the Journal of Strength and Conditioning Research™

Is Performing Repetitions to Failure Less Important Than Volume for Muscle Hypertrophy and Strength?

Lucas T. Lacerda,[1] Rodrigo O. Marra-Lopes,[1] Rodrigo C.R. Diniz,[1] Fernando V. Lima,[1] Sara A. Rodrigues,[1] Hugo C. Martins-Costa,[1,2] Michael G. Bemben,[3] and Mauro H. Chagas[1]

[1]Weight Training Laboratory, School of Physical Education, Physiotherapy and Occupational Therapy, Federal University of Minas Gerais, Belo Horizonte, Minas Gerais, Brazil; [2]Pontifical Catholic University of Minas Gerais, Belo Horizonte, Minas Gerais, Brazil; and [3]Department of Health and Exercise Science, University of Oklahoma, Norman, Oklahoma

Abstract

Lacerda, LT, Marra-Lopes, RO, Diniz, RCR, Lima, FV, Rodrigues, SA, Martins-Costa, HC, Bemben, MG, and Chagas, MH. Is performing repetitions to failure less important than volume for muscle hypertrophy and strength? *J Strength Cond Res* XX(X): 000–000, 2019—The aim of this study was to investigate the effects of muscle failure (MF) or not to MF (NMF) training on strength and muscle hypertrophy relative gains (average and individual data). Ten men untrained in resistance training participated in the study. Each leg was allocated in 1 of 2 unilateral training protocols (MF or NMF with equal volume) on knee extension exercise. Both protocols were performed with 3–4 sets, 3 minutes' rest, and 55–60% of one repetition maximum (1RM). Rectus femoris and vastus lateralis muscles cross-sectional area (CSA), maximal muscle strength (1RM and maximal voluntary isometric contraction), and muscular endurance (maximum number of repetition) were assessed before and after 14 weeks. In addition, neuromuscular activation by normalized root mean square of the electromyographic signal (EMG_{RMS}) was measured in 2nd and 35th training sessions. The average results showed that both training protocols were similarly effective in inducing increases in strength and muscle hypertrophy gains. However, individual analysis data suggest that NMF protocol with equal volume may promote similar or even greater muscle hypertrophy (vastus lateralis) and muscular endurance performance when compared with MF protocol. Also, normalized EMG_{RMS} responses analyzed during 2nd and 35th sessions were similar in MF and NMF protocols for rectus femoris and vastus lateralis muscles. In conclusion, MF and NMF protocol conducted with the same total repetition numbers produced similar maximal muscle strength performance and neuromuscular activation. Nevertheless, NMF training could be a more appropriate strategy to increase muscle hypertrophy (vastus lateralis) and muscular endurance performance in untrained individuals when compared with MF.

Key Words: muscle failure, muscle cross-sectional area, strength performance, repetition number, electromyography

Introduction

Resistance training (RT) performed to muscle failure (MF training) has been used as a strategy to maximize strength performance and muscle hypertrophy (36), which could be partially explained by the high level of effort required when performing repetitions to MF in all sets (36). In this sense, it has been reported that MF training heightens energy demands resulting in a greater metabolite accumulation (15). Although the mechanisms by which metabolic stress influences muscle hypertrophy have yet to be fully clarified, an integration of multiple local and systemic factors likely contribute to muscle development (e.g., increased fiber recruitment, elevated hormonal release, altered myokine production, cellular swelling, and production of reactive oxygen species) (40). However, it is possible that a threshold exists for metabolic stress beyond which no further beneficial effects are observed (41). In addition, it has been previously suggested that MF training would induce a greater fatigue of the active motor units requiring additional higher threshold motor units to be recruited for the maintenance of force production to complete a given task (36,43). However, Nóbrega et al. (33) verified similar neuromuscular activation between protocols performed to MF and volitional interruption (repetitions performed to the point when subjects voluntarily stop the exercise) with same intensity did not indicate the occurrence of a greater recruitment of motor units during MF training. Furthermore, given that MF and volitional interruption are 2 different criteria characterizing protocols performed with maximum repetition numbers, data from that study does not allow a better understanding about the effect of MF and not to muscle failure (NMF) protocols. Thus, despite limitations in the interpretation of data provided by surface electromyography (EMG) (45), understanding if MF and NMF protocols would have differing effects on neuromuscular activation could provide additional insight how they impact muscle strength and hypertrophy adaptations.

Review studies suggest that MF training could induce greater gains in strength and muscle hypertrophy when compared with NMF training (12). However, data from a recent meta-analysis published by Davies et al. (9) investigating MF vs. NMF training effects on maximal strength response, demonstrated that both training strategies provided similar muscle strength gains. Among the previous studies that showed contradictory results (MF vs. NMF), some reported superiority for MF (14,36), others reported support for NMF training (20), and some reported similar outcomes (21,28,33,35,42). These differences in observed results between studies could be partially due to interindividual differences in responsiveness to different training protocols (8). In fact,

Address correspondence to Dr. Mauro H. Chagas, mauroufmg@hotmail.com.

Journal of Strength and Conditioning Research 00(00)/1–12

large variabilities of interindividual responses have been reported for muscular strength and hypertrophy even when subjects perform standardized training protocols, and hence, studies with intraindividual experimental designs have been performed to minimize this problem (33). However, to the best of our knowledge, no study with an intraindividual design has evaluated the chronic effects of both training strategies (MF and NMF) using individual analyses.

It should be emphasized that many studies that have investigated MF and NMF training effects did not equate the variables that configure the training protocols investigated, such as intensity (14) and volume (14,20,33). However, although it is known that both variables may have an influence on the chronic adaptations induced by RT (10,26), volume has not often been equalized between different protocols (14,20,33). Thus, considering previous studies that have not equated different training protocols makes it difficult to interpret their strength and muscle hypertrophy responses and makes it impossible to conclude that the results found in these studies were due only to performing repetitions to MF.

Given the importance of being able to equate training protocols when comparing chronic adaptations, some studies have tried to match the volume performed between MF and NMF protocols to account for this potential confounding factor (21,28,35,36,42). Recently, Martorelli et al. (28) observed that MF and NMF training, equated by load volumes (sets × repetitions × load), increased maximum strength, measured by one repetition maximum (1RM), and muscular endurance in young active women after 5 and 10 weeks of training. In addition, Martorelli et al. (28) also demonstrated that the 2 groups with equal load volumes increased the elbow flexors muscle thickness throughout the training period, whereas a third group (lower volume load than the others) did not show an increase in muscle thickness. Although there were no statistically significant differences between groups using the same load volumes, the relative changes substantially favored MF when compared with MNF training (17.5 vs. 8.5%, respectively) (28). Nevertheless, the large interindividual variability (CV ~20%) may impair the possibility to detect differences between protocols. In the study of Da Silva et al. (42), performed with a resembling experimental design to the study mentioned above, both MF and NMF training (equated by load volume) provided similar increases in quadriceps muscle thickness and 1RM test performance for elderly men. In addition, no significant muscle hypertrophy was observed in a third group that did not train to MF and performed less volume than the other 2 training groups (42). These results suggest that load volumes may be a determinant variable when investigating the effect of MF training (41). Still regarding the study of Da Silva et al. (42), despite the similar load volumes, the average repetition numbers performed were different between MF and NMF protocols in at least 10 of the 12 training weeks. The relative differences in the average repetition numbers ranged from 4.5 to 20%, which was higher for the MF protocol in most training weeks; therefore, it is not possible to assume that the volume was equated for both training groups. However, despite the unequal volumes, it is important to emphasize the similar impact of MF and NMF protocols observed in the adaptations of muscle strength and hypertrophy. Also, another aspect that may have influenced the results found by Da Silva et al. (42) concerns the fact that in addition to RT, all groups performed the same endurance training program that may have caused a bias in the training groups responses given that the combination may induce an interference effect (mainly in strength gains) compared with RT only (7). This interference effect may be even more pronounced when both training programs are performed in the same training session as in the aforementioned study (31). Thus, based on the contradictory outcomes and the methodological limitations found in the studies that investigated this issue, the chronic adaptations provided by MF and NMF training still need better clarification.

Therefore, the aim of this study was to investigate the effects of performing MF or NMF training on strength and muscle hypertrophy relative gains (average and individual data). A secondary aim was to verify the effects of these training strategies on EMG amplitude responses. It was hypothesized that increases in muscle strength and hypertrophy, as well as in neuromuscular activation (before and after training period), would be similar between the 2 equalized protocols.

Methods

Experimental Approach to the Problem

In this study, an intraindividual experimental design was used. Volunteers performed 2 different seated unilateral knee extension training protocols (MF or NMF) for 14 weeks, with each lower limb performing one of the protocols. Pre- and post-test measures included the following: maximal voluntary isometric contraction (MVIC), 1RM, and maximum number of repetition (MNR) tests. It was used a design in which each subject's lower limb was allocated in a randomized and balanced way, according to lower-limb dominance, to one of the 2 training protocols. To balance the use of the lower limb between protocols, half of volunteers performed the MF protocol with their preferred limb while the other volunteers performed the NMF protocol with their preferred limb. This procedure aimed to minimize the influence of possible strength discrepancies between limbs and the impact on the neuromuscular responses induced by the 2 training protocols. To determine lower-limb dominance, the voluntaries were asked: "If you would shoot a ball on a target, which leg would you use to shoot the ball?"

