Differential changes in muscle oxygenation between voluntary and stimulated isometric fatigue of human dorsiflexors

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McNeil, Chris J., Brad J. Murray, and Charles L. Rice. Differential changes in muscle oxygenation between voluntary and stimulated isometric fatigue of human dorsiflexors. J Appl Physiol 100: 890–895, 2006. First published November 10, 2005; doi:10.1152/japplphysiol.00921.2005.—The purpose of this study was to compare fatigue and recovery of maximal voluntary torque [maximal voluntary contraction (MVC)] and muscle oxygenation after voluntary (Vol) and electrically stimulated (ES) protocols of equal torque production. On 1 day, 10 male subjects [25 yr (SD 4)] completed a Vol fatigue protocol and, on a separate day, an ES fatigue protocol of the right dorsiflexors. Each task involved 2 min of intermittent (2-s on, 1-s off) isometric contractions at 50% of MVC. For the ES protocol, stimulation was delivered percutaneously to the common peroneal nerve at a frequency of 25 Hz. Compared with the Vol protocol, the ES protocol caused a greater impairment in MVC (75 vs. 83% prefatigue value; Pre) and greater increase in 50-Hz half relaxation time (165 vs. 117% Pre) postexercise. After acute (1 min) recovery, MVC impairment was similar for both protocols, whereas 30-Hz half relaxation time was still greater in the ES than Vol protocol. Total hemoglobin decreased to a similar extent in both protocols during exercise, but it was elevated above the resting value to a significantly greater extent for the ES protocol in recovery (18 vs. 11 μM). Oxygen saturation was significantly lower in the ES than Vol protocol during exercise (46 vs. 57% Pre), but it was significantly greater during recovery (120 vs. 105% Pre). These findings suggest that despite, equal torque production, ES contractions impose a greater metabolic demand on the muscle that leads to a transient greater impairment in MVC. The enforced synchronization and fixed frequency of excitation inherent to ES are the most likely causes for the exacerbated changes in the ES compared with the Vol protocol.

near-infrared spectroscopy; electrical stimulation; oxygen saturation; contractile slowing

ELECTRICAL STIMULATION (ES) is a commonly applied technique used to evoke muscle contractions to assess muscle fatigue; in animals it is used because volitional tasks are often not appropriate, and in humans it is used to negate the influence of central factors and spinal reflexes. As a result, considerable insight into fatigue mechanisms has been gained with ES. In addition to research on fatigue, there is interest in the potential of ES contractions to counteract muscle atrophy and strength loss in immobilization, rehabilitation, or paralysis. Regardless of the purpose, to maximize the application of ES, it is important to understand how skeletal muscle responds to ES compared with voluntary (Vol) contractions.

Several studies in humans have focused on how metabolism is affected by ES compared with Vol contractions, and the consensus is that ES invokes a greater energy demand. Magnetic resonance spectroscopy results have indicated a greater turnover of ATP and PCr as well as a decrease in pH in ES vs. Vol contractions (25, 29, 30). In support of these findings, other studies have reported that energetic substrate requirements, blood lactate concentration, respiratory exchange ratio, and intramuscular pressure are higher in ES compared with Vol tasks (13, 17, 18). Measures of anaerobic metabolism have received greater research focus because only three studies (18, 27, 29) have examined the aerobic response of muscle (the quadriceps in all cases) to ES contractions. Using magnetic resonance spectroscopy (29), direct blood sampling (18), and positron emission tomography (27), ES resulted in greater cytoplasmic myoglobin desaturation (29) and greater muscle oxygen consumption (18, 27) than Vol contractions. Muscle blood flow measures have yielded conflicting results, because two studies reported higher blood flow during ES (18, 27) but one study reported no difference between ES and Vol contractions using venous occlusion plethysmography (23). Although it does not provide information regarding blood flow per se, near-infrared spectroscopy (NIRS) is a versatile method to noninvasively monitor the relative balance of local muscle oxygen delivery and utilization. NIRS has been minimally utilized in studies of isometric fatigue, and it has not been used to assess oxygenation changes induced by ES contractions in healthy subjects.

