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The effects of nitric oxide on the maximum shortening velocity of frog and mouse skeletal muscle

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The maximal velocity of shortening (V_{max}) is the single most important mechanical parameter of skeletal muscle fibres, since it indicates the maximum rate of cross-bridge cycling in the muscle. It is measured from the time needed to take up a slack after a rapid release (Edman, 1979). V_{max} varies considerably among muscles, because of differences between myosin isoforms. Muscle fibres are able to change their phenotype by suppressing the expression of a myosin isoform and expressing another one, as for example by training. This process is slow, however, requiring several weeks, because the turnover of myosin is quite slow. Up to now, no physiological factor has been reported that might modulate V_{max} of a living skeletal muscle within a time scale of a few seconds.

We report here on a mechanism to control V_{max} that, in contrast to the genetic mechanism, acts very quickly, possibly within a time scale of a few seconds. It is based on the local production of nitric oxide (NO), a radical whose half-life is very short in tissues. NO is generated enzymatically from L-arginine by NO synthase (NOS), the activity of which is very high in skeletal muscle. We blocked NOS of isolated skeletal muscle (1 h in an oxygenated saline solution containing 1 mM nitro-L-arginine for frog sartorius, 4 °C, 1 mM nitro-indazole sodium for frog tibialis anterior, 7 °C, and 10 mM nitro-L-arginine for mouse muscles, 20 °C). The drugs depressed V_{max} by one-fourth (Table 1), without change in maximum isometric force (methods described in Maréchal *et al.* 1995). When the drug was washed out, V_{max} returned to the control value. The effect was observed in fast muscles of frog and mouse and in a slow muscle of mouse (Table 1). This indicates that suppression of NO production depresses V_{max} reversibly in most skeletal muscles, beyond their particular phenotype or species, except possibly in rat diaphragm (Morrison *et al.* 1996).

Table 1. Means ± S.E.M. ($n = 9$) of V_{max} in muscle fibre length per second

Muscle	Control	NOS blocked	Difference (%)
SART	2·97 ± 0·20	2·48 ± 0·13	−17*
TA	3·94 ± 0·20	2·83 ± 0·21	−28†
EDL	8·11 ± 0·16	5·90 ± 0·32	−27†
SOL	5·37 ± 0·26	3·92 ± 0·16	−27†

SART, frog sartorius; TA, frog tibialis anterior; EDL, mouse extensor digitorum longus; SOL, mouse soleus. Paired t tests: * $P < 0·01$; † $P < 0·001$.

Two major problems should be solved before we can accept a regulatory role for nitric oxide during physiological contractions: first, how does the muscle fibre regulate NO synthase?; and second, which mechanism explains the action of NO concentration on V_{max}?

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