Wide-pulse-high-frequency neuromuscular stimulation of triceps surae induces greater muscle fatigue compared with conventional stimulation

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Submitted 5 September 2013; accepted in final form 26 March 2014

Wide-pulse-high-frequency neuromuscular stimulation of triceps surae induces greater muscle fatigue compared with conventional stimulation. J Appl Physiol 116: 1281–1289, 2014. First published March 27, 2014; doi:10.1152/japplphysiol.01015.2013.—We compared the extent and origin of muscle fatigue induced by short-pulse-low-frequency (conventional [CONV]) and wide-pulse-high-frequency (WPHF) neuromuscular electrical stimulation. We expected CONV contractions to mainly originate from depolarization of axonal terminal branches (spatially determined muscle fiber recruitment) and WPHF contractions to be partly produced via a central pathway (motor unit recruitment according to size principle). Greater neuromuscular fatigue was, therefore, expected following CONV compared with WPHF. Fourteen healthy subjects underwent 20 WPHF (1 ms–100 Hz) and CONV (50 μs–25 Hz) evoked isometric triceps surae contractions (work/rest periods 20:40 s) at an initial target of 10% of maximal voluntary contraction (MVC) force. Force-time integral of the 20 evoked contractions (FTI) was used as main index of muscle fatigue. MVC force loss was also quantified. Central and peripheral fatigue were assessed by voluntary activation level and paired stimulation amplitudes, respectively. FTI in WPHF was significantly lower than in CONV (21.717 ± 11.541 vs. 37.958 ± 9.898 N·s P<0.001). The reductions in MVC force (WPHF: −7.0 ± 2.7%; CONV: −6.2 ± 2.5%; P<0.01) and paired stimulation amplitude (WPHF: −8.0 ± 4.0%; CONV: −7.4 ± 6.1%; P<0.001) were similar between conditions, whereas no change was observed for voluntary activation level (P>0.05). Overall, our results showed a different motor unit recruitment pattern between the two neuromuscular electrical stimulation modalities with a lower FTI indicating greater muscle fatigue for WPHF, possibly limiting the presumed benefits for rehabilitation programs.

NEUROMUSCULAR ELECTRICAL STIMULATION (NMES) is widely used in rehabilitation to prevent/minimize muscle mass and force loss. Conventional NMES with muscle surface electrodes does not recruit motor units according to the size principle (which states that smaller, fatigue-resistant motor units are recruited before larger, more fatigable ones) (20). NMES leads to random recruitment of fast- and slow-twitch muscle fibers by depolarizing terminal motoneuronal branches, with the main factor influencing their recruitment being their distance and orientation toward the stimulating electrodes (19), but not motor unit size. This results in a greater involvement of fast-twitch muscle fibers for any given level of force compared with voluntary contractions. Furthermore, contrary to volitional efforts during which motor units fire out of phase and at low frequency to minimize fatigue (5), NMES induces synchronous activation of muscle fibers and, therefore, requires high stimulation frequencies to obtain fused contractions (19). This altered recruitment pattern is associated with high metabolic demand (e.g., Ref. 32), and the ensuing muscle fatigue, which has been defined as exaggerated, is an important limiting factor of NMES.

