REVIEW ARTICLE

Physiological and methodological considerations for the use of neuromuscular electrical stimulation

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Abstract The main aim of this review is to discuss some evidence-based physiological and methodological considerations for optimal use of neuromuscular electrical stimulation (NMES) in healthy and impaired skeletal muscles. After a quick overview of the main applications, interests and limits of NMES use, the first section concentrates on two crucial aspects of NMES physiology: the differences in motor unit recruitment pattern between NMES and voluntary contractions, and the involvement of the nervous system during peripheral NMES. The second section of the article focuses on the most common NMES parameters, which entail the characteristics of both the electrical current (the input) and the evoked contraction (the output).

Keywords Strength training · Rehabilitation · Muscle function · Quadriceps

Introduction

Definition of NMES

Neuromuscular electrical stimulation (NMES) involves the application of a series of intermittent stimuli to superficial skeletal muscles, with the main objective to trigger visible muscle contractions due to the activation of the intramuscular nerve branches (Hultman et al. 1983). Electrical stimuli are generally delivered using one or more active

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Neuromuscular Research Laboratory, Schulthess Clinic, Lengghalde 2, 8008 Zurich, Switzerland e-mail: nicola.maffiuletti@kws.ch electrodes positioned in proximity to the muscle motor points (Fig. 1), and pre-programmed stimulation units. An intact motor nerve is a prerequisite for eliciting muscle contractions with NMES.

Main applications of NMES

NMES is used as a valid research tool for in vivo assessment of the neuromuscular function of healthy and impaired muscles, in both fresh and fatigued conditions (Horstman et al. 2008; Martin et al. 2004; Wust et al. 2008). As an example, with this technique it is possible to evaluate the contractile function of intact muscle in a standardized way (e.g., force–frequency relationship, fatigability during constant stimulation) as well as the level of voluntary activation using the twitch interpolation technique (Gandevia 2001).

More importantly, NMES is largely adopted in both research and clinical settings as a rehabilitation/training method [henceforth referred to as (re)training]. Depending on the status of the muscle being stimulated, NMES can be used (1) for the preservation of muscle mass and function during prolonged periods of disuse or immobilization (Gibson et al. 1988), (2) for the recovery of muscle mass and function following prolonged periods of disuse or immobilization (Snyder-Mackler et al. 1995), (3) for the improvement of muscle function in different healthy populations: elderly subjects (Caggiano et al. 1994), adult subjects (Currier and Mann 1983), recreational and competitive athletes (Babault et al. 2007; Delitto et al. 1989; Maffiuletti et al. 2002a; Pichon et al. 1995), and also as a preoperative strengthening modality (Walls et al., personal communications), i.e. "prehabilitation" (Fig. 2).

Thus, NMES (re)training programs have been implemented in the following fields:



Fig. 1 Typical settings of NMES exercise for the quadriceps muscle: a frontal view, b lateral view. Two active electrodes are positioned over the motor points of vastus medialis and vastus lateralis muscles, with one dispersive electrode closing the stimulation loop. The stimulated limb is maintained in isometric conditions so as to record



Fig. 2 Main uses and effectiveness of NMES (re)training programs

- *Cardiovascular medicine* Patients with chronic or refractory heart failure (Harris et al. 2003; Quittan et al. 2001), cardiac transplant (Vaquero et al. 1998), chronic obstructive pulmonary disease (Roig and Reid 2009; Vivodtzev et al. 2008);
- Orthopedic medicine Patients with anterior cruciate ligament reconstruction (Delitto et al. 1988; Eriksson and Haggmark 1979; Fitzgerald et al. 2003; Lieber et al. 1996; Snyder-Mackler et al. 1991), bone fracture (Gibson et al. 1988), knee osteoarthritis (Gibson et al. 1989; Zizic et al. 1995), rheumatoid arthritis (Piva et al. 2007), total knee arthroplasty (Petterson and Snyder-Mackler 2006; Stevens et al. 2004), total hip arthroplasty (Suetta et al. 2004), meniscectomy (Gould et al. 1983), patellofemoral pain (Callaghan et al. 2001);
- Neurological medicine Patients following stroke (Glinsky et al. 2007; Newsam and Baker 2004), spinal cord injury (Belanger et al. 2000; Crameri et al. 2000;

