FATTY ACIDS ARE NEEDED FOR BRAIN GROWTH AND DEVELOPMENT

Polet Barkhooy

The lipids of our central nervous system contain high proportions of arachidonic acid (20:4 n-6, AA) and docosahexaenoic acid (22:6 n-3, DHA) which are the two most important polyunsaturated fatty acids in the brain. Levels of linoleic acid (18:2 n-6) and alpha-linolenic acid (18:3 n-3) are low, usually less than 1% to 2% of total fatty acids (Innis, S78-79). Linoleic acid and alpha-linolenic acid are precursors to AA and DHA; they are elongated and desaturated to form AA and DHA (Clandinin, 27). The brain growth in humans begins early in the third trimester of pregnancy. This is the most important period for brain AA and DHA accumulation (Innis, S78-79). Therefore, the composition of fat in the brain during this period is very important for normal growth and development of the brain. Any changes in the balance of the fatty acids in the dietary fat intake will result in changes in the membrane functioning of brain cells.

During this prenatal life, lipids are mostly needed for structural and regulatory functions. After birth, the infant is challenged by changes in the lipid sources. The response to these changes can be altered by changes in the diet composition. For example, a newborn infant’s response to human milk is considered to be ideal, therefore baby formulas try to mimic that response (Biervliet, S101). Studies have shown that fatty acid accumulation in the brain increases as the pregnancy progresses. It reaches the maximum level of accumulation toward the end of the pregnancy. But there are differences in the rate of accumulation of these fatty acids. For example, DHA levels in the cerebrum increase as the percentage of the total fatty acid, whereas AA levels decrease during the last trimester (Martinez, S130-131). This reduction in arachidonic acid levels is caused by the addition of eicosapentaenoic acid (20:5 n-3, EPA) and DHA in the diet. DHA and eicosapentaenoic acid are known to inhibit the desaturation of n-6 fatty acids. Therefore, there is a reduction in AA synthesis (Innis, S81). Eicosapentaenoic acid is the other precursor of DHA besides alpha-linolenic acid (18:3 n-3). Studies done on chicks show that addition of EPA to the diet increased the brain and retinal DHA as much as when DHA was added to the diet. These studies have also shown that dietary alpha-linolenic acid (18:3 n-3) is a less efficient precursor for DHA in animals with low delta-6 desaturase activity. Thus, it is possible that humans have a stronger preference for dietary DHA over dietary alpha-linolenic acid as the source of tissue DHA (Anderson, 90,95). During the postnatal development, DHA is the only n-3 fatty acid that is present in significant amounts in the brain. Adrenic acid (22:4 n-6), which is the third most abundant fatty acid in the brain, increases very rapidly during this period (Martinez, S132). If the amount of these fatty acids in the diet is not sufficient to maintain an adequate supply of the essential fatty acids, then the body responds by making these fatty acids in the nervous system.

Since the percentage of DHA increases and the percentage of AA decreases in the brain during prenatal development, for a preterm infant, the balance in the dietary ratio of linoleic acid/ alpha-linolenic acid is very crucial to the brain development. For example, an increase in this dietary ratio means low levels of alpha-linolenic acid and as a result a decrease in DHA levels. Without enough DHA, an infant's requirements for brain growth cannot be fullfilled (Martinez, S133). Therefore, since preterm infants do not go through a normal prenatal development, they usually have a decreased DHA/AA ratio. Studies have also shown that dietary deficiency in alpha-linolenic acid (18:3 n-3) during brain development results in impaired cognitive, visual, and motor skill development (Innis, S79). Some of the problems caused by a deficiency in linoleic acid (18:2 n-6) are poor growth, skin lesions, loss of muscle tone, impaired water balance, and increased susceptibility to infections in infants.

These problems disappear after providing an adequate diet that includes linoleic acid. This suggests that linoleic acid / alpha-linolenic acid ratio in milk formulas is very important to brain development in infants (Martinez, S133).

For example, human milk contains the two most important polyunsaturated fatty acids: arachidonic acid and docosahexaenoic acid, but these two important fatty acids are not present in the commercial baby formulas. These milk formulas, however, contain linoleic (18:2 n-6) and alpha-linolenic (18:3 n-3) acid which are elongated to form AA and DHA. The desaturation and elongation of linoleic and alpha-linolenic acids to AA and DHA is very crucial for the infant's brain development. This desaturation and elongation of (18:2 n-6) and (18:3 n-3) to AA and DHA depends on the dietary content and ratio of linoleic acid / alpha-linolenic acid (Arbuckle, 289). During initial postnatal life, the chain elongation-desaturation enzymes are not fully active in an infant; thus it is very important that the infant is fed dietary AA and DHA instead of the precursor fatty acids, 18:2 n-6 and 18:3 n-3 (Uauy, S174).