Despite the number of studies that have compared ES with Vol, there are important factors that have either not been assessed or have been poorly controlled. Most important and pervasive is the imbalance between ES and Vol protocols in the amount of work performed. Often, with ES the torque is lower compared with a Vol protocol (25, 29) or the initial matching of ES and Vol torques becomes unequal because no attempt is made to maintain the ES torque output at the desired level as the exercise progresses (1, 16). One factor yet to be considered is the quantification of maximal voluntary contraction (MVC) torque after both protocols, and thus it is uncertain whether the same degree of torque loss (fatigue) is induced by ES vs. Vol contractions.

The recruitment pattern of motor units (MUs) during ES cannot be generalized; however, it is well known that the pattern is not the same as the orderly recruitment from small to large MUs that occurs during Vol contractions (1, 9, 19). The method used to induce electrical activation of the target muscle will affect the MU recruitment pattern and is therefore an influential factor in ES studies on humans. Percutaneous stimulation over the muscle belly will excite a small and selective fraction of the fibers (1) that are near to the surface of the muscle.
Stimulation over a nerve trunk, particularly at lower intensities, may preferentially activate larger axons (presumably of type II MUs) because of a lower input resistance. Although nerve trunk stimulation will not eliminate the bias of axonal input resistance, it avoids the muscle fiber-depth bias and therefore would seem to be a better method of ES delivery than percutaneous muscle stimulation.

Finally, many studies do not utilize physiological frequencies of excitation during ES, often using frequencies of 50 Hz for contraction intensities of <40% MVC (1, 27). During brief sustained isometric contractions, normal voluntary average MU firing frequencies in human limb muscles at MVC are between 25 and 40 Hz, and thus electrical synchronous excitation at ≥50 Hz is unnaturally high and may cause high-frequency fatigue (8, 16).

The purpose of this study was to address some of the limitations of past studies by comparing the fatigue and muscle oxygenation induced by a Vol protocol and an ES protocol controlled to mimic voluntary contractions as precisely as possible (i.e., equal torque-time integrals (torque production) and with similar frequencies of excitation). Using the tibialis anterior (TA) muscle, we monitored torque, contractile slowing, total hemoglobin (HbT), and oxygen saturation during fatigue and a brief (1 min) period of recovery. The TA model minimizes some of the problems of using ES in that it is a rather homogenous muscle being composed of close to 80% type I fibers (15) and its nerve trunk can be readily stimulated. The TA is also suitable for NIRS measurement because the relatively small muscle size would suggest that the area beneath the probe is more representative of the whole muscle than would be the case in a muscle group like the quadriceps.

We hypothesized that the ES protocol would cause a greater loss of MVC torque with more contractile slowing (fatigue) and a greater local oxygen desaturation compared with the Vol protocol.

METHODS

Subjects. Ten young men [25.3 yr (SD 3.9), 178.7 cm (SD 8.6), 80.4 kg (SD 9.8)] recruited from the university environment participated in this study. All subjects were healthy with no evidence of neuromuscular disease and were moderately active but not involved in any specific exercise program of the lower limbs. The study was conducted in accordance with the guidelines for experimentation on human subjects established by the local university's ethics review board, and informed, written consent was obtained from each of the 10 subjects.

Experimental setup. Subjects were seated in a custom-built isometric dynamometer (21) with their right ankle positioned at 30° of plantar flexion and an angle of 90° at both the hip and knee joints. This ankle angle was selected to minimize the antagonistic effect of the peroneal muscles, weak plantar flexors that are innervated by the same main nerve as the TA (21). A C clamp pressing down on the distal aspect of the right thigh minimized hip flexion during the dorsiflexion contractions. Velcro straps across the toes and the dorsum of the foot secured the limb to the dynamometer footplate. The dynamometer transducer was calibrated using a series of weights with known masses and demonstrated a linear output.

A computer-triggered stimulator (model DS7AH, Digitimer, Welwyn Garden City, Hertfordshire, UK) provided the ES at a pulse width of 50 μs, 400 V, and a current intensity ranging from 20 to 75 mA. A stimulating bar electrode, with a 3-cm anode-to-cathode spacing, was held in place by the operator over the common peroneal nerve slightly inferior and posterior to the fibular head.

