EFFECTS OF MULTIPATH AND CONVENTIONAL NMES ON MAXIMUM COMFORTABLE STIMULUS AND TORQUE PRODUCTION

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Abstract

A novel multipath NMES (m-NMES) device has shown improved outcomes relative to conventional NMES (c-NMES) during recent basic and training studies. However, the mechanisms by which m-NMES outperformed c-NMES remain unclear. This study aimed to better understand these mechanisms by comparing the effects of m-NMES and c-NMES on maximum comfortable stimulus intensity and the subsequent NMES-induced torque, as these variables ultimately impact NMES training intensity, which is considered to be the primary determinant of NMES effectiveness.

We measured maximum comfortable stimulus intensity and the subsequent NMES-induced torque while participants performed NMES-induced contractions under two conditions (m-NMES and c-NMES). Maximum comfortable stimulus intensity was significantly greater under the m-NMES condition, but the subsequent NMES-induced torque was not significantly different across conditions.

m-NMES does not appear to influence the outcomes in a clinically meaningful manner, since it performed similarly to c-NMES with respect to peak NMES-induced torque.

Key words multipath, NMES, quadriceps

Introduction

Neuromuscular electrical stimulation (NMES) treatments are common in orthopedic clinical settings as they can be used for a variety of purposes (Gondin, Cozzone, Bendahan, 2011; Holcomb, 1997; Lake, 1992). Despite this versatility, NMES is most often used for the specific goal of enhancing muscular strength. The effectiveness of NMES for this purpose is believed to be primarily determined by NMES training intensity (Maffiuletti, 2010; Maffiuletti, Minetto, Farina, Bottinelli, 2011), which is often defined as the ratio of NMES-induced torque to torque produced during a maximum voluntary isometric contraction (expressed as % MVIC) (Gondin et al., 2011). Accordingly, clinicians are encouraged to maximize NMES training intensities to the degree possible (Maffiuletti,
2010), but the ability to achieve and maintain appropriate NMES training intensities is limited by a variety of factors; which include: patient discomfort (Gobbo, Maffiuletti, Orizio, Minetto, 2014; Gondin et al., 2011; Maffiuletti, 2010), muscle fatigue (Doucet, Lam, Griffin, 2012; Lauffer, Elboim, 2008; Maffiuletti, 2010; Maffiuletti, Vivodtzev, Minetto, Place, 2014) and spatially limited motor unit recruitment (Gobbo et al., 2014; Maffiuletti, 2010; Maffiuletti et al., 2014).

The Kneehab® XP (Theragen LLC, Leesburg, VA) is an electrical stimulator that has received substantial attention in the literature (Asakawa, Jung, Koh, 2014; Bremner Holcomb, In-press; Bruce-Brand et al., 2012; Coote, Hughes, Rainsford, Minogue, Donnelly, 2015; Feil, Newell, Minogue, Paessler, 2011; Maffiuletti et al., 2014; Morf, Wellauer, Casartelli, Maffiuletti, 2015; Paessler, 2012; Walls, McHugh, O’Gorman, Moyna, O’Byrne, 2010), because it implements a novel strategy designed to address the aforementioned primary factors limiting NMES training intensity (Neurotech®, 2012a; Paessler, 2012; Walls et al., 2010). The stimulator uses multipath™ technology, which distributes the electrical current between four large electrodes integrated within a neoprene thigh garment via two separate channels while also altering pulse durations (Maffiuletti et al., 2014; Morf et al., 2015; Paessler, 2012; Walls et al., 2010); thus it is referred to as multipath NMES (m-NMES). In contrast, conventional NMES (c-NMES) stimulators distribute the electrical current in each channel via a single fixed path between a pair of electrodes. It has been suggested that m-NMES is advantageous because it provides an asynchronous stimulus and improves spatial distribution through dynamically changing the pathways by which current is distributed and by dynamically altering the pulse duration (Feil et al., 2011; Gobbo et al., 2014).

