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The Effects Of Stimulation Frequency And Fatigue On The Force-Intensity Relationship For Human Skeletal Muscle

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Abstract

Objective—Functional electrical stimulation (FES) has not gained widespread application for a number of factors; two of which are rapid muscle fatigue and imprecise control in force. Stimulation intensity is adjusted during FES to overcome the decline in muscle force due to fatigue and precisely control muscle force output. The purpose of this study was to understand the relationship between muscle force output and stimulation intensity and to see how this relationship changes with fatigue.

Methods—Quadriceps femoris muscles of 10 able-bodied adults were tested isometrically. Pre- and post-fatigue muscle force responses to stimulation trains with different intensities and frequencies were recorded and analyzed. In addition, a case study using a subject with spinal cord injury was presented to illustrate the use of the force-intensity relationship to reduce muscle fatigue and improve the control of muscle force during repetitive electrical stimulation.

Results—An exponential relationship between muscle force and stimulation intensity was observed; interestingly, the normalized force-intensity relationship did not change with stimulation frequency or fatigue.

Conclusions—The observed consistencies in the force-intensity relationship should assist scientists and clinicians to more accurately predict the forces produced by a muscle with changes in pulse duration during repetitive electrical stimulation.

Significance—The findings of this study provide guidelines for clinicians and researchers to adjust the stimulation intensity to achieve precise control of force repetitively during the application of FES.

Keywords

Functional electrical stimulation (FES); Quadriceps femoris muscles; force-intensity relationship

Introduction

The use of electrical stimulation to activate paralyzed muscles and restore functional movements for individuals with upper motoneuron lesions is termed Functional Electrical Stimulation (FES). After first being introduced by Liberson and colleagues (Liberson et al., 1961) to prevent foot drop during the swing phase of gait for patients with hemiplegia, FES has been applied to restore functional movements such as grasping (Prochazka et al.,

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1997;Snoek et al., 2000), standing (Davis et al., 2001;Kuzelicki et al., 2002) and walking (Graupe et al., 1998,Kobetic and Marsolais, 1994) for individuals either post-stroke or with spinal cord injury (SCI).

Although FES has the potential advantage of improving functional mobility for individuals with upper motoneuron lesions, it has not gained widespread clinical use due to limitations, such as rapid muscle fatigue and imprecise control of muscle forces (Isakov et al., 1986;Nathan, 1984;Peckham and Knutson, 2005; Reiner, 1999). Unlike voluntary contractions (Henneman et al., 1965), during electrically elicited contractions, smaller and more fatigue-resistant motor units are not always recruited prior to larger and more fatigable ones (Binder-Macleod et al., 1995;Feiereisen et al., 1997;Heyters et al., 1994;Knaflitz et al., 1990;Trimble and Enoka, 1991); therefore, rapid muscle fatigue was thought to result in part due to the difference in recruitment order between electrical stimulation and voluntary activation of motor units. In addition, the physiological and mechanical complexity and nonlinearity of the neuromuscular system increased the difficulty for FES to precisely control muscle force output and to perform functional movements. Imprecise control during FES may result in either an undershoot or an overshoot in muscle force output compared to the actual forces needed to produce a functional movement. An undershoot in peak force could cause muscles to fail to complete a functional task; an overshoot in peak force will affect the smoothness and accuracy of the movements. Also, because higher metabolic expenditure was observed when higher peak forces are generated during repetitive electrical stimulation (Russ et al., 2002), an overshoot in peak force may also cause rapid muscle fatigue.