Traditional NMES current characteristics [hereafter referred to as conventional (CONV)] consist of relatively short pulse durations (<400 μs) delivered at low to moderate stimulation frequencies (15–40 Hz) and high stimulation intensities (9), which elicit depolarization of the sarcolemma and muscle contraction mainly through the orthodromic activation of terminal motoneuron axon branches in the muscle. Short pulses preferentially activate motor axons as they present a lower strength-duration time constant than sensory fibers (22, 26), and the use of relatively high stimulation intensities leads to a large antidromic volley blocking any orthodromic action potentials descending from the spinal cord (3, 13). Recently, a different NMES modality was suggested to overcome some of the limitations of CONV NMES (10, 11, 13). The combination of large pulse durations (~1 ms) with high stimulation frequencies (>80 Hz) [hereafter referred to as wide-pulse-high-frequency (WPHF) NMES] was reported to result in contractions partly originating from a central pathway (10, 11, 13). This was supported by the presence of H reflexes and asynchronous activity (2), allegedly resulting from large-diameter afferent sensory fiber depolarization and reflex activation of motor axons in the spinal cord, which would follow the size principle (9). Such sensory fiber activation is favored by the use of wide pulses, as they have a longer strength-duration time constant and a lower rheobase compared with terminal axonal branches of motoneurons (22, 26, 33). At low force levels [5–10% of maximal voluntary contraction (MVC)], WPHF has been shown to induce a progressive increase in electrically evoked force, despite constant stimulation intensity (the so-called “extra force”), in some cases reaching >40% MVC (2, 9), suggesting progressive recruitment of slow-twitch motor units. Consequently, as a result of this potential slow-twitch motor unit recruitment, less muscle fatigue could be expected, despite greater force production. In contrast, the presumably higher involvement of the central nervous system (reflex loop) in WPHF could lead to a higher degree of central fatigue. Since
the effectiveness of CONV NMES is linearly related to the level of evoked force (24, 25) and is limited by the magnitude and early onset of fatigue (32), it follows that, if a central recruitment occurs, the use of WPHF NMES may be highly beneficial for clinical use.

The present study was designed to assess whether central recruitment occurred during WPHF and CONV contractions and to compare the extent and origin of muscle fatigue induced by both stimulation paradigms in the plantar flexor muscles. Based on the theoretical differences in motor unit recruitment by both stimulation paradigms in the plantar flexor muscles. Furthermore, if a different recruitment occurs in WPHF, with reflexively induced spinal recruitment of motor units, we hypothesized that central fatigue may contribute more to the fatigue generated by WPHF compared with CONV, for which peripheral alterations would prevail.

METHODS

Subjects

Fourteen healthy subjects (11 men, 3 women; 27 ± 4 yr; 175 ± 5 cm; 72 ± 9 kg) took part in this study after having been informed of the experimental procedures and possible risks. They were physically active without being enrolled in any regular training. The study protocol was approved by the Ethics Committee of the Geneva University Hospital (protocol 11–287) and was in accord with the latest update of the Helsinki Declaration. All subjects gave written, informed consent before their participation.

Experimental Protocol

After participating in a familiarization session, subjects were asked to visit the laboratory on two occasions separated by 9 ± 6 days to avoid residual fatigue. On both occasions, neuromuscular function was evaluated before and immediately after a series of NMES fatiguing contractions evoked by WPHF or CONV. The order was counterbalanced between subjects. All experiments were performed on the dominant leg, which was determined according to the revised Waterloo questionnaire (15) during the familiarization session.

At subject arrival on test days, after surface electromyography (EMG) and stimulating electrodes placement, supramaximal stimulation intensity for tibial nerve stimulation was determined. Thereafter, the position of all EMG and stimulation electrodes was marked on the muscle belly with an interelectrode (center-to-center) distance of 2 cm. The reference electrode was placed over the ipsilateral patella. The position of all EMG electrodes was tolerated between the two last MVCs during which paired stimuli at 100 Hz were delivered to evoke a superimposed doublet. All MVCs were followed by paired stimuli at 100 Hz (2 s after the MVC) to evoke a potentiated resting doublet and a twitch, as in the prefatigue tests.

Data Collection

Force recordings. Voluntary and evoked forces developed by the plantar flexors were recorded using an isometric ergometer consisting of a custom-built chair equipped with a pedal coupled to a strain gauge (S2 1,000 N, sensitivity 2 mV/V, HBM). Subjects were seated on the chair with the foot strapped to the pedal at the ankle and metatarsal levels. Angles were 90° at the ankle and knee joints and 100° between the trunk and the thigh. To limit the contribution of muscle groups other than plantar flexors, the thigh was clamped down to the chair proximal to the knee, while harnesses limited upper body movements. Force signals were recorded at 1 kHz using an analog-to-digital conversion system (MP150, BIOPAC, Goleta, CA).

