Neuromuscular Fatigue Following Isometric Contractions with Similar Torque Time Integral

Authors V. Rozand, T. Cattagni, J. Theurel, A. Martin, R. Lepers

Affiliation INSERM U1093, Université de Bourgogne, Dijon, France

Key words
- isometric contraction
- voluntary activation
- EMG activity
- percutaneous neurostimulation
- knee extensor muscles

Abstract

Torque time integral (TTI) is the combination of intensity and duration of a contraction. The aim of this study was to compare neuromuscular alterations following different isometric sub-maximal contractions of the knee extensor muscles but with similar TTI. Sixteen participants performed 3 sustained contractions at different intensities (25%, 50%, and 75% of Maximal Voluntary Contraction (MVC) torque) with different durations (68.5±33.4 s, 35.1±16.8 s and 24.8±12.9 s, respectively) but similar TTI value. MVC torque, maximal voluntary activation level (VAL), M-wave characteristics and potentiated doublet amplitude were assessed before and immediately after the sustained contractions. EMG activity of the vastus lateralis (VL) and rectus femoris (RF) muscles was recorded during the sustained contractions. MVC torque reduction was similar in the 3 conditions after the exercise (−23.4±2.7%). VAL decreased significantly in a similar extent (−3.1±1.3%) after the 3 sustained contractions. Potentiated doublet amplitude was similarly reduced in the 3 conditions (−19.7±1.5%), but VL and RF M-wave amplitudes remained unchanged. EMG activity of VL and RF muscles increased in the same extent during the 3 contractions (VL: 54.5±40.4%; RF: 53.1±48.7%). These results suggest that central and peripheral alterations accounting for muscle fatigue are similar following isometric contractions with similar TTI. TTI should be considered in the exploration of muscle fatigue during sustained isometric contractions.

Introduction

Voluntary sustained sub-maximal contractions lead to neuromuscular fatigue, characterized by a decrease in maximal voluntary contraction (MVC) force [8,20,31]. Neuromuscular fatigue can be defined as an exercise-induced reduction in maximal voluntary muscle force. It may arise not only due to peripheral changes at the level of the muscle (peripheral fatigue), but also because the central nervous system fails to drive the motoneurons adequately (central fatigue) [14]. It has been proven that the amount of peripheral and central alterations may depend on the muscle used [5], fatiguing exercise protocol (isometric vs. dynamic, continuous vs. intermittent), load type (force vs. position tasks [19–21,25]), muscle length [31] or contraction intensity [5,12,23].

By comparing different levels of isometric contraction performed until exhaustion, some authors reported a greater decrease in MVC force after low (~20–35% MVC) vs. high (~65–80% MVC) level of contraction [13,39]. However, in these studies the underlying mechanisms responsible for the decrease in MVC were different. In fact, Fuglevand et al. [13] observed a greater peripheral fatigue (i.e., a reduction of muscle twitch amplitude and M-wave amplitude) following low-intensity contraction (20% MVC) than high-intensity contraction (65% MVC) of the index finger abductors. In contrast, although Yoon et al. [39] found similar peripheral fatigue after elbow flexors contractions carried out at 20% and 80% MVC, central fatigue (i.e., a reduction of maximal voluntary activation level) was only observed at 20% MVC contraction level. Similarly, on the knee extensor muscles, contractions at 25% MVC induced a greater central fatigue than contractions at 50% MVC [5]. More interestingly, after sustained contractions of the quadriceps muscle performed at 35% vs. 65% of MVC, Iguchi et al. [22] observed similar central and peripheral alterations when an identical amount of fatigue was reached (i.e., 65% MVC reduction). Although conflicting results were

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Correspondence
Vianney Rozand
Université de Bourgogne
INSERM U1093
Faculté des Sciences du Sport
Dijon Cedex
France 21078
Tel.: +33/631/488 543
Fax: +33/380/396 749
vianney.rozand@u-bourgogne.fr

observed after sustained isometric contractions performed at different intensities, it seems that the relative contribution of central and peripheral alterations to muscle fatigue were similar for an identical amount of MVC loss. Another approach to analyse the neuromuscular alterations following sustained isometric contractions would be to consider submaximal contractions matched for torque time integral (TTI).