Most current FES systems have used a constant stimulation frequency (usually between 20 to 40 Hz) and adjusted stimulation intensity (either pulse amplitude or duration) to control muscle force output and overcome muscle fatigue during repetitive electrical stimulation (Lyons et al., 2000;Mourselas et al., 2000;Peckham and Knutson, 2005;Prochazka and Wiles, 1983;Staniè et al., 1977). Thus, understanding the relationship between muscle force output and stimulation intensity is essential for precise force output control during FES. To date, only a few studies reported the force-intensity relationship for non-fatigued animal muscles (Crago et al., 1980;Gorman and Mortimer, 1983) and human skeletal muscles (Durfee & MacLean, 1989;Levy et al., 1990;Livshitz et al., 2000;McDonald et al., 2005). All previous studies reported a steep rising phase at lower intensities and a plateau phase at higher intensities. Because of the differences in fatigability of motor units within a muscle, the force-intensity relationship may change with muscle fatigue. No studies, however, have described the changes in the force-intensity relationship with fatigue; in addition, no studies have investigated how the force-intensity relationship changes with stimulation frequency. Thus, the purpose of this study was to investigate the relationship between human skeletal muscle force and stimulation intensity across a wide range of clinically relevant stimulation frequencies and to determine how this relationship changes as a consequence of muscle fatigue.

In the current study, human quadriceps femoris muscles were stimulated isometrically using different frequencies and intensities to obtain the force-intensity relationships at different stimulation frequencies for both non-fatigued and fatigued conditions. In addition, a case study using a subject with spinal cord injury (SCI) was presented to illustrate how precise control in muscle force output during repetitive electrical stimulation could be achieved using the force-intensity relationship identified in the current study. The results showed that the force-intensity relationship was exponential and the normalized force-intensity relationship did not change with stimulation frequency or fatigue.

Materials and Methods

Subjects

Ten able-bodied (6 females, 4 males; 24.3 ± 2.58 years old) and one SCI subject (male; 15 years old; T-10 level of injury; ASIA A; 8 years post injury) with no history of lower extremity orthopedic disorders voluntarily participated in this study. All 10 able-bodied subjects participated in the main experiments, which evaluated the effects of stimulation frequency and fatigue on the human quadriceps muscle force-intensity relationship. The SCI subject was recruited for the case study. Able-bodied subjects were recruited from the general population of students at the University of Delaware and individuals in the surrounding community; the SCI subject was recruited at Shriners Hospital for Children in Philadelphia. Each subject was made aware of the nature of the research, the procedures and the potential risks involved. All able-bodied subjects signed an informed consent that was approved by the Human Subjects Review Board of University of Delaware. The subject with SCI and his parent signed an informed consent and an assent form that was approved both by the Human Subjects Review Board of University of Delaware and the Institutional Review Board of Temple University.

Experimental setup

The experimental setup was the same for the able-bodied subjects and the subject with SCI. Subjects were seated on a computer-controlled dynamometer (KinCom III 500–11 (able-bodied); KinCom II (SCI), Chattecx Corp., Chattanooga, TN) with their hips flexed to approximately 85° and knees flexed to 90° . The axis of the dynamometer was aligned with the axis of the subject's knee joint. The trunk, waist and thigh were stabilized using inelastic straps with Velcro closures. Isometric quadriceps muscle forces were measured by a force transducer placed at the anterior aspect of the tibia, with the lower edge of the transducer pad positioned 2.5 cm proximal to the lateral malleolus. The right quadriceps muscle was stimulated using a voltage regulated Grass S8800 stimulator with an SIU8T stimulus isolation unit (Grass Instrument Co., Quincy, MA). A personal computer equipped with a PCI-6Q24FDAQ board, a PCI6602 counter-timer board, and custom written LabVIEW software (National Instruments, Austin, TX) was used to control the timing of all stimulation pulses during testing. A custom-made pulse duration control switch was connected in series with the Grass stimulator for the modulation of pulse duration. For the able-bodied subjects, two, 7.6×12.7 -cm, self-adhesive electrodes (Versa-stim, Conmed Corporation, Utica, NY) were used to deliver electrical stimulation. For the subjects with SCI, two, 7.5×10 -cm, self-adhesive electrodes (Pals Platinum, Axelgaard Manufacturing Co., Ltd, Fallbrook, CA) were used. The electrode connected to the anode of the stimulator was placed over the motor point of rectus femoris and the cathode was placed over the motor point of vastus medialis (Barnett et al., 1991). The force data were sampled at a rate of 200 Hz and stored on the computer's hard disc.

