

THE ROLE OF GENETICS IN A PERSONALIZED APPROACH IN PATIENTS WITH FEEDING PROBLEMS, OVERWEIGHT AND OBESITY

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Abstract. Aim: For the last 20 years a large amount of data was gathered showing a genetic predisposition to overweight and obesity. The aim of this study was to demonstrate a personalized, genetic-based approach in normalizing the patients' weight and eating habits. **Materials and methods:** Eight patients – seven women and one man – aged 28-51 years with BMI ranging from 17,58 to 38,95 kg/m² were examined. Two of them were underweight, two – with normal weight, two – overweight, and two – obese. Patients were genotyped for: APOA2 (rs5082), ADIPOQ, (rs17300539), FTO (rs9939609), KCTD10 (rs10850219), LIPC (rs1800588), MMAB (rs2241201), PPARG (rs1801282), ANKK1/DRD2 (rs1800497), TAS2R38 (rs1726866), LEPR (rs2025804) and SLC2A2 (rs5400). Based on the genetic results, the type of diet (balanced, Mediterranean, low-fat and low-carbohydrate) was determined; the predisposition to unhealthy eating habits was described and followed by a genetic counseling to clarify the findings as well as a dietitian consultation to formulate a personalized diet. **Results:** Our results showed that the patients' actual diet was equivocally different from the genetically determined one. All patients, except for one, had hereditary predispositions to a particular unhealthy eating habit. **Conclusion:** The inclusion of genetic testing and personalization of the diet facilitates the long-term maintenance of optimal body weight.

Key words: gene, diet, predisposition, eating disinhibition, nutrigenetics

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INTRODUCTION

The key to optimal therapeutic results lies in the personalized treatment targeting the specific problems for a human being. Genetic testing is the base of such treatments, as it helps determining the individual steps in the disease control and prevention. This approach is nowadays used in the

treatment of monogenic disorders (cystic fibrosis, mucopolysaccharidoses) and some cancers (breast cancer, ovarian cancer, colon cancer, etc.) but it is still not of broad use in polygenic diseases (type 2 diabetes, hypertension, obesity, etc.).

A large amount of genetic data worldwide reveals predisposition to overweight and obesity, as well as gene variants protective for these pathologies. Stud-

ies report some genes influencing the metabolism of different nutrients. Those genes are responsible for the predisposition to some eating habits such as food desire, satiety, eating disinhibition, snacking, and cravings. These genes include: *ANKK1* (ankyrin repeat and kinase domain containing 1) and *DRD2* (dopamine receptor D2), which are responsible for the role of dopamine receptors in the brain and are associated with predisposition to eating disorders and addictions [1-3]; *TAS2R38* (taste receptor 2 member 38) associated with bitter taste and glucose metabolism [4, 5]; *FTO* (fat mass and obesity), involved in energy expenditure, energy balance and caloric intake [6, 7]; *LEPR* (leptin receptor) of a great importance in the regulation of food intake [8]; and *SLC2A2* (solute carrier family 2 member 2) needed for the regulation of postprandial glucose level and sweet tooth [9].

Complex research in the field of genetics and dietetics may contribute to the determination of a healthy diet. Four diets are approved by the World Health Organization – the balanced one, the Mediterranean, low-fat and low-carbohydrate diets. The genes associated with the selection of a specific diet are: *APOA2* (apo lipoprotein A2), *ADIPOQ* (adiponectin Q), *FTO* (fat mass and obesity-associated), *KCTD10* (potassium channel tetramerization Domain Containing 10), *LIPC* (lipase C, hepatic type), *MMAB* (metabolism of cobalamin associated B) and *PPARG* (peroxisome proliferator-activated receptor gamma) [10-17].

AIM

The aim of the present study was to demonstrate the possibility of applying a personalized, genetically-based approach in normalizing the patients' body weight and eating habits.

MATERIALS AND METHODS

Eight patients were included in this study. All of them signed an informed consent before the genetic testing was conducted. Patients were asked to fill in a questionnaire about their age, gender, height, weight, medical history, health condition, physical activity, allergies, diet, and family history.

