Altered bioenergetics in skeletal muscle of young *mdx* mice

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Introduction

Duchenne muscular dystrophy (DMD) is an X-linked genetic disorder that affects one in 3,500 male births, and is due to a deficiency in the protein dystrophin on the membrane of muscle fibers (Hoffman et al. 1987). ^{31}Phosphorus magnetic resonance spectroscopy (^{31}P-MRS) has revealed several metabolic differences between dystrophic and unaffected skeletal muscle (Heier et al., 2014; Percival et al., 2013). However, how metabolic status is affected at a young age during the peak inflammatory phase in *mdx* mice is unclear. Therefore, in this study we compared *mdx* to wild-type mice at a young age using ^{31}P-MRS.

Experimental

^{31}P-MRS data were acquired in male wild-type (n =5) and B10-*mdx* (n=5) at 6-8 weeks of age using an 11.1 T MR system with a Bruker spectrometer at the Advanced Magnetic Resonance Imaging and Spectroscopy (AMRIS) facility of the University of Florida. Data from the posterior compartment of the left lower hindlimb were acquired at rest and during and following stimulated muscle contractions. Muscle contractions were performed at the rate of 5 Hz for 2 min with 10 min recovery. PCr peaks were fit using principal component analysis. The time constant of PCr recovery (PCrτ) was calculated using a mono-exponential equation.

Results and Discussion

At rest, the ratios of inorganic phosphate (Pi) to phosphocreatine (PCr), phosphomonoesters (PME) to ATP, and phosphodiesterases (PDE) to ATP are elevated in B10-*mdx* compared to wild-type (Figure 1). Furthermore, PCr recovery was slower in B10-mdx (PCrτ = 216.2 ±13.2s) than wild-type (156.3±10.0s). No differences were observed between groups in pH at rest or at end of exercise.

Conclusions

Overall, our results indicate that metabolic status of dystrophic muscle as assessed with ^{31}P-MRS is altered in young *mdx* mice. The slower PCr recovery in B10-*mdx* may be due to reduced oxygen delivery and metabolism, possibly as a consequence of lack of nNOS (Sander et al. 2000; Nelson et al. 2015).

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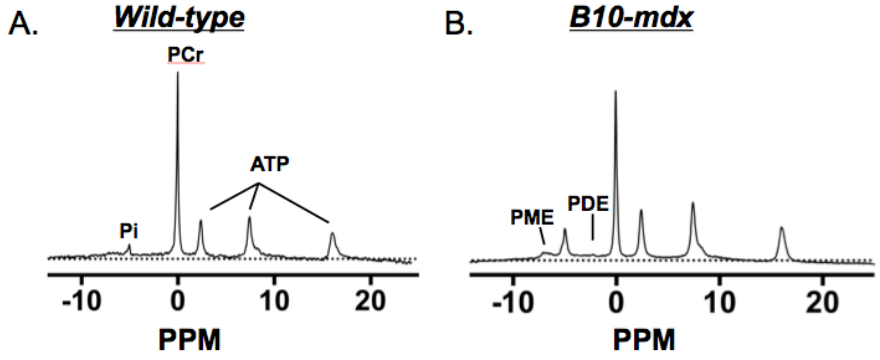

Fig.1. Example ^{31}P spectra acquired at 11.1 T in a control (A) and B10-*mdx* mouse (B). Note the increased inorganic phosphate (Pi) and phosphomonoesters (PME) and reduced phosphocreatine (PCr) in *mdx* compared to wild-type.