In session 1, volunteers were familiarized with all the procedures, limb dominance was determined, and training protocols were assigned to each limb. In the next session, ultrasound images were recorded to determine rectus femoris and vastus lateralis muscle cross-sectional areas (CSAs). Sessions 3 and 4 were separated by at least 48 hours and the MVIC, 1RM, and MNR tests were performed. In sessions 5–39 (14 weeks of training period), volunteers performed 5 training sessions per week, with each session separated by a minimum period of 24 hours. Two or 3 weekly training sessions were performed with each limb, alternating the limb to be trained throughout the sessions. Thus, a minimum interval of 48 hours was given between sessions for the same limb. In sessions 6 and 39, the rectus femoris and vastus lateralis neuromuscular activation were assessed through surface EMG on each lower limb while subjects performed their respective training protocols. After 72–120 hours after the last training session (session 40), the same ultrasound procedures were performed as in session 2. Finally, in session 41, the MVIC, 1RM, and MNR after tests were executed for both lower limbs.

Subjects

The sample size calculation was performed by using the software G.Power for Windows version 3.1.9.2 (Düsseldorf, Germany) and by following the guidelines proposed by Beck (2), with a priori statistical power (1 − ß) of 0, 8, and 5% significance level.

Ten men aged between 18 and 30 years (mean ± *SD*: age = 23.7 ± 4.9 years; height = 1.77 ± 0.09 m; body mass = 80.1 ± 20.1 kg; body fat percentage = 20.5 ± 8.5%) participated in this study. The inclusion criteria for participation were as follows: (1) no RT during the last 6 months; (2) no functional limitations that would influence the 1RM test or the training protocols; and (3) no use of pharmacological substances or ergogenic supplements, and no other modes of resistance exercise during the study period. Subjects were informed about the study aims, procedures, and risks and signed an informed consent form. The local ethics committee of the Federal University of Minas Gerais approved this study, which complied with international standards. In addition, each subject was instructed not to do any physical activity immediately before the testing sessions and to maintain the same dietary practices before each session.

Procedures

Experimental Session 1 (Anthropometric Measurements). After receiving information about the study and giving written consent, the volunteers answered the Physical Activity Readiness Questionnarie (PAR-Q) and were submitted to an anamnesis to verify possible limitations related to participating in the study. In addition, height, body mass, and fat percentage (skinfold thickness) measurements also were performed. Immediately afterward, the volunteers were positioned on the seated knee extension machine (Master; Minas Gerais, Brazil) to maintain the hip at an angle of 110° (angle between the backrest and the equipment seat). The lateral epicondyle of the femur was aligned with the rotational axis of the device and the distal support of the device placed approximately 3 cm above the medial malleolus. These positions were registered to future replication during the subsequent tests and training sessions. All tests sessions were performed at the same time of the day for each volunteer.

Experimental Sessions 2 and 40 (Ultrasound Measurements). During these sessions, ultrasound images were recorded to analyze the CSA of rectus femoris and vastus lateralis muscles. The acquisition procedure for the CSA images was performed as described by Noorkoiv at al (34). Initially, volunteers remained lying in dorsal decubitus position on a stretcher for 15 minutes. During this period, the anterior regions of both thighs were marked to identify the points where the images were later acquired by the ultrasound equipment. In sequence, the major trochanters and lateral epicondyles of the femurs were identified, and femur length was measured (Figure 1A). From the proximal extremity, 40, 50, 60, and 70% of femur length were identified and marked on volunteer's thigh by using a tape measure and a pachymeter positioned parallel to the thigh. Then a line with a microporous adhesive tape was positioned 2 cm from each percentage point on the thigh (Figure 1B) to delimitate the location where the probe guide of the ultrasound would be placed during image acquisition (Figure 1C). Finally, the distances between the intercondylar line and each percentage point on the thighs were recorded for post-test replication. The procedures used to acquire images in the pre-test were the same for the post-test session (40th session), which was completed after 72 hours after the last training session.

An ultrasound (MindRay DC-7, Shenzhen, China) was used in extended-field-of-view mode, with a 4-cm linear transducer. The equipment was configured with 10-MHz frequency, acquisition rate of 21 frames·s^{-1}, depth of image capture ranging from 7.7 to 9.7 cm, and gain between 50 and 64 dB. The settings were adjusted for each volunteer to produce the clearest images of the analyzed muscles. The same trained evaluator (~120 hours of training and 600 images acquired before of the study) performed the acquisition of 2 images at each percentage of femur length (40, 50, 60, and 70%). The probe was placed transversely in parallel to intercondylar line using a coupled guide on the volunteer's thigh (Figure 1C). This procedure was performed with constant speed (controlled by metronome) and lasted between 12 and 15 seconds, varying according to the volunteer's thigh circumference. Sixteen images per volunteer were obtained for rectus femoris and vastus lateralis muscles CSA analysis (8 pre-test + 8 post-test). Afterward, CSA of each muscle scan were manually demarcated by a blinded examiner using specific software (OsiriX MD 6.0, Bernex, Switzerland) (Figure 2). For data analysis, the rectus femoris and vastus lateralis muscle CSA mean values were calculated using 2 images acquired at each percentage of femur length. Finally, based on the lengths of 40, 50, 60, and 70% of the femur, the sum of 4 CSAs of each analyzed muscle were calculated, generating a single CSA value per muscle. This was used in the statistical analysis. For intraclass correlation coefficient (ICC) calculations, the 2 CSA measures of the rectus femoris and vastus lateralis in each lower limb for pre- and post-test sessions were considered. The intrarater reliability values found in these sessions were up to 0.99 for both analyzed muscles.

Although it is commonly used in literature, CSA measured at a single point on a muscles length may not adequately represent the entire muscle hypertrophic response (1). Thus, the CSA analysis using several points along the muscle length should provide a more accurate depiction of the hypertrophic muscle response (1).

Experimental Sessions 3, 4, and 41 (Strength Tests). Strength tests were executed during the third session to familiarize the subjects with procedures that would be performed during the following session. After positioning the volunteer in the equipment, a familiarization MVIC test was performed, which consisted of 2 attempts of 5 seconds in duration at knee flexion angle of 60° (knee extended = 0°) and the knee-joint angle that has been reported as the position where maximum isometric force occurs for the seated knee extension exercise. Maximal voluntary isometric contraction tests were performed with both lower limbs with 2-minute rest periods between each attempt. Testing order was randomized between limbs, and that order was maintained during the post-test session. The highest peak force value registered for each attempt was used in later analyses. During the MVIC test, a verbal signal was given and the volunteer applied maximum force against the fixed lever of the knee extensor machine. Visual feedback of the force trace was provided as well as verbal stimuli from the evaluators to achieve maximum strength.

The 1RM test familiarization was performed 10 minutes after the completion of the MVIC test. Initially, according to procedures described in Lacerda et al. (24,25), subjects performed 10 repetitions without any weight on the equipment. The 1RM was determined in concentric mode within a maximum of 6 attempts, with 5-minutes rest periods between each attempt (25). In addition, a 5-minute rest period was given between the tests executed with each of the lower limbs.

After the 1RM test, volunteers rested for 10 minutes and then performed the MNR test. This test consisted of a single set to MF at 70% 1RM, and the subjects completed each repetition in 4 seconds (2-second concentric and 2-second eccentric). Considering that the repetition duration influences the MNRs performed (37), this procedure attempted to standardize this variable for both pre- and post-training MNR outcomes. The subjects were

