

A new paradigm of neuromuscular electrical stimulation for the quadriceps femoris muscle

Nicola A. Maffiuletti · Isabelle Vivodtzev ·
Marco A. Minetto · Nicolas Place

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Abstract

Purpose Neuromuscular electrical stimulation (NMES) with large electrodes and multiple current pathways (m-NMES) has recently been proposed as a valid alternative to conventional NMES (c-NMES) for quadriceps muscle (re)training. The main aim of this study was to compare discomfort, evoked force and fatigue between m-NMES and c-NMES of the quadriceps femoris muscle in healthy subjects.

Methods Ten healthy subjects completed two experimental sessions (c-NMES and m-NMES), that were randomly presented in a cross-over design. Maximal electrically evoked force at pain threshold, self-reported discomfort at different levels of evoked force, and fatigue-induced force declines during and following a series of 20 NMES contractions were compared between c-NMES and m-NMES.

Results m-NMES resulted in greater evoked force ($P < 0.05$) and lower discomfort in comparison to c-NMES ($P < 0.05$)

($P < 0.05$ –0.001), but fatigue time course and magnitude did not differ between the two conditions.

Conclusions The use of quadriceps m-NMES appears legitimate for (re)training purposes because it generated stronger contractions and was less uncomfortable than c-NMES (due to multiple current pathways and/or lower current density with larger electrodes).

Keywords Quadriceps · Discomfort · Evoked force · Fatigue

Abbreviations

c-NMES	Conventional neuromuscular electrical stimulation
m-NMES	Multipath neuromuscular electrical stimulation
MVC	Maximal voluntary contraction
NMES	Neuromuscular electrical stimulation
SD	Standard deviation
VAS	Visual analogue scale

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N. A. Maffiuletti (✉)
Neuromuscular Research Laboratory, Schulthess Clinic, Zurich,
Switzerland
e-mail: nicola.maffiuletti@kws.ch

I. Vivodtzev
HP2 Laboratory (Hypoxia: Pathophysiology), Inserm U1042,
Université Grenoble Alpes, Grenoble, France

M. A. Minetto
Division of Endocrinology, Diabetology and Metabolism,
Department of Medical Sciences, University of Turin, Turin, Italy

N. Place
Institute of Sport Sciences and Department of Physiology,
Faculty of Biology-Medicine, University of Lausanne, Lausanne,
Switzerland

Introduction

Neuromuscular electrical stimulation (NMES), that is commonly employed to generate muscle contractions for (re)training purposes, is conventionally applied through single pairs of surface electrodes positioned on either side (proximally–distally or medially–laterally) of superficial skeletal muscles. The three main limitations of conventional NMES (c-NMES) are the excessive discomfort caused by the transcutaneous stimuli (Delitto et al. 1992; Vanderthommen and Duchateau 2007), the limited spatial recruitment of motor units (Adams et al. 1993; Maffiuletti 2010; Vanderthommen and Duchateau 2007) that impedes attaining high levels of evoked force, as well as the premature

decline in evoked force (i.e., fatigue) that inevitably occurs during a conventional treatment session (Parker et al. 1986). These limitations are mainly due to the distinctive pattern of motor unit recruitment imposed by NMES, that is basically superficial, synchronous and relatively incomplete (Bickel et al. 2011; Gregory and Bickel 2005; Maffiuletti 2010). Taken as a whole, these shortcomings seriously compromise the acute application and therefore the effectiveness of NMES therapy, particularly in frail and sensitive populations of patients.

In the last few years, several attempts have been made to maximize the electrically evoked force, i.e., the main determinant of NMES effectiveness (Lai et al. 1988; Maffiuletti et al. 2011), and to minimize discomfort and fatigue associated with NMES, mainly by manipulating current parameters such as pulse waveform, frequency and duration (Alon 1985; Bennie et al. 2002; Bowman and Baker 1985; Gorgey and Dudley 2008; Gregory et al. 2007; Kebaetse et al. 2001; Kesar et al. 2008; Laufer et al. 2001; Naaman et al. 2000) as well as surface electrode characteristics such as size, type and location (Gobbo et al. 2011; Lieber and Kelly 1991; Lyons et al. 2004; Malesevic et al. 2010; Naaman et al. 2000). However, the evidence of effectiveness for these strategies has been found to be quite inconsistent. Interestingly, a relatively new paradigm of NMES with large electrodes and multiple current pathways (m-NMES) has recently been shown to be more effective than c-NMES for restoring quadriceps strength and physical performance following anterior cruciate ligament reconstruction (Feil et al. 2011). The main originality of this NMES modality is that current is “dynamically” distributed to multiple pairs of electrodes within each pulse (Paessler 2012; Walls et al. 2010), while a single current pathway is always applied between an electrode pair with c-NMES. The authors of this previous study suggested that m-NMES would have reduced discomfort and thus allowed for higher evoked force than c-NMES (Feil et al. 2011), but none of these variables were compared between the two stimulation modalities. Based on the distinctive electrode configuration and/or wider current distribution, it may be conjectured that m-NMES could cause less discomfort and recruit more motor units than c-NMES, which could in turn maximize the level of evoked tension and perhaps reduce fatigue.

The main aim of this study was to compare evoked force-related, discomfort-related and fatigue-related outcomes between m-NMES and c-NMES of the quadriceps femoris muscle in healthy subjects. We hypothesized that the use of multiple dynamically changing current pathways and large stimulating electrodes in m-NMES would result in greater evoked force, less discomfort and fatigue compared to c-NMES. We chose the quadriceps muscle because, owing to its important functional role and

accessibility, it is one of the most-commonly stimulated muscles (Bax et al. 2005).