As no physical work is performed during isometric contraction, TTI, i.e., intensity × duration combination, reflects the isometric work and the energy expenditure of an isometric contraction, and thus correlates to the ATP consumption [6, 35]. The studies that have analysed neuromuscular fatigue following sustained contractions at different intensities did not generally control the TTI. The intensity of submaximal fatiguing contractions is usually imposed, while the duration of the contractions is determined by the time to exhaustion. For instance, in the study of Behm and St-Pierre [5] the contraction at 25 % MVC that induced a greater muscle fatigue lasted 19 min, whereas the contraction at 50 % MVC lasted only 4 min. Even though the TTI value was not quantified in this study, there is no doubt that the isometric work was different in the 2 contractions. In a study related to neuromuscular electrical stimulation in rats, Gondin et al. [17] controlled the TTI and showed similar neuromuscular fatigue following evoked contractions with high vs. low frequency stimulations. They concluded that fatigue and metabolic changes were independent of the combination of stimulation frequency and pulse duration. Interestingly, Doix et al. [11] recently showed that voluntary and evoked contractions of human triceps surae with different current intensities, but similar TTI, induced the same reduction in MVC torque with identical central and peripheral alterations. The question whether muscle fatigue would be similar following sustained voluntary contractions at different intensities but with identical TTI can be raised.

In this context, the purpose of the present study was to compare central and peripheral alterations following voluntary isometric sustained contractions of the knee extensor muscles with the same TTI, but with different intensity-duration combinations. According to previous findings observed for neuromuscular electrical stimulation contractions, we hypothesized that neuromuscular alterations would be similar after different sustained voluntary contractions with a similar TTI.

Methods

Subjects

Sixteen physically active male subjects (age = 24.0 ± 6.4 (Mean ± SD) years, body mass = 72.7 ± 6.7 kg, height = 177.8 ± 5.3 cm), recruited at the Faculty of Sport Sciences, volunteered to participate in this study. None of them had performed resistance training on the lower limbs. Voluntary consent was obtained from the subjects following an explanation of the experimental procedures and the possible risks involved. The study protocol was approved by the local ethical committee, and all procedures were conducted according to the Declaration of Helsinki as well as the ethical standards in sports and exercise science research [18].

Torque recording

Torque of the isometric knee extension was measured by a dynamometer (Biodex Shirley Corporation, NY, USA). Subjects were seated upright with the trunk-thigh angle at 90°, and performed isometric contractions of the right quadriceps muscle. They were secured with a seat belt, shoulder and thigh straps to prevent unwanted movements. They crossed their arms and held the shoulder strap. The right leg was positioned with a knee angle fixed at 90°, and dynamometer axis was aligned with the knee joint axis. The lever arm was attached to the shank above the ankle with a strap. Torque was recorded during exercise and during maximal voluntary contraction (MVC) using software (Acqknowledge 4.1, Biopac Systems Inc, USA) synchronized with the dynamometer. TTI during isometric sustained contractions was determined as the area under the torque traces over the contraction duration [28] and was calculated on line, using the free software previously mentioned.

Electromyographic (EMG) recording

EMG activity of the vastus lateralis (VL) and rectus femoris (RF) muscles was recorded with circular (recording diameter of 10 mm) bipolar silver chloride surface electrodes (Contrôle Graphique Médical, Brice-Comte-Robert, France). After shaving and cleaning the skin over the VL and RF muscles using alcohol pads to obtain low impedance (< 5 kΩ), electrodes were positioned parallel to the muscle fibres over the muscle belly with an interelectrode (center to center) distance of 20 mm. The electrodes were placed at a distance of 2/3 between the anterior spina iliaca superior and the lateral side of the patella for the VL muscle, and midway between the anterior spina iliaca superior and the superior part of the patella for the RF muscle. The reference electrode was placed on the opposite patella.

