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Research Article

Effects of verbal instruction on maximal isometric force and rate of force development in people with multiple sclerosis and healthy controls

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HIGHLIGHTS

- Isometric maximum force and rate of force development are key clinical outcomes.
- Both outcomes are altered in people with multiple sclerosis (PwMS).
- The values of both outcomes are influenced by verbal instruction.
- An "As fast and as hard" instruction can evaluate both outcomes simultaneously in PwMS.

ABBREVIATIONS

AF	As fast as possible
AFH	As fast and as hard as possible
AH	As hard as possible
ANOVA	mixed factor analysis of variance
EDSS	Expanded Disability Status Scale
GF	Grip force
KE	Knee extension
MaxF	Isometric maximum force
MaxRFD	Maximum rate of force development
η^2	Eta squared
PwMS	People with multiple sclerosis

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BACKGROUND: Isometric maximum force (MaxF) and rate of force development (MaxRFD) obtained from sustained contractions are two important outcomes used in clinical and research settings that evaluate strength and power of an individual, respectively. These outcomes are often impaired in people with multiple sclerosis (PwMS) and are associated with functional limitations. The values of these isometric outcomes can be influenced by the verbal instructions given to the participants prior to contraction.
AIM: We investigated the effects of two common instructions - "as hard as possible" (AH) and "as fast and as hard as possible" (AFH) - on MaxF and MaxRFD in both upper and lower extremities in PwMS and in controls.
METHODS: Twenty-seven PwMS (median EDSS=2.0, range: 0-5.5) and age- and gender-matched healthy controls completed isometric assessments of grip force (GF) and knee extension (KE) under both AH and AFH instructions.
RESULTS: Instructions did not significantly affect MaxF in either group or muscle group ($p>0.05$). However, AFH instruction yielded a significantly higher MaxRFD compared to AH in both GF and KE across both groups ($p<0.001$).
INTERPRETATION: MaxF is unaffected by instruction type, while MaxRFD is sensitive to instruction that emphasizes both speed and magnitude of a contraction. Therefore, AFH instruction enables efficient and simultaneous assessment of both outcomes in neuromuscular evaluations, including clinical populations like PwMS where both outcomes may be impaired, and where the effects of disease could be more prevalent in the lower extremity than the upper extremity.

KEYWORDS: Assessment | Motor function | Motor control | Performance

INTRODUCTION

Assessment of the maximal capacity of the neuromuscular system is crucial for evaluating neuromuscular function across diverse populations, such as athletes, older adults, and individuals with neurological diseases. One commonly employed method for this assessment involves sustained isometric contractions, where individuals are asked to exert their maximal effort for 3-5 seconds. Analyzing the resulting force-time curves allows for the calculation of two key outcomes: maximum force (MaxF) and maximum rate of force development (MaxRFD). MaxF is calculated as the highest value of the recorded force time curve, while MaxRFD is usually calculated as the highest slope (i.e., the highest value of the time derivative of the force-time curve) achieved during the initial phase of the force generation [1-3]. Consequently, MaxF assesses the maximum strength of an individual, which is highly correlated with intrinsic muscular factors such as cross-sectional area and fiber type composition [4]. However, it is important to note that in populations with neurological impairments, such as people with multiple sclerosis (PwMS) neural factors may also significantly influence MaxF [5]. In contrast to MaxF, MaxRFD assesses an individual's explosive strength (i.e., power), which mainly relies on neural factors including the number of double discharges and discharge rates of motor units [1,6]. Therefore, MaxF and MaxRFD are used to evaluate different properties of an individual's neuromuscular system.

Both MaxF and MaxRFD are widely utilized in clinical and rehabilitation settings to provide objective assessment of

neuromuscular function [7], monitor disease progression [8], and evaluate the effectiveness of therapeutical and rehabilitative interventions [9,10] in PwMS. Previous literature demonstrated the external validity of both outcomes in PwMS by showing the relationships to a number of daily functional tasks, such as walking speed and distance, standing up from a chair [8,9,11]. In addition to their functional relevance, both MaxF and MaxRFD have shown high reliability [11] and sensitivity [8,12] in detecting motor impairments in PwMS. Therefore, accurate measurement of these outcomes is essential in both clinical and rehabilitative settings.