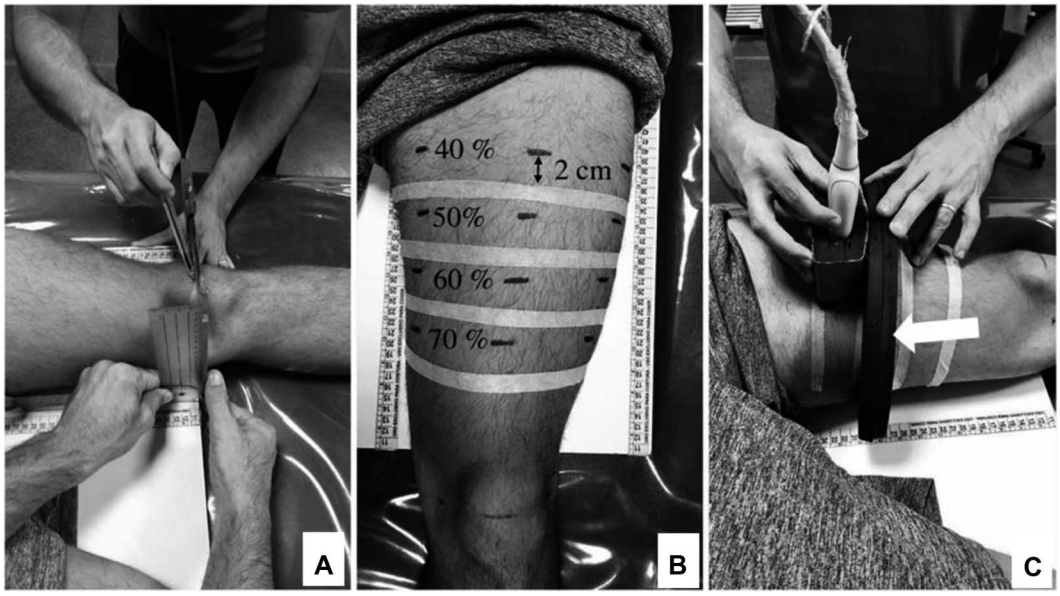

Figure 1. Thigh marking procedures (A and B) and ultrasound images acquisition (C). Probe guide (white arrow).

verbally encouraged by the researchers to perform the MNRs, and this value represented muscular endurance. The range of motion (ROM) in 1RM, MNR tests, and training protocols was maintained at 70°, with 30° and 100° of knee-joint angles corresponding maximum and minimum angular positions, respectively.

In session 4, the MVIC, 1RM, and MNR tests executed in the familiarization session were repeated. These tests were also repeated in the 41st experimental session after a maximum interval of 48 hours after session 40 (ultrasound measurements). The data measured in sessions 4 and 41 were used for statistical analysis. Based on familiarization and pre-test sessions data, the ICC intersession values observed were 0.97 (MICV), 0.98 (1RM), and 0.68 (MNR), respectively.

Experimental Sessions 5–39 (Training Period). After the initial testing period, the 14-week training began (35 training sessions). It is worth noting that all subjects completed 100% of the training sessions. The overall experimental protocol consisted of 3–4 sets

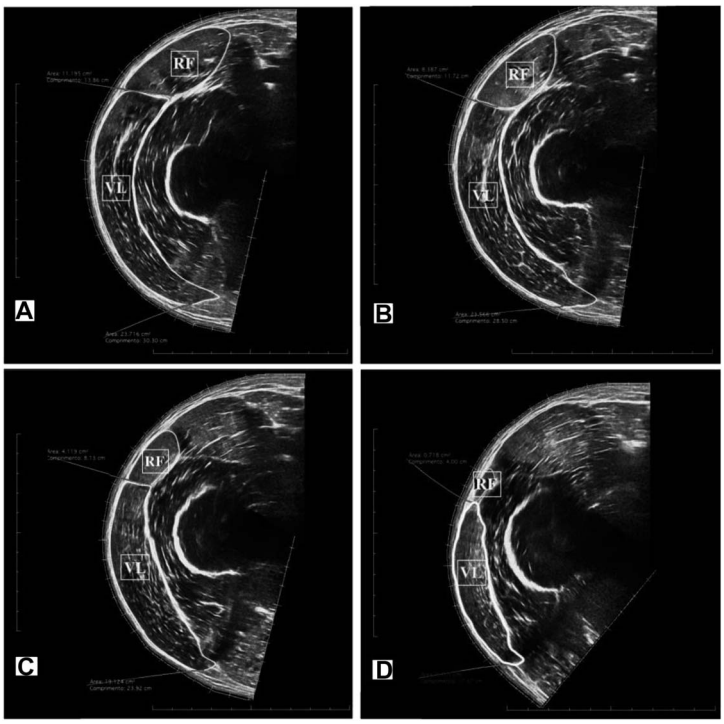

Figure 2. Ultrasound images and cross-sectional areas (CSAs) at 40% (A), 50% (B), 60% (C), and 70% (D) of femur length. RF = rectus femoris and VL = vastus lateralis.

(each repetition 3-second concentric and 3-second eccentric) at 50–60% 1RM with 3-minute rest periods between sets and the protocols complied with recommendations for RT and muscle hypertrophy. In addition, training protocols with similar concentric and eccentric durations were investigated previously in of our laboratory (24,25).

All protocols started the training period by performing 3 sets at 50% of 1RM. At week 3 (sixth training session), the intensity was increased to 60% of 1RM. In addition, one set was added at week 9 (20th training session), so the volunteers started the study by performing 3 sets and ending with 4 sets. In this study, the training load configuration and progression were controlled, considering that the manipulation of other variables in addition to MF could lead to a bias in the responses induced by both training protocols.

Every 2 weeks, also beginning in the third week (sixth training session), 1RM tests were reassessed before the first weekly training session with each of the lower limbs. These procedures aimed to maintain the relative intensity (50–60% 1RM) within the proposed training protocol settings throughout 14 weeks of training. A 10-minute rest period separated the 1RM test and the start of the training session. During these sessions, the 1RM test occurred at the same time of day as the pre-test to standardize the circadian rhythm that can influence strength performance.

An initial pilot study was conducted to test the feasibility of the MF and NMF protocols with volume equated. In MF training, all sets were performed until the subjects were unable to execute the concentric action of the pre-established ROM (70°). To equate the volume between the MF and NMF training protocols, the total number of repetitions performed in MF training from the previous training session was divided by the number of sets to be completed (3 or 4 sets), resulting in a mean number of repetitions per set. This procedure allowed a homogeneous distribution of the total repetition numbers throughout the sets in NMF protocol. When the total number of repetitions performed during the MF protocol was not a multiple of the number of sets, one repetition was added in the first and/or second set to maintain the same number of repetitions in the NMF protocol.

To ensure that the subjects always performed the MF protocol with the maximal number of repetitions, an estimated repetitions-to-failure scale with 11 points ("0" to "10 or greater") was used to estimate the number of repetitions that volunteers would still be able to perform at the end of each set. According to Hackett et al. (16), an estimated repetitions-to-failure score of "10 or greater" indicates that the subject can complete 10 or more repetitions, whereas a score of "0" indicated that the subject can complete no additional repetitions. In addition, a repetition was removed in the last set of the NMF protocol when the volunteers reported at the end of the penultimate set that they could not perform any further repetition (score "0"). This procedure was used to minimize the possibility of volunteers reaching MF in the last set, and proved to be effective, since MF occurred in only 0.8% of the set performed in NMF protocol.

The Borg 15-Category Scale for rating of perceived exertion (RPE) was also used to measure the volunteers' subjective perception of effort at the end of each set for both training protocols. The procedure for the establishment of the low ("7" score) and high ("19" score) anchors for each individual's perceived exertion was read to volunteers during performing one repetition in unilateral knee extension exercise without adding weight to the equipment and in NMR test, respectively. In this manner, volunteers established a perceptual relationship for the 7–19 range on the Borg 15-Category Scale based on the sensations that they perceived after performing one repetition with the free weight and immediately after NMR test. According to Gearhart et al. (13), standard instructions for the use of the RPE scale were read before the start of each training session, and the volunteers estimated their effort sensation after each set. The subjects were asked to assign an RPE score for the local effort from the active muscles. These subjective perceptions were recorded immediately after the end of each set, and the mean RPE value was calculated and used in the statistical analysis as mean perceived exertion of the training session.

Experimental Sessions 6 and 39 (2nd and 35th Training Sessions) (Electromyography Measurements). The surface EMG procedure (Biovision, Wehrheim, Germany) followed the recommendations of Hermens et al. (18). Bipolar surface electrodes (Ag/AgCl—3M-2223, Brazil) were placed parallel to the muscle fibers on the rectus femoris and vastus lateralis muscles. The skin areas were shaved and cleaned with alcohol and a cotton pad before placing the electrodes in pairs, 2 cm apart from their centers at the point of the greatest muscle area. The ground electrode was fixed to the patella. After the electrodes were attached, a silk paper was used to register their positions, as well as the patella and relevant marks on the skin. In addition, the volunteer's 2 lower limbs were photographed with the electrodes positioned. These procedures performed in second training session aimed at mapping the electrode positions on the thigh, allowing reproducibility in the 35th training session.

To measure the ROM and the muscle action durations during both protocols, the angular displacement was recorded using a potentiometer coupled to the rotational axis of the mechanical arm of the knee extension equipment for all training sessions. The potentiometer raw data were converted into angular displacement data and filtered through a fourth-order Butterworth low-pass filter with a cutoff frequency of 10 Hz. The duration of each muscle action comprised the time spent between the maximum (100° of knee flexion) and minimum (30° of knee flexion) angular positions, and thus, the concentric duration corresponded to the period between the maximum and minimum angular positions while the eccentric duration corresponded to the minimum and maximum angular positions. In addition, concentric/eccentric and repetition durations were determined throughout the angular displacement time. The data provided by the potentiometer also allowed the volunteers to have online access to the duration and ROM data of each muscle action on a laptop screen during all training sessions and tests (24,25). In addition, a metronome was used to help volunteers maintain pre-established repetition durations.

