Associations between the occurrence of the *ACTN3* R577X, *ACE* I/D, *BDKRB2* +9/-9 polymorphisms and anaerobic performance among a group of elite fencers

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Abstract

Introduction: This research aims to detect possible associations between the *ACTN3* R577X, *ACE* I/D, *BDKRB2* +9/-9 genetic polymorphisms, and selected anaerobic performance indicators among elite and sub-elite fencers. *Methods*: The sample of participants included a group of 20 fencers (males, age 25.5 ± 6.9 years; height 185.1 ± 5.8; weight 78.3 ± 9.8). We obtained genotype analysis for selected polymorphisms (*ACTN3* R577X, *ACE* I/D, *BDKRB2* +9/-9) through buccal swabs. 30-second Wingate test was used for the anaerobic performance where the following variables were monitored: the maximal anaerobic performance – P_{max} [W], the anaerobic capacity – AnC [kJ], the total number of revolutions – TR [n], the peak blood lactate concentration – LA_{peak} [mmol·l^{-1}]. *Results*: Within *ACTN3* R577X polymorphism, no differences were found in the observed variables between genotypes. However, *ACE* I/D heterozygotes reached higher P_{max}, AnC, and LA_{peak} values than homozygotes. Furthermore, *BDKRB2* +9/-9 polymorphism homozygotes with -9 allele reached higher P_{max} and AnC values than homozygotes with +9 allele. No statistical differences were found in all monitored variables between genotypes of monitored polymorphisms. *Conclusions*: The research findings might serve as another useful piece of knowledge related to the existing statements in the field of genetics, focusing on speed-strength performance problems. It should be highlighted that current studies are only the first steps in helping us better understand the associations between genetic factors and performance in sports.

Keywords: fencing, genotype, Wingate tests, genetic predispositions

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INTRODUCTION

A remarkable number of studies [1,2] address the associations between genetic markers and sports performance. Still, this field is exceptionally vast, so this question continues to be relevant. The well-known critical factors for reaching a high level of sports performance include quality of training, technical and tactical skills, nutrition. Still, sports performance is also associated with more than 350 genetic variants [3]. Some of the authors [4,5] associate up to 62 genetic markers with an anaerobic performance, which is also introduced in this study. Szalata et al. [6] present their findings of associations between sports performance and selected polymorphisms in their review. Regarding speed-strength predispositions, these markers are described as being *ACTN3* Arg577, *ACE* D, *NOS3* rs2070744 T, *PPARA* rs4253778, *PPARG* 12Ala, *AMPD1* Gln12, among others. On the other hand, there are studies [7] where the focus is only on speed-strength performance, and the authors address 14 different markers (parts of the genes *ACE*, *ACTN3*, *AGT*, *AGTR2*, *AMPD1*, *NOS3*, *PPARA*, *PPARG*, *SOD2*, *TRHR*). Ben-Zaken et al. [8] also looked for associations between genetic predispositions and anaerobic performance (polymorphisms *ACTN3* R577X, *AGT* Met235Thr, *PPARD* T/C). Petr et al. [9] searched for associations between polymorphism *PPARA* C/G and the performance reached in an anaerobic test among a group of elite ice-hockey players. Authors such as Norman et al. [10] or Bouchard and Hoffman [11] contributed to research focused on associations between athletes' anaerobic performance athletes and genetics anaerobic performance. The *ACTN3* R577X (α-actinin-3) and *ACE* I/D (angiotensin-I-converting enzyme) polymorphisms are the most prominent ones in the available studies [2,12,13]. Therefore, they are presented in this study, as well. Gene polymorphisms are also monitored in vasodilation, metabolism, or muscle fibers' transformation [14].

