

# EFFECTS OF PULSE DURATION ON MUSCLE FATIGUE DURING ELECTRICAL STIMULATION INDUCING MODERATE-LEVEL CONTRACTION

WOOHYOUNG JEON, MS, and LISA GRIFFIN, PhD

Department of Kinesiology and Health Education, University of Texas at Austin, 2109 San Jacinto Boulevard, D3700, Austin, Texas 78712, USA

Accepted 27 August 2017

**ABSTRACT:** *Introduction:* Neuromuscular electrical stimulation (NMES) is used to prevent muscle atrophy. However, the effect of pulse duration modulation for reducing muscle fatigue and pain is unknown. *Methods:* Two 2-minute stimulation protocols were applied to the knee extensors of 10 healthy individuals. In 1 session, a long pulse duration (1,000  $\mu$ s) and a low current amplitude (LL), set to evoke 25% maximal voluntary contraction at 30 Hz, were applied. The other session was identical except that a short pulse duration (200  $\mu$ s) and a high current amplitude (SH) were used. *Results:* Muscle fatigue was lower for LL than for SH ( $P < 0.01$ ). Force recovery rate was higher for LL than for SH ( $P < 0.05$ ). Pain scores were also lower for LL than for SH ( $P < 0.05$ ). *Discussion:* The use of 1-ms pulse durations reduces fatigue and pain during NMES for moderate-level contractions compared with 200- $\mu$ s durations.

*Muscle Nerve* 57: 642–649, 2018

Neuromuscular electrical stimulation (NMES) is currently used for preventing muscle atrophy and restoring function after damage to the central nervous system.<sup>1</sup> Many surface electrical stimulation systems are commercially available. There are devices available for assistance with ambulation, cycling, and hand function. These systems are used by individuals with paralysis from spinal cord injury and stroke and also for neuromuscular disorders.<sup>2,3</sup> Rapid onset of muscle fatigue and discomfort, however, are major obstacles preventing the effective use of these systems.<sup>4,5</sup> Muscle force production during NMES is dependent on the stimulation parameters of pulse duration, amplitude, and frequency.<sup>6</sup> Increasing either pulse duration or amplitude will increase force production through recruitment of additional motor units.<sup>7</sup> Although motor unit recruitment order during NMES has been found to be non-selective and random with increases in stimulation intensity,<sup>8</sup> it is possible that the type of muscle fibers recruited

may differ depending on whether pulse duration or amplitude is increased.<sup>9–11</sup> Typical functional electrical stimulation (FES) systems use pulse durations of 200–400  $\mu$ s and frequencies of 30–50 Hz.<sup>5</sup>

Many studies have investigated variations in stimulation frequency over time to slow the progression of fatigue.<sup>6</sup> Although starting with initially high frequencies can exacerbate fatigue,<sup>12,13</sup> slowly increasing frequency from 20 to 40 Hz during the course of a fatigue task resulted in prolonged force output over time.<sup>13</sup> Few studies have addressed the effect of different pulse durations on fatigue rate.

Veale *et al.* found that, at low levels of stimulation intensity, shorter pulse durations (<200  $\mu$ s) primarily recruit motor neurons, whereas longer pulse durations ( $\geq 1$  ms) are more effective at recruiting the larger type Ia afferents.<sup>9</sup> Similarly, Lagerquist and Collins found that pulse durations of 1 ms generated larger H-reflexes at low levels of intensity<sup>10</sup> and after high-frequency stimulation, when compared with 50- $\mu$ s pulses.<sup>11</sup> Recruiting more motor units through reflex pathways for a given level of force output should reduce fatigue rates because reflex pathways recruit motor units in order of voluntary recruitment (from small to large motoneurons<sup>14</sup>), and low-threshold motor units typically contain more slow-twitch, fatigue-resistant muscle fibers.<sup>15</sup> It should be noted, however, that the orderly recruitment described by Henneman<sup>14</sup> was investigated in an animal model with nerve cuffs. Nevertheless, at low levels of intensity [2%–15% maximal voluntary contraction (MVC)] during stimulation of human nerves, longer pulse durations appear to recruit more low-threshold motor units than shorter pulse durations, presumably via Ia afferent reflex pathways.<sup>11</sup> It is unknown whether longer pulse durations would recruit more low-threshold motor units than shorter pulse durations during higher intensity contractions with stimulation over the muscle as currently used in most NMES systems. It is possible that higher stimulation intensity could cause more antidromic collision and not influence reflex response. However, it is also possible that longer current durations could spread deeper into the muscle and access more type I muscle fibers.<sup>16,17</sup>

Additional Supporting Information may be found in the online version of this article.

