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Neuromedin Beta: P73T Polymorphism in Overweight and Obese Subjects

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Summary

Neuromedin beta (*NMB*) is a member of the bombesin-like peptide family expressed in brain, gastrointestinal tract, pancreas, adrenals and adipose tissue. The aim of our study was to compare the frequency of P73T polymorphism in overweight and obese patients (37 men: age 50.6±11.7 years, BMI 41.1±7.8 kg/m^2; 255 women: age 49.0±11.9 years, BMI 37.9±6.8 kg/m2) with that of healthy normal weight subjects (51 men: age 28.2±7.1 years, BMI 22.3±2.0 kg/m^2; 104 women: age 29.1±9.1 years, BMI 21.5±1.9 kg/m^2) and to investigate the polymorphism's influence on anthropometric, nutritional and psychobehavioral parameters in overweight/obese patients both at the baseline examination and at a control visit carried out 2.5 years later, regardless of the patient´s compliance with the weight reduction program. No significant differences in the genotype distribution were demonstrated between normal weight and overweight/obese subjects. Male T allele non-carriers compared to T allele carriers had higher energy (p=0.009), protein (p=0.018) and fat (p=0.002) intakes and hunger score (p=0.015) at the beginning of treatment. Male T allele non-carriers had a more favorable response to weight management at the follow-up, as they exhibited a significant reduction in waist circumference, energy intake and depression score as well as a significant increase in dietary restraint. No significant differences between carriers and non-carriers were demonstrated in women at the baseline examination. Both female T allele carriers and non-carriers demonstrated similar significant changes in nutritional parameters and in restraint score at the follow-up. Nevertheless, only female non-carriers showed a significant decrease in the hunger score.

Key words

Neuromedin beta • Obesity • Gene polymorphism • Eating behavior • Nutrient intake • Weight loss

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Introduction

Neuromedin beta (*NMB*) is a member of the bombesin-like peptide family, a subfamily of ranatensins. These peptides are initially released from the gastrointestinal tract in response to food ingestion and bridge the gut and brain, through neurocrine means, to inhibit further food intake. Northern blot analysis revealed two *NMB* gene transcripts of 750-850 bases in human brain and gastrointestinal tissues with high expression levels in the hypothalamus, stomach, colon and low levels in cerebellum, pancreas, adrenals and adipose tissue (Ohki-Hamazaki 2000). *NMB* was identified in the hypothalamus (Krane *et al.* 1988), where afferent signals reflecting the nutritional state and efferent pathways that control feeding behavior and energy expenditure are integrated (Oeffner *et al.* 2000). *NMB* exerts its effect by binding to *NMB* receptor, a G-protein coupled receptor (Ohki-Hamazaki 2000).

As shown in Figure 1, human *NMB* is encoded by a 121-amino acid precursor consisting of an N-terminal hydrophobic signal sequence followed by the prohormone *NMB*-32 and then a carboxy-terminal extension peptide (Oeffner *et al.* 2000). The gene for this precursor is localized on chromosome 15 (15q22.3-q23) and is comprised of three exons. This chromosome region contains a gene for the Bardet-Biedl syndrome (BBS) type 4 (Bruford *et al.* 1997). BBS is a rare disease described in the early 1920s (Biedl 1922) which is associated with severe obesity and congenital abnormalities such as retinal dystrophy, polydactyly,

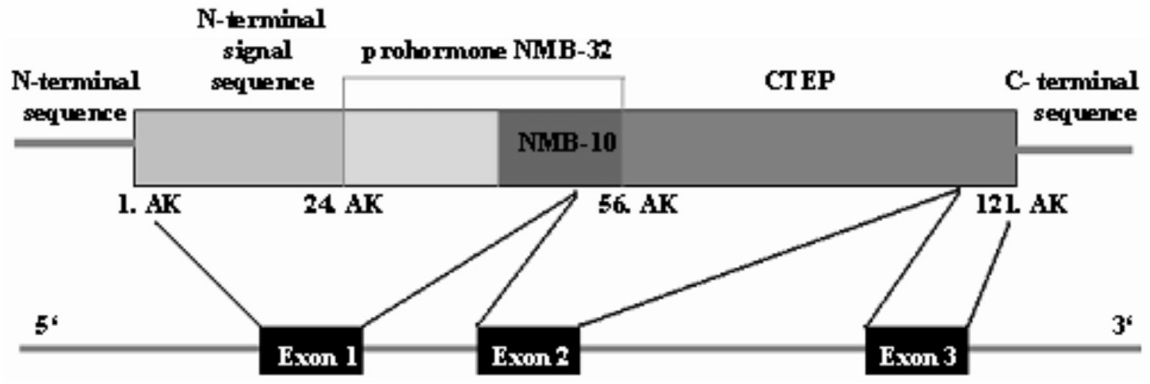

Fig. 1. The structure of human neuromedin beta gene (CTEP – Carboxy-Terminal Extension Peptide)

