

Abstract

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Neuroprotectin D1-mediated anti-inflammatory and survival signaling in stroke, retinal degenerations, and Alzheimer's disease.

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BACKGROUND: Docosahexaenoic acid (DHA), the main omega-3 fatty acid, is concentrated and avidly retained in membrane phospholipids of the nervous system. DHA is involved in brain and retina function, aging, and neurological and psychiatric/behavioral illnesses.

DISCUSSION: Neuroprotectin D1 (NPD1), the first-identified stereoselective bioactive product of DHA, exerts neuroprotection in models of experimental stroke by down-regulating brain ischemia reperfusion (BIR)-induced leukocyte infiltration, proinflammatory signaling, and infarct size. Moreover, NPD1 inhibits cytokine-mediated cyclooxygenase-2 (COX-2) expression. Photoreceptor membranes display the highest content of DHA of any cell. Retinal pigment epithelial cells participate in the phagocytosis of the tips of photoreceptor cells (photoreceptor outer segment renewal). There is a DHA retrieval-intercellular mechanism between both types of cells that conserves this fatty acid during this process. NPD1 promotes homeostatic regulation of the integrity of these two cells, particularly during oxidative stress, and this protective signaling may be relevant in retinal degenerative diseases. Moreover, neurotrophins are NPD1-synthesis agonists, and NPD1 content is decreased in the CA1 region of the hippocampus of Alzheimer's patients.

CONCLUSIONS: Overall, NPD1 promotes brain cell survival via the induction of antiapoptotic and neuroprotective gene-expression programs that suppress Abeta42 production and its neurotoxicity. Thus, NPD1 elicits potent cell-protective, anti-inflammatory, prosurvival repair signaling.

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