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THE FACTORS OF MECHANICAL POWER IN SLOW TWITCH MUSCLE

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1. The concepts.

In order to obtain maximum efficiency of contraction, the mechanical power exerted by the contracting muscle must be matched to the power required to move the load. The maximal mechanical power P_{max} sets the maximal physiological performance of muscle, liberated if all its fibres are stimulated. In most physiological contexts, animals modulate the number of fibres activated and thus are able to obtain the desired match. In muscle artificially stimulated for cardiac assistance, the situation is however different, since the number of fibres stimulated is presumably maximal. No provision is made to match the muscle power to the power requirement of the failing heart. There is thus a large probability that power mismatch occurs, entailing low efficiency. It is thus important to analyze the factors whose combined action are basic to the production of muscle mechanical power.

We limit our analysis to those factors that are closely linked to the contractile machinery, leaving aside the factors that limit the supply of energy to the muscle, such as blood flow, extent of capillary bed, activities of glycolytic and oxidative enzymes, etc. It is also obvious that P_{max} depends on the size of the muscle. We shall be concerned only with the factors that control the maximum mechanical power per unit volume of muscle. The units used for the physical variables are chosen such that P_{max} is expressed in microwatt of mechanical power per cubic millimeter of muscle.

The basic theory is well exposed in the book of Woledge and al., 1985 (10) P_{max}. can easily be deduced from the force-velocity curve of the muscle. It will thus be based on a series of measurements performed as follows. The muscle is isolated and tetanically contracted: its maximum force is measured. This force is divided by the area of muscle section perpendicular to the line of force: in this way, we know the maximal force per square millimeters of muscle, which is defined as S_o, the maximal isometric stress. The isometrically contracting muscle is then released at a controlled velocity: the stress S

(force per muscle area) maintained during the release depends on the velocity V of shortening according to the hyperbolic Hill's equation:

$$S = S_o(b - V.a/S_0)/(b+V) \quad \text{(Eq. 1)}$$

In this equation, V is the independent variable, controlled by the experimenter, S is the measured variable. In order to compute P_{max} in the required units, V is measured in mm/s per mm of muscle fibre length (a unit often called muscle length per s, Lf/s) and S is in mN/mm^2.

Eq. 1 has three independent parameters: S_o, the maximal isometric stress defined above, b, the velocity constant (measured in Lf/s) and a/S_o the force constant (dimensionless). The meaning of the constants can be assessed simply by noticing that a muscle shortening at a velocity V equals to b maintains a stress slightly lower than half the isometric stress, So the difference being measured by a/S_o.

P_{max} is simply computed as the product of three independent parameters:

$$P_{max} = S_o.b.f(a/S_o) \quad \text{(Eq. 2)}$$

in which $f(a/S_o)$ is a rather complicated function of a/S_o

$$f(a/S_o) = 1 + a/S_o - 2\,SQR[(a/S_o)/2 + a/S_o] \quad \text{(Eq. 3)}$$

It is interesting to point out that these parameters allow us to compute the maximum velocity of contraction under zero load:

$$V_{max} = b/(a/S_0) \quad \text{(Eq. 4)}$$

2. Mouse soleus, a slow-twitch muscle.

Soleus muscle of mouse is a slow-twitch muscle fatigue resistant and therefore a good model for the analysis of the contribution of the factors of power in the frame of an understanding of the conditions that are important to consider in muscle assisted cardiac support. We examined soleus muscle of two mouse strains: black mice (C57) are quick, while white mice (NMRI) are calm. We observed noticeable differences in the properties of their soleus muscle (Table 1).

Table 1: Mechanical power of mouse soleus muscle (means ± sem)

Strains i	NMRI (n=46)	C57 (n=11)
S_o (mN/mm^2)	158 ± 6	115 ± 8
b (mm/s per mm)	0.47 ± 0.01	0.60 ± 0.02
a/S_0 (%)	0.12 + 0.01	0.12 + 0.02
P_{max} (µW/mm^3)	38	37
V_{max} (mm/s per mm)	0.9	1.4

The maximum mechanical power, P_{max} computed using Eq. 2 with the means of the parameters, is the same for the two strains. This seems reasonable since the body weight of the two strains is similar. However, among the parameters whose product makes up P_{max}, only the force constant is identical in the two strains. The velocity constant is smaller in the white mouse: this is probably explained by its being a quieter animal. The decrease in velocity constant is compensated by an increase in maximum stress S_o such that the product b. S_o does not change. This entails a consequence of great physiological importance, namely that the two strains develop the same maximum power at velocities of shortening V_{max} noticeably different, about 50 % higher for the black mouse. Thus black mouse will tend to shorten its soleus muscle at higher velocities, in order to obtain the best power match. We are thus led to the concept that the velocity of shortening V_{max} required to produce P_{max} can be adjusted by suitable modifications of the factors of P_{max} in such way that P_{max} itself does not change.

