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Association of the ACTN3 R577X polymorphism in Polish rowers

Zbigniew Jastrzebski
Faculty of Tourism and Recreation, Gdansk University of Physical Education and Sport in Gdansk, Poland,
zbigniew.jastrzebski@awf.gda.pl

Agata Leonska-Duniec
Faculty of Physical Culture and Health Promotion, University of Szczecin, Poland

Marek Kolbowicz
Faculty of Physical Culture and Health Promotion, University of Szczecin, Poland

Tomasz Tomiak
Faculty of Physical Education, Gdansk University of Physical Education and Sport in Gdansk, Poland

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Association of the ACTN3 R577X polymorphism in Polish rowers

Abstract

Background: The ACTN3 R577X polymorphism has been associated with an elite athlete status. Several studies have determined that the R allele is connected with power-oriented athletic performance, whereas the nonfunctional XX genotype may give some beneficial effect for endurance performance. The main aim of the study was to determine the possible interaction between the ACTN3 R577X polymorphism and an endurance athlete status in a group of Polish rowers in comparison with sedentary individuals. Material/Methods: 121 male Polish rowers, members of academic sports clubs, and 115 unrelated volunteers were recruited for the study. Genotyping for the R577X variant was performed by PCR–RFLP. Results: The genotype distribution amongst the rowers (52.06% RR, 38.85% RX, 9.09% XX) was significantly different from that amongst sedentary individuals (RR-33.5%; RX-49.60%; XX-17,35%; P = 0.024). A significant excess of the R allele was noted in the rowers (71.48%, P = 0.008) when comparing with the controls (60.0%). Conclusions: The obtained results show that the ACTN3 X allele and XX genotype are underrepresented in Polish rowers and they are not advantageous for the endurance-type athletes in the studied population. On the contrary, the R allele seems to be useful for a top-level rower. However, additional studies are needed to clarify this problem.

Keywords

gene polymorphism, endurance athletes

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Authors' Contribution:
A – Study Design
B – Data Collection
C – Statistical Analysis
D – Data Interpretation
E – Manuscript Preparation
F – Literature Search
G – Funds Collection

Zbigniew Jastrzebski [1 ABEG], Agata Leonska-Duniec [1,2 BDEF], Marek Kolbowicz [2 BC], Tomasz Tomiak [3 B]

[1] Faculty of Tourism and Recreation, Gdansk University of Physical Education and Sport in Gdansk, Poland
[2] Faculty of Physical Culture and Health Promotion, University of Szczecin, Poland
[3] Faculty of Physical Education, Gdansk University of Physical Education and Sport in Gdansk, Poland

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Conclusions: *The obtained results show that the ACTN3 X allele and XX genotype are underrepresented in Polish rowers and they are not advantageous for the endurance-type athletes in the studied population. On the contrary, the R allele seems to be useful for a top-level rower. However, additional studies are needed to clarify this problem.*

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Corresponding author:
Prof. nadzw. dr hab. Zbigniew Jastrzebski
Gdansk University of Physical Education and Sport in Gdansk
1 Kazimierza Gorskiego St., 80-336 Gdansk
Phone: +48 58 554 7323
E-mail: zb.jastrzebski@op.pl

Introduction

An individual's athletic status is a complex multifactorial phenotype which has a well confirmed strong genetic basis. In recent years 'the human gene map for performance and health-related fitness phenotypes' recognized over 200 genetic markers potentially associated with some physical performance phenotypes [1,2]. However, the latest literature search showed that about 79 DNA polymorphisms are connected with an elite athlete status. These include 59 endurance-related and 20 power-related gene variants [3]. Nowadays, *ACTN3* (α-actinin-3 gene) is one of the most frequently investigated genetic markers in the context of genetic conditioning of athletic predisposition.

The human *ACTN3* gene is located on chromosome 11 in position 11q13-q14. The product of the gene is the cytoskeletal protein named the α-actinin-3, which is found in fast, glycolytic type II muscle fibers, which are responsible for generating forceful contractions at high velocity [4,5]. The protein is a key structural component of the Z-line, where it anchors actin thin filaments, helping to maintain the myofibrillar array [6,7]. Beside the mechanical role, the α-actinin-3 interacts with numerous muscle proteins involved in some signaling and metabolic pathways [4,8].

