

[Physical Therapy]



Can the Use of Neuromuscular Electrical Stimulation Be Improved to Optimize Quadriceps Strengthening?

Neal R. Glaviano, MEd, ATC,*[†] and Susan Saliba, PhD, ATC, PT[‡]

Context: Neuromuscular electrical stimulation (NMES) is a common modality used to retrain muscles and improve muscular strength after injury or surgery, particularly for the quadriceps muscle. There are parameter adjustments that can be made to maximize the effectiveness of NMES. While NMES is often used in clinical practice, there are some limitations that clinicians should be aware of, including patient discomfort, muscle fatigue, and muscle damage.

Evidence Acquisition: PubMed was searched through August 2014 and all articles cross-referenced.

Study Design: Clinical review.

Level of Evidence: Level 3.

Results: Clinicians can optimize torque production and decrease discomfort by altering parameter selection (pulse duration, pulse frequency, duty cycle, and amplitude). Pulse duration of 400 to 600 μ s and a pulse frequency of 30 to 50 Hz appear to be the most effective parameters to optimize torque output while minimizing discomfort, muscle fatigue, or muscle damage. Optimal electrode placement, conditioning programs, and stimulus pattern modulation during long-term NMES use may improve results.

Conclusion: Torque production can be enhanced while decreasing patient discomfort and minimizing fatigue.

Keywords: myoelectric stimulation; therapeutic modalities; weakness

Injury and surgical intervention often lead to muscle weakness and long-term muscle inhibition.³⁴ Clinicians can use many possible interventions to address quadriceps weakness during the rehabilitation process. One common intervention used is neuromuscular electrical stimulation (NMES).^{12,31,34} There is conflicting evidence with respect to NMES parameter selection, electrode placement, and training effects on its effectiveness or best application to improve quadriceps strength and function.^{34,36} Results vary regarding quadriceps muscle reeducation, measureable strength improvements, patient-reported outcomes, and functional return using NMES.³⁴ NMES is more effective than volitional exercise in the rehabilitation of muscle mass preservation after immobilization³⁴ but not more

successful than traditional exercise to recover muscle mass or to improve healthy muscle.⁴⁴

Potential limitations may be responsible for suboptimal NMES outcomes,³⁴ such as differences between physiological and electrically induced contractions and decreased functional applications.⁵ NMES may preferentially target fast motor units, which is beneficial for fast-twitch muscle fibers that are often fatigued after injury and surgery.³⁴ The trade off with electrical stimulation targeting fast motor units is early muscular fatigue, greater patient discomfort, and an increased possibility of muscle damage with the treatment.⁴⁶ NMES may not follow the size principle, and motor units are recruited in a nonselective manner.³⁴ While a random recruitment pattern of motor units

From the [†]Department of Kinesiology, Exercise and Sport Injury Laboratory, University of Virginia, Charlottesville, Virginia, and [‡]Curry School of Education, Department of Kinesiology, University of Virginia, Charlottesville, Virginia

*Address correspondence to Neal R. Glaviano, MEd, ATC, Exercise and Sport Injury Laboratory, University of Virginia, Memorial Gymnasium, PO Box 400407, Charlottesville, VA 22904 (email: ng2w@virginia.edu).

The authors report no potential conflicts of interest in the development and publication of this article.

DOI: 10.1177/1941738115618174

© 2015 The Author(s)

Table 1. Patient discomfort due to NMES treatment

Study	Subjects, n	Results
Lyons et al ³¹	12	Using a 19.63-cm ² electrode decreased pain when compared with a 38.48-cm ² electrode
Rooney et al ⁴⁶	27	Altering frequency does not decrease pain tolerated
Gondin et al ¹⁶	12	Intensity varied between 30 and 120 mA due to pain threshold of subjects
Jubeau et al ²⁷	10	Intensity varied between 21 and 121 mA due to pain threshold of subjects
Maffiuletti et al ³⁶	20	Intensity varied between 60 and 100 mA due to pain threshold of subjects
Broderick et al ¹⁰	20	17/20 patients had increased VAS scores during NMES treatment
Vanderthommen et al ⁴⁷	16	Increase VAS scores >4/10 after NMES
Forrester and Petrofsky ¹³	6	Increase VAS scores >6/10 after NMES
Vanderthommen et al ⁴⁸	10	Increase VAS scores >2/10 after NMES

