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The Effect of Succinic Acid on Metabolic Profile in High-Fat Diet-Induced Obesity and Insulin Resistance

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Obesity, insulin resistance, and poor metabolic profile are hallmarks of a high fat diet (HFD), highlighting the need to understand underlying mechanisms. **PURPOSE:** To determine the effect of succinic acid (SA) on metabolism in high fat diet-induced obesity. **METHODS:** Animals were randomly assigned to either low fat diet (LFD) or a high fat diet (HFD). Mice consumed their respective diets for 4.5 months and then assigned to the following groups: LFD+vehicle, LFD+SA (0.75 mg/ml), HFD+vehicle, or HFD+SA. Body weight (BW), food and water intake, were tracked weekly. After 6 weeks, insulin, glucose, and pyruvate tolerance tests were completed, and spontaneous physical activity was assessed. Epididymal white adipose tissue (EWAT) mass and *in vitro* measurements of oxidative skeletal muscle (soleus) respiration were obtained. **RESULTS:** Expectedly, the HFD increased BW and EWAT mass, and reduced glucose and insulin tolerance. SA significantly reduced EWAT mass, more so in HFD ($p < 0.05$), but had no effect on any *in vivo* measurements (BW, insulin, glucose, or pyruvate tolerance, nor physical activity, all $p > 0.05$). A significant ($p < 0.05$) interaction was observed between mitochondrial respiration and treatment, where SA increased respiration, likely owed to greater mitochondrial content, as assessed by complex IV activity in both LFD and HFD. **CONCLUSION:** In HFD-induced obesity, coupled with insulin desensitization, no favorable effect of succinic acid on glucose regulation was found, but reduced adiposity was observed. In oxidative skeletal muscle, there was a tendency for increased mitochondrial respiratory capacity, owed to greater mitochondrial content, suggestive of a succinic acid-induced mitochondrial biogenesis.