The electromyographic and potentiometer signals were synchronized and converted using an A/D board (Biovision, Wehrheim, Germany) and sampled at a frequency of 4,000 Hz. Appropriate software (DasyLab 11.0; Measurement Computing Corporation, MA) was used to record and treat the data. The electromyographic data acquisition was amplified 500 times and filtered (4th-order Butterworth band-pass filter of 20–500 Hz) to calculate the EMG amplitude as the root mean square (EMG_{RMS}). Before commencing each training session (second or 35th), subjects were asked to perform an MVIC test for 5 seconds on the knee extension machine exercise at 60° knee flexion (controlled by the potentiometer). The EMG_{RMS} value found during the MVIC test was then used as a reference for the normalization of the subsequent protocol measurements (normalization test). The mean EMG_{RMS} of concentric muscle actions for each protocol was then calculated. These values were divided by the respective reference values previously described, generating the normalized

EMG_{RMS} per protocol. The mean for each of the 2 protocols of EMG_{RMS} was used in the statistical analysis as the mean neuromuscular activation for each training session. For EMG_{RMS} acquisition during training sessions 2 and 35, subjects performed 3 sets with 50% of the most recent 1RM value for each protocol.

The $ICC_{[3,\ 1]}$ interprotocol was calculated using the EMG_{RMS} values obtained during the normalization test from experimental sessions 6 and 39. This procedure aimed to evaluate the reliability of EMG_{RMS} measurements in different lower limbs of the same individual, hence the feasibility of comparing the EMG_{RMS} responses of the 2 training protocols in this study. The EMG_{RMS} interprotocol values for both sessions were 0.84 for the rectus femoris and 0.80 for the vastus lateralis.

Statistical Analyses

Statistical analysis was performed with SPSS for Windows version 20.0 (SPSS, Inc., IL). Initially, paired-sample *t*-tests were implemented to test for differences in absolute baseline values for all variables analyzed, and no differences were identified between protocols. In addition, both protocols demonstrated increases in CSA, 1RM, MVIC, and MNR; hence, analysis of relative data was used instead. Therefore, considering the purpose of the study to verify the change caused by training protocols performed until MF or MFN, initially, the CSA, MVIC, 1RM, and MNR test performance data were transformed into relative responses ((Post-test − Pre-test)/Pre-test × 100). Data are presented as mean ± *SD*, as well as 95% confidence interval [CI] and individual values. The normality and homogeneity of variances were verified using Shapiro-Wilk and Levene's tests, respectively. Cohen's *d* values were calculated using the equation $d = (M_{MF} - M_{NMF})/((SD_{MF} + SD_{NMF})/2)$, in which M_{MF} is the mean of the MF protocol, M_{NMF} is the mean of the NMF protocol, and *SD* is the standard deviation in each protocol. These values are reported to reflect the magnitude of the differences (effect size) in each treatment where ≤0.20 was considered "trivial"; 0.21–0.49 "small"; 0.50–0.79 "moderate"; and ≥0.80 "large." The intrarater reliability was verified by the ICC ($ICC_{[3,\ 1]}$).

To compare the CSA relative responses between both training protocols, a paired-sample *t*-test for each muscle was performed. In addition, the maximum isometric strength (MVIC), dynamic strength (1RM), and strength endurance (MNR) relative responses also were compared using paired-sample *t*-tests.

To analyze the EMG_{RMS} normalized data for the rectus femoris and vastus lateralis muscles, the mean from the 3 sets obtained during the 6th and 39th sessions (2nd and 35th training sessions) were used for both protocols. A two-way (protocol × session) analysis of variance (ANOVA) with repeated measures assessed the normalized EMG_{RMS} for each muscle. When necessary, a post hoc Bonferroni honest significant difference test was used to identify the differences reported in the ANOVAs. One individual was removed from the EMG_{RMS} analysis due to technical problems in data collection ($n = 9$).

The individual analyses for CSA, 1RM, MVIC, MNR, and EMG_{RMS} tests were calculated according to Damas at al (8). Therefore, if an individual had a difference from the relative response from MF and NMF training within 2 typical errors (2 TEs), no difference in the response between protocols was considered. The TE was calculated using the equation TE = *SD*diff/$\sqrt{2}$, in which *SD*diff is the standard deviation of the difference scores observed between the 2 measurement performed.

In view of the control variables adopted in this study, paired-sample *t*-tests were used to compare the repetition durations (training sessions and MNR tests) and ROM between training protocols. Finally, considering that the total number of repetitions, the estimated repetitions-to-failure and the RPE data (for session) do not meet the precepts for a parametric analysis, Mann-Whitney-Wilcoxon tests were used to compare the responses of these variables for both protocols. These data are presented as median and interquartile range values. Probability was set at $p \leq 0.05$ for statistical significance for all tests.

Results

Cross-Sectional Area

The relative response for the rectus femoris muscle CSA showed no significant difference between MF (15.89 ± 11.71%, CI = [8.63–23.15]) and NMF protocols (20.11 ± 10.32%, CI = [14.49–27.29]) ($t_9 = -1.10$, $p = 0.30$, $d = -0.38$) (Figure 3A). Also, no significant difference was observed between protocols for the vastus lateralis muscle CSA (MF: 15.06 ± 14.20%, CI =

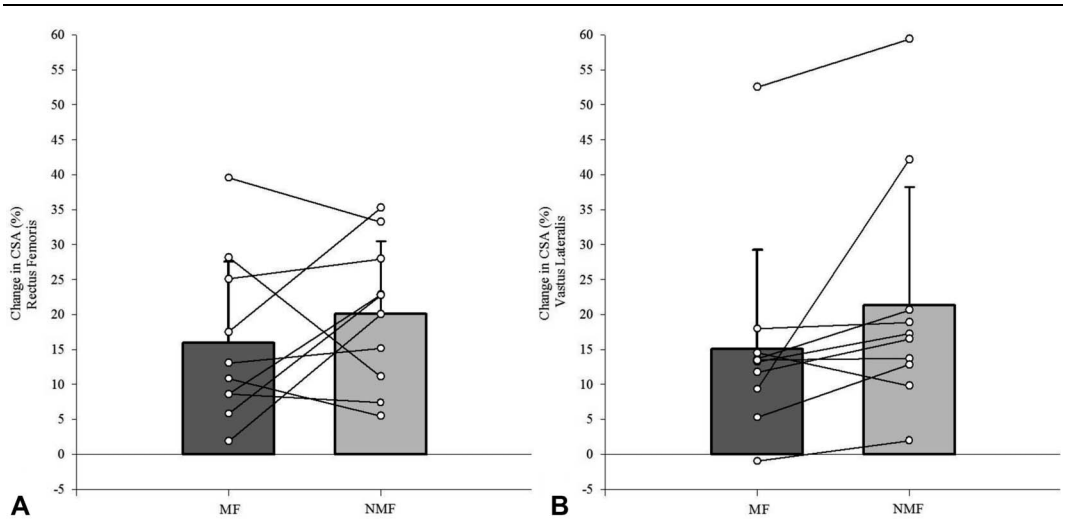

Figure 3. Changes in rectus femoris (A) and vastus lateralis (B) muscle cross-sectional areas (CSAs) at post-test relative to baseline for each training protocol: mean (vertical bars), standard errors (vertical lines), individual values for each training protocol (white circle), and link between individual values for each training protocol (sloping lines).

[6.26–23.86]; NMF: 21.30 ± 16.90%, CI = [10.82–31.77]) (t_9 = −1.90, p = 0.08, d = −0.40) (Figure 3B). Typical error values for rectus femoris and vastus lateralis muscles CSA were 1.96 and 2.94%, respectively. Two pre-test CSA measurements in each lower limb were used to calculate the TE.Individual analyses of the rectus femoris muscle CSA verified that 4 individuals (40% of the sample) responded more for NMF, 3 individuals (30% of the sample) responded more for MF, and the remaining 3 individuals (30% of the sample) showed no difference in the hypertrophic responses between training protocols (the difference was within 2 TE = 3.92%) (Figure 3A). Regarding the vastus lateralis muscle CSA, it was observed that 4 individuals (40% of the sample) responded more for NMF, and the other 6 individuals (60% of the sample) showed no difference in the hypertrophic responses between training protocols (2 TE = 5.87%) (Figure 3B).

One Repetition Maximum, Maximal Voluntary Isometric Contraction, and Maximum Number of Repetition

Concerning the strength performance tests, paired-sample *t*-tests indicated no significant differences between MF and NMF protocols for the 1RM (MF: 12.68 ± 12.53%, CI = [4.91–20.44]; NMF: 15.02 ± 12.87%, CI = [7.04–22.99]) (t_9 = −0.61, p = 0.55, d = −0.18) (Figure 4A), MVIC (MF: 13.85 ± 8.30%, CI = [8.70–18.99]; NMF: 14.96 ± 9.03%, CI = [9.36–20.56]) (t_9 = −0.40, p = 0.70, d = −0.13) (Figure 4B), and MNR performance (MF: 14.27 ± 21.11%, CI = [1.19–27.35]; NMF: 31.44 ± 34.53%, CI = [10.04–52.84]) (t_9 = −1.58, p = 0.15, d = −0.60) (Figure 4C).

