

Taurine homeostasis in Duchenne Muscular Dystrophy and the use of the amino acid as a therapeutic intervention

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Duchenne Muscular Dystrophy (DMD) is a fatal muscle wasting disease. Dystrophic muscle undergoes severe myofibre necrosis, the cause of which is not fully understood, however excess intracellular calcium, inflammation and oxidative stress are implicated. Pharmacological compounds that target these pathological mechanisms are of interest, since the current drug treatment for DMD, corticosteroids, are limited in efficacy and are associated with severe side effects. One such compound, the amino acid taurine, improves strength of muscle from the mdx mouse model for DMD, which is also has been shown to be deficient in taurine. Whilst a taurine deficiency has been observed in mdx mice, and taurine treatment has been shown to be beneficial, the cause of taurine deficiency and mechanisms of action of endogenous taurine treatment in dystrophic muscle have not been established. Additionally, the effects on taurine treatment on mdx myofibre necrosis, as well as indices of *ex vivo* muscle function, are undetermined. Taurine homeostasis involves the balance of multiple processes including synthesis, transport and excretion. These processes were investigated in various mdx tissues, to identify the cause of taurine deficiency in dystrophic muscle. Additionally, the effect of taurine treatment on myofibre necrosis was investigated, as was effect of taurine treatment on *ex vivo* muscle function. To determine the mechanism of action of taurine in dystrophic muscle, the anti-inflammatory and antioxidant effects of the drug were investigated. We show that taurine homeostasis is perturbed in mdx muscle, liver and kidney. These observations highlight the importance of using animal models to understand how dystrophy is affecting whole body taurine metabolism. Taurine treatment of mdx mice prevented myofibre necrosis, and improved and *ex vivo* force generation, most likely due to the potent ant-inflammatory and antioxidant effects of taurine in dystrophic muscle. These data support continued research into the role of taurine in dystrophic muscle, as well as further preclinical investigation into the use of taurine as a therapy for DMD.