renal anomalies and hypogonadism in males. BBS is characterized by an autosomal recessive mode of inheritance (Beales *et al.* 1997).

It has been shown that weight loss maintenance is significantly influenced by psychobehavioral factors such as eating behavior assessed by the Eating Inventory and the level of depression evaluated by the Beck Depression Inventory (Hainer *et al.* 2005, Vogels *et al.* 2005, Kabrnová-Hlavatá *et al.* 2008). Eating Inventory evaluates three factors: dietary restraint, dietary disinhibition and hunger (Stunkard and Messick 1985). Dietary restraint is a conscious behavior aimed at limiting food intake. Disinhibition characterizes eating behavior of a person prone to non-compliance with a weight loss regimen and to overeating in response to stress, increased alcohol intake, anxiety, depression etc. Hunger score quantifies perceived hunger. Different contributions of hereditary components in determination of the factors of the Eating Inventory have been demonstrated in the Québec family study (Provencher *et al.* 2003). The heritability of disinhibition and susceptibility to hunger was found to be 19 % and 32 %, respectively, whereas the heritability of cognitive restraint was not statistically significant. Bouchard *et al.* (2004) found a significant association between the missense polymorphism P73T (or C253A) in exon 2 of the *NMB* and levels of disinhibition and susceptibility to hunger, increased body weight, body mass index (BMI), waist circumference and fat mass. The primary aim of our study was to compare the frequences of *NMB* P73T polymorphisms in overweight and obese patients with that of healthy normal weight subjects. The second aim of our study was to investigate the influence of P73T polymorphism on selected anthropometric, nutritional and psychobehavioral parameters in overweight/obese patients both at their baseline visit to the Obesity Management Centre and at the follow-up visit carried out 2.5 years later regardless of compliance with the weight reduction program.

Methods

Subjects

The overweight and obese patients (37 men: age 50.6±11.7 years, BMI 41.1±7.8 kg/m^2; 255 women: age 49.0±11.9 years, BMI 37.9±6.8 kg/m^2) were examined in the Obesity Management Centre of the Institute of Endocrinology in Prague and in the Obesity Management Unit of the Clinical Centre ISCARE IVF in Prague. Frequency of the P73T polymorphism was compared with healthy normal weight subjects without family history of morbid obesity or diabetes type 2 (51 men: age 28.2±7.1 years, BMI 22.3±2.0 kg/m^2; 104 women: age 29.1±9.1 years, BMI 21.5±1.9 kg/m^2). Essential characteristics of the overweight and obese patients are presented in Table 1.

Our study was carried out over a 3-year period. The comprehensive weight management program included low energy diet (recommended daily energy deficit cca 2.5 MJ), increased physical activity (recommended 30 minutes of aerobic exercise per day such as walking, cycling etc.) and behavioral lifestyle modification provided by a psychologist. All patients underwent a control examination 2.5 years after the baseline visit without regard to their adherence to the weight reduction program or their attendance in regular check-ups. Even the patients who dropped out from the study (in 39 % patients less than three visits per year were recorded) were able to participate at the control visit.