The magnitude of the outcomes obtained from isometric contractions also depends on methodological factors, with one of the most easily manipulated being the instructions given to subjects prior to contraction. Previous literature has studied the effects of instruction on the values of the MaxF and MaxRFD in isometric contractions [13-17]. These studies explored the effects of providing instructions for performing muscle contractions: as hard (AH), as fast and as hard (AFH), and as fast (AF) as possible, in sustained isometric contractions. Bemben et al., (1990) found that the AFH instruction elicited the greatest MaxF values compared to the AH and AF instructions, while Christ et al. (1993) found larger MaxF under AH than AF instruction. Following these studies, several other studies have failed to find a significant difference between AF and AFH [15-17] or AH and AFH [13] instructions on MaxF. Since MaxF is an outcome of strength, measured as the maximum force level produced, we believe that the instruction should focus solely on the magnitude and should not include the contraction speed. However, if AFH does not reduce MaxF compared to AH, it could be a more efficient instruction for neuromuscular assessments, allowing both outcomes to be measured in a single test, thereby optimizing assessment time.

Regarding MaxRFD, most previous studies have used the AF instruction, which has been found to produce greater MaxRFD than both the AH [14] and AFH [15,16] instructions. However, in these studies, participants were also instructed to sustain isometric contractions to achieve a maximal force level, regardless of the instruction. As a result, they were inherently asked to contract as hard as possible. Since MaxRFD is a measure of neuromuscular power [18], which requires the rapid generation of high levels of muscle force, and its value is positively correlated with the peak value of force achieved [19], the most appropriate instruction for testing MaxRFD has been suggested to be AFH [1,13].

Studies examining the effects of instruction on the isometric outcomes have primarily focused on healthy populations and have generally been limited to either upper [20] or lower [13,16] extremities. However, given the well-documented neural component of motor impairment in PwMS and the critical role of the neural contributions to MaxRFD, it remains unknown whether the instructional effects observed in healthy populations generalize to PwMS. Furthermore, literature suggests that MaxRFD may be differentially impaired compared to MaxF in PwMS [21,22], which warrants the valid measurement of both outcomes in this group. Therefore, we aimed to investigate the effects of verbal instruction on MaxF and MaxRFD in both PwMS and age- and sex- matched controls. We examined both upper extremity (grip force muscles) and lower extremity (knee extensors) muscles, as these differ in function and muscle mass, and also disease-related effects are generally more pronounced in the lower extremities than in upper extremity in PwMS [21], especially in those with longer disease duration [23].

METHODS

Subjects

The participant cohort and the raw force data used in this study were included in our earlier analyses on the sensitivity of isometric outcomes for assessing neuromuscular function in PwMS [12]; however, different analyses were performed on the same raw data to calculate MaxF and MaxRFD to address the current research question. Twenty-nine PwMS and 29 age- and sex-matched controls participated in the study (see Table 1 for descriptive data). Data from two PwMS were excluded from the analysis due to data-overwrite issues; consequently, their matched control data were also excluded to preserve the study's design. Inclusion criteria for PwMS included 18-65 years of age, clinically stable relapsing-remitting type of MS, and Expanded Disability Status Scale (EDSS) < 6. Exclusion criteria for both groups included any musculoskeletal injuries affecting the upper- or lower-extremity function, inability to communicate with investigators, and inability to walk or stand without assistance from another person. Individuals signed an informed consent, and the study protocol was approved by university's institutional review boards.

Experimental Set-Up

Individuals completed isometric assessments for both upper (i.e., grip force - GF) and lower-extremity (i.e., knee extensors - KE) muscles. If a participant with PwMS reported a more affected limb, that limb was tested; otherwise, the dominant limb was tested. Control participants were tested on the limb matching the dominance of the limb assessed in their corresponding PwMS counterpart. For example, if a PwMS reports symptoms on their left side and they are right-side dominant, we tested the control counterpart's non-dominant side.

For GF testing, subjects sat on a bench next to a table, with the tested forearm resting on the table and wrist hanging freely in a neutral position (Figure 1a). Using a power grip, participants grasped a custom-made GF measuring device composed of two vertical grasping surfaces connected by a single-axis force transducer (SML-900N, Interface Inc. Scottsdale, AZ, USA).

