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The Effects of Training on Fatigue and Twitch Potentiation in Human Skeletal Muscle

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Twitch postactivation potentiation (PAP) in skeletal muscle is a well recognized and accepted phenomenon. However, the mechanisms responsible for potentiation are not understood in detail, and the possible role of potentiation in normal human movement has remained unclear. It is known that potentiation is increased in fatigued compared to rested muscle. We hypothesized that if fatigue and potentiation were directly linked, a training program should increase PAP and reduce fatigue in parallel. Six subjects underwent a muscle stimulation protocol in which twitch contractions were elicited in the knee extensor muscles before and after a 10-s maximal voluntary contraction (MVC) to detect the degree of PAP. This was done before and after subjects underwent a protocol designated to induce low-frequency fatigue (knee extensions at $180 \cdot s^{-1}$, organized in three repetitions of 60-s bouts, separated by 3 min). This whole protocol was done before and after a 4-week period of isokinetic training, consisting of two sets (5-min interval) of 10 single MVCs (10-s intervals), at $90° \cdot s^{-1}$. In non-fatigued muscles, PAP was greater after training (51.2 ± 4.8%) than before training (44.4 ± 2.4%). In fatigued muscles, PAP was similar before and after training (59.9 ± 2.8% and 60.2 ± 2.6%, respectively). Low-frequency fatigue was observed before training, as twitch force decreased to 66.8 ± 3.1% of the pre-fatigue value. After the training period, low-frequency fatigue was attenuated, as force decreased only to 81.8 ± 2.6% of the pre-fatigue value. Therefore, it appears that training decreases low-frequency fatigue and increases PAP. Therefore, the hypothesis that potentiation is partially linked to fatigue in voluntary contracting human skeletal muscles was confirmed.

Key Words: potentiation, low-frequency fatigue, fatigue, force regulation, light chains

Key Points:

•The role of twitch postactivation potentiation (PAP) in human skeletal muscle is unclear. It may be a mechanism to counteract muscle fatigue. If this is the case, a training program that increases PAP should reduce fatigue in parallel.

•Six subjects underwent a muscle stimulation protocol in which PAP and fatigue were induced before and after a 4-week period of isokinetic training.

•Training increased PAP and decreased low-frequency fatigue. Therefore, it seems that potentiation is partially linked to fatigue in voluntary contracting human skeletal muscles.

Introduction

Postactivation potentiation (PAP) is the activity-dependent enhancement of twitch-developed tension following a tetanic or a maximal voluntary contraction (MVC) observed in human skeletal muscles (8, 11, 13, 25). Overwhelming evidence suggests that the mechanism responsible for twitch potentiation is a Ca^{2+}-dependent phosphorylation of the regulatory light chains of myosin (RLC; 13, 19) . Studies with animals have shown that RLC phosphorylation increases Ca^{2+} sensitivity and force development for a given stimulation (21, 23), resulting in a bigger twitch amplitude, compared to situations in which the RLC are not phosphorylated.

Although PAP is a common phenomenon observed in skeletal muscles, little is known about the practical implications of this form of force regulation. It has been suggested that PAP represents a cellular mechanism used to compensate for the decline in force observed during low-frequency muscle fatigue (8, 10, 11). Low-frequency fatigue has been referred to as the depression of the contractile response at low-frequency muscle stimulation and is associated with a decrease in active force production in human skeletal muscle (7, 11). Since human muscles are not maximally activated during regular activity, PAP would have an important physiological implication if it would counterbalance low-frequency fatigue. Although this hypothesis is attractive, it is based exclusively on the fact that PAP and low-frequency fatigue were found to coexist during low (11) and intermediate (8) frequencies of muscle stimulation, and also after MVC (9, 13). However, the hypothesis that low-frequency fatigue and PAP are related has not been tested following adaptations in the neuromuscular system, like muscle atrophy, neuromuscular disease, or systematic muscle training.

