RESOLUTION OF INFLAMMATION IN ALZHEIMER'S DISEASE - ROLE OF MICROGLIA

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Introduction: The involvement of inflammation in Alzheimer's disease (AD) is well known. A successful inflammatory response ends with the resolution phase, in which homeostatic and protective activities dominate. The inflammation in AD is chronic and never resolved. In chronic inflammation phagocytosis is inhibited, while phagocytosis is prominent in the resolution phase. Failure in the removal of β-amyloid peptide by phagocytosis has been proposed as a contributing factor in AD.

Hypothesis: Induction of resolution with associated increased phagocytic clearance of amyloid and secretion of growth factors would be beneficial for the affected, and at the same time the harmful influence of chronic inflammation is removed.

Methods: To test the hypothesis if resolution can influence AD-related pathology in a beneficial way we incubated human microglia with Ab-peptide or latex beads, together with the omega-3 fatty acids DHA and EPA which are known to be precursors for pro-resolving mediators. In addition to phagocytosis, cellular and secreted levels of inflammatory proteins were assessed.

Results: We found that incubation with DHA and EPA had a stimulatory effect on phagocytosis of Aβ. EPA decreased the number of cells expressing inflammatory markers, while DHA increased the cellular expression of IL-1β. EPA had a bimodal influence on the secretion of IL-6. Cells showing phagocytosis of Aβ had a higher expression of inflammatory markers.

Conclusions: Our results, together with data from earlier studies, indicate a positive influence on AD by omega-3 fatty acids that may be mediated by pro-resolving mediators.