

BAM'98 International Conference on Muscle Plasticity

In this issue the BAM News present Program and Abstracts of the "Fifth Abano Terme Meeting on Rehabilitation, BAM'98 - International Conference on Muscle Plasticity" which will be held in Abano Terme and Padova (Italy), June 14-16, 1998.

The Conference Topics range from Activity-induced Muscle Damage to Muscle-related Gene Therapy, but Muscle Plasticity and its Medical Applications are main goals.

Local Organizers and the Members of the International Scientific Committee hope that numerous participants will meet in Abano Terme to: 1) exchange information on the latest developments in four interconnected sub-fields (Activity-induced muscle damage, Contribution of skeletal myopathies to Chronic Heart Failure, Dynamic Cardiomyoplasty and Skeletal Muscle Circulatory Assistance, and Muscle-related Gene Therapy), 2) organise a European Study Group on Skeletal Muscle Circulatory Assistance, and 3) extend the Italian Trial on Demand Dynamic Cardiomyoplasty.

Beside others topics, clinical effectiveness of Dynamic Cardiomyoplasty will be discussed and some exciting news will be presented. Indeed, using a skeletal muscle to support a failing heart is the result of a multidisciplinary approach, which asks much more than surgery and a trivial device. Among new developments in this surgical therapy of the cardiac heart failure world-class leader in the field will present their expertise in: i) Minimally invasive video assisted Cardiomyoplasty, ii) Vascular delay before LD wrapping, iii) Monitoring of cardiac function, iv) Protocols for conditioning and regime stimulation of LD wrap, v) Bedside monitoring of the dynamic characteristics of LD flap, and vi) Demand Dynamic Cardiomyoplasty.

Organizers gratefully acknowledge Siemens and Hewlett Packard which, even at such a short notice, were so kind to provide, respectively, a Megacart polygraph, and a cardiac Echo Doppler with Tissue Imaging to be used on patients during the Tutorial on LD Flap Monitoring.

Let us hope that the perspectives open by the Conference will attract new interested and interesting scientists, surgeons and doctors to developments and implementations of the new approaches.

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Letter to Basic and Applied Myology

In their interesting paper [3] Duan and his colleagues examine the chronic effects of stimulating rabbit latissimus dorsi muscle with a burst pattern. They report that peak isometric force had fallen to half the control level after 6 weeks of stimulation for 24 hours/day, but had risen to twice that of control after 12 weeks of stimulation for 12 hours/day.

Their seemingly remarkable findings nevertheless present a significant problem. The ability of a muscle to generate force is directly proportional to its cross-sectional area, yet the morphological changes reported by Duan et al. for the intermittent pattern (Figure 5) are minimal. If we multiply the percentage of SO, FOG and FG fibres by their respective mean cross-sectional areas and add the 3 results, we can use the data to estimate the change in the overall cross-sectional area of the muscle. For the intermittent pattern there is actually a reduction of 5% in cross-sectional area (mainly because of the smaller proportion of the larger FG fibres) compared to a reported increase of 105% in peak isometric force. How do we reconcile these conflicting results?

The simple answer is that 'peak isometric force' measured in this study does not equate to the maximum force-generating capability of the muscle. To explain this statement we need to refer back to protocols worked out many years ago for measuring the rate of tension development and amplitude of tetanic contraction in fast and slow muscles [1,2, 7].

When a fast rabbit muscle is stimulated at successively higher frequencies, a fused contraction is not normally achieved until about 100 Hz and peak isometric tetanic tension continues to increase up to at least 150 Hz. Duan et al. state that they made their measurement of peak isometric force with the same pattern used for conditioning - that is to say, with a maximum frequency of only 25 Hz. This would not elicit maximum isometric tension from the control muscles.

The important corollary is that with such a stimulation protocol 'peak isometric force' would be a sensitive function of the contractile speed of the experimental muscles. Duan et al. give no figures for contractile speed, but in another study the time to peak twitch contraction of muscles subjected to a similar aggregate amount of activity increased by about 100% [6]. The greater degree of fusion produced by this slower contractile speed could easily generate the doubling of tension reported by the authors, even in the absence of any concomitant change in the mass or cross-sectional area of the muscle.

What of the results for 'continuous' stimulation? For this group there is an estimated reduction of 34% in overall cross-sectional area, somewhat smaller than that expected from the reported decrease of 48% in peak isometric force. Muscles subjected to this amount of stimulation would typically show substantial fusion, even at 25 Hz [5, 7]. However, because of a very slow time course of rise of

tetanic tension they would achieve full contraction only after about 500 ms of tetanic stimulation [1,2,7]. Duan et al. measured peak isometric tension with tetani of 250 ms duration, and a tetanus of this short duration would underestimate the tension-generating capacity of the muscle.

Duan and his colleagues are in all probability correct when they argue that the capacity to produce force is better preserved in the long term by a less continuous pattern of stimulation. Indeed, Ferguson et al. [4], whom they cite, came to a similar conclusion. However, for the reasons stated here, it is unfortunately not possible to place any reliance on the figures they report for the size of this effect.

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Response

Professor Salmons raises some interesting issues concerning our recent report on muscle training via interval burst stimulation (BAM 1998; 8 (1): 35-39). He is, of course, quite right in asserting that our measurements of peak isometric force do not equate to the maximum force-generating capability of the muscle. This however, was not our intent. The principal goal of this work was to determine whether periodic intervals of rest can improve the functional capacity of fatigue-resistant muscle stimulated under conditions generally accepted for clinical use. While we recognize the importance of characterizing skeletal muscle function under a wide range of stimulation and [loading conditions, such extensive testing would likely have fatigued the control muscle and impaired our ability to assess chronic work capacity. Moreover, in practical terms, preserving a given fiber type distribution over the long term requires that skeletal muscle be activated with the same pulse pattern used during training. We therefore chose to limit testing to a single stimulation regimen (25 Hz, 250 ms burst duration, 5 contractions/min) which had been used to train the muscle and has been proven safe for clinical use.