We were interested in investigating the effects of systematic muscle training on the interaction between PAP and low-frequency fatigue. It is known that certain isokinetic muscle training programs increase muscle endurance (1, 17) and force production (1–3, 17). Further, it has been shown that athletes with a high endurance capacity have an enhanced PAP that may counteract fatigue during repetitive exercise (12). If there is a training-induced increase in fatigue resistance, and twitch potentiation really balances low-frequency fatigue, then an increased resistance to fatigue should be associated with an increased PAP. Therefore, the working hypothesis of this study was that training decreases low-frequency fatigue and increases PAP.

Methods

Subjects

Six healthy individuals volunteered to participate in this study. They were moderately active physical education students and were familiarized with the procedures of the study before testing. None of the individuals had lower limb injuries. All procedures were approved by a Committee on the Ethics of Human Studies of the Federal University of Rio Grande do Sul, and each subject gave written informed consent to participate in the study.

Apparatus

For this study, an isokinetic dynamometer (CYBEX NORM) was used for measurement of the torque output of the knee extensor muscles. Subjects were seated in the CYBEX straight-backed chair, with their hips and chest restrained by elastic straps. The axis of rotation of the CYBEX arm was aligned with the apparent axis of rotation of the knee. The dynamometer pad was positioned on the anterior aspect of the leg, about 5 cm above the lateral malleolus.

During the voluntary and elicited isometric contractions, the knee angle was kept constant at 120° (180° = full extension), the angle at which maximal torque output is normally reached in isometric and slow-velocity contractions (14). Also, it is known that PAP in human muscles is greater when the muscle is shortened, compared to a 90° angle (25). During the dynamic testing, subjects performed contractions through a range from 90° to 180°.

The dynamometer was equipped with a special arm containing a homemade linear differential force transducer. The tension output from the transducer was recorded (3000 Hz) and visualized on a computer during the experiments.

Procedures

During testing, subjects performed MVC, and isometric, electrically elicited twitch contractions. During MVC, subjects were told to build up to maximal force over the first 2 to 3 s, and maintain the maximal effort for 10 s. Verbal encouragement was given to the subjects throughout the contractions.

Twitch contractions were given by electrical stimulation using 50 μs square wave pulses from a GRASS S88 stimulator. Two stimulation electrodes were placed proximally and distally on the anterolateral surface of the thigh. The stimulation was in series with an isolation unit approved for human use. The stimulation voltage was determined to be maximal for each subject prior to the testing by increasing the current until the twitch force response plateaued.

Potentiation and Fatigue Protocols

Initially, three twitch contractions were elicited (20-s intervals) from the relaxed muscle at a knee angle of 120° for reference purposes. After a 1-min interval, these twitches were repeated to check for reliability. After a further 5-min rest, an isometric MVC (duration 10 s) was performed at a knee angle of 120° that was immediately followed by eight postactivation twitches at 30-s intervals.

After a further 5-min rest, an exercise protocol was performed to elicit low-frequency fatigue, as described previously (11). Specifically, subjects performed maximal knee extensions through a range of 90–180° at an angular speed of $180 \cdot s^{-1}$. Three bouts of 60 s were performed with a rest of 3 min between bouts. Following the fatigue protocol, a potentiation protocol identical to that given before the fatigue protocol was given to the subjects.

Training Protocol

After the first session of data collection, subjects started a 4-week training period, based on that described by Caiozzo et al. (2). Subjects trained three times a week (Monday to Friday) separated by at least one day. The training consisted of two sets (5-min interval) of 10 single MVC at an angular velocity of $90° \cdot s^{-1}$, with intervals of 10 s between individual efforts.

After completion of the final training session, a period of maximally 3 days was given before the subjects repeated a testing session identical to the one performed before the training period.

Statistics

The three reference twitch contractions recorded at the beginning of the protocol were compared to the three twitches recorded after a 1-min interval to evaluate the reproducibility of these measurements. This analysis was done before and after the training program. The effect of the fatigue protocol on force production was determined by calculating the decrease in peak MVC and twitch force from the pre- and post-fatigue trials. This decrease caused by the fatigue protocol was compared before and after training. Finally, the degree of PAP (post-activation twitch/pre-activation twitch) was compared before and after fatigue, for the untrained and trained situations. All comparisons were done with the Wilcoxon's non-parametric test, and a value of $p < .05$ was used for all analysis.

