Quadriceps Muscle Fatigue and Comfort Generated by Neuromuscular Electrical Stimulation with Current Modulated Waveforms

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Abstract: *Introduction:* Neuromuscular electrical stimulation (NMES) is used by physical therapists in the clinic. The efficacy of NMES is limited by the rapid onset muscle fatigue. The role of NMES parameters is muscle fatigue is not clear. *Objective:* To determine the effects of shape waveform on muscle fatigue, during NMES. *Methods:* Twelve healthy subjects participated in the study. Subjects were assigned to 1 of 3 groups, randomly. Group assignment determined the order in which they were tested using 3 different shape waveforms. Maximal voluntary isometric contraction (MVIC) was measured during the first session. Fatigue test was applied with amplitude required to elicit 50% of the MVIC. In each 3 testing sessions torque of contraction and level comfort were measured, and percent fatigue was calculated. Analysis of variance tests for dependent samples was used to determine the effect of shape waveform on muscle fatigue and comfort scores *Results:* The results showed no one shape waveform was most fatigable and that SQ wave induced more uncomfortable stimulus.

1 INTRODUCTION

Neuromuscular electrical stimulation is a commonly used tool by physical therapists in sports and clinical conditions characterized by motor impairments such as stroke, cerebral palsy, and spinal cord injury (Glinsky, Harvey and Van, 2007; Maffiuletti *et al.*, 2000; Newsam and Baker, 2004; Stackhouse *et a*l., 2007; Snyder-Mackler, Delitto and Stralka, 1994). The common neuromuscular adaptations that characterize the aforementioned conditions are muscle weakness and atrophy resulting from disuse or neurological injury (Maffiuletti, 2010; Snyder-Mackler *et al.*, 1994).

However, during electrical stimulation, skeletal muscles fatigue more rapidly during repetitive stimulation than during voluntary contractions (Riener, 1999; Vanderthommen *et al.*, 2003). Muscle fatigue is defined as a reduction in the peak force, with continuous and repeated activation (Mulla, Sepulveda and Colley, 2011). Rapid fatigue during NMES is thought to result from the differences in motor unit recruitment order, higher activation frequencies and imprecise control of muscle force comparing voluntary contractions (Peckham and Knutson, 2005). The problem of muscle fatigue is aggravated by the fact that paralyzed muscle show greater fatigability than healthy muscle. Muscle fatigue is an important factor limiting the clinical use of NMES (Gerrits *et al.*, 2003).

New commercial stimulators provide many different waveforms and pulse settings (Snyder-Mackler *et al.*, 1994; Kantor, Alon and Ho, 1994). Researchers have attempted to identify preferred stimulation settings in terms of force contraction (Doucet, Lam and Griffin, 2012; Laufer, Ries and Leninger, 2000), fatigue (Binder-Macleod and Snyder- Mackler, 1993; Gorgey, Black, Elder and Dudley, 2009; Kesar and Binder-Macleod, 2006) and comfort (Kantor *et al.*, 1994). The stimulation variables that are thought to have the greatest impact on muscle fatigue include pulse amplitude and duration and pulse train frequency (Binder-Macleod and Snyder Mackler, 1993; Doucet *et al.*, 2012). However, because the number of factors considered in the different studies is extremely variable, is it difficult to take definitive conclusions concerning the optimal settings that can elicit the strongest contractions with minimal fatigue.

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The independent effects of these 3 parameters on muscle fatigue are still controversial. Conflicting results exist on the role of current amplitude on muscle fatigue: for instance while one study demonstrates fatigue increasing with amplitude (Binder-Macleod, Halden and Jungles, 1995), others show no change in fatigue with increasing current amplitude (Slade, Bickel, Warren and Dudley, 2003). In certain cases the frequency of pulses has been shown to accelerate muscle fatigue (Gorgey *et al.*, 2009; Lieber and Kelly, 1993). Nonetheless, a full understanding of the role of pulse duration on muscle fatigue has not been reached.

