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ORIGINAL ARTICLE

The Relationship between Swimming Styles and Il-6 Rs1800795 Polymorphism in Professional Swimmers

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ABSTRACT
Background: Athletic performance can be improved with regular training, the contribution of genetic factors, nutrition and psychological factors. The aim of this study is to determine the effect of IL-6 rs1800795 polymorphism in Turkish swimmers and to compare the results with sedentary individuals.
Material and Methods: 75 people, including 45 professional swimmers and 30 healthy and sedentary individuals (control), participated in the study. DNA isolation from buccal specimens of athletes was performed using the commercial kit Invitrogen (Van Allen Way, Carlsbad, CA, USA). Genotyping was performed with real-time PCR.
Results: GG genotype and G allele were found to be higher in athletes. GG genotype and G allele were found to be higher in the control group. There was no statistically significant difference between the athletes and controls in terms of IL-6 rs1800795 polymorphism. In our study, when the IL-6 rs1800795 gene polymorphism was compared between the groups in terms of swimming styles-distances and genotypes, no significant difference was found.
Conclusion: Our study is the first to analyze the IL-6 rs1800795 polymorphism in Turkish swimmers. More studies are needed in terms of IL-6 rs1800795 to reveal the importance of genetic factors in determining the sports performance of the athlete and to clarify their effects on athletic performance. This first report, which includes relevant genetic markers and swimmers, will guide scientists for further studies.
Keywords: Genetics, Polymorphisms, Sports Genetics, Single Nucleotide Polymorphism, Swimmers, IL-6

INTRODUCTION
An individual's physical capacity reflects a complex phenotype influenced by genetic and environmental factors. How these related polymorphisms and metabolic pathways affect individual performance is a current research and interest in sports genetics, as it is important to identify genetic variants that make significant contributions to an individual's sports performance.

There are many polymorphisms that give us information about the systems that directly affect the genetic and environmental factors that affect an individual's athletic performance. Combinations of these polymorphisms give us phenotypic information. Since these polymorphisms and how the metabolic pathways they directly or indirectly affect contribute to individual performance, it is important to identify genetic variants that make great contributions to athletic performance, so studies on sports genetics have become extremely important. Sports genetics also aims to direct the talented athletes to appropriate training programs at young ages and investigates the contribution of genetic predispositions to sports performance.

Swimming is defined as the whole of meaningful movements that an individual makes to move a certain distance by moving in or on the surface, while sports swimming is defined as the ability of the athlete to complete certain distances in the liquid with free, back, breaststroke, butterfly, and mixed techniques in the shortest time[1]. During swimming, almost all the muscles and joints of the body, especially the arms and legs, work.

Interleukin-6 (IL-6), encoded by IL-6, is a cytokine that plays a role in the immune system response. IL-6 is found at 7p15.3 and, although its primary role is in immune functions, it has important roles in muscle repair and hypertrophy processes. IL-6 is a pro-inflammatory agent secreted by macrophages and T cells, stimulating the inflammation response especially in burns, trauma, and other tissue injuries, and also plays an important role in the formation of acute phase response and temperature regulation.

A common, functional C/G rs1800795 polymorphism in the 5′ flanking region of the gene is previously described[2]. Studies have shown that IL-6 rs1800795 polymorphism provides genetic predisposition to individuals in endurance sports. The minor “C” allele has been associated with the low level of plasma IL-6, and the “G” allele is thought to be associated with power-focused sport performance before[3]. IL-6 is the first muscle derived cytokines and muscle derived cytokines are defined as myokines.

In the present study, we analyzed IL-6 rs1800795 polymorphism in Turkish swimming athletes and compared the results with sedentary individuals. This is the first study to analyze the IL-6 rs1800795 polymorphism in Turkish swimming athletes. Our aim is to gain knowledge about the allelic distribution of the relevant polymorphisms and to evaluate the possible effects of these markers on the success of the athlete.