NMES, neuromuscular electrical stimulation; VAS, visual analog scale.

may occur with electrical stimulation, early fatigue may still occur due to the stimulus to identical muscle fibers.³⁴

Additionally, NMES has limited functional applications since it is commonly applied in an open kinetic chain position.³⁴ The majority of clinical research utilizes NMES applications on individuals during isometric quadriceps sets, straight leg raises, or knee extension tasks.⁴³ While these activities are beneficial during early rehabilitation, they do not translate to functional tasks where pathological individuals present with long-term muscle dysfunction.³⁶

While NMES is used in a variety of settings and pathologies, establishing ways to maximize its effectiveness should become a priority for clinicians using this modality. This review evaluates common limitations and presents ways from NMES treatments to optimize this modality.

METHODS

PubMed, Ovid MEDLINE, SPORTDiscus, CINAHL, and the Cochrane Library were searched for articles published between 1975 and August 2014 pertaining to electrical stimulation theory and clinical use, parameters, and limitations of NMES. Articles that were not written in English and did not use human participants were excluded. Bibliographies were cross-referenced to locate additional research articles of interest.

Patient Discomfort

As the intensity of the stimulus is increased, excitation of sensory, motor, and pain fibers occurs (Table 1).³¹ While the excitation of the motor neurons is the fundamental premise behind NMES,

those motor points that need to be stimulated to elicit a muscular contraction are located near free nerve endings and nociceptive receptors, which results in discomfort, pain, and a burning sensation.²⁵ There is a linear relationship between amplitude of the current and quadriceps torque production.⁶ The challenge is that by increasing amplitude of the current to recruit additional motor units and subsequent torque production, there is an increase in patient discomfort.¹⁰ The charge density, product of the pulse duration, and amplitude also play a role in patient discomfort and muscle damage.²⁴ Identical total charges with varying combinations of pulse duration and amplitude play a role in pain, fatigue, and torque production.²¹

Sex and body type differences should also be taken into consideration with the onset and severity of patient discomfort with NMES treatments.^{37,38} Female patients present with increased pain levels and earlier perception of the stimulus when compared with their male counterparts.^{37,38} Obese individuals also have greater pain levels during electrical stimulation treatments, with obese female patients presenting with the lowest pain tolerance.³⁸ To optimize NMES treatment, a balance between maximal quadriceps activation with minimized patient discomfort is vital.

Fatigue

Neuromuscular electrical stimulation often produced muscular fatigue at a faster rate than repetitive voluntary contractions (Table 2).^{4,6,7,18,49} One suggestion for fatigue is that electrically induced muscular contractions place different stresses on the muscle fibers than if an individual performed a physiological muscle

Table 2. Fatigue after NMES treatment

Study	Subjects, n	Results
Binder-Macleod et al ⁶	50	20% MVIC produced the least fatigue compared with 50% MVIC
Zory et al ⁴⁹	12	20% reduction in MVIC after NMES; EMG of the VL and RF decreased by 17.3% and 14.5%, respectively
Jubeau et al ²⁶	9	NMES resulted in a 22% decrease in MVIC compared with a 9% decrease with voluntary contraction
Botter et al ⁹	18	EMG-assessed fatigue was found in the VMO and VL after NMES
Bickel et al ⁴	13	A low-frequency protocol resulted in a 25% decline in torque production; a low-pulse duration protocol resulted in a 50% decline in torque production; a low-voltage protocol resulted in a 48% decline in torque production
Gorgey et al ¹⁸	7	A low-frequency protocol resulted in a 39% decrease in torque production; a short phase duration protocol resulted in a 71% decrease in torque production; a low-amplitude protocol resulted in a 70% decrease in torque production
Kesar and Binder-Macleod ²⁸	12	A low frequency-long pulse duration protocol resulted in a 22% decrease in torque production; a medium frequency-medium pulse duration protocol resulted in a 28% decrease in torque production; a high frequency-short pulse duration protocol resulted in a 46% decrease in torque production

