Effects of anti-oxidant therapies with N-acetylcysteine or extra virgin olive oil on increased body metabolisms promoted by conjugated linoleic acid in C57Bl/6 mice.

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Daily intake of conjugated linoleic acid (CLA) prevents white adipose tissue (WAT) gain and improves body energy expenditure. The latter effect is associated to upregulation of uncoupling protein (UCP)-2 in several tissues. As UCPs expression in liver depends on the increase in reactive oxygen species production, here we investigate whether anti-oxidant therapy with extra virgin olive oil (EVOO) or N-acetylcysteine (NAC) could prevent the rise in the mitochondrial and body metabolism promoted by CLA.

For EVOO therapy, male mice were divided into one of four groups: CLA (1:1 cis-9, trans-11: trans-10, cis-12 - 18:2 isomers), EVOO, CLA plus EVOO or control (linoleic acid). Each mouse received 3g/kg b.w of stated oil by gavage on alternating days. For the NAC treatment, mice from CLA or control supplemented groups received NAC in the drinking water (daily intake of 0.1 g/kg b.w). After 30 days, body metabolism was monitored by indirect calorimetry and glucose tolerance test was performed. The mice were euthanized and liver, WAT and skeletal muscle were subsequently analyzed. Liver mitochondria were isolated by differential centrifugation. Tissue and mitochondrial respirations were monitored using an oxygraph (Oroboros).

Diet supplementation with CLA reduced the WAT gain and increased body VO\textsubscript{2} consumption, VCO\textsubscript{2} production and energy expenditure, but promoted liver enlargement and insulin resistance. In the liver, CLA in also increased UCP-2 expression and UCP activity in isolated mitochondria. Supplementation with EVOO did not change any metabolic parameters in control or CLA groups, and reduced insulin resistance and liver enlargement in CLA group. Interestingly, high body metabolism and liver UCP-2 expression/UCP activity induced by CLA were abolished by therapy with NAC, suggesting an oxidative-dependent pathway. Therefore, this study clarifies the mechanism of UCPs induction in the liver by CLA and demonstrates for the first time the beneficial effects of combined CLA and EVOO supplementation.