ORIGINAL ARTICLE

Effect of obesity-related gene polymorphisms on weight loss of female wrestlers

Authors' Contribution:
A Study Design
B Data Collection
C Statistical Analysis
D Manuscript Preparation
E Funds Collection

Mio Nishimaki[1ABCDE], Shizuo Sakamoto[2ABCDE]

[1] Department of Sports Science, Japan Institute of Sports Sciences, Tokyo, Japan
[2] Faculty of Sport Sciences, Waseda University, Saitama, Japan

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ABSTRACT

Background and Study Aim: Many wrestlers undergo extreme dieting, with rapid weight loss and fluid restriction, to achieve rule weight as measured before a match. Insight into the genetics of weight loss has been gained from studies of patients with lifestyle-related diseases, including obesity and diabetes, who show weight loss resistance in the face of therapeutic interventions such as diet and exercise. However, the effect of single nucleotide polymorphisms (SNPs) in obesity-related genes on the rapid weight loss that athletes experience in weight-class sports such as wrestling remains to be elucidated. The purpose of this study was the effect of SNPs in *ADRB3*, *ADRB2*, and *UCP1* on rapid weight loss in female wrestlers.

Material and Methods: Twenty-two female wrestlers who sought weight loss before a match participated in this study. We performed real-time polymerase chain reaction using a quenching probe to determine subject genotypes.

Results: Thirteen subjects had the *ADRB3* (Trp/Trp) wild-type genotype, whereas 9 had the *ADRB3* (Trp/Arg) polymorphic genotype. Five subjects had the *ADRB2* (Arg/Arg) genotype, and 17 had the *ADRB2* (Arg/Gly) polymorphic genotype. Five subjects had the *UCP1* (−3826A/A) genotype, and 17 had the *UCP1* (−3829A/G) polymorphic genotype. No statistically significant associations were detected between genotypes of obesity-related genes with any of the weight loss indicators measured.

Conclusions: SNPs in the obesity-related genes *ADRB3*, *ADRB2*, and *UCP1* do not appear to affect weight loss in female wrestlers during rapid weight loss regimens prior to a match.

Keywords: beta-2 adrenergic receptor • beta-3 adrenergic receptor • uncoupling protein 1

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Author's address: Mio Nishimaki, Department of Sports Science, Japan Institute of Sports Sciences, 3-15-1, Nishigaoka Kita-ku, Tokyo 115-0056, Japan; e-mail: mionishimaki@gmail.com

Wrestling – noun a sport in which two contestants fight by gripping each other using special holds, each trying to force the other's shoulders onto a mat [24].

Weight loss – noun the fact of losing weight or of becoming thinner [24].

Weight-loss plan – noun a scheme to reduce body weight, usually by reducing calorie intake, increasing physical activity or a combination of both [24].

Weight reduction – noun same as weight loss [24].

Dehydration – noun a dangerous lack of water in the body resulting from inadequate intake of fluids or excessive loss through sweating, vomiting or diarrhoea [24].

Heatstroke – noun a condition in which someone becomes too hot and his or her body temperature rises abnormally, leading to headaches, stomach cramps and sometimes loss of consciousness [24].

Hyponatraemia – noun a lack of sodium in the blood caused by excessive sweating, persistent diarrhoea or overuse of diuretic drugs [24].

Spasm – noun a sudden, usually painful, involuntary contraction of a muscle, as in cramp [24].

Glycogenolysis – noun the breakdown of glycogen into glucose [24].

Performance – noun the level at which a player or athlete is carrying out their activity, either in relation to others or in relation to personal goals or standards [24].

INTRODUCTION

Weight-class sports, including wrestling, judo, and boxing, match opponents according to strength, power, and agility using weight classes. This sets up a scenario by which players attempt to rapidly lose weight to be eligible to fight in a lower weight class and thus gain an advantage over their opponents. Such rapid weight loss is generally achieved by a dehydration strategy, wherein the body water content is reduced over a short period [1, 2]. Players, especially combat sports athletes generally choose weight loss methods that include excessively reducing both food and water intake, as well as wearing a sauna suit while training and otherwise to increase perspiration [3-7]. These weight-loss methods have raised concerns about the potential associated health problems such as heatstroke, muscle spasm, and hyponatremia [8]. Short-term weight reduction is mostly limited to a reduction in lean body mass with little change in the body fat content [9]. Lean body mass comprises the muscles and bones, and thus plays an important role in physical performance. Therefore, development of a weight-loss method that can effectively reduce body fat without compromising health or performance is important, since body fat is the main energy source that is indispensable for exercise. In addition to their role in energy storage, fat tissues, including white, brown, visceral, and subcutaneous fat, possess other unique characteristics related to the expression of specific genes and associated metabolic functions.

