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RESEARCH ARTICLE

ACTN3 R577X variant: could it be a determinant of sports performance in elite athletes in a Turkish population?

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Abstract. *ACTN3* gene, which encodes α-actinin-3 and actin-binding protein, has been found to be associated with strong athletic performance, especially among track and field athletes. Therefore, in this study, our aim was to compare the allelic and genotype frequencies of the ACTN3 R577X variant among elite athletes specialized in different branches, and nonathletic controls in Turkey. In the present study, 316 subjects, including 168 athletes and 148 sedentary controls were genotyped for the *ACTN3* R577X variant. Genotyping was conducted by polymerase chain reaction (PCR) method. Additionally, we evaluated the groups by dividing them as females and males. There were 48 females and 120 males in the athletes group, and 43 females and 105 males in the control group. Genetic associations were evaluated by chi-squire test or Fisher's exact test. There was a significant difference between the athletes and controls in terms of the *ACTN3* R577X variant. *ACTN3* RR and XX genotypes increased in the controls compared to the athletes, while RX genotype was higher in the athletes than the controls ($P = 0.030$). Then we evaluated the groups by separating them as females and males. Genotype distribution of the *ACTN3* R577X differed between the male athletes and the male controls ($P = 0.046$). *ACTN3* R577X RX genotype increased in the male athletes compared to the male control ($P = 0.046$). But *ACTN3* R577X genotype and allele distribution was not significant between female athletes and female control group ($P > 0.05$). As far as we know, this study is the largest series examining the *ACTN3* R577X variant in Turkish athletes. Our results support that the *ACTN3* R577X variant has a heterozygous advantage in athletic performance in the Turkish population. However, epigenetic, gene–gene and gene–environment interactions affects athlete performance should not be forgotten.

Keywords. elite athletes; *ACTN3* gene; variant; Turkish population.

Introduction

Athletic performance is affected by the environment (e.g., training, diet, and sociodemographic factors) and heredity (e.g., sex, genetics, and epigenetics) as a complex trait. In this regard, there is exponentially increasing evidence that genetics significantly contributes to athletic performance, and it is well recognized that 'nurture' and 'nature' affect the ability to be extremely good at sport (Antero *et al.* 2018). Both twin and familial studies show that genetic factors of speed, power, and strength form 35–80% of the variation among individuals (Tiainen *et al.* 2009). With the completion of the Human Genome Map (HGM), the productivity of human genomics research has been greatly increased. Several genetic studies on sports performance have been conducted assuming that the human genome affects individual physical functions, such as muscle strength, equilibrium, endurance, flexibility, coordination, and even psychological motivation.

Alpha-actinin-3, an actin-binding protein with a pivotal role in metabolism and muscle structure, is encoded by the human *ACTN3* gene. It has been found that there is an association between the *ACTN3* R577X variant and power athletic performance, particularly among track and field athletes. Association studies have found an association between several genetic variants and training responses and traits related to sport, such as skeletal muscle mass, recovery ability, strength, and composition of muscle fibre. One of the most-researched genes associated with physical performance characteristics of muscle endurance and strength is alpha-

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actinin-3. Alpha-actinin-3 contributes to the regulation of blood pressure, higher resistance to muscle fatigue, and the contractile capacity of skeletal muscle (Ortiz *et al.* 2020). The ACTN3 protein in humans is an F-actin cross-linking sarcomeric protein that binds actin to various intracellular structures (exclusively in fast-twitch type II muscle fibres) and regulates the myofibril contraction coordination (MacArthur *et al.* 2007). *ACTN3* gene is located on the 11th chromosome long arm (11q13.1). Single-nucleotide polymorphism in the *ACTN3* gene has a negative effect on the α-actinine-3 expression. The p.R577X single-nucleotide polymorphism (SNP) specifically causes to replace an arginine with a premature stop codon. Consequently, those with two identical alleles of a gene for this stop codon in the *ACTN3* gene experience deficiency of α-actinin-3. Contrarily, a functional α-actinin-3 is expressed by those with RR or RX genotypes. In addition, the *ACTN3* genotype has been proposed to control the muscle function and sarcomeric composition dependently on the dose, indicating that RR individuals have higher α-actinine-3 in the muscle than the RX individuals (Hogarth *et al.* 2016).