NMES force; this latter is then expressed relative to MVC force to provide NMES training intensity (see Fig. 5). Current intensity is consistently increased by the subject themselves to the maximal tolerated level throughout the session

Dudley et al. 1999), cerebral palsy (Merrill 2009; Stackhouse et al. 2007);

- *General medicine* patients with hemophilia (Querol et al. 2006), cancer (Crevenna et al. 2006) and critically ill patients (Gerovasili et al. 2009);
- *Geriatric medicine* Healthy (Amiridis et al. 2005; Caggiano et al. 1994) and unhealthy (Stevens et al. 2004) elderly subjects;
- *Space medicine* Astronauts (Convertino 1996; Mayr et al. 1999), simulated microgravity (Duvoisin et al. 1989);
- *Sports medicine* Healthy and injured athletes of individual and team sports (Delitto et al. 1989; Maffiuletti 2006).

Surprisingly, such an extensive use of NMES has been mainly restricted to the quadriceps femoris muscle (Bax et al. 2005; Hortobagyi et al. 1992).

Interests of NMES

The most unique aspect of NMES is the activation order of motor units, which is quite different from the physiological recruitment pattern ("size principle" of Henneman et al. 1965) and would favor the activation of fast motor units in addition to the slow ones (i.e., "disorderly" recruitment), even at relatively low levels of evoked force (Gregory and Bickel 2005) (see "Physiological considerations for the use of NMES"). This unique feature has important implications for the use of NMES in the context of rehabilitation and sport training, e.g., for those patients presenting with atrophy of fast muscle fibers (Gosker et al. 2002) or for athletes requiring high levels of muscle strength and power (Babault et al. 2007; Delitto et al. 1989).

The use of NMES as a (re)training modality allows preservation (Gibson et al. 1988) or recovery (Eriksson and

Haggmark 1979) of muscle mass and function in patients. and improves muscle strength in healthy subjects (Bax et al. 2005; Gondin et al. 2005) and sportsmen (Maffiuletti 2006). Compared to voluntary training and conventional rehabilitation procedures, NMES (combined or not with voluntary exercise) could be (1) more effective to preserve muscle function during a phase of reduced activity/immobilization (Bax et al. 2005; Glinsky et al. 2007; Vivodtzev et al. 2006), (2) equally effective to recover muscle function after an immobilization period (Bax et al. 2005), also when treatment intensities are matched (Lieber et al. 1996), (3) equally or less effective to improve healthy muscle function (Bax et al. 2005; Hainaut and Duchateau 1992) (Fig. 2). That is to say, NMES (re)training may provide better results than volitional training only for partially or totally immobilized subjects (to substitute for voluntary activation of muscle), when they are unable to perform volitional exercise or to sustain an adequate volitional training intensity and duration to gain benefit from the intervention, e.g., because of breathlessness in cardiovascular patients (Vivodtzev et al. 2008), limited or no cooperation in neurological (Glinsky et al. 2007) and critically ill patients (Gerovasili et al. 2009), reflex inhibition (Morrissey 1988) and limited effectiveness of voluntary isometric training in immobilized orthopedic patients (Eriksson and Haggmark 1979; Gould et al. 1983). It seems that more impaired patients would even respond more effectively to NMES (Morrissey 1988; Roig and Reid 2009).