Gorgey *et al.* (2009) concluded that altering the pulse duration does not appear to influence fatigue in NMES. Compared to the influence of current amplitude, frequency and pulse duration, the role of shape waveform on muscle fatigue is even less well established.

According to the literature, the most efficient stimulation of the nerve fiber is carried out using square shape waveform (Robertson, Ward, Low and Reed, 2006). However, if pulse duration is sufficiently short (250 µs or less) triangular shape waveforms are functionally equivalent to square waves (Robertson *et al.*, 2006). Laufer *et al.* (2000) showed stimulation with sinusoidal polyphasic waveform resulted in more rapid muscle fatigue than stimulation with square monophasic and biphasic waveforms, both tested on quadriceps muscle in individuals without impairment. In addition, stimulation with polyphasic waveform elicited weaker electrically induced contractions.

Another factor to take into consideration during NMES, is the subjective comfort of stimulation. Many previous studies attempted to determine waveform parameters or combination of parameters which caused the least subjective discomfort. In one study, there was no simple answer, individuals having their own preference for sinusoidal, triangular, or square waveform (Delitto and Rose, 1986). A symmetric biphasic square waveform was generally preferred for the large quadriceps muscle group, whereas an asymmetric biphasic square waveform was preferred for the smaller forearm musculature when compared to a monophasic paired spike and three medium frequency waveforms (Baker, Bowman and McNeal, 1988).

The main aim of our study was to investigate the effect of shape waveform on quadriceps muscle fatigue with three different shape waveforms, in individuals without impairments. . A second purpose was to determine whether changing the shape waveform (square, triangular and quadratic) could improve the comfort level of subjects.

2 METHODS

2.1 Subjects

The subjects who volunteered to participate in the study were the following: six female averaging 25 years old (SD=2,7); six male averaging 24 years old (SD=2,8) All subjects reported having no known neuromuscular, skeletal, vascular or dermatological impairment. Each one received a detailed explanation of the study and gave informed consent prior to participation. The Scientific Committee of Health School of Technology of Lisbon approved the present study.

2.2 Instrumentation

A portable electrical stimulator with wireless data communication was used to elicit muscle contraction (Bio Signals Plux). This device allows the modulation of different shape waveforms. **Table 1** presents a characteristics summary of the electrical stimulation settings used. The current charge difference from each waveform was taken into account in the data analysis. The stimulation charge was computed accordingly to the stimulation intensity and waveform, based on the following formula:

$$Q= \int t1 I \, dt \qquad (1)$$

Where *I* represent the current intensity and *t1* to *t2* is the stimulus time range, being considered in this case constant. The charge of the different waveform types have been equalized, for each current intensity, maintaining the amplitude and varying the pulse-duration time.

Table 1: Summary of stimulation characteristics for 3 waveforms.

Stimulation parameters	**SQ**	**TR**	**QU**
Type of waveform	Monophasic	Monophasic	Monophasic
Pulse duration (µs)	175	375	500
Frequency (Hz)	50	50	50
Maximal peak intensity (mA)	100	100	100

Abbreviations: SQ - Square waveform TR - Triangular waveform QU - Quadratic waveform

Two 10 x 5 cm rectangular, reusable, self-adhering electrodes were used in each participant; a isokinetic dynamometer (Biodex) $_{[25]}$ was used to assess torque generated by right quadriceps muscle group during MVIC and during all electrically induced isometric quadriceps muscle contractions. The reliability of the Biodex system dynamometers for knee extensors and knee flexors peak torque measurements in isometric, concentric and eccentric tests has been studied. Interclass correlation coefficients indicated high to very high reproducibility for isometric, concentric and eccentric peak torques (0,88-0,92), and moderate to high reliability for agonist-antagonist strength ratios (0,62-0,73) (Araújo *et al.*, 2014).

2.3 Protocol

Each subject participated in 3 sessions, separated by at least a 48 hours period. Subjects were assigned to 1 of 3 groups, determining the order in which they were tested using 3 different electrical stimulation shape waveforms. Group assignment was random. Participants were not informed of the shape waveform being used during each testing session.