**Abbreviations:** ANOVA, analysis of variance; FES, functional electrical stimulation; MVC, maximal voluntary contraction; NMES, neuromuscular electrical stimulation; LL, parameter set with long pulse duration and low current amplitude; SH, parameter set with short pulse duration and high current amplitude

**Key words:** current amplitude; evoked contractions; pain; pulse duration; stimulation parameters

**Correspondence to:** L. Griffin; e-mail: l.griffin@austin.utexas.edu

© 2017 Wiley Periodicals, Inc.  
Published online 1 September 2017 in Wiley Online Library (wileyonlinelibrary.com). DOI 10.1002/mus.25951

To determine whether longer pulse durations are more beneficial for fatigue reduction in NMES systems, it is essential to test fatigue protocols at moderate levels of intensity. At 20% MVC, protocols that used longer pulse durations (600  $\mu$ s) with very low frequencies (11.5 Hz) of stimulation induced a smaller decline in peak force than protocols that used shorter pulse durations (131–150  $\mu$ s) and medium-to-high frequencies (30–60 Hz) of stimulation.<sup>18</sup> However, it is well known that high frequencies of stimulation induce greater rates of fatigue than lower frequencies.<sup>12</sup> When stimulation frequencies were held constant at 60 Hz, there was no difference in fatigue during evoked contractions starting at 25% MVC when long (600  $\mu$ s) vs. short (167  $\mu$ s) pulse durations were used.<sup>19</sup> When using constant frequency in the lower range normally used for FES ( $\sim$ 30 Hz) for moderate functional force levels ( $\sim$ 25% MVC), it is unknown whether long pulse durations are more beneficial than short pulse durations in reducing muscular fatigue and pain during NMES. It is important to start with matched force levels in this type of study to ensure that differences in fatigue are due to differences in neuromuscular activation by the stimulation rather than contraction load. Thus, long pulse durations will require less current than short pulse durations to generate a given force output.

The purpose of this study was to investigate rates of fatigue across protocols with moderate stimulation frequencies (30 Hz) with long (1 ms) vs. short (200  $\mu$ s) pulse durations during fatiguing evoked intermittent contractions at a moderate force level (25% MVC). We chose pulse durations of 1 ms because this duration is known to be best for targeting Ia afferents. We chose 200  $\mu$ s because this pulse duration is commonly used in NMES systems and it primarily targets the smaller nerve fibers.<sup>9,20</sup> We hypothesized that, during moderate levels of contraction and stimulation frequency (which are typically used during FES), the 1-ms duration with lower current amplitude would elicit less fatigue than the 200- $\mu$ s duration with higher current amplitude during intermittent stimulation protocols.

## METHODS

**Subjects.** Ten healthy, recreationally active individuals (5 males and 5 females,  $23.9 \pm 3.5$  years of age) participated in this study. All participants completed a questionnaire confirming that they had no neuromuscular, cardiovascular, or metabolic disease and no previous surgery on the dominant leg. All participants refrained from strenuous exercise for at least 48 hours before participating in the study. All individuals signed an informed consent form before study participation. All procedures were approved by the institutional review board of the University

of Texas at Austin and were in accord with the Helsinki Declaration of 1975.

**Experimental Set-Up.** Each participant was seated in a chair with an ankle cuff placed around their dominant leg (refer to Fig. S1 in the Supplementary Material, available online). The ankle cuff was attached to a strain-gauge force transducer with a capacity of 1,000 N and output 2 of mV/V (Entran Sensors & Electronics, Fairfield, New Jersey). The force was digitized at 2,000 Hz using an A/D converter (Micro 1401 A/D converter, Cambridge Electronic Design, Cambridge, UK), and collected through Spike2 version 7.09 software (Cambridge Electronic Design). The participant's back was supported with the hips flexed at approximately 80° between the thighs and the torso using the anatomical position of upright standing as 0°. The knees were flexed at 90°. Velcro straps were used to stabilize the participant's upper trunk and waist.

**Electrical Stimulation.** Electrical stimulation was delivered via 2 self-adhesive surface electrodes (5 cm  $\times$  10 cm; Axelgaard PALS Platinum Self Adhesive Stimulation Electrodes, Axelgaard Manufacturing Co., Fallbrook, California) placed over the middle of the quadriceps. The anode was placed covering the proximal portion of the rectus femoris and vastus lateralis muscles and the cathode was placed covering the distal portion of rectus femoris and vastus medialis muscles.<sup>18</sup> The area of the skin where the electrodes were placed was first cleaned with a 70% isopropyl alcohol swab before and after shaving the area with a disposable razor. A constant-current stimulator (Digitimer DS7A, Digitimer, Ltd., Welwyn Garden City, UK) was used to deliver electrical stimulation. Commands were sent to the stimulator from an A/D converter with programmable digital output capacity (Micro 1401, Cambridge Electronic Design). A modified Burke fatigue protocol<sup>21</sup> (intermittent 30 Hz), which lasted for 2 minutes, was used, with a stimulation intensity set to produce 25% MVC force at the start of the fatigue protocol for both tests. Each cycle was composed of 10 300-ms trains and each train consisted of 10 monophasic square-wave pulses. There was a 700-ms rest after each train. Each cycle of 10 trains lasted 10 seconds (see Fig. S2 in Supplementary Material online). There was a 5-s rest between cycles of 10 trains with a total of 80 trains over the 2 minutes. After the fatigue task, participants were asked to rate their pain during the stimulation using a visual analog scale (VAS) over a range of 0–10, with 0 corresponding to “no pain” and 10 corresponding to “the worst possible pain.”

