Long-chain n-3 PUFA and cognition in older people: interaction with Apolipoprotein E genotype

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Epidemiological studies and basic research suggest a protective role of dietary long-chain omega-3 poly-unsaturated fatty acids (n-3 PUFA) against Alzheimer's disease while most intervention studies of supplementation with n-3 PUFA have yielded disappointing results so far. Such discordant results may stem from inadequate targeting of individuals who could actually benefit from a supplementation because of their genetic susceptibility to Alzheimer's disease. The epsilon4 allele of the Apolipoprotein E gene (APOE4) is the main genetic risk factor for late-onset Alzheimer's disease. Apolipoprotein E plays a key role in the transport of cholesterol and other lipids involved in brain composition and functioning. The aim of this presentation is to review studies supporting an interaction between dietary n-3 PUFA and APOE genotype on the risk for Alzheimer's disease. Several epidemiological studies have observed a protective effect of long-chain n-3 PUFA on cognitive decline only in those who do not carry the APOE4 with however, some conflicting results. Plasma DHA was found to be more responsive to dietary fish intake or n-3 PUFA supplementation in older APOE4 non-carriers compared to carriers. A sub-group analysis of a randomized controlled trial of DHA supplementation in patients with mild to moderate Alzheimer's disease found that APOE4 non-carriers receiving DHA had a significantly lower cognitive decline compared to placebo while no effect was evidenced in APOE4 carriers. The PREDIMED-NAVARRA trial evidenced a different effect of the Mediterranean diet on some cognitive tests according to APOE genotype but also CLU and CL1 polymorphisms involved in genetic susceptibility for Alzheimer's disease. Further research is needed to explain these gene X diet interactions on Alzheimer's disease.