Exercise for a precocious detection of impairment in mdx mice model
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Introduction: The mdx mouse with essential dystrophin deficiency is an established animal model of Duchenne’s muscular dystrophy (DMD) in human. However, hindlimb muscle of mdx mice does not exhibit severe and progressive muscle weakness before 15 months excepted for the diaphragm which is severely affected earlier by the disease (Dupont-Versteegden, 1996). The ventilation of old mdx mice (16 months) has been shown to be altered (Gayraud, 2007) and by consequence could affect oxygen uptake (VO\textsubscript{2}), which has never been measured in this model and running performance (V\text{peak}).

Aim: To determine the evolution of running performance and aerobic and anaerobic metabolism in mdx mice between 5 and 9 months old.

Hypothesis: As mice are animals with mostly anaerobic displacements and mdx mice are not severely impaired before 15 month-old, we hypothesized that running performance should not be greatly affected conversely to maximal oxygen consumption in mdx mice between 5 and 9 months.

Methods: 6 mdx mice of 5 months and 6 mdx mice of 9 months of age were tested on a treadmill inserted into a metabolic chamber (Columbus Instrument, USA). Exercise protocols were performed to determine the maximal velocity (V\text{peak}) and the critical speed (CS, Fig 1) as well as the VO\textsubscript{2max} (Billat et al. 2005, Ferreira et al., 2007). The blood lactate concentration was measured at the beginning and the end of exercise (Arkray, JA). Statistical differences were assessed by Mann-Whitney non parametric test (p < 0.05).

Results: In contrast with our hypothesis, the performance of mdx mice (V\text{peak}) decreased between 5 and 9 months (-30%), but not VO\textsubscript{2max}. Furthermore the [La] and the anaerobic distance capacity (ADC) were not different between the 5 and 9 month-old mdx mice, whereas the critical speed (CS) decreased significantly (-30%), eventhough this decrease was not correlated with the decrease of performance.

Discussion: VO\textsubscript{2max} and anaerobic metabolism ([La] and ADC) are not good markers of the mdx pathology in contrast with the performance (V\text{peak}) and the endurance index (CS), which could reflected the progressive diaphragm impairment in mdx mice. However, the endurance capacity (CS) decreased significantly but was not correlated with the performance decrease. Furthermore, this performance decrease was limited thanks to the maintaining of the anaerobic metabolism ([La] and ADC). V\text{peak} and CS are very early sensitive to the mdx pathology. Therefore exercise, allowed to underline deficiency precociously (9 months) compared with other in vivo parameters used in the litterature (around 15 months). Further analyses are in progress to determine the respective part of the diaphragm and skeletal muscle energetics impairment responsible for this severe decrease of performance in mdx mice. Thus exercise can be a usefull tool for pathological models, included in the mdx model.


Fig 1: CS and ADC determination in one mice 5 month-old and one mice 9 month-old (Billat et al., 2005).

Fig 2: Evolution of performance and aerobic and anaerobic metabolisms in 9 versus 5 month-old mdx mice.