[RESEARCH REPORT]

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Effects of Electrical Stimulation Parameters on Fatigue in Skeletal Muscle

STUDY DESIGN: Experimental laboratory study.

OBJECTIVES: The primary purpose was to investigate the independent effects of current amplitude, pulse duration, and current frequency on muscle fatigue during neuromuscular electrical stimulation (NMES). A second purpose was to determine if the ratio of the evoked torque to the activated area could explain muscle fatigue.

BACKGROUND: Parameters of NMES have been shown to differently affect the evoked torque and the activated area. The efficacy of NMES is limited by the rapid onset of muscle fatigue.

METHODS AND MEASURES: Seven healthy participants underwent 4 NMES protocols that were randomly applied to the knee extensor muscle group. The NMES protocols were as follows: standard protocol (Std), defined as 100-Hz, 450-μs pulses and amplitude set to evoke 75% of maximal voluntary isometric torque (MVIT); short pulse duration protocol (SP), defined as 100-Hz, 150-μs pulses and amplitude set to evoke 75% of MVIT; low-frequency protocol (LF), defined as 25-Hz, 450-μs pulses and amplitude set to evoke 75% of MVIT; and low-amplitude protocol (LA), defined as 100-Hz, 450-μs pulses and amplitude set to evoke 45% of MVIT. The peak torque was measured at the start and at the end of the 4 protocols, and percent fatigue was calculated. The outcomes of the 4 NMES protocols on the initial peak torque and activated cross-sectional area were recalculated from a companion study to measure torque per active area.

RESULTS: Decreasing frequency from 100 to 25 Hz decreased fatigue from 76% to 39%. Decreasing the amplitude and pulse duration resulted in no change of muscle fatigue. Torque per active area accounted for 57% of the variability in percent fatigue between Std and LF protocols.

CONCLUSIONS: Altering the amplitude of the current and pulse duration does not appear to influence the percent fatigue in NMES. Lowering the stimulation frequency results in less fatigue, by possibly reducing the evoked torque relative to the activated muscle area. *J Orthop Sports Phys Ther 2009;39(9):684-692. doi:10.2519/jospt.2009.3045*

KEY WORDS: *amplitude, frequency, NMES, pulse duration*

Neuromuscular electrical stimulation (NMES) is a promising tool in the rehabilitation of individuals with a limited ability to activate their skeletal muscles,[13,35,36] as well as a method of strength training and short-term resistance training in athletic populations.[26,27] During NMES application, the capacity to maintain performance is compromised compared to voluntary exercise, resulting in a higher rate of muscle fatigue.[23] Muscle fatigue is defined as a reduction in the peak force, with continuous and repeated activation that could impair functional or therapeutic goals.[14,15] Muscle fatigue could result from either increasing the metabolic cost of muscular contractions or from the pattern of motor units recruitment during stimulation.

Measuring the peak torque or torque-time integral (TTI) has been used as an index to reflect the metabolic cost of the stimulated muscle,[5,29-31] because the force-generating capacity is a function of the number of cross-bridges between actin and myosin myofilaments which are directly related to ATP hydrolysis.[32,33] Additionally, the initial peak torque has been correlated to fatigue resulting from NMES.[29] Moreover, during stimulation, muscle fiber recruitment patterns vary from the well-known size principle recruitment that occurs during voluntary contractions.[20,21] Evidence suggests that muscle recruitment during NMES occurs in a random order, likely depending on the position of the stimulating electrodes,[1,18,21,24] and that motor units are activated in a synchronous and repeated manner.[1,8,24] This pattern of motor unit activation may lead to greater fatigue by preventing the cycling of motor unit activation that is thought to occur during submaximal voluntary muscle actions.[1,8,24]

NMES parameters (eg, current amplitude, frequency, and pulse duration) are known to play a critical role in torque production during repeated contrac-

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tions.[1,8,16,17] It is generally accepted that increasing current amplitude, frequency, and pulse duration will increase evoked torque; however, the independent effects of these parameters on motor units recruitment are less appreciated. Previous studies have clearly established that increasing current amplitude leads to increased torque production via the activation of additional motor units.[1,17] Binder-Macleod et al[8] showed that increasing the current amplitude results in steep rise of the torque, followed by a plateau at a high level of stimulation. Increasing pulse duration has also been shown to increase the evoked torque by possibly increasing motor unit activation.[17] A pulse duration of 450 μs elicited 22% and 55% greater torque output compared to pulse durations of 250 and 150 μs, respectively.[16,17] However, increasing the frequency of NMES has been shown to increase evoked torque by increasing the torque per active muscle area of skeletal muscle.[9,17]

Because increasing the frequency and pulse duration increase the evoked torque per unit of activated muscle,[9,17] it causes an increased energy demand that cannot be supplied by the muscle and thus leads to muscular fatigue.[4,28] These findings may illustrate that fatigue during NMES is not necessarily related to peak muscle torque production, but may in fact be related to the metabolic demand placed upon each activated motor unit. Thus torque per active area, rather than torque production, could provide a better indicator of the metabolic demand during stimulation.