EMG signals were amplified (× 1000) to be analysed and recorded (sampling frequency = 2 kHz) using commercially available software (Acqknowledge 4.1, Biopac Systems Inc, USA).

Evoked contractions

The electrically evoked contractions were induced using a high voltage stimulator (DS7 model, Digitimer, Hertfordshire, UK). The femoral nerve was stimulated using a monopolar cathode ball electrode (0.5 cm diameter) pressed into the femoral triangle by the experimenter. The site of stimulation was marked on the skin so that it could be repeated for each condition. The anode was a large (10 × 5 cm) rectangular electrode (Compex SA, Ecublens, Switzerland) located in the gluteal fold opposite the cathode. The optimal intensity of stimulation, determined with single stimuli, was considered to be reached when an increase in the stimulation intensity did not induce a further increase in the amplitude of the twitch force and the peak-to-peak amplitude of the compound muscle action potential (M wave) of the VL muscle, the EMG activity of which has been shown to be more reliable compared to the RF muscle [32]. Once the optimal intensity was found, it was increased by 25 % to ensure supra-maximal stimulation, and kept constant throughout the session for each subject. During the protocols, only doublets were delivered. The stimulus duration was 1 ms, and the Integral of the stimuli in the doublets were 10 ms (100 Hz).

Experimental protocol

The experimental protocol took place during a single session in the laboratory. The aim of the experimental protocol was to produce a similar TTI during sustained isometric contractions of the knee extensor muscles at 3 different intensities.

Before each exercise, a standard warm-up consisted of 10 brief non-fatiguing submaximal contractions of the knee extensor muscles [32, 38]. A 3-min rest was taken between warm-up and exercise to avoid a fatiguing effect of the warm-up.

First, participants performed 2 isometric MVC of the knee extensor muscles, or more if the difference between the 2 contractions was too high (>5%). Doublets were delivered during (superimposed doublet) and after (~3 s; potentiated doublet) MVC to estimate voluntary activation level (% VAL) using the twitch interpolation technique [27].

After a few minutes of rest, the TTI value of reference was determined for each participant. Subjects performed a MVC of the knee extensor muscles until they could not maintain more than 75% of the initial MVC torque, represented by a red line on the visual screen. When torque reached a value lower than 75% of the initial MVC torque for more than 2 s, the experimenter asked the participants to stop their effort. Verbal encouragements were given during the contraction. The reference TTI value was calculated from this sustained MVC lasting 20.0±8.0 s.

Subjects had therefore to perform 3 sustained contractions in a random order at an intensity corresponding to 25%, 50% and 75% of MVC with the same TTI value, calculated on-line by software (Acqknowledge 4.1, Biopac Systems Inc, USA). The target torque was represented by a red line on a visual screen. The experimenter controlled the TTI value on another screen (not seen by the subjects) during each contraction, and the contractions were stopped when the required TTI value was reached. Immediately after the end of the sustained contractions, subjects were asked to perform a MVC with a superimposed doublet as fast as possible (the interval duration between the end of the sustained contraction and the MVC was close to 1 s). A potentiated doublet was delivered 3 s after the MVC to assess neuromuscular fatigue. A 45-min rest period was taken between each contraction. A MVC was performed before each condition to verify that subjects had fully recovered (difference <5% from the first MVC torque of the protocol). If they had not fully recovered, more rest was allowed until they could perform the same MVC torque as at the beginning of the protocol.