The TE values were 3.18% (1RM), 3.69% (MVIC), and 16.10% (MNR) and were obtained from measures during the third (familiarization) and fourth (pre-test) sessions. A minimal interval of 48 hours was observed among sessions for each strength test procedures. The individual analyses for the 1RM tests showed that 2 individuals (20% of the sample) responded more for NMF, 1 individual (10% of the sample) responded more for MF, and the remaining 7 individuals (70% of the sample) showed no difference in maximal dynamic strength performance between training protocols (2 TE = 6.36%) (Figure 4A). Similarly, for the MVIC relative response, it was observed that 2 individuals (20% of the sample) responded more for NMF, 1 individual (10% of the sample) responded more for MF, and the

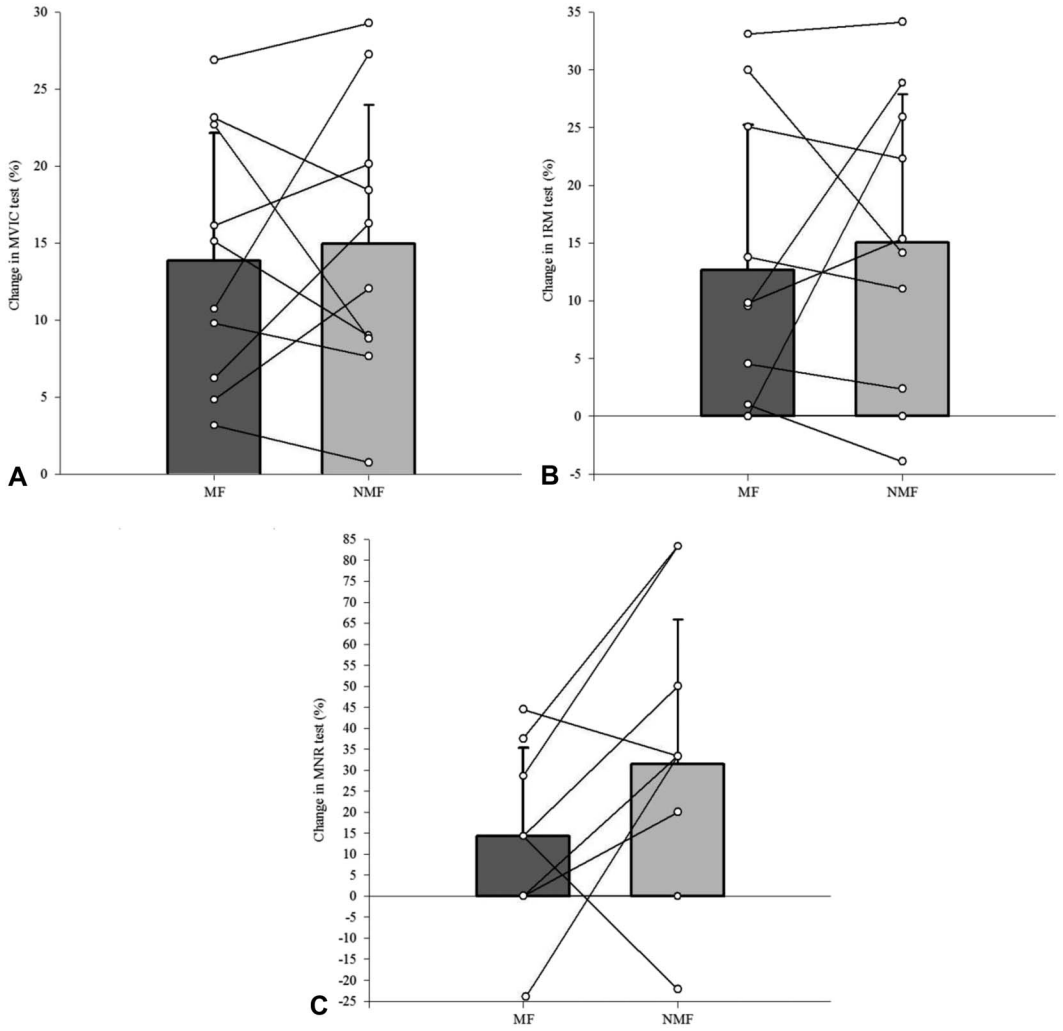

Figure 4. Changes in maximal voluntary isometric contraction (MVIC) (A), one repetition maximum (1RM) (B), and maximum number of repetition (MNR) (C) tests at post-test relative to baseline for each training protocol: mean (vertical bars), standard errors (vertical lines), individual values for each training protocol (white circle), and link between individual values for each training protocol (sloping lines).

other 7 individuals (70% of the sample) showed no difference in maximal isometric strength performance between training protocols (2 TE = 7.39%) (Figure 4B). Finally, regarding the MNR test performance, 5 individuals (50% of the sample) responded more for NMF, 1 individual (10% of the sample) responded more for MF, and the other 4 individuals (40% of the sample) showed no difference in muscular endurance performance between training protocols (2 TE = 32.10%) (Figure 4C).

EMG_{RMS} Normalized

There were no statistically significant differences in the neuromuscular activation between the MF and NMF training protocols during the second (rectus femoris—MF: 72.39 ± 16.72%, CI = [62.03–82.75]; NMF: 68.42 ± 23.75%, CI = [53.70–83.14]) (vastus lateralis—MF: 66.26 ± 12.05%, CI = [58.79–73.73]; NMF: 63.07 ± 19.40%, CI = [51.05–75.10]) and the 35th training sessions (rectus femoris—MF: 64.33 ± 14.43%, CI = [55.39–73.27]; NMF: 58.49 ± 19.65%, CI = [46.31–70.67]) (vastus lateralis—MF: 70.09 ± 19.20%, CI = [58.19–81.99]; NMF: 62.22 ± 11.83%, CI = [54.89–69.55]) (Figure 5A, B). More specifically, no significant interaction (time × protocol) was observed for the normalized EMG_{RMS} data for the rectus femoris ($F_{1,8} = 0.12$; $p = 0.74$) and vastus lateralis muscles ($F_{1,8} = 0.29$, $p = 0.60$). There were also no significant main effects for time ($F_{1,8} = 1.76$; $p = 0.22$; $d = 0.48$) ($F_{1,8} = 0.08$, $p = 0.78$, $d = -0.10$) and for protocol ($F_{1,8} = 0.65$, $p = 0.44$, $d = -0.26$) ($F_{1,8} = 1.56$, $p = 0.25$, $d = 0.35$) for the rectus femoris and vastus lateralis muscles, respectively.

In addition, the TE values for EMG_{RMS} were 15.60% (rectus femoris) and 20.10% (vastus lateralis). The EMG_{RMS} values for the MVIC tests performed during the fourth (pre-test) and second training sessions were used for the TE calculation. Similar to strength measures, a minimal interval of 48 hours was observed among sessions for each EMG tests procedures. Regarding EMG_{RMS} of the rectus femoris during the second training session, individual analyses verified that 2 individuals (22% of the sample) responded more for MF, whereas the other 7 individuals (78% of the sample) showed no difference in the EMG responses between training protocols (2 TE = 31.20%) (Figure 5A). In the 35th training session, all 9 individuals (100% of the sample) showed no difference in the EMG_{RMS} for the rectus femoris between training protocols (Figure 5B). Similarly, for EMG_{RMS} for the vastus lateralis during the 2nd and 35th training sessions, all 9 individuals (100% of the sample) showed no difference in the EMG_{RMS} for the rectus femoris between training protocols (2 TE = 40.20%) (Figure 5C, D).

