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Influence of Pulse Waveform and Frequency on Evoked Torque, Stimulation Efficiency and Discomfort in Healthy Subjects

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ABSTRACT

Objective: To determine the influence of neuromuscular electrical stimulation (NMES) pulse waveform and frequency on evoked torque, stimulation efficiency and discomfort at two NMES levels.

Design: Repeated measures study. The quadriceps muscle of 24 healthy men was stimulated at submaximal ($NMES_{sub}$) and maximal ($NMES_{max}$) levels using two pulse waveforms (symmetrical, asymmetrical) and three pulse frequencies (60, 80, 100 Hz). Repeated measures analysis of variance and effect sizes (ES) were used to verify the effect of pulse waveform and pulse frequency on stimulation efficiency (evoked torque/current intensity) and discomfort and to assess the magnitude of the differences, respectively.

Results: Stimulation efficiency was higher for symmetrical ($NMES_{sub}$: 0.88 ± 0.21 Nm/mA; $NMES_{max}$: 1.27 ± 0.46 Nm/mA) compared to asymmetrical ($NMES_{sub}$: 0.77 ± 0.21 Nm/mA; $NMES_{max}$: 1.02 ± 0.34 Nm/mA; $P \leq 0.001$; ES = 0.56-0.66), but did not significantly differ between frequencies ($P = 0.17$). At both NMES levels, there were no statistically significant differences in discomfort between pulse waveforms or frequencies.

Conclusions: The higher stimulation efficiency of symmetrical pulses suggests that this waveform would be preferred to asymmetrical pulses in clinical practice. Stimulation frequencies between 60 and 100 Hz can be used interchangeably due to similar efficiency and discomfort.

Keywords: frequency; waveform; stimulation efficiency; NMES

What Is Known: Electrical stimulation parameters largely impact both the amount of torque that is produced and the discomfort perceived by the patient, consequently influencing the effectiveness of the technique.

What Is New: A symmetrical pulse waveform has greater stimulation efficiency (more torque with less current intensity) than an asymmetrical one, for a comparable level of discomfort.

INTRODUCTION

Neuromuscular electrical stimulation (NMES) consists in the application of trains of electrical stimuli to superficial muscles with the goal to generate involuntary contractions, whereby motor units are non-selectively recruited by depolarizing motor axons in proximity of the stimulating electrodes.[1] Electrical current parameters, such as pulse waveform, pulse frequency, pulse duration and current intensity, have a great influence on the amount of tension generated by a muscle during NMES (evoked torque) as well as on the level of discomfort perceived by the subject.[2] NMES is universally considered more efficient when it produces the highest torque with the smallest current intensity, as reflected by the highest possible stimulation efficiency in Nm/mA,[3] while subjective discomfort is also an important clinical outcome that should potentially be kept to the lowest possible level.[4]

The waveform of an electrical pulse represents the current intensity level variation over time. It can be symmetrical or asymmetrical, and is often represented by geometric shapes.[5] The area below an electrical current curve - which is influenced by pulse waveform, pulse duration and current intensity - represents the level of electrical charge delivered to the muscle, this latter being proportional to torque production.[6] Although pulse waveform is a very important NMES parameter, its impact on evoked torque has mainly been evaluated while modifying other parameters concurrently.[7,8] Consequently, there is still poor knowledge on how pulse waveform per se affects evoked torque and stimulation efficiency.

The impact of different NMES parameters on evoked torque has been extensively studied, and more particularly so for the functionally-important and commonly-stimulated quadriceps muscle.[6–11] However, it is still unclear how tetanic stimulation frequencies - which are known to maximize evoked torque -[12] in combination with different pulse waveforms (particularly symmetrical vs. asymmetrical pulses) may affect stimulation efficiency, as well as the level of perceived discomfort. Therefore, the main aim of this study was to determine the influence of pulse waveform and frequency on evoked torque, stimulation efficiency and discomfort at two different NMES levels: a standard submaximal level and the maximally tolerated current level. It was hypothesized that both NMES-evoked knee extension torque and current intensity - and therefore stimulation efficiency - as well as perceived discomfort would be comparable for equal-charge symmetrical and asymmetrical pulse waveforms. On the other hand, because more electrical charge is delivered at higher frequencies with the same current intensity, it was also expected that stimulation efficiency would increase in direct proportion to the increase in pulse frequency.

METHODS

Subjects

In order to reduce between-subject heterogeneity in NMES current levels and evoked torque,[13] only healthy and physically active men were considered for this study. Subjects were recruited through social networks amongst physical education students of the university in which the study was conducted. Physical activity level and medical history were self-reported. In order to participate in the study, subjects should have reported a minimum of 150 minutes of exercise a week, no lower limb injuries in the previous 6 months and no history of cardiovascular or neurological disease. The STROBE guidelines were used to ensure the reporting of this observational study (Supplemental Digital Content 1, http://links.lww.com/PHM/B76). All participants signed an informed consent form to participate in the study, which was approved by the university’s ethics committee (CAAE number 79564217.9.0000.5347).