The independent effects of these 3 parameters on muscular fatigue are still controversial. Conflicting results exist on the role of current amplitude on muscle fatigue, with 1 study demonstrating an increase fatigue with increasing amplitude[8] and others demonstrating no change in fatigue with increasing current amplitude.[1,34] Increasing the frequency of pulses has been shown to accelerate muscle fatigue.[7,25] For example, a stimulus at a frequency of 85 Hz has been shown to cause more fatigue compared to 25 Hz[10] because of the high metabolic cost associated with stimulation at 85 Hz.[29,30] Yet another study showed that this general rule is debatable when settings of 80 Hz and 100 Hz demonstrated no significant difference in muscular fatigue.[31] Compared to the influence of current amplitude and frequency, the role of pulse duration on muscle fatigue is even less well established.

The primary purpose of this study was to examine the independent effects of current amplitude, frequency, and pulse duration on muscle fatigue after altering the evoked torque and muscle recruitment. To accomplish this purpose, the current amplitude was increased from that needed to evoke 45% of maximal voluntary isometric torque (MVIT) to that needed to evoke 75% of MVIT, pulse duration was increased from 150 to 450 μs, and the frequency was increased from 25 to 100 Hz. A second purpose was to examine the relationship between the evoked torque adjusted to the activated area and muscle fatigue. The rationale was based on the hypothesis that altering the NMES parameters to increase the initial peak torque relative to the activated area would lead to a concomitant increase in muscle fatigue.

METHODS

THIS STUDY USED DATA COLLECTED, but not analyzed, in an earlier study of the effects of NMES on specific tension (ie, the evoked torque relative to the activated area). Because of the inherent difficulties in determining the physiological variables (pennation angle, moment arm, and fiber length) used to estimate specific tension for the knee extensor muscle group, we have separated these data into 2 sets to address different research questions using the same NMES protocols.

Subjects

Seven healthy participants (6 males and 1 female) were recruited from the university community. None had a history of knee or hip pathological conditions. They were (mean ± SD) 28 ± 4 years old, weighed 68 ± 9 kg, and were 173 ± 9 cm tall. They all had previous experience with similar research protocol to address different research questions. The associated benefits and risks of participating in the study were explained to each subject, and each subject signed a written informed consent. The Institutional Review Board of The University of Georgia approved the protocol for this study.

Procedure

Familiarization Session One week prior to data collection, subjects participated in a 30-minute practice session to acquaint themselves with the NMES protocols. In this session, each subject was asked to perform 3 trials of maximum voluntary isometric knee extension efforts for both lower extremities. The highest trial for each lower extremity was considered the MVIT effort. To demonstrate tolerance of the 4 NMES protocols, each knee extensor muscle group was assigned 2 protocols and was then stimulated. Each stimulation protocol delivered 30 isometric contractions to the knee extensor muscle group. The procedure was performed to determine if all participants could tolerate stimulation at 75% of their MVIT.

Maximum Voluntary Isometric Torque MVIT of the left and right knee extensors were determined for each participant, as described previously.[1,34] The participant sat on a custom-built chair, with a hip angle of 110° and the knee secured at approximately 60° of flexion. The shin of the lower leg was firmly secured to a rigid lever arm with an inelastic strap, to ensure that the knee extensors could perform only isometric actions. A lever arm was established by placing a load cell perpendicular to, and 33 cm away from, the axis of rotation of the lever arm. The participant was asked to contract the knee extensors as fast and forcefully as possible, while verbal encouragement was provided. Trials were repeated if the difference between the peaks of 2 separate trials was greater than 5%. The load cell, interfaced with a personal computer, was used to measure knee extension torque expressed in Nm. All force data were corrected for gravity and then saved for future analysis.

