Acta Kinesiologiae Universitatis Tartuensis, 2017. Vol. 23, pp. 34–41
https://doi.org/10.12697/akut.2017.23.03

THE *AGT* M235T (RS699, 4072T>C) POLYMORPHISM IS NOT ASSOCIATED WITH ELITE WEIGHTLIFTING PERFORMANCE

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ABSTRACT

It is now well established that genetic background influences an athlete's ability to excel in different sport disciplines. Previous studies have demonstrated that among power athletes, single nucleotide polymorphism (SNP) in the *AGT* genotype (Thr-Thr), was significantly more prevalent among weightlifters compared to sprinters and jumpers indicating that despite the common features of these sport subtypes (short and very intense), they vary in their strength and speed abilities, as well as in their genetic make-up. The aim of the present study was to assess whether the *AGT* SNP can be used also to distinguish elite from national levels weightlifters. The *AGT* M235T genotype frequencies were assessed in 47 weightlifters (30 elite, 17 national level) and 86 non-athletes control. The Thr-Thr genotype was significantly higher among weightlifters (29.8%) compared to controls (12.8%) (p=0.048). Thr allele frequency was significantly higher among weightlifters (55.3%) compared to controls (37.8%) (p=0.021). However, there was no difference in the prevalence of the polymorphism between national level and elite athletes. In conclusion, the results suggest that the AGT polymorphism cannot predict elite competitive weightlifting performance.

Keywords: *genetic profile; athletic performance; weightlifting*

INTRODUCTION

Anaerobic-type sport events are characterized by high intensity activities lasting few seconds using different proportions of power, speed and strength. Weightlifting is considered one of the more explosive-type anaerobic events characterized by maximal force production and slow velocity lifts. The initiation of the lifting movement is explosive, but the subsequent movement is at a rather slow velocity due to the high load and the associated lifting biomechanics [3, 9, 16]. However, during training weightlifters use both standard resistance exercise techniques, including heavy load, slow velocity movements as well as explosive type lifts such as snatch, clean and jerk [12]. This allows for the use of heavy loads and high velocities simultaneously, thus producing higher power outputs [9, 10] and increasing concurrently muscle strength and power [13].

It is now well known that genetic background influences an athlete's capability to excel in different sport disciplines like weightlifting. Genetics have a large influence on muscle cross-sectional area and size, muscle fibre type (fast versus slow twitch) and muscle strength [1, 5, 8, 21–24]. Genetics may also regulate the muscle adaptation to training and it was found that improvement in one repetition maximum (1RM), static strength, and concentric flexion were influenced by genetic-environment interactions [20]. AGT encodes for angiotensinogen, an activity modulator of the renin-angiotensin system (RAS) [6], known to affect muscle growth and power. We recently demonstrated that single nucleotide polymorphism (SNP) in the AGT genotype (Thr-Thr), was significantly more prevalent among weightlifters compared to sprinters, jumpers and controls [19]. The results indicated that despite common features of these sport subtypes (short and very intense), they vary in their strength and speed abilities, as well as in their genetic make-up. The aim of the present study was to assess whether the AGT SNP can be used also to distinguish elite from national levels weightlifters.

MATERIALS AND METHODS

Participants

Forty-seven weightlifters (38 males and 9 females, age 20–49) and 86 non-athletes controls (55 males and 31 females, age 17–39) participated in the study. All athletes competed in national and/or international level meets on a regular basis. Thirty weightlifters were classified as elite athletes (participants and winners in international competitions, including European and World Championships, and Olympic Games). Controls were not engaged

in physical activity on a regular basis. The study was approved by the Institutional Review Board of the Hillel Yaffe Medical Center, Hadera, Israel, according to the Declaration of Helsinki. A written informed consent was obtained from each participant.

Genotyping

Genomic DNA was extracted from samples of peripheral venous blood according to the salting-out procedure. Genotypes were determined using the Taqman allelic discrimination assay. The Assay-by-Design service (www.appliedbio-systems.com) was used to set up a Taqman allelic discrimination assays. Primer sequences were: forward: CCGTTTGTGCAGGGCCTGGCTCTCT, reverse: CAGGGTGCTGTCCACACTGGACCCC. Probe sequences were for M235T, forward: VIC- CTATCGGGAGGGTTG, reverse: FAM- CTATCGGAAGGGTTG.

The PCR reaction mixture included 5ng genomic DNA, 0.125µl TaqMan assay (40*, ABI), 2.5µl Master mix (ABI) and 2.375µl water. PCR was performed in 384 well PCR plates in an ABI 9700 PCR system (Applied Biosystems Inc., Foster City, CA, USA) and consisted of initial denaturation for 10 min at 95 °C, and 40 cycles with denaturation of 15s at 92 °C and annealing and extension for 60s at 60 °C. Results were analyzed by the ABI Taqman 7900HT using the sequence detection system 2.22 software (Applied Biosystems Inc).

Data Analysis

The SPSS statistical package, version 20.0, was used to perform all statistical evaluations (SPSS, Chicago, IL, USA). A $\chi 2$-test was used to confirm that the observed genotype frequencies were within the Hardy-Weinberg equilibrium and to compare alleles and genotype frequencies between athletes and controls, as well as between athletes from different competitive levels. If observed or expected values included a cell with a value of 5, we used Fisher's exact test to compare alleles and genotype frequencies.

RESULTS

The complete allele and genotype frequencies data are presented in Table 1. The genotype subtype did not differ by age or sex. The *AGT* M235T genotype distribution was in agreement with the Hardy-Weinberg equilibrium in controls (p=0.54), national-level weightlifters (p=0.75), and top-level weightlifters (p=0.97).

