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Interaction between Familial History of Obesity and Fat Intakes on Obesity Phenotypes

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Key Words
Familial history of obesity · Fat intakes

Abstract
Aim: To evaluate whether familial history of obesity (FHO) interacts with dietary fat intake (DFI) on obesity-related phenotypes. ***Methods:*** We recruited 664 participants aged between 18 and 55 years. A positive FHO (FHO+) was defined as having at least 1 obese first-degree relative and a negative FHO (FHO–) as no obese first-degree relative. Dietary intakes were collected from a food-frequency questionnaire. Body mass index, weight and waist girth were recorded using standard procedures. Fat mass and fat-free mass were assessed by electrical bioimpedance. ***Results:*** Significant interaction effects (FHO · DFI) were observed for body mass index, weight, waist girth and fat mass (p interaction = 0.05, 0.04, 0.04, 0.02, respectively). Among FHO+ individuals, indices of obesity increased with an increasing amount of DFI, whereas these associations were not observed in FHO– individuals. We also found that FHO+ individuals consuming a high-fat diet were at higher risk of obesity than FHO– individuals consuming a low-fat diet (3.6, CI 2.1–6.2). ***Conclusion:*** These results suggest a stronger relationship between DFI and obesity-related phenotypes in individuals with FHO+.

Introduction

Obesity has now reached epidemic proportions [1]. This multifactorial disease is influenced by a variety of factors including dietary intakes and genetics [2]. The role of dietary fat intakes (DFI) in the etiology of obesity has been well-explored in the past, and it is generally accepted that a high-fat diet induces an overconsumption of energy, which can lead to the development of obesity [3–5]. However, the impact of dietary intakes on weight differs significantly between individuals [6, 7], suggesting that an individual's genetic background remains an important determinant of susceptibility to obesity [8]. Indeed, it has been shown that the presence of obese family members increases the risk of offspring being obese [9–12], suggesting that heredity or the presence of a positive familial history of obesity (FHO) play a significant role in the development of obesity. Familial history data could be used as an indicator of genetic susceptibility on the assumption that FHO+ individuals are more likely to have a genetic predisposition for obesity than FHO– individuals.

Thus, it is hypothesized that genetics and diet could interact together to modulate obesity-related phenotypes. The purpose of this study was to examine the influence of DFI, FHO and their interaction on obesity-related phenotypes.

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Methods

Study Population and Study Design

Participants of the present study were Caucasian adults aged between 18 and 55 years. They were recruited in the Quebec City metropolitan area through advertisements in local newspapers and radio stations and by electronic messages sent to university and hospital employees. A trained research assistant conducted a 15-min telephone interview with people who responded to the advertisement messages. After the interview, the eligible participants were invited to come to the laboratory to meet a trained research assistant to collect anthropometric measurements and to have a dietitian complete a validated food frequency questionnaire (FFQ) [13]. Participants received 25 dollars (Canadian) to cover transportation and parking expenses after the appointment. The enrolment of the participants took place between May 2004 and March 2007. The final study sample consisted of 664 individuals. All participants gave their written consent to participate in this study, which has been approved by the Ethics Committee of the local university.

Familial History of Obesity

A cross-sectional study was previously conducted to validate the method used to classify individuals with and without FHO [14]. Briefly, individuals were first asked to report, on a self-administrated questionnaire, their own weight and height and to estimate the weight and height of each of their family members (mother, father and siblings). Subjects had to answer the following questions: What is your current weight?, What is your current height? What is the current weight of your mother, father and siblings? What is the current height of your mother, father and siblings? Secondly, volunteers had to identify whether any of their family members were obese. If the participant identified at least 1 obese first-degree relative, the FHO was determined as positive (FHO+), and the FHO was considered negative (FHO–) if no obese first-degree relative was identified. Substantial agreement between the FHO reported by the participants and the one obtained by each family member was observed (kappa = 0.72; $p < 0.0001$). Sensitivity (90.5%), specificity (82.6%), positive (82.6%) and negative (90.5%) predictive values of the FHO were very good.