In a study done by Wilcoxon, the serum lipid and lipoprotein status of breast-fed and formula-fed infants were compared. The serum cholesterol, cholesteryl esters, and high-density lipoprotein subfractions in breast-fed infants were measured during the first thirty days of their life. These measurements were compared with the measurements of infants fed a typical formula, formula supplemented with cholesterol, or formula supplemented with the gamma-linolenic acid, the precursor of arachidonic acid. By day 30, breast-fed infants had higher total cholesterol levels than any of the formula-fed groups. But by day 30, breast-fed infants had significantly higher cholesteryl-oleate and cholesteryl-palmitate levels than the formula-fed infants. By day 30, the high-density lipoprotein cholesterol levels were also higher in breast-fed infants (Biervliet, S103-104). High-density lipoproteins are particles that consist of a core of hydrophobic lipids surrounded by polar lipids and apoproteins. High-density lipoproteins solubilize hydrophobic lipids and contain cell-targeting signals (Stryer, 697). Cholesterol levels are very significant in the body due to the effect of cholesterol on the fluidity of membranes. Cholesterol prevents the crystallization of fatty acyl chains by fitting itself between them. The opposite effect of cholesterol is to block large motions of fatty acyl chains, therefore decreasing membrane fluidity. Cholesterol moderates the fluidity of membranes (Stryer, 280). In a long-term follow-up study of mental development in breast-fed versus formula-fed children, early breast feeding was associated with higher intelligence at eight years of age and better scores in math, nonverbal ability, and sentence completion at fifteen years of age (Uauy, S177).

As this study demonstrates, human milk contains three to four times more cholesterol than any of the baby formulas. As it was mentioned before, since the baby formulas contain plant fats, they do not have the long polyunsaturated fatty acids (n-3) and (n-6) that are present in the human milk. Cholesterol is a major component of nerve membranes. Therefore, by providing high levels of both cholesterol and arachidonic acid, the human milk assists in delivering needed amounts of arachidonic acid to the developing brain. The breast-fed infants had higher serum cholesterol concentration than had formula-fed infants, and they had higher levels of cholesteryl arachidonate. This cholesteryl fatty acid is needed for cell growth. Dietary cholesterol also affects the maturation of high-density lipoproteins. This effect on the distribution and composition of high-density lipoproteins in newborn infants may be important in adulthood. Adult rats tolerate dietary cholesterol better after a neonatal challenge with cholesterol (Biervliet, S106-107).

In order for normal brain growth and development to take place in infants, a diet that contains docosahexaenoic acid (DHA) (22:6 n-3), arachidonic acid (AA) (20:4 n-6), linoleic acid (18:2 n-6), and alpha-linolenic acid (18:3 n-3) is needed. A deficiency in these fatty acids may result in visual and motor skill impairment. Studies have shown that when linoleic acid (18:2 n-6) and alpha-linolenic acid (18:3 n-3) or only n-3 fatty acids are deficient, the levels of AA and DHA in the brain decrease. When the DHA levels decrease, docosapentaenoic acid (22:5 n-6) values go up in the cells (Uauy, S169). The explanation that is given for this rise in docosapentaenoic acid is that when the amount of alpha-linolenic acid (18:3 n-3) in the diet is not sufficient to maintain an adequate supply of docosahexaenoic acid (22:6 n-3), docosapentaenoic acid (22:5 n-6) (which is made only in the nervous system when DHA levels are low) becomes the preferred long chain n-6 fatty acid substitute for docosahexaenoic acid. Therefore, when there is a decrease in 22:6 n-3 levels, there is an increase in 22:5 n-6 levels (Pawlosky, 1288). This deficiency in DHA changes brain and retinal fatty acid composition. The change in fatty acid composition affects membrane functioning by modifying membrane fluidity and affecting membrane thickness and excitability (Uauy, S169).

A study was done on children five to twelve years of age who were maintained on fat-free total parenteral nutrition (TPN) for two to six months in order to characterize the effect of long-term essential fatty acid deficiency on sleep organization. They found out that children with a fat-free TPN had less slow-wave sleep (a stage of sleep associated with a lower metabolic rate than other stages of sleep) than children who received TPN with the essential fatty acids (Uauy, S170). It has been suggested that the absence of fat intake is related to decreased lipolysis and changing fuel metabolism. So, there is evidence for impaired functioning of the central nervous system when there is a low intake or dietary absence of linoleic and alpha-linolenic acid (Uauy, S170).

