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## Original article

## Plasma fatty acid biomarkers are associated with gait speed in community-dwelling older adults: The Three-City-Bordeaux study

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## SUMMARY

**Background & aims:** Nutritional factors, such as fatty acids (FA), could modulate physical performance in the elderly. In particular, the opposite properties of long-chain n-3 and n-6 polyunsaturated FAs (LC PUFAs) could impact muscle function. We aimed to assess the cross-sectional association between plasma FAs and gait speed in French elderly community-dwellers.

**Methods:** Elderly participants from the Bordeaux centre of the Three-City Study were included. The proportion of 12 FAs, and gait speed (m/s) were measured concomitantly at enrollment. Low gait speed (LGS) was defined as below the first quartile of gait speed. FA patterns were derived from the 12 individual FAs using principal component analysis. Multivariate logistic regression models were used and odds-ratios (OR) were expressed per one additional standard-deviation unit of each plasma FA or per one additional unit of pattern score.

**Results:** Among 982 participants, 239 (24.3%) had a low gait speed (<0.63 m/s) at baseline. Regarding individually each FA, a higher proportion of eicosapentaenoic acid (EPA) and of docosahexaenoic acid (DHA) were associated with lower odds of LGS (OR = 0.76; 95% CI: 0.63–0.93 and OR = 0.79; 95% CI: 0.67–0.95 respectively). Conversely, a higher arachidonic acid (AA):(EPA + DHA) ratio was associated with higher odds of LGS. Three main FA patterns were identified. A higher score on the FA pattern characterized by higher proportions of LC n-3 PUFAs was associated with lower odds of LGS (OR = 0.78; 95% CI: 0.67–0.90).

**Conclusions:** A FA pattern mainly driven by high plasma concentrations of LC n-3 PUFAs is cross-sectionally associated with higher gait speed in community-dwelling older adults, while a higher AA:(EPA + DHA) ratio is associated with lower gait speed. These findings suggest a potential protective effect of n-3 PUFA on physical performance decline.

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**Abbreviations:** 3C study, Three-City study; AA, arachidonic acid; ALA,  $\alpha$ -linolenic acid; FA, fatty acids; LA, linoleic acid; LGS, low gait speed; PCA, principal component analysis.

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## 1. Introduction

Low gait speed (LGS), marker of the age-related decline of physical performance also used for sarcopenia definition [1], has been identified as a good predictor of mobility disability, institutionalization and mortality in older persons [2]. Thus, identification of modifiable risk factors for physical performance decline is essential to set up efficient primary prevention strategies for disability in older people. Among them, nutrition should be a 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 [3]. As modulators of inflammatory processes, the fatty acids (FAs) have been rarely studied in association with physical performance to date. The ability of saturated fatty acids (SFA) to promote inflammation and insulin resistance may result in a potential deleterious effect on muscle metabolism [4] while an anti-inflammatory effect of mono-unsaturated fatty acids (MUFA) has been biologically ascertained [5]. A potential role of n-3 polyunsaturated fatty acids (PUFA) in preventing age-related physical decline could partly be explained by their anti-inflammatory properties and their ability to increase muscle protein synthesis [6,7], while n-6 PUFAs and their derivatives exhibit inflammatory properties [8]. So far, few studies have explored the association between dietary intake of n-3 PUFA and physical performance in older adults and have provided inconsistent results [9,10]. A reason for such discrepancies may be the recall bias inherent to available dietary assessment methods, which could lead to subsequent misclassification of the dietary n-3 PUFA exposure [11]. To our knowledge, a single study to date showed a cross-sectional positive association between higher gait speed and higher plasma n-3 PUFA concentrations, which surpass limits of dietary surveys, in Italian older adults [12]. This finding needs to be replicated in various populations before its generalization and the consideration of n-3 PUFAs as potentially preventive factors. Moreover, study of individual FAs may ignore important interrelations among FA families, which are absorbed and metabolized through common enzymatic pathways [13], suggesting that the investigation of FA patterns could be more informative. Indeed, FAs are strongly linked in the diet and their individual effect cannot be easily disentangled from that of other synergistic or antagonist FAs. The aim of the present study was to evaluate the cross-sectional association between plasma FAs, considered either individually or grouped in patterns, and gait speed in a sample of French community-dwelling older adults.

