

# Abstract

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## Low plasma eicosapentaenoic acid and depressive symptomatology are independent predictors of dementia risk.

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**BACKGROUND:** The potential preventive role of polyunsaturated fatty acids (PUFAs) in Alzheimer disease has aroused increasing interest. Plasma n-3 PUFAs have been shown to be inversely related to the risk of dementia and to depression, which is frequently associated with dementia.

**OBJECTIVE:** The objective was to ascertain whether plasma PUFAs predict the risk of incident dementia in a cohort of older persons, independently of their depressive status.

**DESIGN:** Of 1214 nondemented participants in the Three-City Study from Bordeaux (France) who were followed up for 4 y, 65 developed dementia. The association between the proportion of plasma fatty acids at baseline and the risk of incident dementia was assessed by multivariate proportional hazard models, taking into account depressive status assessed on the basis of the Center for Epidemiologic Studies Depression scale.

**RESULTS:** A higher plasma eicosapentaenoic acid (EPA) concentration was associated with a lower incidence of dementia [hazard ratio (HR) for 1 SD = 0.69; 95% CI: 0.48, 0.98], independently of depressive status and after adjustment for age, education, apolipoprotein E epsilon4 allele, diabetes, and baseline plasma vitamin E and triacylglycerol. The relations between docosahexaenoic acid (DHA), total n-3 PUFAs, and incident dementia did not remain significant in multivariate models. Higher ratios of arachidonic acid (AA) to DHA and of n-6 to n-3 fatty acids were related to an increased risk of dementia, particularly in depressive subjects (n = 90): ratio of AA to DHA (HR: 2.65; 95% CI: 1.07, 6.56) and ratio of n-6 to n-3 (HR: 1.61; 95% CI: 1.04, 2.47).

**CONCLUSIONS:** A high plasma EPA concentration may decrease the risk of dementia, whereas high ratios of n-6 to n-3 fatty acids and of AA to DHA may increase the risk of dementia, especially in depressed older persons. The role of EPA in dementia warrants further research.

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