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BRAIN RESEARCH

Review

Dietary omega 3 fatty acids and the developing brain

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ABSTRACT

The ω-3 fatty acids are essential dietary nutrients and one of their important roles is providing the fatty acid with 22 carbons and 6 double bonds known as docosahexaenoic acid (DHA) for nervous tissue growth and function. Inadequate intakes of ω-3 fatty acids decrease DHA and increase ω-6 fatty acids in the brain. Decreased DHA in the developing brain leads to deficits in neurogenesis, neurotransmitter metabolism, and altered learning and visual function in animals. Western diets are low in ω-3 fatty acids, including the 18 carbon ω-3 fatty acid alpha linolenic acid found mainly in plant oils, and DHA, which is found mainly in fish. The DHA status of the newborn and breast-fed infant depends on the maternal intake of DHA and varies widely. Epidemiological studies have linked low maternal DHA to increased risk of poor child neural development. Intervention studies have shown improving maternal DHA nutrition decreases the risk of poor infant and child visual and neural development. Thus, sufficient evidence is available to conclude that maternal fatty acid nutrition is important to DHA transfer to the infant before and after birth, with short and long-term implications for neural function. However, genetic variation in genes encoding fatty acid desaturases also influence essential fatty acid metabolism, and may increase requirements in some individuals. Consideration of ω-3 fatty acid to include brain development, optimizing ω-3 and ω-6 fatty acids in gestation and lactation, and in fatty acid nutrition support for intravenous and formula-fed neonates is important.

Contents

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1. Introduction

The long chain ω-3 fatty acid with 22 carbons and 6 double bonds known as docosahexaenoic acid (DHA) is the most abundant ω-3 fatty acid in the mammalian central nervous system, and is specifically concentrated in membrane lipids of brain grey matter and the visual elements of the retina. The levels of DHA in the brain increase during development (Martinez 1992; Svennerholm 1968) and decrease with aging (Guisto et al., 2002; Rotstein et al., 1987; Soderberg et al., 1990), and both the retina and brain levels of DHA are altered by the dietary ω-3 and ω-6 fatty acid supply (Innis, 1991, 2005a). Epidemiological and intervention studies have linked low plasma and blood cell lipid DHA to increased risk of poor visual and neural development in infants and children (Bouwstra et al., 2003; Dunstan et al., 2006; Helland et al., 2003; Hibbeln et al., 2007; Innis and Friesen, 2008; Innis et al., 2001; Oken et al., 2005; Uauy and Danqour, 2006; Williams et al., 2001), and to an increased risk of dementia and cognitive decline in older individuals (Dullemeijer et al., 2007; Kalmijn et al., 2004; Morris et al., 2003; Nurk et al., 2007; Schaefer et al., 2006; Van Gelder et al., 2007). A growing body of information now provides cause to carefully weigh the possibility that dietary fatty acids, potentially influenced by genetic variation in fatty acid metabolism, contribute to poor central nervous system (CNS) functioning in infants and children, and do so with long-lasting sequelae. Understanding the importance of dietary ω-3 fatty acids in contributing to human CNS development, however, is challenging because of the complexity of fatty acid metabolism, and incomplete knowledge of the pathways of transfer and fatty acid uptake in the brain, and the functional roles of DHA. This review aims to provide a background on ω-3 fatty acids and current knowledge relating early fatty acid nutrition to cognitive and behavioral development.

2. Dietary omega 3 fatty acids and their metabolism

Unsaturated fatty acids are classified by the position of the first double bond from the methyl end (ω) of the fatty acid carbon chain, while the desaturase enzymes are denoted by the carbon counting from the carboxyl end (Δ) at which hydrogen atoms are removed to create the carbon–carbon double bond (Fig. 1). Because animals lack a Δ-15 or Δ-12 desaturase, they are unable to form ω-3 or ω-6 fatty acids *de novo* and must obtain these fatty acids from their diet (Innis, 2003). Humans and other animals obtain DHA either as the 18 carbon chain precursor α-linolenic acid (18:3ω-3), or as DHA itself and intermediates between 18:3ω-3 and DHA, notably eicosapentaenoic acid (20:5ω-3), usually abbreviated as EPA (Fig. 2). However, DHA not 18:3ω-3 or 20:5ω-3, is the major ω-3 fatty acid esterified in the glycerophospholipids that form the structural matrix of brain grey matter and retinal membranes (Guisto et al., 2002; Sastry, 1985). DHA accumulation in the brain and retina, as in other organs, depends on the amount and types of ω-3 fatty acids in the diet, and on dietary intake of ω-6 fatty acids which interact and compete with ω-3 fatty acids in the fatty acid metabolic pathway (Arbuckle et al., 1994; Bourre et al., 1989, 1990; Galli et al., 1971; Hrboticky et al., 1990, 1991; Innis, 1991; Neuringer et al., 1986). Central questions in human nutrition are which and how much of the different ω-3 fatty acids are needed in the diet, and whether the current high intakes of ω-6 fatty acids, or low intakes of ω-3 fatty acids contribute to poor infant neural development and function.

Synthesis of DHA occurs in phytoplankton and animals, but not plants (Fig. 2). This means that DHA is absent from foods of plant origin, including vegetable fats and oils, grains, nuts and seeds. However, DHA is present in animal tissue lipids, with the richest dietary source being fatty fish (Chow, 2000). The meat and milk of ruminants also contain very low amounts of DHA. The 18 carbon ω-3 fatty acid 18:3ω-3 is also relatively sparsely distributed in foods, with higher levels in soybean, canola and flax seed oils, but common oils such as corn oil, safflower oil, sunflower oil and olive oil all contain<1% 18:3ω-3. The 18 carbon ω-6 fatty acid, linoleic acid (18:2ω-6) is the precursor of the ω-6 fatty acids and is abundant in modern food supplies, with over 50% of all the fatty acids in soybean, corn, safflower and sunflower oils being 18:2ω-6.

Once obtained from the diet, 18:3ω-3 can be further metabolized by Δ-6 desaturation, elongation and Δ-5 desaturation to 20:5ω-3, while 18:2ω-6 is metabolized using the same enzymes to the 20 carbon chain ω-6 fatty acid, arachidonic

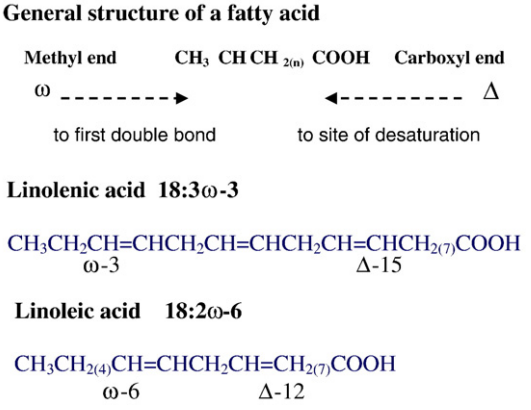

Fig. 1 – Schematic of the general structure and nomenclature of fatty acids. Fatty acids are denoted by the number of carbons:number of double bonds and position of the first double bond from the methyl end. Desaturase enzymes are denoted by the carbon at which they introduce double bonds from the carboxyl end. Humans and other animals lack Δ-15 and Δ-12 desaturase.