Docosahexaenoic acid-thyroid hormone combined protocol as a novel approach to metabolic stress disorders: Relation to mitochondrial adaptation via liver PGC-1? and sirtuin1 activation

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 Docosahexaenoic acid (DHA) and 3,3?,5-triiodothyronine (T 3) combined protocol affords protection against liver injury via AMPK signaling supporting energy requirements. The aim of this work was to test the hypothesis that a DHA + T 3 accomplish mitochondrial adaptation through downstream upregulation of PPAR-? coactivator 1? (PGC-1?). Male Sprague?Dawley rats were given daily oral doses of 300 mg DHA/kg or saline (controls) for three consecutive days, followed by 0.05 mg T 3 /kg (or hormone vehicle) ip at the fourth day, or single dose of 0.1 mg T 3 /kg alone. Liver mRNA levels were assayed by qPCR, NAD + /NADH ratios, hepatic proteins, histone 3 acetylation and serum T 3 and ?-hydroxybutyrate levels were determined by specific ELISA kits. Combined DHA + T 3 protocol led to increased liver AMPK, PGC-1?, NRF-2, COX-IV, and ?-ATP synthase mRNAs, with concomitant higher protein levels of COX-IV and NRF-2, 369% enhancement