Role of dietary fat in modulating the biosynthesis of endocannabinoids and congeners in humans

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The endocannabinoid system contributes to the regulation of energy metabolism influencing body fat distribution and metabolism. Overweight and obese subjects are often characterised by high levels of endocannabinoids in plasma associated to dislipedemia and body fat distribution. Dietary n-3 HPUFAs by modulating arachidonic acid availability in phospholipids, may modify the levels of endocannabinoid biosynthetic precursors. Our studies in humans indicate that dietary strategies aimed at increasing the incorporation of n-3 HPUFAs in tissue phospholipids influenced endocannabinoid levels and ameliorated dislipidemia e leptin resistance. However, this was not merely the result of a decreased arachidonic availability, but rather to a modified n-6/n-3 HPUFA ratio irrespective of the absolute levels of arachidonic acid in phospholipids. In fact, decreasing plasma n-6/n-3 HPUFA after 3 weeks of dietary cheese naturally enriched in alpha linolenic, conjugated linoleic and vaccenic acids, in hypercholesterolemic overweight subjects resulted in a an almost 50% decrease of anandamide and 7% decrease of LDL cholesterol. In addition, dietary fatty acids may modify the biosynthesis of AEA congeners N-palmitoylethanolamide (PEA) and N-oleoylethanolamide (OEA) both avid ligands of PPAR alpha but not of CB receptors, having therefore distinct biological activity with respect to AEA.
Therefore the biosynthesis of the endocannabinoids and their congeners is modified by dietary fatty acids, influencing the onset of the metabolic syndrome and its cardiovascular consequences.