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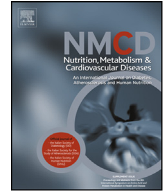

Associated factors of estimated desaturase activity in the EPIC-Potsdam study

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Abstract *Background and aims:* Altered activity of desaturase enzymes may be involved in the development of metabolic diseases like type 2-diabetes. Desaturase activities might be modifiable by diet and lifestyle-related factors, but no study has systematically investigated such factors so far. We aimed to evaluate the association of demographic, anthropometric, dietary and lifestyle characteristics with estimated Δ5-, Δ6- and Δ9-desaturase activity.
Methods and results: A subsample ($n = 1782$) of the EPIC-Potsdam study was used for a cross-sectional analysis, involving men and women, mainly aged 35–65 years. Fatty acid (FA) product-to-precursor ratios, derived from the FA composition of erythrocyte membrane phospholipids, were used to estimate desaturase activities. Multiple linear regression models were used with estimated Δ5-, Δ6- and Δ9-desaturase activity as outcome and demographic (age, sex), anthropometric (BMI, WHR), dietary intake (FAs, carbohydrates) and lifestyle (physical activity, smoking, alcohol consumption) factors as exposure variables.

Alcohol intake was positively associated with estimated Δ6- (explained variance in desaturase activity: 1.52%) and estimated Δ9-desaturase activity (explained variance: 5.53%). BMI and WHR showed a weak inverse association with estimated Δ5-desaturase activity (explained variance: BMI: 1.07%; WHR: 1.02%) and weak positive associations with estimated Δ6-(explained variance: BMI: 1.17%; WHR: 1.19%) and estimated Δ9-desaturase activities (explained variance: BMI: 0.70%; WHR: 0.96%). Age, sex, physical activity, smoking and dietary factors were only weakly associated with the estimated desaturase activities.
Conclusion: Our findings suggest that alcohol intake as well as obesity measures are associated with the FA ratios reflecting desaturase activity.
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Introduction

The fatty acid (FA) composition of biological tissues is influenced by the amount and the quality of dietary fat as well as the endogenous FA metabolism, where desaturases play an important role [1]. Desaturase enzymes catalyze the formation of unsaturated FA by inserting double bonds into the FA carbon chain. Δ5- and Δ6-desaturase synthesize highly unsaturated FAs with linoleic acid (LA) and α-linolenic acid (ALA) as substrates. Δ9-desaturase catalyzes

Abbrevations: BMI, body mass index; FA, fatty acid; FFQ, food frequency questionnaire; ALA, α-linolenic acid; LA, linoleic acid; MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid; SFA, saturated fatty acid; T2D, type 2 diabetes; WHR, waist to hip ratio.

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the formation of monounsaturated FAs (MUFA) from palmitic acid and stearic acid. All three desaturases catalyze the rate-limiting step for the endogenous synthesis of MUFAs and polyunsaturated FAs (PUFA) [2]. In epidemiological studies, the activity of these desaturases has traditionally been estimated using FA product-to-precursor ratios that are derived from the FA composition of lipid fractions from blood or adipose tissue.

A number of epidemiological studies indicated a strong inverse relation of the estimated Δ5-desaturase activity and a strong positive relation of the estimated Δ6-desaturase and Δ9-desaturase activity to diabetes risk as well as to the risk of obesity, mortality and cancer [1–6]. Therefore, the regulation of all desaturases seems to be of considerable physiological importance. In addition to genetic variations, environmental factors are assumed to be involved in the regulation of the desaturase activities [7]. However, data from studies in humans on how desaturase activity is modified are scarce. In a controlled cross-over dietary intervention study, the FA composition in the diet was associated with changes in the estimated desaturase activities [8]. In the SLIM-study, changes in estimated desaturase activity were related to lifestyle changes (diet and physical exercise) [9]. Further, an observational study suggested an association between estimated desaturase activity and lifestyle factors including smoking, physical activity and fat intake as well as markers of obesity [3]. While these studies indicate that the estimated desaturase activities might be modifiable by diet and other lifestyle-related factors, no study has systematically investigated the association of anthropometric, demographic, dietary and lifestyle factors so far.