Contrary to voluntary training procedures, NMES can be used to selectively (re)train specific muscles, e.g., erector spinae for low-back pain prevention (Kahanovitz et al. 1987), or to alter the relative magnitude of recruitment of certain heads within a muscle group (Lake 1992), e.g., selective stimulation of the vastus medialis in subjects with patellofemoral problems (Morrissey 1988). Additionally, the acute application of NMES has been found to promote unique facilitatory effects of the contralateral homologous muscle (Howard and Enoka 1991), and NMES (re)training has been shown to result in greater cross-education compared to voluntary training (Hortobagyi et al. 1999). Such cross-limb effects of NMES are likely to be especially important in patients with disorders predominantly affecting one side of the body.

Limits of NMES

The two main limitations of NMES are the strong discomfort associated with the peripheral stimulation (Delitto et al. 1992; Lake 1992) and the limited spatial recruitment of muscle fibers, which is quite superficial (Vanderthommen et al. 2003) and largely incomplete (see "Physiological considerations for the use of NMES"). Both of these factors, which are strictly related to the current dose, inevitably limit the use of NMES in frail subjects as well as its effectiveness as a valid treatment intervention. In order to improve NMES acceptability, researchers have long attempted to minimize the discomfort and maximize the spatial recruitment by altering the characteristics of NMES parameters (see "Methodological considerations for the use of NMES"), but only with limited success.

Peripherally, NMES exercise imposes a great metabolic demand and thus hastens the onset of muscle fatigue, mainly because of the repeated contractile activity within the same muscle fibers (i.e., fixed recruitment). Moreover, as stimulations are generally delivered at a fixed joint angle (Lieber and Kelly 1993), the effects of NMES (re)training programs are considered to be poorly related to functional activities of daily living or to sporting activities (Enoka 2002b). Methodological precautions may nevertheless be taken to minimize the impact of these limitations on NMES application (Maffiuletti et al. 2002a).

Aims of the review

As discussed above, the use of NMES (re)training could be particularly appropriate during a period of reduced activity/ immobilization. Paradoxically, however, the large majority of the NMES (re)training studies have focused on healthy rather than on impaired muscles (Bax et al. 2005), so that the real potential of NMES remains largely unexplored. Additionally, several clinicians are still reluctant to apply NMES in patient populations because of the unclear benefits compared to volitional training, and because of the scarce knowledge of the physiological (Lieber 1986) and methodological issues (Reed 1997; Vanderthommen and Duchateau 2007) related to its use. As an example, there is still a lack of objective evidence on how motor units are activated by the electrical current (see Gregory and Bickel 2005), as well as on the central mechanisms that mediate acute adjustments and chronic adaptations in response to NMES (Collins 2007; Vanderthommen and Duchateau 2007). In the same way, since manufacturers' claims and personal experience generally prevail over scientific evidence, NMES stimulation parameters are often determined on an empirical basis (Reed 1997; Vanderthommen and Duchateau 2007).

Therefore, the main aim of this review is to discuss some evidence-based physiological and methodological considerations for optimal use of NMES in healthy and impaired skeletal muscles. The intention is to provide practical information for clinicians, physical trainers and researchers working with NMES.

Physiological considerations for the use of NMES

This section will focus on two aspects of NMES physiology that have been the subject of numerous discussions in the last 20 years: the differences in motor unit recruitment pattern between NMES and voluntary contractions, and the involvement of the nervous system during peripheral NMES.

Motor unit recruitment

The involvement of motor units during NMES contractions is considerably different from that underlying voluntary activation (Table 1). The first logical difference between the two modalities of activation deals with the temporal recruitment of motor units, which is quite asynchronous during voluntary actions, while it is imposed by the stimulator in a synchronous manner during NMES (Adams et al. 1993).

