Altered mitochondrial oxidative phosphorylation capacity in horses suffering from polysaccharide storage myopathy

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Introduction: Polysaccharide storage myopathy (PSSM) is a widely described cause of exertional rhabdomyolysis that has been found in more than 35 equine breeds. Recent studies identified a dominantly genetic defect in the skeletal muscle glycogen synthase (GYS1) enzyme at the basis of the Type-1 PSSM phenotype (McCue et al., 2008). The condition is characterized by increased skeletal muscle glycogen concentration, and abnormal polysaccharide accumulation in myofibers. Gene expression studies (Barrey et al., 2009) indicated a down-regulation of some mitochondrial genes and we hypothesized that, in type-1 PSSM-affected horses, the energetic production through the oxidative phosphorylation (OXPHOS) in the mitochondria of myofibres might be impaired.

Our aim was to explore the muscle mitochondrial function of PSSM-affected horses using the High Resolution Respirometry, a sensitive diagnostic of the mitochondrial activity recently validated in the equine species (Votion et al., 2010).

Materials and Methods:

- Eight horses (mean age 8.1 - 4.4 y.o.), different breeds
- History of recurrent exertional rhabdomyolysis, exercise intolerance, increased serum CK/AST
- Specific complementary exams were performed to exclude other possible causes of exercise intolerance
- The presence of the GYS1 mutation was tested on each horse (EDTA whole blood sent to the Royal Veterinary College of London, England)
- Muscular biopsies were collected on the m. gluteus medius and m. triceps brachii muscles of each horse using the microbiopsy technique
- Histological analysis and high resolution respirometry (HRR) were realised on the muscle samples

Results: Four horses were tested positive to type-1 PSSM (GYS1 mutation) at the genetic test and were included in the study. Histology revealed the presence of Periodic Acid Schiff (PAS)-positive accumulations of abnormal glycogen. A severe depression of the maximal oxidative phosphorylation capacity was observed (minus 38±14%) by HRR, therefore confirming altered mitochondrial function in type-1 PSSM horses. Surprisingly, one PSSM-positive horse showed very high levels of mitochondrial respiration, even higher than control sport horses.

Conclusions

- All horses suffering from exertional rhabdomyolysis showed a severe decrease of mitochondrial respiration
- PSSM+ horses respiration was lower than PSSM- case
- In the m. gluteus medius the decrease of mitochondrial respiration was more pronounced than in the m. triceps brachii
- Is there a possible mitochondrial recovery/compensatory response?
- Equine PSSM is more than a glycogen storage disease?