Evoked contractions. Electrical stimuli were delivered to the triceps surae muscle belly (for NMES purposes) and to the tibial nerve (for testing purposes) by using a high-voltage (maximal voltage 400 V) constant-current stimulator (model DS7AH, Hertfordshire, UK). For NMES, two large electrodes (10 × 5 cm, Compex, Ecublens, Switzerland) were placed over the gastrocnemius (~5 cm below the popliteal fossa) and soleus (~10 cm above the calcanean) muscles, as described by Collins et al. (10, 11). Current characteristics were 100-Hz frequency/1-ms pulse duration for WPHF and 25-Hz frequency and 50-μs pulse duration for CONV. The intensity was set to evoke an initial force level corresponding to 10% MVC for a train lasting for 1 s. For tibial nerve stimulation, single and paired pulses lasting 1 ms were delivered through a circular cathode (1-cm diameter, Kendall Meditrace 100, Tyco) positioned in the popliteal fossa. The anode (5 × 10 cm, Compex, Ecublens, Switzerland) was placed on the anterior surface of the knee. The optimal intensity of stimulation was considered to be reached when no further increase in peak twitch force nor in any of the agonist M-wave amplitudes was observed, despite a current increase of 20 mA. The optimal stimulation intensity was then further increased by 20% to ensure supramaximal stimulation.

EMG recordings. The EMG activity of the soleus gastrocnemius lateralis, and gastrocnemius medialis was recorded using pairs of silver chloride (Ag-AgCl) circular (recording diameter: 1 cm) surface electrodes (Kendall Meditrace 100, Tyco) positioned lengthwise over the muscle belly with an interelectrode (center-to-center) distance of 2 cm. The reference electrode was placed over the ipsilateral patella. The position of all EMG and stimulation electrodes was marked on the skin with indelible ink to allow identical repositioning in the second session. To obtain low interelectrode resistance (<10 kΩ), the skin was shaved and cleaned with alcohol. EMG signals were amplified (gain = 1,000) with a frequency window between 10 and 500 Hz, digitized at a sampling frequency of 2 kHz, and recorded by the analog-to-digital conversion system. Isometric force and EMG data were stored and analyzed offline with commercially available software (AcqKnowledge, BIOPAC, Goleta, CA).

Discomfort. A horizontal visual analog scale (100 mm) was shown to the subject after the 1st and after the 19th evoked contraction. Subjects placed a vertical mark between “no discomfort” (0 mm) and “worst possible discomfort” (100 mm) to rate the discomfort induced by NMES.

Data Analysis

Force data. Isometric MVC force was considered as the highest force attained during the contraction. Before the fatigue inducing task, the MVC producing the highest force was used for all of the following analyses. The pre-to-postfatigue MVC force loss was considered as an index of global muscle fatigue (8). Maximal voluntary activation level (VAL; main index of central fatigue) was estimated according to the following formula:

\[
\text{VAL} = \frac{\text{MVC}_{\text{post}}}{\text{MVC}_{\text{pre}}} 
\]

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VAL = \left[ 1 - \left( \text{superimposed doublet amplitude/} \text{resting doublet amplitude} \right) \right] \times 100 \quad (I)

When the superimposed doublet was elicited slightly below the actual MVC force, a correction was consistently applied to this formula \((31)\). Contractile properties were assessed with potentiated twitch and doublet amplitudes evoked on a relaxed muscle following the highest prefatigue MVC. Doublet amplitude changes were considered as the main index of peripheral fatigue, as doublets have been reported to be more reliable than twitches [which, therefore, were considered as a secondary index of peripheral fatigue \((28)\)].

The force-time integral (FTI) of each contraction evoked by NMES and the sum of the 20 evoked contractions (total FTI) were also quantified for both conditions as a surrogate of fatigue of the recruited motor units. Since sustained force after cessation of NMES has been considered as evidence of central recruitment \((23)\), we measured the time between the end of the stimulation (no more stimulation artifact observed on the EMG channel) and the return of the force to baseline values after each contraction. The coefficient of variation (SD/mean × 100) of the average force produced over the 20 s by the 20 evoked contractions was also calculated in each protocol to assess the variability of the force production between protocols.

