EFFECT OF VALINE AND VALINE-CATABOLITE, 3-HYDOXYISOBUTERATE ON CELL METABOLISM, MITOCHONDRIAL BIOGENESIS AND BCAA CATABOLISM

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BACKGROUND: Valine and other branched chain amino acids (BCAAs) are known to have favorable effects including increased muscle mass and possibly enhanced oxidative capacity (via increased mitochondrial content), which may provide benefit for athletes. Interestingly, circulating BCAAs correlate with insulin resistance, although a causal relationship between BCAA consumption and disease development/progression has not been established. It is likely the relationship between elevated circulating BCAAs and insulin resistance is a byproduct of reduced BCAA catabolism, likely resulting from excess fat consumption. Recently, valine catabolite 3-hydroxyisobuterate (3HIB) was shown to enhance cellular lipid uptake contributing to insulin resistance. To further investigate the roles of valine and 3HIB in metabolic perturbations, this work examined the effect of both metabolites on skeletal muscle metabolism and related gene expression.

METHODS: C2C12 myotubes were treated with varying concentrations of valine or 3HIB for 48 hours. Metabolic gene expression was measured via qRT-PCR, mitochondrial metabolism was measured via O2 consumption, and glycolytic metabolism was quantified using extracellular acidification rate.

RESULTS: Neither valine nor 3HIB altered expressional indicators of mitochondrial biogenesis. 3HIB at 100μM significantly increased peak oxygen consumption compared to control. Conversely, supraphysiological 3HIB treatment (5mM) suppressed basal mitochondrial and glycolytic metabolism without altering metabolic gene expression. Valine treatment significantly decreased glycolytic metabolism (both basal and peak) as well as BCAA catabolic gene expression, which was not observed in 3HIB-treated cells. CONCLUSION: 3HIB may dose-dependently alter metabolism independent of mitochondrial biogenesis, while valine may uniquely suppress glycolytic metabolism and BCAA catabolic enzyme expression.

REFERENCES