For example, greater spatial distribution of the NMES stimulus may result in greater torque production, as improved spatial distribution may maximize the number of motor units recruited by the stimulus (Maffiuletti et al., 2014). To date, a single randomized controlled trial comparing the use of m-NMES and c-NMES on clinical outcomes has been completed, with S. Feil et al. (2011) observing greater improvements following ACL reconstruction while using the m-NMES device. However, the authors acknowledged that the mechanism(s) responsible for their observations remain unclear. Subsequent basic studies have attempted to identify the possible mechanism(s) by which m-NMES outperformed c-NMES, with mixed results. Two studies comparing m-NMES and c-NMES observed improved fatigue and discomfort related outcomes while using m-NMES (Maffiuletti et al., 2014; Morf et al., 2015), but substantially different electrode configurations were used across conditions; thus the authors’ ability to attribute their observations to the novel multipath current distribution method was limited. Consequently, a similar basic study was performed in our laboratory while using similar electrode configurations because this approach allowed us to better examine the influence of the novel multipath current distribution method on these outcomes (Bremner, Holcomb, in-press). Using this approach, we did not observe any clinically relevant differences across the two conditions.

We standardized the NMES stimulus intensity across conditions during our previous study to limit baseline differences, which is necessary when comparing fatigue and discomfort related outcomes. However, this methodology did not allow us to examine differences in maximum comfortable stimulus intensity and the subsequent NMES-induced torque; which are also important outcomes when comparing NMES treatment conditions because they impact NMES training intensity (Bremner, Holcomb, Brown, 2015; Dantas, Vieira, Siqueira, Salvini, Durigan, 2015; Holcomb, Golestani, Hill, 2000). To the best of our knowledge, the influence of m-NMES on maximum comfortable stimulus intensity and the subsequent NMES-induced torque while using similar electrode configurations has yet to be examined. Each of these outcome measures are clinically relevant and warrant further investigation, as they ultimately impact the NMES training intensity. Therefore, the purpose of this study is to compare the effects
of m-NMES and c-NMES on the clinically relevant maximum comfortable stimulus intensity and subsequent NMES-induced torque outcomes. We hypothesize that the maximum comfortable stimulus intensity and subsequent NMES-induced torque will be greater while using m-NMES.

**Methods**

**Design**

We performed a single-blind counterbalanced crossover study with 1 independent variable (NMES condition at 2 levels: m-NMES and c-NMES) and 2 dependent variables (maximum comfortable stimulus intensity and NMES-induced torque). We assigned participants to one of two permutations designed to counterbalance the session order in which the c-NMES and m-NMES treatment conditions were performed.

**Participants**

We performed an *a priori* power analysis using G*Power software (version 3.1.9.2) to determine a target sample size (Faul, Erdfelder, Lang, Buchner, 2007). We determined a target sample size of 17 participants in order to maintain adequate power (1 – β = 0.80) and detect a medium to large effect size (d = 0.650) while using a dependent *t*-test (Cohen, 1988). We selected medium to large effect sizes for the power analysis because we believe that any statistically significant differences with corresponding effect sizes smaller than this threshold would lack clinical relevance for the outcomes included in our study.

A convenience sample of 21 participants (age = 23.9 ±5.1 years, height = 175.1 ±7.4 cm, mass = 78.1 ±11.7 kg, BMI = 25.3 ±2.6 kg/m²) from the university and community completed two study sessions. As has been done previously (Gorgey, Dudley, 2008), participants in our current study had prior NMES experience due to their participation in an earlier study (Bremner Holcomb, In-press). We elected to use participants from a previous study because an individual’s tolerance to NMES is likely to improve over the first few exposures to NMES treatments (Alon, Smith, 2005).