Anthropometric parameters (body weight, height, waist and hip circumferences) were measured according to the WHO recommendations (WHO Expert Committee 1995). Body composition (fat mass %, fat free

Table 1. Anthropometric, nutritional and psychobehavioral characteristics of the overweight/obese subjects at baseline and follow-up visits (lower quartile; **median**; upper quartile)

	MEN			**WOMEN**		
	The beginning of the treatment	**The control visit after 2.5 years**	**Statistics[a] (p)**	**The beginning of the treatment**	**The control visit after 2.5 years**	**Statistics[a] (p)**
number	**37**		--	**255**		--
BMI (kg/m^2)	35.9; **39.4**; 47.1	33.9; **38.6**; 46.1	0.331	33.1; **36.8**; 42.1	32.4; **36.2**; 41.2	**0.002**
Body weight (kg)	109.2; **126.8**; 152.8	104.9; **121.0**; 146.0	0.361	89.6; **100.2**; 113.1	87.1; **97.4**; 110.8	**0.003**
Waist circumference (cm)	119.4; **126.5**; 135.8	110.3; **124.0**; 133.0	**0.044**	99.0; **108.0**; 117.0	98.0; **107.0**; 117.0	0.113
Fat mass (%)	30.2; **35.0**; 37.3	30.4; **33.4**; 37.5	0.673	41.7; **44.5**; 48.1	41.6; **44.7**; 47.8	0.960
Fat free mass (%)	62.7; **65.0**; 69.8	62.5; **66.6**; 69.6	0.673	51.9; **55.5**; 58.3	52.2; **55.3**; 58.4	0.960
Energy intake (kJ/day)	7028; **8455**; 12120	5813; **6584**; 9633	0.088	5919; **7321**; 9017	5271; **6144**; 7343	**0.000**
Protein intake (g/day)	59.7; **79.2**; 91.8	57.6; **66.3**; 88.6	0.256	56.3; **65.6**; 79.0	52.4; **62.3**; 70.8	**0.000**
Carbohydrate intake (g/day)	185.5; **259.8**; 405.8	115.4; **206.7**; 258.0	0.108	168.7; **211.4**; 272.1	145.9; **181.2**; 220.5	**0.000**
Fat intake (g/day)	57.9; **77.9**; 107.6	49.2; **54.7**; 76.8	0.218	49.5; **63.4**; 85.1	40.6; **52.1**; 62.7	**0.000**
EI – restraint score	3.3; **7.0**; 12.3	9.0; **12.0**; 14.0	**0.034**	6.0; **10.0**; 14.0	10.0; **14.0**; 16.8	**0.000**
EI –disinhibition score	7.0; **4.0**; 9.0	3.5; **5.0**; 7.0	0.776	3.0; **6.0**; 9.0	3.0; **6.0**; 9.0	0.830
EI – hunger score	2.3; **4.5**; 8.0	1.0; **6.0**; 6.0	0.455	2.0; **4.0**; 7.0	1.0; **3.0**; 6.0	**0.000**
BDI – depression score	4.0; **9.0**; 16.8	3.0; **11.5**; 15.5	0.337	6.0; **11.0**; 16.0	5.8; **9.0**; 17.0	**0.029**

[a]Wilcoxon test, BMI – body mass index, EI – Eating Inventory, BDI – Beck Depression Inventory

mass %) was assessed using a bipedal – bimanual bioimpedance analyser – TANITA BC-418MA.

Daily energy and macronutrients (protein, carbohydrate, fat) intakes were evaluated from a one-week dietary record, which was performed at the baseline and follow-up visits. A computerized version of the Czech Nutrition File „Vyziva", which includes almost 3000 food items, was used for dietary intake assessment.

A validated Czech version of the Eating Inventory (Stunkard and Messick 1985) was used to measure dietary restraint, disinhibition and susceptibility to hunger. This Three Factor Eating Questionnaire was used in our previous studies involving obese patients (Hainer *et al.* 2005) and in a quota sample of Czech adults (Hainer *et al.* 2006). The depression score was measured by the Beck Depression Inventory (Beck *et al.* 1961).

The study was conducted in accordance with the Declaration of Helsinki and was approved by the Ethic Committee of the Institute of Endocrinology. All subjects signed informed consent before the study initiation.

Genotyping

Genomic DNA was isolated from peripherial blood leukocytes using the QIAamp® DNA Blood Kit (QIAGEN, Germany). Genomic DNA was amplified by polymerase chain reaction (PCR; T-Gradient Cycler, Biometra, Germany). Reactions were performed in a final volume of 12 μl. Primers were designed in accordance with Oeffner *et al.* (2000). In order to find variants of the P73T polymorphism (PP, PT, TT) the sequencing method was used (ALFExpress II, Amersham Pharmacia Biotech, USA). For screening of P73T polymorphism the Single Strand Conformation Polymorphism (SSCP) method was employed, using control genotypes in every run (ALFExpress II, Amersham Pharmacia Biotech, USA). Allele determinations were performed independently by two experienced persons. Detailed procedures of the methods used are available from the corresponding author.