The right quadriceps muscle was used for all tests.

During the initial session, MVIC of the right quadriceps muscle was measured. This measurement was followed by determination of the current amplitude required to elicit 50% of the MVIC test and by a fatigue test using 1 of the 3 shape waveforms. The procedure for each the ensuing sessions was similar to the initial procedure, with the following exceptions: MVIC was determined at the initial session only; the type of shape waveform being used for the electrical stimulation component of the protocol differed and was determined by group assignment. Testing was carried out in the FMH Exercise Physiology Laboratory.

MVIC test. Biodex was used to measure MVIC at a 60 degree knee flexion. Subjects' leg, thigh, and pelvis were stabilized by seating system pads and belts. Backrest was set at 110 degree posterior incline. The fulcrum of the lever arm was aligned with the most inferior aspect of the lateral epicondyle of the right femur. The inferior portion of the shin pad was adjusted superior to the medial malleolus. Before the test, participants warmed up and then stretched the major muscle groups of the lower extremity, holding each stretch for 15 seconds. Subjects did 3 consecutive 5-second MVIC trials of the right quadriceps muscle group, with 60 seconds of rest between trials. They were asked to keep their arms crossed over their chest and to contract knee extensors as fast and forcefully as possible, while verbal encouragement was provided**.**

Participants were not allowed to view the measurements on the computer screen. The highest measured torque was used to calculate 50% of the MVIC level.

Determination amplitude required to elicit 50% of the MVIC. A 5 minute rest period was allowed between the MVIC test and the determination current amplitude required to elicit 50% of the MVIC. Each subject's right thigh was cleaned with alcohol. The distal electrode was placed on the vastus medialis approximately 5 to 7 inches from the top margin of the patella; the proximal electrode was placed on the lateral border of the femoral rectus muscle approximately 2/3 of its length above the top edge of the patella (**Figure 1**).

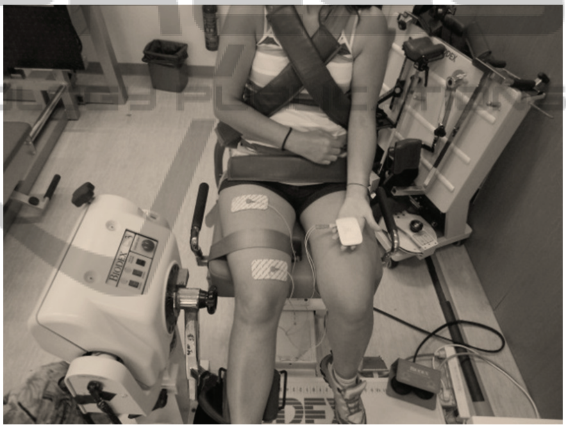

Figure 1: Frontal view: Two electrodes are positioned over vastus medialis and on the lateral border of the femoral rectus. The stimulated limb is maintained in isometric conditions.

The electrodes being set, subjects were placed in the Biodex in the same position used for the MVIC testing. The current amplitude was determined by delivering 3-second trains of progressively greater amplitude. At least 1 minute separated each train. Three to four trials per participant were performed to determine the amplitude of the current in milliamps (mA).

Fatigue test. After a 15-minute rest period, to ensure muscle fatigue recovery, the fatigue component othe protocol was performed, using the current amplitude previously identified and an identical positioning in the Biodex. The fatigue test consisted in nineteen 3-second contractions were evoked 2-minute period (work-to-rest cycle of 3 seconds on and 3 seconds off) As in other portions of the study, subjects were instructed to keep their arms crossed over their chest and to try to relax during the electrically stimulated muscle contractions. They were not able to view the torque measurements displayed on the computer screen. After the three first contractions, the subjects were asked to express their perceived discomfort on a visual analogue scale (VAS) 10 cm long labeled at the left extreme "maximum discomfort" and at the right "no discomfort".

The fatigue index was measured and reflects the difference between the torques of the initial and final contractions divided by the torque of the initial contraction.

