

The Impact of n-3 Polyunsaturated Fatty Acids on the Sphingolipid Metabolism in the Human Circulatory System

Jakob H. Mathiassen¹, Philip C. Calder², Elizabeth A. Miles² and Lars I. Hellgren¹,

¹BioCentrum-DTU, Technical University of Denmark, 2800 Kgs. Lyngby, Denmark. ²Inst. of Human Nutrition, Univ. of Southampton, Southampton, United Kingdom.

Sphingomyelin (SM), ceramide (Cer), sphingosine (Sph), and sphingosine-1-phosphate (S-1-P) are metabolically linked through a reversible pathway. These sphingolipids (SL) have different roles in regulating intra- and extracellular physiological processes. For instance, Cer and Sph induce growth arrest and apoptosis, while S-1-P ensures cell survival. Hence, the polarization of the SL metabolism can determine cell fate. The enzymes necessary for transformation of SM to S-1-P are secreted into the circulatory system. The involved enzymes are the secretory acid sphingomyelinase (S-A-SMase), neutral ceramidase (neutral CDase) and sphingosine kinase-1, where they can act on SLs in both lipoprotein particles and in the outer monolayer of the plasma membrane of blood cells.

The S-A-SMase are activated by inflammatory cytokines and since the ratio between the intake of n-6 and n-3 polyunsaturated fatty acids (PUFAs) has been shown to influence inflammatory conditions, this provides a possible link between the intake of dietary fatty acids and the polarization of the extracellular SL metabolism.

Therefore, we have determined the effect of varying intake of eicosapentanoic acid (EPA) and linoleic acid on the activity of S-A-SMase and neutral CDase in plasma from healthy young males (age 18-42). The subjects were divided in four different treatment-groups; no EPA (placebo group), low, moderate and high intakes. Linoleic acid (from corn oil) intake decreased from the placebo group to the high EPA group. The diets also contained minor amounts of docosahexaenoic acid, with the amount increasing from the low to the high EPA group. The enzyme activities were measured in plasma collected immediately before the interventions began and after 12 weeks of intervention.

No dose-related effects of EPA, nor any differentiated effect of the n-6 versus n-3 PUFA intake, were observed on the activities of the two enzymes. However, the average activity of the neutral CDase was decreased in all four treatment-groups, indicating that intervention as such, affected the activity of this enzyme