Insight into the genetics of weight loss has been gained from studies on patients with lifestyle-related diseases, including obesity and diabetes, who show weight loss resistance in the face of therapeutic interventions such as diet and exercise. There is high individual and racial variation in the onset of lifestyle-related diseases, including diabetes and hypertension, as well as in the adverse events of the drugs used for their treatment, which are due to background factors, including sex and age, environmental factors such as diet, smoking, and exercise, as well as genetic factors. Indeed, single-nucleotide polymorphisms (SNPs) in various obesity-related genes may be related to this variation as well as the weight-loss resistance in these patients. An SNP is an individual change in a gene sequence and is a representative genetic factor (constitution/predisposition) that makes an individual unique. The most typical obesity-related genes include beta-3 adrenergic receptor (*ADRB3*), beta-2 adrenergic receptor (*ADRB2*), and uncoupling protein 1 (*UCP1*). *ADRB3* is expressed in adipocytes and visceral fat, and is involved in the regulation of lipolysis and thermogenesis. *ADRB3* is involved in a feedback mechanism that prevents excessive obesity, where overeating and obesity stimulate and activate the sympathetic nervous system, thereby promoting lipolysis [10]. However, an SNP in *ADRB3* in which a thymine (T) at the 190th base is replaced by cytosine (C), resulting in replacement of tryptophan (Trp) at the 64th residue with arginine (Arg), has been shown to decrease the basal metabolism by approximately 200 kcal and is associated with an increased risk for obesity [11]. Therefore, it is possible that an *ADRB3* polymorphism would contribute to the individual variations in exercise performance and ultimately affect weight loss from exercise differently among different players. However, the effect of SNPs in obesity-related genes on the rapid weight loss that athletes experience in weight-class sports such as wrestling remains to be elucidated.

Table 1. Change in body composition measurement of 22 female wrestlers one month before the match (T1) and one day before the match (T2).

Variable	Measurement period	
	T1 pre	T2 after
body mass (kg)	57.0 ±8.0	54.7 ±7.6**
lean body mass (kg)	44.4 ±4.6	42.9 ±4.3**
fat mass (kg)	12.6 ±3.9	11.7 ±3.7**
relative body fat (%)	21.7 ±3.8	21.1 ±3.9*

*p<0.05, **p<0.01

Table 2. Physical characteristics of the subjects by genetic polymorphism for each receptor (mean and SD) 22 female wrestlers.

Variable	Genetic polymorphism for each receptor					
	ADRB3		ADRB2		UCP1	
	Trp/Trp (n = 13)	Trp/Arg (n = 9)	Arg/Arg (n = 5)	Arg/Gly (n = 17)	–3826A/A (n = 5)	–3826A/G (n = 17)
body mass (kg)	58.0 ±8.7	55.7 ±7.1	58.3±10.4	56.6 ±7.5	55.6 ±9.1	57.5 ±7.9
lean body mass (kg)	44.5 ±5.2	43.6 ±3.2	45.8 ±5.6	44.0 ±4.3	43.3 ±4.9	44.8 ±4.6
fat mass (kg)	13.5 ±3.8	10.2 ±2.2	12.6 ±4.9	12.6 ±3.7	12.3 ±4.4	12.7 ±3.8
relative body fat (%)	22.9 ± 3.3	19.8 ±3.9	20.9 ±4.3	21.9 ±3.7	21.6 ±4.4	21.7 ±3.8

Accordingly, the aim of this study was the effect of SNPs in *ADRB3*, *ADRB2*, and *UCP1* on rapid weight loss in female wrestlers.

MATERIAL AND METHODS

Participants and General Study Design

Twenty-two female wrestlers (average age: 18.2 ±2.1 years, height: 156.6 ±4.9 cm) who sought weight loss before a match participated in this study. The impedance method was used to measure body weight, body fat percentage, lean body mass, body fat, and body fat mass twice, one month before the match during the usual training period (T1) and one day before the match (T2), using a body composition meter (Omron body scan, HBF-362).

The research plan for this study was examined and approved by the Ethics Committee of Shigakkan University (Japan) prior to conducting the study.

DNA Collection and Extraction/ Purification

Approximately 2 mL of saliva was collected from the subjects using a DNA collection kit (OG-500 tube type, Kyodo International, Inc., Japan). The subjects' DNA was extracted and purified using the QP Genotyping Probe/Primer Set (Code No. 201-001, 201-002, 201-003, Nippon Steel Eco-Tech, Corp., Japan) based on the manufacturer's protocol.

