Docosahexaenoic Acid

Docosahexaenoic acid (DHA) is an omega-3 fatty acid that is a primary structural component of the human brain, cerebral cortex, skin, sperm, testicles, and retina. It can be synthesized from alpha-linolenic acid or obtained directly from maternal milk or fish oil.

DHA, in particular, promotes neuronal survival 12–14, neurogenesis15, neurite development16–17, neuronal cell migration18, synaptogenesis17, and modulation of inflammatory cascade 19.

Docosahexaenoic acid (DHA), an essential omega-3 fatty acid, protects mitochondria in various diseases. This study aimed to investigate the neuroprotective role of DHA in ischaemic stroke models in vitro and in vivo and its involvement in mitophagy and mitochondrial dysfunction. A mouse model of ischaemic stroke was established through middle cerebral artery occlusion (MCAO). To simulate ischaemic stroke in vitro, PC12 cells were subjected to oxygen-glucose deprivation (OGD). Immunofluorescence analysis, western blotting (WB), electron microscopy (EM), functional behavioral tests, and Seahorse assay were used for analysis. DHA treatment significantly alleviated brain infarction volume, neuronal apoptosis, and behavioral dysfunction in mice with ischaemic stroke. In addition, DHA enhanced mitophagy by significantly increasing the number of autophagosomes and LC3-positive mitochondria in neurons. The Seahorse assay revealed that DHA increased glutamate and succinate metabolism in neurons after ischaemic stroke. JC-1 and MitoSox staining, and evaluation of ATP levels indicated that DHA-induced mitophagy alleviated reactive oxygen species (ROS) accumulation and mitochondrial injury. Mechanistically, DHA improved mitochondrial dynamics by increasing the expression of dynamin-related protein 1 (Drp1), LC3, and the mitophagy clearance protein Pink1/Parkin. Mdivi-1, a specific mitophagy inhibitor, abrogated the neuroprotective effects of DHA, indicating that DHA protected neurons by enhancing mitophagy. Therefore, DHA can protect against neuronal apoptosis after stroke by clearing the damaged mitochondria through Pink1/Parkin-mediated mitophagy and by alleviating mitochondrial dysfunction [1)].

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Sun E, Zhang J, Deng Y, Wang J, Wu Q, Chen W, Ma X, Chen S, Xiang X, Chen Y, Wu T, Yang Y, Chen B. Docosahexaenoic Acid Alleviates Brain Damage by Promoting Mitophagy in Mice with Ischaemic Stroke. Oxid Med Cell Longev. 2022 Oct 8;2022:3119649. doi: 10.1155/2022/3119649. PMID: 36254232; PMCID: PMC9569200.