Fine Motor Kinematic Analysis in the MDX Mouse Model of Duchenne Muscular Dystrophy: a Longitudinal Study of Chronically Exercised VS Non-Exercised MDX Mice

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BACKGROUND

Duchenne Muscular Dystrophy (DMD) is an X-linked neurodegenerative disorder that progressively leads to loss of muscle function and death. It is among the most common of inherited diseases affecting around 1/3500 live male births. MDX (mdx) muscle dystrophy mice only partially encapsulate the disease in humans and display weakness in muscles, muscle damage and death during a period (anterior to the "critical period" between 2 – 4 weeks of age) when these mice go through cycles of muscle degeneration and regeneration. After this period the animals revert to a relatively "normal" status with respect to muscle damage and can live a relatively normal lifespan. During this period and thereafter, there are no discernible changes in gait that can be readily seen.

MATERIALS & METHODS

Animals

All animal experiments were carried out according to the National Institute of Health (NIH) guidelines for the care and use of laboratory animals, and approved by the National Animal Experiment Board. Animals used for the study were handled according to all relevant governmental regulations, and good scientific practice. Animals were randomly allocated to the different groups. The ml of the entire trial all mice were observed for the entire period of the study.

Training

Mice were trained on a lane treadmill (Exer 3/6 Treadmill; Columbus Instruments, Columbus, OH, USA) and the mice were placed in treadmill slots 6 at a time. Training took place using a 6 slope. Treadmill challenges started immediately after the acclimatization period at 4 weeks of age. Training sessions that started at approximately 4 weeks of age - where speed was gradually built up - 3 Mdx and 3 WT mice of the same age were exposed to an exercise regime of 3 X 20 minute training sessions per week at maximum speed (14 meters/min). All training sessions were performed at 4 weeks of age.

The fine motor kinematic test system (MotoRater, TSE Systems GmbH, Bad Homburg, Germany) is used for standardized quantitative analysis of gait. The system can be used for standardized objective kinematic evaluation of fine motor skills of rodents. A second cohort of age matched N=5 Mdx (C57BL/10ScSn-Dmdmdx/J) and N=5 WT mice were subjected to a training regime for use as controls. The same age were exposed to an exercise regime of 3 X 20 minute training sessions per week at maximum speed (14 meters/min). Analysis of variance (ANOVA) was used to determine whether the differences among treatment groups if these are improvements brought on by the rigorous training exercise program or actual improvements in muscle function. If the difference is not due to the exercise intervention, but is because of the underlying condition and in some parameters we see changes that are in line with the improvement in muscle function evident in WT trained mice.

Kinematic analysis

Kinematic analysis is examined by PCA that can be used to identify changes in principle components. From different angles and the relationship between certain components are tracked by drawing vectors from specific mathematical analyzing the relationship of specific components. There are clear differences in the presentation and analysis of PCA associated with of some defects associated with DMD. There are differences in the presentation and analysis of PCA associated with of some defects associated with DMD.

Fine Motor Kinematic Analysis

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CONCLUSION

There are clear differences to be found in trained vs. untrained MDX mice beyond the “critical period”. However, the question still remains as to whether or not as can be evidenced by changes in the WT trained groups if these are improvements brought on by the rigorous training exercise program or actual improvements in muscle function. If the difference is not due to the exercise intervention, but is because of the underlying condition and in some parameters we see changes that are in line with the improvement in muscle function evident in WT trained mice.

REFERENCES

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