Genotype Determination

We used real-time polymerase chain reaction (ABI 4300) to determine whether the *ADRB3*, *ADRB2*, and *UCP1* showed the wild-type or mutant genotype in each sample using the quenching probe (QP) method.

Statistical Analysis

Data are presented as mean and standard deviations (±). The unpaired *t*-test was used to compare the frequencies of wild and heterozygous genotypes of each gene. One-way analysis of variance was used to compare measurement data in all subjects. Analyses were performed with the use of SPSS (version 21.0). A *p*-value of less than 0.05 was considered statistically significant.

RESULTS

On an average, the body weight of the subjects significantly decreased from 57.0 ±8.0 kg at T1 to 54.7 ± 7.6 kg at T2 ($p< 0.01$). The rate of weight loss was −4.1 ±2.6%. The mean body fat percentage was 21.7 ±3.8% at T1 and was 21.1 ±3.9% at T2 ($p<0.01$). Lean body mass also significantly decreased from 44.4 ±4.6 kg at T1 to 42.9 ±4.3 kg at T2 ($p<0.01$). Body fat mass significantly decreased from 12.6 ±3.9 kg at T1 to 11.7 ±3.7 kg at T2 ($p< 0.01$) (Table 1).

Thirteen subjects had the *ADRB3* (Trp/Trp) wild-type genotype, whereas 9 had the *ADRB3* (Trp/Arg) polymorphic genotype. Five subjects had the *ADRB2* (Arg/Arg) genotype and 17 had the *ADRB2* (Arg/Gly*) polymorphic genotype. Five subjects had the *UCP1* (−3826A/A) genotype and 17 had the *UCP1* (−3829A/G) polymorphic genotype (Table 2).

There were no statistically significant associations detected between genotypes of obesity-related genes with any of the weight loss indicators measured (Figures 1 to 3).

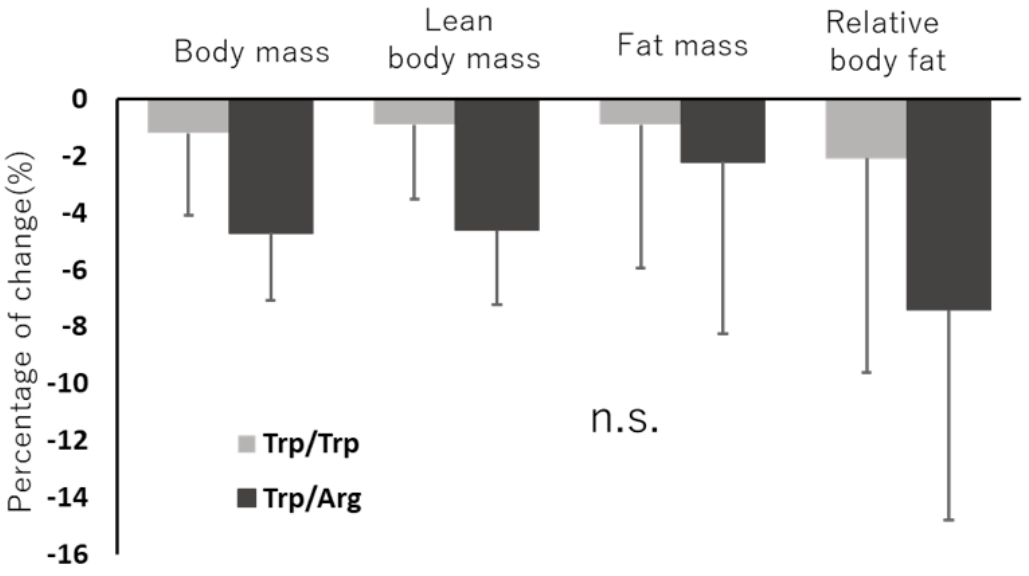

Figure 1. The rate of change in body weight, lean body mass, body fat percentage, and body fat mass for ADRB3.

DISCUSSION

In this study, we examined the association of variation in changes in weight loss for 22 female wrestlers with the ADRB3 (Trp/Trp genotype and Trp/Arg genotype), *ADRB2* (Arg/Arg genotype and Arg/Gly genotype), and *UCP1* (−3826 A/A genotype and −3826 A/G genotype) polymorphisms. There was no difference in the change in body composition due to weight loss between subjects with the SNP and wild-type genotypes of *ADRB3*, *ADRB2*, or *UCP1*. It is, therefore, possible that these three polymorphisms have little effect on the change in body composition associated with the weight loss that female wrestlers undergo before a match.