Experimental procedure for able-bodied subjects

Each able-bodied subject participated in one testing session. Subjects were asked to refrain from strenuous exercise 24 hours before the testing session. At the beginning of the testing session, each subject's maximal voluntary isometric contraction (MVIC) was determined using the burst superimposition technique (Snyder-Mackler et al., 1993). The burst superimposition technique used an 11-pulse ($600 \mu\text{s}$ pulse duration, 135 V), 100-Hz train to stimulate the muscle while the subjects performed a maximum voluntary contraction of their quadriceps muscles. The MVIC was accepted if the volitional contraction was $\geq 95\%$ of the "superimposed" tetanic force. If the peak force of volitional contraction was $< 95\%$ of the superimposed tetanic force, subjects rested for 5 minutes before attempting to perform another MVIC testing. All subjects were able to perform successful MVICs within 3 attempts. Subjects rested for 5 minutes after MVIC testing.

Quadriceps muscles were potentiated before setting the stimulation amplitude. One, 12-pulse (600 μ s pulse duration), 14-Hz train was delivered to the quadriceps muscles every 5 seconds over a ~ 60 second period to potentiate the muscles (240 total pulses) (Binder-Macleod et al., 2002). The stimulation intensity was then set using 60-Hz (600 μ s pulse duration), 300 ms long trains. The stimulation amplitude was increased gradually until the muscle peak force responses reached 20 % of the subject's MVIC. Previous work showed that if rather than using a 300-ms train, the train duration was extended to ~ 1 second, this stimulation intensity would produce ~ 40 % of subject's MVIC (Ding et al., 2003). Thus, the current intensity was recruiting approximately 40 % of the quadriceps femoris muscle. The amplitude was then held constant throughout the remainder of the session. Although stimulation intensity can be modulated by varying either pulse amplitude or duration, pulse duration modulation was chosen in the present study as it was easier to control and may require less charge per stimulus pulse compared to stimulation amplitude modulation (Crago et al., 1974).

Testing trains were delivered right after setting the stimulation intensity. Each subject received a testing protocol consisting of a pre-fatigue portion, a fatiguing portion and a post-fatigue portion. For the pre-fatigue portion, a series of 300-ms long testing trains with different frequency (10, 12.5, 20, 30, 40 and 60 Hz) and pulse duration (100, 200, 300, 400 and 600 μ s) combinations were delivered to the quadriceps muscles to examine the force responses to different stimulation frequencies and intensities before muscle fatigue. These testing trains were delivered in a random order at the rate of 1 train every 10 seconds to avoid fatigue, and then repeated in a reversed order (N.B., the same random order was used for all subjects). The force responses to the same train were averaged for later analysis. Next, a modified Burke's fatigue protocol (Burke et al., 1973) consisting of a series of 40-Hz, 300-ms trains, with pulse duration at 600 μ s, was delivered to the muscle at a rate of one train every second for a total of 180 trains to fatigue the quadriceps muscles. The post-fatigue portion was delivered to subject's quadriceps muscle immediately after the fatigue portion. Stimulation in this portion was continued at a rate of 1 train per second. Post-fatigue testing included the same sequence of testing trains as used in the pre-fatigue portion, but each of the testing trains was separated by two fatiguing trains (e.g., 40-Hz, 300-ms train with pulse duration at 600 μ s) to maintain a steady state of fatigue. The force responses to the same train were averaged for later analysis.

A simple test was performed to determine if fatigue was produced during the pre-fatigue portion of testing. Because the first and last stimulation trains (20 Hz; 300 μ s pulse duration) of the pre-fatigue protocol were identical (see above), the peak forces produced by the first and last trains were compared. Analysis of these data using paired t-test showed no significant difference (first trains' peak force=99.5 $\pm$ 11.3 N; last trains' peak force=100.2 $\pm$ 10.7 N; P=0.72). Similarly, a comparison of the peak forces produced by the first and last testing trains of the post-fatigue protocol showed no significant difference (first trains' peak force=28.19 $\pm$ 3.5 N; last trains' peak force=26.88 $\pm$ 4.1 N; P=0.31). Thus, we concluded that there was no fatigue produced during the pre-fatigue portion and a steady level of fatigue was maintained during the post-fatigue portion.