Methods

Subjects

Ten healthy subjects (5 men and 5 women; mean age \pm SD: 31 \pm 6 years, height: 174 \pm 9 cm, mass: 71 \pm 13 kg) volunteered to participate in the study. They were recreationally active, free from known cardiovascular, neurological or orthopedic problems, and relatively inexperienced with both NMES modalities. The study protocol was approved by the local ethics committee (KEK-ZH-Nr. 2013-0013), and written consent forms were signed prior to participation. The experiments conformed to the standard sets by the declaration of Helsinki.

Experimental procedure

Participants completed two identical experimental sessions, except for the type of NMES (c-NMES, m-NMES) and the stimulated side (left, right), that were randomly presented in a cross-over design. Examiners and participants were both aware of which NMES modality was administered. The experimental sessions were separated by 24 h, completed at the same time of day, and arranged in four main phases (Fig. 1): an initial neuromuscular evaluation (pre-test), a NMES ramp trial, a NMES fatigue trial, and a final neuromuscular evaluation (post-test). The entire experiment was conducted in isometric conditions and lasted approximately 60 min. Subjects were comfortably seated in a custom-built dynamometer, with the tested knee at 90° and the trunk–thigh angle at approximately 100°. Isometric knee extension force was continuously recorded by means of an S-shaped load cell (STS 2,500 N, sensitivity 2 mV/V and 1.7 mV/N, SWJ, China) that was posteriorly attached to the leg, 2–3 cm above the lateral malleolus. Participants were fixed to the dynamometer chair using two crossover shoulder harnesses and a belt across the abdomen. Force signal was fed directly from the load cell into a 16-bit A/D converter (MP150, Biopac Systems, Goleta, USA), then into a computer sampling at 2 kHz using Acqknowledge software (Biopac Systems).

Neuromuscular evaluation

Neuromuscular function of the quadriceps muscle was investigated at pre-test and post-test to quantify the decline in maximal voluntary contraction (MVC) force (as a marker of muscle fatigue; Gandevia 2001) as well as the decline in doublet twitch force evoked by femoral nerve

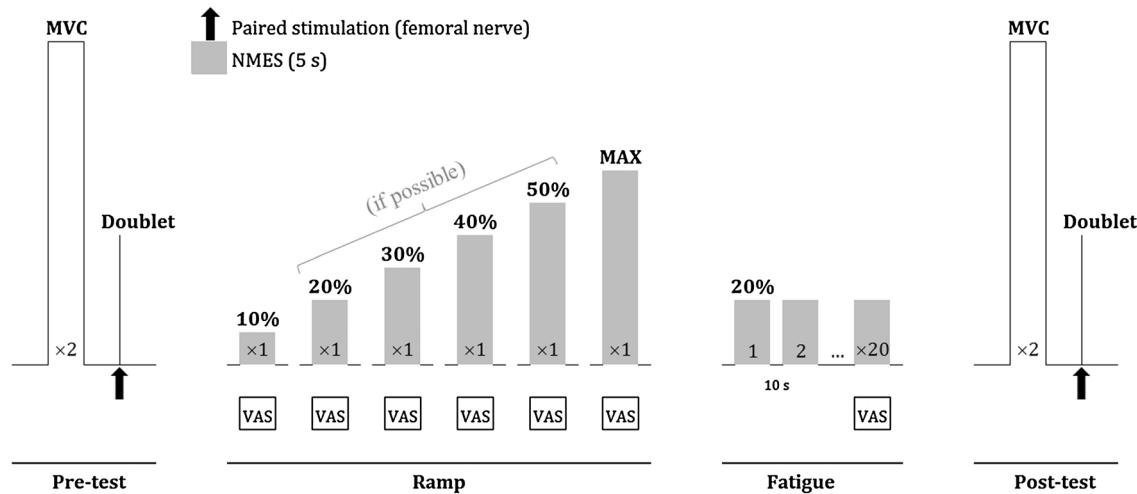


Fig. 1 Overview of the experimental protocol. VAS for discomfort. 10–50 %: steps of the NMES ramp trial starting at 10 % MVC force and followed by 10 %-MVC increments (if possible) up to the maximal tolerable level (MAX)

stimulation (as a marker of peripheral fatigue; Place et al. 2007). The femoral nerve was stimulated using a circular (diameter: 5 cm) self-adhesive electrode positioned in the groin, 3–5 cm below the inguinal ligament. A large (5 × 10 cm) self-adhesive electrode was fixed on the gluteal crease to close the stimulation current loop. Monophasic rectangular pulses of 1 ms were produced via a modified constant-current stimulator (Digitimer DS7AH, Hertfordshire, UK), either as single or paired stimuli (inter-stimulus interval: 10 ms). At pre-test, current intensity of a single stimulus was progressively increased from 0 mA to the intensity corresponding to peak twitch force. This current intensity was further increased by 10 % to ensure stimulus supramaximality (Neyroud et al. 2012), which was attained at 209 ± 57 and 196 ± 42 mA for c-NMES and m-NMES sessions, respectively. Subsequently, subjects completed 8–12 submaximal (20–80 % of the estimated MVC) voluntary isometric contractions as a warm-up. At both pre-test and post-test, the neuromuscular evaluation consisted of two MVC (separated by ~30 s), each followed by supramaximal paired stimulation of the femoral nerve. Subjects were instructed to contract their knee extensors as forcefully as possible for 4–5 s during the MVC, and to relax completely before the supramaximal paired stimuli were applied (~2 s after the end of the MVC).