With regard to spatial recruitment, constant-intensity NMES imposes a continuous contractile activity to the same population of superficial muscle fibers (i.e., those with the axonal branches in proximity to the stimulating electrodes), and such fixed recruitment diminishes proportionally with increasing distance from the electrode (Vanderthommen et al. 2000). On the other hand, if current intensity is progressively increased throughout the (re)training session (Theurel et al. 2007), new fibers located at a greater distance from the electrode (i.e., deeper) could be depolarized, while the superficial ones maintain their contractile activity despite the occurrence of neuromuscular transmission-propagation failure (Zory et al. 2005). Using magnetic resonance imaging to map the muscle activity elicited by very high-intensity NMES [up to 75% of maximal voluntary contraction (MVC) force], Adams et al. (1993) indicated that the recruitment pattern was not exclusively superficial, but rather dispersed and different among subjects. Despite a relatively small sample size (N = 7 healthy subjects), they also proposed a formula to predict the activated muscle cross-sectional area

 Table 1 Motor unit recruitment during voluntary and NMES contractions

Voluntary contraction	NMES contraction
Temporal	
Asynchronous	Synchronous
Spatial	
Dispersed	Superficial (close to the electrodes)
Rotation is possible	Spatially fixed
Quasi-complete (even at the maximum)	Largely incomplete (even at the maximum)
Orderly	
Yes, selective (slow to fast)	No, nonselective/random/ disorderly (slow and fast)
Consequence	
Partially fatiguing	Extremely fatiguing



Fig. 3 Quadriceps muscle cross-sectional area (*CSA*) activated by NMES can be predicted using NMES training intensity (% of *MVC*), according to the equation proposed by Adams et al. (1993)

as a function of NMES training intensity (Fig. 3). This formula substantiates the main limitation of NMES-induced contractions that is the limited spatial recruitment of muscle fibers. As an example, for the normal range of NMES training intensities previously discussed (40–60% MVC), the amount of activated cross-sectional area would only be 29–43% of the total muscle, which indirectly suggests that only a limited portion of the targeted muscle could be (re)trained by NMES.

As already discussed, superficial, fixed and incomplete muscle recruitment with NMES does not represent good reasons for the use of this modality in the context of muscle (re)training. However, there are at least three strategies that would maximize spatial recruitment during NMES exercise. First, stimulation intensity should be increased whenever possible by the subject themselves, ideally after each contraction, in order to depolarize new and deeper muscle fibers at each evoked contraction. Secondly, stimulation electrodes should be moved after a series of contractions (within the same session and between training sessions), so as to change the population of superficial fibers preferentially activated by NMES current. Thirdly, it is also recommended to alter muscle length by manipulating joint angle, to vary the position of muscle fibers with respect to the electrode, but also to modify the likely contribution of cutaneous (Garnett and Stephens 1981) and joint receptors to the evoked contraction.

The main argument supporting differences in motor unit recruitment order between voluntary and stimulated contractions is that large-diameter axons are more easily excited by electrical stimuli (i.e., they have the lowest threshold of activation), which would reverse the activation order during NMES (Enoka 2002a). This is even favored by anatomical factors, at least for the quadriceps muscle, since larger motor units are mainly located in superficial regions of the vastus lateralis muscle (Knight and Kamen 2005), which would inevitably reduce the distance between the larger axons and the active electrode. Moreover, input from cutaneous afferents via reflex inhibition may alter the recruitment threshold of motor units, as demonstrated by Garnett and Stephens (1981), and favor reversal of motor unit recruitment order. However, human studies have produced contradictory findings on motor unit recruitment order with some studies suggesting preferential or selective activation of fast motor units with NMES (Cabric et al. 1988; Heyters et al. 1994; Trimble and Enoka 1991), and others demonstrating minimal or no difference between voluntary and electrically elicited contractions (Binder-Macleod et al. 1995; Feiereisen et al. 1997; Knaflitz et al. 1990). In an excellent review paper, Gregory and Bickel (2005) suggested that motor unit recruitment during NMES is nonselective or random (see also Jubeau et al. 2007); that is motor units are activated without obvious sequencing related to unit types (i.e., "disorderly" recruitment). This implies that NMES can activate some fast motor units, in addition to slow units, even at relatively low force levels. Indirect evidence suggests that the relative proportion of fast and slow motor units in a muscle activated by NMES at different force levels would be quite constant, as twitch contractile speeds were not found to differ between NMES training intensities of 20, 40 and 80% of MVC (Binder-Macleod et al. 1995).