The appropriate sample size was calculated a priori using G*Power software (version 3.1.9.6; University of Trier, Trier, Germany). An ANOVA: Repeated measures, within-between interaction (F tests family) was used, with a level of significance set at $P = 0.05$, power set at 0.95 in order to detect a medium effect ($f^2 > 0.35$) (Correlation among repeated measures = 0.5; Number of groups = 2; Number of measurements = 3; Non-sphericity correction $\varepsilon = 1$).[14] Based on these calculations, twenty-four subjects (age: 25 ± 4 years, range: 20-35 years; BMI: 23.7 ± 2.9 kg/m²; 22 Caucasian) were recruited and completed all phases of the study.

Procedures

A repeated measures design was used in which all the subjects completed two NMES sessions in the laboratory separated by a 2-week interval to avoid any possible carryover effect. The two sessions were identical, except for the type of pulse waveform (symmetrical or asymmetrical; Fig. 1B) that was randomly presented. Both NMES sessions consisted of a preparation phase without NMES (positioning, warm up and assessment of MVC torque), a preparation phase with NMES (motor point localization and familiarization) and an experimental phase (determination of NMES levels and testing using three different frequencies with symmetrical/asymmetrical pulses at two NMES intensity levels) (Supplemental Digital Content 2, http://links.lww.com/PHM/B77). All procedures and assessments were conducted on the quadriceps/knee extensors of the dominant side (kicking leg) under static conditions (except warm-up contractions).

The dependent variables were evoked torque, current intensity, stimulation efficiency and perceived discomfort. The independent variables were pulse waveform (symmetrical vs asymmetrical), pulse frequency (60 vs 80 vs 100 Hz) and NMES level [submaximal (NMES_{sub})

vs maximal ($NMES_{max}$)]. Submaximal NMES was consistently used first, while pulse waveform and pulse frequency were randomized. Block randomization (n = 4) was used to guarantee that the symmetrical and asymmetrical waveforms were used for an equal number of subjects (n = 12) on the first session. Similarly, each of the six possible orders in which the three frequencies could be organized were used for an equal number of subjects (n = 4) for each session and intensity level. A new randomization was performed for each session and level (i.e. the randomization used for $NMES_{sub}$ on the symmetrical day did not influence the one used for $NMES_{max}$ on the asymmetrical day).

Preparation Phase without NMES

Subjects were positioned in the chair of an isokinetic dynamometer (Biodex System 3 Pro, Biodex Medical System, Shirley, NY, USA) with the hip joint flexed at ~90° (Fig. 2B). They initially warmed-up by performing 10 reciprocal concentric knee extension/flexion cycles at an angular velocity of $90°.s^{-1}$. Subsequently, their knee joint was fixed at 90° of flexion and maximal voluntary contraction (MVC) torque (in Nm) was evaluated using three efforts of 4-5 s separated by 2-min rest periods. Only the trial with the highest MVC torque was further considered.

Preparation Phase with NMES

NMES was consistently delivered with a multifunctional electrical stimulator designed and manufactured by the Bioengineering Department of a collaborating hospital, which allowed pulse waveform and frequency to be manipulated while controlling current intensity.[15] Both the symmetrical and the asymmetrical waveforms had a quasi-rectangular positive phase with a 500-

µs duration but differed in their negative phase. The negative phase of the symmetrical waveform was also quasi-rectangular (500-µs duration), while the negative phase of the asymmetrical pulse was triangular, with a slope increasing slowly and steadily until all the energy was dissipated (Fig. 1B).

To determine the exact location of the rectus femoris motor point, saline gel was applied on the skin covering the muscle belly, and a pen-shaped electrode was used to locate the motor point (Fig. 2A). Single pulses (biphasic symmetrical waveform with 100-µs duration) were delivered with a frequency of 1 Hz at a sufficient intensity to produce a visible quadriceps contraction.[16] The pen-shaped electrode was displaced over the skin, and the location where the pulse produced the largest knee extensor torque was identified as the motor point.

Two 7.5 x 13 cm rectangular electrodes with integrated self-adhesive gel (Arktus, Santa Tereza do Oeste, Brazil) were positioned proximally over the previously determined motor point, and distally ~5 cm above the patella's upper edge (Fig. 2). With this configuration, subjects were familiarized to low-intensity NMES trains (duration: 6 s with ramp-up and ramp-down phases of 2 and 1 s, respectively) at the three experimental frequencies and the waveform selected for the specific session, with two trains per frequency. Trains were interspersed with rest periods of 2-min.