Experimental procedure for the subject with SCI

Quadriceps femoris muscle's maximal twitch force (MTF) was first determined using single pulses (600 μ s pulse duration). Stimulation amplitude was gradually increased until a plateau in the MTF was reached. Next, the stimulation voltage was adjusted to produce tetanic force equal to MTF level using a 1-s, 100-Hz stimulation train (pulse duration of 600 μ s). The MTF of paralyzed skeletal muscles are about 15 to 25 % of the maximal tetanic force (Gerrits et al., 1999; Scott et al., 2006). Next, a series of 1-sec long stimulation trains with different frequency (12.5, 20, 33.3, 50 and 80 Hz) and intensity (150, 250, 350 and 600 μ s) combinations were delivered to the quadriceps femoris muscles. These 20 testing trains were delivered in a random

order at the rate of one train every 10 seconds to avoid fatigue, and then repeated in a reversed order. The force responses to the train with the same frequency and intensity were averaged and analyzed to obtain each subject's force-intensity relationship and intensity modulation steps (Details in the next section). The stimulation amplitude was readjusted using a series of 60-Hz (600- μ s pulse duration), 300-ms long trains. The stimulation amplitude was gradually increased until the muscle force responses reached subject's $2 \times$ MTF. The stimulation amplitude was then held constant for the remainder of the session. Quadriceps muscle was then stimulated repetitively at the rate of one train every 1.1 second using a series of 300-ms long, 30-Hz trains with a pulse duration (226 μ s) that produced a peak force equal to the subject's MTF. To precisely maintain muscle force output, the stimulation pulse duration was increased in a stepwise manner every time the peak forces declined more than 10% from the targeted force level (i.e., MTF) due to muscle fatigue. The experimental protocol was terminated when muscle peak forces could not be maintained above 90% MTF at the maximum pulse duration (600 μ s).

The pulse duration modulation steps were calculated based on the force-intensity relationship of the subject. Five calculation steps were needed to determine each pulse duration step (Fig. 1):

Step 1: The force-intensity relationship curve (black curve) obtained for the subject was fitted with equation 1, and the parameter values for A , PD_0 and τ for the force-intensity relationship curve were then determined.

Step 2: The starting pulse duration was identified by locating the pulse duration that produced peak forces equal to the targeted force level (dark point). In the case study, stimulation trains were delivered once every second; therefore, muscle peak force output gradually declined due to muscle fatigue.

Step 3: We predetermined that the stimulation pulse duration would be modulated when the peak force drops 10% from the targeted force level (gray point).

Step 4: When the peak force dropped 10% from the targeted force level, a new curve that represented the relationship between force output and stimulation intensity at that point of time could then be identified. Based on the results of the study with able-bodied subjects (See "Results" section), only parameter A changed with fatigue. Thus, with all other parameter values known (determined from Step 1), the new A value for the new force-intensity relationship curve (gray curve) could then be determined.

Step 5: By locating the pulse duration that produced peak forces equal to the targeted force level from the new force-intensity relationship curve, the next modulation step for pulse duration could be identified.

By repeating these steps, a family of the force-intensity relationship curves for the subject was identified (Fig. 2). As expected, the force-intensity relationship scaled down as the muscle fatigues. All the pulse duration modulation steps for the subject were determined by locating the intersections between the curves and the targeted force level. Calculation was stopped when the longest pulse duration (600 μ s) was reached.

Data management and analysis

To analyze the force-intensity relationship, the peak force responses to each of the testing trains were measured and plotted as a function of pulse duration for each frequency tested for both pre- and post-fatigue conditions. Each force-intensity relationship curve was normalized to the peak force produced at the longest pulse duration (600 μ s).