TABLE 1 SUMMARY OF THE 4 NMES PROTOCOLS AND THEIR OUTCOMES*

Protocol	Amplitude (mA)	Frequency (Hz)	Pulse Duration (μs)	Torque (Nm)	Activated CSA (cm^2)	Torque per Active Area (Nm/cm^2)
Std	74 ± 18	100	450	166 ± 41	30 ± 7	5.7 ± 1.2
SP	76 ± 16	100	150†	78 ± 40‡	18 ± 10‡	4.3 ± 1.3‡
LF	72 ± 18	25†	450	137 ± 30‡	36 ± 8	3.9 ± 0.9‡
LA	56 ± 13†	100	450	109 ± 35‡	22 ± 12‡	5.8 ± 2.1

Abbreviations: CSA, cross-sectional area; LA, low-amplitude protocol; LF, low-frequency protocol; NMES, neuromuscular electrical stimulation; SP, short pulse duration protocol; Std, standard protocol.

* *Values, except those of frequency and pulse duration, are mean ± SD.*

† *Different from the Std protocol.*

‡ *Significantly different from Std ($P<.05$).*

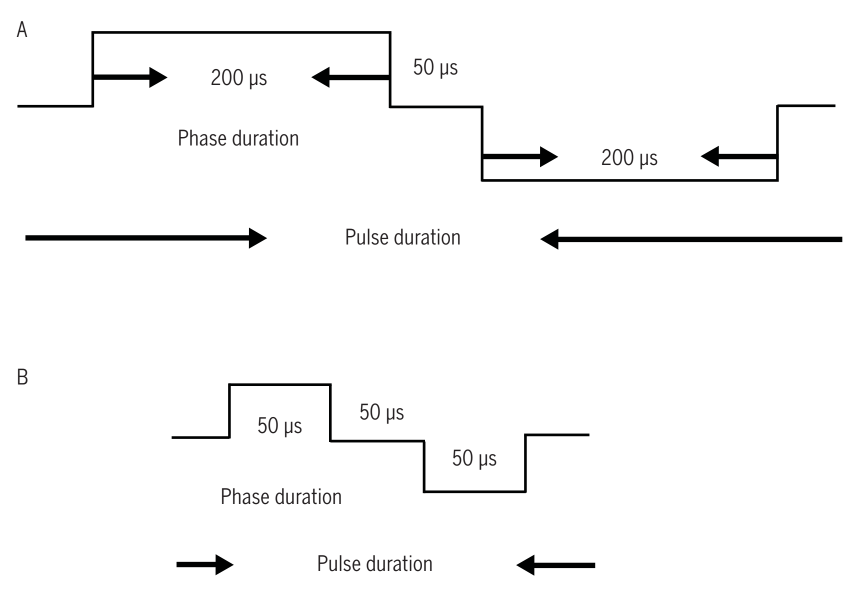

FIGURE 1. Illustration of the durations (450 and 150 μs) of the symmetrical biphasic pulses used for the Std, LF, LA (450 μs), and SP (150 μs) protocols. The phase duration was 200 and 50 μs for the 450 and 150 μs pulses, respectively.

After determining the MVIT, each subject was asked to assess his/her ability to tolerate NMES. A Theratouch 4.7 NMES unit (Rich-Mar Corporation, Inola, OK) was used. The current amplitude required to elicit 75% of the MVIT for each lower extremity was determined by delivering 1-second trains of progressively greater amplitude at a frequency of 100 Hz, with a 450-μs pulse duration. At least 1 minute separated each train. All participants were asked to completely relax, and the current was progressively increased. Three to 4 trials per participant were performed to determine the amplitude of the current in milliamps (mA).

NMES was applied to the knee extensor muscle group via large (8 × 10-cm) surface electrodes (Uni-Patch Inc, Wabasha, MN), as done previously.[1,13,34] One electrode was placed on the skin 2 to 3 cm above the superior aspect of the patella, over the vastus medialis muscle, and the other lateral to and 30 cm above the patella, over the vastus lateralis muscle. The anatomical location of each pair of electrodes was marked with a permanent marker to ensure similar positioning in subsequent protocols.