Therefore, we aimed to compare allelic and genotype frequencies of the *ACTN3* R577X variant among elite athletes specializing in different branches and nonathletic controls in Turkey.

Materials and methods

Study population

The study group consisted of 168 athletes representing the Department of Sport Management. The control group consisted of age-gender-matched voluntary sedentary individuals. The participants included both genders, were of Turkish descent, and aged between 18 and 30 years. Informed written consent was obtained from all subjects before enrollment in the study. According to the Declaration of Helsinki's ethical guidelines, the Ethical Committee approved the investigation.

Genotyping

Two mL of venous blood was taken from each participant (athletes and controls), and DNA was extracted from all the samples using the commercial kit based on the manufacturer's instructions. *ACTN3* R577X variant was genotyped by the polymerase chain reaction (PCR) method described previously (Orysiak *et al.* 2014).

Statistical analysis

Data were analysed using the Statistical Package for Social Sciences (SPSS) software v. 20.0 for Windows (SPSS, Chicago). Mean and standard deviation were used for the presentation of continuous quantitative variables. Frequencies and percentages were used for categorical data. The *ACTN3* overall genotype distribution was compared by the chi-square (χ^2) test, and the specific genotype and allele distributions were compared using Fisher's exact test. The odds ratio (OR) and 95% confidence intervals (CI) were used to determine the relationships between the *ACTN3* allelic and genotypic variants, and their occurrence in the groups. The *P* values below 0.05 were considered statistically significant.

Results

In the present study, 316 subjects, including 168 athletes and 148 controls, were genotyped for the *ACTN3* R577X variant. Baseline demographic features of the subjects are shown in table 1. The distribution of genotypes and alleles of *ACTN3* between athletes and controls are shown in table 2. There was a significant difference between the athletes and controls in terms of the R577X variant of the *ACTN3* gene. *ACTN3* RX genotype was higher in the athletes than the controls ($P = 0.030$). No statistically significant association was observed between the athletes and the controls in terms of RR + RX. We found no significant difference between the athletes and the controls in terms of the allelic frequencies of the *ACTN3* variant. Further, we genotyped the groups by dividing them into females and males. The *ACTN3* genotype and allele distribution in females and males are presented in tables 3 and 4. There were 48 females and 120 males in the athletes group, and 43 females and 105 males in the control group. There was no statistically significant difference between the female athletes and female controls in terms of genotype and allele distribution ($P > 0.05$). Genotype distribution of the *ACTN3* R577X differed between the male athletes and male controls ($P = 0.046$). *ACTN3* R577X RX genotype increased in the male athletes compared to the male controls. Allelic frequencies of *ACTN3* R577X were similar between the male groups ($P > 0.05$).

Discussion

An individual has enormously complex ability to maximize personal potential. There is no doubt that some factors, such as the motivation, volume of training, and environment, are due to an athlete's success (Baker and Davids 2006). However, while training is a crucial determinant of increasing an athlete's level of body strength, agility, speed, and endurance, it appears to be an overarching factor of human physical performance as the genetic factor is more responsible for determining a person's innate potential. The consistent main effect of genetics on exercise adaptation has been explored well in the last 20 years and more. Although genetics clearly has a certain effect on exercise performance,

Table 1. Demographical features of the subjects.