EMG, electromyography; MVIC, maximal voluntary isometric contraction; NMES, neuromuscular electrical stimulation; RF, rectus femoris; VL, vastus lateralis; VMO, vastus medialis oblique.

contraction.³⁴ During a physiological contraction, the number of recruited motor units is dispersed, varies in the number active at a given time, and often occurs in a rotational pattern (termed *spatial recruitment*), which is a neurophysiological adaptation to minimize fatigue.^{5,34} However, during an electrically stimulated muscle contraction, there is a nonselective order of recruitment where only the motor units located between the electrodes are activated.^{5,34} This is termed *incomplete muscle recruitment* since the entire muscle is not stimulated, just those motor units between the electrodes.³⁴ Because of this incomplete and superficial activation, identical motor units will be activated repetitively, resulting in a fixed spatial recruitment.³⁴ The inability to alter the motor units being recruited results in the decrease of force production because of fatigue.^{5,8}

Muscle Damage

There has been growing evidence that electrical stimulation can have temporary detrimental effects on the muscle being stimulated (Table 3).^{3,22,26,32,33,41} A positive relationship has been found between amplitude and the force per area unit being stimulated.³⁰ Greater muscular fatigue, increased creatine kinase levels, histological damage to the muscle fibers, soreness, and changes in muscle volume measured by magnetic resonance imaging (MRI) are seen with increased force per unit area, suggesting that lower amplitudes may be more advantageous during NMES treatment.³⁰

Muscle damage has also been measured directly by identifying histological changes after electrical stimulation treatments.³³ While the number of studies examining direct measures is limited, it has been reported that electrical stimulation causes histological changes of macrophage infiltration, extracellular matrix alterations, muscle fiber disturbance, and Z-line disruption.^{32,33,41}

Indirect measures of muscle damage include creatine kinase circulating within the blood 24 to 96 hours after both single and multiple electrical stimulation treatments.^{3,26,32} Delayed onset muscle soreness with decreased flexibility and increased pain with palpation can occur after NMES treatments.^{3,26,47} Rhabdomyolysis resulting from a home electrical stimulation unit has been reported.²² For NMES to be beneficial, muscle damage must be reduced.

OPTIMIZING NMES OUTCOMES

Stimulus Pattern

Repetitive isometric NMES contractions commonly use duty cycles that do not mimic functional activities. Altered stimulus patterns exist in both acute rehabilitation and functional activities.^{12,23} While altering stimulus patterns is a novel intervention for NMES applications, there is great promise for more functional uses of NMES.^{12,23}

During the phases of rehabilitation, multiple electrodes produce beneficial results.^{12,39} Increasing the number of

Table 3. Muscle changes after NMES

Study	Subjects, n	Results
Mackey et al ³²	7	Increased muscle tenderness to palpation, stretch, and tenderness 1-4 days post-NMES (increase in VAS between 3 and 7/10) Z-line disruption after NMES when assessed by muscle biopsy Increase CK levels from baseline (200 IU/L) at day 2 (400 IU/L), day 4 (>1000 IU/L), and day 7 (800 IU/L) Increased cell inflammation and desmin staining when assessed by immunohistochemistry
Guarascio et al ^{22a}	1	Rhabdomyolysis (CK, 2917 mU/mL)
Aldayel et al ³	9	Increased pain 1-4 days after NMES during palpation and squat; increase in baseline CK levels 3 and 4 days after NMES
Vanderthommen et al ⁴⁸	10	Increase in baseline CK (136 ± 50 IU/L) day 1 and day 2 after NMES (927 ± 613 IU/L and 3021 ± 2693 IU/L) Decrease in muscle flexibility by 13°
Jubeau et al ²⁶	9	Increase in baseline CK levels 2 days (>1000 IU/L) and 3 days (>3000 IU/L) after NMES