Statistical analysis

Genotype frequencies were tested by the χ^2-test. The differences between groups were evaluated using the robust Mann-Whitney test, while the differences between the beginning of the treatment and the control visit at the 2.5-year follow-up were assessed by Wilcoxon's paired robust test. The PC programs NCSS 2004, QC.Expert 2.7 and Microsoft Excel 2007 were used for statistical analysis.

Results

Table 1 summarizes essential anthropometric, nutritional and psychobehavioral characteristics of the overweight/obese subjects at the baseline and follow-up visits. The cohort of men was made up of less individuals, most likely due to the fact that Czech men tend to not be as motivated as women to participate in a long term life style modification program. In men a significant reduction in waist circumference was revealed at the follow-up visit. In both genders an observed significant increase in dietary restraint score could have contributed to a better control of energy intake. A minor but significant decrease in body weight and BMI in women at the follow-up visit might reflect a significant decrease in energy and nutrient intakes as well as a decline in hunger and depression scores.

Table 2 shows the frequencies of genotypes (PP, PT, TT) in overweight and obese population and in healthy normal weight persons. No significant differences in the frequencies of genotypes were demonstrated between the two groups studied (χ^2=2.08, p=0.353).

Due to the low frequency of TT homozygotes, overweight and obese patients were divided into two groups – T allele non-carriers (homozygotes PP) and T allele carriers (heterozygotes PT together with homozygotes TT). Table 3 shows anthropometric, psychobehavioral and nutritional parameters before the treatment and after the 2.5-year follow-up period in overweight and obese men classified as T allele carriers or non-carriers. Male T allele non-carriers had higher energy intake (p=0.009), protein intake (p=0.018), fat intake (p=0.002) and hunger score (p=0.015) at the beginning of treatment in comparison with male T allele carriers. After the follow-up period, significant decreases in waist circumference (p=0.021), energy intake (p=0.038), carbohydrate intake (p=0.038), dietary restraint (p=0.021) and score of depression (p=0.032) were observed in male T allele non-carriers. Changes in energy and carbohydrate intakes over the follow-up period significantly differed between male T allele carriers and non-carriers (p=0.043, p=0.034 respectively). T allele carriers increased and T allele non-carriers decreased energy intake and carbohydrate consumption. Maximum weight loss observed at follow-up was higher in T allele non-carriers than in T allele carriers (median: 15.1 vs. 11.5 kg). However, the difference in weight loss between the two groups was not statistically significant (p=0.365).

Table 2. The frequencies of genotypes in overweight/obese patients and in normal weight subjects

	PP		**PT**		**TT**	
	overweight and obese n (%)	**normal weight n (%)**	**overweight and obese n (%)**	**normal weight n (%)**	**overweight and obese n (%)**	**normal weight n (%)**
men	17 (45.9)	28 (54.9)	18 (48.6)	20 (39.2)	2 (5.4)	3 (5.9)
women	128 (50.2)	59 (56.7)	108 (42.4)	36 (34.6)	19 (7.5)	9 (8.7)
total	145 (49.7)	87 (56.1)	126 (43.2)	56 (36.1)	21 (7.2)	12 (7.7)

χ^2=2.08, p=0.353 (for total numbers)

Table 4 shows anthropometric, psychobehavioral and nutritional parameters before the treatment and after the 2.5-year follow-up period in overweight and obese women who were classified as T-allele carriers or non-carriers. At the beginning of the treatment no significant differences between carriers and non-carriers were demonstrated in women. In neither men nor women did P73T polymorphism affect the maximum weight loss achieved (median: 9.9 vs. 10.0 kg, p=0.434). Both female T allele carriers and non-carriers exhibited significant decreases in energy, protein, carbohydrate and fat intakes and increases in restraint scores. However, a decrease in BMI and body weight was revealed in T allele carriers only. In contrast to T allele carriers, female non-carriers significantly decreased in the hunger score. Nevertheless, changes in anthropometric, psychobehavioral and nutritional parameters at the follow-up were not significant for either female T allele carriers or non-carriers.