Results

The control twitch contractions (1-min interval) recorded at the beginning of the protocol were compared to check reliability of data collection throughout the experiments. The difference between these twitches before and after training was –0.26 ± 1 N and 0.53 ± 0.6 N, respectively. Therefore, the reliability of data collection between trials was satisfactory.

Before training, the MVC amplitudes were 175.1 ± 15.2 N · m and 155.3 ± 17.1 N · m, for non-fatigued and fatigued muscles, respectively. After training, the MVC amplitudes were significantly greater, with values of 189.1 ± 21.6 N · m and 175.2 ± 21.5 N · m, for non-fatigued and fatigued muscles, respectively. The amplitude of the MVC was always significantly lower after fatigue than before.

Table 1 shows the values for the twitch contractions for the different experimental situations. The post-activation twitches were significantly greater than the pre-activation twitches—that is, PAP was observed in this study before and after fatigue, as well as before and after training. The twitch forces were significantly lower after fatigue compared to before. Therefore, the protocol caused low-frequency fatigue for all conditions. As shown in the last row of Table 1, PAP was increased by training in the non-fatigued muscle. Further, PAP was always greater in the fatigued compared to the non-fatigued muscles.

Table 1 Developed Tension of Pre-Activation (Pre-MVC) and Post-Activation (Post-MVC) Twitch Contractions, Recorded Before Fatigue (BF) and After Fatigue (AF), in Untrained and Trained Conditions

Variable	Untrained		Trained	
	BF	AF	BF	AF
Pre-MVC (N · m)	35.7 ± 3.0	23.9 ± 2.1	36.4 ± 1.9	29.6 ± 1.0
Post-MVC (N · m)	51.7 ± 4.5	38.3 ± 3.6	54.9 ± 2.8	47.4 ± 1.8
Potentiation (%)	44.4 ± 2.4	59.9 ± 2.8	51.2 ± 4.8	60.1 ± 2.6

Note. Values are mean ± *SEM*.

In order to better understand the effects of training on fatigue, the decrease in force caused by the fatigue protocol was compared before and after training. Before training, the force of the twitch contractions decreased to 66.8 ± 3.1% of the pre-fatigue value. After training, the force decreased to 81.8 ± 2.6% of the pre-fatigue value, and this decrease was significantly smaller than the one observed before training. Therefore, the training protocol produced an increased muscle endurance to low-frequency fatigue.

Figure 1 shows the time course of twitch amplitudes over a period of 4 min, recorded after the MVCs. In Figure 1a, the data from one representative subject are shown, with twitches recorded before the MVCs (time zero) and after the MVCs. The force enhancement after the MVC is apparent, and it is greater in the fatigued compared to the non-fatigued muscles. Note that training did not increase the twitch amplitude but increased PAP. Also, the pattern of change in twitch force is not different over the 4-min period for the fatigued and non-fatigued muscles. As expected, the twitch amplitude of the fatigued muscles is smaller at the end of the 4-min period than the corresponding values obtained in the non-fatigued muscles.

Figure 1b shows the mean relative potentiation for all experimental conditions. The pattern of force decrease over time is similar in all conditions. Fatigued muscles had a greater PAP than non-fatigued muscles. This increased PAP in fatigued muscles was observed for about 3 min following the end of MVCs. After 2 min, potentiation was highly depressed, and after 4-min potentiation was virtually absent in all situations.

