Force output during fatigue with progressively increasing stimulation frequency

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Abstract

There is currently a controversy over whether stimulation frequencies should increase or decrease to optimize force output over time. This study compared changes in thenar muscle force and M-wave amplitude during progressively increasing (20–40 Hz), decreasing (40–20 Hz) and constant (20 Hz) frequency stimulation of the median nerve continuously for 3 min. Twenty-three individuals participated in three sets of experiments. There was no significant difference in the force–time integrals between the three fatigue tasks. The rate of fatigue was not correlated to the number of stimulation pulses delivered (20 Hz: 3600, 20–40 and 40–20 Hz: 5400). All fatigue tasks caused a significant reduction in M-wave amplitude and the reduction was largest for the 20–40 Hz protocol. However, multiple linear regression analysis revealed that the M-wave amplitude could not predict the changes in force over time for the 20 Hz or 20–40 Hz protocols. Thus during sustained evoked contractions with stimulation frequencies within the physiological range, frequencies can vary significantly without changing the overall force–time integral.

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1. Introduction

There has been conflicting evidence as to how stimulation frequencies should be manipulated during sustained evoked contractions. Bigland-Ritchie et al. (1979) originally proposed that during sustained evoked maximal contractions, stimulation frequencies should decrease (80–20 Hz) over time in order to prevent neuromuscular transmission failure (measured as a reduction in M-wave amplitude) associated with constant high frequency (80 Hz) stimulation. Fuglevand and Keen (2003) found that during submaximal evoked contractions, when frequencies were within the range of natural motor unit firing, a reduction in frequency (30–15 Hz) exacerbated force loss over a 1 min sustained contraction compared to constant 30 Hz stimulation.

Substantial evidence exists that indicates that a stimulation frequency pattern that increases over time when stimulating within the physiological range would result in greater force output compared to continuous constant frequency stimulation. Several studies have delivered brief trains of electrical stimulation at different frequencies before and after various fatigue tasks to investigate relative force loss across a range of frequencies. These studies found that higher frequencies were required to evoke the same absolute force after fatigue compared to before. This shift in the force–frequency distribution occurs in both single motor units (Thomas et al., 1991; Fuglevand et al., 1999) and whole muscle (Edwards et al., 1977; Bergstrom and Hultman, 1990; Binder-Macleod and McDermond, 1992; Meyers et al., 2001; Russ et al., 2002). In addition, relatively more force is lost at low compared to high frequencies of stimulation following fatigue termed ‘low frequency fatigue’ (Grabowski et al., 1972; Edwards et al., 1977; Westerblad et al., 1993).
To date, only one study has investigated the use of increasing stimulation frequency during evoked contractions (Kebaetse et al., 2005). During repeated intermittent submaximal dynamic evoked contractions of the quadriceps muscles in spinal cord injured individuals, (Kebaetse et al., 2005) found that a stimulation pattern that increased from 20 to 66 Hz decreased the rate of fatigue compared to constant frequency intermittent stimulation of 20, 33 or 66 Hz. These promising results suggest that the same benefits would ensue during continuous rather than intermittent stimulation during sustained contractions of the muscles of the hand. We hypothesized that stimulation frequencies within the physiological range (<40 Hz) would not severely disrupt neuromuscular transmission because frequencies above 40 Hz can greatly exacerbate fatigue (Zhou et al., 1987). We also hypothesized that an increase in stimulation frequency over time would maximize force output over time by overcoming ‘low frequency fatigue’. Thus, the purpose of this study was to test whether during sustained evoked contractions in the hand, an increase in stimulation frequency would improve force output over time compared to constant frequency stimulation. The second aim of this study was to investigate whether changes in the force output during fatigue were correlated to changes in M-wave amplitude.

2. Methods

2.1. Subjects

Twenty-three individuals (19 male, 4 female) between the ages of 20 and 36 (29 ± 1) years with no history of neuromuscular, or metabolic disorder participated in this study. Prior to participating, all volunteers signed a consent form. All procedures were approved by the Institutional Review Board of the University of Texas at Austin.

Ten individuals participated in the main experiment which consisted of performing two fatigue protocols that were separated by at least 48 h to ensure recovery from fatigue. These protocols were designed to compare muscle fatigue responses between two, 3 min evoked fatigue tests; one of constant stimulation frequency (20 Hz) and the other continuously increasing frequency (20–40 Hz).

