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Correlation between Lingual *CD36* Gene Polymorphism (AA), Eating Disorder and Obesity in Algerian Adolescents

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Abstract

Background: Altered lipid perception might influence obesity risk by affecting feeding behavior. The goal of the present study was to compare eating habits between adolescents with AA polymorphism of *CD36* gene with their obese and lean counterparts.

Methods and Findings: The study population (n=165, age=13.9 ± 1.1 years) was divided into two groups. The first group was composed of 65 adolescents with AA genotype of *CD36* lingual gene (35 obese, 30 control), 76 adolescents with AG genotype (43 obese, 33 control) and 24 adolescents with GG genotype (5 obese, 19 control). The second group included adolescents with (n=83) and without (n=82) obesity based on the body mass index (BMI) z-score. The BMI z-score, oleic acid sensitivity test and eating habits were assessed in all subjects. Adolescents with AA genotype of *CD36* lingual gene had the same eating habits than adolescents with obesity without AA genotype in terms of eat-containing products consumption (meat in general, sausages and offal), French fries, milk and soda (p<0.05). Eating habits of adolescents with AA-allele of *CD36* gene polymorphism are similar to those of adolescents with obesity in foods containing fat, which may explain the increase in detection threshold for emulsions containing fatty acids in subjects with obesity.

Conclusion: The AA genotype of the *CD36* gene and the higher detection threshold for fatty acids may play a significant role in eating disorder and the development of obesity in our population of Algerian adolescents.

Keywords: Adolescent; Obesity; *CD36* polymorphism; Fat detection threshold; Eating habits

Introduction

Obesity and overweight in adolescents are reaching important proportions in the whole world and raise a large interest in the world health research. Indeed, 70%-80% of adolescents with obesity will remain obese at adult age which increases morbidity risk [1]. Moreover; adolescence is a vulnerable period including puberty, where many metabolic, hormonal, psychological and behavioral disorders promote weight and fat gain [2].

Obesity is a complex disease and is mainly affected by behavioral determinants partly genetically determined including reduction in physical activity [3,4], and alimentary disorders [5,6]. In addition, heritability of obesity is between 40%-70%. Other studies demonstrated that the *CD36* protein or GPR120, a G protein-coupled receptor present in the tongue, is implicated in the detection of long-chain fatty acids both in humans and animals [7,8]. Indeed, it has been shown in mice that, GPR120 is an essential protein for the detection of solutions with oily extracts [7,9]. The intake of dietary fats is one of the main factors involved in the development of obesity because of their high energy density, palatability and slight effect on satiety [10]. This fat intake might be influenced by their gustatory detection. Indeed, studies in humans reported that variations in sensitivity to fatty acid taste influence the consumption of fat and then predisposition to obesity [7,11]. Interestingly, Stewart et al. showed that subjects with obesity were hyposensitive to dietary fatty acids compared to their lean counterparts and that their palate to the oleic acid altered their BMI and consumption of fat [12,13]. These results suggest that altered fats perception might

influence obesity risk by affecting feeding behavior in adolescents.

The AA polymorphism of the *CD36* gene decreases the expression of the receptor in the tongue which increases in parallel the lingual detection threshold for fatty acids in obese individuals [14]. Keller et al. observed an association between obesity and the *CD36* gene polymorphism with oral detection of high-fat foodstuff in adults [15]. In line with the previous findings, it has been demonstrated that only in obese subjects expressing the AA genotype of the *CD36* gene exhibited a higher oral detection thresholds for fat-containing products structure than subjects with AG and GG genotypes [14]. All these results highlight a new of thinking the obesity treatment in humans. A recent study conducted in young lean and obese Algerian children showed that *CD36* gene AA polymorphism was present both in young lean and in obese children and associated with high threshold for fatty acid taste sensitivity in children with obesity only [16]. In our study conducted in 165 Algerian adolescents [17], we found that adolescents with obesity exhibited a significantly higher detection threshold (lower sensitivity) of oleic acid compared to age-matched lean participants. Moreover, we found that A-allele frequency of rs1761667 polymorphism of the *CD36* gene was higher in obese than in lean participants. Our results suggest that fat-containing products might influence fats gustatory detection leading, in long term, to alimentary disorders and predisposition to obesity.

