Membrane Composition and Cellular Responses to Fatty Acid Intakes and Factors Explaining the Variation in Response

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The relative abundance of polyunsaturated fatty acids (PUFA) in the diet has a major influence on the composition of membrane bilayers. Moreover, the association between membrane composition and the intake of n-6 and n-3 PUFA with the diet and especially the dietary n-3/n-6 ratio may be attributed to the capacity of PUFA belonging to the two metabolic series to substitute for each other [1]. Both n-6 and n-3 PUFA are the biologically active fatty acids (FA). Within the n-6 series, linoleic acid, the first recognized essential FA, gives origin by desaturation and elongation processes to arachidonic acid, precursor of the eicosanoid families, and therefore one of the most essential components for life. The compound of the n-3 family with a shorter chain and lower unsaturation degree, α-linolenic acid, can be converted to the more biologically active very long-chain n-3 PUFA eicosapentaeanoic acid, and docosahexaenoic acid (DHA). Also in this case the process occurs by a series of desaturation and elongation reactions.

Within this context, by increasing the contents of eicosapentaenoic acid and DHA in membranes, it is possible to modify the pattern of production of different lipid mediators [2]. These changes can affect membrane order, intracellular signaling processes, and, most important, gene expression, leading to changes in the production of both lipid and peptide mediators. Neurocognitive performance, visual development, immune function, inflammatory reactions and surrogates of the metabolic picture connected with the cardiovascular health (i.e. arterial blood pressure, cardiac rhythm, insulin sensitivity, overweight and obesity development) represent the main functional outcomes, at least in neonates and children. They share similar biological mechanisms and have been evaluated in relation to changes in FA intake to explain the association with dietary FA.
In the last years, the prominent role of the interindividual genetic variability in metabolism, incorporation, synthesis of biochemical intermediates and even effects on gene expression, has been shown to be closely connected with the individual asset of the aplotypes, including single-nucleotide polymorphisms (SNPs), associated with PUFA metabolism. Indeed, in addition to diet, common polymorphisms in the FA desaturase (FADS) gene cluster have very marked effects on human PUFA and LC-PUFA status. In intervention studies on the biological effects of linoleic acid, α-linolenic acid and LC-PUFA, and the effects of genetic variants in FADS1 and FADS2, 5-LO and cyclooxygenase-2 should be taken into consideration both in the determination of nutritional requirements and chronic disease risk [3]. New data have become available to show that FADS SNPs also modulate DHA status in pregnancy as well as LC-PUFA levels in children and in human milk. There are indications that FADS SNPs modulate the risk for allergic disorders and eczema, as well as the effect of breastfeeding on asthma symptoms and later cognitive development [4]. Based on these observations in human-based research, two take-home messages may be derived: (1) that the genetic variability may have a transgenerational effect via breastfeeding, and (2) that the genetic variation in human desaturase genes affects enzyme activity and, consequently, disease risk factors. Smoking and alcohol consumption may influence the absorption, biosynthesis, or metabolism of serum FA. The negative effects of smoking observed in the maternal-fetal dyad are summarized in table 1, and ethanol consumption may negatively affect the supply of FA from the maternal compartment to the fetus [5]. The differences observed in PUFA metabolism associated with variants in human genes and environmental factors suggest that different amounts of dietary PUFA may

**Table 1. Effects of smoking on PUFA metabolism observed in the maternal-fetal dyad**

- In mothers: higher plasma lipid levels and lower milk total fat and DHA content in the first months of lactation
- In mammary gland cells: exposure to cigarette smoke negatively affects the synthesis of n-3 LC-PUFA from the precursor
- In infants: reduction in LC-PUFA pools, particularly of the n-3 series, in infants born to smoking mothers in spite of lack of differences in maternal dietary intakes vs. nonsmokers in association with reduced fetal growth
- Speculative associations: in breastfed infants, a lower total fat content of human milk is negatively associated with developmental indices at 12 months; in adults: negative relationship between maternal smoking during the third trimester and offspring adult intelligence
be necessary in order to meet the requirements for these nutrients in development and disease prevention on individual basis, but individual phenotypic indicators are still lacking.

References