FTI was considered as the main index of muscle fatigue in the present study, as the initial evoked force was kept well below MVC force (to minimize antidiromic block). Indeed, in our experiment, the extent of muscle fatigue when quantified by MVC force loss may well be underestimated because many motor units recruited during MVC were not recruited with NMES.

**EMG data.** M-wave peak-to-peak amplitude and duration as well as total M-wave area were measured to monitor action potential transmission/propagation from EMG responses obtained following single stimulation of the tibial nerve. M-wave properties were considered as a secondary index of peripheral fatigue. EMG signals recorded during MVCs were quantified as the root mean square (RMS) amplitude averaged over 250 samples \(2\, \text{kHz}\) for a 500-ms interval around MVC force \(250\, \text{ms} \text{before and after MVC force}\) for all agonist muscles and normalized by their respective M-wave amplitude \((\text{RMS/M})\) to assess muscle activation \((\text{secondary index of central fatigue})\). Sustained EMG activity was also quantified as another indicator of central recruitment \(\text{(alongside sustained force)}\); sustained EMG activity was considered when EMG bursts could be noticed on all three agonist muscles and was measured as the duration between the last stimulation artifact on the EMG channels and the last EMG burst of each tetanus.

**Current charge.** To compare the amount of current delivered by each modality of stimulation, the current charge was calculated as follows:

\[
\text{charge} \quad (C) = \text{intensity} \times \text{frequency} \times \text{pulse duration} \quad (s)
\]

**Statistical Analysis**

All statistical analyses were performed with SigmaPlot software for Windows \(\text{version} 11\); Systat, Chicago, IL). Data normality was checked with a Kolmogorov-Smirnov test. Two-way repeated-measures ANOVAs \[\text{condition (WPHF vs. CONV)} \times \text{time (prefatigue vs. postfatigue)}\] were performed to assess differences in MVC force, RMS/M, VAL, doublet amplitude, peak twitch, and M-waves properties. Two-way repeated-measures ANOVAs \[\text{condition (WPHF vs. CONV)} \times \text{time (contraction 1 to contraction 20)}\] were performed to assess differences in sustained force, sustained EMG activity, and FTI. Post hoc \(\text{(Holm-Sidak)}\) analyses were used to test for differences among pairs of means when appropriate. Depending on the outcome of the normality test, paired \(t\)-tests or Wilcoxon signed-rank tests were performed to compare the total FTI, MVC force loss, VAL changes, potentiated twitch and doublet amplitude losses, stimulation intensity, and current charge between the two conditions. The \(\alpha\)-level for statistical significance was set to \(P < 0.05\). Data are presented as means ± SD in text and Tables 1–3 and means ± SE in Fig. 1, except when specified otherwise.

**RESULTS**

**Neuromuscular Fatigue**

Total FTI in WPHF was 1.7-fold smaller compared with CONV \(21.717 \pm 11.541\, \text{vs.} \, 37.958 \pm 9.898\, N\text{s}, \, \text{Fig. 1A}, \, P < 0.001\). During the WPHF protocol, FTI was decreased by contraction 2 \(P < 0.001, \text{Fig. 1B}\) and remained constant thereafter, whereas it remained constant during the whole protocol in CONV \(P > 0.05\). MVC force was similarly decreased after both protocols \(\text{(WPHF: from 884} \pm 164 \text{to 831} \pm 205\, \text{N), i.e., } -7.0 \pm 2.7\% , \, P < 0.01; \, \text{CONV: from 917} \pm 165 \text{to 864} \pm 190\, \text{N), i.e., } -6.2 \pm 2.5\% , \, P < 0.01\)\). VAL remained unchanged after WPHF \(\text{(prefatigue: 86.8} \pm 11.5\% , \, \text{vs. postfatigue: 85.2} \pm 12.9\% , \, P > 0.05)\) and CONV \(\text{(prefatigue: 88.0} \pm 9.5\% , \, \text{vs. postfatigue: 87.7} \pm 11.4\% , \, P > 0.05)\). Similarly, no change in RMS/M was observed in any muscle after NMES \(\text{Table 1}, \, P > 0.05\).