KE test was performed with the subjects seated on a custom-made wooden box with their knee and hip joints at approximately 70° and 90° of flexion from full extension, respectively. A bisected PVC pipe with a firm rubber insert was attached to a single-axis force transducer (SM-500lbf, Interface Inc., Scottsdale, AZ, USA), which was fixed to the box on a surface perpendicular to the ground. The

tested leg was secured with a cuff, placed just above the lateral malleoli using a rubber insert. The thigh and hip of the tested leg were also secured using straps to isolate the knee extensors and minimize unwanted compensations. Subjects crossed their arms on their chest during KE testing (Figure 1b). The reliability and validity of the experimental protocol used for KE and GF testing was shown in our previous research [7,11,24]. The ICC and CV (%) values for MaxF were 0.92 and 8.49 in the upper, and 0.95 and 9.20 in the lower extremity, while for MaxRFD ICC and CV (%) values were 0.93 and 7.63 in the upper, 0.89 and 11.69 in the lower extremity [11].

Table 1. Participant demographics

	MS		Controls	
	Mean	St Dev	Mean	St Dev
Sex (F/M)	15/12		15/12	
Age (years)	47.85	8.91	47.15	8.63
Height (cm)	171.69	12.39	170.46	12.21
Weight (kg)	82.10	25.84	80.45	18.45
	Median	Range		
EDSS	2	0 - 5.5		

EDSS: Expanded Disability Status Scale; St Dev: Standard deviation

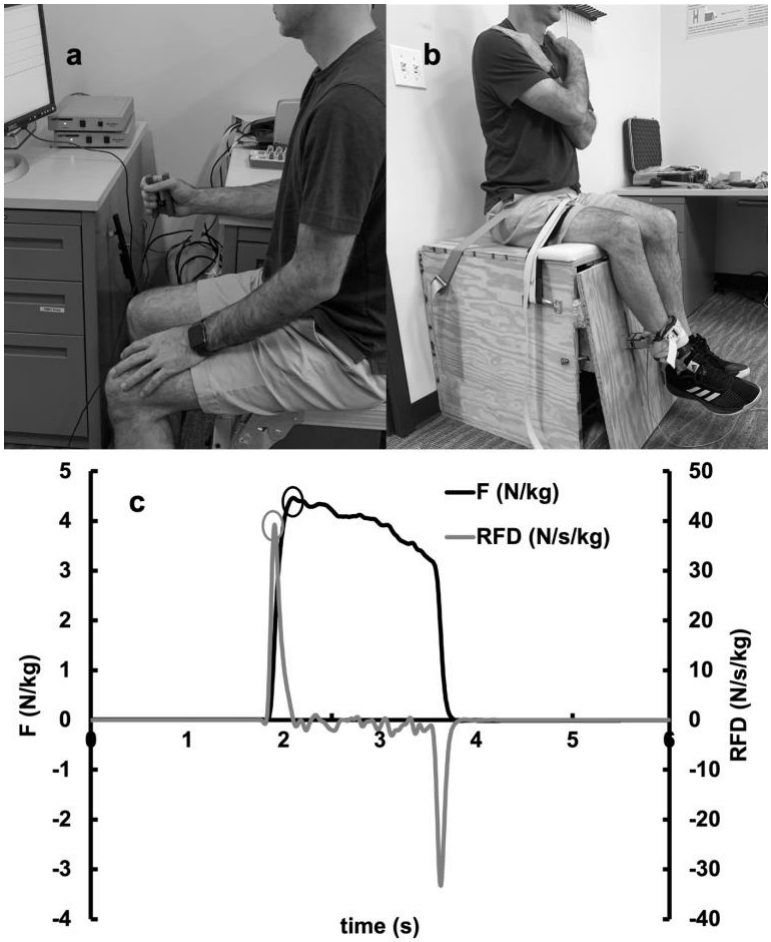

Figure 1. Experimental setup for the testing of (a) grip force and (b) knee extension. (c) A sample recording of force (black line) and the time-derivative of the recorded force, representing rate of force development (gray line). Circles represent the maximum values of force (black) and rate of force development (gray).