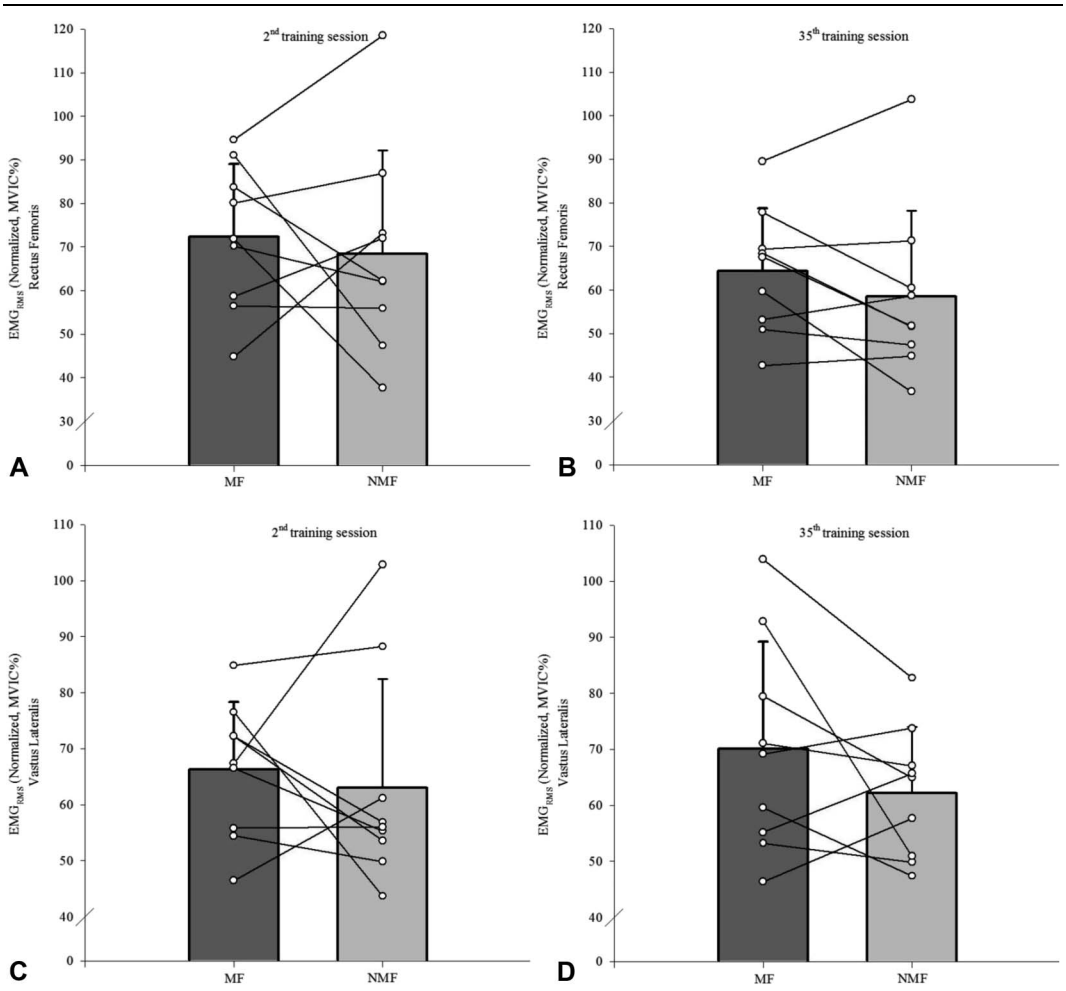

Figure 5. Normalized EMG_{RMS} of the rectus femoris (A and B) and Vastus lateralis (C and D) muscles for 2nd and 35th training sessions: mean (vertical bars), standard errors (vertical lines), individual values for each training protocol (white circle), and link between individual values for each training protocol (sloping lines). EMG_{RMS} = root mean square of the electromyographic signal.

Repetition Duration, ROM, Total Number of Repetitions, and Rating of Perceived Exertion

Concerning the control variables analyzed in this study, the MF and NMF protocols had similar repetition durations during the training sessions (MF: 5.99 ± 0.27 seconds; NMF: 6.00 ± 0.31 seconds) ($t = 0.50$, $p = 0.88$, $d = -0.03$) and MNR tests (MF: 4.00 ± 0.28 seconds; NMF: 3.99 ± 0.26 seconds) ($t = 0.12$, $p = 0.90$, $d = 0.04$). In addition, no significant differences were found for the average ROM between the MF and NMF protocols (MF: 71.14 ± 1.40°; NMF: 71.09 ± 1.27°) ($t = 0.88$, $p = 0.37$, $d = 0.03$). Regarding the total number of repetitions for each training protocol, Mann-Whitney-Wilcoxon test indicated differences between the MF (total repetitions = 739 [826-668]; first set = 8 [9-7], second set = 6 [7-5], last set (third or fourth) = 5 [6-4]) and NMF protocols (total repetitions = 734 [816-656]; first set = 6 [7-6], second set = 6 [7-6], last set (third or fourth) = 6 [6-5]) ($U = -2.67$; $p = 0.01$; $d = 0.08$); however, the magnitude of the difference between median values was less than 0.7% and deemed as trivial based on ES. For estimated repetitions to failure, significant differences were verified between the MF (Session = 0 [0-0]; first set = 0 [0-0], second set = 0 [0-0], last set (third or fourth) = 0 [0-0]) and NMF protocols (Session = 1 [2-0]; first set = 2 [2-1], second set = 1 [2-0], last set (third or fourth) = 0 [1-0]) ($U = -27.70$; $p = 0.0001$; $d = 1.36$). Finally, we observed significantly higher RPE values for the MF protocol (Session = 19 [19-19]; first set = 19 [19-19], second set = 19 [19-19], last set (third or fourth) = 19 [19-19]) compared with the NMF protocol (Session = 17 [18-15]; first set = 15 [17-15], second set = 17 [18-16], last set (third or fourth) = 18 [19-17]) ($U = -24.30$; $p = 0.0001$; $d = 1.20$).

Discussion

The purpose of this study was to compare the strength and muscle hypertrophy responses induced by MF or NMF training, as well as the level of activation of the rectus femoris and vastus lateralis muscles. To the best of our knowledge, no other studies have compared lower limbs chronic adaptations between different training protocols performed with MF or with NMF with equal training volumes, and analyzing average and individual data. The main results showed that both training protocols were similarly effective at inducing increases in strength and muscle hypertrophy gains, confirming the study hypothesis. Also, the normalized neuromuscular activation, in both rectus femoris and vastus lateralis muscles, was similar in MF and NMF protocols analyzed during the 2nd and 35th sessions; hence, the protocols promoted a similar neuromuscular demand. Overall, for untrained individuals, it is possible to suggest that an increased volume may be a more important variable than performing repetitions to MF for the chronic adaptations associated with RT. However, it is important that NMF training be performed with a relatively high degree of effort. Still on the effect of volume on chronic adaptations, Da Silva et al. (42) also showed similar strength and muscle hypertrophy gains for MF and NMF training when volumes were equalized. In addition, these protocols were superior to a lower volume training program based on muscle hypertrophic response but not for maximal strength performance. Thus, training volume probably has a greater impact on muscle hypertrophy gains than on strength performance gains (28,42).

The rectus femoris muscles of each trained leg had a similar average hypertrophy response for both MF and NMF protocols after 35 training sessions, with a small effect size ($d = -0.38$). In agreement with the average hypertrophic responses, the individual analyses demonstrated that a significant proportion of subjects showed no difference between protocols (30% of the subjects for rectus femoris). Nevertheless, some individuals greatly increased the rectus femoris muscle CSA in response to MF (40% of the subjects) while others responded better to the NMF training (30% of the subjects). A similar average hypertrophy response ($p = 0.08$) was also verified for the vastus lateralis muscle, also with a small effect size ($d = -0.40$). In addition, 60% of the subjects showed no difference between MF and NMF protocols for this muscle. Conversely, 40% of the subjects had a greater hypertrophic response to the NMF protocol, and no one responded more to the MF protocol. Therefore, the vastus lateralis hypertrophy individual responses suggest that NMF training with equal volume may promote similar or even greater muscle hypertrophy when compared with MF training. Recent studies found similar hypertrophic responses for MF and NMF training, specifically when attempting to match volume between protocols (28,33,42). Thus, taken together, the results of this study and previous investigations (28,33,42) indicate that the assumption that MF training maximizes muscle hypertrophy is not supported, as speculated in some previous reviews (12). In fact, it has been shown that protocols performed with repetitions to MF induce greater metabolic disturbance (e.g., ratios of adenosine triphosphate and adenosine diphosphate or monophosphate [ATP/ADP and ATP/AMP] and lower pH values) compared with submaximal repetitions (15). Regarding the association between hypertrophy and metabolic stress, it has been proposed that an accumulation of metabolites may increase the hormone concentrations related to muscle growth, which would make the environment more favorable for anabolism, thus enabling a subsequent accumulation of muscle proteins (32). It should be emphasized that changes in the AMP/ATP may also activate AMP-activated protein kinase (17), which decreases activation of protein kinases in the mammalian target of rapamycin (mTOR) signal transduction pathway (5). Although mTOR is involved in the protein synthesis process, a reduced activity could be detrimental to muscle hypertrophy gains. The elevation of post-exercise hormone responses would also increase the likelihood of hormone-receptor binding, initiating a cascade of intracellular events that could favor muscle growth (23). It is also suggested that acute elevations in hormone concentrations after resistance exercise would have a greater association with muscle tissue growth and remodeling than any hormonal changes measured at rest during a training period (23). According to Schoenfeld (40), an elevated metabolic stress may induce peaks in insulin-like growth factor (IGF-1), growth hormone, and testosterone, thereby providing an increase in post-exercise muscular proteins synthesis. However, metabolic and hormonal responses were not analyzed in this study, yet, the similar hypertrophic responses between MF and NMF protocols reinforce the reasoning that there is a threshold for metabolic stress beyond which no further beneficial effects are realized (41). Therefore, the high level of effort required to perform repetitions to MF in all sets was not able to promote a sufficient training stimulus to provide greater chronic adaptations compared with the NMF protocol (36).