	Controls, n = 148 (%)	Athletes, n = 168 (%)
Female/male (n/n)	43/105 (%29.1/70.9)	48/120 (%28.6/71.4)
Age (years)	22.49±2.99	21.90±2.84
Min–max	18–30	18–30
Weight (kg)		
40–49	0	1 (0.6)
50–59	18 (12.2)	25 (14.9)
60–69	39 (26.4)	46 (27.4)
70–79	47 (31.8)	51 (30.4)
80–89	25 (16.9)	25 (14.9)
90–99	18 (12.2)	16 (9)
100–109	1 (0.7)	4 (2.4)
Height (cm)		
150–159	5 (3.4)	6 (3.6)
160–169	21 (14.2)	26 (15.5)
170–179	70 (47.3)	76 (45.2)
180–189	40 (27)	32 (19)
190–200	12 (8.1)	28 (16.7)
BMI		
Lower than 18.5	1 (0.7)	1 (0.6)
18.5 up to 25	115 (77.7)	136 (81)
25 up to 30	31 (20.9)	28 (16.7)
30 upwards	1 (0.7)	3 (1.8)
Smoking (day)		
0	103 (69.6)	137 (81.5)
5–9	6 (4.1)	11 (6.5)
10–15	39 (26.4)	20 (11.9)
Alcohol consumption (month)		
0	121 (%81.8)	150 (89.3)
1–4	0	1 (0.6)
5–9	7 (%4.7)	5 (3)
10–14	12 (%8.1)	6 (3.6)
15–20	8 (%5.4)	6 (3.6)
Sports branch		
Football	–	39 (23.2)
Basketball		37 (22)
Volleyball		66 (39.3)
Wrestle		26 (15.5)
Training (week)		
2	–	1 (0.6)
3		60 (35.7)
4		63 (37.5)
5		44 (26.2)
Family history		
–	138 (93.2)	104 (61.9)
Football	7 (4.7)	16 (9.5)
Basketball	3 (2)	5 (3)
Volleyball	0	9 (5.4)
Wrestle	0	27 (16.1)
Judo	0	5 (3)
Athleticism	0	1 (0.6)
Swimming	0	1 (0.6)
Disease		
No chronic disease	135 (91.2)	150 (89.3)
Chronic disease	13 (8.8)	18 (10.7)
Years		
1–5		24 (14.3)
6–10		100 (59.5)
11–20		44 (26.2)

the effect of individual SNPs or a combination of SNPs on this process is examined in fewer studies. DNA polymorphisms with 1% or higher frequency in the population and rare mutations of DNA (below 1% frequency) can be generally classified as the genetic markers of power, endurance, and strength (or combined strength/power) of the athlete status. The specific genetic marker related to sport is significantly based on several criteria, such as frequency of the polymorphism in a specified population, its type, the number of cross-sectional and case–control studies with negative or positive (controversial) results, the total number of the investigated athletes, and proof from the functional studies (knockout or overexpression models, analysing the luciferase activity with specific allele, etc.) (Ahmetov *et al.* 2014).

A family of actin-binding proteins is the α-actinins, which are related to dystrophin. Two genes encode skeletal-muscle α-actinins in humans: *ACTN3* restricted to fast fibres and ACTN2 expressed in all fibres (Mills *et al.* 2001). The α-actinin-3 protein expression is almost exclusively limited (Mills *et al.* 2001). Phenotypic analysis of an *Actn3* knockout mouse model mechanistically explains the impact of α-actinin-3 deficiency on performance and skeletal muscle traits (MacArthur *et al.* 2008). *Actn3* knockout muscles show that fibre size of type 2, fast-twitch glycolytic muscle is significantly reduced, anaerobic activity decreases, and oxidative phosphorylation increases compared to wild-type littermates (Seto *et al.* 2013). The metabolic properties of fast glycolytic muscle fibres are slowed by the decreased activity of glycogen phosphorylase (Quinlan *et al.* 2010) and, are reversed by replacement or 'rescue' of α-actinin-3 after birth in skeletal muscle (Garton *et al.* 2018).

The variant of the *ACTN3* R577X gene is recognized as a nonsense mutation, specifically occurring in codon 577 of exon 16, where the arginine codon production is altered to a premature stop codon through the translation at nucleotide position 1747 (North *et al.* 1999). Homozygosity for the prevalent polymorphism of a single null nucleotide in the *ACTN3* gene causes full deficiency of the α-actinin-3 protein in the estimated 18% of humans all over the world (North *et al.* 1999). The null and wild-type mutations for the *ACTN3* R577X variant are characterized by *X* and *R* alleles, respectively. The *R* allele codes *ACTN3* gene producing α-actinin-3 protein, while the X allele contains a series of changes that completely stops the production of the functional α-actinin-3 protein (North *et al.* 1999). MacArthur *et al.* (2007) stated that losing ACTN3 protein alters the metabolism of skeletal muscle to aerobic metabolism with higher efficiency. Based on these various physiological functions, possessing the *R* and *X* alleles may beneficially affect the power/strength and activities of endurance, respectively. In addition, the RR genotype, i.e., two copies of R allele, were found more frequently in power/strength-

Table 2. Genotype and allele frequencies of *ACTN3* R577X in study participants.