According to Bouchard and Hoffman [11], the *ACTN3* gene is responsible for producing the α-actinin-3 in skeletal muscles, and its expression is restricted exclusively to type II muscle fibers. The presence of the α-actinin-3 isoform is associated with athletes' speed-strength predispositions. A common genetic variant in the *ACTN3* gene leads to the replacement of arginine (R) with a premature stop codon at position 577 of the amino acid chain (Arg577stop, rs1815739 polymorphisms) [15]. Slizik et al. [16] mention that the *ACE* I/D polymorphism is associated with a physiological response to aerobic performance. The *ACE* I/D (rs1799752) polymorphism is formed from two alleles that differ from each other by the insertion or deletion of a 287-bp long element in the intron 16 on chromosome 17 [13]. The conclusions of the studies regarding the *ACE* I/D polymorphism often differ concerning the monitored allele's presence. While allele I is associated with endurance performance, the presence of allele D might affect speed and strength performance, as presented in some studies [15]. Another kind of polymorphism, *BDKRB2* +9/-9, shown in this study, has been examined to associate skeletal muscle metabolic efficiency, vascular contractility, and blood flow [17]. Bradykinin is a potent vasodilator that significantly lowers blood pressure thanks to the bradykinin β2 receptor encoded by the *BDKRB2* gene [5]. According Eynon et al. [17], the bradykinin receptor's activation can increase the level of calcium in cells. Our study focuses on a specific sports discipline (fencing), where one of the basic predispositions for successful performance is the speed of movement (offensive and defensive). Therefore, speed is considered a fundamental ability that affects sports performance in fencing. Without a doubt, other factors (technique, tactics, psyche, etc.) are also essential for optimal match performance.

The genetically determined predominance of fast muscle fibers among fencers can be considered an essential component of sports performance. The course of matches in individual fencing disciplines (épée, foil, sabre) corresponds to these facts. By revealing possible associations between selected polymorphisms and the results obtained during the anaerobic test, there is a possibility to widen the knowledge of genetics and sports performance associations.

This study investigates possible associations between the *ACTN3* R577X, *ACE* I/D, *BDKRB2* +9/-9 polymorphisms, and the selected variables determined through an anaerobic test WT30. These variables are P_{max} [W], AnC [kJ], TR [n], LA_{peak} [mmol·l^{-1}]. The possible associations found in this study might be useful for extending the existing knowledge in genetics and sports, adding another sport discipline where sports performance is based on speed [18]. The results of partial studies focused on sports genetics can provide additional information that complements the current knowledge state.

MATERIAL AND METHODS

Participants

The participants' sample included 20 fencers (males, 18 épée fencers, 2 foil fencers) aged 25.5 (± 6.9). The average active training time was 13.4 (± 6.5), height 185.1 (± 5.8), weight 78.3 (± 9.8). The participants were both elite (the Czech Republic national team, participating in world cup competitions) and sub-elite fencers (participating in international and national competitions). The research was approved by Charles University, Faculty of Physical Education and Sport's Ethical Committee in Prague under reference number 095/2013. All participants voluntarily participated in the testing after being informed of the research's purpose and signed written consent.

Procedure

DNA Analysis

Genetic material was obtained through buccal swabs. A sampling set known as a cytology kit (CytoSoft, Medical Packaging, USA) was used for collecting samples. The genotypic analysis of selected polymorphisms was processed in both the accredited genetic laboratory Genomac – Research Institute, s.r.o., Czech Republic, and the molecular diagnostics laboratory at the Department of Biology and Medical Genetics of the 1st Medical Faculty of Charles University. These laboratories used polymerase chain reaction (PCR) for basic genetic testing.

Three different polymorphisms were examined. For *ACTN3* polymorphism (Arg577stop, rs1815739) SNP detection was optimized and performed using PCR to form heteroduplexes and subsequent DCE separation (ABI PRISM 3100 Genetic analyzer; Applied Biosystems, Foster City, NJ, USA, now a part of ThermoFisher Scientific). This principle of the method has been described in previous study [19]. The primer sequences were 5´CGCCCGCCGCGCCCCGCGCCCGTCCCGCCGCCCCC GCCCGCGATCAGTTCAAGGCAACAC 3´ - forward (5´Fluorescent-labeled) and 5´ TTCTGGATCTCACCC TGGAT 3´- reverse for *ACTN3*. The annealing temperature was 64°, and the separation temperature was 56°C. For primer sequences were used methods from previous studies for *ACE* I/D polymorphism (rs1799752) [20] and for *BDKRB2* +9/-9 polymorphism (rs1799722) [21].