CK, creatine kinase; NMES, neuromuscular electrical stimulation; VAS, visual analog scale.

^aCase study.

electrodes over the quadriceps modulates the stimulus pattern using multiple pathways to improve torque production and minimize the common limitations of muscle damage and fatigue.¹² By alternating the quadriceps fibers being recruited by the stimulus, more motor units are being activated to produce greater strength gains while ample recovery time is provided to minimize fatigue. Two novel devices can improve outcomes by altering stimulation patterns (Kneehab and Patterned Electrical Neuromuscular Stimulation [PENS]).^{12,14,23} The Kneehab uses a neoprene sleeve with multiple electrodes where a current is altered between 4 differently sized electrodes (10 × 20 cm, 3 × 18 cm, 10 × 7.5 cm, and 7 × 14 cm); electrical current is alternated between the 4 electrodes to stimulate multiple motor units.¹² Kneehab produced significant improvements in quadriceps strength, single-leg hop test, and running speed performance and allowed for a quicker return to work time period and higher intensity quadriceps contractions with less discomfort.¹² PENS provides an electrical stimulation pattern to both agonist and antagonist muscle groups to mimic healthy firing patterns based off electromyography studies.¹¹ Spinal alterations are replicated by the rhythmical contraction of the agonist and antagonist muscles seen in the pattern of PENS.⁴⁰ This rhythmical contraction replicates muscle stretch receptor and motor neuron stimulation that occurs during locomotion.⁴⁰ A 6-week training study with PENS improved vertical jump height by 10%,²³ and PENS was found to have an immediate improvement on pain and gluteus medius activation in individuals with patellofemoral pain during functional tasks.¹⁴

Neuromuscular Electrical Stimulation Parameters

Pulse Duration

Pulse durations between 400 and 600 μs selectively target motor fibers as shorter durations target sensory fibers and have a positive influence on torque production without negative factors of muscle fatigue or metabolic demands.^{16,19,28} Pulse durations closer to 400 μs produce greater quadriceps cross-sectional activation compared with 150 μs.²⁰ Pulse duration is often preselected depending on the NMES unit, requiring clinicians to evaluate and compare NMES devices.

Pulse Frequency

Pulse frequency directly correlates with torque production; however, it comes at the cost of muscle fatigue.²⁸ A linear relationship also exists between increases in pulse frequency and metabolic demands, including pH levels, greater inorganic phosphocreatine ratio values, and energy costs.¹⁶ These metabolic demands may cause early muscle fatigue and muscle damage after NMES treatments.¹⁶ The threshold between increasing torque production and fatigue due to increased metabolic demands appears to be between 30 and 50 Hz.^{7,16}

Duty Cycle

Duty cycle commonly uses a 1:5 ratio, which consists of 10 seconds on and 50 seconds of rest.⁴² This cycle is an acceptable ratio for minimizing muscular fatigue compared with

1:1 and 1:3.⁴² The 1:5 ratio produces less fatigue and is often used⁴²; inconsistency with this parameter is seen with varying ratios: 10:80,⁴⁴ 8:12,⁷ 4:25,³⁵ and 3:17.³⁶ The optimal duty cycle selection is unclear, and additional clarity is needed comparing multiple duty cycle ratios with regard to fatigue and discomfort.