Experimental Phase

Stimulation trains with a combination of symmetrical/asymmetrical pulses and 60, 80 and 100 Hz were delivered at two different levels: $NMES_{sub}$ (20% of the MVC torque) and $NMES_{max}$ (maximum tolerated current intensity). The 20% MVC torque target was selected because it corresponds to the lowest range of the therapeutic window,[17] is close to what has been used in previous studies,[18,19] and produces a minimum discomfort due to a relatively low stimulation intensity. The maximal tolerated current condition was selected as it corresponds to the most widely used NMES level in strength training[20,21] and rehabilitation.[22,23]

For all waveform-frequency combinations, the current intensity required to reach the $NMES_{sub}$ level was determined by gradual increases until the desired torque was reached. After a 2-min rest interval, testing was performed by increasing current intensity during 2 s (ramp up) until the determined value was reached, maintaining it constant for 3 s, and finally decreasing to zero in 1 s (ramp down). After the three frequencies (with symmetrical or asymmetrical pulses, depending on the day) were tested for the $NMES_{sub}$ level, subjects rested for 10-min. Afterwards, the same protocol was performed for the $NMES_{max}$ level, where the required current intensity was determined by gradual increases until subjects signaled verbally that they had reached the highest tolerated current level.

During testing, the highest torque generated by each train was recorded by the dynamometer. The associated current intensity provided by the stimulator was also retained. Stimulation efficiency was calculated by dividing the evoked torque by the concomitant current intensity (in Nm/mA).[3] Immediately after each stimulation train, subjects were asked to report their discomfort level by making a vertical mark on a 0-10 visual analogue scale (VAS), where 0 represented no discomfort and 10 the worst possible perceived discomfort.[24] Subjects were blinded as to which pulse waveform and frequency were used.

Statistical Analyses

Paired t-tests were used to compare the MVC torque between the two sessions (symmetrical vs asymmetrical). To verify the effect of pulse waveform and pulse frequency on current intensity, evoked torque and discomfort at both $NMES_{sub}$ and $NMES_{max}$ levels, a repeated measures two-way analysis of variance (ANOVA) was used (factors: frequency and waveform). To verify the effect of pulse waveform, pulse frequency and NMES level on stimulation efficiency, a repeated measures three-way ANOVA was used (factors: waveform, frequency and stimulation level). Bonferroni *post hoc* tests were used to identify specific differences when appropriate. All analyses were performed with SPSS 20.0 (SPSS Inc., Chicago, IL, USA) software package adopting a significance level of 5% ($P < 0.05$). In addition, effect sizes (ES, Cohen's "d") were calculated to assess the magnitude of the differences. ES were classified as small if d = 0.2, medium if d = 0.5 and large if d ≥ 0.80.[25] Results are presented as mean ± standard deviation (SD), unless otherwise stated.

RESULTS

MVC torque was 235 ± 50 and 235 ± 58 Nm for symmetrical and asymmetrical sessions, respectively ($P = 0.94$). ES will only be shown for statistically significant comparisons, because ES were small (d < 0.2) for all non-significant comparisons.

For NMES_{sub} (Fig. 3), there was a main effect of pulse waveform on current intensity, but not on evoked torque ($P = 0.27$) and discomfort ($P = 0.13$). Current intensity was lower ($P \leq 0.001$) for symmetrical compared to asymmetrical pulses, with medium ES (d range: 0.71-0.76). There was a main effect of pulse frequency on evoked torque, but not on current intensity (intensity $P = 0.44$) and discomfort ($P = 0.96$). Evoked torque was higher ($P = 0.04$) at 80 Hz than at 60 Hz, with small ES (d range: 0.05-0.14). There was no significant interaction between pulse waveform and frequency for any of the dependent variables (current intensity: $P = 0.83$; evoked torque: $P = 0.57$; discomfort: $P = 0.42$).

For $NMES_{max}$ (Fig. 3), there was a main effect of pulse waveform on current intensity and evoked torque, but not on discomfort ($P = 0.76$). Current intensity was lower ($P \leq 0.001$) while evoked torque was higher ($P = 0.04$) for symmetrical compared to asymmetrical pulses, with small to medium ES (d range: 0.25-0.52 for current intensity, 0.26-0.37 for evoked torque). There was no main effect of pulse frequency for any of the dependent variables (current intensity: $P = 0.26$; evoked torque: $P = 0.80$; discomfort: $P = 0.61$). There was a significant interaction between pulse waveform and frequency for current intensity ($P = 0.04$). No interaction was found for the other dependent variables (evoked torque: $P = 0.66$; discomfort: $P = 0.69$).

