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Review

Omega-3 fatty acids intake and risks of dementia and Alzheimer's disease: A meta-analysis

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ABSTRACT

Background: We systematically reviewed the association of omega-3 fatty acids intake with the incidence of dementia and Alzheimer's disease (AD) in this meta-analysis of prospective cohort studies, as evidence from previous studies suggests inconsistent results.
Methods: We identified relevant studies by searching PubMed, EmBase, and Web of Science databases up to June 2013. Prospective cohort studies reporting on associations of dietary intake of long-chain omega-3 fatty acids or fish with the incidence of dementia and AD were eligible.
Results: Comparing the highest to lowest category of long-chain omega-3 fatty acids intake and fish intake, the pooled relative risks (RRs) for dementia were 0.97 (95% CI 0.85–1.10) and 0.84 (95% CI 0.71–1.01), respectively. Evidence synthesis for AD risk did not show a statistically significant association with long-chain omega-3 fatty acids intake (RR = 0.89, 95% CI 0.74–1.08). However, a higher intake of fish was associated with a 36% (95% CI 8–56%) lower risk of AD. Dose–response meta-analysis showed that an increment of 100 g per week of fish intake was associated with an 11% lower risk of AD (RR = 0.89, 95% CI 0.79–0.99). There was limited evidence of heterogeneity across studies or within subgroups.
Conclusion: A higher intake of fish was associated with a lower risk of AD. However, there was no statistical evidence for similar inverse association between long-chain omega-3 fatty acids intake and risk of dementia or AD, nor was there inverse association between fish intake and risk of dementia.

Contents

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1. Introduction

Alzheimer's disease (AD), accounting for more than 70% of all cases of dementia, is the most dreaded disease and the fifth leading cause of death in persons aged 65 and older (Brookmeyer et al., 1998; Alzheimer's Association, 2008). The role of nutrition in prevention of dementia and AD arouses increasing hope with particular interest in dietary intake of omega-3 fatty acids, for brain tissue membranes are rich in omega-3 fatty acids, including docosahexaenoic acid (DHA) (Youdim et al., 2000). Eicosapentaenoic acid (EPA) also plays a protective role for nervous system (Kou et al., 2008). Experimental evidence indicates that a DHA-enriched diet can protect the brain from cognitive decline and reduce neurodegenerative pathology in aged rats (Calon and Cole, 2007; Lim and Suzuki, 2000). However, evidence from observational and epidemiological studies suggests an inconsistent relationship between dietary intake of omega-3 fatty acids and risk of dementia and AD. Some human studies suggest that higher intakes of omega-3 fatty acids from dietary sources are related to reduced risk of dementia and AD (Barberger-Gateau et al., 2002; Morris et al., 2003), while other studies failed to find this association (Schaefer et al., 2006; Engelhart et al., 2002).

Given the inconsistency in the literature on the role of omega-3 fatty acids and risk of dementia and AD, we conducted a meta-analysis to review current evidence on the associations of dietary intake of long-chain omega-3 fatty acids or fish (an important source of omega-3 fatty acids) and the incidence of dementia and AD. We restricted the meta-analysis to prospective cohort studies, because case-control studies may be biased by recall of past dietary habits after disease has been diagnosed, especially for patients with dementia or AD, and heterogeneity between study results may be assumed to be smaller by focusing on one study design.

2. Methods

We followed the guidelines published by the Meta-analysis of Observational Studies in Epidemiology (MOOSE) group to complete the meta-analysis (Stroup et al., 2000) (see Table S1).

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2.1. Study selection

Prospective cohort studies on dementia and AD that included data on the exposure to "omega-3 fatty acids" or "fish" were considered eligible for meta-analysis. A systematic literature search of PubMed, EmBase, and Web of Science for identification of articles published between 1965 and June 2013 was performed by two investigators (Wu and Ding). No language restriction was imposed. In addition, we also manually reviewed the references of all retrieved articles and recent reviews to identify relevant studies.

The eligible studies should meet the following inclusion criteria: (1) use of prospective cohort design; (2) examination of dietary intake of omega-3 fatty acids or fish as the variable of interest; (3) determination of incidence of dementia or AD as the outcome of interest; (4) at least one year of follow-up and involved general populations or people at high risk of dementia or AD (e.g. the elderly); and (5) reporting the relative risks (RRs) of dementia or AD calculated according to the highest category with the lowest category of dietary intake of omega-3 fatty acids or fish, and their 95% confidence intervals (CIs). The studies about animal experiment, review research and mechanistic research were excluded.

2.2. Study quality evaluation

The quality of each study was assessed by two investigators (Wu and Mao), using the Newcastle-Ottawa Scale (Wells et al., 2000). This scale judges each study on three broad categories: selection of the study groups, the comparability of the groups, and the ascertainment of the outcome of interest. It ranges from 1 to 9 stars based on the quality of the study, and we considered a study awarded 7 or more stars as a high-quality study in current study, as no standard criteria has been established.

2.3. Statistical analysis and data synthesis

We performed meta-analyses of risk estimates comparing the highest category of exposure with the lowest category. As dietary intake of fish is a major source of omega-3 fatty acids but not the final form of omega-3 fatty acids intake, we pooled the data on dietary intake of long-chain omega-3 fatty acids (including total long-chain omega-3 fatty acids, DHA, and EPA) and fish separately. Dose–response meta-analyses of fish intake and risks of dementia and AD were then conducted using methods previously reported (Larsson and Orsini, 2011; Greenland and Longnecker, 1992), which facilitated the calculation of a pooled relative risk across studies with a common unit of comparison with studies, assuming a linear dose–response relation. In this study, we estimated the relative risk per unit of 100 g increment of fish intake per week for each study and then pooled them together. For studies that reported results for fish intake in servings only, we derived grams by assuming that one serving equals 100 g (Bouzan et al., 2005; Guevel et al., 2008). We converted the level of fish intake categories based on the calculated midpoint of fish intake if the study did not report the median of exposure category. Table S2 shows the definition of fish intake and the means of conversion of categories within each study. These analyses were carried out for fish intake and risks of dementia and AD only, as there was insufficient data for total long-chain omega-3 fatty acids, DHA, and EPA.

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A fixed effects model was used to estimate the pooled RRs and 95% CIs if there was no evidence of heterogeneity; otherwise, a random effect model was used. The chi-square (χ^2) test and I-squared (I^2) statistic were used to explore the heterogeneity among studies. Publication bias was assessed by Egger's regression test and Begg–Mazumdar test (Egger et al., 1997; Begg and Mazumdar, 1994). Subgroup analyses were performed on fish intake and risk of dementia and AD, according to follow-up duration, geographic location, study quality, and difference between highest intake categories, to test the possible impact factors.

Statistical analyses were conducted using Stata Version 12.0 software (Stata Corp, College Station, TX). All statistical tests were two sided and used a significance level of $p < 0.05$.