A study was done to examine the effect of consumption of eggs from hens fed diets of 0%, 10%, and 20% ground flaxseed would have on plasma and platelet lipids of male volunteers. These male volunteers were fed four eggs per day for two weeks. There were no significant changes in the total cholesterol levels in the volunteers consuming eggs from flaxseed-fed hens. However, there was a significant increase in total n-3 fatty acids and in DHA content. There was also a decrease in the ratio of n-6 to n-3 fatty acids. From studies done on humans, they have found out that platelet n-3 fatty acids increase in human subjects consuming the n-3 fatty acids EPA and DHA. As a result of this increase, a mild high-density lipoprotein cholesterol elevating effect has been observed. These platelet lipid alterations have been associated with a reduced risk of thrombosis. There is evidence that suggests diets containing increased n-3 fatty acids such as alpha-linolenic acid are associated with reduced risk of cardiovascular disease and all-cause mortality. Dietary alpha-linolenic acid through its limited conversion to the longer-chain polyunsaturated fatty acid EPA and DHA also reduces the risk of coronary heart disease (Ferrier, 81).

In conclusion, docosahexaenoic acid is a significant fatty acid in the development of the brain. It accumulates in the retina and brain of all mammals during prenatal and postnatal development. Studies of animals suggest that high levels of DHA in neural tissues such as the retina and cerebral cortex are very important for proper function. Human milk contains high amounts of DHA, AA, linoleic, and alpha-linolenic acid, whereas commercial milk formulas only contain linoleic and alpha-linolenic acid. Breast feeding infants leads to a normal mental development whereas feeding infants the commercial milk formulas may cause deficiencies in DHA and other essential fatty acids. The deficiency of these essential fatty acids can result in decreased visual acuity, impaired growth and development, etc. Therefore, adequate amounts of the major polyunsaturated fatty acids of the brain should be provided in the diet of an infant.

Works Cited

Anderson, Gregory J., Connor, William E., and Corliss, Julie D. "Docosahexaenoic acid is the preferred dietary n-3 fatty acid for the development of the brain and retina." Pediatric Research. 27 (1). Jan 1990, 89-97.

Arbuckle, Dianne L., MacKinnon, Murray J., and Innis, Sheila M. "Formula 18:2(n-6) and 18:3(n-3) content and ratio influence long-chain polyunsaturated fatty acids in the developing piglet liver and central nervous system." The Journal of Nutrition. 124(2). Feb 1994, 289-98.

Clandinin, M.T., Jumpsen, J., and Suh, Miyoung. "Relationship between fatty acid accretion, membrane composition, and biologic functions." The Journal of Pediatrics. 125(5)(P2). Nov 1994, S25-S32.

Ferrier, Les K, Caston, Linda J, Leeson Steve, Squires, James, Weaver, Bonnie J, and Holub, Bruce J. "Alpha-Linolenic acid and docosahexaenoic acid -enriched eggs from hens fed flaxseed: influence on blood lipids and platelet phospholipid fatty acids in humans." The American Journal of Clinical Nutrition. 62 (1). July 1995, 81-6.

Innis, Sheila M. "Plasma and red blood cell fatty acid values as indexes of essential fatty acids in the developing organs of infants fed with milk or formulas." The Journal of Pediatrics. 120(4)(pt 2). Apr 1992, S78-86.

Martinez, Manuela. "Tissue levels of polyunsaturated fatty acids during early human development." The Journal of Pediatrics. 120 (4)(pt 2). Apr 1992, S129-38.

Pawlosky, Robert J, and Salem, Norman Jr. "Ethanol exposure causes a decrease in docosahexaenoic acid and an increase in docosapentaenoic acid in feline brains and retinas." The American Journal of Clinical Nutrition. 61 (6). June 1995, 1284-9.

Stryer, Lubert. Biochemistry. Fourth edition. W.H. Freeman and Company, New York. 1995, 687-88.

Uavy, Ricardo, Birch, Eileen, Birch, David, and Peirano, Patricio. "Visual and brain function measurements in studies of n-3 fatty acid requirements of infants." The Journal of Pediatrics. 120 (4)(pt 2). Apr 1992, S168-80.

Van Biervliet, J.P., Vinaimont, N., Vercaemst, R., and Rosseneu, M. "Serum cholesterol, cholesteryl ester, and high-density lipoprotein development in newborn infants: Response to formulas supplemented with cholesterol and gamma-linolenic acid." The Journal of Pediatrics. 120(4)(pt 2). Apr 1992, S101-8.