Anthropometric Measurements

Participants were standing and dressed in light indoor clothing without shoes for anthropometric measurements. A beam scale with height rod graduated in centimeters was used (Detecto, Webb City, Mo., USA) to obtain a measure of weight and height. Weight was measured to the nearest 0.1 kg, and height was measured to the nearest 0.5 cm. The scale was calibrated before the examination. The body mass index (BMI) was computed as weight in kilograms divided by height in meters squared. The waist girth was measured to the nearest 0.5 cm midway between the lower rib margin and the iliac crest in the horizontal plane. Fat mass and fat-free mass were measured by a bioelectrical impedance meter (101-RJL Systems, Detroit, Mich., USA). To minimize variations in anthropometric measurements, they were obtained by the same experienced staff member.

Dietary Assessment

Dietary intake over the past month was assessed by a 91-item FFQ administered by a dietitian. This FFQ has been previously validated in French Canadian men and women [13]. Briefly, the mean value for intake of most nutrients assessed by the FFQ and the 3-day food record were not statistically different. Energy-adjusted correlation coefficients for the principal macronutrients (proteins, carbohydrates, fat and subtypes of fat) ranged from 0.36 to 0.60 [13]. The FFQ was structured to reflect food habits of the Quebec population. Participants were asked how often they consumed each item per day, week, month or none at all during the last month. Many examples of portion size were provided for a better estimation of the real portion consumed by the respondent.

Lipid Profile

Blood samples were collected from an antecubital vein and put into vacutainer tubes containing EDTA in the morning after a 12-h overnight fast. Blood samples were immediately centrifuged. Cholesterol and triglyceride concentrations were determined in plasma and lipoprotein fractions using OLYMPUS AU400e (Olympus America Inc., Melville, N.Y., USA). HDL fraction was obtained after precipitation of LDL in the infranatant ($d > 1.006$ g/ml) with heparin-manganese chloride [15]. LDL-C concentrations were estimated by the equation of Friedewald et al. [16].

Statistical Methods

Analysis of variance and covariance were used to explore differences in participants' characteristics between FHO+ and FHO– individuals. To explore the interaction between FHO and DFI, an analysis of covariance was performed where the FHO, the DFI (which was categorized using the median value of fat intake: $\leq$ or $>$33.1% of the total energy intake from fat), and the interaction term (FHO·DFI) were included in the model together with age, sex and energy intake as covariates. Logistic regression analysis was performed to assess the odds ratio of being obese (BMI $\geq$30) in FHO+ individuals with FHO+ having a high-fat diet ($>$33.1%) compared to FHO– individuals having a low-fat diet ($\leq$33.1%). All statistical analyses were performed in SAS statistical software, version 9.1 (SAS Institute Inc., Cary, N.C., USA) and statistical significance was defined as $p < 0.05$.

Results

Anthropometric measurements and blood lipid levels are shown in table 1. Individuals with FHO+ were older and had higher values for all obesity-related phenotypes (BMI, waist girth, weight, fat mass and fat-free mass) than individuals with FHO–. Blood lipid levels were similar for individuals with FHO+ and FHO–. Energy and nutrient intakes were similar for individuals with FHO+ and FHO– (table 2).

To verify whether FHO interacts with DFI to modulate the obesity indices, covariance analyses were performed, with age, sex and energy intake as covariates. Significant

Table 1. Anthropometric measurements and blood lipid levels according to FHO

	FHO+ (n = 277)	FHO– (n = 387)	p
Men/women ratio, %	36/64	48/52	0.003*
Age, years	39.7 ± 11.2	34.8 ± 10.9	<0.0001
BMI	28.9 ± 5.6	25.8 ± 5.1	<0.0001**
Waist girth, cm	93.1 ± 15.6	85.3 ± 14.8	<0.0001**
Weight, kg	81.0 ± 18.1	73.9 ± 17.5	<0.0001**
Fat mass, kg	28.1 ± 10.5	22.0 ± 9.3	<0.0001**
Fat-free mass, kg	52.7 ± 11.5	51.9 ± 11.9	<0.0001**
Total cholesterol, mmol/l	4.70 ± 1.00	4.47 ± 1.01	0.73***
LDL cholesterol, mmol/l	2.92 ± 0.96	2.83 ± 1.00	0.75***
HDL cholesterol, mmol/l	1.37 ± 0.42	1.43 ± 0.42	0.43***
Triglycerides, mmol/l	1.30 ± 0.80	1.11 ± 0.80	0.49***
Total cholesterol/HDL cholesterol, mmol/l	3.75 ± 1.62	3.38 ± 1.21	0.17***

* p value from χ^2. ** p value adjusted for age and gender. *** p value adjusted for age, gender and BMI. Results are expressed as mean ± SD.