Seven individuals participated in a second set of experiments that were designed to compare changes in M-wave amplitude throughout the constant 20 Hz and the 20–40 Hz fatigue tests. This experiment controlled for the effects of possible reductions in M-wave amplitude due to waveform cancellation of consecutive M-waves during continuous stimulation (Fuglevand and Keen, 2003) that can result from M-wave slowing with fatigue (Bigland-Ritchie et al., 1979; Thomas et al., 2003). All procedures were identical to the main experiment except that the stimulation during the fatigue tests was interrupted by 1 s rest intervals every 45 s during which three single, non-overlapping M-waves were evoked.

Six additional subjects participated in a third experiment to compare the forces, M-wave amplitudes and force–time integrals during a 3-min constant 20 Hz stimulation and a 3-min protocol in which stimulation frequency continuously decreased (40–20 Hz) throughout the fatigue task.

2.2. Experimental setup

The experimental set up was similar to that used in previous investigations (Griffin et al., 2002; Thomas et al., 2003). Each participant sat in a chair with their right upper arm strapped to the chair back. The wrist and forearm were restrained in a supinated position within a thermoplastic splint (Smith and Nephew, Rolyan, USA) secured to a laminar base mounted to a laboratory table. A metal plate stabilized both the hand and fingers to isolate thumb adduction and flexion forces. The thumb was positioned against a custom made force transducer (Mechanical Engineering Shop, University of Texas at Austin) that recorded the isometric adduction and flexion forces which were at right angles to each other. The resultant force was calculated from the addition and flexion forces and was displayed on a computer monitor positioned in front of the participant.

Surface EMG was recorded with two surface electrodes placed approximately 1.5 cm apart over the central portion of the thenar eminence. Electrodes were pre-gelled, 1 cm diameter circles composed of Ag/AgCl (Danlee Medical Products, Inc., US). A ground electrode was placed on the pisiform bone slightly below the hypothenar eminence. A depiction of the experimental set up is displayed in Fig. 1.

2.3. Stimulation

A stimulating electrode was placed over the median nerve. Stimulation of the nerve enabled maximal motor unit recruitment and produced a significant delay between the stimulus artifact and the resulting M-wave at the thenar musculature. Duration pulses (50 μs) were delivered to the median nerve with a variable current stimulator (Digitimer D57A, UK). After the best stimulating electrode position was obtained, it was secured with tape over the participants’ wrist. The current was gradually increased until the M-wave reached maximum amplitude. The stimulation current was set at approximately 15% greater than that which evoked the maximal M-wave amplitude. The sequence of stimulation for each fatigue task was controlled by a programmable output system (Spike 2, version 5, Cambridge Electronic Design (CED), UK).

2.4. Experimental protocol

In the first and third sets of experiments, two fatigue protocols were administered to each participant in random order. The interval between all testing days was at least 48 h to ensure recovery from fatigue. After the experimental set up and electrode placement, the median nerve was stimulated with five single pulses. Three 5 s maximal voluntary contractions (MVCs) were then performed.

Following the MVCs, one of the fatigue protocols was administered. One fatigue protocol consisted of stimulation at a constant 20 Hz frequency for 180 s and the other protocol consisted of progressively increasing the stimulation frequency from 20 to 40 Hz over 180 s. This program was created such that each consecutive interval was decreased until a stimulation rate of 40 Hz was reached by the end of the 3 min. Twenty Hertz was used as the baseline constant frequency because it produces a fairly fused, moderate level of contraction force (Krajl and Bajd, 1989). The upper level was selected as 40 Hz since this frequency elicits a force close to maximum (Zhou et al., 2005).
et al., 1987) and represents the upper limits of physiologically relevant frequencies see (Enoka and Fuglevand, 2001) for review. Five M-waves were recorded before the fatigue task and after 2 min of rest following the fatigue test to measure recovery of the M-wave and verify stability of the stimulating electrode throughout the fatigue task.

Seven individuals (6 male, 1 female) participated in two additional experiments to measure changes in the M-wave amplitude periodically throughout the fatigue tasks without the interference of waveform cancellation from consecutive M-waves during the continuous stimulation. For these experiments, all procedures were identical to the main study except that the 3 min evoked fatigue protocols of constant (20 Hz) and continuously increasing (20–40 Hz) frequencies were interrupted every 45 s by a 1 s interval in which three single pulses were delivered. Fig. 2 displays the surface EMG and stimulation data for these ‘intermittent’ fatigue tasks for one participant. One M-wave from each 1 s rest is expanded below the surface EMG trace.

