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single fibres that have multiple deformities. This is the type of *mdx* skeletal fibre that we concluded was most susceptible to damage by eccentric contractions.

(2) *Muscle fibre types.* Our second area of concern is the classification by Moens and colleagues of mouse soleus as a typically slow muscle. In adult *mdx* soleus muscle is a mixture of slow oxidative and fast oxidative glycolytic fibres in a ratio of 45:55, this compares with the EDL muscle which is an approximately 50:50 mixture of fast oxidative glycolytic to fast glycolytic (Anderson *et al.*, 1988) this means that of the fast twitch muscle fibres only fast glycolytic fibres are unique to EDL. Given that the EDL muscles that we tested from young *mdx* mice, where less than 5% of the muscle fibres are deformed, were not affected by the eccentric contraction protocol we feel that it is reasonable to infer that dystrophin-negative deformed fast glycolytic fibres, which are only present in EDL muscle from older *mdx* animals of the age groups used both in our study and in Moens and colleagues, are the most prone to activity-induced damage. This is an important conclusion given that Weller and colleagues (1990) showed that the fast glycolytic fibres are the first to show evidence of necrosis in Duchenne muscular dystrophy, although in this case it was not known if these fibres were deformed.

(3) Finally, the authors state that McArdle and colleagues (1991) did not find a difference in stretch induced damage between *mdx* and controlled animals. Moens and colleagues concluded that the eccentric contraction protocol used by McArdle and colleagues may have been below the threshold that would damage the muscle fibres. This is a misinterpretation of McArdle and co-worker's paper where in fact they used such a punishing eccentric contraction protocol that both the control and *mdx* muscles showed a drop of 94% in the level of maximal tetanic force they could sustain, and in any case they were using mice of 6 weeks of age at which time few deformed muscle fibres would be present in the *mdx* mice.

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To the Editors,

In the preceding letter Head and colleagues raise a number of points concerning our 1993 paper (Moen *et al.*, 1993).

(1) *Deformed fibres.* We did not discuss branching of fibres (a.o. Isaacs *et al.*, 1973; Head *et al.*, 1990, 1992; Schmalbruch, 1984) in our paper (Moens *et al.*, 1993), since we had found no evidence for their presence in our serial cross-sections, contrary to the suggestion of Head and colleagues in their letter. Besides, even if there were any, it would not change our conclusion that the percentage of red-stained cross-sectional area (indicating fibres with damaged plasma membrane) is proportional to the force drop resulting from eccentric contractions.

In their letter, Head and colleagues propose that our observed *grouping* of damaged, red fibres is 'most likely' reflecting branched, deformed fibres. However, groups containing about 40 fibres were often observed in cross-sections taken from the middle part of the muscle. We cannot rule out that these groups contained some branched fibres that escaped our analysis, but there is no reason to believe that one fibre could subdivide into 40 branches. Therefore, grouping of damaged fibres is genuine.

Along the same lines, Head and colleagues presume that red stained fibres, occurring only in proximal or caudal parts of the muscle and which we included in our total red cross-sectional surface area, probably also result from fibre splitting. This presumption requires that they should always be found next to a fibre stained red in the central section. However, this was often not the case; quite often they were found in isolation. Moreover, longitudinal sections more often showed partly red fibres.

In their letter, Head and colleagues state that we have used 21–71-week-old *mdx* mice, whose EDL muscles should be rich in deformed fibres (Head *et al.*, 1992). This is not true; the bulk part of our experiments was performed on mice of 21 weeks and younger. As is clearly shown

by our Fig. 2, only one *mdx* mouse of 500 days was used. In fact, 14 mice on a total of 19 were 3 to 15 weeks old, the age group that displays less than 5% deformed fibres (Head *et al.*, 1992). Nevertheless, EDL from these mice displayed force drops of up to 40% of maximal isometric tension after eccentric contractions. Therefore, it seems clear to us that deformed fibres cannot explain the susceptibility to stretch of EDL from young *mdx* mice.

(2) *Fibre types.* We classified adult *mdx* soleus muscle as a typically slow muscle because the time to peak of its twitch is 3–4 times longer than that of EDL. Although *fast* oxidative fibres of mouse soleus stain like type IIA fast-twitch fibres, their force–velocity relation is similar to that of *slow* tonic type I fibres, which are much slower than type IIA fibres of EDL. In addition, their myosin heavy chains are different (Maréchal & Beckers-Bleukx, 1993). Therefore, it is incorrect to equate the fast oxidative fibres of soleus and EDL. It is an attractive hypothesis to postulate that, in *mdx* mice, fast glycolytic fibres are most sensitive to stretch, but it is even more attractive to postulate that the stretch-induced damage depends on the mechanical properties of the fibres, and, eventually, on the myosin isoform. As the content in oxidative or glycolytic enzymes does not strictly correlate with the mechanical properties and the type of myosin isoform, we feel that it may be misleading to infer resistance to stretch-induced damage from the glycolytic profile of the muscle fibres.

(3) *Misinterpretation of McArdle and colleagues (1991).* McArdle and colleagues (1991) stimulated EDL muscles for 30 min and measured the force before and after the period of stimulation. They found a large decrease in force, which was not modified by stretching the muscle during the stimulation and which was identical in *mdx* and C57 mice. Unfortunately, they did not measure the force during the period of stimulation. Under their conditions of stimulation (short tetani of 0.5 s, 100 Hz, every 2 s at 37° C) fibres fatigue very rapidly and force produced would drop to less than 5% within a few minutes (compare with our experiments: tetani of 0.35 s, 125 Hz, every 3 minutes at 20° C: in such conditions the isometric force remains constant for at least 20 tetani; note also that the normal intralimb temperature of EDL muscle is close to 25° C). Because of this, stretching the muscle during activation may be anticipated to yield force levels probably not much greater than the resting force, which is well below the threshold necessary to produce stretch-induced damage (see our Fig. 3). In our opinion, this explains why McArdle and colleagues (1991) did not find differences between EDL from *mdx* and control mice after contractions with stretch. We believe that we did not misinterpret the experiment of McArdle and colleagues (1991), but we acknowledge that we should have made this point clearer in our discussion.

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