Multi-parametric MRI at 14T for muscular dystrophy mice treated with gene therapy

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Introduction

Duchenne muscular dystrophy (DMD) is one of the most common forms of muscular dystrophy in humans. There is no cure for this deadly disease. Although magnetic resonance (MR) has emerged as a noninvasive tool capable of generating valuable information on tissue characteristics, clinical muscle MRI has been dependent on T1 and T2 weighted imaging to monitor inflammatory myopathies in patients with muscular dystrophy (1,2). These methods are useful because of their sensitivity to a wide range of mechanisms, but this generality means that they may not be able to identify specific cellular processes in the affected areas. Here we performed multi-parametric MRI to monitor treatment responses for mdx mice after adeno-associated virus (AAV) vector mediated gene therapy. We used quantitative T2, diffusion and magnetization transfer (MT) MRI to evaluate treatment effects for the AAV vector medicated gene therapy.

Methods

Eleven mdx mice and three normal C57Bl/6 mice were used for this study. Among 11 mdx mice, 7 were systemically treated with 10^{13} vg of AAV virus containing a codon-optimized micro-dystrophin at 12 weeks of their ages. Multi-parametric 1H MRI was carried out for mdx mice on a Bruker 14T Avance MR spectrometer (Bruker Corp., Billerica, MA). The high resolution MRI protocol includes scout imaging (gradient echo; TR (recycle delay)/TE (echo time) = 30/1.3 ms), planning for image planes (multislice RARE (Rapid acquisition with refocused echoes): TR/TE = 668/4.5 ms), high resolution 2 dimensional imaging with thin slices (200 micron thick) (multi-slice RARE: TE/TE = 4000/6 ms) for muscle volume evaluation, multi-TE RARE imaging (TR/TE = 4000/ 6 ~ 75 ms, 12 echoes) for T2 measurements, magnetization transfer imaging, diffusion imaging with three b values of 0, 500 and 1000 s/mm2 sequence (TR/TE = 4000/25 ms) and diffusion tensor imaging (DTI) with 4 shot echo planar imaging and b value of 1000 s/mm2 (TR/TE = 4000/18 ms).

Results and Discussion

Conclusions

Our results show T2, apparent diffusion coefficient (ADC) and MT ratio values would be potential MR markers to evaluate the treatment efficacy of gene therapy for muscular dystrophy. These noninvasive MR markers may be useful to timely monitor treatment responses for muscular dystrophy, which facilitates development of effective approaches to treat the deadly disease.

References