The goal of the present study is to compare eating habits between Algerian adolescents with AA, AG and GG polymorphisms of the lingual *CD36* gene with their obese and lean counterparts.

Materials and Methods

Subjects

We recruited one hundred and sixty five (165) adolescents (13.9 ± 1.1 year old) from public colleges of the district of Constantine, Algeria. Female and male adolescents with chronic pathologies such as cardiovascular diseases, type I and II diabetes and with kidney or liver diseases were excluded from our study as well as smokers.

Ethics

The study was achieved according to the Declaration of Helsinki of 1975 (as revised in 2008) of the World Medical association and to the ethical guidelines for research in humans. The research council of the University of Constantine 1 approved the protocol (number of agreement: #683). The material used has been validated by the National Agency for the Safety of Medicines and Health Products.

BMI z-score and eating habits

We used the WHO references to calculate the BMI expressed as z-score in our population. Normal-weight adolescents had a BMI z-score below 1 and above -1 and adolescents with obesity had a BMI z-score more than 2. Overweight adolescents (with

BMI z-scores were excluded from the study to avoid resemblance and confusion of results between the groups of obese and lean adolescents. To determine eating habits, the adolescents were asked to fill the feeding pattern questionnaire that consisted of 17 questions corresponding to 17 different types of food and beverages. The subjects answered how often they consumed a particular product on a rating scale from 1 to 4 (1-never, rarely; 2-once a week/month; 3-a few time each week; 4-every day). After data collection, we calculated the mean consumption frequency in our experimental population considering that never, rarely = 1 point; one a week/month = 2 points; a few time each week = 3 points and every day = 4 points.

The oral sensitivity oleic acid test

This procedure was performed previously and described in our published papers [16,17]. Briefly, adolescents were asked to taste three solutions (one with oleic acid and acacia gum at 0.01% and two with acacia gum only) in an isolated chamber using a nose clip to reduce olfaction hints as they performed the test.

Determination of genotype in adolescents

This procedure was performed previously and described in our published papers [16,17]. Briefly, the DNA was purified in blood samples using commercially available kit (Promega, USA) and amplified using PCR procedures. The determination of the AA, AG and GG genotypes was performed using electrophoresis with a 2% agarose gel.

Statistical analysis

Statistical analyses have been conducted by Statistica 14 software (Statsoft, USA). Two-way ANOVA with repeated measures was used to compare the difference between parameters in the study groups. We used Spearman rank correlations to study the correlation between various parameters. Fisher exact test was performed to compare allelic and genotype frequencies between the different groups of subjects in the study. The difference between variables was considered statistically significant when $p < 0.05$. Data were expressed as means ± SEM.

Results

Characteristics of the study population

A One group of adolescents was divided in 3 subgroups: a group of 65 adolescents with the AA genotype (35 obese and 30 lean), a group of 76 of adolescents were with the AG genotype (43 obese and 33 lean) and a group of 24 adolescents with the GG genotype (5 obese and 19 lean) of the *CD36* lingual gene. The other group of adolescents was divided into 2 subgroups. Eighty three (83) adolescents with a BMI z-score higher than 2 (females = 39, males = 44, z-score 2.67 ± 0.29 and 14.01 ± 0.19 years respectively) and 82 adolescents with a BMI z-score below 1 (females = 37, males = 45, z-score 0.03 ± 0.0, 13.92 ± 0.23

years respectively). The average age of the global population was 13.9 ± 1.1 years.

Oleic acid sensitivity and *CD36* genotyping

In this part, we only complete the main results obtained in our previous published papers [16,17]. Adolescents with obesity exhibited almost twofold oleic acid detection threshold than lean participants (2.57 ± 0.29 vs. 1.33 ± 0.15 mmol/L, $p < 0.01$ respectively).