ACTN3 R577X	Controls n = 148 (%)	Athletes n = 168 (%)	OR (95%CI)	P	P
Genotypes					
RR	49 (33.1)[a]	51 (30.4)[a]	1		0.030*
RX	66 (44.6)[a]	96 (57.1)[b]	0.716 (0.433–1.182)	0.191	
XX	33 (22.3)[a]	21 (12.5)[b]	1.636 (0.834–3.206)	1.152	
RX+XX	99 (66.9)	117 (69.6)	0.881 (0.548–1.416)	0.600	
Alleles					
R	164 (55.40)	198 (58.92)	1	0.372	0.372
X	132 (44.60)	138 (41.08)	1.155 (0.842–0.1584)		

[a,b]No significant differences between groups that share the same letter in the same column.
*P<0.05.

Table 3. *ACTN3* R577X genotype and allele distribution in the female group.

ACTN3 R577X	Female controls n = 43 (%)	Female athletes n = 48 (%)	OR (95%CI)	P	P
Genotypes					
RR	13 (30.2)	17 (35.4)	1		0.442
RX	17 (39.5)	22 (45.8)	1.010 (0.387–2.640)	0.983	
XX	13 (30.3)	9 (18.8)	1.889 (0.619–5.762)	0.467	
RX+XX	30 (69.8)	31 (64.6)	1.266 (0.525–3.049)	0.599	
Alleles					
R	43 (50)	56 (58.33)	1		0.260
X	43 (50)	40 (41.67)	1.400 (0.779–2.515)		

Table 4. *ACTN3* R577X genotype and allele distribution in the male group.

ACTN3 R577X	Male controls n = 105 (%)	Male athletes n = 120 (%)	OR (95%CI)	P	P
Genotypes					
RR	36 (34.3)[a]	34 (28.3)[a]	1		0.046*
RX	49 (46.7)[a]	74 (61.7)[b]	0.625 (0.346–1.130)	0.120	
XX	20 (19)[a]	12 (10)[b]	1.574 (0.669–3.703)	0.299	
RX+XX	69 (65.7)	86 (71.7)	0.758 (0.430–1.334)	0.336	
Alleles					
R	121 (57.63)	142 (59.17)	1		0.740
X	89 (42.37)	98 (40.83)	1.066 (0.732–1.552)		

[a,b]No significant differences between groups that share the same letter in the same column.
*P<0.05.

oriented athletes, such as elite-level bodybuilders and powerlifters (Roth *et al.* 2008), Russian power athletes (Druzhevskaya *et al.* 2008), Indian power athletes (Kothari *et al.* 2011), Polish power athletes (Cieszczyk *et al.* 2011), gymnasts (Massidda *et al.* 2009), compared with the controls and endurance athletes. Yang *et al.* (2003) also suggested that sprint ability could be enhanced by the *R* allele of *ACTN3* R577X variant due to the presence of at least one copy of *R* allele in all female elite sprint and male Olympian power athletes. Niemi and Majamaa (2005) reported that there were similar findings with a lower frequency of the *R* allele in endurance athletes and a higher frequency of the *R* allele in Finnish sprinters. None of the top Finnish sprinters were reported to be predisposed for two copies of the X allele. Eynon *et al.* (2009) reported similar findings that the R allele had a significantly higher frequency in sprinters than in the controls and endurance athletes of the Israeli population (Eynon *et al.* 2009). Unlike the positive findings, the effect of the R allele possession on power/strength performance was not identified in several studies. A study exhibited individuals with XX genotype with higher relative and absolute one-repetition maximum gain after the resistance training (Clarkson *et al.* 2005), and higher vertical jump and grip strength (Ginevičienė *et al.* 2011), than the RR carriers. The reasons for

such inconsistent findings may be limited reports from the Asian population and the factor of ethnicity. However, Yusof *et al.* (2016) found that the multi-ethnic groups of Malaysian athletes had no varying ACTN3 alleles and genotype frequencies. Its relationship with physical performance indicated no interaction between *ACTN3* variant and ethnicity to affect the strength and endurance performances in the Malaysian population. This finding suggested a universal effect of the *ACTN3* variant on human physical performance among different Malaysian ethnic groups. Further, they identified an association between the presence of the R allele and higher strength performance among the multi-ethnic Malaysian population in line with the previous study on the Asians (Kothari *et al.* 2011) and the findings related to Caucasian athletes (Yang *et al.* 2003; Eynon *et al.* 2009).