Local tissue oxygenation levels were recorded from the TA using a NIRS unit (Hamamatsu NIRO 300, Hamamatsu Photonics KK, Tokyo, Japan). The theory and specifics of NIRS have been described in detail elsewhere (7, 22). Briefly, near-infrared light is transmitted via a fiber-optic cable and passed into the tissue of interest through an emitting optode. Any light that is transmitted through the tissue is acquired by a detector optode and carried by a second fiber-optic cable to a photon detector (photomultiplier tube) in the spectrometer. The NIRO 300 uses laser diodes set at four different wavelengths (776, 826, 845, and 905 nm) to provide the light source signal, which is pulsed in rapid succession and detected by the photomultiplier tube.

The emitting and detecting optodes of the NIRS unit were placed over the belly of the TA muscle 6 cm inferior and 2 cm lateral to the tibial tuberosity. An interoptode spacing of 4 cm was used to separate the emitting from the detecting sensor (26). The optodes were held within a black rubber housing that maintained constant optode spacing. The housing was taped to the skin and covered with an optically dense, black vinyl sheet that was also affixed with tape. The housing and vinyl sheet minimized the loss of near-infrared light from the field of interrogation as well as the intrusion of light from the environment.

The full assembly was further secured with an elastic bandage that encircled the leg.

Experimental procedures. The Vol and ES protocols were performed on different days separated by a minimum of 2 days and by no more than 7 days. To ensure all subjects were able to perform the volitional task, the Vol protocol was performed before the ES protocol. Unless otherwise stated, the following experimental procedures were conducted on both visits.

Sampling of the NIRS signal began at the completion of subject setup and continued uninterrupted until the end of testing. Subjects sat motionless for 5 min to obtain stable resting measures. To determine maximal ES intensity, doublet stimulations (2 pulses at 100 Hz) were delivered at increasing levels of current until a plateau in torque was achieved. This current intensity was increased a further 15% (supramaximal) to be certain that all motor axons in the peroneal nerve would be activated during assessment of voluntary activation and contractile slowing. Peak isometric torque was assessed from four MVCs of the dorsiflexors, with each sustained for 3–4 s and separated by 3 min of rest. The extent of voluntary activation was assessed during the third and fourth MVCs by use of the interpolated twitch technique modified to employ a supramaximal doublet rather than single pulse (11). To quantify voluntary activation, the torque amplitude of a doublet (Ts) delivered during the MVC was compared with a resting doublet (Tr) delivered after the MVC using the formula: [%activation = (1 – (Ts/Tr)) × 100]. A supramaximal 50-Hz train (1 s) was delivered after the resting doublet, and the torque response of this train was used to determine contractile slowing (i.e., half relaxation time; 50Hz-HRT). After the final MVC, for the ES fatigue protocol only, a small number (2–4 of 25-Hz (1 s) stimulation trains were delivered separately at submaximal intensities to determine the current that evoked a torque output equal to 50% of the peak MVC. After baseline measures, a 10-min rest period was given to allow the muscle to return to resting conditions before administering a fatigue protocol.

Both the ES and the Vol protocol involved 2 min of intermittent (2-s on, 1-s off) isometric contractions at 50% MVC. A constant stimulation frequency of 25 Hz was employed throughout the ES protocol. However, to match the Vol torque production, the current intensity was manipulated manually, as necessary, throughout the protocol to maintain the evoked torque response at the target of 50% MVC. On average, the increase in current intensity necessary to maintain 50% MVC at 2 min was ~30%. Immediately after the protocol (Post) and at 1 min of recovery, an MVC with an interpolated doublet was performed and a 50-Hz train was delivered (at the prefatigue supramaximal current intensity) to assess torque loss (fatigue), voluntary activation, and 50Hz-HRT (contractile slowing).
RESULTS

Strength, voluntary activation, and half relaxation time. Prefatigue MVC torque was the same for the ES and Vol visits [41.3 N·m (SD 4.4) vs. 41.4 N·m (SD 3.5), respectively]. The target torque of 50% MVC during the fatigue protocols was closely matched during both ES and Vol protocols [49.4% MVC (SD 1.5) vs. 50.1% MVC (SD 1.4), respectively]. Despite the equal torque production, MVC torque was significantly more impaired after the ES, compared with the Vol protocol [75.4% (SD 6.7) vs. 82.9% (SD 4.9)] of prefatigue, respectively; Fig. 1]. This protocol-related difference in MVC was temporary, because maximal torque values were similar in both protocols after 1 min of recovery [88.8% (SD 7.6) vs. 92.9% (SD 5.5)] of prefatigue, respectively; Fig. 1]. For both protocols, voluntary activation was near maximal (>99%) at all time points.