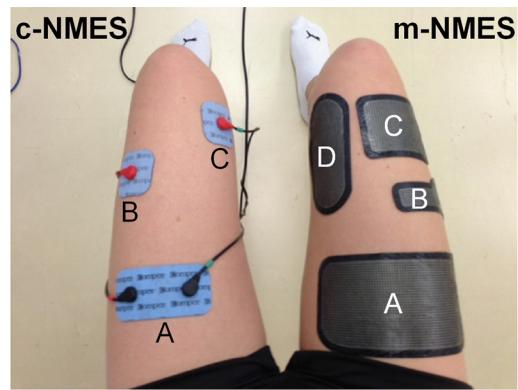
NMES ramp trial

Following the pre-test, NMES was delivered at progressively increasing current intensity (starting from 0 mA in both conditions), in an attempt to attain the following force levels: 10, 20, 30, 40 and 50 % MVC (NMES ramp trial). Current was initially increased throughout one or more (up

to three) NMES-evoked contractions until the 10 % MVC target was reached; when this force level was successfully attained (as verified online), one additional NMES trial at constant intensity was completed and the discomfort induced by NMES was evaluated by means of a 0–10 cm horizontal visual analogue scale (VAS), where 0 indicates no discomfort and 10 indicates maximum discomfort. After a 3-min rest period, stimulation current intensity was further increased to attain the 20 % MVC target (if possible) and the same procedure was repeated for the different force levels. If one or more of the NMES ramp levels could not be attained (because of excessive discomfort), or if all the levels (including the 50 % MVC) were attained, current intensity was increased up to the maximal tolerable level (pain threshold) and maximal evoked force was quantified.

c-NMES was delivered with a portable and programmable stimulator unit (Compex 3, Compex Médical SA, Ecublens, Switzerland; maximum current output: 120 mA) connected to three self-adhesive pre-gelled electrodes (two active channels). Two 5 × 5 cm electrodes were positioned on the belly of the vastus lateralis and vastus medialis muscles (electrodes B and C on the left thigh in Fig. 2), and one 5 × 10 cm electrode was placed transversally on the proximal aspect of the quadriceps muscle (electrode A), as per manufacturer's instructions (http://www.compex.info/en_UK/Electrode_Placement.html). m-NMES was delivered with a two-channel Kneehab XP device (Bio-Medical Research, Galway, Ireland), which consists of a modified stimulation unit (maximum current output: 200 mA) connected to a garment that wraps around the thigh and incorporates four large self-adhesive pre-gelled electrodes (10 × 20; 3 × 18; 10 × 7.5; 7 × 14 cm; respectively, electrodes A, B, C and D on the right thigh in Fig. 2). The thigh

Fig. 2 Electrode positions and pulse current pathways for c-NMES (left thigh) and m-NMES (right thigh). See “Methods” for details



brace was positioned according to the recommendations of the manufacturer (<http://www.neurotechgroup.com/uk/products/kneehab-xp>). Besides differences in electrode configuration and current distribution (see below) between m-NMES and c-NMES, all current characteristics were strictly identical for the two NMES modalities (frequency: 50 Hz; pulse characteristics: 400-µs-long biphasic rectangular pulses; on/off ratio: 5/10 s with a ramp-up of 1 s and a ramp-down of 0.5 s).

The main differences in current pathways between m-NMES and c-NMES are that current is distributed to multiple pairs of electrodes within single channels with m-NMES, while a single current pathway is always applied between an electrode pair with c-NMES (Fig. 2). Additionally, m-NMES current pathways are dynamically changing within single pulses, with a temporal shift between pairs of electrodes for the first channel (electrodes A–C and A–D for the first 300 µs followed by A–B for the last 100 µs of each pulse) and different pulse durations for the two active channels (400 µs for channel 1 and 100 µs for channel 2).

NMES fatigue trial

Following the NMES ramp trial, and after 5 min of passive recovery, subjects completed a short treatment session that entailed 20 NMES cycles (on/off ratio: 5/10 s) completed at a predefined starting intensity of 20 % MVC (as determined during the NMES ramp trial), in order to evaluate

the self-reported discomfort (VAS score) and the fatigue-related decline in NMES-evoked force.

Data analysis

Evoked force-related outcomes were the proportion of subjects having attained each level of the NMES ramp trial (provided the level was attained), and the maximal force evoked by NMES expressed as a percentage of pre-test MVC force (Fig. 3a). Discomfort-related outcomes were the VAS scores obtained at each level of the NMES ramp trial (provided the level was attained), the VAS score recorded during the NMES fatigue trial (before the last stimulation cycle) as well as the proportion of subjects having preferred m-NMES, c-NMES or with no preference. Participants were asked to answer the following question at the end of the second experimental session: “what NMES modality did you prefer/would you choose for an eventual (re)training program?”. Fatigue-related outcomes were the decline in evoked force recorded during the NMES fatigue trial (linear regression using the maximal force evoked at each stimulation cycle), as well as the pre- to post-test decline in MVC force and doublet peak force.

Statistical analysis

Normal distribution was assessed using Shapiro–Wilk tests. Normally distributed data were expressed as mean and SD,