Discussion

NMB is a member of the bombesin-like peptides family. These peptides have many biological effects that may be related to eating behaviors and obesity (Bouchard *et al.* 2004). Monitoring P73T polymorphism in *NMB* revealed many associations with dietary disinhibition, susceptibility to hunger and fat mass change over time (Bouchard *et al.* 2004). Recent results from the Québec Family Study confirmed a significant contribution of *NMB* polymorphism to the adiposity changes in adult subjects with a wide range of adiposity (BMI range from 17.5 to 55.6 kg/m^2) who were followed over a period of 6-10 years (Bouchard *et al.* 2007). It was therefore considered possible that *NMB* could play a role in the regulation of eating behavior and thus might affect body weight.

Several gene polymorphisms have been implicated in the determination of weight loss and weight loss maintenance (Hainer *et al.* 2008). As weight loss maintenance remains an essential target in weight loss strategies (Wadden *et al.* 2004), the aim of our study was to evaluate the influence of P73T *NMB* polymorphism on anthropometric, nutritional and psychobehavioral indexes in obese patients at baseline examination and at a 2.5-year follow-up visit.

The frequency of P73T genotypes in our cohort was not different between healthy normal weight control group and overweight/obese subjects. Frequency of T allele in overweight/obese patients and in healthy control group was similar (28.8 % vs. 25.8 %). This our finding confirms that of Oeffner *et al.* (2000), who monitored obese German children and adolescents, and also did not detect an association of the T allele to body weight. In their study frequencies of this allele in severely obese (29.03 %) were similar to those observed in underweight subjects (26.60 %). However, they revealed a significant association between the G401A polymorphism in the *NMB* gene and body weight (Oeffner *et al.* 2000). Bouchard *et al.* (2004) who studied a randomized sample of the Québec population did not find significant differences in P73T genotypes with regard to body weight, BMI, waist circumference, fat mass (kg), restraint score and intakes of macronutrients. However, TT homozygotes exhibited significantly higher level of disinhibition and hunger when compared to P allele carriers. TT homozygotes gained significantly more fat over a 6-year follow-up than PP homozygotes.

Our study demonstrated the influence of P73T polymorphism on anthropometric, nutritional and psychobehavioral parameters, esp. in men. At the beginning of the treatment male T allele non-carriers exhibited higher susceptibility to hunger (p=0.015) and higher dietary disinhibition (of borderline significance

Table 3. Baseline anthropometric, nutritional and psychobehavioral characteristics of overweight/obese men (classified as T-alelle carriers or non-carriers) and their changes at follow-up (lower quartile; **median**; upper quartile)

MEN	The beginning of the treatment			The follow-up change				
	T allele non-carriers	T allele carriers	Statistics[a] (p)	T allele non-carriers	Statistics[b] (p)	T allele carriers	Statistics[b] (p)	Statistics[a] (p)
BMI (kg/m^2)	36.2; **39.1;** 46.9	35.8; **39.6;** 47.7	0.855	-2.3; **-1.0;** 0.8	0.102	-1.3; **0.3;** 1.6	0.779	0.247
Body weight (kg)	109.0; **123.0;** 152.0	111.0; **131.0;** 154.0	0.626	-7.8; **-2.8;** 2.3	0.113	-4.2; **0.9;** 4.3	0.779	0.300
Waist circumference (cm)	119.0; **125.0;** 132.0	121.0; **127.0;** 137.0	0.490	-5.0; **-4.0;** -2.0	**0.021**	-3.0; **-2.0;** 4.0	0.491	0.153
Fat mass (%)	33.0; **35.8;** 37.2	30.2; **31.9;** 37.3	0.622	-8.0; **-0.7;** -0.2	0.091	-1.0; **1.0;** 3.6	0.286	0.071
Fat free mass (%)	63.0; **64.0;** 67.0	63.0; **68.0;** 70.0	0.622	0.2; **0.7;** 8.0	0.091	-3.6; **-1.0;** 1.0	0.286	0.071
Energy intake (kJ/day)	8379; **11540;** 14469	5955; **7460;** 10151	**0.009**	-5536; **-3079;** -1216	**0.038**	-718; **211;** 1101	0.779	**0.043**
Protein intake (g/day)	77.4; **90.4;** 107.8	55.3; **63.5;** 85.0	**0.018**	-36.5; **-12.8;** -7.7	0.139	-4.1; **0.5;** 7.7	0.674	0.102
Carbohydrate intake (g/day)	222.0; **322.0;** 410.0	168.0; **231.0;** 272.0	0.067	-204.0; **-76.0;** -64.0	**0.038**	-13.0; **2.0;** 49.0	0.674	**0.034**
Fat intake (g/day)	81.0; **107.0;** 129.0	50.0; **62.0;** 78.0	**0.002**	-40.2; **-33.9;** 5.1	0.139	-11.2; **2.7;** 12.2	0.889	0.149
EI – restraint score	2.5; **6.5;** 9.0	3.8; **7.0;** 14.3	0.391	4.0; **5.0;** 8.0	**0.021**	-3.0; **1.0;** 5.0	0.593	0.132
EI – disinhibition score	5.3; **8.0;** 10.0	3.0; **4.0;** 9.0	0.060	-3.0; **-1.0;** 0.0	0.233	-1.0; **1.0;** 3.0	0.257	0.101
EI – hunger score	5.3; **7.5;** 9.0	1.8; **3.0;** 4.8	**0.015**	-4.0; **-1.0;** 0.0	0.134	-2.0; **1.0;** 2.0	0.717	0.195
BDI – depression score	4.3; **15.0;** 17.0	3.0; **7.5;** 11.5	0.318	-9.0; **-2.0;** -1.0	**0.032**	-4.0; **2.0;** 9.0	0.594	0.157

