Histochemical and Fatigue Characteristics of Conditioned Canine Latissimus Dorsi Muscle


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SUMMARY. To induce fatigue resistance in the latissimus dorsi muscle of the dog in preparation for possible myocardial assistance, eight adult male beagles underwent unilateral electrical stimulation of the thoracodorsal nerve at a frequency of 2 Hz (120 stimuli/min) and 10 Hz (600 stimuli/min) for a 6-week period. The conditioned muscles were compared with their unconditioned contralateral controls by fiber typing, pyrophosphate gel electrophoresis, isometric characteristics, and fatigue rates. At the end of the period of stimulation, the conditioned muscles had a greater percentage of slow-twitch, fatigue-resistant fibers on acid and alkaline stains (100 ± 0.7% and 83 ± 15.3%), respectively, than did their contralateral controls (45 ± 7.6% and 43 ± 7.0%). Pyrophosphate gel electrophoresis revealed an increase in the slow myosin and a decrease in the fast myosin content in the conditioned muscles; the stimulated muscles also demonstrated a slower contraction time (87 ± 20 msec vs. 57 ± 17.9 msec), a lower initial tension (4.4 ± 1.45 kg vs. 7.2 ± 2.11 kg), and a slower fatigue rate during a 30-minute fatigue test than did their contralateral controls. The muscles stimulated at 2 Hz had fatigue rates similar to those stimulated at 10 Hz, but generally had less diminution in muscle fiber diameters and less interfiber connective tissue. Thus, it is possible to make canine latissimus dorsi muscles more fatigue resistant, and, theoretically, more capable of myocardial assistance by electrical stimulation of the thoracodorsal nerve at a frequency as low as 2 Hz—the natural canine heart rate. (Circ Res 58: 298–304, 1986)

BECAUSE of the many problems inherent in the use of artificial hearts or heart transplantation, many investigators have attempted to utilize skeletal muscle for myocardial assistance (Kantrowitz, 1960; Nakamura et al., 1964; Kusaba et al., 1973; Spotnitz et al., 1974; Macoviak et al., 1981; Dewar et al., 1984). Despite often encouraging initial results, augmentation of cardiac output has been inevitably thwarted by skeletal muscle fatigue (Nakamura et al., 1964; Kusaba et al., 1973; Spotnitz et al., 1974; Dewar et al., 1984). The relentless demand placed upon the heart, its high metabolic rate, predominantly aerobic metabolism, and slow contraction characteristics make its replacement by skeletal muscle a formidable task. Recently, however, endurance training and chronic low frequency stimulation have been shown to induce physiological and biochemical changes in mammalian skeletal muscle which may make it more capable of the sustained work required of a myocardial substitute (Hudlicka et al., 1977; Salmons and Henriksson, 1981; Armenti et al., 1984).

This experiment was designed to evaluate the effect of electrical muscle conditioning on the latissimus dorsi muscle of the dog through the thoracodorsal nerve at rates of 2 and 10 Hz, and to evaluate the histochemical and functional characteristics of the conditioned muscle.

Methods

Control Experiments

Five adult male beagles that did not undergo previous electrical conditioning were studied to test for possible differences between their right and left latissimus dorsi muscles. All five control animals underwent fatigue testing and histochemical evaluation of the muscles bilaterally. The methods for fatigue testing and histochemical analysis are described below.

Muscle Conditioning

Eight adult, male beagles with a weight range of 10–17 kg underwent unilateral conditioning of the latissimus dorsi muscle. The animals were anesthetized with 30 mg/kg of pentobarbital, intubated, and placed on a Harvard ventilator. A 5-cm longitudinal skin incision was made in the mid-axillary line of the right side, and the latissimus dorsi was reflected from the chest wall. The thoracodorsal nerve was identified and two modified electrodes were placed underneath the nerve, 3 cm apart. The fascia and blood supply on top of the nerve were left intact. Medtronic bipolar electrodes (model 6901R) were shortened and modified by attaching a variable length of stranded, no. 36-gauge, Teflon-coated, stainless steel wire. The stainless steel ends were fashioned to a ¾” diameter loop. The leads were attached to a Medtronic 5984 multiprogrammable pulse generator, set to 3.2 V and 0.22-msec pulse width. One-half inch doughnut-shaped magnets, embedded in Silastic, were bonded to the pulse...
generators to retain an asynchronous mode. The 44-g pulse generators were positioned in a pocket fashioned posterior to the right rectus muscle. The lead extended subcutaneously from the pocket to its position around the thoracodorsal nerve. The pulse generators were programmed to a rate of 2 Hz (120 stimuli/min) in five dogs and to 10 Hz (600 stimuli/min) in three dogs, with a Medtronic custom engineered, hand-held programmer. The muscles were stimulated continuously 24 hours a day. The average duration of chronic continuous stimulation at 2 Hz was 40 ± 4.6 days; the length of chronic continuous stimulation at 10 Hz was 30, 38, and 40 days.