We concur with Professor Salmons that the force-generating capacity of muscle is directly proportional to its cross-sectional area (CAS), but must disagree with his contention that changes in whole muscle CSA can be estimated from the fiber distribution and fiber areas reported in Figures 4 and 5 respectively. In our paper, percent fiber distribution refers to relative number of each fiber type in a given CSA of muscle tissue (note that the percentages always add up to 100). These figures do not indicate the absolute number of fibers present. Thus, it is not possible to estimate the change in whole muscle CSA in the manner suggested without assuming that the total number of muscle fibers remains constant with training (an assumption for which there is little basis). It therefore remains quite possible that the muscles trained via interval stimulation actually increased CSA by increasing the total number of muscle fibers in a manner analogous to exercise training (1).

Admittedly, measurements of whole-muscle mass and CSA would have been helpful in determining the physiologic basis for the large power increases seen in the interval stimulation group but the amount of tissue needed to perform electrophoresis, histochemical, and biochemical analyses made this impossible. We can only hypothesize that the improved contractile performance described in our report was due to some combination of muscle hypertrophy (seen qualitatively), increased number and recruitment of FOG motor units (2), and reduced contractile speed (as Professor Salmons has suggested). However, this does not diminish the fact that interval training has been shown to improve chronic muscle performance under clinically-appropriate stimulation conditions. This is the

central tenet of this work, a message which we hope has been clarified through this correspondence.

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Letter to Basic and Applied Myology

I read with interest Professor Salmons' letter [Basic Appl myol 1998; X (x): 0-0] commenting our latest BAM publication [4]. Professor Salmons is correct regarding the difficulty of reconciling the 105% increase in peak isometric force in the 12-week interval stimulation group over control muscles. However, recognizing that the aim of this study was not to prove or disprove basic principles [1, 3,6], established long before the start of biomechanical cardiocirculatory assist with skeletal muscle, but to research into the new ones that must regulate muscle physiology under the novel electro stimulating patterns utilized for clinical purposes, such reconciliation becomes easier.

In our clinically oriented work we did not intend to elicit maximum isometric tension or to generate maximum isometric force. Indeed, Professor Salmons is right in stating that in our study 'peak isometric force' does not equate to the maximum force-generating capability of the muscle. Our protocol did not call for it to be so. A close review of our manuscript reveals the use of the term maximum in only two occasions, in: Results, paragraph 1, lines 2 and 3. We assumed, as the reviewers and most readers probably did, that maximum under the testing protocol was understood, as opposed to absolute maximum, incompatible with clinical use in circulatory assist. We apologize for the inconvenience. Elsewhere throughout the paper, the term peak isometric force is used.

We recognize with Professor Salmons the ability of a whole muscle to generate force is directly proportional to its cross-sectional area (CSA), and that a fast muscle (fast oxidative [FO] fibers) does not normally achieve a fused contraction until about 100 Hz, and continues to increase up to around 150 Hz. Recognizing however that peak isometric contraction, regardless of generated force, is

dependent upon the number (percentage) of fiber recruited at one time, we elected to utilize a stimulation pattern equal to that used for muscle conditioning. Our specific aim was to demonstrate what difference had made the conditioning pattern in treated muscles as compared to controls. A 25 Hz burst of 250 ms duration, with pulse width of 210 usec was chosen for its closeness to clinical electrostimulation programs. Frequencies higher than 35 Hz and burst durations longer than 150 ms have proven to be deleterious for long-term application of muscle powered circulatory assist [5].

We cannot agree with Professor Salmons' interpretation of figures 4 and 5. An estimation of the change in the overall CSA of the muscles in each group is irrelevant to the purpose of our research. Other observations related to non-clinically applicable basic principles are irrelevant as well.

Fast glycolytic (FG) fibers are abundant in the latissimus dorsi muscle and take the largest portion of the CSA. They are strong and respond well to high frequencies (100 Hz +), but for our purpose are useless in account of being very prone to fatigue. Distribution of slow oxidative (SO) fibers increases dramatically with continuous stimulation but occupy the smallest CSA in so stimulated muscles. They respond well to low frequencies (10 Hz +) and are resistant to fatigue, but for our purpose are also useless because muscles conditioned in this manner become significantly weaker and slower.

Fast oxidative glycolytic (FOG) fibers on the other hand, retain much of the best of the other two types over the long periods of time. Muscles trained under an interval stimulation protocol of 12 weeks, with burst at a frequency of 25 Hz and pulses of 210 usec amplitude, proved to develop the highest peak isometric force with this set of parameters and, following an initial decrease, to maintain the highest contractile function for as long as 170 minutes, and that is an undisputable fact. The explanation is found in the proper interpretation of figures 4 and 5 of our paper. Under the interval stimulation protocol, fiber distribution (%) of FOG fibers increased significantly over controls, and FOG fibers were the only ones to reach significance in fiber CSA increase. These findings suggest that FOG fibers are more energy-efficient from the thermodynamic point of view [2], which possibly makes them responsible for better long-term contractile performance and fatigue resistance, and that interval stimulation may be able to yield and sustain a larger proportion of FOG fibers of greater CSA, in an otherwise healthy working muscle.

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EDITORIAL & LETTERS TO THE EDITOR

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Response

The estimation was based on published evidence that the number of fibres does not increase in chronically stimulated muscle [1, 2]. In our view, experimental data that provide an insight into mechanism will ultimately be of the most value clinically, particularly when those data are derived from small laboratory animals.

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