The frequency of alternate muscle activity is associated with the attenuation in muscle fatigue

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Submitted 12 October 2005; accepted in final form 12 May 2006

Kouzaki, Motoki, and Minoru Shinohara. The frequency of alternate muscle activity is associated with the attenuation in muscle fatigue. J Appl Physiol 101: 715–720, 2006. First published May 25, 2006: doi:10.1152/japplphysiol.01309.2005.—Alternate muscle activity between synergist muscles has been demonstrated during low-level sustained contractions [≤5% of maximal voluntary contraction (MVC) force]. To determine the functional significance of the alternate muscle activity, the association between the frequency of alternate muscle activity during a low-level sustained knee extension and the reduction in knee extension MVC force was studied. Forty-one healthy subjects performed a sustained knee extension at 2.5% MVC force for 1 h. Before and after the sustained knee extension, MVC force was measured. The surface electromyogram was recorded from the rectus femoris (RF), vastus lateralis (VL), and vastus medialis (VM) muscles. The frequency of alternate muscle activity for RF-VL, RF-VM, and VL-VM pairs was determined during the sustained contraction. The frequency of alternate muscle activity ranged from 4 to 11 times/h for RF-VL (7.0 ± 2.0 times/h) and RF-VM (7.0 ± 1.9 times/h) pairs, but it was only 0 to 2 times/h for the VL-VM pair (0.5 ± 0.7 times/h). MVC force after the sustained contraction decreased by 14% (P < 0.01) from 573.6 ± 145.2 N to 483.3 ± 130.5 N. The amount of reduction in MVC force was negatively correlated with the frequency of alternate muscle activity for the RF-VL and RF-VM pairs (P < 0.001 and r = 0.65 for both) but not for the VL-VM pair. The results demonstrate that subjects with more frequent alternate muscle activity experience less muscle fatigue. We conclude that the alternate muscle activity between synergist muscles attenuates muscle fatigue.

MUSCLE FORCE IS PRODUCED by the activation of pools of motor units that are composed of motoneurons and their innervating muscle fibers. Muscle fatigue has been defined as an acute, exercise-induced reduction in the maximum force-generating capacity of a muscle (2, 10). A reduction in the net excitatory input to the motoneuron pool and a change in intrinsic properties of the motoneurons in the spinal cord are considered the major factors for central fatigue, whereas the impairment of the processes located at or distal to the neuromuscular junction is considered peripheral fatigue (10). To compensate for the progressive loss of force due to peripheral fatigue during a prolonged submaximal contraction, the nervous system usually increases the excitatory input to the motoneuron pool monotonically and progressively until task failure.

Specific muscle activation patterns other than monotonic increase in muscle activity, however, can appear during sustained isometric contractions in some conditions. For example, intermittent muscle activity was observed in all elbow flexor muscles during isometric elbow flexion at 20% of maximal voluntary contraction (MVC) in 7 of 11 subjects who underwent 4 wk of limb immobilization (27, 28). The intermittent muscle activity was characterized by clear bursts with intervals of reduced activity without necessarily a concurrent compensating reduction or increase in muscle activity in other agonist muscles. Interestingly, this intermittent muscle activity was present only in subjects whose endurance time was prolonged after immobilization. Although the relation between the amount of intermittent muscle activity and level of muscle fatigue was not quantitatively examined in these studies, the findings imply that muscle fatigue can be influenced by the pattern of muscle activation.

Another specific pattern of muscle activation is a clear alternating pattern of muscle activation between synergist muscles in a variety of synergist muscle groups, including knee extensor (32) and ankle extensor (33) muscles, during sustained low-force contractions. This alternating pattern (32, 33) appears to be distinct from the intermittent muscle activation in elbow flexor muscles (27, 28) in that when one muscle is active, the other muscle is silent. Recently, our laboratory termed this specific muscle activation pattern between synergist muscles as “alternate muscle activity” (Fig. 1) (17–19). However, the functional significance of this specific pattern of muscle activity has not been elucidated with regard to muscle fatigue.

In the earlier studies (32, 33), the number of alternate muscle activity was not quantified nor was it examined whether the alternations in muscle activity were made intentionally by subjects. Our laboratory then confirmed that the alternate muscle activity during knee extension was completely involuntary and established a method to quantify the number of alternate muscle activity in knee extensor muscles (18). Our laboratory also revealed that blood circulation is locally impaired by the alternate muscle activity even during a low-level contraction (2.5% MVC force) (19). Furthermore, an increase in physiological tremor due to muscle fatigue was modulated by the alternate muscle activity (17). These findings suggest that the alternate muscle activity is related to muscle fatigue, but the mechanism is still unknown.