M-wave amplitude was significantly reduced for gastrocnemius lateralis and gastrocnemius medialis muscles \(P < 0.05\) after the fatiguing task with no difference between WPHF and CONV \(P > 0.05, \text{Table 2}\). Soleus M-wave duration was slightly increased postfatigue \(P < 0.05\) with no differences across conditions \(P > 0.05\). For both conditions and for all muscles, M-wave area was unchanged after the fatiguing task \(P > 0.05\). We also observed a reduction in doublet and twitch amplitudes after the fatiguing task \(P < 0.001, \text{Table 3}\), with no differences across conditions \(P > 0.05\).

**Differences Between Protocols**

The stimulation intensity required to evoke the initial target of 10% MVC force was eightfold greater in CONV \(144 \pm 19\, \text{mA} \text{compared with WPHF (18} \pm 8\, \text{mA, } P < 0.001\). Actual current charge was 10-fold higher with WPHF \(1.8 \times 10^{-3} \text{vs.} \, 8.2 \times 10^{-4}\, \text{C} \text{compared with CONV \(1.8 \times 10^{-4} \text{vs.} \, 2.4 \times 10^{-5}\, C, \, P < 0.001\). Discomfort scores were comparable for CONV \(17 \pm 13 \text{vs.} \, 14 \pm 10\, \text{mm after the 1st and 19th evoked contractions, respectively) and WPHF (15} \pm 14 \text{and 21} \pm 17\, \text{mm after the 1st and 19th evoked contractions, respectively; } \, P > 0.05\).

The force recordings of the 20 contractions evoked in CONV and WPHF for each subject are depicted in Figs. 2 and 3, respectively. The difference in force production pattern between the two protocols and the high intra- and interindividual variability in WPHF can be clearly seen. Accordingly, a greater coefficient of variation of the averaged evoked force was found in WPHF compared with CONV \(58.5 \pm 44.8\% \text{vs.} \, 9.4 \pm 8.1\% , \, P < 0.001\). The sustained force was considered to highlight central recruitment and appeared to be longer after WPHF compared with CONV \(867 \pm 431\, \text{vs.} \, 661 \pm 351\, \text{ms, } P < 0.01\). Central recruitment evidenced by sustained EMG activity was also compared between the two NMES paradigms, but it did not reach statistical significance \(\text{average of the 20 contractions: } 556 \pm 1372\, \text{ms in WPHF and 347} \pm 768\, \text{ms in CONV, } P = 0.1\); this sustained EMG activity was highly variable in both protocols.
DISCUSSION

Based on the literature pointing to a central recruitment during WPHF (10, 11, 23), we expected WPHF to induce a central recruitment and thus to result in less muscle fatigue compared with CONV. Contrary to this hypothesis, in some subjects a central recruitment was observed with both stimulation paradigms. Furthermore, FTI was more reduced in WPHF compared with CONV. Finally, the extent and origin of MVC force loss was similar between both stimulation paradigms.

Extent and Origin of Neuromuscular Fatigue

Based on the literature suggesting a central recruitment with WPHF (10, 11, 23), we expected CONV would mainly lead to a random recruitment of muscle fibers determined by terminal motoneuron axonal branches orientation and distance from the stimulating electrodes (19), while WPHF would activate muscle fibers through the same peripheral pathway, but also through a central pathway, i.e., reflex loop activation of motoneurons accordingly to the size principle (20). If these assumptions were correct, CONV would have activated a greater proportion of type II, fast-twitch motor units compared with WPHF (a higher stimulation intensity would induce a greater peripheral, random motor unit recruitment) and would thus have resulted in a greater amount of muscle fatigue.