Participants were required to be healthy, recreationally active, males, between the ages of 18–35. Participants also had to have a body mass index (BMI) ≤30 kg/m² to be included, as NMES tolerance and motor thresholds have been shown to differ between individuals with a BMI above and below 30 kg/m² (Maffiuletti, Morelli, et al., 2011). To be included in our current study participants had to tolerate a NMES training intensity of at least 30% MVIC during a previous study. This study was approved by the University’s institutional review board and participants provided written informed consent. To facilitate participant recruitment, we incentivized participants via a lottery for a chance to win one of four $50 gift cards.

**Instrumentation**

We used a Quickset 4 Biodex dynamometer (Biodex Medical Systems Inc., Shirley, New York) to measure and record isometric knee extension torque following procedures used previously (Bremner, Holcomb, In-press). We applied the c-NMES treatment using the same Sonicator® Plus 940 stimulator (Mettler Electronics® Corp., Anaheim, CA). To maintain consistency across the two NMES conditions, we set the c-NMES parameters as similar as possible to the parameters used with the Kneehab® XP program 6 (Table 1). We used four self-adherent electrodes to deliver the c-NMES current (two – 5 cm × 9 cm [Metron™, Bolingbrook, IL], one – 10.79 cm × 17.78 cm...
[TENS Products, Grand Lake, CO], one – 7 cm × 14 cm electrode (SME INC., Wilmington, NC; Figure 1). To guide the placement of the c-NMES electrodes, we manually identified four motor points that would allow us to place the c-NMES electrodes in a similar fashion to the m-NMES electrode configuration (proximal and distal vastus lateralis, proximal rectus femoris and distal vastus medialis) using a pencil electrode (Mettler Electronics XK2, Active Forever, Scottsdale, AZ; Figure 2) (Gobbo et al., 2014).

Note: c-NMES electrodes are on the left side of the photo and m-NMES electrodes are integrated into the neoprene garment on the right side of the photo.

Figure 1. Electrode Configuration Comparison

Note: the photo illustrates the pencil electrode method for manually identifying motor points.

Figure 2. Motor Point Identification

We applied the m-NMES treatment using the same Kneehab® XP stimulator (Theragen LLC, Leesburg, VA), however we assigned each participant a separate Kneehab® XP garment with integrated electrodes. We integrated the m-NMES electrodes into the neoprene garment and subsequently placed the garment on the dominant thigh.
according to the manufacturer’s recommendations (Figure 3) (Neurotech®, 2012b). We set the stimulator parameters to program 6 during all m-NMES treatments (Table 1).

**Table 1. Parameters of Neuromuscular Electrical Stimulation Conditions**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>m-NMES</th>
<th>c-NMES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current distribution</td>
<td>Multipath</td>
<td>Single path within two independent channels</td>
</tr>
<tr>
<td>Waveform</td>
<td>Biphasic Square</td>
<td>Biphasic Square</td>
</tr>
<tr>
<td>Frequency</td>
<td>70 Hz</td>
<td>70 Hz</td>
</tr>
<tr>
<td>Pulse duration</td>
<td>400/100 µsec</td>
<td>400 µsec</td>
</tr>
<tr>
<td>Ramp</td>
<td>1 second up : 0.5 seconds down</td>
<td>1 second up : 0 seconds down*</td>
</tr>
<tr>
<td>On time/off time</td>
<td>10 s/50 s</td>
<td>10 s/50 s</td>
</tr>
<tr>
<td>Stimulus intensity</td>
<td>Maximum comfortable</td>
<td>Maximum comfortable</td>
</tr>
<tr>
<td>Number of electrodes</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Total area of electrodes</td>
<td>427 cm²</td>
<td>360 cm²*</td>
</tr>
</tbody>
</table>

* It was not possible to select a ramp-down of 0.5 seconds with this particular c-NMES device while also maintaining a similar ramp-up and hold time to the m-NMES device, thus a ramp-down was not included. A slightly smaller total area of electrodes was used during the c-NMES condition.

