World Academy of Science, Engineering and Technology
International Journal of Medical and Health Sciences
Vol:9, No:05, 2015

Temporal Profile of T2 MRI and 1H-MRS in the MDX Mouse Model of Duchenne Muscular Dystrophy

Authors : P. J. Sweeney, T. Ahtoniemi, J. Puoliväli, T. Laitinen, K.Lehtimäki, A. Nurmi, D. Wells

Abstract : Duchenne muscular dystrophy (DMD) is an X-linked, lethal muscle wasting disease for which there are currently no treatment that effectively prevents the muscle necrosis and progressive muscle loss. DMD is among the most common of inherited diseases affecting around 1/3500 live male births. MDX (X-linked muscular dystrophy) mice only partially encapsulate the disease in humans and display weakness in muscles, muscle damage and edema during a period deemed the “critical period” when these mice go through cycles of muscular degeneration and regeneration. Although the MDX mutant mouse model has been extensively studied as a model for DMD, to-date an extensive temporal, non-invasive imaging profile that utilizes magnetic resonance imaging (MRI) and 1H-magnetic resonance spectroscopy (1H-MRS) has not been performed.. In addition, longitudinal imaging characterization has not coincided with attempts to exacerbate the progressive muscle damage by exercise. In this study we employed an 11.7 T small animal MRI in order to characterize the MRI and MRS profile of MDX mice longitudinally during a 12 month period during which MDX mice were subjected to exercise. Male mutant MDX mice (n=15) and male wild-type mice (n=15) were subjected to a chronic exercise regime of treadmill walking (30 min/ session) bi-weekly over the whole 12 month follow-up period. Mouse gastrocnemius and tibialis anterior muscles were profiled with baseline T2-MRI and 1H-MRS at 6 weeks of age. Imaging and spectroscopy was repeated again at 3 months, 6 months, 9 months and 12 months of age. Plasma creatine kinase (CK) level measurements were coincided with time-points for T2-MRI and 1H-MRS, but also after the “critical period” at 10 weeks of age. The results obtained from this study indicate that chronic exercise extends dystrophic phenotype of MDX mice as evidenced by T2-MRI and1H-MRS. T2-MRI revealed extent and location of the muscle damage in gastrocnemius and tibialis anterior muscles as hyperintensities (lesions and edema) in exercised MDX mice over follow-up period.. The magnitude of the muscle damage remained stable over time in exercised mice. No evident fat infiltration or cumulation to the muscle tissues was seen at any time-point in exercised MDX mice. Creatine, choline and taurine levels evaluated by 1H-MRS from the same muscles were found significantly decreased in each time-point, Extramyocellular (EMCL) and intramyocellular lipids (IMCL) did not change in exercised mice supporting the findings from anatomical T2-MRI scans for fat content. Creatine kinase levels were found to be significantly higher in exercised MDX mice during the follow-up period and importantly CK levels remained stable over the whole follow-up period. Taken together, we have described here longitudinal prophile for muscle damage and muscle metabolic changes in MDX mice subjected to chronic exercised. The extent of the muscle damage by T2-MRI was found to be stable through the follow-up period in muscles examined. In addition, metabolic profile, especially creatine, choline and taurine levels in muscles, was found to be sustained between time-points. The anatomical muscle damage evaluated by T2-MRI was supported by plasma CK levels which remained stable over the follow-up period. These findings show that non-invasive imaging and spectroscopy can be used effectively to evaluate chronic muscle pathology. These techniques can be also used to evaluate the effect of various manipulations, like here exercise, on the phenotype of the mice. Many of the findings we present here are translatable to clinical disease, such as decreased creatine, choline and taurine levels in muscles. Imaging by T2-MRI and 1H-MRS also revealed that fat content or extramyocellar and intramyocellular lipids, respectively, are not changed in MDX mice, which is in contrast to clinical manifestation of the Duchenne’s muscle dystrophy. Findings show that non-invasive imaging can be used to characterize the phenotype of a MDX model and its translatability to clinical disease, and to study events that have traditionally been not examined, like here rigorous exercise related sustained muscle damage after the “critical period”. The ability for this model to display sustained damage beyond the spontaneous “critical period“ and in turn to study drug effects on this extended phenotype will increase the value of the MDX mouse model as a tool to study therapies and treatments aimed at DMD and associated diseases.

Keywords : 1H-MRS, MRI, muscular dystrophy, mouse model
Conference Title : ICPDMD 2015 : International Conference on Parkinson’s Disease and Movement Disorders
Conference Location : London, United Kingdom
Conference Dates : May 25-26, 2015