NMES Protocols The current amplitude was adjusted until a torque equivalent to 75% of the MVIT was evoked, using the nonfatiguing trains. The current amplitudes were determined for the right, followed by the left, knee extensors.[17] Next, 1 of 4 NMES protocols was randomly applied to the knee extensors: 2 protocols were applied to the right lower extremity and the other 2 applied to the left. The protocols were as follows: (1) a standard protocol (Std) of 100-Hz frequency, 450-μs pulse duration, and a current amplitude set to evoke 75% MVIT; (2) a short pulse duration protocol (SP) of 100-Hz frequency, 150-μs pulse duration, and a current amplitude set to evoke 75% MVIT; (3) a low-frequency protocol (LF) of 25-Hz frequency, 450-μs pulse duration, and a current amplitude set to evoke 75% MVIT; and (4) a low-amplitude protocol (LA) of 100-Hz frequency, 450-μs pulse duration, and at a current that evoked the average of the initial torques of SP and LF, as there was no available consensus on the lowest amplitude that should be used to stimulate the knee extensors (**TABLE 1**). Rectangular symmetrical biphasic pulses were used for the 4 protocols (**FIGURE 1**). Thirty 3-second contractions were evoked over a 3-minute period for each protocol (work-to-rest cycle of 3 seconds on and 3 seconds off).[17] The administration order of the 4 protocols was randomized to each participant and to both knee extensors. At least 120 minutes separated 2 subsequent protocols to ensure muscle fatigue recovery. Before starting a new protocol, the recovery of force was examined by applying Std for 1 second and performing a MVIT. The recovery force and MVIT had to be within 1% of the initial testing to proceed to the next protocol. Pilot work suggested that recovery time should

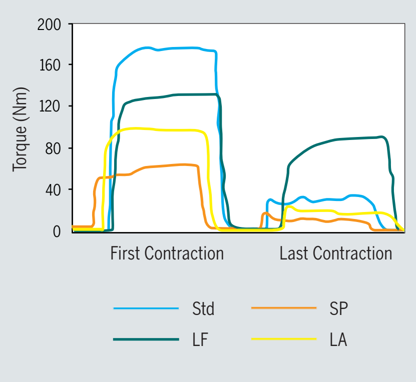

FIGURE 2. Force traces of the 3-second first and last contractions of electrically evoked torque for the 4 stimulation protocols. For the last contraction, Std and LF were only labeled for the purpose of clarity. Abbreviations: LA, low-amplitude protocol; LF, low-frequency protocol; SP, short pulse duration protocol; Std, standard protocol.

TABLE 2 KNEE EXTENSOR TORQUE FOR NUMBER OF CONTRACTIONS BY THE 4 STIMULATION PROTOCOLS*

	Contraction 1	Contraction 11	Contraction 21	Contraction 30
Std	166 ± 41	64 ± 19†	51 ± 17†	40 ± 18†
SP	78 ± 40	36 ± 29†	31 ± 27†	25 ± 14†
LF	137 ± 30	105 ± 36†	88 ± 33†	83 ± 28†
LA	109 ± 35	49 ± 29†	39 ± 26†	37 ± 20†

Abbreviations: LA, low-amplitude protocol; LF, low-frequency protocol; SP, short pulse duration protocol; Std, standard protocol.

* *Knee extensor torque (Nm) was measured at the beginning of each minute (contractions 1, 11, 21) and for the final contraction (30). Values are mean ± SD Nm.*

† *Significantly different from the initial contraction ($P<.05$).*

not exceed 10 minutes after any of the 4 protocols. Therefore, the 2-hour interval provided between the 2 protocols was enough to ensure full recovery of force of the same knee extensors.

Peak Torque Peak isometric torque was reported as the average torque over a 500-millisecond window. The window began after the contraction rose above baseline and recorded torque from 250 to 750 milliseconds (**FIGURE 2**). The peak torque was reported at the beginning of each minute (contractions 1, 11, 21) of the 3-minute session and for the final contraction (contraction 30) (**TABLE 2**). The fatigue index was measured and reflects the difference between the torques of the initial and final contractions divided by the torque of the initial contraction[2,3]: percent fatigue = ([torque of the first contraction – torque of the last contraction]/torque of the first contraction) × 100.

Torque-Time Integral (TTI) The TTI of the first contraction was measured and was used as an index for the force generated during the 3-second isometric contractions of the 4 NMES protocols.[29,30] The TTI of the first contraction was adjusted to the activated cross-sectional area (CSA) to determine its possible role in muscle fatigue.

Torque per Active Area The torque per active area was calculated by dividing the highest torque (Nm) achieved for each NMES protocol by the total activated skeletal muscle area (cm^2).[9,16,17] The torque and the activated CSA values in response to the 4 NMES protocols were previously measured and published.[17] Considering the clinical purpose of the current study, we recalculated these values and presented them as torque relative to the activated CSA (Nm/cm^2): torque per active area = peak torque of the first contraction/the activated knee extensor CSA. The activated CSA was measured using T2 magnetic resonance imaging (MRI).