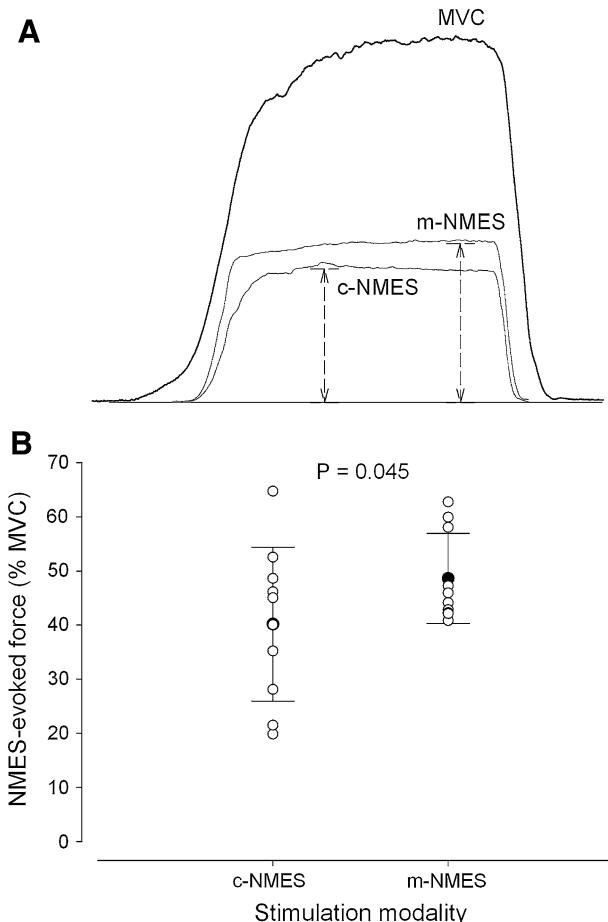


Fig. 3 Experimental force traces recorded from a representative subject during MVC and electrically evoked contractions (a). The dashed arrows indicate the maximal force evoked by c-NMES (37 % MVC for this subject) and m-NMES (44 % MVC). Maximal force evoked by c-NMES and m-NMES as a percentage of MVC force (b); data are individual (white circles), mean (black circles) and SD (error bars)

and were analyzed using paired *t* tests (one-tailed). Non-normally distributed data (only current intensity at the 30 % MVC level) were expressed as median and interquartile range, and were analyzed using Wilcoxon signed-rank sum tests. We also used two-way repeated measure ANOVAs (time \times session) to evaluate pre-to-post-test changes in MVC force and doublet peak force in c-NMES vs. m-NMES conditions, eventually followed by Tukey's HSD post hoc analyses. The threshold of statistical significance was set to $P < 0.05$.

Results

Current intensity at all levels of the NMES ramp trial, including the maximal tolerable intensity, was systematically greater for m-NMES compared to c-NMES, with an

Table 1 Current intensity by contraction intensity level and NMES modality

	c-NMES	m-NMES
10 % MVC (mA)	30 ± 6 [n = 10]	45 ± 6^a [n = 10]
20 % MVC (mA)	39 ± 8 [n = 9]	56 ± 7^a [n = 10]
30 % MVC (mA)	47 (40–57) [n = 5]	66 (63–72) ^a [n = 9]
40 % MVC (mA)	61 ± 19 [n = 4]	73 ± 8 [n = 6]
50 % MVC (mA)	78 ± 27 [n = 2]	87 ± 11 [n = 3]
Maximal tolerable (mA)	53 ± 25	92 ± 25^a

Data are mean and SD (normal distribution) or median and interquartile range (non-normal distribution). The number of subjects having reached each contraction intensity level appears in square brackets

^a m-NMES > c-NMES ($P < 0.05$) as verified with paired *t* test (normal distribution) or Wilcoxon signed-rank test (non-normal distribution)

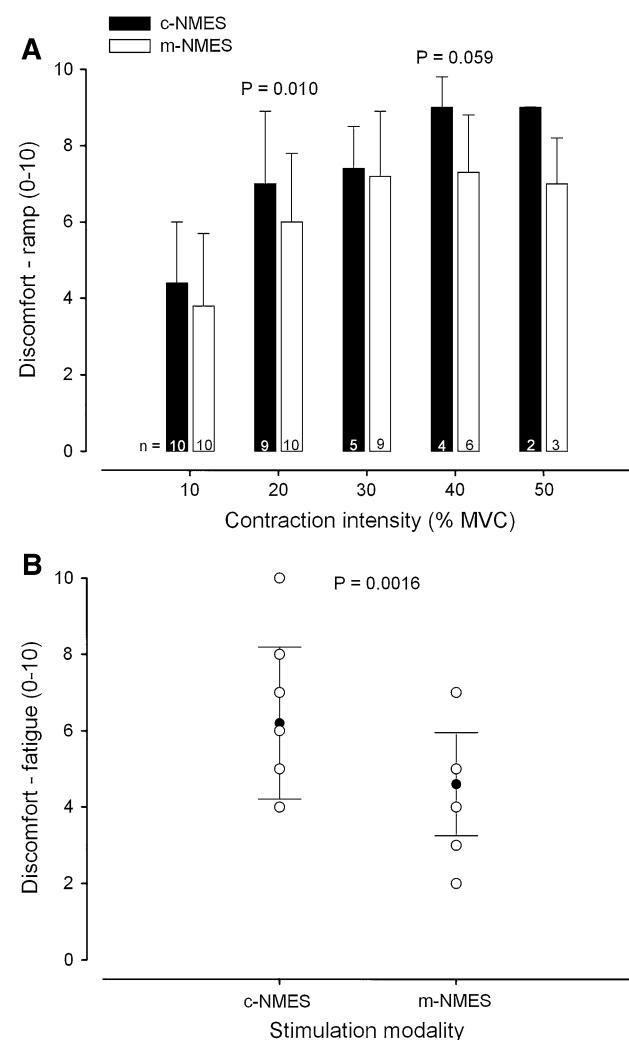


Fig. 4 VAS score for discomfort recorded during the ramp trial by contraction intensity level and NMES modality (a); data are mean and SD. VAS score for discomfort recorded during the fatigue trial by NMES modality (b); data are individual (white circles), mean (black circles) and SD (error bars)

average difference of +39 % (Table 1). The difference was significant at 10, 20, 30 % MVC and at the maximal tolerable level ($P < 0.05$). The proportion of subjects having attained the different levels of the NMES ramp trial was, respectively, for m-NMES and c-NMES, 100 vs. 100 % at 10 % MVC, 100 vs. 90 % at 20 % MVC, 90 vs. 50 % at 30 % MVC, 60 vs. 40 % at 40 % MVC, and 30 vs. 20 % at 50 % MVC (see also Table 1). Figure 3a shows examples of force traces recorded from a representative subject during a MVC and during NMES contractions at the maximal tolerable level. The maximal force evoked by NMES was higher for m-NMES (44 % MVC) compared to c-NMES (37 % MVC). Similar to this example, analysis of group data showed that the maximal force evoked by NMES was significantly greater for m-NMES compared to c-NMES ($P < 0.05$), with an average difference of 8 % (Fig. 3b).