In contradiction with our hypothesis, we noted a rapid decrease in FTI in WPHF, whereas no significant reduction was observed in CONV. Surprisingly, in WPHF, the FTI dropped between the first and second tetanus and then remained constant. It thus appears that the high stimulation frequency combined with large pulse duration used in WPHF and associated with long contraction durations (but necessary to correctly assess an eventual central recruitment), led to premature fatigue of the recruited motor units, which were not able to recover during the 40-s recovery period. Due to this decrease, total FTI was, therefore, smaller in WPHF compared with CONV. This decrease in FTI points to a reduced motor unit mechanical output in WPHF compared with CONV and suggests a higher fatigue level of the recruited motor units in WPHF, possibly due to the higher stimulation frequency (4, 5). Indeed, this higher fatigue level is in accordance with previous results showing that increasing stimulation frequency from 20 to 100 Hz leads to a greater metabolic cost per activated motor unit (17), as shown by an increased ATP and PCr consumption, as well as P_i production in the knee extensors (29). Additionally, WPHF recruited less motor units than CONV as the active area is increased by the higher intensities, but not necessarily by higher frequencies (18). Taken together, these results suggest that WPHF would lead to a greater metabolic cost per unit area compared with CONV, mainly due to higher stimulation frequency. In the only other study where the initial force

Table 1. Root mean square normalized by M-wave amplitude recorded during maximal voluntary contractions before and after the 20 evoked contractions

<table>
<thead>
<tr>
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<th>WPHF</th>
<th>CONV</th>
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<tr>
<td>Pre</td>
<td>Post</td>
<td>Pre</td>
</tr>
<tr>
<td>Sol</td>
<td>0.030 ± 0.017</td>
<td>0.031 ± 0.017</td>
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<tr>
<td>GL</td>
<td>0.031 ± 0.018</td>
<td>0.031 ± 0.020</td>
</tr>
<tr>
<td>GM</td>
<td>0.033 ± 0.021</td>
<td>0.032 ± 0.018</td>
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Values are means ± SD. Sol, soleus; GL, gastrocnemius lateralis; GM, gastrocnemius medialis; CONV, short-pulse-low-frequency (conventional); WPHF, wide-pulse-high-frequency; Pre and Post, before and after the 20 evoked contractions, respectively.

A

Fig. 1. Total force-time integral (FTI) induced by the 20 evoked contractions (A) and FTI time course throughout the 20 contractions (B). *P < 0.05, significant differences across conditions. ***P < 0.001, a significant FTI reduction in wide-pulse-high-frequency (WPHF) compared with short-pulse-low-frequency (conventional (CONV)) in A, and a significant decrease compared with the first evoked contraction in B. In A, median (solid line) and mean (dashed line) values are indicated, as well as upper and lower limits, which represent the 25% and 75% quartiles, and whiskers representing the 10th and 90th percentiles. In B, values are means ± SE.
evoked by NMES was matched between conditions (as in the present study), an increase in frequency from 80 to 100 Hz did not lead to greater muscle fatigue, as shown by similar evoked peak force and FTI (30). This result might be explained by the fact that the two tested frequencies were on the plateau of the force-frequency relationship, while our stimulation frequencies were located on the bottom and top portions of the force-frequency relationship.

In contradiction with the FTI results, the MVC force was reduced to a similar extent after the two NMES paradigms. This finding might be explained by the relatively low evoked force, resulting in the majority of the motor units participating in MVC force production not being recruited during NMES. As such, evaluating MVC force losses might underestimate the muscle fatigue induced by these NMES paradigms.