Table 2. Dietary intakes of individuals according to FHO

	FHO+ (n = 277)	FHO– (n = 387)	p*
Energy, kcal	2,387 ± 634	2,522 ± 813	0.26
Fat, % of energy intake	33.5 ± 5.4	33.2 ± 5.4	0.78
Saturated fatty acids	11.3 ± 6.7	11.3 ± 2.6	0.98
Monounsaturated fatty acids	14.0 ± 2.9	13.7 ± 2.7	0.51
Polyunsaturated fatty acids	5.6 ± 1.4	5.6 ± 1.6	0.70
Carbohydrates, % of energy intake	49.1 ± 6.7	49.5 ± 7.0	0.84
Protein, % of energy intake	16.8 ± 2.5	16.5 ± 2.7	0.50
Cholesterol, mg	314 ± 130	325 ± 147	0.70
Fiber, g	24.9 ± 7.6	25.2 ± 8.5	0.44

* p value adjusted for age and gender. Results are expressed as mean ± SD.

interactions between DFI and FHO were observed on the BMI (p = 0.05), weight (p = 0.04), waist girth (p = 0.04), fat mass (p = 0.02), after adjustment for age, gender, and energy intake (fig. 1). Similar analyses were performed to examine the interaction between FHO and dietary intakes of saturated (≤11.2% or >11.2% of energy from saturated fatty acids, SFA), monounsaturated (≤13.5% or >13.5% of energy from monounsaturated fatty acid, MUFA), and polyunsaturated fatty acids (≤5.4% or >5.4% of energy from polyunsaturated fatty acid, PUFA). Significant evidence of interaction between SFA and FHO was found for body weight (p = 0.04) and fat mass (p = 0.01) (data not shown). However, there were no significant interactions between MUFA or PUFA and FHO. Similar analyses were performed to test the interaction between FHO and other macronutrients (% of energy from carbohydrates, proteins or alcohol); no interaction was observed. The interaction effect on blood lipid levels was also tested after adjustment for the effect of age, sex and BMI, and no significant interaction effects were observed (data not shown).

To evaluate the risk of obesity (BMI ≥30) of individuals with FHO+ consuming a high-fat diet (>33.1% of energy from fat), a logistic regression using age, sex and energy intake as covariates was performed. Individuals with FHO– consuming a low-fat diet (≤33.1% of energy from fat) were considered as the reference group. Figure 2 illustrates the risk of being obese in individuals with FHO– consuming a high-fat diet, in those with FHO+ consuming a low-fat diet and in those with FHO+ consuming a high-fat diet. The results clearly indicate a higher obesity risk in FHO+ individuals and further increase for those consuming a high-fat diet in addition of being FHO+. Indeed, when compared to individuals with FHO– consuming a low-fat diet, the risk of being obese in individuals with FHO+ consuming a low-fat diet was 2.5 (95% CI 1.5–4.4, p = 0.01) and 3.6 (95% CI 2.1–6.2, p < 0.001) in those with FHO+ consuming a high-fat diet.

Discussion

In the present study, significant interactions between DFI and FHO on obesity-related phenotypes were observed. Indeed, individuals with FHO+ consuming a high-fat diet (>33.1% of energy from fat) had higher BMI, weight, waist girth and fat mass than those with FHO– consuming a low-fat diet (≤33.1% of energy from fat). Moreover, some of these interactions were also observed when SFA were taken into account. Indeed, individuals with FHO+ consuming a high-SFA diet (>11.2% of energy from SFA) had higher weight and fat mass compared to individuals with FHO– consuming a low-SFA diet (≤11.2% of energy from SFA). Although individuals with FHO+ and FHO– had similar dietary intakes, total fat and SFA intakes were more closely associated to obesity-related phenotypes in individuals with FHO+. These results suggest that a genetic predisposition to obesity may