Study Protocol and Instructions

In both tests (i.e., GF and KE), individuals were instructed to squeeze (GF) or kick (KE) either “as hard as possible” (AH) or “as

fast and as hard as possible" (AFH) for approximately 3-s. The order of tested extremities (GF and KE) and the order of instructions were counterbalanced. Each participant completed three trials under each instruction (AH and AFH) for each extremity, with one-minute resting period between trials. All contractions were initiated from a relaxed state, which was verified by concurrent visual feedback provided to participants. The same researcher provided all instructions during data collection. Strong verbal encouragement was given throughout the trials, to ensure maximal effort. Recorded forces were corrected by subtracting the baseline force levels obtained during the relaxed state. Participants were not informed of the specific objectives related to the verbal instructions.

Data Acquisition and Analysis

We used custom-written LabVIEW (National Instrument Corp., Austin, Texas, USA) routines for data acquisition and analysis. The signals from the force transducers were sampled at 200 Hz using a 16-bit 500kS/s analog-to-digital converter (NI-6314, National Instruments Corp. Austin, Texas, USA). The raw force data was filtered using a fourth-order low-pass Butterworth filter with a cutoff frequency of 50-Hz. The time derivative of the force data was calculated and filtered with a 5-Hz low-pass filter [25]. MaxF was calculated as the maximum value of the force-time curve, while MaxRFD was calculated as the maximum value of the time derivative of the force-time curve (Figure 1c). Within each instruction, the highest values of MaxF and MaxRFD obtained among the three trials were used in the statistical analysis. Both MaxF (N/kg) and MaxRFD (N/s/kg) were normalized to body mass in each trial.

Statistical Analysis

Statistical analysis was performed using SPSS (version 28, IBM SPSS Statistics, Armonk, NY). The normal distribution of the selected variables was tested by the Shapiro-Wilk's test. As all the variables were normally distributed, mixed factor analysis of variance (ANOVA) was run separately in GF and KE to test the effects of instruction ("as hard" vs "as fast and as hard"; within factor) and group (PwMS vs control; between factor) on the MaxF and MaxRFD. P-value was set at 0.05. Eta squared (η^2) values were calculated and presented to show effect sizes. The η^2 below 0.06, between 0.06 and 0.14, and above 0.14 indicate small, moderate, and large effect sizes, respectively [26]. Some part of the data used in this study was used to evaluate the sensitivity of the outcomes in detecting the presence of multiple sclerosis [12]. To avoid redundancy, the present analysis does not focus on the main effect of *group*. However, any *group*instruction* interactions, central to the novel contribution of this study, are reported and discussed in detail.

RESULTS

Maximum Force

For GF, results revealed neither significant group*instruction interaction (F=0.45, p=0.505, η^2=0.009), nor the main effects of group (F=2.23, p=0.141, η^2=0.041) and instruction (F=1.24, p=0.271, η^2=0.023) on MaxF (Figure 2a). For KE, results also revealed neither instruction*group interaction (F=1.07, p=0.36, η^2=0.02) nor main effect of instruction (F=0.1, p=0.749, η^2=0.002) on MaxF. However, results revealed that controls had higher MaxF in KE than PwMS (F=12.2, p<0.001, η^2=0.19; Figure 2b).