Anaerobic Test

To diagnose anaerobic conditions, the Wingate test (WT30) was used. The test was performed on a calibrated Monark 824E bicycle ergometer (MONARK, Vansbro, Sweden). Before the testing started, participants had a warm-up on the ergometer. The heart rate of 120 beats·min⁻¹ was reached with a gradual increase in the pedaling rate with minimum resistance, which changed when participants reached the maximum pedaling speed. After reaching the top pedaling speed, the WT30 was begun. A 30-second test started with a braking resistance of 6 W·kg⁻¹. The resistance depended on the participants' weight and represented 0.106 kg·kg⁻¹ [22]. Participants were instructed to use their maximum effort for 30 seconds to perform the test. The participants were motivated to their maximal physical performance throughout the WT30 testing to obtain the most objective data possible.

The main focus was on speed-strength predisposition indicators, which can be detected from the WT30. The performance values representing the maximal anaerobic performance (P_{max}) in watts [W] were monitored. The values were determined from the best five-second interval of the test. Furthermore, the anaerobic capacity (AnC) in kilojoules [kJ], the total number of revolutions (TR), and the peak blood lactate concentration (LA_{peak}) in mmol·l⁻¹ were tested. Blood lactate concentration was determined electrochemically by using a Biovendor Super GL system. Capillary blood samples (20 µl) were diluted with a systemic solution (1 ml) immediately after collection to ensure hemolysis and stabilization of the samples. Afterward, Biosen 5030 [23] was used for the analysis of the blood samples. Before each testing, the analyzer was calibrated with a standard 12 mmol·l⁻¹ solution.

Statistical Analysis

For Hardy-Weinberg equilibrium (HWE) and verification of determined frequencies of alleles and polymorphisms, free online software SNPStats [24] was used. The Shapiro-Wilk test found that the data did not have a normal frequency distribution. For this reason, non-parametric statistical

procedures were used. The associations between genotypes of selected polymorphisms, individual variables from WT30 were verified through non-parametric ANOVA (Kruskal-Wallis test). Statistical significance was pre-determined as $p < 0.05$. For post-hoc tests (Mann-Whitney test), the effect size was calculated [25]: small effect r > 0.1, medium effect r > 0.3, large effect r > 0.5. Statistical analysis was performed in the R programming language (version 3.5.2), used in the IDE Rstudio (version 1.1.463).

RESULTS

The results were compared with each other according to a codominant model. The expectations were that each genotype would have its degree/weight on the effect. The following tables represent our findings of a statistically significant difference between selected genotypes. Furthermore, the table displays another combination of genotypes and monitored variables. The Hardy-Weinberg equilibrium confirmed the normal distribution of allele frequencies within *ACTN3* R577X ($p = 0.71$), *ACE* I/D ($p = 0.67$) and *BDKRB2* +9/-9 ($p = 0.48$).

Table 1 provides an overview of the essential characteristics of the monitored variables. As the number of participants in the group fell below 5 in some cases, these relationships were not (for *ACTN3* RX vs. XX and RR vs. XX; for *ACE* I/D vs. D/D and D/D vs. I/I) statistically verified (Table 2).

For *ACTN3* R577X polymorphism, no significant differences were found in the observed variables between genotypes. The *ACE* I/D polymorphism results presented in Table 1 display medium effect size between genotypes I/D vs. I/I in P_{max}, AnC, and LA_{peak} ($r > 0.3$). Participants with I/D achieved better results in the WT30 test (P_{max}, AnC values) and had higher blood lactate levels than participants with I/I. However, no statistically significant difference ($p > 0.05$) was detected here. In the *BDKRB2* +9/-9 polymorphism, a large effect size was found between homozygotes with +9 and -9 allele in P_{max} and AnC ($r > 0.5$) but without statistically significant difference ($p > 0.05$). In FI and LA_{peak}, there was found a difference, in both medium effect size and $r > 0.3$, between a group with genotype +9/+9 and a group with genotype -9/-9.

Table 1. Descriptive statistics of monitored variables.