## 2. Materials and methods

### 2.1. Participants

This cross-sectional study was conducted among participants from the Bordeaux sample of the Three-City (3C) Study. The 3C cohort aims to disentangle the part of vascular risk factors in dementia. This cohort included 9294 community dwellers, selected from electoral rolls of Bordeaux ( $N = 2104$ ), Dijon ( $N = 4931$ ) or Montpellier ( $N = 2259$ ) (France), aged 65 years and over at baseline (1999–2000) [14]. The general methods of the 3C study have been described elsewhere [14] and are available at <http://www.three-city-study.com/the-three-city-study.php>. This research adheres to the principles of the Declaration of Helsinki. The Consultative Committee for the Protection of Persons participating in Biomedical Research of the Kremlin-Bicêtre University Hospital (Paris, France) approved the protocol of the 3C study. All participants gave their written informed consent. The baseline data collection included sociodemographic and behavioral measurements, symptoms and complaints, major chronic diseases, neuropsychological tests, a physical examination, a brief food-frequency questionnaire and blood sampling. The present analyses were restricted to the Bordeaux sample of the 3C cohort, the only center where FA assessment has been performed: 982 (46.7%) participants were included since they had both a baseline evaluation of gait speed and assessment of plasma FA proportions.

### 2.2. Gait speed assessment

Gait speed was assessed via a 6-m walking test during the mobile-unit face-to-face interviews performed at baseline. Due to the length of the mobile-unit, participants were asked to perform a 3-m returned walk from a standing start at their usual speed. Use of their usual technical assistance was allowed for safety reasons. The time needed to cover 6 m was measured by the interviewer, and gait speed was computed as the ratio between distance and time and expressed in m/s.

### 2.3. Assessment of plasma fatty acid

At the baseline visit, 1416 Bordeaux participants underwent a blood drawing and aliquots of plasma samples were frozen immediately to  $-80^{\circ}\text{C}$  until utilization. Then, plasma FA measurements were performed as earlier described [15]. Briefly, separation of isopropyl esters was done on a gas chromatograph (Trace; Thermoelectron, Courtaboeuf Cedex, France) using a 25-m Carbowax capillary column. Using reference FA esters (Sigma Chemical Company, Saint-Quentin Fallavier, France), each peak was identified, and peak areas were measured with an automatic integrator (DP700; Fisons Instruments, Arcueil Cedex, France). Each series of chromatographs was validated by use of internal quality controls (saturated and unsaturated fatty acid methyl esters from Sigma Aldrich, Saint-Quentin Fallavier, France) to ensure accuracy of peak integration. The results of each FA were expressed as percentage of total plasma FAs. Total SFA was the sum of myristic (14:0), palmitic (16:0) and stearic (18:0) acids. Total MUFA was the sum of palmitoleic (16:1 n-7) and oleic (18:1 n-9) acids. Linoleic acid (LA, 18:2 n-6),  $\gamma$ -linolenic acid (18:3 n-6) and arachidonic acid (AA, 20:4 n-6) proportions were summed to compute the total n-6 PUFA proportion and the sum of  $\alpha$ -linolenic acid (ALA, 18:3 n-3), EPA (20:5 n-3), docosapentaenoic acid (22:5 n-3) and DHA (22:6 n-3) proportions represented the total n-3 PUFA proportion. The n-6:n-3 PUFA, LA:ALA and AA:(EPA + DHA) ratios were calculated. At the same time, assessment of red blood cell (RBC) FA has been performed, as described in [Supplementary data](#) among a sub-sample of participants (see [e-Methods](#)).

### 2.4. Other variables

Sociodemographic information recorded at baseline included sex, age and education (in four classes: no education or primary school only, secondary school, high school, and university). Practice of physical activity was defined as regular when doing sport regularly or having at least 1 h of leisure or household activity per day. Vascular risk factors at baseline included BMI [computed as measured weight (kg)/height<sup>2</sup> (m)], smoking status (in three classes: never, ex- or current smoker), self-reported history of cardiovascular or cerebrovascular disease (at least one of the following: angina pectoris, myocardial infarction, stroke, heart failure and peripheral vascular disease), hypertension (systolic blood pressure  $\geq 140$  mmHg or diastolic blood pressure  $\geq 90$  mmHg or antihypertensive treatment), and diabetes (fasting glucose  $\geq 7.0$  mmol/L or antidiabetic treatment). Polypharmacy, defined as taking 5 medications per day (median of total medication consumption in the study sample) or more was used as an indicator of comorbidity (dichotomous variable). Cognitive disorders were defined as Mini-Mental State Examination scores  $< 24$  [16]. Depressive symptomatology was defined as Center for Epidemiologic Studies-Depression scale scores  $\geq 17$  in men and  $\geq 23$  in women [17]. If more than 4 of 20 items of the scale were missing because of severe depression, as ascertained by the psychologist interviewer, the subject was considered to be depressive. Alcohol consumption was

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