A common R577X polymorphism in the *ACTN3* (rs1815739), which results in replacement of an arginine (R) residue with a premature stop codon (X) at amino acid 577 (C→T translation at position 1747 in exon 16), was first described by North et al. [9]. This variation creates two versions of the *ACTN3*: the R allele is the functional version of the gene, whereas the X allele includes a sequence change that stops the production of the functional protein [10]. Though this genetic variation is not related with any known disease, the *ACTN3* R577X polymorphism has been widely studied in the context of physical performance in different ethnic groups. Several studies have determined that the R allele is associated with power-oriented athletic performance [11-13]. There is a positive connection between the presence of the allele and the capacity to perform high-power muscle contractions [14]. Additionally, Vincent et al. [15] have shown that the surface area percentage and the number of type II fibers was higher in healthy men with the RR genotype. Whereas the nonfunctional XX genotype may give some beneficial effect for endurance performance [12,16,17]. This hypothesis seems to be supported by the fact that the loss of α-actinin-3 expression in a knockout mouse model results in a shift in muscle metabolism toward the more efficient aerobic pathway and an increase in intrinsic endurance performance [8,18]. Additionally, the XX genotype occurs at higher frequency in some groups of elite endurance athletes [12,16]. On the other hand, there are also some studies which have found no evidence for such association [19-23]. Thus, the role of the *ACTN3* R577X polymorphism in athletic performance is still unclear.

The main aim of the present study was to determine the possible interaction between the *ACTN3* R577X polymorphism (rs1815739) and the endurance athlete status in a group of Polish rowers, members of academic sports clubs, in comparison with sedentary individuals.

Material and methods

Ethics Committee

The Pomeranian Medical University Ethics Committee approved the study, and written informed consent was obtained from each participant. The study complied with the guidelines set out in the Declaration of Helsinki [24,25].

Subjects

121 male Polish rowers, members of academic sports clubs, were recruited for this study. 28 of them were national representatives with no less than ten years' experience participating in sport. 42 of them were the Poland National Championship medalists. All of them were rowers with no less than six years' experience participating in sport.

For controls, samples were prepared from 115 unrelated volunteers (male students of the University of Szczecin, aged 19-23). The athletes and controls were all Caucasian to ensure no likely racial gene skew and to overcome any potential problems of population stratification.

Protocol

Genomic DNA was extracted from buccal cells using a GenElute Mammalian Genomic DNA Miniprep Kit (Sigma, Germany), according to the producer's protocol.

The 290 bp fragment of the *ACTN3* gene was amplified by polymerase chain reaction (PCR) using forward: CTGTTGCCTGTGGTAAGTGGG and reverse primer: TGGTCACAGTATGCAGGAGGG as recommended by Mills et al. [4]. PCR mixture and thermal-time profile were coequal as described by Cięszczyk et al. [11]. The amplified PCR fragments were subsequently digested with *Dde*I endonuclease (Fermentas, Lithuania) in a condition recommended by the supplier [4]. The alleles were distinguished by the presence (X) or absence (R) of a *Dde*I restriction site. Digestion of PCR products of the X allele yields bands of 108, 97 and 86 bp, whereas digestion of PCR products of the R allele yields bands of 205 and 86 bp. The digested products were visualized by using 3% agarose gels stained with ethidium bromide. The research was performed in the molecular laboratory of Gdansk University of Physical Education and Sport, Poland.

Statistical analysis

Genotype distribution and allele frequencies between the groups of athletes and controls were compared, and significance was assessed by χ^2 test. P values of < 0.05 were considered statistically significant [26].

Results

The *ACTN3* genotype distributions amongst subjects and controls were in Hardy-Weinberg equilibrium, making selection bias less likely. Genotype distribution results of the control group (RR-33.5%; RX-49.60%; XX-17,35%) were similar to those reported in previous studies on Caucasian populations [9,10,17,27]. The distributions of the ACTN3 genotypes and alleles are given in Table 1.

Table 1. Genotype and allele frequencies of the *ACTN3* R577X. This data is presented as absolute and relative values (within parentheses). The P value corresponds to comparisons in the genotype and allele frequencies between rowers and controls

Group	n	*ACTN3* genotype			*P*	*ACTN3* allele		*P*
		RR	RX	XX		R	X	
Rowers	121	63 52.06%	47 38.85%	11 9.09%	0.024	173 71.48%	69 28,52%	0.008
Controls	115	40 33.05%	58 49.60%	17 17.35%		138 60.00%	92 40.00%	

The genotype distribution amongst the rowers (52.06% RR, 38.85% RX, 9.09% XX) was significantly different from that amongst sedentary individuals (RR-33.5%; RX-49.60%; XX-17.35%; P = 0.024). A significant excess of the R allele was noted in the rowers (71.48%, P = 0.008) when comparing with the controls (60.0%).