Such peculiarity of NMES recruitment inevitably entails some disadvantages (e.g., onset and extent of muscle fatigue, see below) but also several advantages, particularly for impaired muscles. For example, elderly individuals and patients presenting a selective atrophy of type II muscle fibers (e.g., chronic obstructive pulmonary disease, chronic steroid myopathy) (Gosker et al. 2002; Kanda et al. 2001), or orthopedic patients who cannot perform high-intensity voluntary contractions because of injury, recent surgery or impaired activation (Petterson and Snyder-Mackler 2006; Stevens et al. 2004), and also athletes requiring high levels of muscle strength and power (Babault et al. 2007; Delitto et al. 1989; Malatesta et al. 2003), would benefit from the use of NMES exercise-even at low intensity-to (re)train at least some of the fast fibers that otherwise can only be activated using high-force voluntary efforts.

The main consequence of such a unique motor unit recruitment pattern for NMES is the exaggerated metabolic cost of an electrically evoked contraction (Vanderthommen et al. 2003), which, compared to a voluntary action of the same intensity, provokes greater and earlier muscle fatigue (Deley et al. 2006; Jubeau et al. 2008; Theurel et al. 2007). According to Vanderthommen and Duchateau (2007), these differences, in motor unit recruitment and thus in metabolic demand between NMES and voluntary contractions, constitute an argument in favor of the non-concomitant combination of these two techniques in the context of muscle (re)training. Differences in spatial recruitment between these two activation modalities, would also contribute, at least in part, to the significant muscle damage produced by NMES but not by voluntary isometric contractions of the same intensity (Jubeau et al. 2008).

Involvement of the nervous system during NMES

Although NMES is commonly viewed as a technique to induce muscle contractions with a negligible contribution of the central nervous system, several lines of evidence indicate a considerable involvement of different neural structures during NMES. These central effects of NMES have been increasingly acknowledged in the last few years (Enoka 2002a; Vanderthommen and Duchateau 2007). In accordance with this contention, it has even been suggested that NMES would provide a multimodal bombardment of the central nervous system (Baker et al. 2000), which results in increased cortical activity (Smith et al. 2003) as well as in spinal motoneuron recruitment (Collins 2007).

Quadriceps NMES, as it is used in clinical settings, has been shown to acutely increase the hemodynamic response in sensorimotor cortex regions (Smith et al. 2003). Importantly, this previous MRI study showed a doseresponse relationship between the current intensity and cortical activity, which allows speculation that high current doses (see "Methodological considerations for the use of NMES") would maximize these supraspinal effects of NMES exercise. On the other hand, the use of wide-pulse (1 ms) high-frequency (50-100 Hz) NMES would favor the recruitment of spinal motoneurons by the electrically evoked sensory volley, leading to the development of central torque (shaded area in Fig. 4), in addition to the peripheral depolarization of motor axons (Collins 2007). Such reflexive recruitment, which activates motor units in the normal physiological recruitment order, is consistent with the development of persistent inward currents in spinal motoneurons or interneurons (Collins 2007) that lead to sustained depolarizations of sensory axons (plateau potentials). Interestingly, central torque can be further maximized by the use of frequencies higher than 80 Hz, long stimulation trains (approximately 20 s) and low contraction intensities (approximately 10% of MVC) (Dean et al. 2007). Even though this spinal contribution remains to be demonstrated for commonly stimulated muscles such as the quadriceps femoris, some of the neural mechanisms that mediate the acute adjustments in response to NMES exercise are now better identified due to these recent findings.