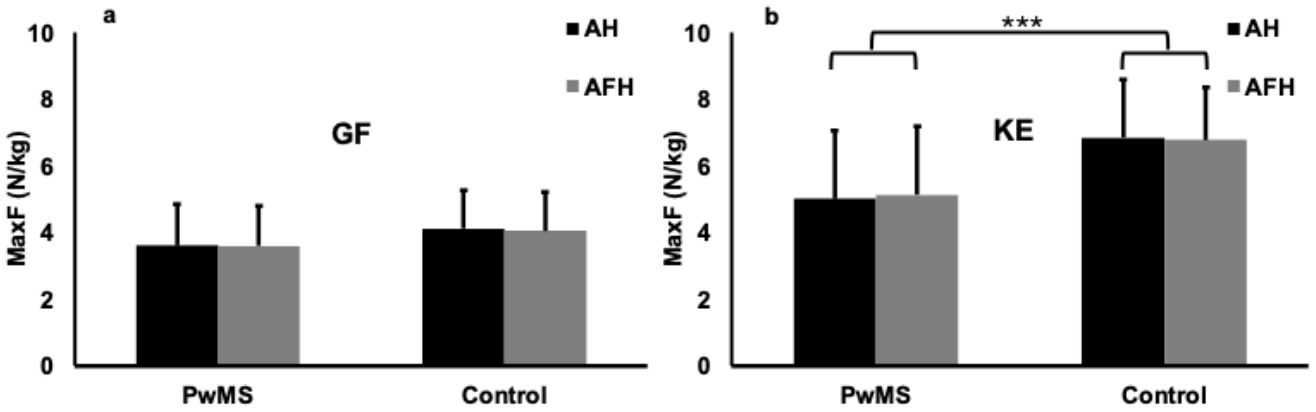

Figure 2. Mean values of (a) maximum force (MaxF) for grip force (GF) and (b) knee extension (KE) obtained from "as hard" (AH; black bars) and "as fast and as hard" (AFH; gray bars) instructions. Error bars indicate standard deviations. *** p<0.001.

Maximum Rate of Force Development

For GF, results revealed neither significant group*instruction interaction (F=0.97, p=0.329, η^2=0.018) nor significant main effect

of the group on MaxRFD (F=3.26, p=0.077 η^2=0.06). However, there was a significant main effect of instruction (F=28.3, p<0.001, η^2=0.353), indicating that MaxRFD obtained under AFH instruction was higher than that obtained under AH instruction Figure 3a. For KE, results revealed no group*instruction interaction (F=3.49, p=0.067, η^2=0.063). However, both the main effects of instruction (F=40.5, p<0.001, η^2=0.438) and group (F=10.1, p=0.003; η^2=0.162) were significant, indicating that AFH instruction yielded a higher MaxRFD than the one obtained under AH and that controls produced higher MaxRFD than PwMS (Figure 3b).

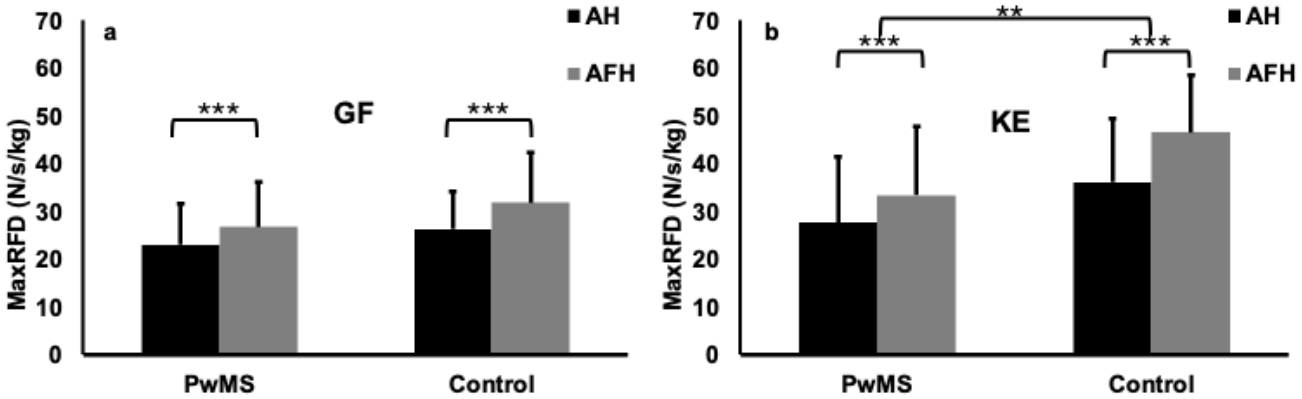

Figure 3. Mean values of (a) maximum rate of force development (MaxRFD) for grip force (GF) and (b) knee extension (KE) obtained from as hard as (AH; black bars) and as fast and as hard (AFH; gray bars) instructions. Error bars indicate standard deviations. **p<0.01; *** <0.001.

DISCUSSION

In this study, we aimed to investigate the effects of instructions – as hard as possible (AH) and as fast and as hard as possible (AFH) – on the values of maximum force (MaxF) and maximum rate of force development (MaxRFD) in the upper (grip force, GF) and lower (knee extensors, KE) extremities in people with multiple sclerosis (PwMS) and healthy controls. Our findings indicate that MaxF was not influenced by the type of instruction in either group or tested muscle groups. However, MaxRFD obtained under AFH instruction was higher than that obtained under the AH instruction in both extremities and in both groups.