VAS scores at all levels of the NMES ramp trial were systematically higher for c-NMES compared to m-NMES (Fig. 4a), with an average difference of +15 %. Due to the dissimilar number of subjects having reached the various contraction levels in the two conditions (see “*n*” in Fig. 4a; Table 1), the difference was significant only at 20 % MVC ($P = 0.01$), and a trend was observed at 40 % MVC ($P = 0.059$). The mean VAS score at the maximal tolerable intensity (pain threshold) was 10 ± 0 for both NMES modalities. The VAS score recorded during the NMES fatigue trial was significantly higher for c-NMES compared to m-NMES ($P = 0.0016$), with an average difference of 35 % (Fig. 4b). The preferred NMES modality was m-NMES for eight subjects (80 % of the sample) and c-NMES for one subject, while one participant had no preference.

The decline in evoked force during the NMES fatigue trial (Fig. 5a) was similar for c-NMES ($-23 \pm 2\%$) and m-NMES ($-26 \pm 7\%$). In the same way, the pre- to post-test reductions in MVC force (Fig. 5b) and doublet peak force (Fig. 5c) were comparable for c-NMES (-23 ± 11 and $-16 \pm 4\%$, respectively) and m-NMES (-25 ± 5 and $-16 \pm 8\%$, respectively).

Discussion

The main findings of this comparative study are that acute application of m-NMES in a group of healthy subjects resulted in greater knee extension evoked force and lower self-reported discomfort in comparison to c-NMES, while the time course and magnitude of quadriceps muscle fatigue did not differ between the two conditions.

Evoked force

When both NMES modalities were applied at the maximal tolerable intensity, m-NMES evoked greater knee

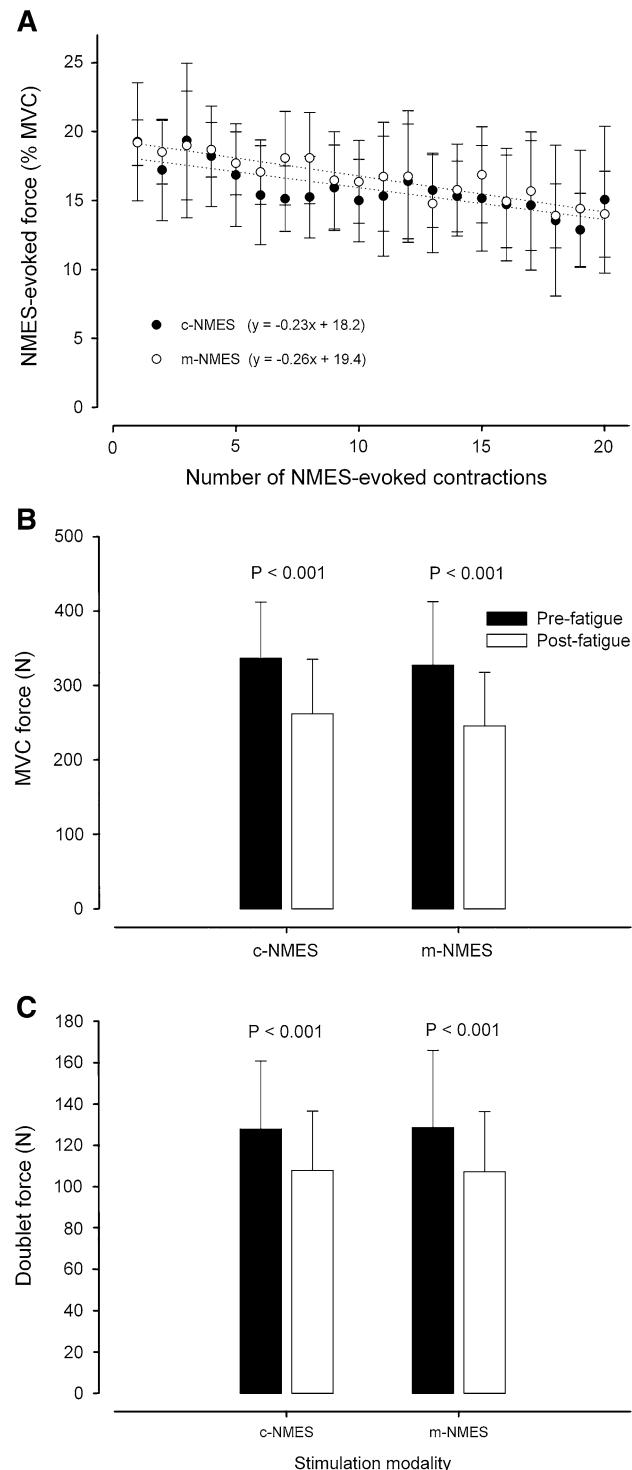


Fig. 5 Fatigue-related outcomes: decline in evoked force during the fatigue trial (a), decline in MVC force (b) and decline in doublet force (c) by NMES modality; all data are mean and SD

extension force in comparison to c-NMES. Two main and not mutually exclusive explanations can account, at least in part, for this interesting finding. First, the higher absolute