An exponential equation,

$$F = A \left(1 - e^{-(PD - PD_0)/\tau} \right) \text{ for } PD \geq PD_0$$

$$F = 0 \text{ for } PD < PD_0, \quad (1)$$

was used to fit each of the force-intensity relationship curves, where parameter A is the scaling factor for the force (F), PD represents the duration of the stimulation pulse (μs). PD_0 represents the threshold pulse duration (μs), above which we predict there is a measurable force. τ is the time constant controlling the rise of the force with increasing pulse duration. Because muscles cannot generate negative force, F will equal to zero when $PD \leq PD_0$. R^2 value between the actual force-intensity relationship curves and the fitting curves was calculated to evaluate the quality of the fit. Two-way (conditions versus frequencies) analyses of variance (ANOVAs) with repeated measures were used to determine if the parameter values for A , PD_0 , or τ changed with frequency or fatigue. Pairwise comparison with a Bonferroni correction was performed if a significant main effect was observed. Statistical significance was accepted at $P \leq 0.05$.

Results

Pre- and post-fatigue force-intensity relationships at frequencies ranging from 10 to 60 Hz were collected for the 10 able-bodied subjects (6 women, 4 men; 24.3 ± 2.58 years old). During the fatiguing protocol, muscle peak forces declined rapidly over the first 60 contractions, declined more gradually between 60th and 150th contractions, and then became stable for the last 30 contractions (Fig. 3). The averaged decline in peak force for all the subjects tested was $48.46\% \pm 12.18\%$ (Mean $\pm$ SE) from the initial peak force level.

Force-intensity relationship

The force responses for a typical subject were shown in Fig. 4. For all the force-intensity relationship curves in the current study, a steep-rising phase at shorter pulse durations (100 – 400 μs) and a gradual rise at longer pulse durations ($> 400 \mu\text{s}$) was observed for all frequencies tested and for both the pre- and post-fatigue data (Fig. 5A & C). For both pre- and post-fatigue conditions, the normalized force-intensity relationships for all frequencies tested superimposed (Fig. 5B & D). For all frequencies tested, the averaged post-fatigue force-intensity relationships scaled down compared to the averaged pre-fatigue force-intensity relationships (Fig. 5E). When plotting the averaged (collapsed across all the frequencies tested) normalized pre- and post-fatigue force-intensity relationships, the 2 curves superimposed with each other (Fig. 5F). Similar results were observed when plotting the pre- and post-fatigue force-intensity relationship curves for each individual frequency.

Equation 1 was used to fit each of the force-intensity relationship curves for each subject. For each subject, equation 1 successfully captured the exponential shape of the force-intensity relationship for all the frequencies tested under both pre- and post-fatigue conditions ($R^2 = 0.99$) (Fig. 6). Statistical analysis showed that the averaged pre-fatigue A value (156.83 ± 55.39) was significantly greater than the averaged post-fatigue A value (68.20 ± 40.71) ($F = 43.57$; $P < 0.05$) (Fig. 7A). In addition, a significant main effect was observed for A value across frequencies. Post-hoc analysis showed that the value of A at each stimulation frequency was significantly different from each other ($F = 50.94$; $P < 0.05$).

The 2-way ANOVA comparing the PD_0 values between the pre- and post-fatigue conditions and across frequencies showed no significant main effect for either the fatigue states or frequencies ($F = 0.157$ & 2.731 , respectively), but did show a significant interaction between the main effects ($F = 4.021$; $P = 0.004$) (Fig. 7B). Subsequent analysis with one-way ANOVAs

showed no significant difference among PD_0 values across frequencies for either pre- or post-fatigue conditions ($F = 0.013$ (pre) & 1.27 (post)), which indicated that the threshold pulse duration (PD_0) did not change with stimulation frequency in either pre- or post-fatigue conditions. In addition, paired t-tests with Bonferroni corrections showed no significant difference between pre- and post-fatigue PD_0 values for any of the frequencies tested, indicating that the threshold pulse duration also did not change with muscle fatigue at frequencies ranging from 10 to 60 Hz. The 2 way ANOVA comparing τ values between the pre- and post-fatigue conditions and across frequencies showed no significant main effect ($F = 3.96$ & 1.46 , respectively), indicating that the rate of rise in force for the force-intensity relationship did not change with stimulation frequency in either the pre- or post-fatigue conditions (Fig. 7C).