Similar to MVC torque, the prefatigue 50Hz-HRT was the same for the ES and Vol visit [126.4 ms (SD 10.6) vs. 128.5 ms (11.7), respectively]. The ES protocol induced a significantly greater slowing of the 50Hz-HRT than the Vol protocol immediately postfatigue [165.1% (SD 28.9) vs. 117.2% (SD 10.0)] of prefatigue, respectively; Fig. 1], and this difference persisted during the 1-min period of recovery [119.2% (SD 11.3) vs. 101.6% (SD 2.4)] of prefatigue, respectively; Fig. 1]. There was a strong and significant negative correlation between MVC and 50Hz-HRT in fatigue and recovery (r = −0.73).

Hb_{tot} and oxygen saturation. As a result of the baseline testing procedures, Hb_{tot} was equally increased (ES: 5 μM, Vol: 3.9 μM) at prefatigue from the resting level in both protocols (Fig. 2). At the midpoint of both protocols, Hb_{tot} had decreased to a value 9.5 μM below the resting level. In the last half of exercise and during recovery, the Hb_{tot} of the ES protocol increased to a greater degree than in the Vol protocol such that ES had a significantly greater concentration after 1 min of recovery [17.8 μM (SD 4.6) vs. 11.1 μM (SD 5.1)] above the resting level, respectively; Fig. 2].

The changes in oxygen saturation for a typical subject during the ES and Vol protocol are depicted in Fig. 3. The prefatigue saturation was the same for the ES and Vol visit [62.9% (SD 5.6) vs. 65.3% (SD 6.0), respectively]. At the onset of exercise,
the half-time of desaturation was significantly shorter for the ES than the Vol protocol [12.9 s (SD 3.2) vs. 17.5 s (SD 4.0), respectively; data not shown]. At the midpoint of both protocols, the ES saturation was significantly lower than the Vol saturation [45.6% (SD 6.5) vs. 58.3% (SD 15.2) of prefatigue, respectively], and this difference was maintained until the end of exercise (Fig. 4). One minute after completion of the protocols, oxygen saturation was significantly greater for the ES protocol [119.7% (8.9) vs. 104.8% (SD 5.7) of prefatigue, respectively; Fig. 4].

DISCUSSION

An ES protocol matched to the torque-time integral and the approximate excitation frequency (25 Hz) of a Vol protocol caused a greater impairment of MVC torque than the volitional task. This functional impairment was likely caused by the combination of a greater aerobic (oxygen desaturation) and anaerobic (contractile slowing) demand induced by the ES vs. the Vol protocol. $Hb_{tot}$ was the same for both protocols during exercise but was significantly greater in the period of recovery after the ES protocol. This suggests a link between the greater anaerobic metabolite accumulation during ES exercise (greater contractile slowing; see Refs. 5, 31) and an enhanced vasodilatory response in the recovery from the ES protocol (12). There are two plausible causes for the differential response to the ES and Vol protocols: dissimilar areas of active muscle (including the possibility of preferential activation of type II muscle fibers) or the synchronicity of MU excitation rates. It seems unlikely that preferential use of type II fibers during ES would have significantly impacted our results because the TA is composed of close to 80% type I fibers (15), and we used nerve trunk rather than percutaneous muscle stimulation. Furthermore, both protocols required enhanced activation either through voluntary recruitment or an increase in electrical current as fatigue developed to maintain torque at 50% MVC. Thus, although we have no direct measures, it would seem that similar and substantial portions of the muscle would be utilized in both protocols, especially during fatigue when additional muscle mass was progressively activated to maintain the target torque. Therefore, the lack of a temporal distribution of MU excitations during ES is the more reasonable candidate mechanism for the greater torque impairment with ES contractions using this design.