Magnetic Resonance Imaging Standard spin echo images of the thighs were collected using a Signa 1.5-T superconducting magnet (General Electric Company, Milwaukee, WI) (**FIGURE 3**). After 30 minutes of lying down supine to avoid body fluid shift, subjects were positioned within the magnet using the whole body coil. Transaxial images were obtained before NMES, and the participant was then moved out of the magnet to a separate room to perform the NMES protocols. After each NMES protocol, the subject was asked to walk to the MRI unit without bearing weight on the stimulated lower extremity so as to repeat the imaging within 3 minutes after ending the electrical stimulation. The total time of the scan was around 4 minutes and 40 seconds. The scout view time and subsequent imaging adjustments (mean ± SD, 2 minutes ± 23 seconds) made the total imaging time almost 7 minutes. The transaxial T2 images (TR/TE = 2000/30, 60) were 1 cm thick and 1 cm apart. They had a 40-cm field of view, with a 256 × 256 matrix size, and the number of excitations was 1. Fourteen to 18 slices for each subject were analyzed for the knee extensors, beginning with the first slice containing the 4 heads of the quadriceps femoris muscle group, and continued distally until the slice just before the proximal pole of the patella. Images were analyzed and T2 values calculated with the NIH Image 1.62 software.[16,17]

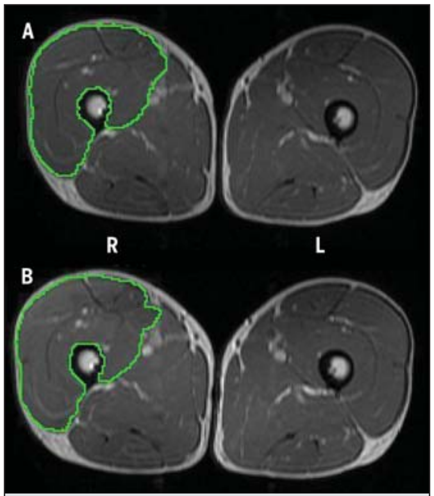

FIGURE 3. Representative anatomically matched axial T2 magnetic resonance images from the mid-thigh region of the knee extensor muscle group before (A) and immediately after (B) stimulation with the Std protocol. Letters R and L denote the right and left thighs, respectively. Note the activation on the R side immediately after stimulation.

Data Analysis

Data were analyzed using a 2-way (protocols by contractions), repeated-measures

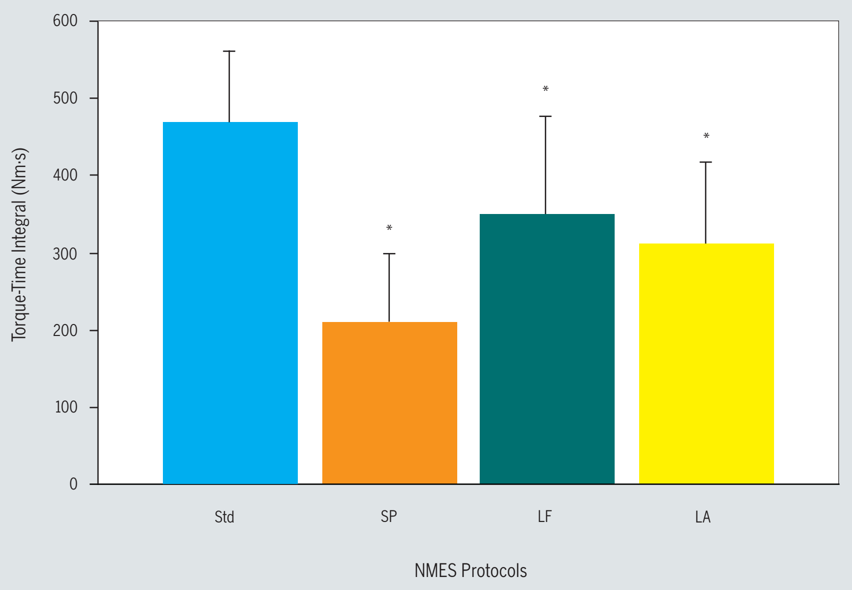

FIGURE 4. Torque-time integral for the first contraction for the 4 NMES protocols. *Significantly different from Std. Values are mean ± SD. Abbreviations: LA, low-amplitude protocol; LF, low-frequency protocol; NMES, neuromuscular electrical stimulation; SP, short pulse duration protocol; Std, standard protocol.