The similar normalized EMG_{RMS} (average and individual responses) for the MF and NMF protocols in the current study did not confirm the premise that training to MF requires additional motor unit recruitment for the maintenance of force production to complete the task. For example, it was previously suggested that training to MF could result in increases in neuromuscular activation, in part due to additional recruitment of motor units for

the maintenance of force production to complete the task (36,38). Reinforcing this expectation, Burd et al. (6) observed a higher protein synthesis response after the execution of a protocol to MF compared with NMF. According to the authors, the increased protein synthesis response they observed could be related to higher motor unit recruitment necessary to perform repetitions to MF. The present findings are similar to a recent study conducted with untrained individuals (33) and may be explained by the EMG amplitude reaching a plateau at some repetitions before MF (44). Conversely, for trained individuals, protocols performed to MF might result in increased neuromuscular activation, which could explain the greater increases in strength and muscle hypertrophy after this training strategy. Given that the EMG amplitude would not truly reflect the recruitment of motor units (45), other factors such as increased firing frequency and motor unit synchronization may also influence neuromuscular activation and should not be disregarded in the interpretation of these outcomes. It is noteworthy that in a study using the automatic decomposition of surface EMG into motor unit action potential trains, the authors reported that higher threshold motor units were recruited when the vastus lateralis muscle was in a fatigued state (43).

In agreement with the CSA responses, the average maximal dynamic strength performance (1RM test) was similar for MF and NMF protocols and had a small effect size (0.18). The 1RM test individual analyses showed that 70% of the sample did not respond differently to the 2 protocols. As observed in this study, the absence of additional maximal dynamic strength increases due to performing repetitions to MF has been shown in meta-analysis completed by Davies et al. (9). Therefore, MF training is not necessary to maximize strength gains, confirming the hypothesis presented by previous studies reporting that training intensity, rather than volume, explains improvements in maximal strength adaptations (27). Given that a greater metabolic demand and neuromuscular fatigue was occurred in MF training, requiring a longer recovery period between training sessions (15), it could be argued that subsequent training sessions could have been affected, so that training would result at a lower intensity or volume (9). Thus, the effectiveness of both MF and NMF training modes on maximal strength would be influenced by the ability to recover and allow for progressive overload that may induce different implications for practitioners based on their performance and training experience (9). Nevertheless, the impact of these assumptions still needs to be verified in future studies.

It has been reported that re-evaluation of 1RM tests every 2 weeks to adjust training intensities may cause a bias in the protocol effect on an individual's performance for this test (29). These repeated measurements could promote the acquisition of a similar motor pattern to perform 1RM test, making it possible that differences between training protocols would not be found (3). Therefore, MVIC tests become a valid alternative to investigate the effects of different training protocols on muscle strength responses. However, the relative increases in the MVIC test performance also were similar for the 2 training protocols investigated (effect size 0.13). The 1RM test individual analyses have shown that 70% of the sample did not respond differently to the 2 protocols, and this finding is in agreement with previous studies (36,42).

Regarding muscular endurance, no differences were observed between MF and NMF protocols ($p = 0.15$). However, the medium effect size (−0.60) suggests that it might be possible that the protocols analyzed have provided distinct effects on muscular endurance performance. Also, the individual analyses reveal that a significant proportion of subjects showed no difference between MF and NMF protocols (40% of subjects). Nevertheless, some individuals greatly increased muscular endurance performance in response to NMF (50% of subjects) but only one had better responses to MF training (10% of subjects). The individual analysis responses suggest that NMF training with equal volumes as MF training induces a similar or even greater muscular endurance gain when compared with MF training. Based on these data, it may be speculated that the subjects who responded better to the NMF training would be more sensitive to fatigue associated with biochemical changes when performing repetitions to MF (e.g., reduced capacity to regenerate ATP), which decrease force and power production during successive sets (15), but this argument needs to be better clarified. It is important to note that the effect of MF training on muscular endurance gains may be dependent on the muscle group trained, training status, and sex (28). Studies investigating the impact of MF and NMF protocols on lower-limb muscular endurance performance found divergent outcomes (21,35). Izquierdo et al. (21) observed similar gains for both training modes, but in a recent study by Prestes et al. (35), the MF protocol (rest pause) was superior to the NMF protocol (traditional multiple set) for muscular endurance in trained individuals. It has been suggested that performing repetitions to MF would be necessary to improve the capacity to tolerate muscle fatigue (21,28); consequently, it may induce greater increases in muscular endurance performance when compared with NMF protocol (21). In addition, it has been reported that RPE (obtained immediately after completion of the sets) has been used to investigate the physiological mechanisms of fatigue associated with resistance exercise (22). However, the higher RPE values during the MF protocol compared with the NMF protocol in this study, and others (11,39) do not corroborate the assumption that an elevated fatigue response would also provide greater muscular endurance performance. According to Santos et al. (39), a possible explanation would be that the higher repetition numbers performed in the initial sets during MF protocols could result in greater RPE values, but if an effort threshold exists to increase the motor unit recruitment and metabolic stress, then the impact of repetitions performed to MF may be dependent on the number of sets being executed. Thus, this impact would be greater in a single-set MF protocol, but during multiple sets, the accumulation of fatigue also may result in elevated efforts in the later sets for NMF protocols (11,39). Therefore, it is possible that both protocols analyzed in this study required similar efforts and muscle fatigue levels following the last set, inducing similar muscular endurance responses. However, based on the contradictory results found in the literature and inconclusive results found in the current study, it is not possible to confirm or refute the expectation of a superior muscular endurance response of MF training compared with NMF training.

A limitation of the intraindividual experimental design is a possible cross-training or cross-education effect (4). There is evidence in the literature indicating that the cross-training effect, if it occurs, could be restricted to neural parameters and muscle strength gains but not morphological changes (e.g., CSA) (4). In addition, the hormonal responses have also not been considered an important factor for the cross-training effect (30). Beyer et al. (4) found an increase in muscle mass only in the trained limb despite the exposure of both limbs to similar hormonal concentrations. One possible explanation for distinct hypertrophic responses between trained and untrained limbs would be that the morphological adaptations associated with resistance training in the content and affinity of anabolic hormones receptors (e.g., testosterone) occur only in the trained limb (23). However,

muscle strength gains in the contralateral limb would reflect an increase in motor neuron activation and probably are not related to morphological adaptations. However, previous studies investigating cross-training effects report increases or no changes in neuromuscular activation of the untrained limb (19). It has been reported that changes in neuromuscular activation of the untrained limb could be related to the training mode performed (e.g., type of muscle action) and similar to gains in muscle strength (19). In addition, it has been suggested that the cross-training effect contributes approximately 7.8% to muscle strength gains of the contralateral limb (30), and this adaptation would result from neural mechanisms involving acute facilitation at the motor cortex to the untrained contralateral limb after excitation of the trained limb (11). The training protocols in the current study were performed with a minimal interval of 24 hours to minimize the potential acute, deleterious effects of unilateral training on muscular strength performance on the contralateral limb. Finally, it has been argued that when both limbs of the same individual are trained by performing different protocols, the cross-training effect is minimal or nonexistent (30), therefore, it could be expected that any difference in strength responses between limbs would be due to the different training protocols (11).

Practical Applications

This study showed that a NMF protocol with equal volumes as an MF protocol produced similar strength and muscle hypertrophy gains. These results suggest that performing repetitions to MF was not a determining factor for the chronic adaptations associated with RT; hence. NMF training (with equal volume to MF) could be an alternative training method for untrained individuals. In addition, based on the vastus lateralis muscle CSA and muscular endurance individual analyses, a higher number of individuals responded better to the NMF protocol. These results could be related to the need for a longer recovery period between sessions for individuals training to MF; thus, an insufficient recovery would induce a greater action of inhibitory mechanisms impairing the adaptations promoted by this training mode.

Strength and conditioning professionals could opt for periodically performing an MF protocol to determine the maximal number repetitions that could be completed by an individual, but then distribute the volume between sets in subsequent NMF training sessions. This training strategy could result in a similar or even better muscle hypertrophy and muscular endurance adaptations compared with performing repetitions to MF in all training sessions, but with lower perceptions of effort. However, these recommendations are limited to the exercise and sample with characteristics similar to those of the current study. Finally, future research is needed to determine the impact of MF protocols on the chronic adaptations associated with RT.

Acknowledgments

Supported by the FAPEMIG; CAPES (Brazil); and PRPq of Universidade Federal de Minas Gerais.