On average, MVC force is reduced by 11–15% after a 1-h prolonged knee extension at 2.5% MVC force (17–19). The amount of reduction in MVC force is variable across subjects and so is the frequency of alternate muscle activity. With the
alteration in muscle activation, it is likely that fatigued muscles may recover from fatigue during their silent phases, leading to an attenuation of muscle fatigue. Hence, we hypothesized that the frequency of alternate muscle activity is associated with the degree of muscle fatigue.

METHODS

Subjects. Data from 41 healthy subjects during a sustained knee extension at 2.5% MVC force were examined. In addition to the existing data set of 19 subjects in previous studies (17–19), the new data set was obtained from 22 subjects. The age, height, and body mass of the 41 subjects (means ± SD) were 26.1 ± 2.5 yr, 171.6 ± 6.7 cm, and 67.4 ± 8.6 kg, respectively. They gave their written, informed consent for the study after receiving a detailed explanation of the purposes, potential benefits, and risks associated with participation in the study. All procedures used in this study were in accordance with the Declaration of Helsinki and were approved by the Committee for Human Experimentation at the Department of Life Sciences, The University of Tokyo.

General procedure and equipment. The basic setup for the knee extension procedure has been described in our laboratory’s previous studies (17–19). Subjects were in a seated position with the hip and knee joint angles flexed 90° (full extension = 0°). The trunk and thigh were strapped to a chair. The knee extension force was measured by a strain gauge force transducer (model 274II, Minebea, Tokyo, Japan), which was coupled with a strain amplifier and attached by a strap to the dorsal aspect of the lower leg just above the medial malleolus. Bipolar surface electromyogram (EMG) was recorded from skin surface over the muscle belly of rectus femoris (RF), vastus lateralis (VL), and vastus medialis (VM), and biceps femoris long head (BF), using Ag-AgCl electrodes with a diameter of 5 mm and an interelectrode distance of 20 mm. After careful abrasion of the skin, the electrodes were placed on the skin over the muscle belly of the respective muscles. The common reference electrode was placed on the iliac crest. The electrodes were connected to a preamplifier and a differential amplifier having a bandwidth of 5 Hz to 1 kHz (model 1253A, NEC Medical Systems, Tokyo, Japan). All electric signals were stored on hard disk of a personal computer at a sampling rate of 1 kHz using a 16-bit analog-to-digital converter (PowerLab/16SP, ADInstruments, Sydney, Australia).

Experimental protocol. Subjects performed MVCs before and immediately after (<1 s) a sustained contraction. The MVC task involved a gradual increase in knee extension force exerted by the quadriceps muscle from baseline to maximum for 3–4 s and then sustained at the maximum for 2 s. The knee extension force was displayed in real-time on an oscilloscope. The onset of the task was based on a verbal count given at 1-s intervals. Vigorous encouragement was provided from the investigator when the force began to plateau. Each subject performed at least three MVC trials with subsequent trials performed if the differences in the peak force of two MVCs were >5% (10), and the trial with the highest peak force was chosen for analysis. After a sufficient rest period (~10 min), the subject sustained a contraction of the knee extensor muscles at 2.5% MVC force for 1 h. The force and the target were displayed as horizontal lines on an oscilloscope in front of the subject to provide visual feedback. Subjects were instructed not to alter joint angles or force directions during the sustained contraction. No verbal feedback or encouragement was provided during the sustained contraction to avoid intentional changes in muscle activation strategy. Furthermore, our laboratory has confirmed that the alternate muscle activity cannot be achieved voluntarily by altering joint angles or force directions (18).

Data analyses. During the MVC tasks, simultaneous recordings of force and EMG signals were analyzed over 1-s periods of steady force output. The mean value of force was calculated for 1 s in each MVC task. The EMG signals were full-wave rectified and averaged for 1 s to calculate the average EMG (AEMG) in each MVC task.

Alternate muscle activity was observed in EMG activity between RF and a set of VL and VM during the sustained contraction (Fig. 1). To quantify the alternate muscle activity between synergist muscles, we focused on marked changes in the EMG sequences between the knee extensor muscles. EMG of BF (antagonist muscle) was small and constant across the sustained contraction, and thus it was not included in further analyses.