Discussion

In the present study we analyzed genotype distribution of the *ACTN3* R577X polymorphism (rs1815739) the X allele frequency among the rowers from Poland, members of academic sports clubs. Given the fact that rowing is generally categorized as an endurance discipline, we expected the XX genotype to be overrepresented in the examined group of athletes. However, the obtained results show that the occurrence of the XX genotype in the Polish rowers was lower compared to the sedentary individuals (P = 0.024). Surprisingly, a significant excess of the R allele was noted in the case of the examined rowers when comparing with the controls (P = 0.008).

Our findings are inconsistent with some other results, which showed a higher frequency of the X allele and the XX genotype in groups of endurance athletes compared to controls [12,16,17,28].

In the first published case-control study Yang et al. [17] revealed that the occurrence of the *ACTN3* XX genotype was higher in Australian endurance athletes compared to controls, although the association reached statistical significance only in females. Additionally, a significantly higher proportion of the XX genotype was found in Israeli top-level long distance runners [16] and Finnish runners and walkers [12] compared with controls and sprinters.

Some investigators have demonstrated that the deficiency of the α-actinin-3, as marked by the X allele, may give some positive effect on endurance performance [17]. Norman et al. [28] also showed that athletes with loss of the protein expression may be predisposed to developing a higher percentage of type I muscle fibers, benefiting endurance performance. In addition, authors have reported that no the *ACTN3* expression supports a change in metabolic pathways favoring aerobic performance in a knockout mouse model [29].

On the other hand, our results are in accordance with some previous research on endurance athletes including top-level rowers from Poland, which revealed a higher frequency of the R allele in the examined athletes compared to controls [23]. Additionally, the hypothesis that the α-actinin-3 deficiency may give some benefit in endurance performance events has not been supported by other independent studies of elite endurance-oriented athletes such as Russian rowers, biathletes, cross-country skiers, road cyclists, triathletes [10], Spanish cyclists [20], Ethiopians and Kenyans athletes [19], Italian rowers [21] and Caucasian triathletes [22]. Additionally, no important associations were identified between the *ACTN3* R577X genotypes and endurance-related traits such as VO_{2max} in Spanish and Russian athletes [20, 30].

The obtained results could be explained by a mixed strength-endurance character of rowing; consequently, this discipline can not be classified as regular endurance sport. It is well determined that rowers should exhibit endurance as well as excellent isokinetic strength and power [10]. Investigators have explained the high percentage of the R allele in the athletes by the fact that rowers use a special physiological pattern of race pacing: they begin exertion with a vigorous sprint that places excessive demands on anareobic metabolism followed by a severely high aerobic steady-state and a fast finish. In addition, in most endurance events in which the races begin with a mass start, the strategies to win contain covering the distance with the top participants of the race for as long as possible, and turning the long-distance fight into an exhausted sprint for the finish [10, 31].

The present study does have some limitations. The investigated group was too small, because of restrictions imposed by the number of rowers who are members of academic sports clubs and agreed to participate in our research. The relatively small size of group in this study may not possess sufficient statistical power for meaningful analysis and interpretation. In addition, athletic performance is a multifactorial and polygenic trait. Over 59 polymorphisms have been connected with top-level endurance performance, while 25% of these markers were positively associated with athlete status in at least two studies [3]. Within the group of genetic factors that are believed to play a role in athletic ability, there are gene variants that have an important impact on human body composition and metabolism such as endurance, power, strength, muscle fibre size and composition, flexibility, neuromuscular coordination, temperament and other phenotypes [3]. It is also worth mentioning that performance in the rowing competition depends on numerous environmental components such as training, nutrition, motivation, lifestyle, advance in equipment, mental toughness, tactical astuteness, team coherence, decision making and other non-physiological factors also determine success [10].

Conclusions

In summary, our results show that the *ACTN3* X allele and XX genotype are underrepresented in Polish rowers, members of academic sports clubs, and they are not advantageous for the endurance-type athletes in the studied population. On the contrary, the R allele seems to be useful for being a top-level rower. However, the identification of the *ACTN3* polymorphism as a genetic marker for a rowing talent should be interpreted with great caution and additional studies are needed to clarify this problem.

Acknowledgements

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