MaxF has been the most widely evaluated isometric outcome across various populations, including athletes and clinical and neurological patients. Consistent with previous literature [13], our results indicate that similar levels of MaxF can be achieved using different instructions, whether emphasizing contraction speed (AFH) or not (AH). This finding is rather expected since in both instructions, individuals are asked to sustain the isometric contractions for a 3-4 s to produce MaxF, which is primarily driven by peripheral muscular factors [4], such as muscle cross-sectional area and fiber type composition, although neural factors may also play a significant role, particularly in neurological populations [8,27]. Our findings contribute unique information to the literature by confirming that instruction similarly affects the MaxF in a group of individuals with neurological impairment, whose central and peripheral nervous systems are affected by the disease. Furthermore, our results also suggest that MaxF can be assessed using different instructions in both upper and lower extremity muscle groups, which differ in functional use, muscle mass, and susceptibility to disease effects (with the lower extremity typically being more impacted in PwMS).

Consistent with previous studies, our findings indicate that the value of MaxRFD, unlike MaxF, is highly sensitive to the type of instructions provided [13,15,16]. Both PwMS and controls exhibited significantly higher MaxRFD values in both upper and lower extremities under the AFH instruction compared to the AH instruction. This difference is likely due to the AFH instruction's emphasis on rapid neural activation, which is caused by early rapid neural drive (e.g., double discharge behavior and high initial firing rates of motor units) [6]. The effect was consistent across both upper (grip force) and lower (knee extensors) extremities, despite the greater disease-related impairments typically observed in the lower limbs of PwMS [21]. These results underscore the importance of contraction speed as a determinant of MaxRFD, even in a neurologically impaired population.

Our findings offer practical implications for clinical assessments. Since a single instruction emphasizing both speed and magnitude of contraction (AFH) effectively evaluates both MaxF and MaxRFD, this approach could reduce the time required for neuromuscular assessments during patient visits, minimizing patient fatigue, and simplifying test administration. A single AFH-based isometric testing protocol thus allows clinicians to obtain comprehensive information on both strength and rapid force generation in one brief, efficient testing session, facilitating more feasible monitoring of neuromuscular function in routine clinical practice. Furthermore, previous research emphasized the value of strength training in managing motor symptoms in PwMS. Given the disproportionate decline in MaxRFD compared to MaxF in PwMS [22], our findings suggest that strength training protocols emphasizing rapid, forceful contractions, such as plyometric exercises or resistance training with a focus on speed, could optimize neuromuscular adaptations and improve

functional outcomes.

One common instruction used to evaluate MaxRFD is to produce force "as fast as possible". However, we did not include this instruction, as traditional isometric testing typically involves sustaining the contraction for a prolonged period to achieve maximal levels of force regardless of the instruction used. This sustained approach differs from the newer isometric testing protocol (i.e., brief force pulse protocol), introduced in the recent literature. Unlike the traditional sustained contractions, the brief force pulse protocol requires individuals to generate isometric forces to various submaximal levels without attempting to sustain muscle contractions [19,24,28]. The instructions used in this protocol is, therefore, emphasize contractions to be as fast as possible without trying to sustain contractions to reach to a maximum amount. While a previous study found that ballistic contractions elicit higher MaxRFD than sustained contractions performed under AFH instruction [29], it remains unclear whether this holds true in PwMS. Therefore, future studies should compare MaxRFD obtained from Gaussian-shaped muscle contractions with that from sustained contractions performed under AFH instruction in PwMS.

Limitations

PwMS participated in this were ambulatory individuals (median EDSS value=2.0; EDSSs of 21/27 of the participants<4). Therefore, our results may primarily generalize to individuals with mild to moderate disease severity. We acknowledge that the sample size was moderate, which may limit the detection of smaller effect sizes. Additionally, we tested two muscle groups that are both functionally relevant to daily activities and commonly used in the literature. However, we still do not know if our findings are generalizable to other muscle groups.

CONCLUSION

For the isometric testing of neuromuscular function, the instruction emphasizing both the speed and magnitude of contraction (AFH) is sufficient to assess both MaxF and MaxRFD in a single trial. Our results demonstrate that this holds true for both upper and lower extremities, including in neurological populations where these extremities may be differentially affected by the disease. These findings highlight the importance of clear verbal instructions in clinical practice during assessment of the maximal neuromuscular capacities.

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