**Fatigue Testing**

At the end of the period of chronic electrical stimulation, the eight conditioned animals’ latissimus dorsi muscles were evaluated. The contralateral non-conditioned latissimus dorsi muscle served as control for the chronically stimulated muscle. The animals were again anesthetized with 30 mg/kg of pentobarbital and placed on a ventilator. A balanced salt solution without glucose was used for intravenous therapy. Arterial blood pressure was monitored through a femoral arterial line. The dog was secured to the operating table with a ⅛” rawhide strap over-riding the pelvic brim or with Steinman pins placed in the femur. The tendons of the latissimus dorsi were detached bilaterally from their insertions into the humerus and attached to Grass strain gauges (FT10) with #0 polyglactin sutures. Muscle temperatures were measured with 22-gauge hypodermic thermistors placed in the muscles and maintained at 36.5 ± 1.5°C with a heat lamp. The thoracodorsal nerves were identified bilaterally, and two modified electrodes were placed around each nerve. An S44 Grass square wave stimulator was used to produce supramaximal pulses (approximately 6 V) 0.22 msec in duration in order to initiate a muscle twitch. Voltage was considered supramaximal when a further increase in voltage failed to result in an increase in peak tension. Whole muscle contraction time was calculated to be the time from initiation of contraction to peak tension.

Twitch times were recorded on a Grass model polygraph with a pen recorder. The accuracy of the Grass recording system for the determination of canine latissimus dorsi twitch times was assessed with a WPI 302 T square wave stimulator, a Tetronix 564 oscilloscope, and a crystal-controlled time mark generator (University of Pennsylvania, Neurosciences). The oscilloscope time base was calibrated using the time mark generator. The output of the stimulator then was adjusted to initiate multiple square wave pulses from 30–200 msec, which were fed into 5 PI Grass preamplifiers. The resulting curved waveforms, taken at a paper speed of 100 mm/sec, were then measured graphically using a transparent curvilinear overlay by an observer unaware of the generated pulsewidths. The mean error rate for pulses between 30 and 100 msec was 5.7 ± 2.7% (range 0–11%); for pulses between 100 and 200 msec, the mean error rate was 4 ± 1.2% (range 2–6%).

Isometric twitch contractions at varying lengths were obtained, and the length which yielded the highest twitch amplitude was utilized for the fatigue test. Two S44 Grass square wave stimulators, modified by a 556 analog timing circuit, were used to produce trains (556 ± 98 msec) of pulses at 25 Hz, followed by 750 msec of rest. Although the duration of stimulation varied slightly between some animals, the duration of stimulation did not vary for the right and left latissimus dorsi muscle in the same dog (mean difference, 18 msec ± 10 msec). Isometric contractions were recorded on a Grass model polygraph; hemodynamic data and muscle temperatures were recorded on an Electronics for Medicine DR-12 recorder equipped with a rapid writer printout. The muscles were stimulated sequentially with the order (right or left) of stimulation variable. The period of stimulation of the fatigue test was 30 minutes (Fig. 1).

The fatigue tests, as described above, were performed on two of the five unconditioned dogs. The right and left muscles of the remaining three dogs were fatigue-tested simultaneously rather than sequentially.

**Histochemistry**

After completion of the fatigue test, the animals were sacrificed and both latissimus muscles were dissected from each animal. Six biopsies were taken from the conditioned muscle and from the six corresponding areas of the contralateral, unconditioned latissimus dorsi. All specimens were quickly frozen in liquid nitrogen. Serial transverse frozen sections, 10 μm thick, were cut on a cryostat and stained for myofibrillar adenosine triphosphatase (ATPase) with acid (pH 4.3) and alkaline (pH 10.4) preincubation (Dubovitz and Brooke, 1983). The slides were reviewed, and three representative muscle bundles were evaluated on both the acid and alkaline stain. The percentages of slow and fast fibers were calculated from each section by averaging the counts from three representative muscle bundles. Cells were identified as fast or slow by Brooke’s ATPase classification (Brooke and Kaiser, 1969). In conditioned muscles with acid stains, a cell was counted as a slow-twitch type if it stained darkly; with alkaline stains, a cell was counted as a fast-twitch type if it stained darkly.