The 2 testing sessions were separated by at least 48 hours and were performed in random order. The frequency and pattern of stimulation were identical in both testing sessions. In 1 session, a parameter set with a *long* pulse duration (1,000  $\mu$ s) and a *low* current amplitude (LL) was used. In the other test session, a *short* pulse duration (200  $\mu$ s) with a *high* current amplitude (SH) was used. Current amplitude was adjusted so that 25% MVC was evoked during a 300-ms contraction. In this way, both protocols evoked the same amount of force over time at the start of the fatigue task.

**Experimental Protocol.** All volunteers first participated in a practice session. The MVCs and stimulation intensity required to generate 25% MVC for the 2 pulse durations was established. Twenty minutes of rest was allotted after

the MVCs and before the stimulation. A maximum of 5 test trains were used for each pulse duration. Each participant performed approximately 5 MVC trials. Participants were provided with visual feedback of their torque production on a computer monitor and received verbal encouragement. The average of the 3 highest MVCs was used to set the stimulation intensity for the 2 stimulation protocols.

**Muscle Fatigue.** The percent decline in peak force was calculated for each fatigue protocol. The difference between the torque of the initial contraction and the torque of the final contraction of each stimulation protocol was divided by the torque of the initial contraction to determine the percent muscle fatigue as follows:

$$\text{Percent muscle fatigue} = \frac{\text{Torque of first contraction} - \text{Torque of last contraction}}{\text{Torque of first contraction}} \times 100$$

**Recovery Rate during Rest Periods.** The rate of increase in peak force during each 5-second rest period was calculated as the difference between the peak force of the

last train before the rest and the first train after the rest divided by the 5-second interval between cycles, as shown by the following equation:

$$\text{Recovery rate during periods of rest (Nm/s)} = \frac{|\text{Peak torque of the last train of a cycle} - \text{Peak torque of the first train of the next cycle}|}{5 \text{ seconds}}$$

**Statistical Analysis.** Current amplitude used during the fatigue protocols and percent muscle fatigue during each fatigue protocol were compared across protocols with 1-way repeated-measures analyses of variance (ANOVAs). Peak forces, contraction times, and half-relaxation times during the first and last trains were compared with 2-way repeated-measures ANOVAs (factors: time and stimulation protocol) with Tukey *post-hoc* analysis. Average peak forces during the first cycle (10 trains) and last cycle (10 trains) were also compared by 2-way repeated-measures ANOVA (factors: time and stimulation protocol) with Tukey's *post-hoc* analysis. The recovery rate during the rest periods was compared over time and between protocols with a 2-way repeated-measures ANOVA (factors: time and stimulation protocol). Pain scores were compared using the Friedman chi-square test. SPSS software (IBM SPSS, Armonk, New York) was used for

all statistical analyses.  $P < 0.05$ , established *a priori*, was considered significant. All data are presented as mean  $\pm$  standard deviation in the text and as mean  $\pm$  standard error in the figures.

## RESULTS

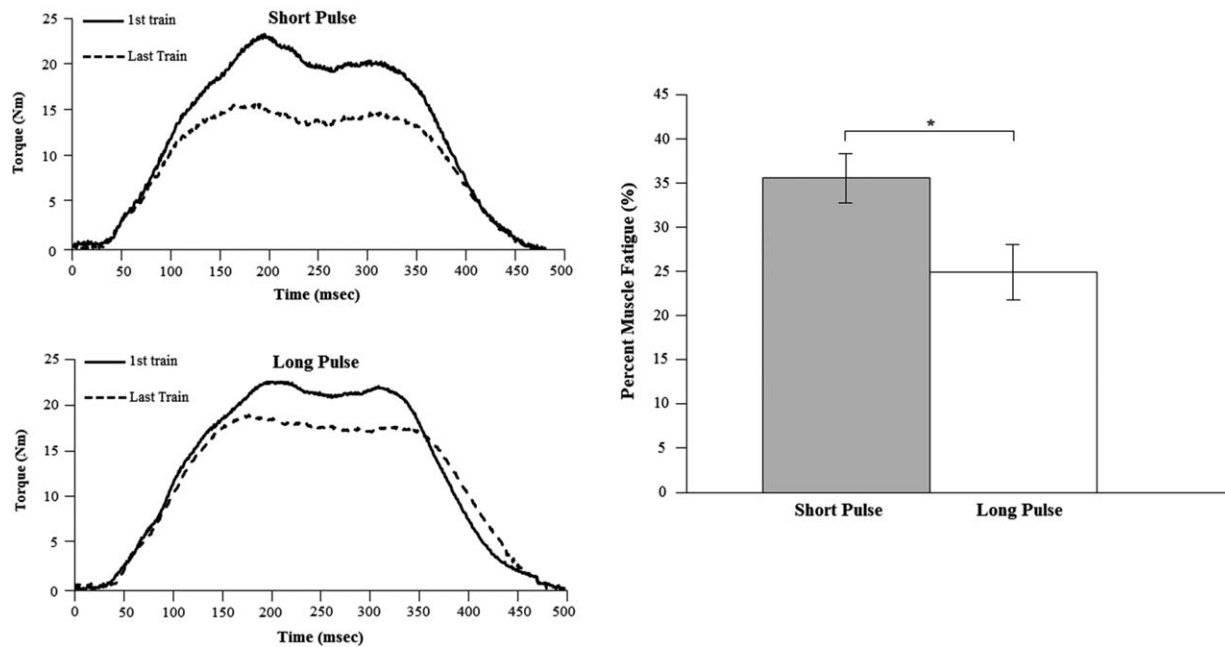
**Current Amplitude.** A lower current amplitude ( $38.2 \pm 17.8$  mA) was required for the LL protocol to generate 25% MVC than was required for the SH protocol ( $76.5 \pm 22.4$  mA) [ $F_{(1,9)} = 352.9$ ,  $P < 0.001$ , observed power = 1.0].