Fig. 4 Representative elbow flexor force traces recorded during conventional NMES (grey line) and wide-pulse highfrequency NMES (black line) of the biceps brachii muscle in a healthy subject. The shaded area indicates the central torque due to the reflexive recruitment of spinal motoneurons by the electrically evoked sensory volley (Collins 2007)



60-second stimulation

The central and peripheral mechanisms of muscle fatigue induced by a conventional session of NMES have been investigated in our laboratory (Boerio et al. 2005), in an attempt to substantiate the acute neural adjustments to NMES exercise. Interestingly, after only 13 min of intermittent NMES of the calf muscles, the exercise-induced reduction in plantar flexor MVC torque (i.e., muscle fatigue) was accompanied by both peripheral (neuromuscular transmission-propagation failure) and central (voluntary activation failure) fatigue, as witnessed by M wave and interpolated twitch findings, respectively (Boerio et al. 2005). Failure of voluntary activation after a single bout of calf NMES has been confirmed and debated recently by Papaiordanidou et al. (2010). As no depression in spinal reflex excitability was reported (Boerio et al. 2005; Papaiordanidou et al. 2010; Tanino et al. 2003), central fatigue induced by NMES could originate from supraspinal rather than from spinal mechanisms. However, we failed to observe a similar neural impairment immediately after application of the same NMES protocol to the quadriceps muscle (Zory et al. 2005), while others have reported a tendency toward a decrease in voluntary activation (Deley et al. 2006), and a significant decline in quadriceps voluntary activation 2 days after the NMES bout (Laurin et al., personal communications).

Besides fatigue experiments, a series of NMES (re)training studies have provided compelling evidence of neural adaptations induced by short-term programs on healthy and impaired muscles. These adaptations include: significant increases in MVC strength after only a few sessions of NMES (Brocherie et al. 2005; Pichon et al. 1995), when there is no reason to believe that increased protein synthesis could have induced significant muscle hypertrophy; strength increases without any significant changes in muscle enzyme activity, fiber size, or

mitochondrial properties (Eriksson et al. 1981) (for a contrary view see (Cabric et al. 1988); voluntary strength gains of the contralateral homologous muscle after unilateral (re)training (i.e., cross-education effect) (Hortobagyi et al. 1999; Lai et al. 1988); and increases in voluntary muscle activation, as witnessed by surface electromyography (Gondin et al. 2006; Maffiuletti et al. 2002b), twitch interpolation (Maffiuletti et al. 2002b; Stevens et al. 2004), and volitional-wave (Gondin et al. 2006) recordings. Surprisingly, NMES (re)training does not seem to influence H reflex excitability (Gondin et al. 2006; Maffiuletti et al. 2003), both at rest and during an actual contraction, so it has been inferred that NMES (re)training-induced adaptations would be mainly located at the supraspinal level.

Interestingly, the time course of neuromuscular adaptations to NMES (re)training appears very similar to the classical model proposed by Sale (1988) for voluntary strength training. In their well-designed, prospective study, Gondin et al. (2005) demonstrated that 4 weeks of NMES significantly increased MVC strength and voluntary activation, while muscle cross-sectional area was not significantly altered. After 8 weeks of NMES (re)training, both neural and muscular adaptations mediated the strength improvement, therefore demonstrating that NMES could elicit morphological changes in the muscle, but only for programs longer than 4 weeks. There is, however, a lack of knowledge on the effects of NMES at the single muscle fiber level, and further studies are required to confirm that NMES (re)training actually induces changes in myosin heavy chain isoforms relative content, single-fiber crosssectional area and specific tension (Maffiuletti et al. 2006).

In light of the above considerations, one can conjecture that conventional NMES (re)training using high training intensities would mainly promote supraspinal adaptations, while wide-pulse high-frequency NMES would likely result in changes at the spinal level. In the same way, the former NMES modality would probably train populations of slow and fast muscle fibers, while the latter would preferentially target slow fibers. These speculation, however, remain to be confirmed by controlled studies in both healthy and patient populations.

