Dietary Lipid Quality and Long-Term Outcome

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The amounts and types of ω-6 and ω-3 fatty acids in the diet are one of the most important aspects of early dietary lipid quality that influence early development with the potential also for long-term effects. The ω-6 and ω-3 fatty acids are needed in the diet due to the absence of desaturase enzymes able to form these double bonds. Linoleic (18:2ω-6, LA) and α-linolenic acid (18:3ω-3, ALA) are found mainly in vegetable oils, while the longer chain arachidonic acid (20:4ω-6, ARA), eicosapentaenoic acid (20:5ω-3, EPA) and docosahexaenoic acid (22:6ω-3, DHA) are found in animal tissue lipids (fig. 1). The maternal dietary intake of ω-6 and ω-3 fatty acids in gestation and lactation is the most important variable determining the amounts and types of ω-6 and ω-3 fatty acids transferred across the placenta, secreted in breast milk and accumulated in developing infant tissues [1]. However, which and how much of the different ω-6 and ω-3 fatty acids are needed in development is still unclear, and understanding needs is complicated by dramatic changes in ω-6 and ω-3 fatty acids in the food supply in recent years and large differences in intake within and among different populations.

A central question is whether the high LA intakes typical of western diets interfere with the ability to form and accumulate long-chain ω-3 fatty acids. In piglets, a formula diet with 1.2% energy from LA and 1.1% energy from ALA led to high DHA in the brain, but this did not occur when LA provided 10% dietary energy, as is common in modern human milk and infant formula (fig. 2) [2]. Small amounts of DHA representing 0.3% energy, however, were readily incorporated in the brain, showing the need for preformed DHA in the modern LA-rich diet.

Recent studies are beginning to question if a high ω-6 and low ω-3 fatty acid supply during early development is linked to later characteristics of the metabolic syndrome, such as dyslipidemia, insulin resistance and hyperphagia. The ω-6 and ω-3 fatty acids play important roles
in membrane lipids, regulation of gene expression and inter- and intracellular communication, and through these roles they have powerful effects on the integration of energy substrate metabolism [1]. During early development, key hormones and metabolites serve as important cues that regulate the development of hypothalamic feeding circuitry.

**Fig. 1.** Schematic of major steps of essential fatty acid desaturation and elongation with dietary sources of ω-6 and ω-3 fatty acids.
and peripheral energy substrate metabolism. Mathai et al. [3] showed that maternal ω-3 fatty acid deficiency in gestation and lactation led to long-term changes in glucose-regulatory appetite sensing in adult offspring. In recent proteomic studies, we found 14-3-3 protein zeta/delta was increased in the ω-3 fatty acid embryonic and neonatal brain: this protein is a known target of insulin, which in turn plays a role in development of neurons in the hypothalamus involved in feeding behavior.

In the liver, fatty acids regulate the expression of key lipogenic, lipolytic and glycolytic genes [4]. In recent studies, we showed that higher EPA and DHA in neonatal liver was associated with altered protein and gene expression of enzymes regulating not only fatty acid and glucose, but also amino acid metabolism [5]. Our results indicate that ω-3 fatty acids are important in the metabolic transition at birth to enable processing of the high-fat milk diet, conserving glucose for essential functions, sparing of protein from oxidation, and avoiding lipotoxicity by increasing fatty acid oxidation. Further attention should be given to the possibility that ω-6 and ω-3 fatty acids in early

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**Fig. 2.** DHA in ethanolamine phosphoglyceride in brain, liver and heart of piglets fed formula with, as percent dietary energy, 1.2% LA, 1.1% ALA (balanced LA/ALA); 1.2% LA, <0.1% ALA (ω-3 deficient); 10.7% LA, 1.1% ALA (high LA); 10.7% LA, 1.1% ALA, 0.3% DHA, 0.3% ARA (DHA + ARA supplemented). Values are means ± standard error of 5–7 piglets/diet. Bars with different superscripts are significantly different by ANOVA with Tukey’s test for post-hoc analysis, p < 0.05.
life have effects that extend beyond roles in neural and visual development to complex roles in energy metabolism, with implications for later susceptibility to metabolic syndrome.

References