MATERIALS AND METHODS
Literature review: The literature search was searched in Google Academic and PUBMED databases with the keywords "sport, athlete, genetics, IL-6, polymorphism, sports genetics, swimming" and their combinations.
Study Group: In this study, which was conducted to determine the distribution of IL-6 rs1800795 polymorphisms in swimmers and their effects on athlete success, the study group consisted of 45 professional swimmers. The control group was selected from 30 healthy and sedentary individuals who did not have a regular sports history and were included in the study. All individuals had Turkish ancestry. The study protocol was carried out in accordance with the Declaration of Helsinki. Informed consent form was obtained from the parents of each child after the aim and protocol of the study were understood and accepted.
Genotyping: DNA isolation from buccal cells was performed using a commercially available DNA Isolation kit (Invitrogen; Thermo Fisher Scientific, Inc.) according to the manufacturer’s protocol. A mean total of 20 ng of the DNA was isolated from each sample, and the purity of the isolates were assessed based on the OD260/280 spectrophotometric ratio (Implen NanoPhotometer, München, Germany). Genotyping of the IL-6 rs1800795 polymorphism was performed using reverse transcription-quantitative PCR on a QuantStudio 3 (Thermo Fisher Scientific, Inc.) using a TaqMan Genotyping assay according to the manufacturer’s protocol (cat. no. 4362691; Thermo Fisher Scientific, Inc.).

Statistical analysis: Genotype distribution and allele frequencies between groups of athletes and controls were then compared by χ^2 testing using the GraphPad InStat statistical package. p values of <0.05 were considered statistically significant.

RESULT

Briefly, 28 (62,2%) of the swimmers were found to be as GG, 12 (26,7%) as GC and 5 (11,1%) CC for IL-6 rs1800795 polymorphism. Allelic distributions were counted as 75,6% for G allele, and 24,4% for C allele. In the control group, 15 (50%), 13 (43,3%) and 2 (6,7%) athletes had GG, GC and CC genotypes, respectively. For the allelic counts, G and C allele was counted as 43 (71,7%) and 17 (28,3%), respectively. When we examined the genotype distributions of our study group, we found that the GG genotype was superior. Likewise, G allele was superior to C allele, as expected. In statistical results, in both genotypes and alleles, no statistically significant difference was found between groups (p>0.05). The respective p values for genotypes and alleles of the athletes and controls were 0.3088 and 0.5948. The results are listed in Table 1.

Table 1: The genotype and allele comparison of the study cohort.

		Genotypes			p-value	Alleles		p-value
		GG	GC	CC		G	C	
Swimmers	Number	28	12	5	0,3088	68	22	0,5948
	Percentage	62,2%	26,7%	11,1%		75,6%	24,4%	
Controls	Number	15	13	2		43	17	
	Percentage	50%	43,3%	6,7%		71,7%	28,3%	

We also detected no statistically significant difference between swimming types, genotypes and average time (Table 2).

Table 2: Comparison of the swimming type times of the swimmers by genotype distributions (The ungiven genotypes were not detected in the swimmers)

Swimming Type	Genotype	N	Avg. time (Seconds)	±SD	p
50 m Breaststroke	GG	6	33.00	±2,28	0.542
	CC	3	32.00	±2,00	
100 m Breaststroke	GG	7	74.00	±5,35	0.264
	CC	3	70.00	±2,64	
200 m Breaststroke	GG	4	163.75	±12,03	0.255
	CC	3	153.66	±0,80	
100 m Butterfly Stroke	GG	3	60.00	±2,00	0.315
	GC	3	61.66	±1,52	
200 m Freestyle	GG	10	123.00	±3,80	1.000
	GC	3	123.00	±7,21	
50 m BackStroke	GG	3	30.00	±1,00	0.692
	GC	3	29.33	±2,51	
100 m BackStroke	GG	4	63.50	±2,88	0.836
	GC	3	64.33	±7,09	
200 m BackStroke	GG	3	138.00	±9,00	0.863
	GC	3	140.00	±16,52	

DISCUSSION

After intense and prolonged exercises, disturbances in the immune system of the cell and increased inflammation are observed. IL-6 is not only related to immune functions, but also a pleiotropic cytokine that regulates exercise-related muscle damage, muscle regeneration function, and metabolism during intense training[4, 5, 6].