Table 1. *AGT* Met235Thr Genotypes and alleles frequencies, n (%)

	Control	Weight lifters		
		National level	Top level	Total
n	86	17	30	47
Met-Met	32 (37.2)	4 (23.5)	5 (16.7)	9 (19.2)
Met-Thr	43 (50.0)	8 (47.1)	16 (53.3)	24 (51.0)
Thr-Thr	11 (12.8)	5 (29.4)	9 (30.0)	14 (29.8)
Thr allele carriers	54 (62.8)	13 (76.5)	25 (83.3)	38 (80.8)
Met allele	107 (62.2)	16 (47.1)	26 (43.3)	42 (44.7)
Thr allele	65 (37.8)	18 (52.9)	34 (56.7)	52 (55.3)

$\chi^2(1)=3.90$; p=0.048 for *AGT* Thr-Thr genotype frequency, Weight lifters vs. Controls
$\chi^2 2(1)=5.35$; p=0.021for *AGT* Met235Thr allele frequency, Weight lifters vs. Controls

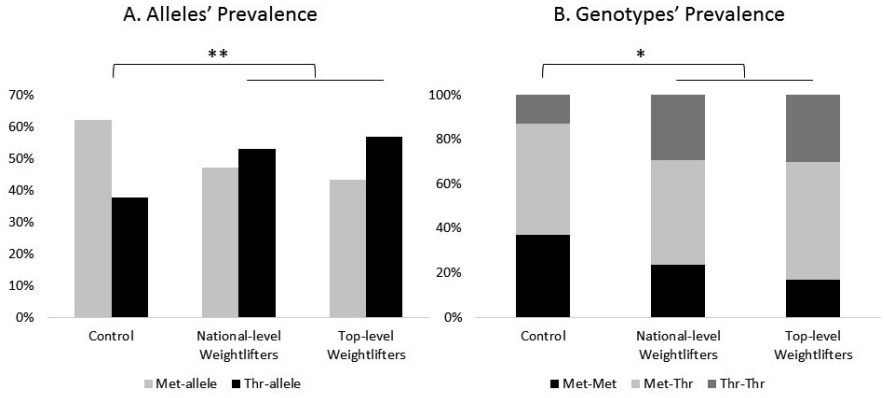

Figure 1. AGT Met235Thr alleles and genotype frequencies among weightlifters.

*$\chi^2(1)=3.90$; p=0.048 for *AGT* Thr-Thr genotype frequency, Weight lifters vs. Controls
**$\chi^2(1)=5.35$; p=0.021 for *AGT* Met235Thr allele frequency, Weight lifters vs. Controls

AGT Met235Thr genotype and allele frequencies are presented in Figure 1. The *AGT* Met235Thr genotype frequencies were different among weightlifters compared to controls. Overall, the Thr-Thr genotype was significantly higher among weightlifters (29.8%) compared to controls (12.8%) (p=0.048). Thr allele frequency was significantly higher among weightlifters (55.3%) compared to controls (37.8%) (p=0.021). However, The *AGT* Met235Thr genotype and allele frequencies were not significantly different among top-level compared to national-level weightlifters.

DISCUSSION

Recent studies attempted to identify genetic variants associated with elite athletic performance. These studies relied primarily on the candidate gene approach and SNP relations with top world class performance using frequently small sample size cohorts from different geographic areas and ethnicities. However, while several genes have been found to potentially assist in sport selection and explain athletic success, and while genetic assessment may eventually become part of future talent identification, genetic testing predictive value is poor at the present time [17]. In the present study, we assessed the prevalence of the *AGT* M235T (rs699, 4072T>C) polymorphism among national level and elite weightlifters. Our main findings were a significantly higher prevalence of *AGT* 235T polymorphism among weightlifters compared to controls. However, there was no difference in the prevalence of the polymorphism between national level and elite athletes suggesting that this polymorphism cannot determine or predict elite competitive weightlifting performance.

Angiotensinogen (AGT) plays an important role in the renin-angiotensin system (RAS) by activation of angiotensin I and II (ANG I & II) production [6]. The RAS controls cardiovascular and renal functions, inflammatory cytokine and free radical production [4] as well as cell growth and proliferation [7]. M235T (rs699, 4072T>C) is a missense polymorphism that leads to T to C transition at position 4072 in exon 2 and results in a replacement of the amino acid methionine (M) by threonine (T) at residue 235 of the mature AGT. The M235T polymorphism effects plasma *AGT* concentration, with C allele (Thr) carriers having 10–30% higher AGT levels [14], and subsequently a higher ANG II level, a skeletal muscle growth factor [18]. Mechanisms that may explain the ANG II effect on muscle performance include a direct skeletal muscle hypertrophic effect, and redistribution of intra-muscular blood flow from the slow type I to the fast and powerful type II fibers, thereby augmenting power and strength capability [15]. Consistent with that previous studies have reported a higher prevalence of the *AGT* CC genotype in power athletes [11, 25]. In addition, we recently demonstrated [19]a high prevalence of the *AGT* CC genotype (Thr-Thr) among weightlifters (25.9%) compared to extremely low prevalence among sprinters (4.2%). This suggests that different genetic makeups enable athletic excellence in speed-oriented (e.g., sprints and jumps), and strength-oriented events (e.g., weightlifting). Moreover, the results suggest that combining different disciplines in sports genetic research should not be done, or at least should be done with extreme caution [2].

In conclusion, the main finding of the present study was that despite the higher prevalence among weightlifters, the *AGT* polymorphism cannot distinguish between top and national level athletes. Although it is possible that other genetic polymorphisms may determine weightlifting success, this finding emphasizes the concept that while a favourable genetic predisposition is essential in sports, other associated factors such as training experience, superior equipment and facilities, adequate nutrition, greater familial support, and motivational factors, are crucial for top-level sports development as well.

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