References

1. Antonio J. Nonuniform response of skeletal muscle to heavy resistance training: Can bodybuilders induce regional muscle hypertrophy? *J Strength Cond Res* 14: 102–113, 2000.
2. Beck T. The importance of a priori sample size estimation in strength and conditioning research. *J Strength Cond Res* 27: 2323–2337, 2013.
3. Bernardi M, Solomonow M, Nguyen G, Smith A, Baratta R. Motor unit recruitment strategy changes with skill acquisition. *Eur J Appl Physiol Occup Physiol* 74: 52–59, 1996.
4. Beyer KS, Fukuda DH, Boone CH, et al. Short-term unilateral resistance training results in cross education of strength without changes in muscle size, activation, or endocrine response. *J Strength Cond Res* 30: 1213–1223, 2016.
5. Bolster DR, Crozier SJ, Kimball SR, Jefferson LS. AMP-activated protein kinase suppresses protein synthesis in rat skeletal muscle through down-regulated mammalian target of rapamycin (mTOR) signaling. *J Biol Chem* 277: 23977–23980, 2002.
6. Burd NA, Andrews RJ, West DWD, et al. Muscle time under tension during resistance exercise stimulates differential muscle protein sub-fractional synthetic responses in men. *J Physiol* 590: 351–362, 2012.
7. Cadore EL, Pinto RS, Lhullier FLR, et al. Physiological effects of concurrent training in elderly men. *Int J Sports Med* 31: 689–697, 2010.
8. Damas F, Barcelos C, Nóbrega SR, et al. Individual muscle hypertrophy and strength responses to high vs. low resistance training frequencies. *J Strength Cond Res* 33: 897–901, 2019.
9. Davies T, Orr R, Halaki M, Hackett D. Effect of training leading to repetition failure on muscular strength: A systematic review and meta-analysis. *Sport Med* 46: 487–502, 2016.
10. Figueiredo VC, de Salles BF, Trajano GS. Volume for muscle hypertrophy and health outcomes: The most effective variable in resistance training. *Sport Med* 48: 499–505, 2018.
11. Fisher J, Blossom D, Steele J. A comparison of volume-equated knee extensions to failure, or not to failure, upon rating of perceived exertion and strength adaptations. *Appl Physiol Nutr Metab* 41: 168–174, 2016.
12. Fisher J, Steele J, Smith D. Evidence based resistance training. *Med Sport* 17: 217–235, 2013.
13. Gearhart RE, Goss FL, Lagally KM, et al. Standardized scaling procedures for rating perceived exertion during resistance exercise. *J Strength Cond Res* 15: 320–325, 2001.
14. Gieβsing J, Fisher J, Steele J, et al. The effects of low-volume resistance training with and without advanced techniques in trained subjects. *J Sports Med Phys Fitness* 56: 249–258, 2016.
15. Gorostiaga EM, Navarro-Amézqueta I, González-Izal M, et al. Blood lactate and sEMG at different knee angles during fatiguing leg press exercise. *Eur J Appl Physiol* 112: 1349–1358, 2012.
16. Hackett DA, Johnson NA, Halaki M, Chow C-M. A novel scale to assess resistance-exercise effort. *J Sports Sci* 30: 1405–1413, 2012.
17. Hardie DG. Sensing of energy and nutrients by AMP-activated protein kinase. *Am J Clin Nutr* 93: 891S–896S, 2011.
18. Hermens HJ, Freriks B, Disselhorst-Klug C, Rau G. Development of recommendations for SEMG sensors and sensor placement procedures. *J Electromyogr Kinesiol* 10: 361–374, 2000.
19. Hortobágyi T, Lambert NJ, Hill JP. Greater cross education following training with muscle lengthening than shortening. *Med Sci Sports Exerc* 29: 107–112, 1997.
20. Izquierdo-Gabarren M, Expósito R, García-Pallarés J, et al. Concurrent endurance and strength training not to failure optimizes performance gains. *Med Sci Sport Exerc* 42: 1191–1199, 2010.
21. Izquierdo M, Ibañez J, González-Badillo JJ, et al. Differential effects of strength training leading to failure versus not to failure on hormonal responses, strength, and muscle power gains. *J Appl Physiol* 100: 1647–1656, 2006.
22. Keller JL, Housh TJ, Hill EC, et al. Neuromuscular responses of recreationally active women during a sustained, submaximal isometric leg extension muscle action at a constant perception of effort. *Eur J Appl Physiol* 118: 2499–2508, 2018.
23. Kraemer W, Ratamess N. Hormonal responses and adaptations to resistance exercise and training. *Sports Med* 35: 339–361, 2005.
24. Lacerda LT, Costa CG, Lima FV, et al. Longer concentric action increases muscle activation and neuromuscular fatigue responses in protocols equalized by repetition duration. *J Strength Cond Res* 33: 1629–1639, 2019.
25. Lacerda LT, Martins-Costa HC, Diniz RCR, et al. Variations in repetition duration and repetition numbers influence muscular activation and blood lactate response in protocols equalized by time under tension. *J Strength Cond Res* 30: 251–258, 2016.
26. Lasevicius T, Ugrinowitsch C, Schoenfeld BJ, et al. Effects of different intensities of resistance training with equated volume load on muscle strength and hypertrophy. *Eur J Sport Sci* 18: 772–780, 2018.
27. Mangine GT, Hoffman JR, Gonzalez AM, et al. The effect of training volume and intensity on improvements in muscular strength and size in resistance-trained men. *Physiol Rep* 3: e12472, 2015.

28. Martorelli S, Cadore EL, Izquierdo M, et al. Strength training with repetitions to failure does not provide additional strength and muscle hypertrophy gains in young women. *Eur J Transl Myol* 27: 113–120, 2017.
29. Morton RW, Oikawa SY, Wavell CG, et al. Neither load nor systemic hormones determine resistance training-mediated hypertrophy or strength gains in resistance-trained young men. *J Appl Physiol* 121: 129–138, 2016.
30. Munn J, Herbert RD, Gandevia SC. Contralateral effects of unilateral resistance training: A meta-analysis. *J Appl Physiol* 96: 1861–1866, 2004.
31. Murach KA, Bagley JR. Skeletal muscle hypertrophy with concurrent exercise training: Contrary evidence for an interference effect. *Sport Med* 46: 1029–1039, 2016.
32. Nishimura A, Sugita M, Kato K, et al. Hypoxia increases muscle hypertrophy induced by resistance training. *Int J Sports Physiol Perform* 5: 497–508, 2010.
33. Nóbrega SR, Ugrinowitsch C, Pintanel L, Barcelos C, Libardi CA. Effect of resistance training to muscle failure vs. volitional interruption at high- and low-intensities on muscle mass and strength. *J Strength Cond Res* 32: 162–169, 2018.
34. Noorkoiv M, Nosaka K, Blazevich AJ. Assessment of quadriceps muscle cross-sectional area by ultrasound extended-field-of-view imaging. *Eur J Appl Physiol* 109: 631–639, 2010.
35. Prestes J, Tibana R, Sousa E, et al. Strength and muscular adaptations following 6 weeks of rest-pause versus traditional multiple-sets resistance training in trained subjects. *J Strength Cond Res* 33(suppl 1): S113–S121, 2019.
36. Rooney K, Herbert R, Balnave R. Fatigue contributes to the strength train stimulus. *Med Sci Sports Exerc* 26: 1160–1164, 1994.
37. Sakamoto A, Sinclair PJ. Effect of movement velocity on the relationship between training load and the number of repetitions of bench press. *J Strength Cond Res* 112: 1015–1025, 2006.
38. Sale DG. Influence of exercise and training on motor unit activation. *Exerc Sport Sci Rev* 15: 95–151, 1987.
39. Santos WDND, Vieira CA, Bottaro M, et al. Resistance training performed to failure or not to failure results in similar total volume, but with different fatigue and discomfort levels. *J Strength Cond Res*, 2019. Epub ahead of print.
40. Schoenfeld B. Potential mechanisms for a role of metabolic stress in hypertrophic adaptations to resistance training. *Sports Med* 43: 179–194, 2013.
41. Schoenfeld B, Grgic J. Does training to failure maximize muscle hypertrophy? *Strength Cond J* 41: 108–113, 2019.
42. Da Silva LXN, Teodoro JL, Menger E, et al. Repetitions to failure versus not to failure during concurrent training in healthy elderly men: A randomized clinical trial. *Exp Gerontol* 108: 18–27, 2018.
43. Stock MS, Beck TW, Defreitas JM. Effects of fatigue on motor unit firing rate versus recruitment threshold relationships. *Muscle Nerve* 45: 100–109, 2012.
44. Sundstrup E, Jakobsen MD, Andersen CH, et al. Muscle activation strategies during strength training with heavy loading vs. repetitions to failure. *J Strength Cond Res* 26: 1897–1903, 2012.
45. Vigotsky AD, Halperin I, Lehman GJ, Trajano GS, Vieira TM. Interpreting signal amplitudes in surface electromyography studies in sport and rehabilitation sciences. *Front Physiol* 8: 1–15, 2018.