FORCE TRAINING INDUCES CHANGES IN HUMAN MUSCLE MEMBRANE PROPERTIES

Werner J. Z'Graggen MD[1,2*], Joël P. Trautmann[2], and Hugh Bostock PhD[3]

[1] Department of Neurosurgery, Inselspital, Bern University Hospital and University of Bern, Bern, Switzerland

[2] Department of Neurology, Inselspital, Bern University Hospital and University of Bern, Bern, Switzerland

[3]Sobell Department of Motor Neuroscience and Movement Disorders, Institute of Neurology, University College London, London, UK

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Correspondence to: W.J. Z'Graggen, email: werner.zgraggen@insel.ch

Running title: Training and muscle membranes

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Abstract

Introduction: Human muscle membrane properties can be assessed *in vivo* by recording muscle velocity recovery cycles (MVRCs). This study was undertaken to study the effect of muscle force training on MVRC parameters.

Methods: MVRCs with 1 to 5 conditioning stimuli were recorded from brachioradialis muscle before and after 2 weeks of muscle force training in 12 healthy subjects. The effects of training on relative refractory period and early and late supernormality were quantified.

Results: Force training induced a reduction of relative refractory period ($P<0.0001$), while early supernormality was increased ($P<0.02$) and peaked earlier ($P<0.01$). Late supernormality and the increases in late supernormality due to 2 and 5 conditioning stimuli remained unchanged.

Discussion: Muscle force training leads to hyperpolarization of the resting muscle membrane potential, probably caused by an increase in the number of sodium pump sites.

Keywords: force training, muscle velocity recovery cycle, relative refractory period, early supernormality, muscle membrane potential

Introduction

Changes of muscle membrane potential and alterations of muscle ion channel function can be assessed *in vivo* by recording multi-fiber muscle velocity recovery cycles (MVRCs) [1-6]. The technique is based on the principle that an elicited action potential induces a depolarizing afterpotential, which declines in 2 phases over about 1 sec (early and late supernormality) to its resting membrane potential [7]. If a second action potential is evoked during this period, its propagation velocity will be increased, depending on the inter-stimulus interval [7-10].

Force training has been shown to induce functional, structural, and molecular muscular plasticity [11]. The aim of this study was to investigate whether muscle strength training results in changes in multi-fiber MVRC measurements.

Methods

Twelve healthy right-handed subjects (4 women and 8 men; age 22-27 years, mean 23.4 years) participated in this study. Ethical approval was obtained from the local ethics committee (Kantonale Ethikkommission Bern, Switzerland) and conformed to the Declaration of Helsinki. Subjects provided written informed consent.

Recording of multi-fiber muscle velocity recovery cycles

In all subjects the left (non-dominant) brachioradialis muscle was examined. Cutaneous temperature was maintained at 32°C. MVCR studies were performed using a recently described protocol [7,10]. MVRCs with test stimuli alone, single, paired, and 5 conditioning stimuli were recorded. The inter-stimulus interval (ISI) between the

conditioning stimulus and the test stimulus was varied between 1000 and 2ms in 34 steps. For recording and analysis the QTRAC program (written by H. Bostock, copyright Institute of Neurology, London, UK) was used. The following MVRC parameters were analyzed: 1) Relative refractory period, i.e. the interpolated ISI at which velocity first reached its unconditioned value; 2) early supernormality, measured as the peak percent increase in velocity at ISIs shorter than 15 ms; 3) the interpolated ISI at which the peak early supernormality occurred; 4) late supernormality, measured as the average percentage increase in velocity at ISIs of 50-150 ms; 5) extra late supernormality in recordings with 2 conditioning stimuli; and 6) extra late supernormality in recordings with 5 conditioning stimuli, measured as the peak percent increase in velocity at ISIs of 50-150 ms due to the extra conditioning stimuli.

Experimental protocol and training

MVRCs were tested on days 0 and 14, and training sessions undertaken on days 1, 3, 5, 7, 9, and 11. The training sessions involved exerting voluntary force by raising the left forearm against resistance (elastic band), for 30s every minute for 10 minutes. Brachioradialis force was measured just before recording MVRCs. The subject was asked to bend the elbow maximally with the forearm in the semi-pronated position against a weight transducer fixed underneath a shelf. A measure of endurance was provided by the time for which a force two-thirds of maximal could be maintained within 10 Newtons.

Statistics

Measurements before and after training in the same subject were compared by a 2-tailed paired *t*-test (*t*-test of differences), and *P* values computed by the QTRAC software. $P<0.05$ was considered significant.