For stimulation efficiency (Fig. 4), there was a main effect of pulse waveform and stimulation level, but not of pulse frequency ($P = 0.17$). Symmetrical pulses showed greater efficiency than asymmetrical pulses ($P \leq 0.001$), with medium ES (d range: 0.56-0.66). Stimulation efficiency at $NMES_{max}$ was higher than at $NMES_{sub}$ ($P \leq 0.001$), with a large ES (d = 1.10). There was no significant interaction between pulse waveform, pulse frequency and stimulation level ($P = 0.96$). There was a significant interaction between pulse waveform and stimulation level ($P = 0.02$), but no interaction was found between pulse waveform and frequency and between frequency and stimulation level ($P = 0.66$ and 0.65, respectively).

DISCUSSION

The main findings of this study were that stimulation efficiency of symmetrical pulses was greater compared to asymmetrical pulses, despite similar discomfort. This study also demonstrated that stimulation efficiency and discomfort were not influenced by pulse frequency, and stimulation efficiency was higher at $NMES_{max}$ compared to $NMES_{sub}$.

Stimulation efficiency of symmetrical pulses was greater than asymmetrical pulses at both $NMES_{sub}$ and $NMES_{max}$ levels. Since the only difference between the two pulse waveforms was the negative phase slope, the results suggest that the shape and/or duration of the negative phase (long triangular for asymmetrical), as opposed to a 500-μs quasi-rectangular negative phase (symmetrical), may have affected evoked torque. In biphasic pulsed currents, the first phase (or stimulating phase) is used to elicit the desired physiological effect, such as initiation of an action potential, while the second phase, or reversal phase, is used to reverse electrochemical processes occurring during the stimulating pulse.[26] Therefore, as the negative phase of the asymmetrical pulse extended until the next pulse was initiated, the reversal of the electrochemical processes might not have been complete, thereby impeding some of the new action potentials to be produced, consequently affecting stimulation efficiency.

Stimulation efficiency was expected to increase proportionally with pulse frequency, since electrical charge is greater at higher frequencies for the same current intensity. However, efficiency did not differ between the three pulse frequencies, probably due to the fact that these frequencies are all too close to the plateau of the force-frequency relation.[10] These results are similar to those reported in previous studies that evaluated the influence of stimulation frequency on NMES evoked torque, in which the frequency producing the highest torque was above 60 Hz,[10] between 80 and 100 Hz,[27] or close to 100 Hz.[11] In these studies, however, stimulation efficiency was not reported.

Stimulation efficiency was higher for $NMES_{max}$ than for $NMES_{sub}$, suggesting a non-linearity of the relationship between current intensity and evoked torque from submaximal to maximal levels. More specifically, progressively increasing current intensity beyond the 20% MVC torque level apparently resulted in the recruitment of stronger motor units per unit of current compared to those recruited at lower intensities. These surprising results do not support the assumption that motor unit recruitment induced by NMES is random/non-selective (i.e., muscle fibers are activated without obvious sequencing related to fiber types),[28] but they rather suggest that motor units could be recruited in order of their size also during NMES. If confirmed, these findings may have important implications for individuals showing specific impairments in fast muscle fibers (e.g., elderly, critically ill patients), as submaximal levels of NMES would probably not be able to activate these fibers sufficiently to promote beneficial adaptations.

From a clinical perspective, there are at least two important requirements for the utilization of NMES as a valid therapeutic modality: maximizing the presumed effectiveness by applying trains that produce the highest evoked torque with the lowest current intensity (i.e., maximizing stimulation efficiency),[29,30] and/or minimizing the level of discomfort induced by NMES. In terms of efficiency, these results - despite having been obtained in healthy subjects and in acute conditions - suggest that symmetrical pulse waveforms seem to be more appropriate than asymmetrical pulses, while frequencies in the 60-100 Hz range may be used interchangeably. In terms of discomfort, no pulse waveform-frequency combination appeared superior to minimize self-reported discomfort, as already demonstrated in similar NMES studies.[24,31,32] Taken together, these results seem to indicate an inconsistency between the subjective sensations resulting from actual muscle stimulation/contraction and objective characteristics of the stimulation (current intensity) or the contraction (evoked torque). This inconsistency invalidates, at least in part, the use of self-reported discomfort as a single main criterion for optimizing NMES use.