**Procedures**

Participants reported at the same time of day (±2 hours) on two occasions and each session lasted approximately 1 hour. Each participant’s dominant leg, which was defined as the leg with which they would use to kick a soccer ball, served as the leg of interest throughout the study (20 right, 1 left). We also instructed participants to report well hydrated and to refrain from strenuous activities for 12 hours prior to reporting.

Each session began with the participants completing a standardized warm-up following procedures used previously (Bremner, Holcomb, in-press). Participants rested for 8 minutes following the warm-up, during which we identified the motor points using the pencil electrode method and cleaned the leg of interest with an alcohol free wipe. Although motor point identification was not necessary for the m-NMES condition because the electrodes were integrated within the garment, we still identified motor points during both sessions in an effort to blind participants to treatment condition.

To continue the warm-up, participants performed maximum voluntary isometric contractions (MVICs) of the quadriceps for 6 seconds in duration and then rested for 5 minutes prior to performing the NMES procedures, during which we placed the Kneehab® XP garment with integrated electrodes or the c-NMES electrodes over the participant’s shaved dominant thigh. We also placed an empty Kneehab® XP garment over the c-NMES electrodes in an effort to blind participants to treatment condition (Figure 3) (Morf et al., 2015). As has been done previously to limit fatigue (Bremner et al., 2015), participants performed a single NMES-induced contraction during each session (c-NMES or m-NMES) while using a self-selected maximum comfortable stimulus intensity; which is defined as the highest intensity that does not cause pain (Holcomb, Rubley, Girouard, 2007). The maximum comfortable stimulus intensity was determined following procedures used previously (Figure 3) (Bremner, Holcomb, in-press).
Outcome Measures

Maximum Comfortable Stimulus Intensity. We manually recorded the maximum comfortable stimulus intensity selected by each participant (expressed in milliamps [mA]). The m-NMES device does not express the stimulus intensity in mA units, thus a conversion table provided by the manufacturer was used to convert the observed m-NMES stimulus intensities into the appropriate units.

Normalized NMES-induced Torque. The isokinetic dynamometer measured and recorded the NMES-induced peak torque under each condition. In an effort to reduce inter-participant variability, we normalized the NMES-induced peak torque values to each participant’s body mass, which converts the unit of measure to Newton-meters per kilogram (Nm/kg) and has been done previously (Bremner et al., 2015; Holcomb et al., 2000).

Statistical Analysis

We used the Statistical Package for Social Sciences (SPSS) version 23.0 (IBM Corporation, Armonk, NY) to analyze the data. We performed a separate dependent t-test to analyze each outcome measure. To examine the magnitude of the differences, we calculated Cohen’s d effect sizes (Cohen, 1988). We calculated Cohen’s d effect sizes corresponding to within groups comparisons using the equation suggested by Cumming (2012) which uses the average standard deviation of the paired data as the standardizer (d_{sav}). Since d statistics are believed to overestimate the population effect size, Cumming recommended that an unbiased Cohen’s d (d_{unb}) also be provided. Accordingly, we calculated d_{unb} values using the equation provided by Cumming.
Results

Prior to analyzing the data, we assessed the tenability of the applicable statistical assumptions, and the data were considered to be normally distributed without any outliers.

Maximum Comfortable Stimulus Intensity

The maximum comfortable stimulus intensity (mA) was significantly higher during the m-NMES condition ($t_{20} = 2.817; P = 0.006; d = 0.581; 95\%\ CI$ for effect size: $-0.133, 1.018; d_{unb} = 0.559$; Figure 4).

Note: * Significantly greater maximum comfortable stimulus intensity ($P = 0.006$). Error bars indicate 95% confidence intervals calculated using a critical $t$-value as has been recommended (Cumming, 2012).

Figure 4. Maximum Comfortable Stimulus Intensity

Note: error bars indicate 95% confidence intervals and were calculated using a critical $t$-value as has been recommended (Cumming, 2012).