The results from the case study were shown in Fig. 8. Each data point represented a peak force response for 1 contraction. During repetitive electrical stimulation with a constant pulse duration, quadriceps muscle peak forces gradually declined due to muscle fatigue. When the peak forces dropped more than 10% from the targeted level, pulse duration was increased based on the calculated modulation steps. Increasing pulse duration resulted in recruiting more motor units; peak force responses, therefore, increased every time the pulse duration was modulated. Peak force responses reached the targeted level after each modulation step, and no significant overshoot in peak force was observed (Fig. 8), suggesting that the pulse duration modulation step calculation method accurately predicted the required pulse durations. The results of the case study showed that when increasing pulse duration in a stepwise manner according to the modulation steps calculated using the method described in the Methods section, quadriceps muscle isometric forces could be maintained at a targeted level during repetitive electrical stimulation.

Discussion

The present study was the first to investigate the effects of stimulation frequency and muscle fatigue on the force-intensity relationship for human quadriceps femoris muscles. Our results showed that the force-intensity relationship was exponential with a steep-rising phase at shorter pulse durations and a more gradual rising phase at longer pulse durations. In addition, the value for both PD_0 , threshold pulse duration, and τ , rate of rise in force with increasing pulse duration, were consistent across frequencies and fatigue conditions, and only A , the scaling factor, changed with changes in stimulation frequency or muscle fatigue.

The shape of the force-intensity relationship curve

To date, only a few studies have reported the force-intensity relationship for non-fatigued animal (Crago et al., 1980; Gorman and Mortimer, 1983) or human skeletal muscles (Durfée & MacLean, 1989; Levy et al., 1990; Livshitz et al., 2000; McDonald et al., 2005). Similar to the present study, a steep rising phase at lower intensities and a plateau phase at higher intensities were observed. The shape of the force-intensity relationship can be explained by the number of motor units and the force generated by each recruited motor unit at different stimulation intensities. The steep rise in force at lower intensities (shorter pulse durations) could be due to: (1) more motor units being recruited for each increment in pulse duration at shorter pulse durations and/or (2) larger motor units being recruited at shorter pulse durations. When a rectangular pulse is applied to an excitable membrane, due to the resistive and capacitive properties of the membrane, the membrane potential depolarizes exponentially with a steeper rise at the beginning of the stimulation and gradually reaches a plateau (Koester and Siegelbaum, 2000). When the membrane potential reaches the activation threshold, an action potential is generated, propagates along the motoneuron axon, reaches the neuromuscular junction, and produces a muscle contraction.

The passive depolarization of the membrane potential that initiates the triggering of the action potential can be described with the following equation (Koester and Siegelbaum, 2000),

$$\Delta V = IR(1 - e^{-t/\tau}), \quad (2)$$

where ΔV is the change in membrane potential, I and R represent the current and resistance across the membrane, t is the stimulation pulse duration, and τ is the membrane time constant determining the rate of rise for the membrane potential. The value of τ is the product of the resistance and capacitance of the membrane. The values for I , R , and τ depend on the electrical properties of the tissues through which the current flows and the distance between the stimulation electrodes and motoneurons. Thus, when applying a rectangular pulse to a motor nerve within a muscle, each motoneuron will have one set of parameter values for I , R , and τ to describe its membrane depolarization. Based on equation 2, the changes in membrane potential (ΔV) are exponential, with greater changes in membrane potential at shorter versus longer pulse duration for the same increment in pulse duration. Thus, at shorter pulse durations, relatively more additional motor units will be recruited for each increment in pulse duration and greater force augmentation for each increment in pulse duration will be observed. On the other hand, at longer pulse durations, the amount of membrane depolarization for each increment in pulse duration becomes smaller, resulting in fewer additional motor units recruited for each increment in pulse duration and smaller force increments will be observed. Thus, greater motor unit recruitment and force augmentation at shorter pulse durations due to faster rise in membrane potential at the beginning of the excitation may play a significant role in determining the shape of the force-intensity relationship found in the current study.