2.4 Data Analysis

The mean value of each contraction was extracted for all subjects and for all the signals resulting from the different waveforms. For that, we computed the mean and standard deviation (SD) value of the contraction above 90% of its maximum value. The results were extracted automatically and visually validated manually by two experts.

Descriptive analysis was performed. Frequency or means and standard deviations were calculated for each of the demographic variables.

To check if the variables approached a normal distribution we used Shapiro-Wilk test. The level of significance used was $\alpha = 0{,}01$.

Data was analyzed using ONE-WAY ANOVA, comparing groups in age and Body Mass Index (BMI), discomfort and fatigue percent or Kruskal-Wallis test if the assumption of normality or homogeneity was not verified.

To examine the effects of the 3 shape waveforms on muscle fatigue and discomfort we used ANOVA for 3 dependents samples or ANOVA Friedman test. The independent variables were the shape waveforms (SQ, TR and QU), the contraction number were 1, 9, 13, 19 and dependent variables were peak torque, perceived discomfort and fatigue percent. When applying variance analysis led to the identification of differences, post-hoc tests were used.

The level of significance used to inferential statistics was $\alpha = 0{,}05$.

3 RESULTS

Of the 12 subjects who participated, two of them have not reached values close to50% MVIC with TR and QU shape waveforms. There was no differences between the 3 groups in the age ($F_{2,9} = 5{,}42$, $P = 0{,}029$) , BMI ($X^2_{kw}(2) = 3{,}500$, $P = 0{,}174$) and sex (**Table 2**). The groups are also similar in physical exercise practice, not being given the intensity of the exercise.

Table 2: Demographic variables in 3 groups.

Variables	**Groups** **Group 1 (n = 4)**	 **Group 2 (n= 4)**	 **Group 3 (n = 4)**
Sex			
Female	2 (33,3%)	2 (33,3%)	2 (33,3%)
Male	2 (33,3%)	2 (33,3%)	2 (33,3%)
Age*	22 ± 3,2	25 ± 1,3	27 ± 2,7
BMI*	21 ± 2,8	22 ± 2,0	19 ± 0,8
Dominant leg			
Right	4 (33,3%)	4 (33,3%)	4 (33,3%)
Left	0	0	0
Exercise practice			
Yes	3 (37,5%)	3 (37,5%)	2 (25,0%)
No	1 (25,0%)	1 (25,0%)	2 (50,0%)

Group 1: SQ, TR and QU; Group 2: QU, SQ and TR; Group 3: TR, QU and SQ.
*Data presented in form of means and standard deviations.

The mean ± SD current amplitudes for SQ, TR and QU shape waveforms were 77± 14; 92± 8 and 99 ± 2, respectively. The SQ, TR and QU waveforms evoked mean ± SD percents of MVIC of 50,5% ± 2,4%, 47,2% ± 11,1% and 45,6% ± 10,1%, respectively (**Figure 2**). It was noted the SQ wave generates higher percent of MVIC than the others with lower current amplitudes. FRIEDMAN'S test did not reveal statistical difference between evoked percents of MVIC by 3 shape waveforms in the first contraction of the fatigue test ($X^2_{AF}(2) = 3{,}362$, $P = 0{,}186$).

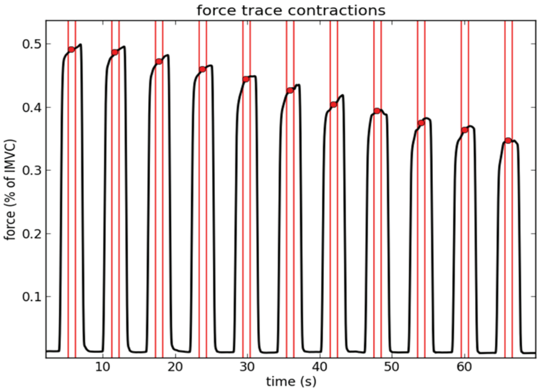

Figure 2: Declining torque of a subject, during fatigue test with SQ shape waveform.