An alternate muscle activity between synergist muscles was defined and counted according to previously established methods (18). Briefly, EMG signals during the sustained contraction were full-wave rectified and averaged over 15 s to yield AEMG every 15 s. Calculated AEMG of each muscle head was smoothed by five-point moving average and differentiated (dAEMG/dt); an outlier was defined as dAEMG/dt that exceeds ± 3 SD of the first eight sample points; the extracted outliers were classified into positive and negative outliers; the alternate muscle activity was defined as the case in which the positive and negative outliers overlapped between the synergist muscles; and the number of the alternate muscle activity was counted in each muscle combination, i.e., between RF and VL (RF-VL), between RF and VM (RF-VM), and between VL and VM (VL-VM) throughout the sustained contraction. The total number (frequency) and combinations of alternate muscle activity were determined by this.
method throughout the sustained contraction. Detailed account of the methodology has been given elsewhere (18). In addition, mean AEMG of the 1-h contraction was calculated in each muscle.

Statistical analyses. Relative changes in MVC force and AEMG after the sustained contraction were calculated as the difference in these values between the MVC tasks before and after the sustained contraction divided by the values before the sustained contraction. A linear regression analysis was also performed between the relative change in MVC force and the relative change in AEMG during MVC. A one-way ANOVA with repeated measures and a Tukey’s post hoc test were used to identify significant differences in the relative change in AEMG during MVC across muscles. The level of significance for all comparisons was set at $P < 0.05$ and corrected for multiple comparisons. Values are given as means ± SD in the text and means ± SE in the figures.

RESULTS

All subjects were able to complete the 1-h contraction without volitional exhaustion. The alternate muscle activity was observed in EMG between RF, VL, and VM muscles (Fig. 1) in all subjects. The reduction in MVC force after the sustained contraction ranged from 4.6 to 23.5%. On average, MVC force decreased by $14.1 \pm 5.2\%$ ($P < 0.01$) from $573.6 \pm 145.2$ N to $493.3 \pm 130.5$ N. During the sustained contraction, AEMG of RF amounted to $17.2 \pm 4.6\%$ (range: 10.9–30.2%) of its maximal value when it was most active. AEMG in VL ($11.9 \pm 7.7\%$, range: 4.3–20.9%) and VM ($10.1 \pm 3.4\%$, range: 3.6–18.9%) was significantly smaller compared with RF ($P < 0.05$ for both) when each of these muscles was most active.

The alternate muscle activity for the RF-VL pair and RF-VM pair were frequently concurrent and outnumbered the alternate muscle activity for the VL-VM pair ($P < 0.01$). The frequency of alternate muscle activity ranged from 4 to 11 times/h for the RF-VL ($7.0 \pm 1.9$ times/h) and RF-VM ($7.0 \pm 1.9$ times/h) pairs, but it was only 0 to 2 times/h for the VL-VM pair ($0.5 \pm 0.7$ times/h). A significant negative linear relation was found between the frequency of alternate muscle activity and the amount of reduction in MVC force for the RF-VL and RF-VM pairs ($P < 0.001$ and $r = 0.65$ for each) but not for the VL-VM pair (Fig. 2A). There was no significant correlation between the mean AEMG of the 1-h contraction and the amount of reduction in MVC force in any muscles (Fig. 2B).

After the sustained contraction, AEMG during MVC showed a decrease in all muscles on average, but a significant reduction was found only in RF ($P < 0.01$). In addition, the decrease in AEMG of RF was significantly greater than that in VL and VM (Fig. 3A). A significant correlation was found only between the changes in MVC force and AEMG of RF ($r = 0.40$, $P < 0.01$).

DISCUSSION

In the present study, alternate muscle activity between knee extensor synergist muscles were observed in all 41 subjects,
and the functional significance of this neural strategy on muscle fatigue was investigated. In support of our hypothesis, the reduction in MVC force was negatively correlated with the frequency of alternate muscle activity between muscles. The findings indicate that alternate muscle activity between synergist muscles attenuates muscle fatigue during a low-level sustained contraction.

