Omega-3 Fatty Acids Benefit Microglial Responses to Myelin Pathology

Chen, Songela

Demyelinating diseases, such as multiple sclerosis (MS), are devastating disabling neurological disorders most commonly affecting millions of young adults worldwide. Microglia represent rational but potentially difficult therapeutic targets for MS due to their dual-faced protective (phagocytosis, M2 phenotypic) and toxic (overproduction of inflammatory mediators, M1 phenotypic) effects on myelinating oligodendrocytes. This project aimed to determine whether omega-3 polyunsaturated fatty acids (n-3 PUFAs), specifically docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), could benefit microglial responses to myelin pathology. A disease-simulating in vitro model of inflammation was established using primary microglial cultures treated with purified myelin and/or interferon-gamma (IFN-gamma). Myelin phagocytosis and production of pro-inflammatory mediators, including nitric oxide (NO) and tumor necrosis factor alpha (TNF-alpha), were measured as parameters of microglial function. Multiple M1 and M2 molecular markers were measured using high-throughput PCR array, followed by verification using conventional quantitative real-time PCR for specific genes. DHA and EPA dose-dependently enhanced myelin phagocytosis and inhibited the release of NO and TNF-alpha in response to myelin and IFN-gamma stimulation. Furthermore, DHA and EPA elicited microglial polarization toward the beneficial M2 phenotype under physiological and pathological conditions. Thus, n-3 PUFAs promote microglial responses favorable for remyelination at both functional and molecular levels in a demyelinating disease-simulating model. These results open new possibilities for safe and cost-effective future therapies in demyelinating diseases, potentially benefiting millions of people worldwide.

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