Muscle and Motility
Volume 2

Proceedings of the XIXth European Conference in Brussels

Edited by

G. Maréchal and U. Carraro

Intercept
Andover, Hampshire

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Maximal Isometric Forces of mdx Muscles

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Introduction

Duchenne muscular dystrophy, an X-linked disease, is characterized by the absence of a 400 kDa protein, discovered by Hoffman *et al.* (1), called dystrophin. Zubrzycka-Gaarn *et al.* (2) have localized this protein in the sarcolemma and have suggested that dystrophin is a binding molecule that anchors elements of the internal cytoskeleton to the plasma membrane thereby providing mechanical strength for the sarcolemma.

According to this hypothesis, we would expect muscles lacking dystrophin to develop less force than normal muscles.

Bulfield *et al.* (3) have discovered a mutant of the C57BL10, the mdx mice. These mice have the same gene deletion as in the human Duchenne dystrophy and do not express dystrophin (1).

We have analysed the maximal isometric forces developed by the soleus and extensor digitorum longus (EDL) muscles from dystrophic mice (mdx) and their control strain.

Methods

Six C57 and six mdx mice matched for age (60 ± 5 days) and weight (28 ± 2 g) are killed by neck-breaking. The soleus and EDL muscles of each mouse are dissected, measured, weighted and mounted on a ergometer. Muscles are stimulated isometrically at 20°C in an oxygenated Krebs solution. We have recorded the force of the twitch (*FT*) and the maximal tetanic isometric force

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(*Fo*). The maximal tetanic isometric force was normalized giving the stress (*So*) (*So* = *Fo** fibres length (*Lf*)/ muscle weight (*Wm*); density = 1). The length of the fibres was obtained by microscopic measurements of few superficial fibres. We found that in EDL the fibre length is 0.48% of muscle length, and in soleus it is 0.68%. This is in agreement with Brooks and Faulkner (4). Results are expressed as mean ± SEM.

Results

The length (*Lo*) and the weight (*Wm*) of soleus muscles are not different in the two strains (Fig. 1a). The maximal isometric force (*Fo*) developed by the mdx soleus (243 ± 26 mN) is higher, but not significantly different from that of controls (227 ± 11 mN). The stress (*So*) and the maximal force of the twitch (*FT*) aresimilar in mdx and C57 soleus.

The mdx EDL muscle (Fig. 1b) is shorter (11.7 ± 0.2 mm) than the C57 EDL (12.8 ± 0.2 mm), but there is no difference in the weights. The maximal isometric force of the mdx muscle (33 ± 19 mN) is significantly higher than that of the control muscle (263 ± 21 mN). However, the stress and the maximal

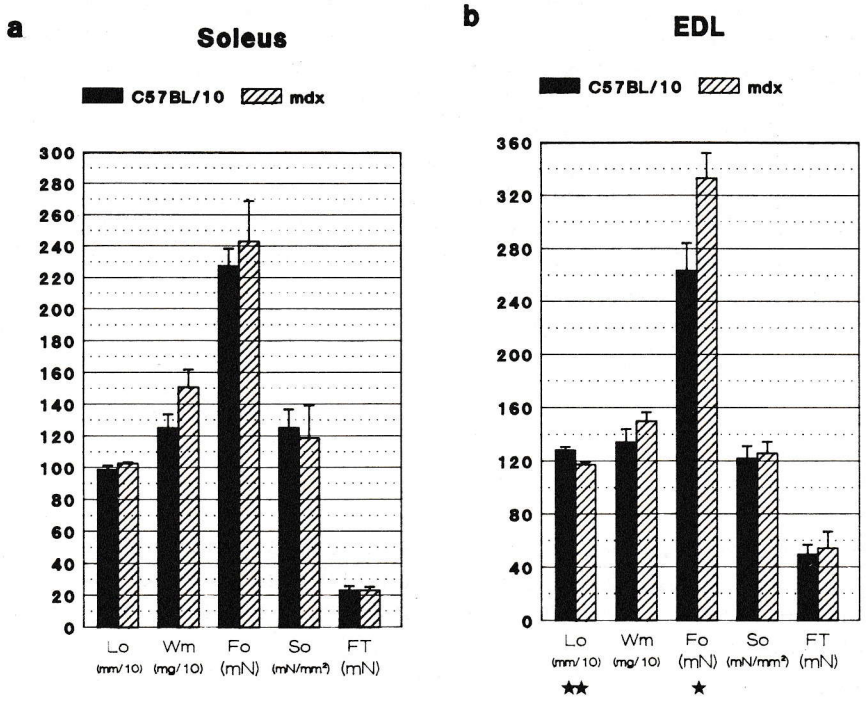

Fig. 1 Comparison between morphological and mechanical parameters of the C57BL/10 and the mdx mice. (a) Soleus muscles (C57: $n = 6$; mdx:$n = 6$). (b) EDL muscles (C57: $n = 6$; mdx: $n = 6$). The bar is the SEM. *$P<5\%$. **$P<1\%$.

force of the twitch are not different between the mdx and the C57 EDL muscles.

Discussion

Our estimates of the maximal isometric force of the soleus muscles are in agreement with those reported by Maréchal and Beckers-Bleukx (5) but they are somewhat greater than those reported by Anderson *et al.* (6) and Coulton *et al.* (7) for both mdx and C57 mice.

The maximal isometric force of the EDL muscle as well as the maximal force of the twitch for the EDL and soleus muscle correspond to the values given by Anderson *et al.* (6). However, they show that the stress of the mdx EDL muscles is significantly lower than the stress of the C57 EDL muscles. We found no differences between the two strains concerning the stress of the muscles. Such differences in the results could be due to the different control strain used. Anderson *et al.* (6) have worked with C57BL/6 mice whilst we used the C57BL/10 strain, the original strain of the mutant mdx (3).

The force developed by the mdx muscle during a twitch and a tetanus was similar to the force developed by soleus and EDL muscles of C57 mice. Thus the absence of dystrophin is not correlated with a decrease of the force developed by the muscle and could not account for the weakness of the muscles characteristic of the Duchenne muscular dystrophy.

Acknowledgements

We are grateful to Dr Partridge and Dr Morgan for donating the animals.

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