Significance of the present study. The present findings provide the first quantitative evidence for the functional significance of alternate muscle activity in attenuating muscle fatigue. Based on an earlier observation by Sjøgaard et al. (32) on alternate activity in EMG and intramuscular pressure during sustained knee extension, Enoka and Stuart (8) speculated that muscle fatigue might be minimized by varying the activity among knee extensor muscles. In line with this speculation, subjects who had longer endurance time in sustained trunk extension had more frequent alternate muscle activity between the left and right erector spinae muscles compared with other subjects who had shorter endurance time (4). In this study (4), however, apparent alternate muscle activity was limited to three of seven subjects, and the relation between the frequency of the alternate muscle activity and the degree of muscle fatigue (reduction in MVC force) was not investigated. Because of these limitations, the previous study (4) was unable to conclusively explain the functional significance of alternate muscle activity.

In the present study, alternate muscle activity was observed in all 41 subjects, and a clear inverse relation was found between the frequency of alternate muscle activity and muscle fatigue defined as a reduction in MVC force. This finding explains the occasional observations of prolonged endurance time with frequent alternate muscle activity during sustained contractions.

Causes of muscle fatigue during low-level sustained contractions. Muscle fatigue during low-level sustained contractions may involve peripheral fatigue: impairment of the processes located at or distal to the neuromuscular junction. According to an increase in the venous plasma potassium concentrations and muscle water content during a 1-h 5% MVC knee extension (31, 32), force of the contracting muscle may be reduced because of a decrease in muscle cell excitability that was caused by a loss of potassium from the cells and because of an impaired substrate transport (increased diffusion distance) within the muscle that was caused by an accumulation of water in the interstitial space. Furthermore, prolonged contractions can impair the release and uptake of calcium by the sarcoplasmic reticulum that may lead to impairment in muscle contractility (11, 13, 21).

A resultant reduction in force needs to be compensated by an increase in the excitatory input to the motoneuron pools, which is manifested as an enhanced EMG activity (7, 23). In the present study, the EMG activity averaged across the 1-h contraction ranged from 1 to 17% of the corresponding maximal value across subjects, but it was not correlated with a reduction in force during the MVC task (Fig. 2B). It is suggested therefore that the amount of peripheral fatigue may not be the primary factor that influences the degree of muscle fatigue during low-level sustained contractions. However, it is
also possible that the AEMG may have been altered due to changes in muscle fiber action potentials. This could result from a probable decrease in muscle cell excitability mediated by a loss of potassium from the cells.

Another potential factor that may contribute to muscle fatigue is central fatigue: a reduction in the net excitatory input to α-motoneurons. Indeed, a reduction in force accompanied a reduction in AEMG in RF during the MVC task after a sustained contraction (Fig. 3A), and there was a positive linear relation between these reductions across subjects (Fig. 3B). Interestingly, there was no reduction in AEMG in other muscles and no significant association between the changes in MVC force and AEMG in these muscles. These results suggest that a reduction in MVC force after low-level sustained knee extension may be primarily dependent on a reduction in the net excitatory input to α-motoneurons in RF.

This reduction of AEMG in RF and not in other muscles implies that the excitatory input from the motor cortex was not reduced, but the net excitatory afferent input to α-motoneurons in RF was reduced after a sustained contraction. According to a similar observation (concurrent reduction in knee extension MVC and EMG only in RF) after prolonged vibration of RF (16), an impairment in Ia afferent functions in RF due to prolonged tremor during alternate muscle activity (17) may be involved as a potential mechanism. Although the sustained contraction might have changed the shape of muscle fiber action potentials, a change in shape is unlikely to explain the significant reduction of AEMG in RF because the change in the area of action potentials due to fatiguing contractions is not systematic but variable (5, 9).

Potential mechanisms for alternate muscle activity. Physiological mechanisms underlying alternate muscle activity remain as yet unknown. It is likely, however, that fatigue in RF plays a major role for the following reasons. RF appears to be most susceptible to fatigue in the knee extensor muscles as examined by EMG (6), mechanomyography (15, 30), functional magnetic resonance image (34), and positron emission tomography (20). In addition, impaired blood circulation associated with phasic activity is observed only in RF during low-level sustained contractions (19). Our laboratory has speculated (19) that this impairment in blood circulation in RF is attributable to greater mechanical stress due to the smaller muscle volume of RF compared with other knee extensor muscles (1). Furthermore, during low-level sustained contractions, the increase in AEMG is greatest in RF, the force tremor is greater when RF is more active, and a majority of the alternate muscle activity was observed predominantly between the RF and the set of VL and VM (17–19). Although contributions of central and peripheral fatigue are unknown, it is likely that fatigue-related feedback information is transmitted from the afferents of RF to α-motoneurons in each knee extensor muscle, probably via interneurons, leading to alternate muscle activity.