Adolescents with obesity also had most frequently the AA and AG genotypes compared to their lean peers (42.2% vs. 36.6%, $p < 0.008$ and 51.8% vs. 40.2%, $p < 0.002$, respectively). In addition, the GG genotype was less frequent in adolescents with obesity compared to lean subjects (6.0% vs. 32.2%, $p < 0.001$, respectively).

Eating habits between lean and obese Algerian adolescents

The mean consumption frequency of fat-containing products (i.e. French fries, meat, sausage and offal, $p < 0.01$) was significantly higher in adolescents with obesity than their lean peers (**Supplementary Table S1**). However, the mean consumption frequency of milk was lower in subjects with obesity than in lean participants ($p < 0.01$) (**Supplementary Table S1**). We also noticed a higher mean consumption frequency of soda in adolescents with obesity compared to lean subjects ($p < 0.05$) (**Supplementary Table S1**). Participants with obesity had a higher mean consumption frequency of fruits than lean participants ($p < 0.05$) (**Supplementary Table S1**). The mean consumption frequency of starchy food and bread was lower in adolescents with obesity than in lean adolescents ($p < 0.01$) (**Supplementary Table S1**). The mean consumption frequency of candies was lower in participants with obesity compared to lean ones ($p < 0.05$) (**Supplementary Table S1**).

Eating habits between Algerian adolescents with AA, AG and GG polymorphisms of the *CD36* lingual gene

The mean consumption frequency of fat-containing products (i.e. French fries, meat, sausage and offal) was not significantly different between adolescents with the AA *CD36* gene polymorphism and those with AG and GG *CD36* gene polymorphisms (**Supplementary Table S2**). However, the mean consumption frequency of soda was significantly higher in adolescents with AA genotype than in adolescents with AG and GG *CD36* gene polymorphisms ($p < 0.05$) (**Supplementary Table S2**). We also noticed a higher mean consumption frequency of candies among adolescents with AA *CD36* gene polymorphism.

Discussion

Obesity is a complex disease eating habits may be one of the most important factors involved in its development all over the world. It was demonstrated that our gustatory system and mostly our tongue could feel fat-containing products [7,18]. In addition, it was reported that GPR120 was implicated in the detection of fatty acids [19]. Thus, a new way of understanding

the pathogenesis of obesity in humans is emerging, linking the oro-gustatory detection of lipids and the eating habits. In this context, the present study is the first one to compare eating habits between Algerian adolescents with AA, AG and GG allele polymorphisms of *CD36* lingual gene with their lean and obese peers.

In our study, AA-allele frequency of *CD36* gene polymorphism was higher in adolescents with obesity than in lean participants [17]. We notably demonstrated that adolescents with obesity had a significant higher mean consumption frequency of the meat-containing products, French fries and soda than lean adolescents. Our results corroborated with other results, which showed a positive association between meat consumption and risk for obesity in an American population [20]. Meat and especially processed one, is rich in saturated fatty acids and cholesterol [21], and its overconsumption has been associated with high BMI [22]. Rouhani et al. also reported a direct association between consumption of red or processed meat intake and obesity, high BMI and waist circumference [23]. We further observed that adolescents with the AA-allele *CD36* gene polymorphism exhibited the same eating habit concerning meat-containing products than adolescents with AG- and GG-allele *CD36* gene polymorphisms. We also observed that adolescents with A-allele of *CD36* gene polymorphism and obese adolescents had a higher mean consumption frequency of French fries than other polymorphism alleles and control participants. Our results agreed with other findings observing that consumption of high energy food including French fries contributes to weight gain and increases the risk of obesity in young children [24] and pointed out the potential role of *CD36* gene polymorphism in this condition. This previous finding is of importance since fat-containing products might influence, in the long-term, the fatty acid oro-sensory detection capacity. Our hypothesis is supported by the observations of Stewart et al. who reported that feeding a high-fat diet significantly increased oleic acid oral detection threshold in lean subjects [25]. In addition, these authors also concluded that hyposensitive subjects consumed significantly more energy, fat, saturated fat, fatty foods, had greater BMI and were lesser perceptive of small changes in the fat content of custard, compared with hypersensitive lean subjects [13]. Similarly, feeding a high-fat diet in mice resulted in high oro-sensory threshold for linoleic acid [26] suggesting that lipid perception may be involved in the development of obesity in adolescents.