Hematoxylin and eosin stains were performed on selected frozen sections and reviewed for regenerative muscle fibers and interfiber connective tissue. Three thousand fibers were surveyed from each conditioned muscle and
the percentage of cells with central nuclei was tabulated. Fiber areas also were computed. Images from muscle fiber sections were projected from a Zeiss microscope onto a video screen by an Optomax video camera and were magnified $1.3 \times 10^3$. The television screen was connected to an Apple graphics tablet. Tracings on the graphics tablet were also projected onto the video screen, permitting accurate outlining of the muscle fibers. A software program for area measurements converted the data from the graphics tablet on an Apple IIe computer. All muscle fibers from two representative muscle bundles were measured in the conditioned muscles and in contralateral controls. Each muscle bundle contained approximately 80 muscle fibers.

Gel Protein Electrophoresis

Myosin isozymes were analyzed from muscle biopsies of similar location for representative control, 2 Hz, and 10 Hz animals. Pyrophosphate gel electrophoreses were performed on slab gells as described in a previous communication (Lyons et al., 1983).

Statistical Analysis

Data analysis was conducted on a DEC-10 computer using BMDP and SPSS statistical packages (Nie et al., 1979; Dixon et al., 1981) with adjunctive Fortran programming. Analyses included repeated measures analysis of variance and Wilcoxon matched pairs signed rank test, where appropriate.

Results

Control Experiments

Five dogs that had served as bilateral controls were evaluated for possible differences between right and left latissimus dorsi muscles; however, no significant differences were found. There was some variation in histochemistry and isometric characteristics among the five dogs, but very little variation in the same dog between the left and right latissimus dorsi muscles. The percentage of slow fibers by acid ATPase staining for the left and right side were $45 \pm 18.2\%$ and $47 \pm 19.5\%$, respectively. The percentage of fast-twitch fibers by alkaline ATPase staining for the left and right side were $59 \pm 18.9\%$ and $61 \pm 15.3\%$, respectively. The twitch times for the left and right latissimus dorsi muscles were $54 \pm 8.9$ msec and $51 \pm 16$ msec, respectively. The peak tensions and fatigue rates from both sides of the control animals were similar to the "contralateral control" values of the conditioned animals (Fig. 1).

Experiments on Conditioned Animals

Histochemistry

In the eight dogs with conditioned latissimus dorsi muscles, the contralateral control muscles were eval-

![Figure 2](http://circres.ahajournals.org/)

**Figure 2.** ATPase stains with acid and alkaline preincubation of latissimus dorsi muscle, respectively (top row, control; middle row, 2 Hz; bottom row, 10 Hz, left column, acid preincubation; right column, alkaline preincubation). Note the 100% conversion (dark staining fibers) on acid stain for both rates of stimulation and the greater number of cells with a suggestion of residual fast myosin (dark-staining fibers) on alkaline stain after 2-Hz stimulation.
Table 1

Percent Slow and Fast Fibers in Control and Conditioned Muscles

<table>
<thead>
<tr>
<th>Dog no</th>
<th>Control Mean ± SD</th>
<th>Conditioned Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% Slow Acid</td>
<td>% Fast Acid</td>
</tr>
<tr>
<td>2 Hz</td>
<td>51 ±8.9</td>
<td>54 ±13.9</td>
</tr>
<tr>
<td>2</td>
<td>53 ± 8.9</td>
<td>49 ± 13.7</td>
</tr>
<tr>
<td>3</td>
<td>32 ± 4.6</td>
<td>73 ± 9.7</td>
</tr>
<tr>
<td>4</td>
<td>44 ± 11.1</td>
<td>61 ± 11.0</td>
</tr>
<tr>
<td>5</td>
<td>39 ± 8.1</td>
<td>61 ± 14.2</td>
</tr>
<tr>
<td>10 Hz</td>
<td>54 ± 10.8</td>
<td>49 ± 10.9</td>
</tr>
<tr>
<td>7*</td>
<td>43 ± 7.4</td>
<td>55 ± 6.4</td>
</tr>
<tr>
<td>8</td>
<td>44 ± 4.6</td>
<td>56 ± 4.8</td>
</tr>
<tr>
<td>Mean ± sd</td>
<td>45 ± 7.6</td>
<td>57 ± 7.8</td>
</tr>
</tbody>
</table>

A comparison of the fiber types on both acid and alkaline (Alk) stain between the conditioned latissimus dorsi muscles and their contralateral controls.

