in PwMS, but this approach requires large isokinetic dynamometer equipment rarely available at this time [27, 28].

Patient-Reported Measures of Spasticity

Patient-reported outcome measures (PROs) have been developed to capture the patient's perspective of spasticity. PROs using validated measures have been used successfully to assess and develop treatments for patients with pain and with depression [29], and the National Institutes of Health and the Food and Drug Administration are putting increased emphasis on the importance of PROs in clinical trials, even in disorders for which there are objective measures.

The Penn Spasm Frequency Scale was an early PRO scale for muscle spasms, a spasticity-related symptom. The Spasm Frequency Scale relies on the patient counting the number of spasms they experience in a specified time frame, typically 1 h. It is scored on a 0–4 scale with 0 reflecting no spasms in the hour, 1 reflecting mild spasms induced by stimulation, 2 reflecting full spasms occurring less than one per hour, 3 reflecting spasms occurring more than once per hour, and 4 reflecting more than 10 spontaneous spasms per hour [30]. The spasms can also be rated for severity with 1 = mild, 2 = moderate, and 3 = severe. The Spasm Frequency Scale was developed for assessing spasticity in SCI, but spasm frequency has also been used as an outcome in studies of spasticity in PwMS [22, 31]. The validity and reliability of the Spasm

Frequency Scale, or other spasm frequency measures, have not been established in PwMS, and these measures only capture a very limited component of the spasticity experience.

The Numeric Rating Scale (NRS) for Spasticity (NRS-S) is a variation of the Visual Analog Scale and the NRS for Pain. The NRS was developed to capture information from the patient's perspective and asks the patient to rate the severity of their symptom on a 0–10 scale. When applied to pain, 0 reflects no pain and 10 reflects the worst possible pain. When applied to spasticity, 0 reflects no spasticity and 10 reflects the worst possible spasticity. The test-retest reliability of the NRS-S is considerably better than that of the Ashworth Scale (ICC 0.83 vs 0.53). In addition, the validity of the NRS-S is supported by a consistent association with the Patient Global Impression of Change (PGIC) scores. A 29.5% improvement on the spasticity NRS-S is considered clinically important and correlates with "much improved" or better on the PGIC, consistent with the widely used NRS for pain where 30% improvement is clinically important. In addition, the 18% Minimal Clinically Important Difference (MCID) for the NRS-S is consistent with 10–20% improvement in pain recognized as the MCID on the NRS for pain [32].

The MS Spasticity Scale-88 (MSSS) is an MS-specific PRO for spasticity. The MSSS was developed as a patient-focused measure to capture patient experience and perception of the impact of spasticity in MS on day-to-day symptoms and during functional activities. The MSSS is a self-report questionnaire, with 88 questions that all begin with "As a result of your *spasticity*, how much in the past two weeks have you been bothered by…" and each question ending with a description of a symptom. Each question can be answered by one of the four responses with 1 reflecting not bothered at all to 4 reflecting extremely bothered. The total score for the MSSS ranges from 88 if a person is not bothered at all by any of the symptoms, up to 352 if they are extremely bothered by all of the described symptoms. The symptoms are organized into eight subscales in clinically relevant areas: spasticity-specific symptoms (muscle stiffness, pain and discomfort, and muscle spasms), physical functioning (activities of daily living, walking, and body movements), emotional health, and social functioning [33, 34]. The MSSS has been proven to be a valid and reliable measure of the impact of spasticity in PwMS, both in English and in several other languages [34, 35]. The need for 88 questions highlights the complexity of the seemingly unidimensional concept of spasticity. Extensive testing, analysis, and evaluation supported the need for the eight scales to cover the breadth of the problem. Both the total score and scores for each of the subscales have proven independent validity and can thus be analyzed and reported independently. Unfortunately, this new tool does not improve our understanding of the relationship between the patient's experience of spasticity and clinician-administered measures, but it does help us understand, and thus potentially improve, the patient's experience of spasticity and quality of life.

Conclusions

Spasticity is an involuntary stimulus to muscle tissue to contract or shorten as part of the upper motor neuron syndrome that is a common, disabling, and multifaceted symptom of MS. Development of effective therapies for spasticity requires accurate assessment and measurement, but there is no single approach that captures and quantifies all aspects of spasticity in MS. The neurological exam, with muscle tone evaluation described in 1949 as "an old, rather crude method, that of moving the patient's legs and attempting to appraise and compare the resistance he feels," is well established and will therefore likely persist as it is and continue to be reported narratively in the neurologist's note [18]. The AS and the TS, and their modified versions, report examiner ratings of resistance to passive stretching. While simple and reproducible, these ratings are subjective and capture only one component of spasticity, the resistance to passive movement, limiting their validity [36–38]. A number of instrumented measures of spasticity have been developed, including instrumented versions of the TS and pendulum scale and EMG and ultrasound-based measures. Although these provide more precision, their use is limited by the need for equipment, expertise, time, and validation. Spasticity-specific PROs, developed to capture the patient experience of spasticity, are available in several languages and have been validated. However, these scales are limited by subjectivity, particularly when evaluating interventions where blinding is difficult or not possible. The ideal spasticity measure depends on the intended use, available equipment, expertise, time, reliability, and validity. Quicker clinical scales are generally most appropriate for the clinical setting, while multiple concurrent measures are likely most appropriate for clinical trials.

Compliance with Ethical Standards

Conflict of Interest Cinda L. Hugos declares no potential conflicts of interest. Michelle H. Cameron reports consulting fees from Adamas Pharmaceuticals and Greenwich Bioscience/GW Pharmaceuticals, outside the submitted work.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

Disclaimer The contents do not represent the views of the U.S. Department of Veterans Affairs or the United States Government.

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