Due to the inverse relationship between neuron axial resistance and fiber diameter (Blair and Erlanger, 1933), it has been traditionally assumed that motor units are recruited in a reverse order of Henneman's size principle (Henneman et al., 1965) during electrical stimulation (Heyters et al., 1994; Sinacore et al., 1990; Trimble and Enoka, 1991). That is, larger motor units are recruited prior to smaller ones when gradually increasing stimulation intensity. A few studies, however, have provided evidence suggesting that the motor unit recruitment order during surface electrical stimulation is not as consistent as previously reported because both the location of the motoneuron with respect to electrodes and the motor axonal diameter are major factors in determining motor unit recruitment order (Binder-Macleod et al., 1995; Feiereisen et al., 1997; Knaflitz et al., 1990). Thus, because larger motor units are not always recruited prior to smaller ones during surface electrical stimulation, the contribution of motor unit recruitment order to the shape of the force-intensity relationship is unknown.

Effect of fatigue and stimulation frequency on the force-intensity relationship

The current study was the first to investigate the changes in force-intensity relationship with fatigue for human skeletal muscles. Interestingly, the normalized force-intensity relationship for human quadriceps did not change after a three-minute fatiguing protocol. Because of the positive relationship between human motor unit force generating ability and its fatigability (i.e., larger motor units are more fatigable) (Fuglevand et al., 1999; Thomas et al., 1991), if motor units were recruited in an orderly fashion with respect to force, a change in the shape for the normalized force-intensity relationship (i.e., changes in the PD_0 and τ values) should be seen with fatigue. In the current study, however, the pre-fatigue normalized force-intensity curve superimposed with the post-fatigue curve and the PD_0 and τ values remained the same, indicating no change in the force-intensity relationship with fatigue. A random recruitment order could diminish the effects of the difference in force generation ability and fatigability of different motor unit types on the shape of the normalized force-intensity relationship. Thus, the fact that we observed no change in the normalized force-intensity relationship supports

previous claims for a random recruitment of motor units during electrical stimulation with surface electrodes (Binder-Macleod et al., 1995; Feiereisen et al., 1997; Knaflitz et al., 1990).

Because muscle contractile properties determine the temporal summation of the twitch forces in response to each stimulation pulse (Botterman et al., 1986; Kernell et al., 1983), motor unit recruitment order may affect how the force-intensity relationship changes with stimulation frequency. If motor units were recruited orderly with respect to their contractile speeds, the contractile properties of the muscle should change with a change in stimulation intensity. For example, if motor units were recruited in order from fast to slow units with increasing stimulation intensity, at shorter pulse durations, muscle contractile speed should be relatively faster than at longer pulse durations. Consequently, a shift in the shape of the force-intensity relationship should be observed when stimulated at different frequencies. Our results, however, showed consistent PD_0 and τ values for the exponential equations at different stimulation frequencies, indicating that the force-intensity relationship did not change with stimulation frequency. Our findings could be explained by the random recruitment order observed during surface electrical stimulation (Binder-Macleod et al., 1995; Feiereisen et al., 1997; Knaflitz et al., 1990). The effect of stimulation frequency on the shape of the force-intensity relationship curve would be minimized if motor units were recruited randomly with respect to contractile speed. However, it should be noted that a few studies have reported that human motor unit contractile speed is not correlated with its force or fatigability (Fuglevand et al., 1999; Thomas et al., 1991), suggesting that weaker, more fatigue-resistant motor units are not necessarily slower contracting. This absence of correlation between motor unit contractile speed and force or fatigability could result in no change in the force-intensity relationship at different frequencies even when motor units were recruited orderly with respect to its force or fatigability.

Skeletal muscles undergo marked morphological and neurophysiological changes towards a faster fiber type composition following upper motoneuron lesions. It has been reported that there are marked decreases in muscle mass (Gordon and Mao, 1994), changes in muscle fiber type composition (Burnham et al., 1997; Round et al., 1993), and changes in contractile properties and fatigability (Gerrits et al., 1999) in paralyzed muscles. Thus, the force-intensity relationship for paralyzed muscles could be expected to be different from non-paralyzed muscles. However, when applying FES to paralyzed muscles using surface electrodes, due to a random motor unit recruitment order, it could be expected that the normalized force-intensity relationship of paralyzed muscles would not change with frequency or fatigue, as observed in the current study. This information regarding the force-intensity relationship during repetitive electrical stimulation enables a more accurate estimation of force output with a given stimulation pulse duration (See example below), and can help clinicians and researchers to precisely control force output during the application of FES.