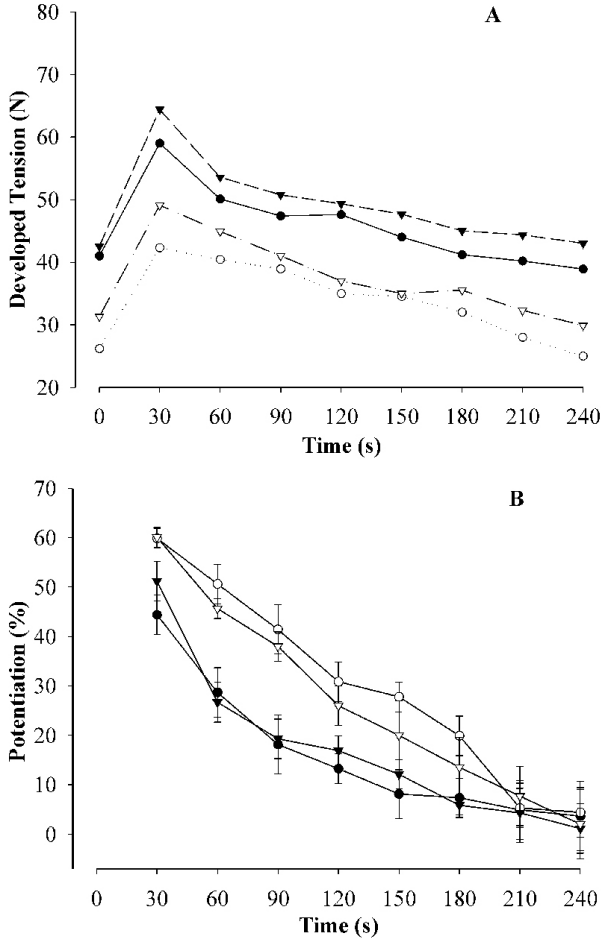

Figure 1 — Time course of twitch amplitudes over a period of 4 min after the MVCs, before (solid symbols) and after fatigue (open symbols), before (circles) and after training (triangles). A. Data from one representative subject, showing twitch developed tension recorded before (time 0) and after MVCs. B. Relative force increase in twitch contractions (mean ± *SEM*) after the MVC, indicating the level of PAP.

Discussion

The main purpose of this study was to evaluate the effects of training on PAP and low-frequency muscle fatigue. It was anticipated that, if training reduces fatigue, and PAP compensates for fatigue, then the degree of PAP would be greater after training. This hypothesis was confirmed.

Muscle training used in this study produced a significant increase in MVC, as has been observed by others (1–3, 17). However, it did not affect the twitch amplitude, also in agreement with previous observations (4, 15, 18). There are some studies in which a training-induced increase in twitch amplitude was found, but they used longer periods of training than the 4 weeks used here (6), or they used endurance athletes who had been training for long periods of time (12).

After the training protocol, resistance to fatigue was increased. Also, training increased PAP. The increased resistance to fatigue in the trained compared to the non-trained muscles might be directly associated with the increased PAP following the training protocol. Krarup (16) suggested that upon contraction, two competing factors are initiated: potentiation, resulting in an increase in force of the contractile machinery for a given activation, and fatigue, resulting in a decrease in force. Training might increase the ability to produce force over time because of an increased ability for potentiation, a decreased fatigue response, or a combination of the two factors. Here, we provide evidence in support of the idea that training results in an increased ability for potentiation, thus potentiation might have contributed to the fatigue resistance observed after training in our subjects.

Post-activation potentiation was greater in fatigued than in rested muscles. Similar results were observed in the in situ rat gastrocnemius (24) and were associated with a decrease in the levels of RLC phosphorylation after fatigue. Likely, RLC phosphorylation was also decreased in the fatigued in vivo human quadriceps compared to the rested muscles. Although fatigue may be caused in several ways, the primary mechanism is thought to be a decreased Ca^{2+} concentration in the myoplasm (26). Although PAP is regulated by the Ca^{2+}-dependent RLC phosphorylation, it has been shown that the effects of RLC phosphorylation on potentiation are greater at low Ca^{2+} concentrations (20, 22). Therefore, the conditions created by fatigue likely act to enhance the effects of RLC phosphorylation, leading to an increased potentiation.

In summary, a short period of systematic training induced an increase in muscle endurance in parallel with an increase in PAP. Therefore, the hypothesis that PAP may balance low-frequency fatigue, at least to a certain extent, must be retained as a distinct possibility. Our results suggest that twitch potentiation may be an effective way for human skeletal muscles to offset the effects of muscle fatigue to a certain extent. Since everyday voluntary contractions are submaximal (5), PAP could play a greater role than might have been thought based on studies of maximal activation. Potentiation may produce more force for a given amount of activation, or similarly, may allow the muscle to produce a given force with less activation than would be required if the muscle was not potentiated. Also, potentiation may represent an effective way to offset, to a certain degree, the loss of muscle force associated with fatigue. Further research is needed to better understand the role of twitch potentiation in human skeletal muscles during everyday movements and sport activities.

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