current intensity (i.e., the charge of the delivered pulses) adopted for m-NMES in comparison with c-NMES generated stronger contractions because the greater the stimulation charge, the larger the voltage changes elicited across the capacitance of the axonal membrane, and therefore the greater the number of activated motor axons (Botter et al. 2009). Interestingly, relative stimulation efficiency (i.e., the intrinsic tissue property relating torque output to current density) at the maximum tolerated level was threefold higher for m-NMES [$753 \text{ Nm}/(\text{mA}/\text{cm}^2)$] than for c-NMES [$249 \text{ Nm}/(\text{mA}/\text{cm}^2)$]. Second, the wider distribution of electrical current via multiple pairs of large electrodes combined with its dynamically changing pathways (within each pulse) likely enabled m-NMES to recruit more motor units than c-NMES, whose recruitment was inevitably restricted to the axons located in the area between the electrodes of a pair (see Fig. 2). Whatever the exact mechanisms underlying the differences in evoked force between m-NMES and c-NMES, the results reported here and in the longitudinal study of Feil et al. (2011) give further support to the concept of NMES “training intensity” (Lai et al. 1988; Maffiuletti 2010, Maffiuletti et al. 2011; Snyder-Mackler et al. 1994), which proposes that the higher the electrically evoked force (expressed as a fraction of the MVC force), the higher the effectiveness of NMES (re)training programs (i.e., the higher the strength/functional gains induced by the treatment). Interestingly, NMES training intensity is increasingly considered as the key parameter to control NMES dosage, and as the main determinant of treatment effectiveness in both healthy and patient populations (Maffiuletti et al. 2011; Vivodtzev et al. 2012).

Discomfort

The excessive discomfort induced by the application of c-NMES represents an important drawback of the technique in the context of muscle (re)training, especially considering that the ability to tolerate high current intensities (and therefore to generate stronger contractions) seems to be correlated to the effectiveness of NMES (re) training (Vivodtzev et al. 2012), at least for the quadriceps muscle. Although current intensities were higher for m-NMES compared to c-NMES, our present results show that m-NMES was able to reduce discomfort at all submaximal force levels in comparison with c-NMES, and more particularly so during the execution of the short treatment session (fatigue trial).

Previous studies have identified the role of selected NMES parameters (such as pulse waveform, electrode size and placement) on the discomfort associated with NMES (Alon 1985; Bowman and Baker 1985; Delitto et al. 1992; Gregory et al. 2007). In the present study, considering that all NMES parameters (pulse frequency, pulse duration,

duty cycle, ramping)—except current pathways—were identical between the two conditions, it could be speculated that the observed differences in discomfort were mainly related to the disparate electrode configurations. The four large electrodes (total surface 427 cm^2) used for m-NMES resulted in lower current density (Alon 1985; Doheny et al. 2010) as compared with the three small c-NMES electrodes (total surface 100 cm^2). As an estimation, current density at the maximum tolerable level was less than half for m-NMES ($0.22 \text{ mA}/\text{cm}^2$) than for c-NMES ($0.53 \text{ mA}/\text{cm}^2$). Since current density in the dermo-epidermal junction is an important determinant of the excitation of nociceptive A δ -fibers (Morch et al. 2011), it is very likely that larger electrodes provoked less discomfort compared to smaller electrodes for evoking the same submaximal forces, in line with previous methodological studies (Alon 1985; Doheny et al. 2010).

Another plausible explanation for the discomfort scores we have obtained is related to the differences in spatial distribution of electrical current between the two NMES modalities. As previously discussed, current pathways change dynamically among multiple electrode pairs during m-NMES (Feil et al. 2011; Paessler 2012; Walls et al. 2010), probably maximizing spatial recruitment, while current distribution is constantly limited to the region of electrodes of a pair with c-NMES. Consequently, it could be hypothesized that the activation of small-diameter sensory fibers (A-fibers and C-fibers) mediating nociceptive inputs (Burke et al. 1975) is shorter for the different portions of the quadriceps activated by m-NMES in comparison to the constant recruitment imposed by c-NMES, which would probably contribute to reduce the discomfort in the former condition.

Fatigue

Contrary to expectations, fatigue-related outcomes were comparable between m-NMES and c-NMES. Both modalities provoked similar declines in NMES-evoked force (-25%), MVC force (-24%) and doublet force (-16%), which are comparable to fatigue estimates previously reported following a single bout of NMES exercise on the quadriceps muscle (Theurel et al. 2007; Zory et al. 2005). Hence, optimization of muscle fiber recruitment facilitated by m-NMES did not reduce the mechanical manifestations of fatigue in comparison with c-NMES. A possible explanation for the lack of differences in fatigue-related outcomes between the two stimulation modalities is that m-NMES resulted in a greater and more dispersed recruitment compared to c-NMES, which would have minimized fatigue, but probably also in a more superficial recruitment—at least for NMES contractions of the same intensity (e.g., 20 % MVC)—which could have maximized

fatigue. It is tempting to suggest that the greater absolute recruitment induced by m-NMES was possibly counterbalanced by the activation of a larger relative proportion of fast fatigable fibers, which are mainly located in superficial areas of the quadriceps muscle (Lexell et al. 1983). These speculations remain, however, to be confirmed by future studies in which motor unit recruitment patterns associated with c-NMES (Bickel et al. 2011; Gregory and Bickel 2005) will be compared to m-NMES with different electrode configurations and current pathways, possibly by means of imaging techniques (Adams et al. 1993; Vanderthommen et al. 2003).