* Sections 2, 5—not converted; sections 1, 3, 4, 6—100% converted.

uated for distribution of slow and fast fibers within six different areas of the muscle. The mean percentage of slow fibers for the unconditioned muscle was 45 ± 7.6% by acid stain; the mean percentage of fast fibers was 57 ± 7.8% by alkaline stain. For each dog there was a close correspondence for the percentage of slow and fast fibers calculated from either the acid or alkaline ATPase reactions. When the six different areas of the unconditioned latissimus dorsi muscle were analyzed separately, the posterior sections of the muscle were noted to have a slightly greater percentage of slow fibers than the middle and anterior sections ($P < 0.01$) on acid stains. This slightly higher percentage of slow-twitch fibers was confirmed in sections preincubated at an alkaline pH ($P < 0.01$).

The latissimus dorsi muscles electrically stimulated for 6 weeks were compared with their contralateral control muscles for percentages of slow and fast fibers (Table 1). Virtually, all muscle cells of conditioned muscles contained evidence of slow myosin (stained darkly) on acid preincubation and were considered converted (Fig. 2). The percentage composition of slow-twitch fibers on acid stain was significantly different between stimulated and control muscles ($P < 0.01$), but no differences were found between muscles stimulated at 2 and 10 Hz.

ATPase staining of conditioned muscle sections with alkaline preincubation revealed that 24 ± 14.1% of cells contained residual fast myosin (stained darkly) after 2 Hz stimulation but only 5 ± 8.1% after 10 Hz stimulation. The difference on alkaline stain between the muscles stimulated at 2 and 10 Hz was significant ($P < 0.05$). With either rate of chronic stimulation, the number of cells containing fast myosin in the stimulated muscles was significantly less than in the controls ($P < 0.01$).

The conditioned muscles demonstrated a uniform histochemical conversion throughout the entire muscle. There were two exceptions to this. In dog 6, posterior sections 2 and 5 showed no evidence of conversion on ATPase stains; however, it appeared...
that the pulse generator electrode was placed distal to the nerve branch that supplied the posterior section of the muscle. In dog 2, section 6 was not converted with no apparent explanation.

A review of selected hematoxylin and eosin stained sections revealed that only 0.55 ± 0.7% of muscle fibers were regenerative (range 0–1.9%). Results of the quantitative fiber analysis are shown in Figure 3. Muscle conditioning at either 2 or 10 Hz resulted in a reduction in the percentage of cells with large cross-sectional fiber areas: conditioned muscles had fewer than 4% of cells with areas greater than 2,100 μm², whereas control muscles had more than 30% of cells with areas larger than 2,100 μm². Muscles conditioned at 10 Hz had a smaller mean fiber diameter than muscles conditioned at 2 Hz (873 ± 505 μm² vs. 995 ± μm², respectively), in spite of the fact that the contralateral unconditioned controls of the 10-Hz muscles were slightly greater than those of the 2-Hz muscles (1856 ± 1071 μm² vs. 1682 ± 1217 μm², respectively). The smaller fiber diameter of the 10-Hz conditioned muscle was accompanied by a greater increase in endomysial connective tissue when compared to the 2-Hz muscle. Control muscles demonstrated the least amount of endomysial tissue.

Pyrophosphate Gel Electrophoresis

Changes in the myofibrillar ATPase activity can be correlated with shifts in the complement of myosin isozymes in the chronically stimulated latissimus dorsi muscles. Figure 4 shows a series of pyrophosphate gels of native myosins isolated from latissimus dorsi muscles of control dogs and of dogs stimulated at 2 Hz and 10 Hz for 6 weeks. The control muscle contains the four isozymes characteristic of a mixed muscle: one slow myosin isozyme, SM2, and the three fast isozymes FM1, FM2, and FM3. If dog muscle is analogous to that of other mammals, FM1, FM2, and FM3 will contain the same fast myosin heavy chains, but will differ in their light chain content.