Variable	ACTN3								
	RX (*n* = 11)			RR (*n* = 6)			XX (*n* = 3)		
	Mdn	*Min*	*Max*	*Mdn*	*Min*	*Max*	*Mdn*	*Min*	*Max*
P_{max} [W]	948.10	828.30	114.90	1087.15	788.10	1109.90	1106.80	749.20	1122.80
AnC [kJ]	24.20	21.70	25.60	26.55	19.80	27.80	25.50	19.70	25.60
TR [n]	52.30	45.70	60.20	50.75	45.50	57.80	47.80	41.60	54.00
FI [%]	37.20	21.00	43.70	35.60	33.90	40.20	44.50	26.20	47.50
LA_{peak} [mmol·l^{-1}]	10.00	7.50	11.90	10.85	8.80	13.30	8.10	6.50	9.50
Variable	ACE								
	I/D (*n* = 9)			D/D (*n* = 4)			I/I (*n* = 7)		
	Mdn	*Min*	*Max*	*Mdn*	*Min*	*Max*	*Mdn*	*Min*	*Max*
P_{max} [W]	1102.10	946.20	1114.90	851.95	749.20	1081.30	948.10	788.10	1122.80
AnC [kJ]	25.50	23.10	27.80	21.70	19.70	25.20	23.90	19.80	26.60
TR [n]	52.30	47.60	57.80	49.80	45.70	53.70	50.80	41.60	60.20
FI [%]	37.40	31.30	44.50	30.80	21.00	38.40	36.00	33.90	47.50
LA_{peak} [mmol·l^{-1}]	10.00	8.50	13.30	9.61	6.50	10.70	9.30	7.50	11.90
Variable	BDKRB2								
	+9/-9 (*n* = 9)			+9/+9 (*n* = 5)			-9/-9 (*n* = 6)		
	Mdn	*Min*	*Max*	*Mdn*	*Min*	*Max*	*Mdn*	*Min*	*Max*
P_{max} [W]	1015.40	788.10	1114.90	852.70	749.20	1106.80	1076.75	875.60	1122.80
AnC [kJ]	24.30	19.80	26.60	21.70	19.70	25.50	25.40	21.70	27.80
TR [n]	52.10	47.60	60.20	47.80	45.50	54.00	52.55	41.60	57.80
FI [%]	37.20	33.90	43.70	31.30	21.00	44.50	37.65	34.10	47.50
LA_{peak} [mmol·l^{-1}]	10.00	7.50	13.30	9.45	6.50	9.90	10.20	8.10	12.90

n – number; P_{max} – the maximal anaerobic performance; AnC – the anaerobic capacity; TR – the total number of revolutions; FI – the fatigue index; LA_{peak} – the peak blood lactate concentration

Table 2. Comparison of the WT30 anaerobic test results in polymorphisms.

Variable	ACTN3								
	RX vs. RR			RX vs. XX *			RR vs. XX *		
	z	p	r	z	p	r	z	p	r
P_{max} [W]	-0.704	0.525	0.171		–			–	
AnC [kJ]	-1.107	0.288	0.268		–			–	
TR [n]	0.704	0.525	0.171		–			–	
FI [%]	0.352	0.752	0.085		–			–	
LA_{peak} [mmol·l^{-1}]	-1.006	0.338	0.244		–			–	
Variable	ACE								
	I/D vs. D/D *			I/D vs. I/I			D/D vs. I/I *		
	z	p	r	z	p	r	z	p	r
P_{max} [W]		–		1.429	0.174	**0.357**		–	
AnC [kJ]		–		1.537	0.133	**0.384**		–	
TR [n]		–		1.006	0.351	0.251		–	
FI [%]		–		0.689	0.516	0.172		–	
LA_{peak} [mmol·l^{-1}]		–		1.271	0.221	**0.318**		–	
Variable	BDKRB2								
	+9/- 9 vs. +9/+9			+9/-9 vs. -9/-9			+9/+9 vs. -9/-9		
	z	p	r	z	p	r	z	p	r
P_{max} [W]	1.533	0.147	**0.410**	-0.589	0.607	0.152	-1.826	0.082	**0.550**
AnC [kJ]	1.133	0.298	**0.303**	-0.708	0.511	0.183	-1.738	0.091	**0.524**
TR [n]	1.400	0.190	**0.374**	0.000	1.000	0.000	-0.730	0.537	0.220
FI [%]	1.268	0.226	**0.339**	-0.354	0.749	0.091	-1.461	0.177	**0.440**
LA_{peak} [mmol·l^{-1}]	1.133	0.298	**0.303**	-0.059	0.979	0.015	-1.278	0.247	**0.385**

