Influence of fish oil treatment on microglial cell behavior and Aβ-like pathology in 5xFAD mice model of Alzheimer's disease

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Defining features of Alzheimer's disease (AD) pathology are the formation of amyloid plaques, neurofibrillary tangles, neuron loss and inflammation. Plaques are encircled by a halo of diffuse Aβ, surrounded by dystrophic neurites (DNs) and activated glia. High level of Aβ suppresses microglial ability to clear Aβ and activate inflammatory response that becomes neurotoxic. These microglial cells become dysfunctional and can further contribute to AD pathology.

We investigated the influence of omega-3 fatty acids, the main compounds of fish oil (FO), on Aβ load, neuritic dystrophy and behavior of microglial cells in parietal cortex in 5xFAD mice.

Three-month old female 5xFAD mice received FO (100μl/animal/day) via oral gavage during 3 weeks period. Aβ-pathology was visualized immunohistochemically. We used ThioflavinS and AmiloGlo to visualize plaques, anti-Aβ42 antibody for soluble Aβ peptide labeling, anti-SMI31 antibody for neuritic dystrophy and anti-Iba-1 antibody for microglial cells. Immunostaining was observed by confocal microscopy. Quantification was done by Image J program.

Our results showed that short-term FO supplementation was capable of: (i) inducing significant decreased of total Aβ levels (ii) preventing the emergence of neuritic dystrophy in parietal cortex of 5xFAD mice; (iii) increasing overall microglial number; and (iv) enhancing clustering of microglial cells around amyloid plaques, representing mechanical barrier that prevents further Aβ aggregation.

This study represents valuable contribution to better biological understanding how FO suppresses AD pathology through typical pleiotropic effect. We believe that FO in combination with other drugs could be good approach for long-term treatment in slowing down AD pathology.