Clinical impact

The m-NMES system adopted in this study could constitute a relevant alternative to c-NMES for healthy subjects and sportsmen who want to improve their quadriceps muscle strength (Gondin et al. 2011), but more particularly for patients who need to restore or preserve their muscle function following or during a period of disuse (Maffiuletti et al. 2013; Stevens-Lapsley et al. 2012). For patients with low tolerance to NMES (i.e., the so-called non-responders; Vivodtzev et al. 2012), which is known to compromise treatment effectiveness, m-NMES would potentially permit to attain higher current intensities (and evoked forces) for a given amount of discomfort, and/or to reduce discomfort scores for a given level of evoked force. Besides the benefits of m-NMES demonstrated in this study, the garment-integrated electrodes and the absence of free cables could possibly improve patient compliance to treatment (Feil et al. 2011) and minimize eventual errors related to motor point identification (Gobbo et al. 2011). Therefore, m-NMES has the potential to become a valuable clinical tool not only for home-based and bed-side rehabilitation of the quadriceps muscle (e.g., in critically ill patients; Maffiuletti et al. 2013), but also for multicenter clinical trials.

Limitations and perspectives

This study presents some limitations. Firstly, because we only evaluated a relatively small sample of healthy subjects the present results remain to be confirmed in a larger population of patients with quadriceps muscle weakness, ideally stratified by sex (Laufer and Snyder-Mackler 2010). Secondly, we used a modified research version of the m-NMES unit, whose maximal current output was 200 mA, but not the commercialized one that is limited at 70 mA. The reason is that, in order to evoke the highest possible force at pain threshold, we preferred to avoid any bias between c-NMES and m-NMES devices due to technical limitations. As a matter of fact, none of the subjects included in our study attained the maximal current output of both

c-NMES and m-NMES units, while all of them except one were able to surpass the 70-mA hypothetical limit of m-NMES. This has implications for manufacturers of present and future m-NMES systems. Thirdly, the current results were only obtained during acute NMES use in subjects who were relatively inexperienced with both forms of NMES. It remains to be confirmed whether the advantages of m-NMES demonstrated here are preserved during multiple treatment sessions, even though the findings of Feil et al. (2011) seem to confirm the superiority of m-NMES for (re)training purposes. Finally, our study design did not allow us to distinguish the contribution of the two features of m-NMES that mainly explain its positive effects in terms of force production and discomfort, namely electrode configuration and current distribution.

Conclusion

Because quadriceps m-NMES generated stronger contractions than c-NMES, and discomfort scores were systematically lower with the former modality, the use of m-NMES appears legitimate for (re)training purposes.

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Conflict of interest The authors declare no conflict of interest regarding this study.

References

- Adams GR, Harris RT, Woodard D, Dudley GA (1993) Mapping of electrical muscle stimulation using MRI. *J Appl Physiol* 74:532–537
- Alon G (1985) High voltage stimulation. Effects of electrode size on basic excitatory responses. *Phys Ther* 65:890–895
- Bax L, Staes F, Verhagen A (2005) Does neuromuscular electrical stimulation strengthen the quadriceps femoris? A systematic review of randomised controlled trials. *Sports Med* 35:191–212
- Bennie SD, Petrofsky JS, Nisperos J, Tsurudome M, Laymon M (2002) Toward the optimal waveform for electrical stimulation of human muscle. *Eur J Appl Physiol* 88:13–19
- Bickel CS, Gregory CM, Dean JC (2011) Motor unit recruitment during neuromuscular electrical stimulation: a critical appraisal. *Eur J Appl Physiol* 111:2399–2407
- Botter A, Merletti R, Minetto MA (2009) Pulse charge and not waveform affects M-wave properties during progressive motor unit activation. *J Electromogr Kinesiol* 19:564–573
- Bowman BR, Baker LL (1985) Effects of waveform parameters on comfort during transcutaneous neuromuscular electrical stimulation. *Ann Biomed Eng* 13:59–74
- Burke D, Mackenzie RA, Skuse NF, Lethlean AK (1975) Cutaneous afferent activity in median and radial nerve fascicles: a microelectrode study. *J Neurol Neurosurg Psychiatry* 38:855–864
- Delitto A, Strube MJ, Shulman AD, Minor SD (1992) A study of discomfort with electrical stimulation. *Phys Ther* 72:410–421

Doheny EP, Caulfield BM, Minogue CM, Lowery MM (2010) Effect of subcutaneous fat thickness and surface electrode configuration during neuromuscular electrical stimulation. *Med Eng Phys* 32:468–474

Feil S, Newell J, Minogue C, Paessler HH (2011) The effectiveness of supplementing a standard rehabilitation program with superimposed neuromuscular electrical stimulation after anterior cruciate ligament reconstruction: a prospective, randomized, single-blind study. *Am J Sports Med* 39:1238–1247

Gandevia SC (2001) Spinal and supraspinal factors in human muscle fatigue. *Physiol Rev* 81:1725–1789

Gobbo M, Gaffurini P, Bissolotti L, Esposito F, Orizio C (2011) Transcutaneous neuromuscular electrical stimulation: influence of electrode positioning and stimulus amplitude settings on muscle response. *Eur J Appl Physiol* 111:2451–2459

Gondin J, Cozzzone PJ, Bendahan D (2011) Is high-frequency neuromuscular electrical stimulation a suitable tool for muscle performance improvement in both healthy humans and athletes? *Eur J Appl Physiol* 111:2473–2478

Gorgey AS, Dudley GA (2008) The role of pulse duration and stimulation duration in maximizing the normalized torque during neuromuscular electrical stimulation. *J Orthop Sports Phys Ther* 38:508–516

Gregory CM, Bickel CS (2005) Recruitment patterns in human skeletal muscle during electrical stimulation. *Phys Ther* 85:358–364

Gregory CM, Dixon W, Bickel CS (2007) Impact of varying pulse frequency and duration on muscle torque production and fatigue. *Muscle Nerve* 35:504–509