**Muscle Fatigue.** There was no difference between torques elicited during the first train of the first cycle between protocols (LL:  $23.8 \pm 9.2$  Nm; SH:  $23.7 \pm 9.3$  Nm) [ $F_{(1,9)} = 0.265$ ,  $P = 0.619$ ,

**Table 1.** MVC, 25% MVC, and current amplitude for individual subject during first train of first cycle between 2 protocols.

Subject	MVC (Nm)	First train of first cycle				Current amplitude	
		SH		LL		SH (mA)	LL (mA)
		Nm	%MVC	Nm	%MVC		
1	75.16	18.37	24.44%	18.61	24.75%	97	50
2	62.35	15.88	25.47%	15.46	24.80%	48	18
3	132.38	33.66	25.42%	32.81	24.79%	97	60
4	102.48	25.40	24.78%	25.54	24.92%	88	40.3
5	162.40	40.26	24.79%	40.11	24.70%	72.4	33.9
6	133.37	32.94	24.70%	33.95	25.46%	99.8	55.5
7	92.27	23.11	25.04%	22.99	24.92%	63.2	33.5
8	81.64	19.97	24.46%	20.74	25.40%	98	57.7
9	63.85	16.00	25.06%	16.00	25.06%	60.5	27.5
10	47.36	11.61	24.52%	11.85	25.02%	41	9.6
Mean	95.33	23.72	24.87%	23.81	24.98%	76.49	38.60
SD	37.05	9.26	0.37%	9.21	0.26%	22.36	17.25

MVC, maximal voluntary contraction; SH, a short pulse duration (200  $\mu$ s) and a high current amplitude; LL, long pulse duration (1,000  $\mu$ s) and a low current amplitude.

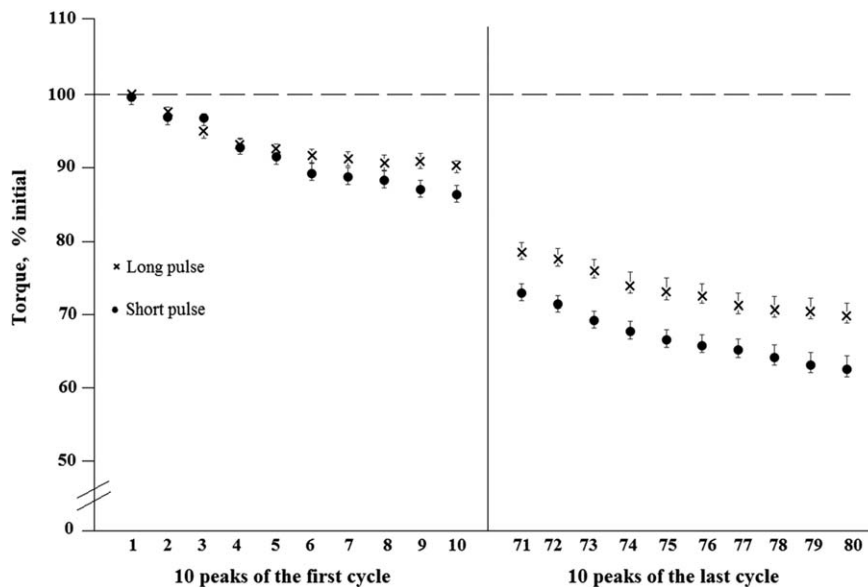


**FIGURE 1.** An example of initial and final peak force profiles from 1 participant are shown on the left. Average values for percent muscle fatigue for both fatigue protocols are plotted on the right. Asterisk (\*) represents a significant difference between the 2 fatigue protocols.