Figure 5. Initial Normalized NMES-induced Peak Torque
Normalized NMES-induced Torque

The normalized NMES-induced torque (Nm/kg) was not significantly different across conditions ($t_{20} = 1.397$; $P = 0.089$; $d = 0.282$; 95% CI for effect size: -0.125, 0.683; $d_{unb} = 0.272$; Figure 5).

Discussion

While using similar electrode configurations, the findings of our study indicate that the maximum comfortable stimulus intensity was significantly higher under the m-NMES condition. However, the higher stimulus intensity did not result in significantly greater NMES-induced torque production during the subsequent NMES-induced contraction. Due to the positive linear relationship between stimulus intensity and NMES-induced torque (Adams, Harris, Woodard, Dudley, 1993; Gorgey, Mahoney, Kendall, Dudley, 2006; Maffiuletti, 2010), the primary clinical objective of using higher stimulus intensities is to enhance the NMES training intensity by increasing NMES-induced torque production. Therefore, the greater maximum comfortable stimulus intensity that we observed during the m-NMES condition does not appear to be clinically meaningful.

Despite our efforts to standardize the electrode configurations, the m-NMES electrodes covered an area of 427 cm$^2$ while the c-NMES electrodes covered a surface area of roughly 360 cm$^2$ (Morf et al., 2015). Since the current was spread over a greater area during the m-NMES condition, the current density (mA/cm$^2$) was subsequently lower during this condition while using the same amount of current (Hooker, 2003). We observed similar values when normalizing the mean stimulus intensities by total electrode area for each condition (m-NMES = 0.16 mA/cm$^2$, c-NMES = 0.17 mA/cm$^2$). Therefore, the difference in electrode sizes is a possible explanation as to why we did not observe significantly greater NMES-induced torque during the m-NMES condition. Although a small difference in the area covered by c-NMES and m-NMES remained during our study (Figure 1), the c-NMES electrode configurations used during previous studies consisted of three electrodes covering only 100 cm$^2$ (Maffiuletti et al., 2014; Morf et al., 2015).

The maximum comfortable stimulus intensities we observed under the m-NMES and c-NMES conditions were 69.1 ±11.3 mA and 62.5 ±11.6 mA, respectively (Figure 4). During a similar study Maffiuletti et al. (2014) reported values of 92 ±25 mA and 53 ±25 mA during their m-NMES and c-NMES conditions. Despite the fact that both of these studies observed significantly greater stimulus intensities under the m-NMES condition, the mean stimulus intensity we observed during m-NMES is much smaller. Two likely explanations for this difference are that Maffiuletti et al. used a maximum tolerable stimulus intensity and a modified m-NMES device that allowed a maximum current output of 200 mA. We elected to use a lower threshold maximum comfortable stimulus intensity because it has been suggested to be more clinically relevant (Holcomb et al., 2007). In addition, Maffiuletti et al. acknowledged that their use of a modified research version of the m-NMES device was a limitation of their study, as it is not available to clinicians, so we elected to use the clinically available m-NMES device with a maximum output of only 79.2 mA.

During the m-NMES and c-NMES conditions we observed normalized NMES-induced torque values of 1.4 ±0.6 Nm/kg and 1.3 ±0.5 Nm/kg, respectively (Figure 5). It is difficult for us to directly compare these values to similar studies comparing m-NMES and c-NMES because normalized torque values were not reported (Maffiuletti et al., 2014; Morf et al., 2015). To facilitate the comparison of our results to these previous studies, we converted the normalized NMES-induced torque values to NMES training intensities using the values recorded during the warm-up MVICs. The subsequent training intensities were 47.9 ±17.1% MVIC and 43.6 ±13.8% MVIC for m-NMES and c-NMES.
respectively. Interestingly, our observed values are near the upper margin of the proposed therapeutic window of 25–50% MVIC (Alon, Smith, 2005). This observation suggests that both devices are capable of producing the torque required for effective NMES treatments, which may be of interest to clinicians as the m-NMES device is portable.