3. Isomyosins of mouse soleus.

Differences in mechanical properties of soleus muscle must ultimately be explained by differences in their myosin isoforms (7,8,9, review in 6). Soleus muscle of mouse contains two different isomyosins (5). Isomyosin SM_2 is typical of Type I fibres: it is composed by heavy chains (MHC_1) and light chains (LC_{1s}; LC_{2s}) of the slow-twitch type. Isomyosin IM is found in Type IIA fibres of slow-twitch muscle (hereafter called Type

IIA_s fibers) : its heavy chain ($MHC2A_s$) is similar or identical to MHC2A, but IM is hybrid in its light chains, some being of the slow twitch type, (LC_{1s}; LC_{2s}) some being of the fast twitch type (LC_{1f};LC_{2f}). Black mice have lower proportion of SM_2 (Table 2). Detailed analysis of the data yields a regression between the velocity constant and the proportion of myosin heavy chain 1 quite similar to the one we reported in an earlier work (4):

$$b = 0.68\ (\pm 0.07) - 0.0032\ (\pm 0.001)\ [MHC_1] \qquad \text{(Eq. 5)}$$

The regression line is shown on Fig. 2 of the paper by Moens et al. in this book. S_0 has an opposite dependence on MHC_1 proportion, such that P_{max} barely depends on the proportion of isomyosins. As expected V_{max} decreases as MHC_1 increases. It is possible to deduce the mechanical properties of Type I and Type IIA_s fibres (4). Both fibres produce similar maximal power, approximately 30 to 35 $\mu W/mm^3$ (at 20°C), but Type IIA_s fibres produce that power at a velocity of shortening twice as high. Type IIA_s fibres of soleus are likely to be fibres belonging to the slow twitch fibres. They are different from the Type IIA fibres found in fast-twitch muscle by their isomyosin type and their mechanical parameters. We conclude that it is possible to control the velocity of shortening P_{max} at which maximum power is produced by changing the proportions of slow type isomyosin SM_2 and IM in the muscle.

Table 2: Isomyosins of mouse soleus muscle (means ± sem)

Isomyosin	Heavy chain	Fibre type	NMRI (n=46)	C57 (n=11)
SM_2	MHC_1	Type I	66 ± 1	35 ± 5
IM	MHC_{2As}	Type IIAs	34 ± 1	65 ± 5

4. Cardiac assistance.

Our conclusions have some implications for cardiac assistance using conditioned skeletal muscle. It is important to match not only the power of muscle to the circulation load, but also to adapt the velocity of shortening of muscle.

Up to now, this goal was not considered, since there was no way to achieve it. Only one type of muscle fibre was judged suitable for cardiac assistance, namely Type 1fibres: the muscle conditioning aimed at inducing transformation of all muscle fibres into Type 1 by programmed artificial stimulation. It may be possible to induce transformation of fibres into the slow form of Type IIA_S fibres and thus control not only maximal power but also the corresponding velocity of shortening. Whether this aim could be obtained by a suitable pattern of artificial stimulation is an objective for future research. Future research must also assess the resistance to fatigue of Type IIA_S fibres: it might be lower than that of Type I fibres since Type IIA_S fibres eventually use more energy to propel a given load than Type I fibres, but still sufficient to allow use of Type IIA_S fibres for cardiac assistance.

5. Methods.

Soleus muscle of 57 mice (46 of strain NMRI and 11 of strain C57) were isolated and tetanized in vitro at 20°C. They were shortened at controlled velocity by an electromagnetic puller. The parameters of the force-velocity relation were computed by a non-linear least square procedure. Soleus muscle were extracted in a Guba-Straub solution and analyzed for their isomyosins and myosin heavy chains content by electrophoresis (2,3). Full details of these methods are reported in (1).

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