In conclusion, the application of peripheral NMES could evoke widespread activity within the central nervous system that is capable of mediating a range of neural adjustments and adaptations. Such central contributions to electrically elicited contractions cannot be ignored any longer.

Methodological considerations for the use of NMES

This section will concentrate on the most common NMES parameters, which entail the characteristics of both the electrical current (the input) and the evoked contraction (the output), and try to provide some clear indications on their appropriate application.

As a foreword, it is important to point out that the effectiveness of a NMES (re)training program does not rely, for the most part, on NMES parameters. Indeed, there is considerable inter-individual variation in response to NMES exercise, and optimization may relate more to the characteristics of the subject than to NMES parameters themselves (Lloyd et al. 1986). I strongly concur with Lieber and Kelly (1991) on the suggestion that NMES effectiveness would not depend on external controllable factors (e.g., current or electrode characteristics), but rather on some intrinsic anatomical properties, such as individual motor nerve branching, which determines the response of the muscle to the application of electrical current over the skin. It is tempting to suggest that NMES success is essentially determined by features that can only be partly controlled by the end user.

In general, NMES current parameters are poorly reported and there is a considerable heterogeneity between the different studies. In the same way, the methods used by researchers to evaluate NMES (re)training effectiveness are quite heterogeneous, so that it is difficult to compare the outcomes of the different NMES studies. Unfortunately, researchers and clinicians tend to consider the different forms of electrical stimulation as a whole, irrespective of the species (human vs. animal), of the model (chronic low frequency stimulation, functional electrical stimulation, transcutaneous electrical nerve stimulation, NMES), of the type of electrode (implanted vs. surface), of the stimulus parameters (subsensory, sensory, motor or supramotor current levels) and of the muscle being stimulated. This inevitably creates confusion and a lack of general consensus regarding the main stimulus parameters for NMES of human skeletal muscles (Maffiuletti 2008; Vanderthommen and Duchateau 2007).

There is nevertheless a sort of agreement on some NMES current characteristics (Vanderthommen and Duchateau 2007). The key factor for optimizing NMES effectiveness has been suggested to be muscle tension, that is the level of evoked force with respect to maximal voluntary force (Lieber and Kelly 1991), which should be maximized, whenever possible, via an appropriate manipulation of the two main NMES current parameters: frequency and intensity. In order to maximize muscle tension, it is strongly recommended to use biphasic rectangular pulses of 100-400 µs delivered at a stimulation frequency of 50-100 Hz (Vanderthommen and Duchateau 2007) and at the highest tolerated current intensity (Lake 1992), and to apply NMES in a static loading condition, so as to strictly control the level of evoked force. It is a common procedure to quantify isometric MVC force at the beginning of a NMES session, and subsequently express the level of each electrically elicited contraction as a percentage of the MVC force (Fig. 5). This important variable, which provides an indication of the intensity of the NMES training achieved, also called NMES training intensity (Selkowitz 1985) or NMES dose (Stevens et al. 2004), is not commonly controlled in both research and clinical settings, therefore invalidating comparisons between studies and between subjects.

There are several lines of evidence indicating that the higher the NMES training intensity, the higher the

Fig. 5 Representative quadriceps force traces recorded during a 5-s MVC (*left*) and a 6-s NMES contraction. NMES training intensity is expressed as the ratio between MVC force and NMES evoked force, as a percentage



effectiveness of NMES (re)training, for both healthy (Lai et al. 1988; Miller and Thepaut-Mathieu 1993; Selkowitz 1985) and impaired muscles (Snyder-Mackler et al. 1994; Stevens et al. 2004). Although few NMES studies actually measured the force generated during the stimulation, typical NMES training intensities for the healthy quadriceps range from 40 to 60% of MVC force, while tension levels greater than 70% of MVC are extremely rare to obtain (Lieber and Kelly 1991). As a unique finding, NMES training intensity was found to exceed the individual's MVC (110% of MVC) in a competitive power lifter (Delitto et al. 1989). Despite low NMES training intensities during the first few training sessions (in subjects nonfamiliarized with NMES), very large increases in current dose and therefore in training intensity are naturally observed during the course of conventional NMES (re)training programs (Lieber et al. 1996; Maffiuletti et al. 2009), due to improved tolerance or accommodation to NMES. It is therefore recommended to adequately familiarize subjects with the NMES current before initiating a (re)training program, in order to maximize training intensity throughout the intervention. Two or three sessions distributed over 7-10 days seem appropriate for this aim.