Limitations and Future Directions

The present study has several limitations worth noting. To avoid the occurrence of neuromuscular fatigue during each session, only one stimulation train per pulse waveform-frequency combination was considered, and in the same way only one train was used to determine the required current intensity for each condition. Nevertheless, the intra-session reliability of evoked torque was tested prior to the study in 15 healthy subjects using three consecutive trains per condition, and ICCs ranging from 0.88 to 0.96 were found (unpublished observations). Therefore, it was assumed that using a single train instead of multiple trains per condition was both valid and suitable for this protocol. Only healthy physically active men were included in this study, so as to reduce the inter-subject heterogeneity in NMES current levels and evoked torque.[13] Therefore, the present results cannot necessarily be generalized to women, elderly subjects or patients with specific needs for NMES therapy. Finally, in the current repeated measure study NMES was exclusively applied twice, and not with a therapeutic goal, so the presumed effectiveness of an actual NMES program can only be inferred from acute differences in stimulation efficiency between conditions. Therefore, future longitudinal studies should aim to investigate the real effectiveness of NMES protocols with different pulse characteristics and following multiple sessions, so as to provide specific clinical recommendations for optimal use of NMES current parameters.

CONCLUSIONS

The results of the present study demonstrated that, when applying NMES to the quadriceps femoris muscle of healthy men at both maximal tolerated and submaximal levels, pulse waveform had a considerable influence on stimulation efficiency, but not on self-reported discomfort. More specifically, greater stimulation efficiency was found for symmetrical compared to asymmetrical pulses. On the other hand, pulse frequency in the 60-100 Hz range had no effect on both stimulation efficiency and discomfort. These findings may help clinicians make an informed decision when choosing the most appropriate pulse parameters for evidence-based NMES therapy in clinical practice.

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FIGURE 1. (a) Schematic representation of the waveforms used for NMES. (b) The total current energy (sum of the positive and negative pulse phases) were similar for both waveforms. NMES pulse shape, phase area (a), pulse area (pA), interpulse interval (I) and pulse amplitude (V) of the symmetrical and asymmetrical waveforms for the three different stimulation frequencies (60, 80 and 100 Hz). (c) Approximated view showing the quasi-rectangular shape.

FIGURE 2. (a) Motor point determination with a pen-shaped electrode. (b) Position of the NMES electrodes on the thigh of a representative subject while seated in the test position.

FIGURE 3. Current intensity, evoked torque and discomfort by pulse waveform and frequency for NMES$_{sub}$ (left) and NMES$_{max}$ (right). Each symbol represents a single data point obtained in each combination between waveform and frequency.

FIGURE 4. Stimulation efficiency by pulse waveform and frequency for NMES$_{sub}$ (left) and NMES$_{max}$ (right). Each symbol represents a single data point obtained in each combination between waveform and frequency.

SUPPLEMENTAL DIGITAL CONTENT 1. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist.

SUPPLEMENTAL DIGITAL CONTENT 2. Protocol flowchart for both data collection days. Torque was measured with the isokinetic dynamometer, intensity was displayed in the electrical stimulator, stimulation intensity was calculated as torque/intensity and discomfort was evaluated with a Visual Analogue Scale.