As a potential neural circuit, inhibitory neural connections between synergist muscles may be involved. In support of the presence of inhibitory neural connections, Gritt and Schieppati (12) demonstrated an inhibition of soleus H reflex by gastrocnemius muscles that was abolished after prolonged vibration to the Achilles tendon. This finding suggests the existence of an inhibitory synaptic input to α-motoneuron pools in the soleus muscle from the Ia afferents originating in the gastrocnemius muscle. According to Gritt and Schieppati and Schieppati et al. (26), this Ia inhibitory connection between the gastrocnemius and soleus muscles may represent the mechanism for adjusting the activity between the monoarticular (soleus) and biarticular (gastrocnemius) muscles in a synergist muscle group. In support of this notion, a Ia inhibitory connection between the biceps brachii (biarticular) and brachioradialis (monoarticular) muscles has been also demonstrated in the elbow flexor synergists in a recent study (24). Because the RF is a biarticular muscle and the VL and VM are monoarticular muscles, it is conceivable that there may be a similar Ia inhibitory connection between these muscles in the knee extensor synergists as well. In addition to Ia afferents circuit, recurrent inhibition supplying synergist muscles via Renshaw cells could be related to reciprocal activation between synergists (14). Hence, these studies are consistent with the idea that there are inhibitory neural connections between mono- and biarticular synergist muscles, which may contribute to alternate muscle activity.

Potential inhibitory neural connections across knee extensor muscles would lead to alternating muscle activity, possibly in the following way. During a sustained low-force contraction, the RF starts to fatigue and increases its activity earlier than the VM and VL because of its greater fatigability (6, 15, 20, 30, 34). This fatigue-induced increase in the RF activity accompanies a reduced activity of both VL and VM and a predominant increase in 8- to 12-Hz oscillations in force (i.e., physiological tremor) (17). This increased physiological tremor may increase Ia afferent input to RF possibly via α-γ-coactivation. The involvement of an increased Ia afferent input is supported by a reduction of fatigue-induced physiological tremor after vibration and nerve block (3), both of which depress Ia afferent input. One consequence of this circuitry is that an increase in Ia afferent input to RF can increase inhibitory input to VL and VM, reducing the activity of these vasti muscles. Another consequence is that a reduction in muscle spindle activity after prolonged discharges of muscle spindles (22, 25, 29) in the RF would reduce inhibitory input to the VM and VL and increase their activity. However, because there are no studies that have directly assessed the alterations of inhibitory neural input to individual knee extensor muscles in relation to alternate muscle activity, these potential mechanisms require further investigations.

Attenuation of muscle fatigue by alternate muscle activity. The significant association between the frequency of alternate muscle activity and muscle fatigue suggests that muscle fatigue during low-force contractions can be explained in part by the frequency of alternate muscle activity. The potential pathways that attenuate muscle fatigue by alternate muscle activity include the following. Although alternate muscle activity temporarily imposes a greater load to particular muscles that are more active, it reduces the load to other muscles that are silent or less active. Hence, frequent alternate muscle activity allows less active muscles to recover from their impaired muscle cell excitability, substrate transport, and Ia afferent functions. In particular, the recovery in Ia afferent functions in RF appears to be most influential to the attenuation of muscle fatigue based on the linear relation between the reduction of force and AEMG in RF during MVC.

In conclusion, muscle fatigue during a low-level sustained contraction is associated with alternate muscle activity among
synergist muscles. The results suggest that the nervous system can employ alternate muscle activity to attenuate muscle fatigue in synergist muscles. Accordingly, if the nervous system employs this specific neural strategy, the endurance time during sustained contractions will be prolonged.

ACKNOWLEDGMENTS

We are grateful to Tetsuo Fukunaga (Waseda University) for invaluable comments on the study. We thank Kevin Keenan (Cornell University), Zachary Riley and Michael Pascoe (University of Colorado) for comments on the manuscript.

GRANTS

This work was supported, in part, by Grant 15700396 from the Ministry of Education, Science and Culture of Japan.

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