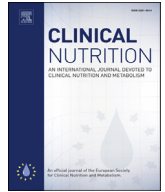




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Randomized Control Trials

Red blood cell membrane omega-3 fatty acid levels and physical performance: Cross-sectional data from the MAPT study

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SUMMARY

Background & aims: Studies have shown that omega-3 polyunsaturated fatty acids (PUFAs) are associated with brain, cardiovascular and immune function, as well as physical performance and bone health in older adults. So far, few studies have highlighted the associations between PUFA status and performance-based tests of physical function. To study the associations between the omega-3 index (red blood cell (RBC) membrane content of omega-3 PUFAs, such as eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA)) and physical performance measured with the Short Physical Performance Battery (SPPB) in a sample of community-dwelling older adults.

Design: Cross-sectional study using the baseline data of the Multidomain Alzheimer's Disease Trial (MAPT), a randomized, placebo-controlled trial.

Participants and measurements: 1449 participants with available data on PUFAs were included. Omega-3 index and Short Physical Performance Battery (SPPB) scores were measured at enrollment and the omega-3 index expressed as the percentage of total fatty acid content was calculated. We also dichotomized the omega-3 index as low (lowest quartile) vs. high (three upper quartiles).

Results: Participants were 75.2 (± 4.4) years old, 64.5% were female. Bivariate analyses found that participants who were in the lowest omega-3 index quartile (Q1) had a SPPB score significantly lower than participants in the three other quartiles (Q2–Q4). However, adjusted (for age, gender, cognitive function, depressive status, Body Mass Index and grip strength) multiple linear regression showed that the omega-3 index–SPPB score association did not reach statistical significance [$\beta = -0.166$; (-0.346 ; 0.013); $p = 0.07$] in our sample.

Conclusion: This cross-sectional study found that participants with a low omega-3 index had worse performance-based test results of physical function than people with a high omega-3 index, but this association did not reach statistical significance once confounders were controlled for. Studies looking at the over-time associations between PUFA status and physical performance changes may shed more light on this topic.

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1. Introduction

Lower Short Physical Performance Battery (SPPB) test results, marker of the age-related decline of physical performance, have been identified as a good predictor of mobility disability, institutionalization and mortality in older persons [1]. Identification of modifiable risk factors for physical performance decline is essential

to set up efficient primary prevention strategies for disability in older people. Among the potential risk factors, nutrition should be in the focus based on its role in the regulation of inflammation, which is a key player in the development of some geriatric diseases leading to physical disability like sarcopenia [2]. Several lines of evidence suggest that polyunsaturated fatty acids (PUFAs) of the omega-3 family have strong anti-inflammatory activity [3] and therefore may be beneficial for the treatment of conditions associated with an increased inflammatory state and subsequent catabolic state, such as muscle mass loss and impairment of physical performance [4]. Moreover, omega-3 PUFAs have been shown to facilitate the transport of red blood cells (RBCs) through the

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capillary bed [5], which could lead to enhanced oxygen delivery to skeletal muscle and a subsequent improvement in physical performance. Finally, a potential role of omega-3 PUFAs in preventing age-related physical decline could partly be explained by their ability to increase muscle protein synthesis [6,7]. The omega-3 index, which is the sum of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) content in RBC membranes, is a biomarker of omega-3 PUFA status [8,9]. The omega-3 index is a good marker of dietary omega-3 intake [10], and it is also considered as a biomarker for long-term essential PUFA intake, because its level changes in parallel with changes in the fatty acid composition of adipose tissues [11]. However, to date few studies have explored the association between the omega-3 index and physical performance in older adults, and those have provided inconsistent results [12]. To our knowledge, only few studies showed a cross-sectional positive association between physical performance (higher gait speed) and higher plasma omega-3 PUFA concentrations [13–15]. This finding needs to be replicated before its generalization and the consideration of omega-3 PUFAs as potentially preventive factors. The aim of the present study was to evaluate the cross-sectional association between the omega-3 index and SPPB scores in a sample of community-dwelling older adults.

2. Methods

The data used in this study comes from the baseline assessments of the Multidomain Alzheimer's Disease Trial (MAPT), a randomized, placebo-controlled trial with four groups: omega-3 PUFA supplementation, omega-3 PUFA supplementation plus multidomain intervention (exercise advice, nutritional counseling and cognitive training), multidomain intervention alone, and a placebo group [16].

2.1. Participants

The MAPT population included older adults aged 70 years and over, living in the community and at risk of cognitive decline.

Inclusion criteria:

- Older persons aged 70 years and over,
 - Spontaneous memory complaint expressed to the general practitioner
- or
- Limitation in one IADL
- or
- Slow walking speed

Exclusion criteria:

- Demented individuals (DSM IV), individuals with MMS <24/30
- ADL < 6/6
- subjects who had taken omega-3 supplementation within the past 6 months

1680 individuals included in MAPT Study

At least one follow-up visit (n=1525)
and
Omega-3 PUFA measure at baseline

1449 participants analyzed

Fig. 1. Study flow chart. ADL, Activity of Daily Living; DSM IV, Diagnostic and Statistical Manual – Revision 4; IADL, Instrumental Activity of Daily Living; MAPT, Multidomain Alzheimer Preventive Trial; MMS, Mini Mental State; PUFA, Polyunsaturated Fatty Acids.

Inclusion criteria were spontaneous memory complaint, limitation in one instrumental activity of daily living (IADL, e.g., ability to use the telephone, to shop, to prepare meals), slow walking speed (i.e., lower than 0.8 m/s). Exclusion criteria were a dementia diagnosis [17], a Mini Mental State Examination (MMSE) score lower than 24/30 [18], dependency in at least one basic activity of daily living (ADL, e.g., bathing, feeding, transferring) [19], and the presence of any disease that could compromise the subject's participation in the multidomain intervention (e.g., Parkinson's disease). In addition, subjects who had taken omega-3 supplementation within the past 6 months were not included. The current analyses were performed in 1449 individuals who have had available data on omega-3 PUFA status at baseline and who have had at least one follow-up visit for the assessment of cognitive function (Fig. 1).

The study protocol has been approved by the Ethical Committee in Toulouse (CPP SOOM II). Written consent was obtained from all participants. The protocol is registered on a public-access clinical trial database (www.clinicaltrials.gov [NCT00672685]).

2.2. Measures

2.2.1. RBC PUFA analysis

At the baseline visit, participants underwent a blood drawing. RBCs were isolated from blood samples drawn into heparin-containing tubes. RBC PUFA membrane composition was analyzed by gas chromatography with flame ionization [8]. Briefly, unwashed packed RBCs were directly methylated with boron trifluoride and hexane at 100 °C for 10 min. The PUFA methyl esters thus generated were analyzed using a GC2010 gas chromatograph (Shimadzu Corporation) equipped with an SP2560 fused-silica capillary column (Supelco, Bellefonte, PA). PUFAs were identified by comparison with a standard mixture of FAs characteristic of RBCs (GLC 727; NuCheck Prep), which also was used to determine individual PUFA response factors.

The addition of RBC membrane DHA plus EPA content (i.e., omega-3 index) expressed as the percentage of total fatty acids in

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