The 1-way ANOVA did not reveal significant difference in fatigue percent for SQ ($F_{2,9} = 1{,}063$, P

= 0,385), TR($F_{2,9}$ = 0,201, P = 0,821) and QU ($F_{2,9}$ = 0,317 P = 0,736) waveform; comfort perception score of SQ ($F_{2,9}$ = 0,66, P = 0,537), TR ($F_{2,9}$ = 1, 725, P = 0, 232) and QU (F2,9 = 2,189, P = 0,168) protocols , among the 3 groups, suggest that the sequence of application of the waves does not interfere with the results.

Figures 2 and **3** illustrate the decline in the evoked torque for the 3 shape waveforms. For all 3 waveforms, there was significant reduction in torque from the initial contraction ($F_{3,2}$ = 189,143, P = 0,000; $X^2_{AF}(3)$ = 32,700, P = 0,00; $X^2_{AF}(3)$ = 32,500, P = 0,000 for SQ, TR and QU waveform, respectively).

No significant differences were observed in fatigue percent among the 3 shape waveforms ($F_{2,2}$ = 2,677, P = 0,091). The TR wave resulted in a lower fatigue when compared to the other 2 shape waveforms (mean ± SD fatigue percent 34,8% ± 12,4% versus 40,3% ± 5,5% and 41,9% ± 9,3%).

Relative to comfort score there were significant difference between 3 shape waveforms (X^2_{AF} = 9,500 , P = 0,009). We verified on **Table 3** that SQ wave differs significantly from TR wave (P = 0,007). The most comfortable shape waveform was the TR wave (mean 5,0 ± 2,5), then the QU wave (mean 5,6 ± 2,9) and finally the SQ shape waveform (mean 6,7 ± 2,7).

Table 3: Pairwise comparisons among waveforms, relative comfort scores.

Shape waveforms	Value test	P
SQ vs TR	9,500	0,007*
SQ vs QU	9,500	0,662
QU vs TR	9,500	0,199

F: Value of ANOVA Friedman test
*Significantly different P < 0,05

4 DISCUSSION

The current study investigated the influence of the waveform (SQ, TR and QU) on muscle fatigue, during NMES. A second purpose was to determine how the wave shape could alter subject comfort level during stimulation.

The results of our study demonstrated that there are no major differences between 3 waves on muscle fatigue. However TR wave (mean 34,8% ± 12,4%) has shown lowest percentage of fatigue than standard wave SQ (mean 40,3% ± 5,5%) and QU waveform (mean 41,9% ± 9,3).

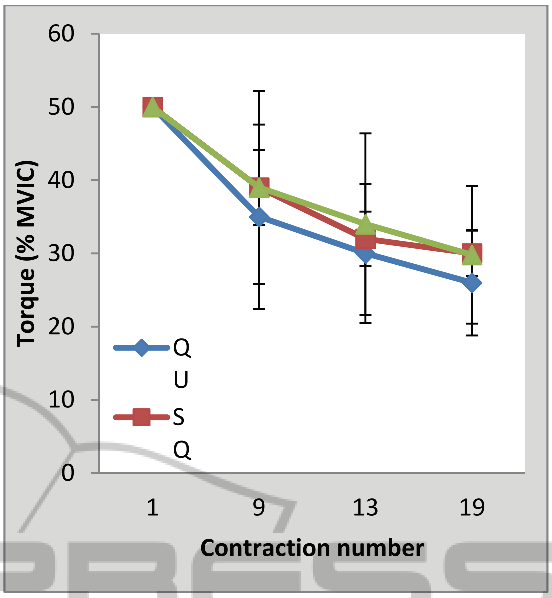

Figure 3: Values are mean ± SD. No significant differences between QU, SQ and TR (P > 0,05). Decline in torque over repeated contractions for QU, SQ and TR.

The difference between the fatiguing effect of TR waveform and that of the other 2 waveforms is difficult to explain. Three of the variables considered to have the greatest effect on muscle fatigue (frequency, electrical charge and time on-off ratios) were the same in all protocols (Binder-Macleod and Snyde-Mackler, 1993; Doucet *et al.*, 2012).