With stimulation of 2 Hz for 6 weeks, most of the fast isozymes disappear; only a small amount of FM3 can be seen. This correlates well with the residual staining for fibrillar ATPase activity seen after alkaline preincubation at this stage. In addition, a larger proportion of SM2 and a smaller proportion of SM1 can be seen.

After 6 weeks of stimulation at 10 Hz, the muscle differs slightly from the sample stimulated at 2 Hz; no fast isozymes can be seen, and the muscle contains a greater proportion of SM1 than after 2-Hz stimulation. Moreover, an isozyme with mobility intermediate between FM3 and SM1 can now be seen. This may represent isozymes with different combinations of fast and slow heavy chains and light chains (Pluskal and Sreter, 1983).

Functional Characteristics

Muscle conditioning resulted in a significant prolongation of peak contraction time: 89 ± 19.1 msec for conditioned muscle vs. 57 ± 18.2 msec for controls (P < 0.02). The conditioned muscles also exhibited a significantly lower initial tension (4.4 ± 1.45 kg) than controls (7.2 ± 2.11 kg, P < 0.02). However, after 30 minutes of fatigue testing, there was no difference in force generated between conditioned or unconditioned muscle (3.7 ± 1.71 kg vs. 3.7 ± 1.45 kg, respectively). The fatigue rates of the conditioned muscles are compared with their contralateral controls in Figure 1. There is a significant slowing of the rate of fatigue in the conditioned muscles compared to their contralateral controls (P < 0.05). The fatigue rates appeared similar for the muscles conditioned at 2 and 10 Hz (not significant).

Discussion

The ultimate goal of our research is to replace nonfunctioning myocardial tissue with a functioning, nonfatiguing substitute, or to augment cardiac output with a muscle-powered assist device. This study shows that chronic stimulation at frequencies...
as low as the natural canine heart rate can effect a uniform transformation of the canine latissimus dorsi from a predominantly fast-twitch muscle into a slow-twitch muscle with fatigue-resistant characteristics. Thus, one aspect of the problem of skeletal muscle fatigue in myocardial augmentation—muscles of mixed fiber type—can be obviated by chronic electrical stimulation.

The latissimus dorsi muscle offers several potential advantages over other skeletal muscles that might be considered for myocardial replacement. It is a large, powerful, broad-based muscle; it can reach the heart with its neurovascular pedicle intact; it is a noncritical muscle which, in fact, has been used by plastic surgeons for cosmetic applications; and it is innervated by a single nerve, the thoracodorsal. This last fact makes it particularly well suited for electrical conditioning. In a previous study, when skeletal muscle was stimulated directly, instead of through its nerve, only a relatively small area of muscle around the stimulating electrode was transformed (Macoviak et al., 1981). In the present study, the entire latissimus dorsi muscle was transformed with a single, appropriately placed electrode by electrical stimulation through the thoracodorsal nerve.

Chronic electrical stimulation for a 6-week period resulted in a significant lowering of peak tension of conditioned muscles. However, the exact role that isometric strength plays in determining the suitability of muscle for myocardial replacement remains undefined. Heart muscle generates a lower peak tension per gram than most skeletal muscle (Mommaerts, 1964). In addition, the right and left ventricles, which are presumably constructed of muscles of equal strength per gram of muscle, have widely different functions. These observations suggest that factors such as ventricular geometry and wall thickness may permit muscle to attain a mechanical advantage, which may be as important in the generation of ventricular pressure as the inherent "strength" of the muscle. Skeletal muscle-powered ventricles have proved unsuccessful thus far, not because of an inability to produce initial physiological pressure and flows, but because of rapid muscle fatigue. In hydraulic pump experiments, initial pressures are often much more than adequate (Spotnitz, 1974). Whether a fatigue-resistant conditioned muscle can perform useful work may be as dependent on how it is used as it is on its isometric strength in a linear model.