2.5. Data collection and analysis

Surface EMG was amplified by 100, high-pass filtered above 13 Hz (Coulbourn V-75 amplifier), analogue to digital converted (Micro 1401, Cambridge Electronics Design, UK) and sampled at 2000 Hz. The adduction and flexion forces were amplified by 100, and sampled at 1000 Hz. The resultant force $[\text{resultant force} = \sqrt{(\text{abduction force})^2 + (\text{flexion force})^2}]$ was calculated with Spike 2 software (CED) and displayed online to the computer monitors. The force and M-wave amplitude were measured at 10 s intervals throughout the fatigue task.

2.6. Statistics

Repeated measures 2-way ANOVA (factors: fatigue and protocol) and Tukey’s post hoc analysis were used to compare the forces and cumulative force–time integrals at 10 s intervals throughout the fatigue tasks. Correlation analysis was performed on the forces and M-waves measured at 10 s intervals throughout the fatigue tasks. Multiple linear regressions were also performed with force as the dependent variable to determine if M-wave amplitude and time could predict force values. Repeated measures ANOVAs were also used to compare the average of the 5 peak-to-peak M-wave amplitudes at the start and end of the fatigue task, and after 2 min of recovery and differences in M-wave amplitudes throughout the fatigue task in the ‘intermittent’ fatigue studies. Paired $t$-tests were used to compare MVC force between fatigue tests. The alpha level of significance for all statistical analysis was $p \leq 0.05$. All data are expressed as mean ± standard error.

3. Results

3.1. Force

There was no significant difference in the MVC force between experiment days. MVC forces were $47.77 \pm 5.01$ N

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Fig. 1. Experimental setup. The participant’s right thumb was positioned in a strain gauge force transducer device that measured force in vertical (adduction) and horizontal (flexion) directions. Surface EMG recording electrodes were placed over the thenar muscle and a ground electrode was placed over the pisiform bone. The stimulating electrode was placed over the median nerve at the wrist.
on the 20 Hz protocol test day and 53.19 ± 5.15 N on the 20–40 Hz test day. There was also no significant difference between the forces at the start of the contraction between the two fatigue tests. Mean forces at 10 s of stimulation were 27.64 ± 4.27 N for the 20 Hz protocol and 28.04 ± 3.53 N for the 20–40 Hz protocol.

Fig. 3 depicts the average forces for every 10 s of contraction for all subjects. There was no main effect for differences in force during the fatigue tasks. The force was significantly lower at the end compared to the start of the contraction in both fatigue protocols. The force at the end of the fatigue task was 8.16 ± 1.76 N for the 20 Hz protocol and 7.58 ± 1.13 N for the 20–40 Hz protocol. There was no significant difference in the overall force time integral (FTI) between the 20 Hz (3.40 ± 0.06 KN s) and the 20–40 Hz (3.26 ± 0.05 KN s) fatigue tasks. For the third set of experiments, there was also no difference between the mean FTI for the 20 Hz (2.50 ± 0.29 KN s) and the 40–20 Hz (2.28 ± 0.41 KN s) fatigue tasks. Mean forces at 10 s intervals for this test are displayed in Fig. 4.

3.2. M-waves

There was no significant difference between the pre-fatigue or recovery M-wave values within or across test days. Pre-fatigue M-wave amplitudes during the 20 Hz and 20–40 Hz fatigue protocols were 13.01 ± 1.49 mV and 13.23 ± 1.15 mV, respectively. M-wave amplitudes at 2 min after the fatigue test were 3.18 ± 1.40 mV and 12.77 ± 1.09 mV for the 20 Hz and 20–40 Hz fatigue tests, respectively.

There was a significant reduction in the M-wave amplitude elicited during both fatigue tests with a significantly greater reduction occurring in the 20–40 Hz stimulation protocol. The M-wave amplitudes at the end of the fatigue protocols were 4.76 ± 0.81 mV and 2.55 ± 0.38 mV for the 20 Hz and 20–40 Hz protocols respectively. Fig. 5 shows mean values of M-wave peak-to-peak amplitudes for all participants before and after the fatigue test and after recovery. There was a significant quadratic relationship between M-wave amplitude and muscle force output during both fatigue tasks (20 Hz, \(r = 0.9\); 20–40 Hz, \(r = 0.9\)).

For the ‘intermittent’ stimulation tests, the difference in peak-to-peak M-wave amplitude between the two protocols was also statistically significant. M-wave amplitude depressed to a greater degree by the end of the 20–40 Hz protocol (35.8 ± 4.0%) than by the end of the 20 Hz protocol (11.84 ± 3.5%). Fig. 6 displays the average M-wave data for the seven individuals who participated in the intermittent fatigue tests.