Genotyping of polymorphisms of the abovementioned genes was performed by using a commercial test – the Pathway Genomics®. The type of diet was evaluated using an algorithm specific for the genetic laboratory. Patients were consulted by a medical geneticist and a dietitian after receiving the genetic results. In a 12-month period an appointment was scheduled to monitor the effect of the recommendations after the test.

RESULTS

Seven women and one man took part in the study. The average age of our patients was 38,5 years (from 28 to 51 years). The participants' BMI ranged between 17,58 and 38,95 kg/m². Two of them were underweight, two had normal weight, two were overweight, and two had obesity (Table 1).

Only three of all participants reported regular physical activity both as strength and endurance training. All of them had normal BMI.

We detected a large variation in personal diet preferences. Three of our patients were vegans/vegetarians, one was on low-carb diet, one was on a balanced diet, and the remaining three had no specific diet to follow. Vegans/vegetarians used their diet plan to lose weight, no moral or religious reasons claimed.

Table 1. Characteristics of the study participants

Personal data	P1	P2	P3	P4	P5	P6	P7	P8
Age, yrs	28	32	44	33	47	37	36	51
Gender	f	f	f	f	f	f	f	m
BMI, kg/m ²	17,58	30,49	21,26	22,68	18,38	26,03	25,68	38,95
Adherence to diet	vegetarian, consumes fish	vegetarian, vegan for six months	vegetarian	balanced	low-carb	non specific	non specific	non specific
Regular physical activity	yes	no	no	yes	yes	no	no	no
Additional data	Eating disorder during teenage years	Vertical sleeve gastrectomy	none	none	none	sedentary lifestyle	none	sedentary lifestyle

Patient 1 (P1) was a female with a BMI of 17,58 kg/m². She had eating disorders during her teenage years. Patients 2 (P2) with a BMI of 30,49 kg/m² had a vertical sleeve gastrectomy at the age of 20. Patients 6 and 8 (P6 and P8) reported having a sedentary life-style with a stressful work environment (Table 1).

The results of genotyping, associated with a specific diet type are presented in Table 2. Genes that are associated with the actual food preferences are presented in Table 3.

Genetic counseling

All patients received their results personally. Patients were consulted by a medical geneticist. He

explained each detail of the test understandably and the patients were able to ask all possible questions. Afterwards the patients received a document with their results, interpretations and personal recommendations.

Nutrition counseling

Seven of the eight patients had a dietitian appointment after receiving their genetic results. All of them were assigned a personal diet plan according to the genetic specificities. Monitoring the effect of the recommendations is planned to be performed in a 12-months period.

Table 2. Genotyping results of the genes associated with determining the appropriate diet. Gene variants of the patients are displayed. "LC" indicates Low-carb diet, "Med" – Mediterranean diet and "Bal" – Balanced diet

Gene	Polymorphism	P1	P2	P3	P4	P5	P6	P7	P8
APOA2	rs5082	CC	TT	TT	CT	CT	CT	TT	CC
ADIPOQ	rs17300539	GG	AG	GG	GG	GG	GG	GG	GG
FTO	rs9939609	AT	AT	AT	AT	AT	TT	TT	AT
KCTD10	rs10850219	GG	GG	GG	GG	GG	CC	GG	CG
LIPC	rs1800588	CC	CC	CC	CC	CC	CC	CC	CC
MMAB	rs2241201	CC	CG	CG	CG	CG	CC	GG	CC
PPARG	rs1801282	CC	CG	CC	CG	CC	CC	CC	CC
Diet type		LC	Med	Bal	Med	Bal	Bal	Bal	LC

Table 3. Genotyping results of the genes associated with a possible eating behavior. Genes and polymorphisms are shown. The processes associated with each of the genes are represented in the third row of the table. The interpretation is independent for each individual