Data analysis

Peak doublet amplitude (Dt), reflecting peripheral fatigue [33] was measured from the peak torque associated with potentiated doublet. Peak-to-peak amplitude of VL and RF maximal M-waves was measured after the second stimulus of the potentiated doublet. The maximal EMG activity for each muscle was determined as the root mean square (RMS) value over a 0.5 s interval when MVC torque was maximal. MVC EMG RMS values were normalized to the M-wave amplitude for the VL and RF muscles obtained at rest, and expressed as EMG RMS/M ratio. Maximal voluntary activation level (VAL) was quantified by measurement of the torque responses to stimulation of the muscle [2,14], using the twitch interpolation technique. The level of voluntary activation was computed using the formula:

VAL=(1 – superimposed doublet/potentiated doublet)×100 [4].

When superimposed doublet was not delivered at the peak torque, a correction was applied in the original equation, as recommended by Strojnik and Komi [36].

During submaximal sustained contractions, EMG activity was quantified by EMG RMS normalized to EMG RMS during the MVC (EMG RMSmax). EMG RMS/EMG RMSmax value was determined over the first second and the last second of the 3 sustained contractions. The rate of increase of EMG RMS/EMG RMSmax during the sustained contractions was calculated between the first and the last second of the contractions. Because the rate of increase of EMG was similar between VL and RF muscles, the data were pooled. We also quantified the EMG-time integral for the VL and RF muscles during each sustained contraction. The EMG signal was rectified by squaring the EMG curve and was then integrated.

Statistical analysis

Assumptions of statistical tests such as normal distribution (Shapiro-Wilk test, $P>0.05$) and sphericity (Mauchly test, $P>0.05$) of data were checked as appropriate. All of the parameters were normally distributed excepted RMS/M ratio. Changes in MVC torque, VAL, peak doublet amplitude and RMS/RMSmax ratio were evaluated by 2-way repeated measurement ANOVAs with *condition* (75% MVC, 50% MVC and 25% MVC) and *time* (pre and post) as intra-subjects factors. RMS/M ratio for the VL and RF muscle were evaluated by a non-parametric Wilcoxon signed-rank test. Changes in contraction time, TTI, EMG activity increase, rate of increase of EMG activity and EMG integral were assessed by one-way (*condition*) repeated measurement ANOVAs. Post-hoc analyses (Tukey HSD) were used to test for differences among pairs of means when appropriate. The statistical analyses were performed by using Statistica software for Windows (Statsoft, version 6.1, Statistica, Tulsa, OK). A significance level of $P<0.05$ was used to identify statistical significance. Data are presented as Mean±SD in the text, the table and the figures.

Results

Torque time integral

The contraction time was significantly ($P<0.05$) different for the 3 conditions (25% MVC: 68.5±33.4 s; 50% MVC: 35.1±16.8 s; 75% MVC: 24.8±12.9 s). TTI value was similar ($P>0.05$) for the 3 conditions (3699±1761 Nm.s or 1714±809% MVC.s for 25% MVC, 3782±1739 Nm.s or 1755±815% MVC.s for 50% MVC and 3726±1659 Nm.s or 1860±939% MVC.s for 75% MVC, respectively).

MVC torque

Knee extensors MVC torque, assessed immediately after the sustained contractions, was similarly reduced (−23.4±2.7%) for the 3 conditions (main effect of *time*, but no *condition* or *time* × *condition* interaction effects): −23.1±13.2% at 25% MVC ($P<0.001$), −26.8±10.1% at 50% MVC ($P<0.001$) and −20.3±12.0% at 75% MVC ($P<0.001$), respectively (**Fig. 1**). There was a large inter-subject variability for the MVC torque reduction (25% MVC:

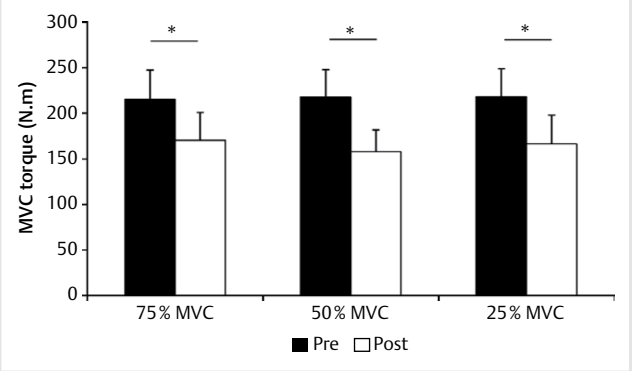

Fig. 1 Mean (±SD) MVC torque pre (black) and post (white) sustained contractions at the 3 different intensities: 75, 50, and 25% of MVC. *: significantly different ($P<0.001$).

