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DISSERTATION SUMMARY

Dynamics of long polyunsaturated fatty acids in rat brain

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The brain is one of the organs rich in phospholipids, especially two polyunsaturated fatty acids (PUFA), docosahexaenoic acid (22:6n-3, DHA) and arachidonic acid (20:4n-6, AA). Although DHA is known to play a very important role in many neural functions including learning and memory, its exact function is still unknown (Sastry1985). On the other hand recent evidence attribute similar function to a proper mixture of n-6 to n-3 octadecapolyenoic fatty acids (Yehuda 1998).

Another factor that might be important to consider is the age of the animal. Aging is a physiological process associated with a loss in cognitive faculties and decreased level of DHA (McGahon BM 1999). Despite the generally accepted idea that it is almost impossible to alter brain fatty acid composition of adult rats we showed that they might have a faster turnover in brain polyunsaturated fatty acids than it was believed till this moment. After one month of feeding with lipid-enriched diet, differences at the molecular level in brain phospholipids appeared to be significant.

Finally it is known that PUFA content affects membrane biophysical properties and it was proposed that the beneficial effect on mental functions of this fatty acid mixture realizes at this level. However, it is evident that storing and processing of incoming information is a more complex process and thus cannot be a simple function of membrane physicochemical properties. Investigating the effect of the lipid composition of the diet it was found, that along with alterations in molecular composition of ethanolamine phosphoglycerides, a number of genes are overexpressed in rat brain.

The aim of our studies was to shed some light on the unravelling mechanism through which the long chain polyunsaturated acids exert its important role in brain. For this purpose several feeding experiments were run and fatty acid and molecular composition of brain lipids was determined. The diet consisted in normal rat chow enriched in different oils depending on their composition. Fish oil, perilla and soybean oil were use to have diets rich in DHA, linolenic acid (18:3n-3, LNA) and linoleic acid (18:2n-6, LA), respectively.

Essential fatty acid-sufficient rats of different ages were fed from conception with oils rich either in LNA, the precursor of DHA, eicosapentaenoic (EPA)+DHA, or with a mixture of oils giving a ratio of LA to LNA 8.2 or 4.7.

Phospholipids were extracted and separated depending on their hydrophilic head by thin layer chromatography from brain, cerebellum and hippocampus. Their composition in fatty acids was determined by gas chromatography after transmethylation.

Phosphoglycerides can be divided in three subclasses depending on the nature of the linkage that binds the fatty acid to the sn-1 position in the glycerol backbone. So, one can distinguish diacyl, alkylacyl and alkenylacyl phosphoglycerides. Only PE and PC, preferentially the first one, showed differences at this level, therefore the analysis were focus on this two particular phospholipids. The molecular composition of the three subclasses was determined by high-pressure liquid chromatography.

Gene expression analysis was done by microarray techniques.

We showed that brain fatty acid and molecular species composition, particularly of PE can be modified by a diet depending manner. The major finding is that the response of brain to dietary fatty acids, like LA, LNA and DHA is faster than that was described so far by others. And the same fact was observed for aged rats.

Despite of this alteration in molecular composition in brain membranes, the rats fed on short time bases, did not perform better in Morris water maze test. Therefore, it was concluded that accumulation of DHA alone cannot explain the beneficial effects of long chain polyunsaturated fatty acids on cognitive functions in rats.

References

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