Gene	ANKK1/DRD2	TAS2R38	FTO	LEPR	SLC2A2
Polymorphysm	rs1800497	rs1726866	rs9939609	rs2025804	rs5400
Process	Appetite	Eating disinhibition	Satiety	Snacking	Sugar cravings
P1	CC	CT	AT	AA	CC
	typical	more likely	typical	typical	typical
P2	CC	CT	AT	AG	CC
	typical	more likely	typical	typical	typical
P3	CC	TT	AT	AG	TT
	typical	high risk	typical	typical	higher
P4	CC	TT	AT	AG	CT
	typical	high risk	typical	typical	typical
P5	CT	TT	AT	AA	CC
	higher	high risk	typical	typical	typical
P6	CC	CC	TT	AA	CT
	higher	less likely	typical	typical	higher
P7	CC	CC	TT	AG	CC
	typical	less likely	typical	typical	typical
P8	CC	TT	AT	AA	CC
	typical	typical	typical	typical	typical

DISCUSSION

In this study we observed an enormous difference between the actual diet of the patients and the most suitable one according to their genotyping information.

P1 – the underweight woman who suffered from an eating disorder was a vegetarian, while her genetic profile revealed that she would benefit most from a low-carb eating plan. Additional information we gained from her gene variants was that she is more likely to have eating disinhibition under stress situations and is less likely to have a specific food desire. Consequently, the vegetarian diet with reduced caloric intake was not suitable for her.

P2 was an overweight female who had been a vegetarian for two years and a vegan for half a year. She had a gastric sleeve surgery at the age of 20. According to her genetic information, she should follow a Mediterranean meal plan and she is at risk of eating disinhibition. During the genetic counseling she confirmed her tendency to eat a lot when put in stressful situations.

P3 was also an overweight woman. She was a 44-year-old woman who adopted a vegetarian diet. The combination of the tested genetic variants revealed that she needed to change for a balanced diet. As to the specific eating habits, she is at risk for eating disinhibition. Therefore she was informed to have this in mind when in emotional situations.

P4 was female, 33 years of age with a BMI within normal limits who had regular physical activity and a balanced diet regimen. The genotyping determined the Mediterranean meal plan as the best option for maintaining her normal body weight. This patient did not tend to have “sweet tooth” but was at risk for eating disinhibition.

P5 was a 47-year-old female with a BMI at the lower limit of the reference range. She stuck to a low-carb eating plan and regular physical activity. Her genetic results revealed that she would benefit most from a balanced diet plan. Moreover, her eating behavior was standard with the exception of slightly elevated risk for eating disinhibition (the risk being not so high as in P3 and P4).

P6 was a woman of 37 years who was overweight and had no special meal plan. The recommendations after the gene variant analysis were to stick to a balanced diet type. She was advised to pay attention to the sugar she consumed. The following conversation with her gave us information that the increased stress at work makes her nervous and she is regularly taking foods with high sugar content.

P7 was an overweight woman at the age of 36 with no specific meal plan. The combined genetic information showed a balanced eating plan as the diet of choice. No predisposition to specific eating behaviors was found.

P8 – a 51-year-old male with extreme obesity and no eating regimen was advised to start a low-carb diet to control his weight. His gene variants associated with eating behaviors showed a tendency for increased appetite.

Genotyping results of our patients displayed that they selected inappropriate diets. Moreover, in P2, the therapeutic measures performed with vertical sleeve gastrectomy to reduce body weight, as well as adherence to an inappropriate diet did not lead to the expected results. In all patients except for P7, hereditary predispositions to a certain eating disorder were established, which underlines the importance of analyzing situations that may lead to such disorders as well as of the motivation to change to a healthy lifestyle.

CONCLUSION

This study demonstrates the possibilities of modern medicine to include genetic testing to personalize the diet, to correct the eating habits of patients and to achieve and maintain long-term healthy body weight. The inclusion of genetic testing of patients can significantly speed up the healing process as it shows the predisposition of the person to a particular diet, the need for micro and macronutrients, as well as information about eating habits and preferences.

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