Burst duty cycles within the delivered current can minimize patient discomfort and change torque output.²⁹ Burst duty cycles of 10% to 20% improve torque production, contractions, and patient discomfort, while burst duty cycles of 50% to 90% produce negative results.²⁹ If the duty cycle is too short, the muscle is not provided adequate recovery time and fatigue is more likely to occur sooner.⁴² The time specified allows for almost complete regeneration of the substrates necessary for repeated contractions.⁴²

Amplitude

Amplitude may be one of the most challenging but important parameters to optimize the effectiveness of an NMES treatment. Amplitude is the intensity of the current administered and is positively related to increased motor unit activation, force generation, and cross-sectional area of the quadriceps activation.^{2,20,48} Since strength development is related directly to dose response, force production must be greater than 50% of the maximal voluntary contraction.⁴⁵ The challenge with producing maximal amplitude intensity is that pain and fatigue increase with greater amplitude.⁶

Body composition between sexes and obese and nonobese individuals also plays a role in the amplitude needed to produce desirable muscular contractions; subcutaneous adipose tissue and intramuscular fat affect the results.^{37,38} The increase in adipose tissue and intramuscular fat functions as insulation to the NMES current, resulting in a greater amplitude level needed to produce full motor contractions.^{37,38} Altering electrode placement and using training effect adaptations over multiple treatments can overcome these limitations.^{5,15,47}

Influence of Electrodes

Traditional electrode placement for the quadriceps is over the distal vastus medialis oblique and proximal vastus lateralis muscles.^{1,44} Placing the electrodes at opposite ends of the muscle should produce a more complete contraction with deeper stimulation during tetanus contraction.⁴⁹ This electrode position can produce measurable contractile activity across all 4 quadriceps muscles when assessed by MRI.¹ Longitudinal electrode position can increase torque production of the quadriceps compared with a transverse orientation.³⁴

Neuromuscular electrical stimulation electrodes placed directly over the motor points can deliver optimal treatment but are yet

to be examined in pathological groups.¹⁵ Motor point reference charts provide a general location; however, emerging evidence suggests a great deal of interindividual variability, and the exact location depends on joint angles of the surrounding muscles.^{9,15} By applying the electrodes and providing stimulation directly over the motor point's motor axon, excitation occurs with less amplitude and less chance for excitation of surrounding sensory nerves.^{9,13,15} Motor point stimulation has been found to significantly increase torque production and decrease patient discomfort.¹⁵

By increasing the number of electrodes delivering a stimulus, spatial recruitment is altered and more motor units are stimulated.³⁴ The utilization of multiple-channel electrodes over a single muscle can decrease fatigue and increase in a more complete contraction.¹²

Electrode size also plays a role in discomfort, since it will recruit axonal branches in close proximity.³¹ Electrode sizes vary from 5 × 5 cm³⁸ to 7 × 10 cm,¹⁹ as well as other diameters.²⁷ Increasing electrode size decreases current density, which is related to discomfort.³¹ Electrodes too large might be detrimental as well by stimulating the wrong motor units and reducing the force produced. Electrodes that are approximately 20 cm² produce the most comfortable stimulus for the quadriceps.³¹

Training Effect

Beneficial results have been found over multiple NMES training sessions due to muscular adaptations to the stimulus.^{17,27,47} Repeated exposure to NMES will produce a training effect that decreases patient discomfort, muscular fatigue, and development of creatine kinase and other indirect measures of muscle damage.^{27,47} There is a protective effect with a preconditioning program with decreases in pain, muscle soreness, and creatine kinase levels and an increase in torque production.⁴⁷ Increasing the amplitude during a single treatment between each individual stimulus may stimulate deeper muscle fibers in the quadriceps muscle.³⁴ Tracking alternating amplitude during the rehabilitation program may ensure depolarization of different motor units over multiple treatments and improve muscular adaptation during NMES.³⁴

CONCLUSION

Subtle changes in NMES can create large positive effects in the treatment for the patient. Quadriceps strength may be improved by utilizing optimal parameters (pulse duration between 200 and 400 μ s and a pulse frequency of 30-50 Hz) over multiple NMES sessions and novel stimulus patterns.