ADRB3 is a seven-transmembrane G protein-coupled receptor found in large quantities in the brown and white adipose tissue. Stimulation by norepinephrine via ADRB3 enhances heat

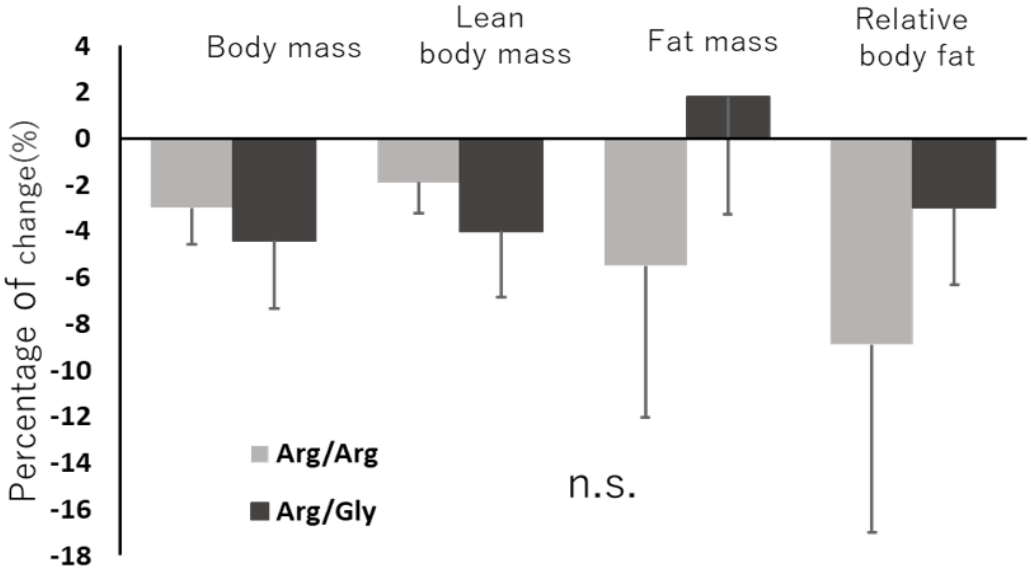

Figure 2. The rate of change in body weight, lean body mass, body fat percentage, and body fat mass for ADRB2.

production in brown adipose tissues and promotes lipolysis in white adipose tissues. The Trp64Arg SNP in the *ADRB3* [12] is associated with an increased risk for obesity, and the basal metabolism decreases by approximately 200 kcal [10, 13, 14]. We found no significant difference in the rate of change in body weight, lean body mass, body fat percentage, and body fat mass during the weight loss period before a match between subjects with the *ADRB3* (Trp/Trp) and *ADRB3* (Trp64Arg) genotypes. These results are different from those obtained in previous studies on the *ADRB3* (Trp64Arg) genotype. For example, researchers evaluating the effect of dietary restrictions and exercise therapy found a difference in weight-loss resistance between subjects with the *ADRB3* (Trp/Trp) genotype and those with the *ADRB3* (Trp64Arg) genotype [11, 15, 16]; however, other researchers have reported the absence of any difference [17, 18]. Thus, the effect of the Trp64Arg mutation in *ADRB3* on weight-loss resistance in middle-aged/elderly obese people cannot be clearly concluded.

ADRB2 is not only found in the heart, bronchi, and smooth muscle cells, but also in the adipose tissue, where it is believed to affect adipocyte degradation. The main effects mediated by ADRB2 include increased gluconeogenesis, glycogenolysis, insulin release, glucagon release, and relaxation of the smooth muscles. The SNP in which adenine (A) is replaced by guanine (G) in *ADRB2* at the 46th base results in replacement of arginine (Arg) with glycine (Gly) at the 16th amino acid in ADRB2 [19] and has been reported to increase the affinity of epinephrine to its receptors by five-fold [20]. This increased affinity, in turn, enhances the effects mediated by ADRB2, leading to an increase in the basal metabolism of people with the Arg16Gly mutation in ADRB2. Oomen et al. [21] reported that heat production mediated by ADRB2 was reduced in the context of the Arg16Arg mutation. Although we found no effect of the *ADRB2* SNP (Arg/Gly) on weight loss indicators in female wrestlers, Sakane et al. [11] focused on the *ADRB2* (Arg/Gly) genotype in middle-aged and elderly obese subjects who underwent exercise and dietary therapy for three months, and found that weight loss was significantly greater in the group with the Arg16Gly mutation [19]. We can, therefore, conclude that weight-loss efficiency is not impacted by the susceptibility for a reduction in body fat percentage. To the best of our knowledge, no previous study has reported enhanced glycogenolysis in patients with the *ADRB2* (Arg/Gly) genotype. However, approximately 3 g of water binds to 1 g of glycogen stored in the body. Thus, it is possible that the Arg16Gly mutation in *ADRB2*