Our results suggest that muscle fatigue can be ascribed to peripheral mechanisms, as revealed by the reduced doublet (−8%) and twitch (−13%) amplitudes. Even though we found slightly altered M-wave amplitudes and durations, the unchanged M-wave areas for all muscles would suggest that neuromuscular transmission-propagation was not compromised after our NMES protocols (6). Thus processes located beyond the sarcolemma likely account for the reduction in evoked force. In agreement with the peripheral origin of muscle fatigue, no changes in VAL and RMS/M (indexes of central fatigue) were observed following NMES in any condition. This peripheral origin of fatigue induced by NMES is consistent with repeated activation of the same muscle fibers and has been widely reported in the literature (7, 21, 25, 34). Boerio et al. (7) observed a comparable MVC force loss (−9.4%) after 30 plantar flexions evoked by NMES. In contrast to the present study, their results point to both a central and peripheral origin of neuromuscular fatigue, as they actually observed a slight but significant decline in VAL (−1.6%), Soleus RMS/M (−11%), as well as in doublet amplitude (−6%). Papaiordanidou et al. (27) reported VAL and RMS/M decreases following 3 series of 17 stimulation trains. Their protocol led to a comparable MVC force loss (−11.5%) as ours. The discrepancy in the etiology of fatigue between the present work and the above-mentioned studies (7, 27) might be explained by the greater target force levels adopted in their protocol, as subjects had to endure maximal tolerable stimulation intensity [e.g., initial target force of 55% MVC in the case of Boerio et al. (7) and of 35–40% MVC in the case of Papaiordanidou et al. (27)]. It thus appears that when NMES protocols are performed at low force levels as in the present study, contractile alterations are the main contributors to muscle fatigue, whereas other mechanisms (including central factors) can be involved at higher levels of evoked force (7, 27, 34).

**Differences Between WPHF and CONV**

Despite the greater stimulation intensity required to elicit the initial force target in CONV than in WPHF, discomfort scores did not differ significantly in the two conditions. This result appears contrary to what one could have supposed, as nociceptors present a higher excitation threshold than motor axons (12); one could have expected that the greater intensity (despite a lower current charge delivered to the muscle) used in CONV would have led to a greater discomfort. But this lack of difference in discomfort levels associated with the two stimulation modalities is most likely the result of the low target force (10% of the MVC force at the beginning of each protocol). Such a low force level, which minimizes antidromic block and would allow central recruitment (3, 13), only led to slight discomfort in both conditions.

A difference in motor unit recruitment was observed between WPHF and CONV as highlighted by Figs. 2 and 3. However, the present data do not allow further explanation and differentiation of the underlying causes of this distinctive force

| Table 2. M-wave properties before and after the 20 evoked contractions |
|-----------------------------|-----------------------------|-------------|-----------------------------|-----------------------------|
|                            | WPHF                        |             | CONV                        |             |
|                            | Pre                         | Post        | Pre                         | Post        |
| Sol                         |                             |             |                             |             |
| Amplitude, mV               | 11.8 ± 2.9                  | 11.6 ± 3.0  | 10.8 ± 3.0                  | 11.8 ± 2.8  |
| Duration, ms                | 2.7 ± 0.5                   | 2.9 ± 0.4*  | 2.8 ± 0.4                   | 2.9 ± 0.4*  |
| Area, mV·ms                 | 0.034 ± 0.020               | 0.029 ± 0.010| 0.025 ± 0.011               | 0.027 ± 0.011|
| GL                          |                             |             |                             |             |
| Amplitude, mV               | 10.6 ± 2.6                  | 10.3 ± 2.7* | 12.1 ± 4.3                  | 11.6 ± 4.2* |
| Duration, ms                | 4.0 ± 1.7                   | 4.0 ± 1.9   | 4.0 ± 1.7                   | 3.9 ± 1.6   |
| Area, mV·ms                 | 0.054 ± 0.044               | 0.049 ± 0.040| 0.055 ± 0.032               | 0.050 ± 0.027|
| GM                          |                             |             |                             |             |
| Amplitude, mV               | 9.5 ± 5.3                   | 8.8 ± 4.9*  | 9.5 ± 4.6                   | 8.4 ± 4.0*  |
| Duration, ms                | 2.5 ± 1.2                   | 2.5 ± 1.3   | 3.0 ± 1.8                   | 2.9 ± 1.8   |
| Area, mV·ms                 | 0.034 ± 0.013               | 0.032 ± 0.014| 0.030 ± 0.014               | 0.030 ± 0.017|

Values are means ± SD. *P < 0.05, significant difference compared with prefatigue.