An important question is whether the decrease in peak tension of the conditioned muscle indicates muscle fiber damage, or simply reflects a decrease in the mass of contractile machinery. Muscle fiber damage, as reflected in the number of regenerative fibers, was minimal in this experiment. Three previously reported observations also suggest that it is the diminution of muscle fiber size, and not muscle damage, that accounts for the decrease in peak tension of conditioned muscles. First, it has been demonstrated that chronic electrical stimulation results in a reduction of the area, but not the number, of muscle fibers (Pette et al., 1976; Salmons and Henriksson, 1981). Second, ultrastructural examination of transforming muscle has revealed "a less well-organized transitional stage," but no sign of muscle fiber destruction or regeneration (Eisenberg and Salmons, 1981). Third, cessation of chronic electrical stimulation has resulted in a complete reversal of fiber transformation with a return to normal fiber size and a significant reduction in the increased endomysial connective tissue seen with muscle conditioning (Eisenberg et al., 1984). In a previous study using chronic electrical stimulation, we did not detect evidence of embryonic isozymes which would be expected to be present if muscle damage and regeneration were occurring (Hoffman, 1985). The possibility that electrical stimulation induces fiber damage raises serious concern over the long-term use of conditioned muscle, and must be further investigated. However, it is not necessary to postulate muscle damage to account for the lower peak tension of conditioned muscles. In addition, the "atrophy" of conditioned muscles, evidenced by the decrease in fiber size, may not be atrophy in the pathological sense, but rather an adaptive response to continuous use. A smaller fiber diameter may be just as important for oxygen delivery as an ingrowth of capillaries.

Although muscles conditioned by either 2- or 10-Hz stimulation demonstrated similar resistance to fatigue, there were differences between the muscles. Both stimulation patterns resulted in an increased concentration of slow myosin in the original fast fibers, as reflected by the histochemistry and the increased slow myosin band on the pyrophosphate gel. However, 10-Hz stimulation resulted in a more complete disappearance of fast myosin evident in histochemical reactions preincubated in an alkaline pH and was confirmed by the complete absence of a fast myosin band on the pyrophosphate gel. Both 2- and 10-Hz stimulation caused a diminution in muscle fiber size with an increased amount of connective tissue, but this effect was generally more pronounced in the 10-Hz animals (Figs. 3, 4). The observation that the 2- and 10-Hz conditioned muscles exhibited similar fatigue rates, yet demonstrated slight differences in fiber size and myosin content, raises the possibility that different stimulation frequencies can induce fatigue-resistant muscles with different capabilities. Further work must be done to characterize any functional differences between 2- and 10-Hz conditioned muscles. In addition, it is necessary to investigate whether a muscle conditioned at 2 Hz, if stimulated for a longer time period, would ultimately appear similar to a muscle conditioned at 10 Hz.

Previous investigators have demonstrated that the increase in fatigue resistance in conditioned muscles appears to be associated with capillary ingrowth and an increase in mitochondrial density (Cotter et al., 1973; Brown et al., 1976; Heilig and Pette, 1980;
Eisenberg and Salmons, 1981). This occurs before complete replacement of fast myosin by slow myosin (Salmons and Henrikkson, 1981). The difference in myosin content after 2- and 10-Hz stimulation, then, would not be expected to result in a difference in fatigue rates, inasmuch as much fatigue is probably more acutely dependent on energy delivery and utilization than on myosin content.

The rationale for muscle preconditioning is to obviate the fatigue demonstrated by skeletal muscle when an attempt is made to utilize the muscle to perform prolonged hemodynamic work. The exact role that conditioned muscle would have as a myocardial substitute, whether as a replacement for diseased ventricular tissue, as an auxiliary skeletal muscle-powered ventricle, or as a power source for an artificial heart, remains to be determined. Consequently, the stimulation parameters that a muscle would be subject to in any long-term study would depend on how it would be used. However, any fatigue-resistant muscle would be expected to have at least some of the characteristics of the 2- or 10-Hz conditioned muscle. Muscles conditioned in this manner might prove useful in evaluating models for muscle-powered myocardial augmentation until more specific stimulation parameters are determined.

In conclusion, this study demonstrates that low frequency stimulation of canine latissimus dorsi effects a uniform transformation of this predominantly fast muscle into a slow muscle with greater fatigue resistance. The study also demonstrates that the transformation can occur at stimulation rates as low as the natural heart rate, and that there may be reasons for preferring the lower stimulation rate. Myofibrillar ATPase stains, pyrophosphate gel electrophoresis, peak contraction times, and fatigue characteristics are evidence to support the muscle conversion. Whether the latissimus dorsi, with its potential natural advantages for conditioning, can be made to perform useful work as a myocardial substitute remains to be elucidated.

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