Annotation

Neonatal brain and dietary lipids

At term the newborn human infant brain weighs about 350 g, which is approximately 10% of the total body weight. During the first year brain weight increases by about 750 g so that the brain is still approximately 10% of body weight at 1 year. The cerebral cortex is composed largely of neurones and astrocytes and makes up about 45% of the total brain weight. Much of the increase in grey matter weight is due to the development of the complex arborisations and synaptosome formation which subserve neuronal function and the learning processes. Myelination proceeds rapidly after birth and in this process neuroglial cells envelope the axons of cortical neurones with sheaths of myelin which speed the rate of transmission of electrical messages between neurones, other central nervous system cells, and end organs such as muscle and skin.

Sixty per cent of the total energy intake of the infant during the first year is utilised by the brain and much of the energy used to construct neuronal membrane and deposit myelin comes from fat in human milk or infant formulas. Fat, however, is not simply a source of hydrocarbon for energy production but is comprised of a series of complex hydrocarbon structures necessary for the creation of membranes.

Membranes

All membranes whether they are at the cell surface or form part of an intracellular organelle such as a mitochondrion are composed of phospholipid bilayers. The main membrane phospholipids contain two fatty acids and a substituted (amino) alcohol attached to a glycerol phosphate backbone. The nature of the alcohol head group and the attached fatty acids have major effects on the biophysical function of that membrane. In myelin the fatty acids are predominantly saturated or monounsaturated whereas those in neuronal membranes particularly at the synaptosomes are polyunsaturated. Each neurone in the cerebral cortical grey matter has 10 000 or more discrete areas of membrane responsible for neurotransmission to other nerve cells through the synaptosomes (boutons) and these areas have high concentrations of polyunsaturated fatty acids (PUFAs) particularly docosahexaenoic acid (C22:6n-3). The major docosahexaenoic acid containing phospholipids in these areas of neuronal membrane are phosphatidyleserine and phosphatidylethanolamine. Docosahexaenoic acid has a highly specific distribution and is the predominant membrane fatty acid of synaptosomes, retinal photoreceptors, mitochondria, and spermatozoa but is scarce in other tissues.1

Essential fatty acids

In the adult there are two essential fatty acids, linoleic acid (C18: 2n-6) and α-linolenic acid (C18: 3n-3) which are the precursors of the PUFAs and must be supplied in the diet. Subcutaneous fat triglyceride in the adult contains variable amounts of these essential fatty acids determined by the adult diet.2 Infant subcutaneous fat, however, contains very little of these essential fats at birth.3 The adult human is able to synthesise arachidonic acid (C20: 4n-6) from linoleic acid and docosahexaenoic acid from α-linolenic acid. The preterm infant and probably the term infant in the first 4–6 months of life have either inactive or relatively inactive enzyme systems required for these conversions of essential fatty acids to the long chain polyunsaturated fatty acids (LCPUFAs). Though the term infant has a small reserve of LCPUFAs,4 this is insufficient for the amount of docosahexaenoic acid that requires to be incorporated into neuronal membranes of the cerebral cortex.

Infant dietary fatty acids

Human milk provides a supply of ready synthesised docosahexaenoic acid and arachidonic acid. In many infant formulas there is little or no docosahexaenoic acid or arachidonic acid and in some there is insufficient essential α-linolenic acid precursor to allow for docosahexaenoic acid synthesis. Human milk docosahexaenoic acid content can range from 0·2% of total fatty acid in British mothers’ milk to 1·2% in North American Inuit mothers.5 The high fish diet of the Inuit apparently provides a plentiful supply of docosahexaenoic acid. The proportion of docosahexaenoic acid in the breast milk of vegan women is lower than in fish and meat eating women but is still substantially greater than in cows’ milk formulas.4

Infant cerebral cortex phospholipid fatty acid composition and diet

Breast fed infants have significantly greater concentrations of docosahexaenoic acid in their cerebral cortex phospholipids than infants fed current infant formulas (J Farquharson et al).6 The deficient docosahexaenoic acid...
is substituted by the insertion of n-6 series LCPUFAs derived from linoleic acid so that the total n-6 fatty acid content in formula fed infants' brains exceeds that of those breast fed. In older infants (>4 months) docosapentaenoic acid (C22: 5n-6) specifically substitutes for the deficiency of docosahexaenoic acid in neuronal membrane phospholipids phosphatidylserine and phosphatidylethanolamine (J Farquharson et al, unpublished observation).

Consequences
It is only in the last 130 years that infant formulas prepared from modified milk of other mammals or created from mixtures of synthetic plant based materials have been fed to newborn human infants. The effects of feeding different milk formulas on the fatty acids attached to the phospholipids of phosphatidylserine and phosphatidylethanolamine in human brain have not been identified. Lucas and his colleagues have demonstrated that preterm infants fed human milk have a higher developmental status at 18 months and a higher intelligence quotient in later childhood than those fed infant formulas. Preterm infants fed standard infant formulas have significantly different electroretinographic patterns indicating a delayed rod photoreceptor maturation compared with those fed human milk or given supplementary docosahexaenoic acid. Visual cortical function as measured by pattern reversal visual evoked potential and forced choice preferential looking visual acuity response are also better in breast fed or fish oil supplemented preterm infants. In a study of experimental infant formulas with 0.2% docosahexaenoic acid provided by marine oil Carlson has shown that the docosahexaenoic acid supplemented preterm infants have higher red blood cell phosphatidylethanolamine docosahexaenoic acid and better visual acuity than standard formula fed preterm infants. The docosahexaenoic acid supplemented infants also performed significantly better than controls on the Bailey mental scale in which perception, memory, learning, problem solving, vocalisation, early verbal communication, and abstract thinking are tested. At present there is no clear evidence that the term infant with more n-6 LCPUFA and less n-3 LCPUFA in neuronal synaptosomes functions differently from the breast fed infant with greater concentrations of docosahexaenoic acid in membrane phospholipid. The short term effect on efficiency of synaptic transmission and longer term effects on neuronal integrity brought about by these neuronal membrane phospholipid fatty acid differences need urgent study.

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