		Intensity of sustained contractions		
		75% MVC	50% MVC	25% MVC
Central parameters				
VAL (%)	pre	93.5±4.4	93.5±4.8	93.7±4.8
	post	91.8±6.5$	90.8±4.1$	89.2±9.6$
EMG RMS/M (VL)	pre	0.074±0.063	0.074±0.054	0.082±0.055
	post	0.145±0.187	0.152±0.198	0.160±0.216
EMG RMS/M (RF)	pre	0.124±0.068	0.128±0.083	0.144±0.115
	post	0.158±0.131	0.165±0.147	0.137±0.097
Peripheral parameters				
Dt amplitude (Nm)	pre	86.1±14.1	85.8±15.8	83.3±22.1
	post	69.2±21.6*	68.0±21.2*	68.2±20.9*
M-wave amplitude VL (mV)	pre	11.0±4.8	10.8±5.0	10.0±5.3
	post	9.1±6.1	8.5±5.6	8.7±5.5
M-wave amplitude RF (mV)	pre	6.0±2.6	5.7±2.6	5.5±2.4
	post	5.5±2.9	5.3±3.1	5.6±2.9

MVC: maximal voluntary contraction; VAL: maximal voluntary activation level; Dt: Doublet torque; VL: vastus lateralis; RF: rectus femoris; $: Pre-Post significant difference (P<0.05); *: Pre-Post significant difference (P<0.001)

Table 1 Means (±SD) of central and peripheral parameters pre and post exercise. Central parameters were assessed during MVCs. Peripheral parameters were assessed from the responses induced by doublet stimulation.

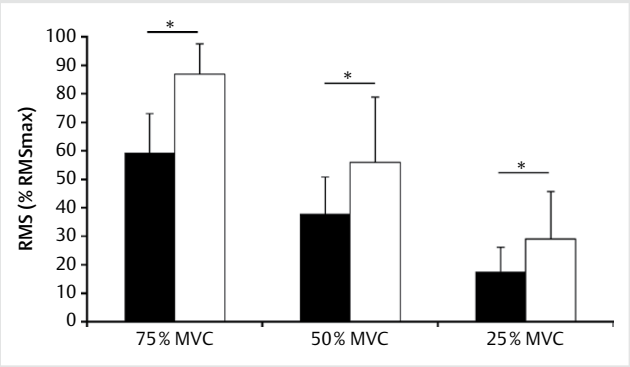

Fig. 2 Mean (±SD) EMG activity of the VL muscle during the first (black) and the last (white) second of the sustained contractions at 75, 50, and 25% of MVC. *: significantly different (P<0.001).

range [−8.2%; −53.0%]; 50% MVC: range [−6.6%; −42.4%]; 75% MVC: range [−5.6%; −49.8%].

Central and peripheral parameters

Maximal VAL was significantly (P<0.05) reduced (−3.1±1.3%; main effect of *time*) in the same amount post exercise for the 3 conditions (**Table 1**). No *condition* or interaction effects were observed. The EMG RMS/M ratio of VL and RF muscles during the MVC was not affected by the sustained contraction in any of the 3 conditions.

The amplitude of the potentiated doublet significantly (P<0.001) decreased in the same amount (−19.7±1.5%, main effect of *time*) after the 3 fatiguing contractions. No *condition* or interaction effects were observed. M-wave amplitude remained stable after the fatiguing contractions for both VL and RF muscles (**Table 1**).