4. Multiple linear regressions

A multiple linear regression was performed with force as the dependent variable to determine if M-wave amplitude and time could predict force values. For the 20 Hz test, time was a significant predictor (\(r^2 = 0.59; P < 0.001\)) of force, but M-wave amplitude was not (\(r^2 = 0.05; P = 0.12\)). The overall \(R^2\) for how well the independent variables (time and M-wave) predicted the dependent variable (force) was 0.21.

For the 20–40 Hz pattern, multiple linear regression showed that time was a significant predictor of force...
For the 40–20 Hz stimulation pattern, both time ($r^2 = 0.18$, $P < 0.001$) and M-wave ($r^2 = 0.11$, $P < 0.001$) were significant predictors of force. The $R^2$ value for this analysis was 0.67.

5. Discussion

The results of this study demonstrate that in a predominantly male subject population, there is a wide range of variability in stimulation frequency that can be used to obtain similar overall force–time integrals. We did not find that progressively increasing or decreasing stimulation frequency over the course of a 3 min sustained contraction significantly altered the overall force–time integral produced when stimulating within the physiological range (20–40 Hz).

The ‘muscle wisdom hypotheses’ proposed that a reduction in frequency could prevent neuromuscular transmission failure and increase force output over time by matching to the slowing of muscle contractile rate during fatigue (Marsden et al., 1983). This hypothesis has been recently challenged.
when (Fuglevand and Keen, 2003) found that force was reduced to a greater degree when frequencies were reduced from 30 to 15 Hz compared to constant 30 Hz stimulation and (Garland et al., 1997) found that motor unit discharge rates declined during submaximal voluntary contractions in the absence of whole muscle contractile rate slowing.

During brief trains of electrical stimulation elicited before and after a fatigue task, higher rather than lower frequencies of stimulation are required to produce the same absolute level of force output after fatigue than before (Edwards et al., 1977; Cooper et al., 1988; Bergstrom and Hultman, 1990; Binder-Macleod and McDermond, 1992). In addition, relatively more force was lost at low compared to high frequencies of stimulation (Grabowski et al., 1972; Edwards et al., 1977; Westerblad et al., 1993). These observations predict that stimulation frequencies should increase over time to maximize force output during fatigue. However, the present study found that no overall difference in the force–time integral occurred with a stimulation pattern that continuously increased during 3 min of stimulation compared to constant low frequency stimulation.

As found in paralyzed muscle (Mizrahi et al., 1994, 1997), the forces produced during the fatigue task were highly correlated to the M-wave amplitude, and the
M-wave amplitude decreased to a greater degree during the protocol with increasing frequency independent of the effects of wave-form cancellation. Changes in the M-wave amplitude could indicate changes in the efficacy of excitation of the sarcolemma of individual muscle fibers or drop out of individual muscle fibers (see Keenan et al., 2006 for review). However, in the present study, the total number of pulses delivered (20 Hz: 3600 pulses, 20–40 Hz: 5400 pulses) had little influence on the overall force output of the muscle over time and multiple regression analysis revealed that force could not be predicted by M-wave amplitude for either protocol. It is possible that increases in dynamic force output over time were found by Kebaetse et al. (2005) because intermittent submaximal stimulation was used, allowing for recovery time for the t-tubules between trains but M-wave amplitudes were not measured in that study.

5.1. Sustained evoked contractions

The design of reducing stimulation frequencies to preserve M-wave amplitude (Bigland-Ritchie et al., 1979) applied only for eliciting contractions of maximal intensity at unphysiologically high frequencies (60–80 Hz). When (Fuglevand and Keen, 2003) compared a 1-min frequency train that progressively decreased from 30 to 15 Hz to a constant 30 Hz train, the decreasing frequency train produced significantly less force overall compared to the constant 30 Hz train. In the present study, we found that progressively increasing or decreasing stimulation frequency within the 20–40 Hz range did not significantly alter the overall force–time integral compared to constant frequency stimulation.

In summary, fatigue is a complex process that commonly involves excitation–contraction failure. We predicted that an increase in stimulation frequency during prolonged evoked contractions of the hand would reduce force loss by overcoming the phenomenon of low-frequency fatigue. The results of this study showed that although significant reductions in the M-wave amplitude occurred during stimulation with frequencies within the physiological range (20–40 Hz), an increase or decrease in stimulation frequency did not significantly alter the overall force–time integral during prolonged sustained contractions of the thenar muscle.

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References


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