Results

The force training successfully increased the maximum force exerted by the subjects (from a mean of 258 to 282 Newtons, $P<0.01$), but endurance time did not increase significantly (from 195 to 220 s, $P=0.66$). MVRCs before and after training are compared in the Figure. Latency changes following a single conditioning stimuli are shown in the upper panel of Fig. 1A, while the extra changes in latency produced with 2 and 5 conditioning stimuli are compared in the lower panel. Figure 1B shows that the reductions in relative refractory period due to training, although small, were highly significant (from 3.2 to 2.9 ms, $P<0.0001$). There was also a significant increase in early supernormality (from 12.0 to 13.6%, $P=0.02$), which peaked earlier after training (at 6.4 ms rather than 7.0 ms, $P<0.01$). There were, however, no significant changes in late supernormality or in the increases in late supernormality with 2 and 5 conditioning stimuli (see lower panel of Fig. 1A).

Discussion

These results show that the force training produced consistent changes in muscle membrane properties that reduced the relative refractory period and increased supernormality. These changes are in the opposite direction to those previously reported in ischemia [1,7], and to those related to hyperkalemia in patients with renal failure [2]. In each of those cases the changes were attributed to membrane depolarization. Our new results therefore suggest that force training causes a slight

hyperpolarization of the muscle membrane. Since it is well established that force training increases the Na^+-K^+ pump density of muscle [12] and since the electrogenic property of the Na^+-K^+ pump will cause increased pump activity to hyperpolarize the muscle membrane, the most likely explanation of the changes we have observed is that the increased Na^+-K^+ pump density due to training causes the hyperpolarization. The reduction in muscle relative refractory period may contribute to the enhanced force production in trained muscles, since training has also been shown to increase the percentage of motor units firing in 'doublets' with ISIs in the range 2-5 ms [13] and doublets lead to motor unit force increase [14].

Abbreviations

ISI = inter-stimulus interval

MVRC = muscle velocity recovery cycle

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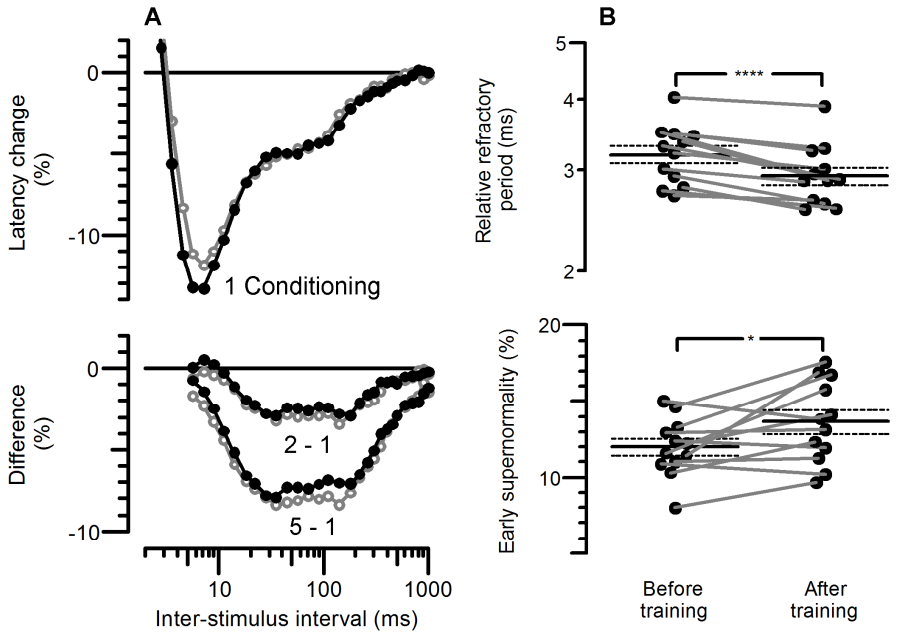

Figure 1 legend

Changes in MVRC measurements before and after training. A) Latency changes as a function of ISI. Open grey circles show recordings before, and filled black circles after training. Upper panel: mean values after single conditioning impulse. Lower panel: mean extra latency changes with 2 and 5 conditioning impulses. B) relative refractory period (upper panel) and peak early supernormality (lower panel) before and after training displayed for each subject measured from recordings with 1 conditioning stimulus. Asterisks indicate *P* values for two-tailed paired t-test: *=$P<0.05$, ****=$P<0.0001$.