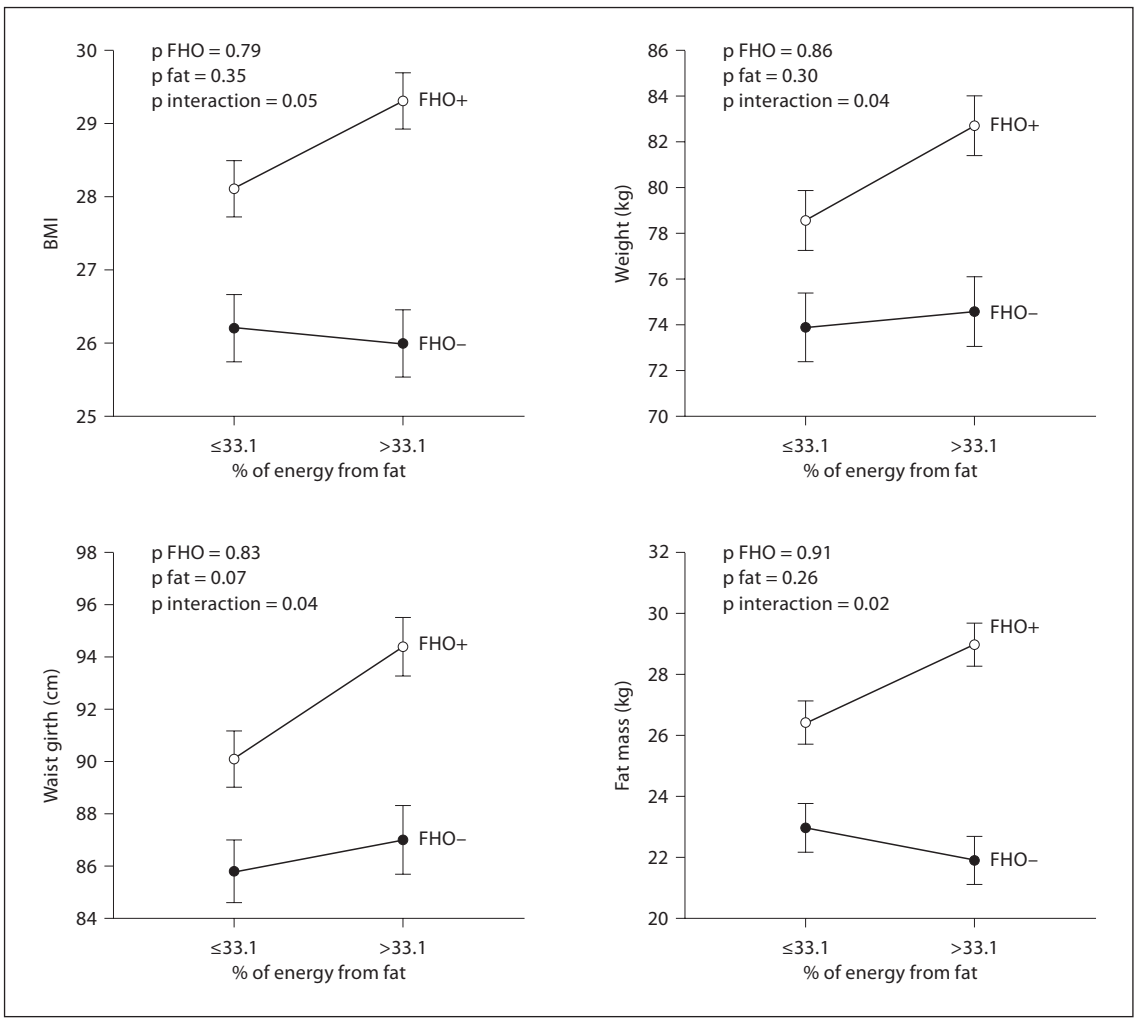

Fig. 1. Interaction between FHO and DFIs on obesity-related phenotypes (means ± SD).