Although the previous studies comparing torque output across m-NMES and c-NMES conditions used a higher threshold maximum tolerable stimulus intensity (Maffiuletti et al., 2014; Morf et al., 2015), the NMES training intensities we observed are comparable to values reported during these studies; which ranged from roughly 35–45% MVIC. Despite using a lower threshold maximum comfortable stimulus intensity, we believe that the comparable NMES training intensities observed during our study are due to the participants’ previous NMES experience, as this likely allowed participants to better acclimate to the NMES stimulus prior to participation in our current study (Alon, Smith, 2005). In contrast, one of the other studies comparing m-NMES and c-NMES did not incorporate familiarization sessions and the other included a single familiarization session (Maffiuletti et al., 2014; Morf et al., 2015).

Although we observed a significantly greater maximum comfortable stimulus intensity under the m-NMES condition, we did not observe a significant difference with respect to the NMES-induced torque across the two conditions. This observation is contrary to the results of previous studies (Maffiuletti et al., 2014; Morf et al., 2015), and methodological differences between our study and the previous studies warrant further discussion. Maffiuletti et al. and Morf et al. hypothesized that a possible mechanism for the significantly greater NMES-induced torque they observed during m-NMES was the novel multipath current distribution method. Maffiuletti et al. suggested that relative to the fixed single path current distribution method of c-NMES, a larger number of motor units may have been recruited during the m-NMES condition due to its greater spatial distribution of the stimulus. However, the m-NMES and c-NMES conditions during these studies differed in two systematic ways, which were the current distribution method and electrode configuration. Morf et al. indicated that as a result of these two systematic differences, it is unclear whether the greater NMES-induced torque they observed was primarily attributable to the multipath current distribution method, larger electrodes or a combination of these factors. Consequently, we standardized the electrode configuration across conditions to the extent possible during our study, as we believe this approach allowed us to better isolate the influence of current distribution method on NMES-induced torque. Since we did not observe significantly greater NMES-induced torque under the m-NMES condition, our results do not support the hypothesis of Maffiuletti et al. and Morf et al. that the multipath current distribution method is a possible mechanism by which m-NMES resulted in greater NMES-induced torque during their studies.

**Limitations**

Eight participants reached the output capacity of the m-NMES device prior to achieving their maximum comfortable threshold during our study. This likely prevented these participants from reaching their true maximum comfortable stimulus intensity during the m-NMES condition, and this may have subsequently reduced the magnitude of our observed effect. Although incorporating the clinically available device during our study may be viewed as a limitation, we feel that it ultimately enhances the clinical applicability of our findings; as the device used in previous studies is a modified version allowing 200mA, but is not available to clinicians.

The extent to which our results are generalizable is unclear, due to our use of healthy participants and exclusion of females. The menstrual cycle has been shown to influence self-reported discomfort levels (Teepker, Peters, Vedder, Schepelmann, Lautenbacher, 2010), thus due to our study design requiring repeated measurements over time we felt it was necessary to exclude females. In addition, during exploratory NMES studies, similar in nature to our study, it is
common practice to use healthy participants (Alon, Smith, 2005; Dantas et al., 2015; Gorgey, Dudley, 2008; Holcomb et al., 2007; Holcomb, Rubley, Miller, Girouard, 2006; Holcomb, Rubley, Randolph, 2011; Maffiuletti et al., 2014).

Conclusions

The results of our study do not indicate that the novel multipath current distribution method improves the outcomes included in our study in a clinically meaningful manner. Contrary to our results, similar previous studies have observed improved outcomes when comparing m-NMES and c-NMES (Maffiuletti et al., 2014; Morf et al., 2015). We believe it is likely that contributing factors for their improved outcomes were differences in electrode configuration and their use of a modified version of the device not available to clinicians; rather than the novel current distribution method.

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References