EMG activity during sustained contractions

EMG activity significantly increased (P<0.001) for the VL and RF muscles during the 3 sustained contractions (**Fig. 2**). The EMG increase was similar in the 3 conditions for VL (62.8±36.8% at 25% MVC, 46.7±42.4% at 50% MVC and 54.1±40.2% at 75% MVC) and RF (68.3±64.7% at 25% MVC, 45.7±34.5 at 50% MVC and 45.3±37.2 at 75% MVC) muscles. The rate of increase in the EMG activity of VL and RF muscles was similar for both muscles and was significantly greater (P<0.01) in the 75% MVC condition (2.3±1.6%.s^{-1}) than in the 50% (1.3±0.6%.s^{-1}) and 25% MVC condition (1.0±0.3%.s^{-1}).

EMG-time integral was significantly greater (P<0.05) for 75% MVC (VL muscle: 16431±18646 V^2.s; RF muscle: 10105±9424 V^2.s) compared to 50% MVC (VL: 9926±9830 V^2.s; RF: 5210±3359 V^2.s) and 25% MVC (VL: 4012±4275 V^2.s; RF: 2278±2710 V^2.s).

Discussion

The aim of the present study was to investigate neuromuscular (central and peripheral) alterations of the knee extensor muscles following isometric sustained contractions with similar TTI but different intensity-duration combinations. The main finding was that sustained contractions with a same TTI lead to the same amount of fatigue, with similar peripheral and central alterations.

The results showed that the level of muscle fatigue quantified by MVC torque loss was similar (~25%) after sustained contractions with similar TTI despite different intensity-duration combination. This finding on sustained voluntary contractions confirms previous results found in human and animal studies using neuromuscular electrical stimulation [10,17]. Similar neuromuscular fatigue with identical central and peripheral alterations was observed following contractions with a same TTI but different stimulation parameters. Gondin et al. [17] suggested that TTI rather than the torque level can be considered as a major determinant of muscle fatigue when neuromuscular electrical stimulation protocols were associated with long stimulation trains. In the present study, MVC reduction following contractions at 75% of MVC was in accordance with the values of Yoon et al. [39] obtained following voluntary contractions of the elbow flexors at 80% of MVC sustained during a similar duration. At low intensities, previous studies observed a greater decrease of MVC torque. At 20% MVC, Fuglevand et al. [13] observed a 40% decrease on the first dorsal interosseous muscle, and Pageaux et al. [30] observed a 28% decrease on the knee extensor muscles, whereas we obtained a 23% decrease at 25% MVC. In these 2 studies, the duration of the contraction sustained until exhaustion were longer (534s and 266s respectively) than in the present study (69s) corresponding also to a greater TTI value (10 680%MVC.s and 5320%MVC.s vs. 1714%MVC.s in the present

study). These data suggest that muscle fatigue may depend on the TTI of the contraction. However, additional studies are required to verify if the amount of muscle fatigue would increase following sustained contractions with greater TTI values.

The decrease in MVC torque following sustained contractions was associated with a slight decrease in VAL, i.e., central fatigue, in the 3 conditions. Neyroud et al. [29] showed an identical 3% decrease in VAL on the knee extensor muscles after a contraction at 20% MVC sustained until exhaustion. On the contrary, Pageaux et al. [30] did not observe any decrease in VAL nor in RMS/M ratio following the same exercise. In the present study, the RMS/M ratio remained constant for both VL and RF muscles. The alteration in voluntary activation may be due to a decrease in muscle activation of untested agonist muscles (e.g. vastus medialis and vastus intermedius). In contrast with previous studies which observed a higher central fatigue after low-intensity contractions compared to high intensities [5,39], the contractions performed at 25%, 50% and 75% MVC induced the same amount of central fatigue. Although it was not calculated by Behm and St-Pierre [5] and Yoon et al. [39], we can presume that TTI was greater at low vs. high intensity in their studies because contractions were performed until exhaustion, which could explain the greater central alterations at low intensity. For the level of TTI value considered in our study, central mechanisms appear to contribute slightly to the decrease in MVC torque.