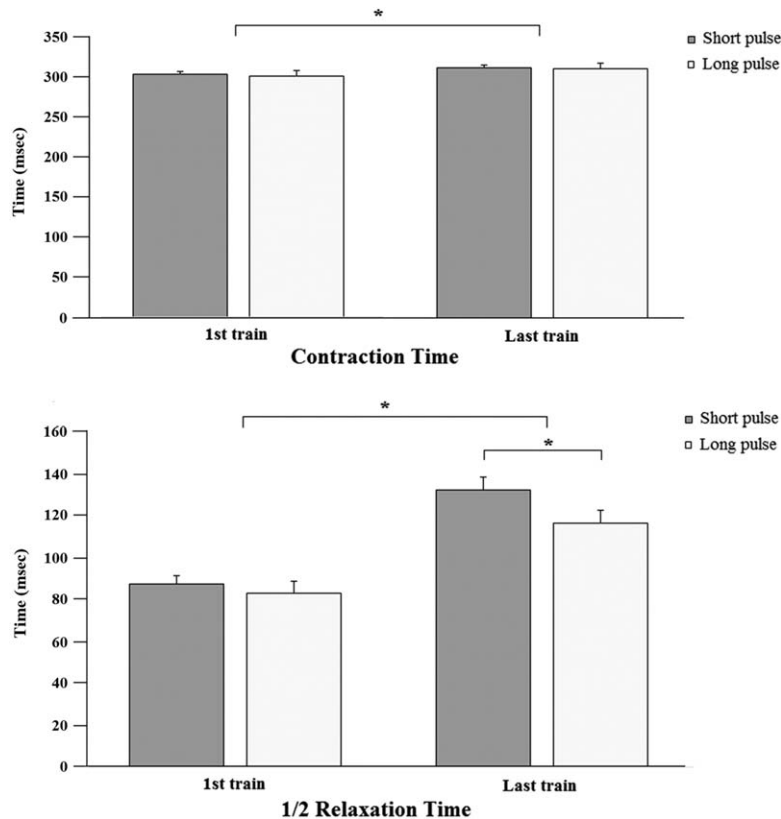
observed power = 0.075] (Table 1). The mean value of the torque during the last train of the last cycle of the LL protocol ( $17.7 \pm 7.4$  Nm) was higher than for the SH protocol ( $15.3 \pm 6.4$  Nm) [ $F_{(1,9)} = 21.3$ ,  $P = 0.001$ , observed power = 0.983]. Figure 1 shows the reduction of peak torque between the initial and final torque profiles of the first and last trains of both protocols in 1 participant and the percent decline in peak torque between initial and final trains of each protocol. There was also a significant difference in average torques of the first (SH:  $21.8 \pm 8.1$  Nm; LL:

$22.2 \pm 8.3$  Nm) and last (SH:  $16.2 \pm 6.1$  Nm; LL:  $18.5 \pm 7.1$  Nm) 10 trains over time [ $F_{(1,99)} = 401$ ,  $P < 0.001$ , observed power = 1.0] and between protocols [ $F_{(1,99)} = 132$ ,  $P < 0.001$ , observed power = 1.0] (Fig. 2). Percent muscle fatigue was greater in the SH protocol ( $36.0 \pm 8.8\%$ ) than in the LL protocol ( $25.6 \pm 9.4\%$ ) [ $F_{(1,9)} = 23.5$ ,  $P = 0.001$ , observed power = 0.99].

There was no significant difference in contraction times between the 2 protocols [ $F_{(1,9)} = 0.107$ ,  $P = 0.751$ , observed power = 0.060]. However, there was a main effect for contraction time over



**FIGURE 2.** Peak forces for all trains in the first (left) and last (right) cycles are shown for both protocols.



**FIGURE 3.** Average contraction and one-half relaxation times for the first and last trains are shown for all participants across both protocols. Asterisk (\*) represents a significant difference.

time [ $F_{(1,9)} = 18.20$ ,  $P = 0.002$ , observed power = 0.966]. Half-relaxation times showed a significant difference between the 2 protocols [ $F_{(1,9)} = 11.7$ ,  $P = 0.008$ , observed power = 0.860] and over time [ $F_{(1,9)} = 51.9$ ,  $P < 0.001$ , observed power = 1.0]. As expected, half-relaxation times slowed more for the SH protocol. Contraction and half-relaxation times before and after fatigue for both protocols are shown in Figure 3.