Concerning QU wave, it may be thought that the largest fatigue percent is due to higher current amplitude (99 mA ± 2 vs 92 mA ± 8). A previous study showed that increasing the current amplitude while keeping other NMES parameters constant modestly increased fatigue (Binder-Macleod *et al.*, 1995). This suggests that as the current amplitude increases, more fast-twitch motor units are recruited, resulting in greater fatigue due their higher metabolic demand in comparison to slow-twitch motor units.

Another possibility relates to high pulse duration (500 µs). Literature reports with increasing pulse duration there is an increase in the evoked torque, possibly increasing motor unit activation (Gorgey, Mahoney, Kendall and Dudley, 2006). A pulse duration of 450 µs elicited 22% and 55% greater torque output compared to pulse durations of 250 and 150 µs, respectively (Gorgey *et al.*, 2006; Gorgey and Dudley, 2008). Because increasing pulse duration increases the evoked torque per unit of activated muscle (Gorgey *et al.*, 2006), it causes a higher energy demand and thus leads to faster muscle fatigue.

However, neither amplitude or pulse duration appears to influence the increased percent fatigue of SQ wave, since it presented lower amplitude and pulse duration than that with the best results (77 mA and 195 µs vs 92 mA and 375 µs). A recent study showed no change in fatigue with increase of current amplitude or pulse duration (Gorgey *et al*., 2009). These parameters cause an increase of active area in stimulated muscle (Gorgey *et al*., 2009). These findings may indicate that, although the differences were not statistically significant, wave shape might be responsible for the slight variations.

We cannot neglect to mention that there are few works that study the effect of the waveform on muscle fatigue and the independent study of the effect of NMES parameters (frequency, pulse duration and amplitude) on fatigue were made using exclusively the standard wave, which gives rise to reserves as to whether generalizations can be made for other waves.

Relatively to level comfort, results indicate that TR wave (mean 5 ± 2,5 on VAS score) is significantly more comfortable than SQ wave (mean 6,7± 2,7, on VAS score). Our work does not confirms the conclusions of Delitto and Rose (1986), who found that individual differences exist as far as tolerance to various waveforms (square, triangular and sinusoidal) is concerned and that no waveform tested can be considered optimally comfortable than the others.

The TR waveform, as used in our study, consisted of higher amplitude and pulse duration than that of the SQ wave, but evoked lower percent of maximum voluntary isometric contraction (MVIC). With longer duration of this pulse within the interval 200-400 µs clinical is which according to some research is a good relationship between efficiency and comfort to the patient (Lyons, Sinkjaer, Burridge and Wilcox, 2002). Best results of the TR wave could suggest that the subjects may find an electrically elicited contraction more comfortable at current amplitude producing lower percentages of the MVIC than amplitude producing higher percentages of the MVIC.

The use of the visual analogous scale (VAS) in this study offers an alternative for measuring the comfort levels (Kersten, 2012). VAS has been reported to be accurate, sensitive, and reproducible instruments for patients to report the degree of pain they are experiencing.

No significant difference in the comfort scores was seen on 3 groups, suggesting the order of the administrations of waves do not interfere with comfort perception, contrary to what Delitto and Rose (1986) suggested.

From the results obtained in this study it is possible to propose that the waveform does not significantly influence muscle fatigue in healthy individuals and that TR waveform provides more comfort than the standard contraction wave, during NMES.

Despite minor differences, the best results of the TR wave compared to the SQ wave (also at the level of muscle fatigue) can be quite relevant for clinical practice. Literature indicates that more efficient stimulation of the nerve fiber is made using the square wave, with pulse durations of less than 250s, but the triangular wave shows equal (Robertson *et al*., 2006) and perhaps better results in improved comfort and reduced fatigue levels for patients.

The new systems of NMES on the market are modifiable, so therapists can set parameters (frequency, pulse duration, shape waveform, etc.) and design custom electrical stimulation programs for patients to use. Therefore future studies should focus on the study of the waveform and its combination with the other parameters, using larger number of subjects. This study should be performed in healthy and clinical populations.

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