Kebaetse MB, Lee SC, Binder-Macleod SA (2001) A novel stimulation pattern improves performance during repetitive dynamic contractions. *Muscle Nerve* 24:744–752

Kesar T, Chou LW, Binder-Macleod SA (2008) Effects of stimulation frequency versus pulse duration modulation on muscle fatigue. *J Electromyogr Kinesiol* 18:662–671

Lai H, De Domenico G, Strauss G (1988) The effect of different electro-motor stimulation training intensities on strength improvement. *Aust J Physiother* 34:151–164

Laufer Y, Snyder-Mackler L (2010) Response of male and female subjects after total knee arthroplasty to repeated neuromuscular electrical stimulation of the quadriceps femoris muscle. *Am J Phys Med Rehabil* 89:464–472

Laufer Y, Ries JD, Leininger PM, Alon G (2001) Quadriceps femoris muscle torques and fatigue generated by neuromuscular electrical stimulation with three different waveforms. *Phys Ther* 81:1307–1316

Lexell J, Henriksson-Larsen K, Sjöström M (1983) Distribution of different fibre types in human skeletal muscles. 2. A study of cross-sections of whole m. vastus lateralis. *Acta Physiol Scand* 117:115–122

Lieber RL, Kelly MJ (1991) Factors influencing quadriceps femoris muscle torque using transcutaneous neuromuscular electrical stimulation. *Phys Ther* 71:715–721

Lyons GM, Leane GE, Clarke-Moloney M, O'Brien JV, Grace PA (2004) An investigation of the effect of electrode size and electrode location on comfort during stimulation of the gastrocnemius muscle. *Med Eng Phys* 26:873–878

Maffiuletti NA (2010) Physiological and methodological considerations for the use of neuromuscular electrical stimulation. *Eur J Appl Physiol* 110:223–234

Maffiuletti NA, Minetto MA, Farina D, Bottinelli R (2011) Electrical stimulation for neuromuscular testing and training: state-of-the art and unresolved issues. *Eur J Appl Physiol* 111:2391–2397

Maffiuletti NA, Roig M, Karatzanos E, Nanas S (2013) Neuromuscular electrical stimulation for preventing skeletal-muscle weakness and wasting in critically ill patients: a systematic review. *BMC Med* 11:137

Malesevic NM, Popovic LZ, Schwirtlich L, Popovic DB (2010) Distributed low-frequency functional electrical stimulation delays muscle fatigue compared to conventional stimulation. *Muscle Nerve* 42:556–562

Morch CD, Hennings K, Andersen OK (2011) Estimating nerve excitation thresholds to cutaneous electrical stimulation by finite element modeling combined with a stochastic branching nerve fiber model. *Med Biol Eng Comput* 49:385–395

Naaman SC, Stein RB, Thomas C (2000) Minimizing discomfort with surface neuromuscular stimulation. *Neurorehabil Neural Repair* 14:223–228

Neyroud D, Maffiuletti NA, Kayser B, Place N (2012) Mechanisms of fatigue and task failure induced by sustained submaximal contractions. *Med Sci Sports Exerc* 44:1243–1251

Paessler HH (2012) Emerging techniques in orthopedics: advances in neuromuscular electrical stimulation. *Am J Orthop* 41:1–8

Parker MG, Berhold M, Brown R, Hunter S, Smith MR, Runhling RO (1986) Fatigue response in human quadriceps femoris muscle during high frequency electrical stimulation. *J Orthop Sports Phys Ther* 7:145–153

Place N, Maffiuletti NA, Martin A, Lepers R (2007) Assessment of the reliability of central and peripheral fatigue after sustained maximal voluntary contraction of the quadriceps muscle. *Muscle Nerve* 35:486–495

Snyder-Mackler L, Delitto A, Stralka SW, Bailey SL (1994) Use of electrical stimulation to enhance recovery of quadriceps femoris muscle force production in patients following anterior cruciate ligament reconstruction. *Phys Ther* 74:901–907

Stevens-Lapsley JE, Balter JE, Wolfe P, Eckhoff DG, Kohrt WM (2012) Early neuromuscular electrical stimulation to improve quadriceps muscle strength after total knee arthroplasty: a randomized controlled trial. *Phys Ther* 92:210–226

Theurel J, Lepers R, Pardon L, Maffiuletti NA (2007) Differences in cardiorespiratory and neuromuscular responses between voluntary and stimulated contractions of the quadriceps femoris muscle. *Respir Physiol Neurobiol* 157:341–347

Vanderthommen M, Duchateau J (2007) Electrical stimulation as a modality to improve performance of the neuromuscular system. *Exerc Sport Sci Rev* 35:180–185

Vanderthommen M, Duteil S, Wary C, Raynaud JS, Leroy-Willig A, Crielaard JM, Carlier PG (2003) A comparison of voluntary and electrically induced contractions by interleaved 1H- and 31P-NMRS in humans. *J Appl Physiol* 94:1012–1024

Vivotzhev I, Debigré R, Gagnon P, Mainguy V, Saey D, Dube A, Pare ME, Belanger M, Maltais F (2012) Functional and muscular effects of neuromuscular electrical stimulation in patients with severe COPD: a randomized clinical trial. *Chest* 141:716–725

Walls RJ, McHugh G, O'Gorman DJ, Moyna NM, O'Byrne JM (2010) Effects of preoperative neuromuscular electrical stimulation on quadriceps strength and functional recovery in total knee arthroplasty. A pilot study. *BMC Musculoskelet Disord* 11:119

Zory R, Boerio D, Jubeau M, Maffiuletti NA (2005) Central and peripheral fatigue of the knee extensor muscles induced by electromyostimulation. *Int J Sports Med* 26:847–853