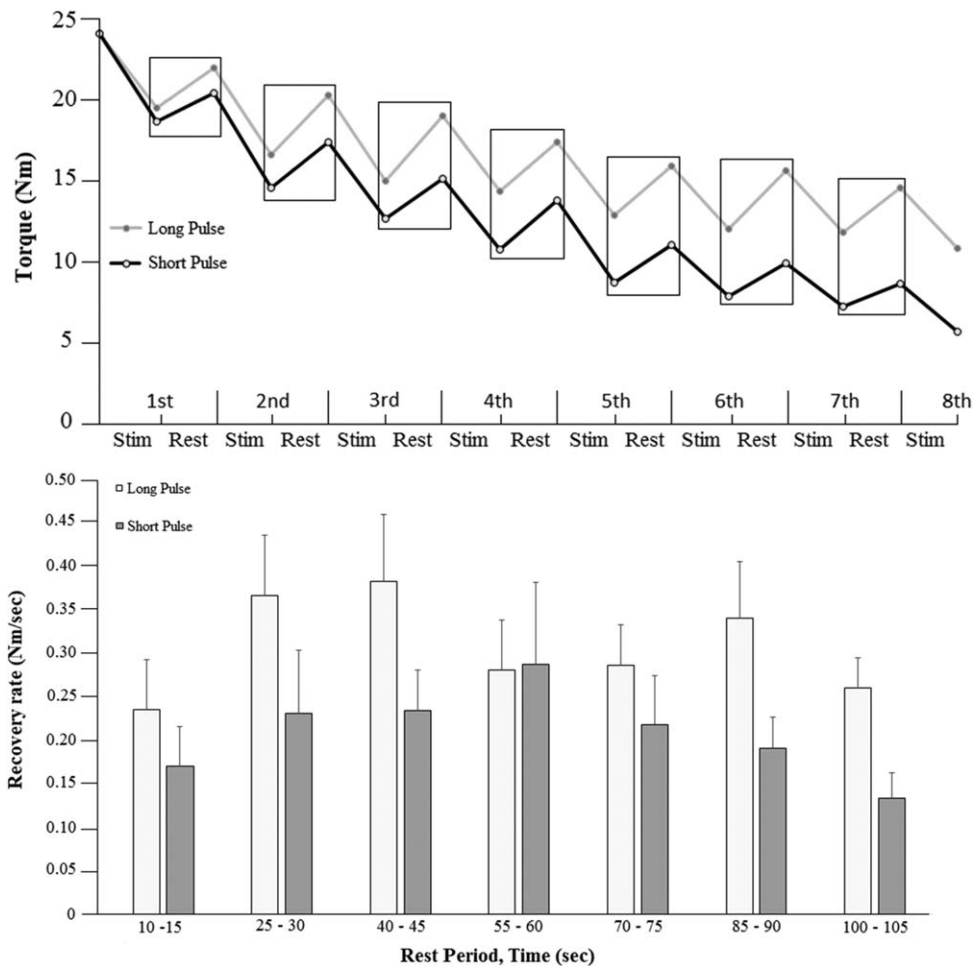
**Recovery Rate during Rest Periods.** Force recovery rate was significantly higher for the LL protocol ( $0.31 \pm 0.06$  Nm/s) than for the SH protocol ( $0.21 \pm 0.05$  Nm/s) [main effect of fatigue protocol:  $F_{(1,9)} = 12.5$ ,  $P = 0.006$ , observed power = 0.880]. However, there was no significant difference between the force recovery rates over time within each fatigue protocol. Figure 4 shows the increasing torque during recovery (top) and the average recovery rates during all 5-second rest periods for both fatigue protocols (bottom).

**Pain.** Self-reported pain associated with the 2-minute NMES protocols was significantly lower for LL than for SH (LL: median = 4; SH: median = 6) [ $\chi^2(1) = 5.4$ ,  $P = 0.02$ ]. However, there was no significant difference for either protocol between men and women [LL: median = 4,  $\chi^2(1) = 1.0$ ,  $P = 0.317$ ; SH: median = 6,  $\chi^2(1) = 0.0$ ,  $P = 1.0$ ].

Pain scores for all participants for both protocols are shown in Table 2.

## DISCUSSION

Motor unit recruitment order during electrical stimulation over a muscle is based on the proximity of the muscle fiber and/or motor neuron to the stimulating electrode<sup>22</sup> and it can be influenced by reflexive motor unit recruitment via Ia afferents.<sup>11</sup> Muscle fiber type distribution in humans is generally random throughout the muscle, with type I fatigue-resistant muscle fibers often located deeper in the muscle.<sup>16,17</sup> Electrical stimulation over the surface of the muscle will also depolarize sensory nerve fibers based on proximity to the stimulating electrode and spread of current through the tissue. To activate sufficient motor unit recruitment to achieve a reasonable force level (25% MVC), stimulation intensity can be increased by increasing pulse amplitude or pulse duration. Increasing pulse amplitude will increase the intensity of the current in a more localized area close to the stimulating electrodes and recruit more nerve fibers with smaller diameters than a longer, more widespread, low-intensity current.<sup>23</sup> The higher level of current required by short pulse durations may also produce more antidromic collision for reflex pathways and decrease the



**FIGURE 4.** Average torque during all 8 cycles are displayed in the top graph. Square boxes are placed around the rest periods showing the force rises during recovery. Recovery rates during 5-second rest periods for both protocols are shown on the bottom.

likelihood of orderly recruitment of low-threshold motor units. In the present study, participants underwent more pain with the shorter pulse duration and higher current amplitude, which indicates

recruitment of more small-diameter nociceptive nerve fibers.<sup>24</sup>

During peripheral nerve stimulation, a longer pulse duration can spread more through the tissue and increases the likelihood of activating more larger Ia afferents.<sup>9,20</sup> Stimulation of Ia afferents can induce an orderly recruitment of motor units through voluntary reflex pathways with the smaller fatigue-resistant motor units being recruited first.<sup>11,14</sup> Collins *et al.* found that “extra contractions” of approximately 21% MVC could be induced with prolonged (>44 seconds) low-intensity stimulation at 100 Hz with 1-ms pulses that initially produced contractions of 2%–7% MVC. They proposed that these extra contractions occurred through Ia afferent reflex pathways because they did not occur with an anesthetic nerve block and could be elicited with stimulation intensities below motor threshold.<sup>25</sup> Although motor unit recruitment order during electrical stimulation over the muscle is based on proximity to the stimulating electrode,<sup>22</sup> there may be a

