MR Characterization of Dystrophic Murine Models with different Genetic background

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Introduction

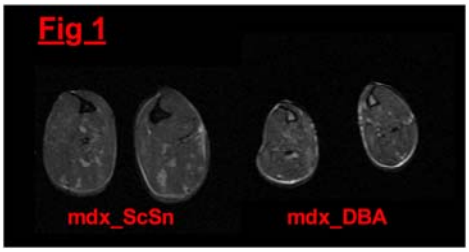
Duchenne muscular dystrophy (DMD) is characterized by progressive muscle weakness and replacement by fibrotic tissue. Muscle fibrosis is a hallmark of several muscular dystrophies and accumulation of fibrosis has been correlated with poor motor outcomes[1]. Different genetic modifiers have been shown to influence phenotypic variability both in humans and animal models[2]. In animal models this can be achieved by knocking out the same gene on different background of mouse strains. The *mdx* mouse model on a typical C57 background show relatively less severity over their lifespan compared to the mouse model on DBA/2 background. Moreover, the *mdx* mouse model on DBA2/J background has shown to accumulate increased fibrotic tissue[3].

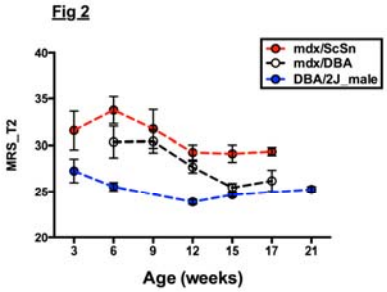
Experimental design

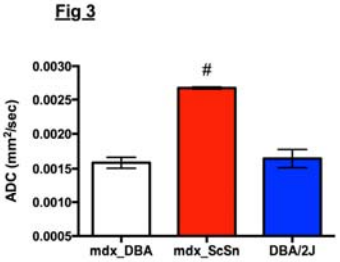
Longitudinal MR measurements were performed every 2-3 weeks over 5 months on C57BL/ScSn-*Dmd*^{mdx} (*mdx*, n=6, 1 month old), D2.B10-*Dmd*^{mdx} (*mdx*_dba, n=5, 1 month old), DBA/2J (n=5, 1 month old) mice within the Advanced Magnetic Resonance Imaging and Spectroscopy (AMRIS) Facility at UF. All mice were imaged on a 4.7T Oxford Magnet with a Varian/Agilent operating system. (1) T_2-weighted single spin–echo images of the hind-limb muscles were acquired (TR 2,000 ms; TE 14 and 40 ms; field of view, 20x20 mm^2; slice thickness, 1.0 mm) using a custom built solenoid coil (2 cm diameter). (2) Stimulated echo acquisition mode (STEAM) spectra was acquired using a solenoid coil in a 1.5x3.0x1.5 mm^3 voxel placed in the posterior compartment of hind limbs with 4 signal averages at TR = 9000 ms; TE: array of 29 TE's spaced between 5-130 ms. (3) 3D-GRE images were acquired using TR/TE = 50/7ms. (4) Apparent diffusion co-efficient (ADC) maps were generated by diffusion weighted images acquired with two gradient intensities (b value of 0 and 900 s/mm^2) with a spin echo sequence (TR/TE = 1,000ms/21 ms). T_2 values were derived using average signal intensity from anterior and posterior hind-limb muscles of each TE using OsiriX software. All values were described as mean ± SD.

Results

*mdx*_dba mice weighed significantly less than age matched *mdx* mice. Furthermore, 3D MR images revealed severe atrophy of hind limb muscles of *mdx*_dba mice (Fig. 1). MRS T_2 revealed significant differences in both strains of *mdx* mice (Fig. 2). ADC data demonstrated significant differences between *mdx* and *mdx*_dba (Fig. 3).







Conclusions

This study shows that MR can detect changes in skeletal muscles of murine models of dystrophy on different genetic backgrounds with the same missing gene. Age related changes in skeletal muscle T_2 were more marked in hind limb muscles of mice on DBA background, which may be attributed to increase in skeletal muscle fibrosis attributed to this strain. These results support that genetic modifiers play a strong role in determining dystrophic phenotype as detected by MRI.

Acknowledgements

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References

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