Figure 1

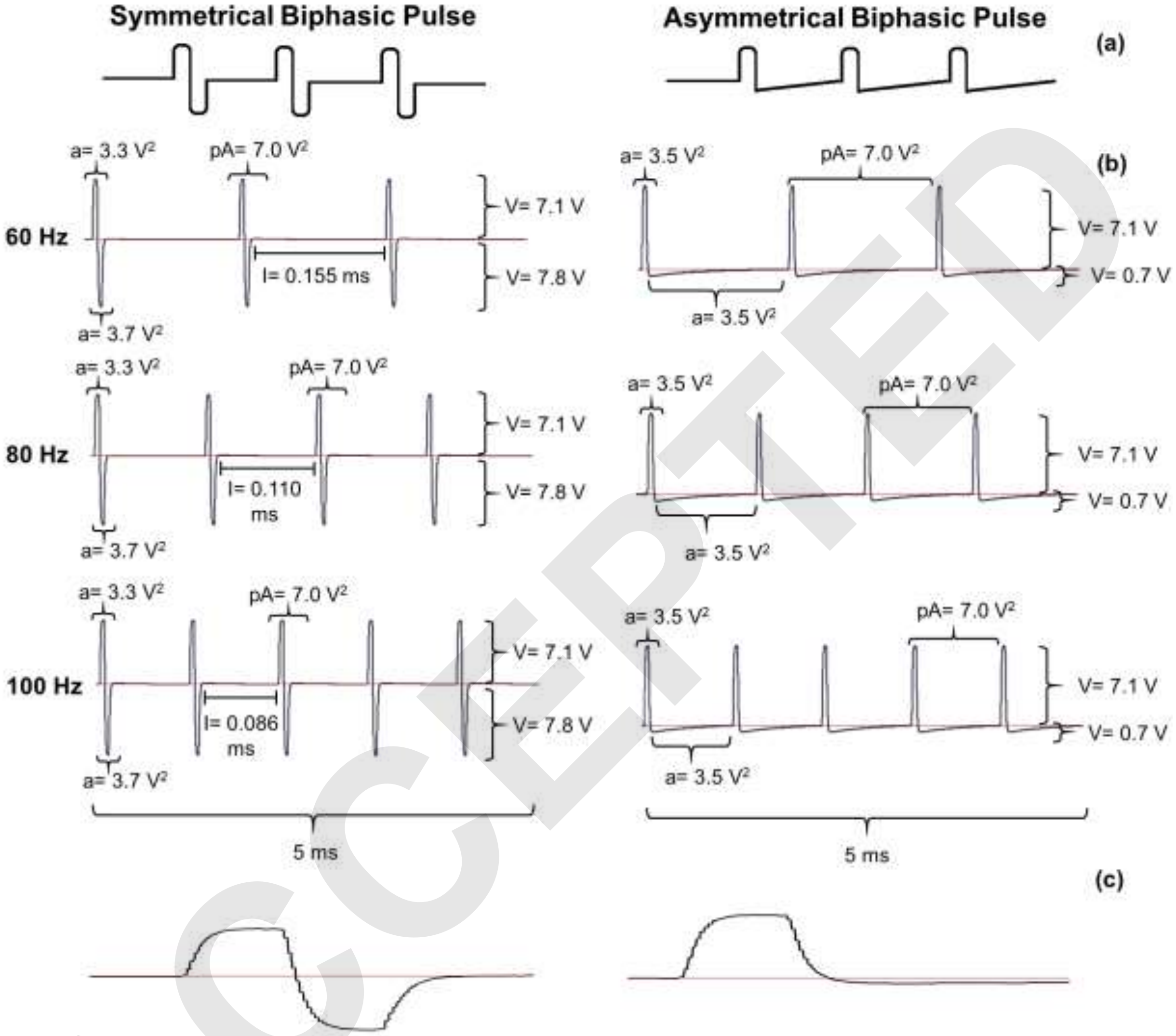

Symmetrical Biphasic Pulse
Asymmetrical Biphasic Pulse
(a)
(b)
a= 3.3 V²
pA= 7.0 V²
60 Hz
V= 7.1 V
I= 0.155 ms
V= 7.8 V
a= 3.7 V²
a= 3.5 V²
pA= 7.0 V²
V= 7.1 V
V= 0.7 V
a= 3.5 V²
a= 3.3 V²
pA= 7.0 V²
80 Hz
V= 7.1 V
I= 0.110 ms
V= 7.8 V
a= 3.7 V²
a= 3.5 V²
pA= 7.0 V²
V= 7.1 V
V= 0.7 V
a= 3.5 V²
a= 3.3 V²
pA= 7.0 V²
100 Hz
V= 7.1 V
I= 0.086 ms
V= 7.8 V
a= 3.7 V²
a= 3.5 V²
pA= 7.0 V²
V= 7.1 V
V= 0.7 V
a= 3.5 V²
5 ms
5 ms
(c)

