Perturbed metabolic profiles associated with muscle weakness seen in adult Ts1Cje mouse model of Down syndrome

ABSTRACT

Down syndrome (DS) is a genetic condition resulting from a partial or full triplication of human chromosome 21. Besides intellectual disability, DS is frequently associated with hypotonia. Ts1Cje, mouse model of DS, displays the muscle weakness characteristic. The metabolic profiles of the skeletal muscle was characterised using 1H nuclear magnetic resonance spectroscopy and multivariate data analysis. Ts1Cje muscle had significantly decreased levels of glutamine, guanidinoacetate, adenosine monophosphate, and histidine, suggesting perturbation of energy, glutamate, and histidine metabolic pathways. Glycine amidinotransferase/arginine glycine amidinotransferase enzyme-linked immunosorbent assay indicated this mitochondrial enzyme was 74% and 50% lower in Ts1Cje kidney and liver than the wildtype respectively. In conclusion, our findings suggest that perturbed metabolite profiles contribute to muscle weakness in Ts1Cje skeletal muscle.

Keyword: Down syndrome, Skeletal muscle, Metabolomics