Clinical Recommendations

SORT: Strength of Recommendation Taxonomy

A: consistent, good-quality patient-oriented evidence

B: inconsistent or limited-quality patient-oriented evidence

C: consensus, disease-oriented evidence, usual practice, expert opinion, or case series

Clinical Recommendation	SORT Evidence Rating
Utilization of NMES can produce limitations such as fatigue, ^{4,6,7,18,34,49} patient discomfort, ^{10,13,37,38,47,48} and muscle damage. ^{3,22,26,30,32,33,41,47}	A
Minor adjustments in NMES parameters (pulse duration of 400-600 μ s and pulse frequency of 30-50 Hz) can improve torque production, minimize fatigue, and improve patient comfort levels. ^{7,16,19,20,28}	B
Increasing the number of stimulating electrodes and electrode placement over motor points have minimized fatigue and patient discomfort while also improving torque production. ^{9,12,13,15,34}	B
Preconditioning NMES training sessions produce muscular adaptations that improve patient comfort levels, decrease muscular fatigue, and minimize muscle damage. ^{17,27,34,47}	B

REFERENCES

- Adams GR, Harris RT, Woodard D, Dudley GA. Mapping of electrical muscle stimulation using MRI. *J Appl Physiol* (1985). 1993;74:532-537.
- Adams OP. The impact of brief high-intensity exercise on blood glucose levels. *Diabetes Metab Syndr Obes*. 2013;6:113-122.
- Aldayel A, Jubeau M, McGuigan MR, Nosaka K. Less indication of muscle damage in the second than initial electrical muscle stimulation bout consisting of isometric contractions of the knee extensors. *Eur J Appl Physiol*. 2010;108:709-717.
- Bickel CS, Gregory CM, Azuero A. Matching initial torque with different stimulation parameters influences skeletal muscle fatigue. *J Rehabil Res Dev*. 2012;49:323-331.
- Bickel CS, Gregory CM, Dean JC. Motor unit recruitment during neuromuscular electrical stimulation: a critical appraisal. *Eur J Appl Physiol*. 2011;111:2399-2407.
- Binder-Macleod SA, Halden EE, Jungles KA. Effects of stimulation intensity on the physiological responses of human motor units. *Med Sci Sports Exerc*. 1995;27:556-565.
- Binder-Macleod SA, Mcdermond LR. Changes in the force-frequency relationship of the human quadriceps femoris muscle following electrically and voluntarily induced fatigue. *Phys Ther*. 1992;72:95-104.
- Boerio D, Jubeau M, Zory R, Maffiuletti NA. Central and peripheral fatigue after electrostimulation-induced resistance exercise. *Med Sci Sports Exerc*. 2005;37:973-978.
- Botter A, Oprandi G, Lanfranco F, Allasia S, Maffiuletti NA, Minetto MA. Atlas of the muscle motor points for the lower limb: implications for electrical stimulation procedures and electrode positioning. *Eur J Appl Physiol*. 2011;111:2461-2471.
- Broderick BJ, Kennedy C, Breen PP, Kearns SR, ÓLaighin G. Patient tolerance of neuromuscular electrical stimulation (NMES) in the presence of orthopaedic implants. *Med Eng Phys*. 2011;33:56-61.
- Cooke JD, Brown SH. Movement-related phasic muscle activation. II. Generation and functional role of the triphasic pattern. *J Neurophysiol*. 1990;63:465-472.
- Feil S, Newell J, Minogue C, Paessler HH. 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*. 2011;39:1238-1247.
- Forrester B, Petrofsky JS. Effect of electrode size, shape, and placement during electrical stimulation. *J Appl Res*. 2004;4:346-354.
- Glaviano NR, Saliba S. Immediate effect of patterned electrical stimulation on pain and muscle activation in individuals with patellofemoral pain. *J Athl Train*. In press.
