Myocardial and Skeletal Muscle T_2 is Reduced in γ-Sarcoglycan Deficient Mice at 7 Months of Age

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Introduction

In striated muscle, γ-sarcoglycan is a protein found at the sarcolemma and a component of the dystrophin-glycoprotein complex. Deficiency of γ-sarcoglycan causes limb-girdle muscular dystrophy type 2C, and is characterized by increased susceptibility of muscle damage and augmented fibrosis (1). In murine models, γ-sarcolemma deficiency in the DBA 2J JAX strain (*gsg-/-*) leads to a more severe phenotype compared to γ-sarcolemma deficiency in other strains and in *mdx* mice, which are lacking the protein dystrophin. A shorter T_2 has previously been associated with fibrosis in the hearts of diabetic rats (2). Therefore, we hypothesized that T_2 would be reduced in g*sg-/-* compared to wild-type (C57Bl6) and *mdx* mice at 7 months of age.

Experimental

MR measurements were performed on C57Bl6 (n=4,7±0 months; mean±SEM), *mdx* (n=4, 7±0 mos), and *gsg-/-* in the DBA 2J JAX strain (n=4, 7±0 months) at the AMRIS Facility. All mice were imaged on a 4.7T Oxford Magnet with a Varian/Agilent operating system. Gated T_2-weighted single spin–echo images of the heart were acquired (TR 750 ms; TE 12.5 and 30 ms; field of view, 25X25 mm^2; slice thickness, 1.0 mm; acquisition matrix size, 256 X 128; averages, 8) using a custom built quadrature volume coil (3.3 cm inner diameter). T_2 values were derived using average signal intensity from the mid-papillary region of each TE using OsiriX software. Single voxel STEAM ^{1}H-MRS of the posterior compartment in the right lower hindlimb was acquired (32 TE's non-linearly spaced between 5-300 ms, TR 9000 ms), and $^1H_20$ analyzed using PCA with a mono-exponential model.

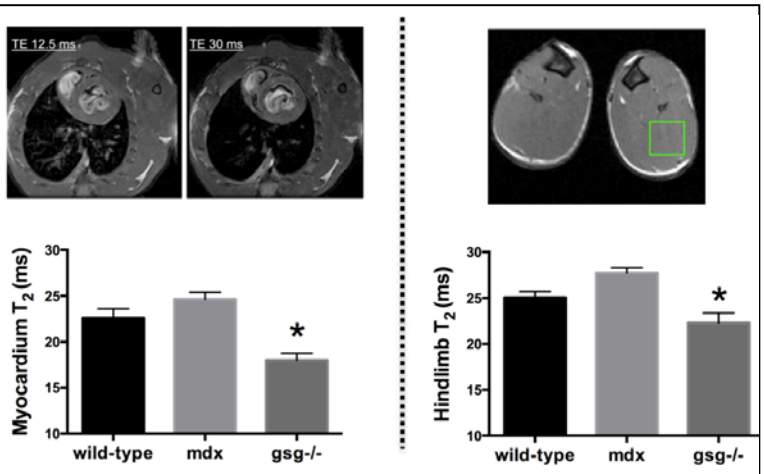

Fig. 1. Example axial images of the heart (top left) and hindlimbs (top right), and corresponding mean T_2 values for wild-type (C57Bl6), *mdx*, and *gsg-/-* mice. *denotes significantly different than wild-type and *mdx*.

Results and Discussion

The mean T_2 of the myocardium and posterior compartment of a lower hindlimb were both reduced ($p<0.05$) in *gsg-/-* than C57Bl6 and *mdx* (Fig. 1).

Conclusions

The findings of this study indicate that a deficiency in γ-sarcoglycan reduces T_2 of the myocardium and skeletal muscle in *gsg-/-* mice, suggesting fibrosis was more prevalent in *gsg-/-* compared to C57Bl6 and *mdx* mice at 7 months of age.

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References

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