**Table 2.** Effect of pulse duration on pain sensation (0–10 numeric pain intensity on VAS).

Subject	Gender	SH	LL
1	F	6	7
2	M	9	6
3	F	7	6
4	F	6	4
5	M	7	4
6	M	5	4
7	M	3	1
8	M	6	6
9	F	4	2
10	F	4	2
Mean	—	5.70	4.20
SD	—	1.77	2.04

VAS, visual analog scale; SH, a short pulse duration (200  $\mu$ s) and a high current amplitude; LL, a long pulse duration (1,000  $\mu$ s) and a low current amplitude ( $P < 0.05$ ).

tendency for longer pulse durations to activate more Ia afferents within the sphere of influence of the stimulating electrode.<sup>9,20</sup> This is likely why the use of longer pulse durations with lower current amplitude produced less fatigue than shorter pulse durations with higher current amplitude in the present study. It is also possible that the current spread with long pulse durations activated more type I muscle fibers deeper in the muscle tissue. Furthermore, because smaller type I muscle fibers typically have more capillary beds and better recovery rates than type II muscle fibers,<sup>26–28</sup> the faster recovery rates during the use of longer pulse durations in the present study is additional evidence that more low-threshold motor units were recruited through reflex pathways.

Others have compared the use of long pulse durations to short pulse durations during evoked fatiguing contractions. Neyroud *et al.*<sup>29</sup> and Wegrzyk *et al.*<sup>30</sup> compared the use of long pulse durations (1 ms) with very high frequencies (100 Hz) of stimulation to short pulse durations (50  $\mu$ s) at low frequencies (25 Hz) of stimulation to induce contractions starting at 10% MVC and found higher rates of fatigue for the contractions with high frequencies. Conversely, Kesar and Binder-Macleod<sup>18</sup> found that the use of long pulse durations (600  $\mu$ s) with very low frequencies (11.5 Hz) produced less muscle fatigue during contraction force levels starting at 50% MVC than short pulse durations (131–150  $\mu$ s) with medium-to-high frequencies (30–60 Hz). The results of these studies are not surprising because it is well known that higher frequencies of stimulation induce rapid rates of fatigue.<sup>12</sup> Bickel *et al.*<sup>19</sup> used constant high-frequency stimulation (60 Hz) and found no difference in fatigue during evoked contractions starting at 25% MVC when long (600  $\mu$ s) vs. short (167  $\mu$ s) pulse durations were used. In the present study, we used moderate-level stimulation frequencies (30 Hz) and found that use of long pulse durations (1 ms) produced less fatigue than short pulse durations (200  $\mu$ s) at moderate starting force levels (25% MVC). Thus, our results show that, for moderate levels of stimulation frequency (30 Hz), the use of longer pulse widths is more effective at maintaining moderate contraction levels.

**Pain.** Reducing pain during electrical stimulation is essential for making NMES systems usable by individuals with preserved sensory function. Our study has demonstrated that the activation of small-diameter pain fibers is dependent more on current amplitude than pulse duration. Small-diameter afferents are abundant throughout the muscle tissue.<sup>24,31</sup> Because a higher current amplitude was necessary to achieve the 25% MVC when

using short pulse durations, many more small diameter afferents in the vicinity of the stimulating electrode were likely activated.

**Future Studies.** It would be of interest to investigate further whether the reduction of fatigue with longer pulse widths is due to reflexive recruitment or to spread of current to deeper type I muscle fibers, or both, and to investigate differences in responders and non-responders to reflexive recruitment during NMES. Future studies should also investigate whether longer pulse durations would be as effective for even higher levels of force output with moderate stimulation frequencies. Also, the impact of different electrode placements should be evaluated. In the present study, we used 1 anode and 1 cathode. The use of multiple cathodes<sup>32</sup> should also be investigated.

In conclusion, our results demonstrate that, during intermittent contractions of moderate force levels (25% MVC) at moderate stimulation frequencies (30 Hz), the use of long pulse durations (1 ms) with low current amplitude reduces fatigue and pain, and improves recovery rate to a greater extent than shorter pulse durations (200  $\mu$ s) with higher current amplitudes. These findings have significant implications with regard to the design of NMES systems for individuals with neuromuscular disability and paralysis.