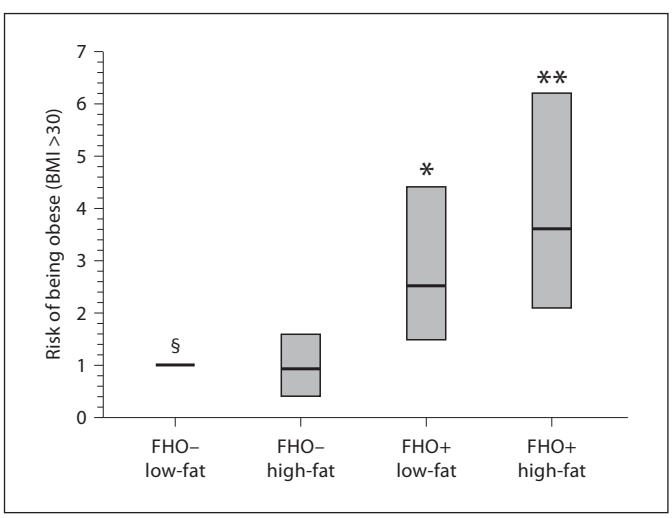

Fig. 2. Obesity risk of individuals according to FHO and DFIs. Odds ratio is represented by the black bold horizontal line and the 95% CI is represented by the grey zone. The median of DFIs was used to classify high- versus low- fat intakes. Obesity was defined as BMI ≥30. The reference group (§) is FHO– low-fat. p values are for the comparison to the reference group. § Reference group. * $p < 0.01$, ** $p < 0.001$.

modify the association between dietary intakes and obesity-related phenotypes.

Multiple studies of families, adoptees, twins and adopted twins have all confirmed that genetic influences play an important role in determining human fatness in adults [9–12, 17–22]. Thus, as expected, individuals with FHO+ had higher values of anthropometric measurements. In this study, the presence of FHO+ was associated with higher BMI, weight, waist circumference, fat mass and a greater fat-free mass.

With regards to dietary intakes, individuals with FHO+ and those with FHO– had similar dietary intakes of energy, fat, SFA, MUFA, PUFA, carbohydrates, proteins, cholesterol and fiber. As previously reported by Heitmann et al. [6], individuals with and without a predisposition for obesity had similar energy and fat intakes.

Although the present study did not look at genes involved in the development of obesity, we can speculate that the obesity-promoting genes may be upregulated by DFI, and that certain individuals are more prone to develop obesity than others when exposed to a high-fat diet. Indeed, the results of the present study suggest that obesity-related phenotypes are influenced by DFI, particularly for individuals with FHO+. Moreover, our results showed that individuals with FHO+ consuming a high-fat diet are 3.6 times more at risk of obesity than individuals with FHO– consuming a low-fat diet. If a higher susceptibility to weight gain on high-fat diets plays a role in the development of overweight and obesity, it is plausible that a reduction in dietary fat may also produce a larger weight loss in susceptible individuals. Thus, this subgroup of the population should benefit from the advice to reduce DFI and could also increase the consumption of water-rich foods such as fruits and vegetables, which are recognized as an effective strategy for weight loss or maintenance [23].

The interest in studying the interaction between FHO and DFI was motivated by a prospective study by Heitmann et al. [6], who showed that only individuals with FHO+ gained weight when consuming high-fat diets. On the assumption that individuals with a positive familial history are more likely to have a genetic predisposition than those without, the familial history can thus be used as a surrogate measure of genetic susceptibility. However, since obesity is a multifactorial disease, environmental factors such as physical activity could be implicated but was not taken into account in the present study. Another limitation is the assessment of dietary intake that constitutes an important issue when evaluating gene-diet interaction effects. However, a study was previously conducted to assess validity and reproducibility of the FFQ used in the present study [13]. The FFQ is considered to be a valid tool to assess dietary intake in epidemiologic studies [24]. Furthermore, the mean fat intake in this sample was 33.1%, which is similar to the fat intake reported in the Quebec population (32–35% of energy from fat) [25].

In conclusion, although genetic differences play an important role in the development of obesity, the relative contribution of genetic, socioeconomic or lifestyle factors, and the ways in which these interact in human societies, are largely unknown. The results of the present study reinforce the hypothesis that variability in response to diet is partly determined by genetic factors. Indeed, there was a stronger relationship between DFI and anthropometric measurement in men and women with FHO+.

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