- Gobbo M, Maffiuletti NA, Orizio C, Minetto MA. Muscle motor point identification is essential for optimizing neuromuscular electrical stimulation use. *J Neuroeng Rehabil*. 2014;11:17-0003-11-17.
- Gondin J, Giannesini B, Vilmen C, et al. Effects of stimulation frequency and pulse duration on fatigue and metabolic cost during a single bout of neuromuscular electrical stimulation. *Muscle Nerve*. 2010;41:667-678.
- Gondin J, Guette M, Ballay Y, Martin A. Electromyostimulation training effects on neural drive and muscle architecture. *Med Sci Sports Exerc*. 2005;37:1291-1299.
- Gorgey AS, Black CD, Elder CP, Dudley GA. Effects of electrical stimulation parameters on fatigue in skeletal muscle. *J Orthop Sports Phys Ther*. 2009;39:684-692.
- Gorgey AS, Dudley GA. The role of pulse duration and stimulation duration in maximizing the normalized torque during neuromuscular electrical stimulation. *J Orthop Sports Phys Ther*. 2008;38:508-516.
- Gorgey AS, Mahoney E, Kendall T, Dudley GA. Effects of neuromuscular electrical stimulation parameters on specific tension. *Eur J Appl Physiol*. 2006;97:737-744.
- Gregory CM, Dixon W, Bickel CS. Impact of varying pulse frequency and duration on muscle torque production and fatigue. *Muscle Nerve*. 2007;35:504-509.
- Guarascio P, Lusi EA, Soccorsi F. Electronic muscular stimulators: a novel unsuspected cause of rhabdomyolysis. *Br J Sports Med*. 2004;38:505.
- Gulick DT, Castel JC, Palermo FX, Draper DO. Effect of patterned electrical neuromuscular stimulation on vertical jump in collegiate athletes. *Sports Health*. 2011;3:152-157.
- He B. Electrical stimulation for the neuromuscular system. In: He B, ed. *Neural Engineering*. New York, NY: Springer; 2005:157-191.
- Jubeau M, Gondin J, Martin A, Sartorio A, Maffiuletti NA. Random motor unit activation by electrostimulation. *Int J Sports Med*. 2007;28:901-904.
- Jubeau M, Sartorio A, Marinone PG, et al. Comparison between voluntary and stimulated contractions of the quadriceps femoris for growth hormone response and muscle damage. *J Appl Physiol*. 2008;104:75-81.
- Jubeau M, Zory R, Gondin J, Martin A, Maffiuletti NA. Effect of electrostimulation training-detraining on neuromuscular fatigue mechanisms. *Neurosci Lett*. 2007;424:41-46.
- Kesar T, Binder-Macleod S. Effect of frequency and pulse duration on human muscle fatigue during repetitive electrical stimulation. *Exp Physiol*. 2006;91:967-976.
- Liebano RE, Waszczuk S Jr, Correa JB. The effect of burst-duty-cycle parameters of medium-frequency alternating current on maximum electrically induced torque of the quadriceps femoris, discomfort, and tolerated current amplitude in professional soccer players. *J Orthop Sports Phys Ther*. 2013;43:920-926.
- Lieber RL, Friden J. Muscle damage is not a function of muscle force but active muscle strain. *J Appl Physiol* (1985). 1993;74:520-526.
- Lyons GM, Leane GE, Clarke-Moloney M, O'Brien JV, Grace PA. An investigation of the effect of electrode size and electrode location on comfort during stimulation of the gastrocnemius muscle. *Med Eng Phys*. 2004;26:873-878.
- Mackey AL, Bojsen-Moller J, Qvortrup K, et al. Evidence of skeletal muscle damage following electrically stimulated isometric muscle contractions in humans. *J Appl Physiol* (1985). 2008;105:1620-1627.
- Mackey AL, Brandstetter S, Schjerling P, et al. Sequenced response of extracellular matrix deadhesion and fibrotic regulators after muscle damage is involved in protection against future injury in human skeletal muscle. *FASEB J*. 2011;25:1943-1959.