In our literature reviews, there is information showing that intensive training causes tissue damage in muscles and joints and in cases where the resting period is insufficient, inflammation starts locally first. Subsequently, it is also found in studies that locally initiating inflammation causes a systemic inflammation[7, 8].

There are studies showing that IL-6 levels are temporarily increased after prolonged exercise, such as marathons, and that post-exercise muscle damage is stimulating for the IL-6 response. 182,183. When we continue to examine the literature studies, it was stated that low muscle glycogen content is an important stimulus for IL-6 gene transcription[9, 10].

In a study conducted in elite athletes, there are studies showing that long-term exercises not only cause immune system suppression, but also cause changes in psychological factors.

In our study, when the genotype (p = 0.3088; p> 0.05) and allele (p = 0.5948; p> 0.05) distributions between athletes and sedentary control group individuals in terms of IL-6 rs1800795 polymorphism are compared, no statistically significant difference was found. In terms of IL-6 rs1800795 genotype distributions, it was determined that in our athlete group, GG was 62.2%, GC 26.7% and CC 11.1% genotype, while the control group genotype was GG 50%, GC 43.3% and CC 6.7%. It is seen that no statistical significance was found in terms of genotype distribution between the groups, but the GG genotype was higher in both groups. In terms of allele distribution of the groups, it was determined that the G allele was 75.6% and the C allele was 24.4% in our athlete group, while the distribution of the G allele in the control group was 71.7% and the distribution of the G allele was 28.3%. It was found that the G allele was at a higher rate in both groups. In our study, when comparing IL-6 rs1800795 gene polymorphism between groups in terms of swimming styles-distances and genotypes (Table 2), no significant difference was found.

Before, Ruiz et al. (2010) examined the same polymorphism in 100 endurance-oriented, 53 power-oriented Caucasian Spanish male athletes and compared their results with 100 non-athletes as a control group. They reported that the GG genotype and G allele were significantly higher in their cohort[11]. In a Polish cohort consisted of 158 Polish power-orientated athletes and 254 volunteers, authors reported that GG genotype and G allele was higher in power athletes when com-pared to sedentary ones[12]. Like the Polish cohort, in an Israel cohort, Eynon et al. (2011) found the high frequencies of GG genotype and G allele endurance and power national and international athletes. Our results were in agreement with the studies in the terms of high GG genotype and G allele.

For the Turkish subjects, similar results to our findings were observed. In a study of elite athletes, authors reported that G allele was found to be more prevalent among elite athletes, but allele distribution was not statistically significant (p>0.05)[13]. Arica et al. (2018) reported the high frequency of G allele and GG genotype in their cohort, consisting of 40 long and short distance runner athletes. They reported no statistically significant difference between short and long-distance runners in the terms of genotype (p=0.07). Akkoc et al. (2020) found a statistically significant difference in Turkish ironman athletes in the terms of G allele[14]. All the previous studies conducted in Turkish samples were in agreement with our findings. The probable reason for these results is that our study cohort was conducted in the same geographic region within the same population.

CONCLUSION

The main limitation of our study is the low numbers of the athletes. Swimming is one of the most popular sport, but it is hard to find a cohort with the same or similar environmental conditions, such as training. Our players are the members of the same club, and they have the same training sessions for a long time.

Since it is the first study in Turkish population and swimming branch, we think that it will contribute to the future studies at national and international level, and the results obtained will increase the statistical power of statistics.

As a result, genetic tests and their effect on athlete selection for clubs use the current debate. At the same time, it is thought that organizing the training models of the athletes according to the haplotype groups after these tests will increase the performance of the athletes and reduce the level of disability. We think that more data on genotype-phenotype relationships are needed in terms of different sports disciplines, gender, ethnicity and different populations worldwide.

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Interest conflict: There are no conflicts of interest to declare.

Availability of data and material: Raw data were generated at [Istanbul, Turkey]. Derived data supporting the findings of this study are available from the corresponding author [Korkut Ulucan] on request.

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