P_{max} – the maximal anaerobic performance; AnC – the anaerobic capacity; TR – the total number of revolutions; FI – the fatigue index; LA_{peak} – the peak blood lactate concentration; * without statistical analysis due to a low number of tested participants in the group

DISCUSSION

This study's focus was to detect whether polymorphisms are expected to positively affect speed to be present in a group of elite fencers. These expectations can be supported by studies focusing on the genetic makeup of various discipline athletes who require speed-strength predispositions [26].

The fencers were deliberately chosen for this research because the sports performance and the fencing movement's character are closely linked to the speed-strength predispositions. This fact can be confirmed by many authors' claims who state that fencing is a discipline where the highest demands are placed on anaerobic performance, visuomotor coordination and reaction time [18].

Revealing the differences between the D/D and I/D genotypes in *ACE* I/D polymorphism (Table 2), where heterozygotes reached higher P_{max} values and AnC, is entirely unexpected because of the initial thoughts. In most available studies, allele I was more often identified among athletes focusing on endurance disciplines [27]. The authors associate the I allele with a higher proportion of type I muscle fibers that indicate higher aerobic performance and higher fatigue resistance. Despite these facts, there are studies [28] in which a more frequent occurrence of the D allele was found among endurance athletes compared to controls and sprinters. Based on these results, it is impossible to unambiguously determine which of the monitored alleles has a decisive influence on maximal anaerobic performance. *BDKRB2* +9/-9 polymorphism group with -9/-9 genotype reached better results in P_{max} and AnC values. Homozygotes with the -9 allele had a higher fatigue index and higher blood lactate levels than homozygotes with the +9 allele. Alves et al. [29] found that the -9 allele was associated with higher metabolic efficiency in skeletal muscles. Therefore, it was considered crucial for the determination of endurance performance. Again, based on the results of various studies [17,23,29], the unequivocal effect of this polymorphism on speed or endurance performance cannot be deduced. This fact is also supported by our results, where fencers reached the best P_{max} values with the -9 allele. Of course,

fencing performance is not limited only for speed but other factors must be taken into account (spatial anticipation, psychomotor factors, personality traits etc.) [30].

As mentioned above, a large number of genes affecting sports performance have been identified, but no gene can be identified as predictive, i.e., a "gene for sport." Most associated studies monitoring a selected group of athletes compared to the control group are based on the assumption that due to their own genetically advantageous dispositions, the talented individuals are more often presented among groups of elite athletes [11]. However, the influence of other external (training, nutrition, methods of regeneration, socio-economic background, etc.) and internal (psyche, health, etc.) factors cannot be underestimated. Thus, it is likely that genetic factors on a particular athlete's sports performance will vary according to the individual. Nowadays, there is a trend to observe the largest possible sample of athletes, which often amounts to several hundred athletes. The presented study examines the performance of a limited number of athletes. Therefore, we do not, in any way, allow ourselves to show the results as objective and unambiguous. In the future similarly focused study, it would be interesting to observe how variables relate to different levels of fencers' performance.

It is necessary to consider that sports performance is supported by many polymorphisms simultaneously and understand it as a polygenic trait. Despite the high numbers of athletes tested in some genetically focused studies in sport, studies with a small number of athletes can also be considered beneficial.

CONCLUSION

The problems mentioned above are still in the phase of searching for the most suitable directions. The increasing number of studies will lead to an objectification of results from genetics and sports. Therefore, even though the study's results suggest associations between the specific genotypes and the performance achieved in selected tests, it is necessary to look at these associations with particular insights. This field of science and the knowledge of the athletes' genetic predispositions can be beneficial for optimizing the training process conditions, minimizing the health damage risk, or reaching the best individuals' abilities to achieve the best sports performance. Overloading athletes can harm their health and could mean the end of their careers.

To prevent all negative effects on athletes' bodies and performances, it could be essential to reveal these associations during childhood or adolescence. It should be highlighted that current studies are only the first steps in helping us better understand the associations between genetic factors and performance in sports.

ACKNOWLEDGMENTS

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