## REFERENCES

1. Carraro U, Rossini K, Mayr W, Kern H. muscle fiber regeneration in human permanent lower motoneuron denervation: relevance to safety and effectiveness of FES-training, which induces muscle recovery in SCI subjects. *Artif Organs* 2005;29:187–191.
2. Nightingale EJ, Raymond J, Middleton JW, Crosbie J, Davis GM. Benefits of FES gait in a spinal cord injured population. *Spinal Cord* 2007;45:646–657.
3. Venugopalan L, Taylor PN, Cobb JE, Swain ID. Upper limb functional electrical stimulation devices and their man-machine interfaces. *J Med Eng Technol* 2015;39:471–479.
4. Marsolais EB, Edwards BG. Energy costs of walking and standing with functional neuromuscular stimulation and long leg braces. *Arch Phys Med Rehabil* 1988;69:243–249.
5. Ibitoye MO, Hamzaid NA, Hasnan N, Abdul Wahab AK, Davis GM. Strategies for rapid muscle fatigue reduction during FES exercise in individuals with spinal cord injury: a systematic review. *PLoS One* 2016;11:e0149024.
6. Doucet BM, Lam A, Griffin L. Neuromuscular electrical stimulation for skeletal muscle function. *Yale J Biol Med* 2012;85:201–215.
7. Gorgey AS, Mahoney E, Kendall T, Dudley GA. Effects of neuromuscular electrical stimulation parameters on specific tension. *Eur J Appl Physiol* 2006;97:737–744.
8. Gregory, CM, Bickel CS. Recruitment patterns in human skeletal muscle during electrical stimulation. *Phys Ther* 2005;85:358–364.
9. Veale JL, Mark RF, Rees S. Differential sensitivity of motor and sensory fibres in human ulnar nerve. *J Neurol Neurosurg Psychiatry* 1973;36:75–86.
10. Lagerquist O, Collins DF. Stimulus pulse-width influences H-reflex recruitment but not H(max)/M(max) ratio. *Muscle Nerve* 2008;37:483–489.
11. Lagerquist O, Collins DF. Influence of stimulus pulse width on M-waves, H-reflexes, and torque during tetanic low-intensity neuromuscular stimulation. *Muscle Nerve* 2010;42:886–893.
12. Bigland-Ritchie BR, Jones DA, Woods, JJ. Excitation frequency and muscle fatigue: electrical responses during human voluntary and stimulated contractions. *Exp Neurol* 1979;64:414–427.
13. Doucet BM, Griffin L. Maximal versus submaximal intensity stimulation with variable patterns. *Muscle Nerve* 2008;37:770–777.
14. Henneman E. Relation between size of neurons and their susceptibility to discharge. *Science* 1957;126:1345–1347.

15. Zajac FE, Faden JS. Relationship among recruitment order, axonal conduction velocity, and muscle-unit properties of type-identified motor units in cat plantaris muscle. *J Neurophysiol* 1985;53:1303–1322.
16. Rosser BW, Norris BJ, Nemeth PM. Metabolic capacity of individual muscle fibers from different anatomic locations. *J Histochem Cytochem* 1992;40:819–825.
17. Knight CA, Kamen G. Superficial motor units are larger than deeper motor units in human vastus lateralis muscle. *Muscle Nerve* 2005;31:475–480.
18. Kesar T, Binder-Macleod S. Effect of frequency and pulse duration on human muscle fatigue during repetitive electrical stimulation. *Exp Physiol* 2006;91:967–976.
19. Bickel CS, Gregory CM, Azuero A. Matching initial torque with different stimulation parameters influences skeletal muscle fatigue. *J Rehabil Res Dev* 2012;49:323–331.
20. Panizza M, Nilsson J, Hallett M. Optimal stimulus duration for the H reflex. *Muscle Nerve* 1989;12:576–579.
21. Burke RE, Levine DN, Tsairis P, Zajac FE III. Physiological types and histochemical profiles in motor units of the cat gastrocnemius. *J Physiol* 1973;234:723.
22. Knaflitz M, Merletti R, Luca CJD. Inference of motor unit recruitment order in voluntary and electrically elicited contractions. *J Appl Physiol* 1990;68:1657–1667.
23. Grill WM, Mortimer JT. The effect of stimulus pulse duration on selectivity of neural stimulation. *IEEE Trans Biomed Eng* 1996;43:161–166.
24. Kaufman MP, Longhurst JC, Rybicki KJ, Wallach JH, Mitchell JH. Effects of static muscular contraction on impulse activity of groups III and IV afferents in cats. *J Appl Physiol* 1983;55:105–112.
25. Collins DF, Burke D, Gandevia SC. Sustained contractions produced by plateau-like behaviour in human motoneurons. *J Physiol* 2002;538:289–301.
26. Andersen P. Capillary density in skeletal muscle of man. *Acta Physiol Scand* 1975;95:203–205.
27. Beltman JGM, Sargeant AJ, Mechelen W, van de Haan A. Voluntary activation level and muscle fiber recruitment of human quadriceps during lengthening contractions. *J Appl Physiol* 2004;97:619–626.
28. Kushmerick MJ, Meyer RA, Brown TR. Regulation of oxygen consumption in fast- and slow-twitch muscle. *Am J Physiol Cell Physiol* 1992;263:C598–C606.
29. Neyroud D, Dodd D, Gondin J, Maffiuletti NA, Kayser B, Place N. Wide-pulse-high-frequency neuromuscular stimulation of triceps surae induces greater muscle fatigue compared with conventional stimulation. *J Appl Physiol* 2014;116:1281–1289.
30. Wegrzyk J, Fouré A, LeFur Y, Maffiuletti NA, Vilmen C, Guye M, *et al.* Responders to wide-pulse, high-frequency neuromuscular electrical stimulation show reduced metabolic demand: a <sup>31</sup>P-MRS study in humans. *PLoS One* 2015;10:e0143972.
31. Hunt CC. Relation of function to diameter in afferent fibers of muscle nerves. *J Gen Physiol* 1954;38:117–131.
32. Maffiuletti NA. Physiological and methodological considerations for the use of neuromuscular electrical stimulation. *Eur J Appl Physiol* 2010;110:223–234.