However, high NMES training intensities cannot always be used with frail populations, mainly because of the discomfort associated with high current doses. The same is true for obese-overweight subjects and for women, who present with large amounts of subcutaneous fat thickness that inevitably limit current diffusion to the targeted muscle (Maffiuletti et al. 2008). Surprisingly, however, NMES (re)training intensities as low as 5% MVC have been shown to be effective for the preservation of muscle mass during limb immobilization (Gibson et al. 1988) and also for the improvement of muscle strength in healthy individuals (Stefanovska and Vodovnik 1985). Lai et al. (1988) clearly demonstrated that high training intensities (50% MVC) produced greater strength gains than low training intensities (25% MVC) in healthy subjects. Nevertheless, a single investigation having compared the effect of low versus high NMES training intensity on mass and function of impaired muscles is still lacking and only a randomized controlled trial will definitely answer this question.

As a practical recommendation, the level of force evoked by NMES should not necessarily be measured during each training session, because of the linear relationship existing between current intensity and NMES force (Fig. 6) (i.e., the latter can be predicted from the former). However, individual current intensity should be consistently measured and, whenever possible, related to the evoked force to give an estimate of stimulation efficiency (in Newtons or Newton-meters per milliamperes) (Lieber and Kelly 1991). It is also recommended to stimulate the muscle under resting conditions in order to



Fig. 6 NMES current intensity is linearly related to NMES evoked force of the quadriceps muscle. Mean data \pm standard deviation (N = 10 healthy subjects)



Fig. 7 Main NMES parameters that should always be reported in research studies

facilitate the quantification of pure NMES evoked force. Nevertheless, frail or current-sensitive subjects could be asked to voluntarily contract their muscle during the first few evoked contractions of a session and/or during the first training sessions of a program so as to decrease the sensation of discomfort associated with NMES. In terms of training effectiveness, whether NMES is performed alone or superimposed with voluntary contraction does not seem to have an influence on the training-induced strength gains (Bax et al. 2005; Currier and Mann 1983; Lieber 1986; Malatesta et al. 2003).

When presenting NMES parameters, it is important to clearly differentiate the characteristics of the electrical current from the characteristics of the evoked contraction (Fig. 7), because the former do not necessarily allow prediction of the latter on an individual basis. Moreover, hardware features and (re)training program parameters, including subject compliance with and tolerance to the NMES intervention, should always be carefully reported in scientific studies. It is also recommended to follow a linear progression in the main NMES training parameters such as current intensity, evoked force and training volume (Maffiuletti et al. 2009), to respect the basic principles of progressive strength training.

Concluding remarks

A good knowledge of the physiological and methodological features of NMES discussed here would allow optimization of NMES use in the clinic and for research purposes. The end user would then turn limitations and unique aspects of NMES to their advantage, so as to ensure effectiveness and safety. As an example, the "disorderly" recruitment of motor units with NMES could be minimized by using nerve instead of muscle stimulation (which would reduce the "confusion"), and wide-pulse high-frequency stimulations to favor the physiological motor unit recruitment order (Collins 2007). In the same way, central effects of NMES could be maximized using wide pulses, high frequencies, long stimulations and low NMES training intensities (Dean et al. 2007). Finally, spatial recruitment of motor units should be maximized by adopting different subterfuges during the training session such as a progressive increase in current intensity, displacement of active electrodes and alteration in muscle length.

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