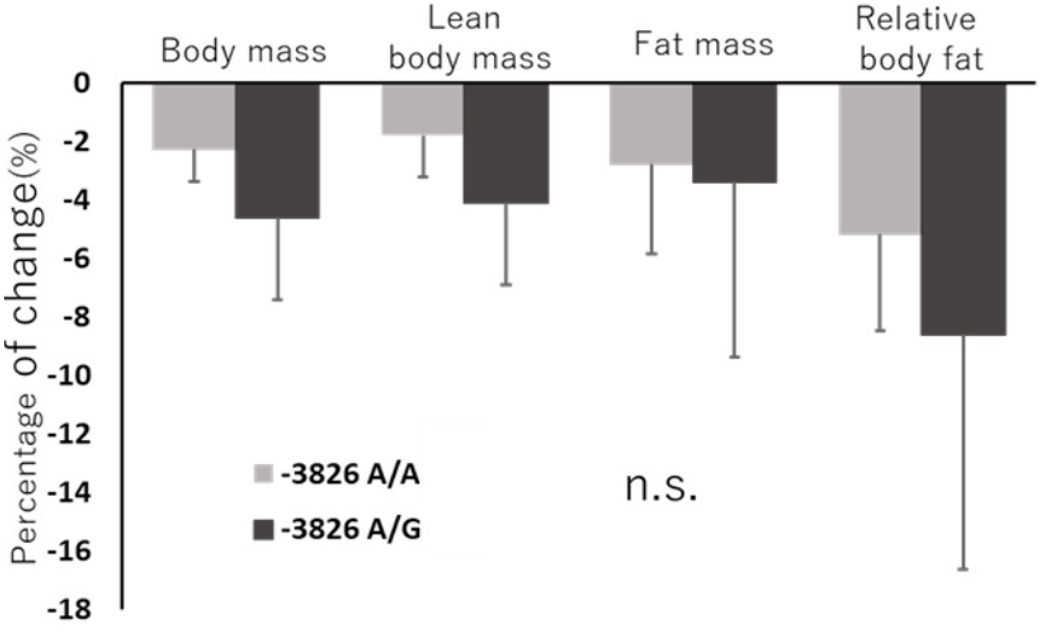

Figure 3. The rate of change in body weight, lean body mass, body fat percentage, and body fat mass for UCP1.

is advantageous for the weight loss that wrestlers undergo if it enhances glycogenolysis, which would facilitate weight loss by dehydration.

UCP1 is located downstream of *ADRB3* in the signalling pathway, and is expressed in the mitochondria of brown adipose cells where it is activated by enhanced sympathetic activity. *UCP1* dissipates energy as heat by uncoupling oxidative phosphorylation reactions in the inner mitochondrial membrane. Cyclic AMP is produced when norepinephrine binds to *ADRB3*; protein kinase A mediates the activation of cyclic AMP response element binding protein (CREB), which is a transcription factor that promotes *UCP1* transcription. Kogure et al. [22] reported that subjects with the −3826 A/G mutation, in which adenine (A) at position −3826 in the upstream region of the sequence is replaced by guanine (G), have significantly lower metabolism at rest compared to those without the mutation, and weight-loss resistance is observed as a result of exercise and dietary interventions [22]. However, in our study, no significant difference was observed in the reduction rates of body weight, lean body mass, body fat percentage, or body fat mass during the weight loss period leading up to a wrestling match between subjects with the *UCP1* (−3826 A/A) or *UCP1* (−3826 A/G) genotypes. Weight-loss resistance has been shown to be even more marked in those with both the *UCP1* (−3826 A/G) and *ADRB3* (Trp/Arg) genotypes than in those with only one of these mutations [23].

CONCLUSIONS

SNPs in the obesity-related genes, *ADRB3*, *ADRB2*, and *UCP1*, do not appear to affect weight loss of female wrestlers during rapid weight loss regimens prior to a match.

HIGHLIGHTS

- Effect of SNPs in obesity-related genes on weight loss in athletes remains to be elucidated.
- The effect of SNPs in *ADRB3*, *ADRB2*, and *UCP1* was studied.
- SNPs in ADRB3, ADRB2, and UCP1 do not affect the rapid weight loss in athletes.

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