In this study, we analysed whether the *ACTN3* genotype affects sports performance. As far as we know, this study is the largest series examining the *ACTN3* variant in Turkish athletes. This study compared 168 athletes with 148 sedentary controls. All subjects live in the Middle Black Sea region. The *ACTN3* R577X genotype distribution was significantly different between the athletes and the controls. *ACTN3* R577X variant RX genotype was higher in the athletes than the controls, while RR and XX genotype was more prevalent in the controls than the athletes (table 2). Then we divided the groups into females and males. While *ACTN3* R577X genotype and allele distribution was not different between the female athletes and female controls, genotype distribution was significantly different between the male athletes and male controls (tables 3 & 4). *ACTN3* R577X RX genotype increased in the male athletes compared to the male controls. This condition can be explained as a heterozygous advantage.

However, there are several limitations in the current case–control analysis. First, the only focus was on one variant in this pathway, and other regulatory genes in this family signalling pathway may affect the mechanism. Second, due to the relatively small sample size, some homozygous variants were less frequent in the groups, decreasing the statistical power. The final limitation is that we do not separate athletes by endurance status and sprint.

Conclusions

Our results support that the *ACTN3* R577X variant has a heterozygous advantage in athletic performance in the Turkish population. However, epigenetic, gene–gene and gene–environment interactions should not be forgotten since it affects athlete performance.

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References

Ahmetov I. I., Donnikov A. E. and Trofimov D. Y. 2014 ACTN3 genotype is associated with testosterone levels of athletes. *Biol Sport.* **31**, 105–108.

Antero J., Saulière G., Marck A. and Toussaint J. F. 2018 A medal in the olympics runs in the family: A cohort study of performance heritability in the games history. *Front Physiol.* **9**, 1313.

Baker J. and Davids K. 2006 Genetic and environmental constraints on variability in sport performance. In *Movement system variability* (K. Davids, S. Bennett and K. M. Newell) Human Kinetics USA.

Cieszczyk P., Eider J., Ostanek M., Arczewska A., Leonska-Duniec A., Sawczyn S. *et al*. 2011 Association of the ACTN3 R577X polymorphism in polish power-orientated. *Athletes J. Hum. Kinet.* **28**, 55–61.

Clarkson P. M., Devaney J. M., Gordish-Dressman H., Thompson P. D., Hubal M. J., Urso M. *et al*. 2005 ACTN3 genotype is associated with increases in muscle strength in response to resistance training in women. *J. Appl. Physiol.* **99**, 154–163.

Druzhevskaya A. M., Ahmetov I. I., Astratenkova I. V. and Rogozkin V. A. 2008 Association of the ACTN3 R577X polymorphism with power athlete status in Russians. *Eur. J. Appl. Physiol.* **103**, 631–634.

Eynon N., Durate J. A., Oliveira J., Sagiv M., Yamin C., Meckel Y. *et al*. 2009 ACTN3 R577X polymorphism and Israeli top-level athletes. *Int. J. Sports Med.* **30**, 695–698.

Garton F. C., Houweling P. J., Vukcevic D., Meehan L. R., Lee F. X. Z., Lek M. *et al*. 2018 The effect of ACTN3 gene doping on skeletal muscle performance. *Am. J. Hum. Genet.* **102**, 845–857.

Ginevičienė V., Pranculis A., Jakaitienė A., Milašius K. and Kučinskas V. 2011 Genetic variation of the human ACE and ACTN3 genes and their association with functional muscle properties in Lithuanian elite athletes. *Medicina (kaunas)* **47**, 284–290.

Hogarth M. W., Garton F. C., Houweling P. J., Tukiainen T., Lek M., Macarthur D. G. *et al*. 2016 Analysis of the ACTN3 heterozygous genotype suggests that α-actinin-3 controls sarcomeric composition and muscle function in a dose-dependent fashion. *Hum. Mol. Genet.* **25**, 866–877.