Conclusions

The present study investigated the relationship between force output and stimulation intensity of human quadriceps muscles at clinically relevant stimulation frequencies and for both pre- and post-fatigue conditions. An exponential relationship between muscle force and stimulation intensity was found, and the normalized force-intensity relationship did not change with stimulation frequency or fatigue. From the aspect of force control during FES, these findings will help researchers and clinicians to better understand the relationship between muscle forces and stimulation intensity and develop strategies to control forces more precisely. Future studies could investigate non-isometric muscle contractions and incorporate the current findings into a closed-loop feedback system for muscle force control during clinical FES.

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Fig 1.

Example for the determination of stimulation pulse duration modulation steps based on the force-intensity relationship curve for a typical subject. (1) represents the initial force-intensity relationship for the subject. (2) Identifying the starting pulse duration by locating the pulse duration that produces peak forces equal to the targeted force level (black point). (3) 10% decline in peak force due to muscle fatigue. (4) the new force-intensity relationship. (5) Identifying the required pulse duration that produces peak forces equal to the targeted level. Not drawn to scale. See text for detail.

Fig 2.

Family of force-intensity relationship curves for the subject with SCI. The force-intensity relationship shifted down with fatigue. The intensity modulation steps (arrows) were determined by locating the intersections between the force-intensity curves and the targeted force level (gray dashed line).

Fig 3. Mean peak force responses ($\pm$ SE, $n = 10$) to 180 stimulation trains in the fatiguing protocol. Peak force responses declined by $\sim 50\%$ from the initial force responses to a steady fatigue state.

Fig 4.

Force responses for a typical subject to 60-Hz stimulation trains with pulse duration ranging from 100 to 600 μ s for both pre- (A) and post-fatigue (B) conditions. Peak forces were then calculated and the force-intensity relationship curve was determined for each condition. The same procedure was used to determine the force-intensity relationship for each of the other 5 frequencies tested.

Fig 5.

Plots of the absolute (A & C) and normalized (B & D) (Mean $\pm$ SE) force-intensity relationships for frequencies from 10 to 60 Hz for both pre- and post-fatigue conditions. For all the frequencies tested, peak force responses increased exponentially as the pulse duration increased, and all the normalized force-intensity curves superimposed with each other. (E) Plot of the averaged (across all the frequencies tested) pre- (triangle) and post-fatigue (circle) peak force responses (Mean $\pm$ SE) as a function of pulse durations (100 to 600 μ s). (F) Plot of averaged ($\pm$ SE) normalized pre- (triangle) and post-fatigue (circle) force-intensity relationships. The pre-fatigue curve superimposed with the post-fatigue curve. For several of the data points the error bars fell within the symbol.

Fig 6.

Example of a curve fitting for force-intensity relationship using exponential equation for a typical subject. Data points shown in triangle and circle represent the pre- and post-fatigue peak force responses to the 60-Hz testing trains, respectively. The dark and gray lines represent the fitting results for the pre- and post-fatigue force-intensity relationship curve. The numbers in the text boxes represent the parameter values for each force-intensity curves.

Fig 7.

Averaged ($\pm$ SE) A (A), PD_0 (B) and τ (C) values for frequencies ranging from 10 to 60 Hz at both pre- (triangle) and post- (circle) fatigue conditions. The averaged A values across frequencies and between conditions were significantly different from each other. On the other hand, PD_0 and τ values were very similar between pre- and post-fatigue conditions for all the frequencies tested.

Fig 8.

Plots of quadriceps femoris muscle peak force responses to repetitive electrical stimulation (one train every 1.1 second) for an SCI subject. Each data point represents a peak force for 1 contraction. The initial pulse duration produced peak forces equaled to subject's MTF. Stimulation intensity was increased every time when the peak force responses dropped 10% from the targeted force level. As shown in the figure, quadriceps muscle isometric force output was successfully maintained within the 10% targeted window for about 175 contractions by modulating stimulation intensity based on the subject's force-intensity relationship.