Therefore, the aim was to investigate the association of anthropometric (BMI and WHR), demographic (age and sex), dietary (intake of FA and carbohydrates) and lifestyle (physical activity, smoking and alcohol consumption) factors with the estimated activity of desaturases.

Methods

Study population

The EPIC (European Prospective Investigation into Cancer and Nutrition)-Potsdam study is a part of the multicenter prospective cohort study EPIC [10]. EPIC-Potsdam includes 16,644 women (mainly aged 35–65 years) and 10,904 men (mainly aged 40–65 years) recruited from the general population between 1994 and 1998 [11]. Baseline assessment included the collection of blood samples, anthropometric measurements, a self-administered validated food-frequency questionnaire (FFQ) and questionnaires as well as interviews on socio-demographic and lifestyle characteristics. For biochemical measurements, a random sample of 2500 subjects was drawn from all participants of EPIC-Potsdam who provided a blood sample ($n = 26{,}444$). We excluded participants with missing values or implausible data on dietary FA intake as estimated from the FFQ ($n = 26$), with unreliable data on erythrocyte FA proportions ($n = 688$) or reported energy intake (<800 or >6000 kcal/d) ($n = 4$). After exclusions, 1782 participants were considered for analysis. Informed consent was obtained from all participants, and approval was given by the Ethics Committee of the state of Brandenburg, Germany.

Dietary assessment

The FFQ assessed the average intake frequency and portion size of 148 foods consumed during the 12 months prior to examination. Intake frequency was measured using ten categories, ranging from ‘never’ to ‘five times per day or more’. Portion sizes were estimated using photographs of standard portion sizes. Information on intake frequency and portion size was used to calculate the amount of each food item in grams consumed on average per day. Nutrient intake was calculated from the food items according to the German Food Code and Nutrient Data Base version II.3. These intakes were then calibrated to 24-h recall data as described in detail elsewhere [15]. For the present analysis, intakes of FAs were expressed as nutrient densities (g per 1000 kcal). Dietary intake of the FAs was estimated from the FFQ, except for the *trans*-FAs, which were measured in erythrocytes as surrogate marker for *trans*-FA intake.

The validity and reproducibility of the FFQ have been described previously [12,13]. Briefly, the correlation coefficients corrected for intra-individual variation in dietary recall data between the FFQ and twelve 24-h-recalls for energy-adjusted intake were 0.76 for SFA, 0.77 for MUFA, 0.70 for PUFA and 0.58 for total carbohydrate [13].

Lifestyle factors and anthropometry

Smoking-history as well as physical activity were assessed with a lifestyle questionnaire (self-administered) and a computer-guided interview [10]. We considered biking and sports activity as physical activity and calculated the average time (hours) spent per week.

Anthropometric measurements included height, weight and waist circumference. Body mass index (BMI) was calculated as body weight (kg) divided by squared height (m^2). Waist to hip ratio (WHR) was calculated as waist circumference (cm) divided by hip circumference (cm). The measurement procedures followed standard protocols [14]. All interviews and examinations were conducted by trained interviewers who were regularly supervised [10].

Fatty acid measurement and estimation of desaturase activities

Thirty milliliters of blood were taken from each participant during baseline examination and were centrifuged at 1000 g for 10 min at 4 °C. Plasma, red blood cells, and buffy coat were removed and stored at −80 °C. The erythrocyte membrane FAs were analyzed between February and June 2008. A detailed description of the laboratory methods can be found elsewhere [15]. Briefly, FA methyl esters (FAME) were separated on a GC-3900 gas chromatograph (Varian Inc, Middelburg, Netherlands) equipped with a 100 m × 0.25 mm ID WCOT-fused silica capillary column

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