Kothari S. T., Chheda P., Chawla S., Chatterjee L., Chaudhry S. K. and Das B. R. 2011 ACTN3 R577X polymorphism in Asian Indian athletes. *Int. J. Hum. Genet.* **11**, 149–153.

MacArthur D. G., Seto J. T., Chan S., Quinlan K. G., Raftery J. M., Turner N. *et al*. 2008 An Actn3 knockout mouse provides mechanistic insights into the association between alpha-actinin-3 deficiency and human athletic performance. *Hum. Mol. Genet.* **17**, 1076–1086.

MacArthur D. G., Seto J. T., Raftery J. M., Quinlan K. G., Huttley G. A., Hook J. W. *et al*. 2007 Loss of ACTN3 gene function alters mouse muscle metabolism and shows evidence of positive selection in humans. *Nat. Genet.* **39**, 1261–1265.

Massidda M., Vona G. and Calò C. M. 2009 Association between the ACTN3 R577X polymorphism and artistic gymnastic performance in Italy. *Genet. Test Mol. Biomarkers* **13**, 377–380.

Mills M., Yang N., Weinberger R., Vander Woude D. L., Beggs A. H., Easteal S. *et al*. 2001 Differential expression of the actin-binding proteins, α-actinin-2 and -3, in different species: implications for the evolution of functional redundancy. *Hum. Mol. Genet.* **10**, 1335–1346.

Niemi A. K. and Majamaa K. 2005 Mitochondrial DNA and ACTN3 genotypes in Finnish elite endurance and sprint athletes. *Eur. J. Hum. Genet.* **13**, 965–969.

North K. N., Yang N., Wattanasirichaigoon D., Mills M., Easteal S. and Beggs A. H. 1999 A common nonsense mutation results in

alpha-actinin-3 deficiency in the general population. *Nat. Genet.* **21**, 353–354.

Ortiz M., Ayala A., Petro J. L., Argothy R., Garzón J. and Bonilla D. A. 2020 Evaluation of ACTN3 R577X and ACE I/D polymorphisms in young Colombian athletes: An exploratory research. *J. Hum. Sport Exerc.* **2**, 1–14.

Orysiak J., Busko K., Michalski R., Mazur-Różycka J., Gajewski J., Malczewska-Lenczowska J. *et al*. 2014 Relationship between ACTN3 R577X polymorphism and maximal power output in elite Polish athletes. *Medicina (kaunas)* **50**, 303–308.

Quinlan K. G., Seto J. T., Turner N., Vandebrouck A., Floetenmeyer M., Macarthur D. G. *et al*. 2010 Alpha-actinin-3 deficiency results in reduced glycogen phosphorylase activity and altered calcium handling in skeletal muscle. *Hum. Mol. Genet.* **19**, 1335–1346.

Roth S. M., Walsh S., Liu D., Metter E. J., Ferrucci L. and Hurley B. F. 2008 The ACTN3 R577X nonsense allele is underrepresented in elite-level strength athletes. *Eur. J. Hum. Genet.* **16**, 391–394.

Seto J. T., Quinlan K. G., Lek M., Zheng X. F., Garton F., MacArthur D. G. *et al*. 2013 ACTN3 genotype influences muscle performance through the regulation of calcineurin signaling. *J. Clin. Invest.* **123**, 4255–4263.

Tiainen K., Sipilä S., Kauppinen M., Kaprio J. and Rantanen T. 2009 Genetic and environmental effects on isometric muscle strength and leg extensor power followed up for three years among older female twins. *J. Appl. Physiol.* **106**, 1604–1610.

Yang N., MacArthur D. G., Gulbin J. P., Hahn A. G., Beggs A. H., Easteal S. *et al*. 2003 ACTN3 genotype is associated with human elite athletic performance. *Am. J. Hum. Genet.* **73**, 627–631.

Yusof H. A., Singh R., Zainuddin Z., Rooney K. and Munir Che Muhamed A. 2016 Alpha-Actinin-3 (ACTN3) R/X gene polymorphism and physical performance of multi-ethnic Malaysian population. *Int. J. Appl. Exer. Physiol.* **5**, 18–30.

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