Figure 2

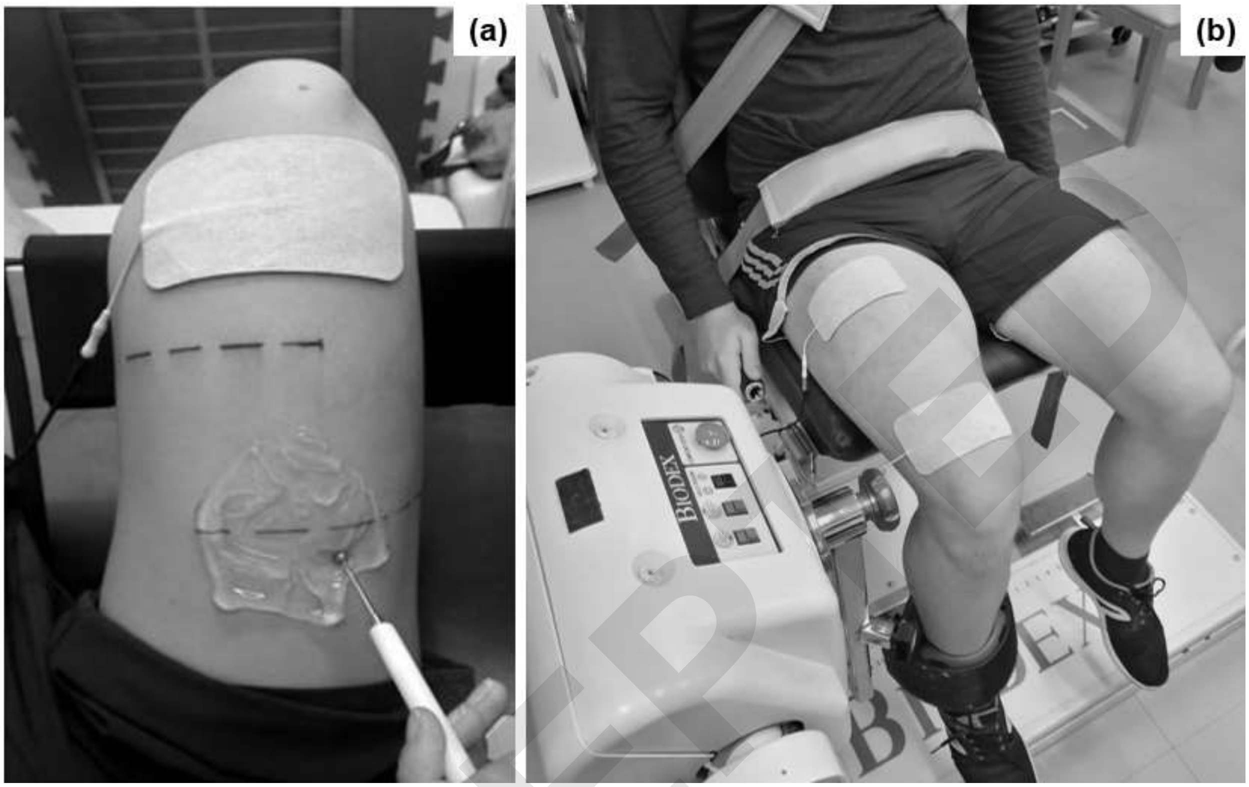
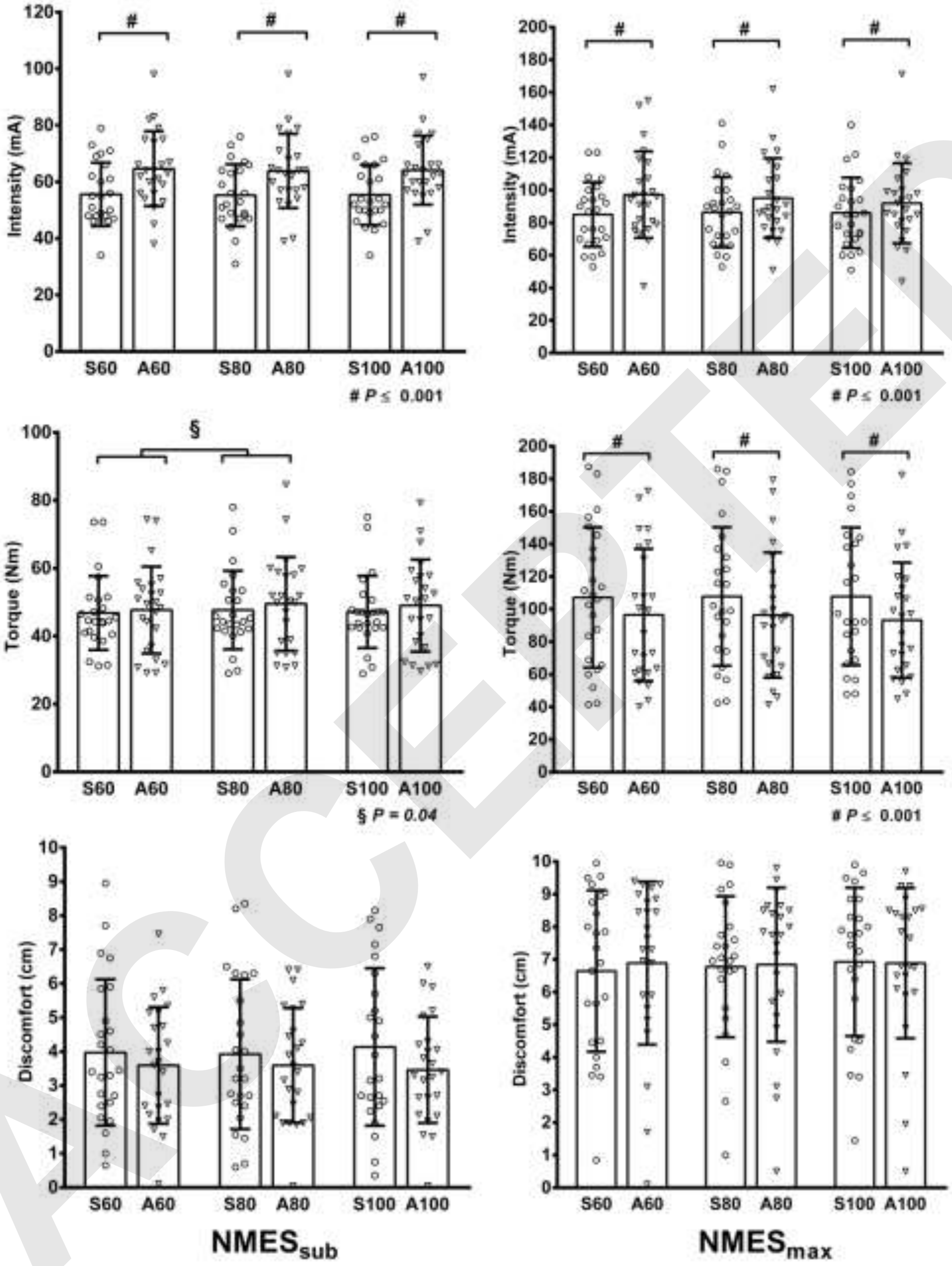
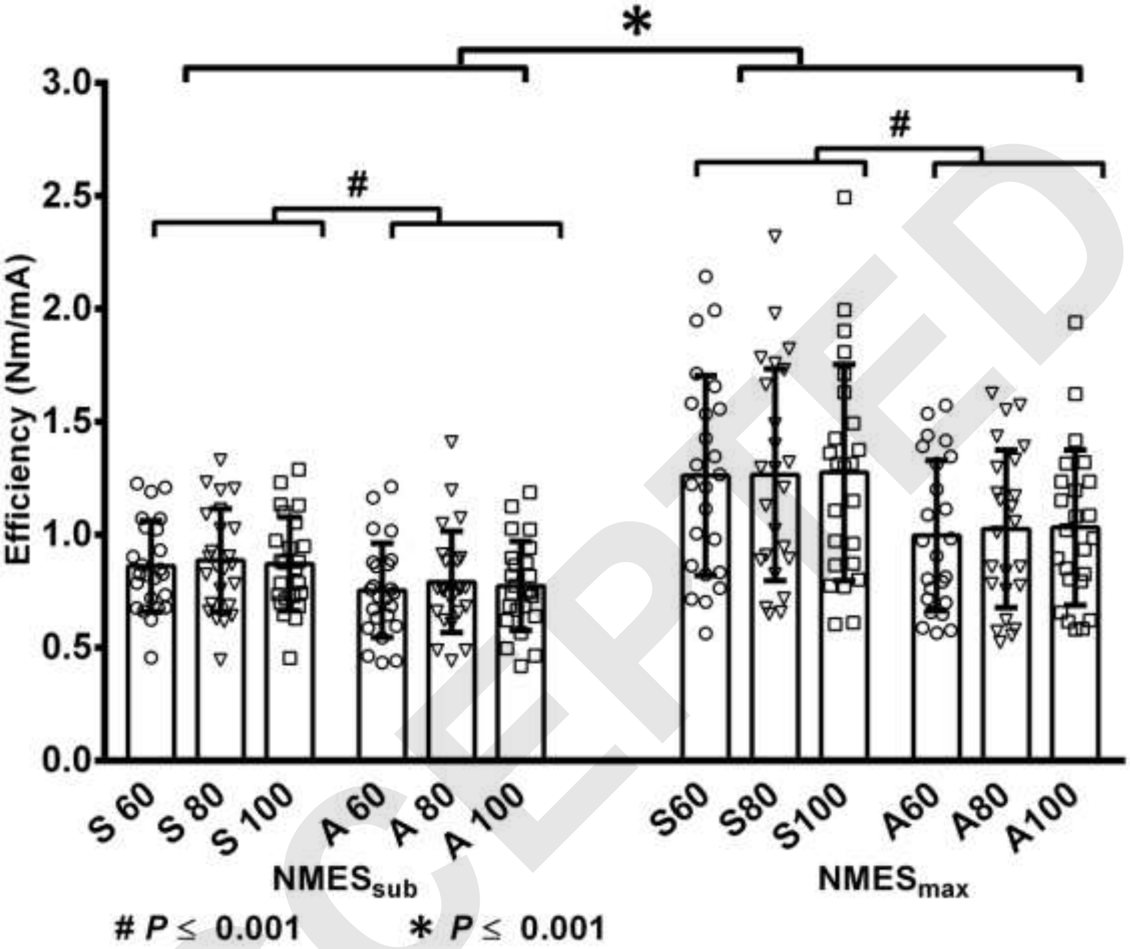


Figure 3



Intensity (mA)
Torque (Nm)
Discomfort (cm)
S60
A60
S80
A80
S100
A100
#
§
P ≤ 0.001
§ P = 0.04
NMES$_{sub}$
NMES$_{max}$

Figure 4



*
#
#
3.0
2.5
2.0
1.5
1.0
0.5
0.0
Efficiency (Nm/mA)
S 60
S 80
S 100
A 60
A 80
A 100
S60
S80
S100
A60
A80
A100
NMES$_{sub}$
NMES$_{max}$
$P \leq 0.001$
* $P \leq 0.001$