[a]Mann-Whitney test, [b]Wilcoxon test, BMI – body mass index, EI – Eating Inventory, BDI – Beck Depression Inventory

Table 4. Baseline anthropometric, nutritional and psychobehavioral characteristics of overweight/obese women (classified as T-alelle carriers or non-carriers) and their changes at follow-up (lower quartile; **median**; upper quartile)

WOMEN	The beginning of the treatment			The follow-up change				
	T allele non-carriers	T allele carriers	Statistics[a] (p)	T allele non-carriers	Statistics[b] (p)	T allele carriers	Statistics[b] (p)	Statistics[a] (p)
BMI (kg/m^2)	32.4; **36.4;** 41.1	33.9; **37.1;** 42.6	0.153	-1.7; **-0.1;** 0.9	0.118	2.7; **-0.5;** 1.0	**0.008**	0.360
Body weight (kg)	86.0; **99.0;** 112	92.0; **101.0;** 115.0	0.163	-4.4; **-0.4;** 2.8	0.126	-7.2; **-1.3;** 2.5	**0.009**	0.651
Waist circumference (cm)	99.0; **108.0;** 115.0	101.0; **110.0;** 118.0	0.374	-5.0; **0.5;** 4.5	0.562	-5.5; **0.0;** 3.0	0.111	0.446
Fat mass (%)	41.2; **44.2;** 47.9	42.3; **44.7;** 48.2	0.548	-1.8; **-0.2;** 2.1	0.574	-2.2; **-0.5;** 2.1	0.728	0.398
Fat free mass (%)	52.0; **56.0;** 59.0	52.0; **55.0;** 58.0	0.548	-2.1; **0.2;** 1.8	0.574	-2.1; **0.5;** 2.2	0.728	0.398
Energy intake (kJ/day)	5948; **7203;** 9090	5904; **7438;** 8936	0.877	-3099; **-927;** 300	**0.000**	-2661; **-836;** 237	**0.000**	0.988
Protein intake (g/day)	54.0; **65.0;** 78.2	57.7; **66.8;** 79.0	0.645	-18.1; **-6.3;** 4.4	**0.006**	-19.8; **-3.5;** 5.5	**0.007**	0.858
Carbohydrate intake (g/day)	167.0; **211.0;** 264.0	171.0; **212.0;** 277.0	0.884	-71.0; **-21.0;** 9.0	**0.000**	-73.0; **-30.0;** 12.0	**0.000**	0.630
Fat intake (g/day)	49.0; **63.0;** 85.0	51.0; **64.0;** 86.0	0.905	-29.9; **-8.6;** 2.3	**0.000**	-30.0; **-11.0;** 4.0	**0.000**	0.821
EI – restraint score	5.0; **9.0;** 14.0	7.0; **11.0;** 14.0	0.132	-1.0; **3.0;** 7.0	**0.000**	0.0; **3.0;** 6.0	**0.000**	0.930
EI – disinhibition score	3.0; **6.0;** 10.0	3.0; **6.0;** 9.0	0.807	-2.0; **0.0;** 1.0	0.991	-1.0; **0.0;** 2.0	0.753	0.833
EI – hunger score	2.0; **4.0;** 7.5	2.0; **4.0;** 7.0	0.356	-2.0; **-1.0;** 0.0	**0.000**	-2.0; **-1.0;** 1.0	0.113	0.111
BDI – depression score	6.0; **11.0;** 17.5	6.0; **10.0;** 16.0	0.818	-5.0; **-1.0;** 2.0	0.072	-4.0; **0.0;** 2.0	0.179	0.667