Moreover, a correlation has been established between the BMI and the hyposensitivity to dietary fatty acids in adult's individuals with obesity [13]. This important finding highlights a potential link between the low capacity to detect fatty acids in fat-containing products and the alteration of feeding behavior leading to overweight and obesity. In line with this statement, we also observed that adolescents with the AA-allele *CD36* gene polymorphism exhibited a higher consumption frequency of soda (i.e. sweetened lemonade) than those with the AG- and GG-alleles *CD36* gene polymorphisms. Interestingly the same eating habit was observed between our adolescents with obesity and lean adolescents, which corroborates other findings [27,28] and allow us to suggest that AA-allele *CD36* gene polymorphism can lead to childhood obesity [27,28] and the

development of cardiovascular diseases [29] given the same dietary habit. We also showed that adolescents with obesity had a higher mean consumption frequency of fruits than lean ones. This surprising higher rate of consumption of fruits might protect them from obesity-related complications by providing them vitamins and polyphenols [30]. We also demonstrated that adolescents with obesity had a lower consumption frequency of candies than lean adolescents and that subjects with AA-allele polymorphism of *CD36* gene had a tendency to consume more frequently candies than adolescents with AG and GG genotypes. Hence, we do not determine the real calories of the candies but the presence of cocoa in the chocolates has been shown to modulate weight gain by several mechanisms, including the decreases in the expression of genes involved in the synthesis of lipids [31]. This latter point may partly explain the higher frequency of AA genotype in our obese adolescent population.

Finally, as we identified particular eating habit in adolescents with the *CD36* gene polymorphism (i.e. high frequency consumption of meat- and fat-containing products), it would be interesting to test the potential of different plant extracts from the Algerian pharmacopoeia to treat pathologies related to obesity. These extracts would have a high affinity agonist (i.e. taste enhancers) to mimic the action of "fake fat" without bringing additional calories. Moreover, because of this specific eating habit in our Algerian adolescents, it would be easier in the future to control their eating habits regarding the high level of pesticides exposure when eating identified products like meat- and fat-containing agricultural products. This last point is in line with a new concept that tries to help conduct health risk assessment regarding unwanted chemicals in agricultural foods by a precise control of eating habit. In fine, this may improve the regulatory process of small pesticide maximum residue limits based on body weight and foods consumption to protect Algerian adolescent's health [32].

Study Limitations

Participants with obesity frequently exhibiting the AA-allele *CD36* gene polymorphism, were not associated with high orodetection threshold for the fatty acid. However, we could not rule out an influence of altered levels of sex hormones in obese adolescents on fat taste perception and other parameters. It was also difficult to determine whether oral fat perception sensitivity affected fat intake or body weight regulation.

Conclusion

Considering the results of the present study, eating habits of adolescents with the AA-allele of the *CD36* lingual gene were similar to those of adolescents with obesity. In addition, the mean consumption frequency of meat-containing products, French fries, milk and soda was also similar between these two groups of adolescents. Finally, our results allow us to infer that eating habits and particularly the intake of foods containing fats, in adolescents with the AA genotype of the *CD36* lingual gene were similar to those of adolescents with obesity. This result may explain the increase in the detection threshold for emulsions containing fatty acids in subjects with obesity and

suggest an "obesity behavior" in adolescents with the AA-allele *CD36* lingual gene polymorphism.

Supplementary Information

<http://www.imedpub.com/supplementary-file/2572-5394-3-S1006s.pdf>

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Competing and Conflicting Interests

No competing and conflicting interests exist.

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