The peripheral alterations were similar in the 3 conditions, the potentiated doublet amplitude decreasing by 20% following the 3 sustained contractions. Neyroud et al. [29] observed the same peripheral alterations following a sustained contraction at 20% MVC of the knee extensor muscles. These findings also agree with a previous study showing peripheral alterations after contractions performed at low (20% MVC) and high (80% MVC) intensity on the elbow flexor muscles [39]. It has been suggested that the decrease in the amplitude of mechanical response to electrical stimulation may be due to several phenomena such as: (i) a reduced number of active cross-bridges due to a decreased release of Ca^{2+}; (ii) a decreased sensitivity of the myofilaments to Ca^{2+}; and/or (iii) a reduced force produced by each active cross-bridge [3,34], related or not with changes in concentration of metabolites. However, these different mechanisms could not be assessed by the present methodology. M-wave amplitude of VL and RF muscle was not altered after the sustained contractions as previously observed [7,29,30], indicating that the neuromuscular propagation-transmission and/or the muscle membrane excitability were not impaired following the 3 sustained contractions. The alteration of the mechanical response to electrical stimulation observed post exercise suggests that sustained sub-maximal contractions with a similar TTI value induce similar alteration of excitation-contraction coupling process.

EMG activity, which reflects the activity of the motor unit [37], increased during the sustained contractions in the same amount in the 3 conditions. During sustained isometric contractions, the increasing EMG activity has been attributed to the recruitment of higher-threshold motor units [10,15,16,26] or to change in firing rate [1,9,10] to compensate for the loss in force output from already active motor units [1]. The relative increase of the EMG activity was similar for the 3 conditions, while the rate of increase in EMG activity was greater in the 75% MVC condition compared to 25% and 50% MVC conditions. The majority of motor units are recruited at high intensity such as 75% MVC [24], leading to a rapid increase in the firing rate to maintain the desired force level. In contrast, the increase in EMG activity during low-force sustained contraction is largely due to the recruitment of larger motor units as the muscle becomes progressively fatigued [12,16]. As a result, the EMG activity increased slowly. Interestingly, the greater EMG level at the end of the contraction at 75% of MVC compared to lower intensities was not associated with a greater muscle fatigue since MVC reductions were similar in the 3 conditions. Similarly, the EMG-time integral, representing the total amount of EMG activity during the sustained contractions, was greater at 75% MVC compared to 25% and 50% MVC conditions, but did not exacerbate muscle fatigue. These findings suggest that EMG-time integral is not related to TTI. Similar TTI and muscle fatigue can be obtained by different EMG-time integral, i.e., total EMG activity.

In practical application our results suggest that the TTI method, which quantifies the physical work, could be used as a complementary approach in strength training programs to control muscle fatigue. Indeed, while the intensity of contraction is usually the main controlled parameter, the force- or torque-time integral value (i.e., intensity × duration combination) could also be an interesting additional parameter for monitoring the fatigue-induced contraction. This supports the idea that during strength training programs, the TTI should be considered in clinical or sport medicine routines.

Conclusions

The present results show that sustained isometric contractions at different intensities but with a similar TTI induced the same level of muscle fatigue with similar central and peripheral alterations. The use of TTI could be an interesting method to compare neuromuscular alteration following fatiguing isometric contractions at different intensities and durations. The correspondence between TTI and muscle fatigue needs to be confirmed for lower (e.g. 10% MVC) and higher (e.g. 90% MVC) contraction intensities (corresponding to different metabolic demands), different muscle length, and other muscle groups (e.g. plantar flexors). Furthermore, additional studies are required to clarify the relation between the amount of TTI of a sustained contraction and the central and peripheral mechanisms of muscle fatigue.

Conflict of interest: The authors declare that they have no conflict of interest.

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