[a]Mann-Whitney test, [b]Wilcoxon test, BMI – body mass index, EI – Eating Inventory, BDI – Beck Depression Inventory

p=0.06) compared to T allele carriers. Higher baseline energy (p=0.009), protein (p=0.018) and fat (p=0.002) intakes in T allele non-carriers probably reflected the higher hunger score. On the other hand, Bouchard *et al.* (2004) found that TT homozygotes had significant higher susceptibility to hunger than P allele carriers. It should be taken into account that Bouchard *et al.* (2004), in contrast to our study, evaluated the items of the Eating Inventory in the whole cohort comprised of both genders while we conducted our evaluation in men and women separately. This our approach seems reasonable as significant gender differences in the items of the Eating Inventory have been demonstrated; restraint score being higher in women whereas disinhibition score and hunger score are higher in men (Hainer *et al.* 2006). However, if we evaluated overall changes at follow-up period we might support some of the conclusions of the study of Bouchard *et al.* (2004). T allele carriers seem to be disadvantaged in several aspects against non-carriers. In our cohort of obese males T allele non-carriers but not T allele carriers exhibited significant decreases in waist circumference and energy intake after the follow-up period. Observed concomitant increase in dietary restraint score and decrease in depression score in T allele non-carriers might contribute to reduction of energy intake and abdominal obesity assessed by waist circumference. The Québec Family Study, which followed subjects over a 6-year period, demonstrated the highest increase of body weight, BMI, body fat (expressed both as kg and %) and waist circumference in TT homozygotes when compared to other genotypes. In agreement with the results of Bouchard *et al.* (2004) it could be presumed that carrying the T allele is a disadvantage in terms of reduction of abdominal obesity and energy intake, however only in men.

In women, the baseline values for anthropometric measures, energy and macronutrient intakes, items of the Eating Inventory and Beck depression score did not differ between the T allele carriers and non-carriers. No significant differences in the maximum weight loss nor in the changes of anthropometric measures over follow-up period were shown between the female T allele carriers and non-carriers. However, a decrease in body weight and BMI was significant only in females who were T allele carriers and a decrease in hunger score achieved statistical significance in female T allele non-carriers. Inconsistency in the results obtained in men and women might be due to gender specific role of genes in the phenotypic manifestation of genotype. Such a gender specific role of genes as determinants of obesity development has recently been shown for perilipin gene (Qi *et al.* 2004) and for β_2- and β_3-adrenergic receptor genes (Ukkola *et al.* 2000, Corella *et al.* 2001).

Several differences in the character of the cohort (ethnicity, age, BMI) and design (duration of follow-up) of our study and in that of Bouchard *et al.* (2004) might explain different outcomes. We followed Czech overweight/obese subjects over 2.5-year period, whereas Bouchard *et al.* (2004) monitored a sample of genetically homogenous Québec adults over 6 years. Our subjects were on average 6.5 years older than those in the Bouchard´s cohort (49.2 vs. 42.7 years) (Bouchard *et al.* 2004). It has been demonstrated that the effect of genes, which contributes to adiposity changes is stronger in the younger than in older subjects (Bouchard *et al.* 2007). The role of gender and age was confirmed in investigations into the influence of the PPARGC1A G482S polymorphism on the risk of obesity (Ridderstråle *et al.* 2006).

Our pilot study demonstrated some gender specific associations of P73T polymorphism of *NMB* with eating behavior and weight changes at 2.5-year follow-up. The results should be confirmed on large groups of men.

Abbreviations

BBS Bardet-Biedl syndrome
BDI Beck Depression Inventory
BMI body mass index
DNA deoxyribonucleic acid
EI Eating Inventory
NMB neuromedin beta

Conflict of Interest

There is no conflict of interest.

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