34. Maffiuletti NA. Physiological and methodological considerations for the use of neuromuscular electrical stimulation. *Eur J Appl Physiol*. 2010;110:223-234.
35. Maffiuletti NA, Bramanti J, Jubeau M, Bizzini M, Deley G, Cometti G. Feasibility and efficacy of progressive electrostimulation strength training for competitive tennis players. *J Strength Cond Res*. 2009;23:677-682.
36. Maffiuletti NA, Cometti G, Amiridis IG, Martin A, Pousson M, Chatard JC. The effects of electromyostimulation training and basketball practice on muscle strength and jumping ability. *Int J Sports Med*. 2000;21:437-443.
37. Maffiuletti NA, Herrero AJ, Jubeau M, Impellizzeri FM, Bizzini M. Differences in electrical stimulation thresholds between men and women. *Ann Neurol*. 2008;63:507-512.
38. Maffiuletti NA, Morelli A, Martin A, et al. Effect of gender and obesity on electrical current thresholds. *Muscle Nerve*. 2011;44:202-207.
39. Maffiuletti NA, Vivodtzev I, Minetto MA, Place N. A new paradigm of neuromuscular electrical stimulation for the quadriceps femoris muscle. *Eur J Appl Physiol*. 2014;114:1197-1205.
40. McCrea DA, Rybak IA. Organization of mammalian locomotor rhythm and pattern generation. *Brain Res Rev*. 2008;57:134-146.
41. Nosaka K, Aldayel A, Jubeau M, Chen TC. Muscle damage induced by electrical stimulation. *Eur J Appl Physiol*. 2011;111:2427-2437.
42. Packman-Braun R. Relationship between functional electrical stimulation duty cycle and fatigue in wrist extensor muscles of patients with hemiparesis. *Phys Ther*. 1988;68:51-56.
43. Palmieri-Smith RM, Thomas AC, Karvonen-Gutierrez C, Sowers M. A clinical trial of neuromuscular electrical stimulation in improving quadriceps muscle strength and activation among women with mild and moderate osteoarthritis. *Phys Ther*. 2010;90:1441-1452.
44. Petterson S, Snyder-Mackler L. The use of neuromuscular electrical stimulation to improve activation deficits in a patient with chronic quadriceps strength impairments following total knee arthroplasty. *J Orthop Sports Phys Ther*. 2006;36:678-685.
45. Rhea MR, Alvar BA, Burkett LN, Ball SD. A meta-analysis to determine the dose response for strength development. *Med Sci Sports Exerc*. 2003;35:456-464.
46. Rooney JG, Currier DP, Nitz AJ. Effect of variation in the burst and carrier frequency modes of neuromuscular electrical stimulation on pain perception of healthy subjects. *Phys Ther*. 1992;72:800-806.
47. Vanderthommen M, Chamayou R, Demoulin C, Crielaard JM, Croisier JL. Protection against muscle damage induced by electrical stimulation: efficiency of a preconditioning programme. *Clin Physiol Funct Imaging*. 2015;35:267-274.
48. Vanderthommen M, Triffaux M, Demoulin C, Crielaard JM, Croisier JL. Alteration of muscle function after electrical stimulation bout of knee extensors and flexors. *J Sports Sci Med*. 2012;11:592-599.
49. Zory R, Boërio D, Jubeau M, Maffiuletti NA. Central and peripheral fatigue of the knee extensor muscles induced by electromyostimulation. *Int J Sports Med*. 2005;26:847-853.

For reprints and permission queries, please visit SAGE's Web site at <http://www.sagepub.com/journalsPermissions.nav>.