Whereas Vol contractions utilize asynchronous firing patterns with somewhat independent firing rates for each MU to maintain a given load with the minimum degree of fatigue (24), MUs activated during the ES protocol were excited synchronously at 25 Hz. Moreover, the muscle wisdom hypothesis suggests that, with continued Vol effort, the firing rates of active MUs will adjust to match the contractile status of the innervated fibers (3, 20). Although recent evidence has called this hypothesis into question (10), if such a central-peripheral matching exists, it would have increased the energy or metabolic efficiency of the Vol protocol. In contrast, the synchronous and fixed stimulation frequency of 25 Hz imposed during the ES protocol would have prohibited any potential central-peripheral feedback loop, and therefore all active fibers were likely working at equal intensity from the onset. Two prior studies concluded that the imposed synchronization of ES caused repeated stimulation of the same muscle fibers, which induced a marked metabolic demand relative to a Vol protocol (1, 27). However, these authors employed a nonphysiological stimulation frequency of 50 Hz to evoke contractions of the quadriceps, so it is possible that high-frequency fatigue influenced their results. In contrast, we employed the same frequency of stimulation as the mean firing rate of TA MUs recorded with intramuscular needle electrodes during brief sustained voluntary contractions at 50% MVC (6).

Although it has been consistently reported that ES contractions are more metabolically demanding than Vol contractions (13, 17, 18, 25, 29, 30), no studies involving isometric contractions have manipulated the stimulation current during the ES protocol to match the Vol output. Moreover, no studies have quantified the change in maximal torque output (MVC) at either the completion of the fatigue protocols or during recovery. Adams and colleagues (1) began intermittent ES and Vol protocols at equal percentages of MVC but allowed ES torque to decline, thereby creating protocols of different total torque production. In two other relevant studies (25, 29), the authors...
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The accumulation of anaerobic metabolites has been associated with contractile slowing (5, 31); hence, we used the 50Hz-HRT parameter as an indirect measure of anaerobic metabolism. The 48% greater change from baseline of the 50Hz-HRT observed at the end of the ES, compared with Vol, fatigue protocol is indicative of a greater anaerobic demand during ES. Use of both the Hb_{tot} and 50Hz-HRT data provides some insight into which process (i.e., production or removal) is most likely responsible for the greater contractile slowing after the ES protocol. As noted above, Hb_{tot} was not different between the two protocols during exercise; therefore, the most likely source of the contractile slowing is a greater production of anaerobic metabolites during the ES protocol. During recovery from the ES protocol, the rapid return toward baseline of 50Hz-HRT suggests expedient removal of anaerobic metabolites (increased blood flow); the greater Hb_{tot} after 1 min supports this suggestion.

Having considered the influence of both aerobic and anaerobic metabolism, it is likely that the greater impairment of MVC in the ES, compared with the Vol, condition was most closely related to fatigue caused by anaerobic metabolite accumulation because of the elimination of an MVC torque difference between the protocols in 1 min of recovery. Such transient fatigue is known to be metabolic in nature. Additional support is provided by the disappearance of the majority of the contractile slowing induced during the ES protocol within the 1-min period of recovery, which suggests that most of the accumulated metabolites were removed. Statistically, there was a strong negative correlation (r = −0.73) between MVC and 50Hz-HRT during fatigue and recovery. Lastly, the 50Hz-HRT of the Vol protocol returned to the prefatigue level after the 1-min recovery, but there was still a torque deficit of 7% that was not different from the 11% deficit in the ES protocol. This suggests that the remaining impairment to torque in both protocols was not related to metabolites and therefore must be due to another peripheral site such as excitation-contraction coupling failure.

In summary, in a controlled comparison of ES and Vol contractions in which the torque-time integral (torque production) was the same, we found that the ES protocol caused a significantly greater deficit of MVC torque. The enforced synchronization and fixed frequency of excitation of the ES are most likely responsible for the greater aerobic (oxygen desaturation) and anaerobic (contractile slowing) demand and the increased blood volume (Hb_{tot}) induced by the ES, compared with the Vol protocol. After only 1 min of recovery, the impairment to MVC was the same for ES and Vol protocols. The transient nature of the functional impairment to ES and the strong correlation between MVC and 50Hz-HRT, therefore, suggest that the accumulation of metabolites associated with the elevated anaerobic demand played a larger functional role than the elevated aerobic demand in the comparison of ES and Vol contractions.

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