| Table 3. Contractile properties measured before and immediately after the 20 evoked contractions |
|-----------------------------------------------|-----------------------------------------------|---------------|-----------------------------|-----------------------------|
| Model                                      | WPHF                                         |             | CONV                        |             |
|                                            | Pre                                           | Post         | Pre                         | Post         |
| Twitch amplitude                           | 240.0 ± 47.7                                 | 208.5 ± 46.1*| 246.9 ± 55.8               | 217.2 ± 50.6*|
| Doublet amplitude                          | 368.1 ± 65.4                                 | 339.4 ± 65.1*| 372.6 ± 77.2               | 344.3 ± 68.2*|

Values are means ± SD in N. *P < 0.001, significant reduction. Doublet, 100-Hz paired stimulation; Δ, variation between Pre and Post.
pattern in WPHF. In contrast to CONV, WPHF data showed large intra- and interindividual variability, as can be seen when comparing Fig. 2 to Fig. 3 and from the higher coefficient of variation of the evoked force observed in WPHF. The intraindividual variability observed in WPHF might be caused by the greater impact of successive sequences of recruitment-derecruitment of some motor units (those with an excitation threshold close to the stimulation intensity), as fewer motor units were contributing to the force production in WPHF than in CONV due to the much lower stimulation intensities used in WPHF. This might have induced relatively large force fluctuations as seen in subjects A, D, E, H, J, K, L, M, and N in Fig.
On the other hand, interindividual variability in electrically evoked force has previously been suggested to originate, at least in part, from differences in monoamine levels between individuals (9). This intervariability could lead to dividing our subjects in groups: the responders showing, on average, a force increase (subjects I–N in Fig. 3), and, therefore, the so-called central force, and the nonresponders showing, on average, a force decrease (no central force, Fig. 3, A–H). Additionally, and in agreement with the sustained activity data, a distinction between responders and nonresponders could also be made for the CONV protocol (see Fig. 2). Evaluation of the monoamine levels in these two groups would be interesting to confirm their possible roles in the occurrence and magnitude of central force.

An increase in H-reflex amplitude, asynchronous activity, as well as sustained activity (2, 3, 10, 11) and changes in intrinsic strength.
muscle fatigue (FTI loss), which can be explained by peripheral pathway, in contrast to nerve stimulation (2). However, according to Bergquist et al. (3), the discomfort associated with nerve stimulation is higher than for stimulation with surface electrodes positioned over the muscle belly, something also observed during our pilot experiments. This led us to opt for the latter, as pain represents an important limitation in rehabilitation. Furthermore, Bergquist et al. (3) reported that stimulation over the muscle belly presented advantages for the triceps surae, such as a reduced susceptibility to movement with electrodes positioned over the muscle belly and higher reliability and consistency of the evoked contraction. Second, we did not use burst (“top hat”) patterns (13), which would have allowed examination of H-reflex and sustained activity during low-frequency stimulation. Third, we used an initial target force of 10% MVC to reduce antidromic block and to keep discomfort low. It is possible that a higher initial target force of 10% MVC to reduce antidromic block and to keep discomfort low. It is possible that a higher initial target force would have resulted in a different outcome (e.g., on MVC force). Finally, even if our results question the greater benefit of WPHF use compared with CONV for rehabilitation, studies in clinical populations are needed, since the present results were obtained in young, healthy subjects.

Conclusions

The present study showed that, whereas motor unit recruitment appeared to differ between WPHF and CONV as highlighted by the differences in FTI and the great variability found in WPHF (Figs. 2 and 3), a central recruitment can occur for some subjects with both types of NMES. However, in contradiction with our hypothesis, WPHF led to a greater level of muscle fatigue (FTI loss), which can be explained by peripheral impairments. Overall, the different motor unit recruitment observed between the two NMES modalities appeared, within the limits of our experimental setup, to question the usefulness of WPHF for rehabilitation purposes, as a lower FTI was observed in WPHF compared with CONV.

ACKNOWLEDGMENTS

The authors thank Marc Buclin for the design and conception of the ergometer, and all of the participants who volunteered to take part in this study.

GRANTS

The study was supported by the Swiss Federal Institute of Sport Magglingen.

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

AUTHOR CONTRIBUTIONS


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J Appl Physiol • doi:10.1152/japplphysiol.01015.2013 • www.jappl.org


