GENES AND EXERCISE INTOLERANCE: INSIGHTS FROM MCARDLE DISEASE

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Abstract

McArdle disease (or glycogenosis type V) is an autosomal recessive disorder of skeletal-muscle carbohydrate metabolism caused by inherited deficiency of *myophosphorylase*, the muscle-specific isoform of *glycogen phosphorylase*, which is the enzyme that initiates muscle glycogen breakdown in this tissue.

Owing to the aforementioned metabolic block, patients are unable to obtain energy from their muscle glycogen stores. This disorder only affects skeletal muscles and is probably the paradigm of exercise intolerance in humans. It thus provides a unique model of study for exercise scientists. In fact, patients present with some quite unique characteristics, such as the so-called second wind phenomenon, frequent rhabdomyolysis episodes (with muscle damage also occurring under basal conditions), or easy fatigability during barely all exercise tasks. Interestingly, they also exhibit a flat (or even decreasing) lactate curve in response to incremental exercise.

Although McArdle patients have been traditionally advised to refrain from physical activity, careful exercise and nutritional prescription can be their best allied because no effective enzyme replacement therapy or 'molecular' treatment is expected to be available in the near future.

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