METABOLISM AND MECHANISMS OF ACTION OF PUFAS IN THE BRAIN

Metabolic fate of AceDoPC, a stable form of LysoPC-DHA to target the brain

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Docosahexaenoic acid (DHA) is preferentially taken up from blood to the brain when esterified at the sn-2 position of lysophosphatidyl-choline[1,2]. However, 1-lyso,2-docosahexaenoyl-glycerophosphocholine (lysoPC-DHA) is not stable in blood plasma where it is rapidly isomerized into 1-DHA,2-lysoPC[3], so we have prevented the DHA migration by acetylating the sn-1 position in lysoPC-DHA[4]. The stable structure is called AceDoPC®, and has been used with success in the experimental stroke treatment[5].

We have recently shown that the structured phospholipidAceDoPC® mimics lysoPC-DHA with similar hydrophobic properties, binds to plasma proteins/lipoproteinsas does a lysophospholipid, and exhibitsa 3D structure close to that of lysoPC-DHA[6].

Using radiolabeled AceDoPC® on the DHA moiety, we were able to show its preferential crossing through a re-constituted blood-brain barrier, compared to non-esterified DHA, as we previously found with lysoPC-DHA[7]. When injected in rat circulation, AceDoPC® provided the brain with DHA more efficiently than non-esterified DHA, whereas the contrary was observed for the heart and liver accretion[6]. AceDoPC® was rapidly processed within the brain with accumulation of DHA into PC first and PE on a longer term, while a small amount of DHA was found associated with lysoPC. The early labeling of PC compared to PE is in favor of lyso-PC re-acylation into PC, followed by redistribution of DHA within brain phospholipids[6].

We conclude that AceDoPC® may mimic lysoPC-DHA to preferentially enter the brain from blood. The advantage of this stabilized form of lysoPC-DHA is to maintain DHA at the sn-2 position during processing to brain phospholipids.

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