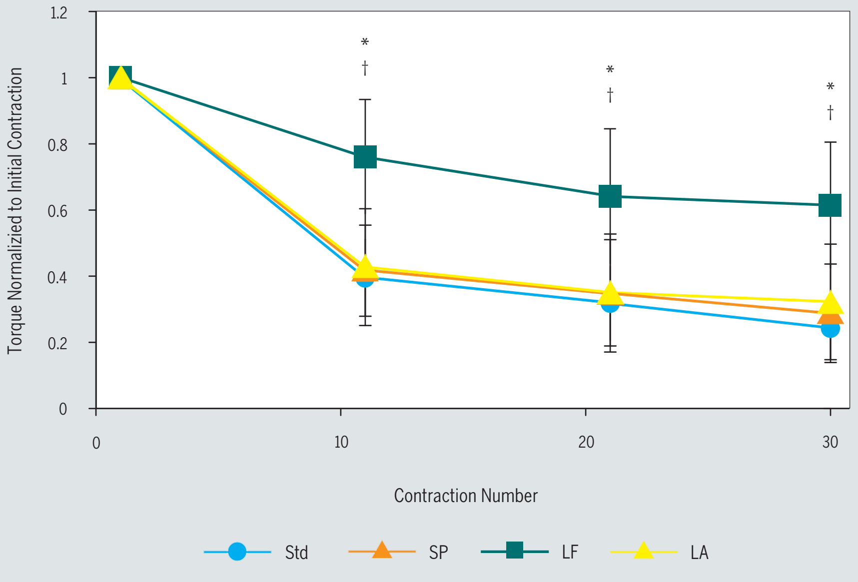

FIGURE 5. Torque for each contraction was normalized to the initial contraction. Values are mean ± SD. *LF was different from Std, SP, and LA ($P<.01$). †Decline in torque over repeated contractions for Std, SP, LF, and LA ($P<.0001$). Abbreviations: LA, low-amplitude protocol; LF, low-frequency protocol; SP, short pulse duration protocol; Std, standard protocol.

analysis of variance (ANOVA) to examine the effects of the 4 NMES protocols on muscle fatigue. The independent variables were the protocols (Std, SP, LF, LA), the contraction numbers were 1, 11, 21, and 30, and the dependent variable was peak torque. If there was an interaction, alpha level was adjusted for pairwise comparison using the Bonferroni correction. A 1-way ANOVA was performed to compare the difference in TTI of the 4 NMES protocols. Simple linear regression was used to examine the relationship between the selected variables (percent fatigue and torque per active CSA). Statistical difference was set at a level of $P<.05$, and values were presented as means ± SD.

RESULTS

THE MEAN ± SD CURRENT AMPLItudes for Std, SP, LF, and LA protocols were 74 ± 18, 76 ± 16, 72 ± 18, and 56 ± 13 mA, respectively (**TABLE 1**). The Std, SP, LF, and LA protocols evoked mean ± SD percents of MVIT of 74% ± 3%, 31% ± 12%, 60% ± 8%, and 45% ± 9%, respectively (**FIGURE 2**). The influence of the 4 NMES protocols on the evoked torque, activated area, and torque per active area are summarized in **TABLE 1**. The 1-way ANOVA revealed a significant difference in the TTI among the 4 protocols ($P<.0001$). TTI was significantly higher for the Std protocol compared to the SP ($P<.0001$), LF ($P<.035$), and LA ($P<.0001$) protocols (**FIGURE 4**). After adjusting for the activated CSA, mean ± SD TTIs were 16 ± 4 and 10 ± 4 Nm·s/cm² for the Std and LF protocols, respectively ($P = .014$).

FIGURES 2 and **5** illustrate the decline in the evoked torque for the 4 NMES protocols. For all 4 protocols, there was a significant reduction in torque from the initial contraction ($F_{3,18} = 12$, $P<.009$). The LF protocol resulted in less fatigue when compared to the other 3 protocols (mean ± SD percent MVIT, 39% ± 19% versus 76% ± 10%; $F_{1,6} = 85.2$; $P<.001$). A significant protocol-by-contraction number interaction ($F_{9,54} = 13.2$, $P<.0001$) was observed, with differences between contractions 11, 21, and 30 for both the Std and LF protocols ($P<.02$), suggesting that lowering the frequency could enhance performance over repeated contractions. No differences in the decline of peak torque over repeated contractions

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