

### The Role of ADRB2, ADBR3 Genes Polymorphism in the Development of Age-Dependent Adaptability, Movement Speed, Speed-Strength Qualities in Junior and Cadet Athletes

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#### ABSTRACT

In the theory and practice of modern sports medicine, an insufficient assessment of the significance of genetic factors, the inability to assess the choice of sports and methods of conducting sports competitions can become an obstacle to the normal formation of the functional capabilities of systems in the body of a young athlete and a decrease in sports results, as well as the achievement of high results by an athlete. This review article is devoted to the significance of ADRB2, ADBR3 gene polymorphism in junior and cadet athletes and its study.

It is known that genetic factors influence performance in sports such as strength and endurance, but only a few studies have investigated the relationship between genetic factors and sports performance in young athletes. Success in every sport requires different athletic qualities. For example, sprinters need qualities that define high speed, long-distance marathoners need endurance, and so on. It will be possible to achieve good sports results only in the conditions where the training process is created taking into account these genetically determined qualities [20; 21, 22].

One of the rapidly developing areas of modern genetics is the development of molecular genetic approaches that allow determining the propensity of a person to various types of activities, which allows to determine the degree of a person's propensity to various types of activities [9; 11; 12.]. Different physical traits are under unequal genetic influence. Manifestation of genetic influences at a young age is evident [1; 5; 6]. Each person has a genetically predetermined threshold for increasing the effects of exercise. Even system-intensive physical exercises cannot increase the functional capacity of the body beyond the limit determined by the genotype [2; 3].

With the help of genetic analysis, it is possible to determine not only the degree of inclination to a certain sport, but also problems in the athlete's health that can be a serious obstacle to sports victories. Based on the recent results of the decoding of the human genome, research is currently being conducted all over the world to determine the heritability of morphological and functional characteristics of a person using molecular genetic methods [4; 7; 8].

Sports genetics can make it possible to calculate the limits of performance of any type of

exercise for an athlete, which depends not only on the nature of the imposed task, but also on genetic components. Human genotype mainly determines important characteristics for athletes, such as strength, endurance, muscle tissue composition and mass, flexibility, neuromuscular coordination and reaction speed. Despite the relatively high heritability of athletic status and performance-related phenotypes, it is difficult to find genetic variants that contribute to success in some sports. To date, 185 DNA polymorphisms associated with athlete performance have been identified over the past 21 years [10; 13; 14]. Among the genetic factors, the athlete's innate talent is one of the important factors for success in sports [15; 16].

The use of the genetic characteristics of the organism leads humanity to new records, because now not only the stamina, regular training, will and motivation of the athlete, but also his "Olympic" heredity are important. The use of modern molecular genetic methods makes it possible to determine the individual characteristics of the human body. To date, about 200 genes associated with the development and manifestation of human physical qualities are known. A detailed study of these genes is necessary for the correct organization of the training process, for predicting the capabilities of athletes.

Genetic analysis gives us information about a person's genetic predisposition to a particular sport. For example, skeletal muscle consists of two types of muscle fibers: fast and slow. Slow-twitch fibers are characterized by a small force of contraction and a low fatigue index, they are involved in long-term work that requires low-intensity power for a long time. Fast fibers are characterized by a strong contraction force, but high fatigue, they are involved in short-term and high-intensity work. Aerobic exercise is very effective for slow-twitch muscles, which include swimming, rowing, tennis, long-distance running, cycling, and walking. And for muscles with a predominance of fast muscle fibers, sports with an anaerobic load (related to strength) are the most effective. These sports include wrestling, sprint running, powerlifting, arm wrestling, and rock climbing, which are examples of physical activity based on muscle anaerobic metabolism [19; 20].

In recent years, many studies have been conducted to investigate the role of different genetic variants in the endurance and strength performance of elite athletes [17]. The results of a number of scientific studies have shown that athletes with a high level of health have a dynamic balance between the functional reserves of the body and the factors affecting it [18; 19]. In addition, the effect of physical activity on the body of athletes increases in proportion to the stages of their professional development, which requires not only high health indicators, but also its optimal sufficient reserve [8; 19]. In this case, the value of the second indicator is the basis of confidence that the athlete can achieve success, and it is an indicator characterized by high efficiency and stability of movements in extreme conditions [1; 9]. A number of anthropometric, compositional parameters that have a greater influence on the choice of the type of sport, physical activity and ability, in particular, the total dimensions of the body, body type, body proportions, have a high genetic basis in sports activities. It allows them to identify promising athletes along with psychological, physiological and biochemical factors. In the last few decades, certain genetic factors responsible for the development of the aforementioned characteristics in humans have been identified. For this reason, sports genetics provides useful information on how to improve performance in competition, which athletes are selected for competition, and which of them are up to the task. Selection of young athletes with high prospects for genetic characteristics (at the same time, assessing the minimal risk of intensive physical activity for their health) is one of the most important priority issues in sports medicine, which can be solved by modern genetic methods [3; 5]. The human genotype determines important characteristics such as strength, endurance, composition and mass of muscle tissue, flexibility, neuromuscular coordination, reaction speed in athletes [18; 19]. The "Human Genome" project ended more than a decade and a half ago [106; p. 860-921.]. Later, the International HapMap Consortium ("haplotype map") of

1,000 genomes and coding human DNA sequences showed similarity in more than 99%. A mere 1 percent variation in a person's DNA can potentially inform a person's athletic ability. Identifying these variations can be important in determining the high performance of athletes [4; 9]. The use of gene profiling methods can be useful for individual optimization of physical training and positive effects on sports performance. Genes affect factors such as the composition of muscle fibers or the activity of aerobic and anaerobic enzymes. In turn, these genetic factors can play a key role in sports performance, as their effectiveness can play a decisive role, especially in the elite sector. To date, the most genetic variants associated with resistance have been studied. Endurance refers to the body's resistance to fatigue and the ability to recover quickly after physical exertion [13; 18].

Identifying the genes responsible for athletic performance is difficult because each gene makes a small contribution to the overall heredity. The detection of these genes is especially important in young athletes. It is recommended that children engage in sports that match their abilities. Therefore, it is necessary to direct children to certain types of sports from adolescence. In general, it has been shown that the use of genetic polymorphisms can serve as an additional tool in the identification of talents and in the selection of sports, as well as in the creation of effective exercise programs for young athletes [1; 6]. Genetic predisposition to endurance or speed is not only determined by more than a dozen genes responsible for cardiovascular function, but each genetic variant probably contributes a small percentage to the total variation in exercise capacity. For this reason, many changes in genetic makeup can alter gene expression and help an individual succeed in endurance or power sports [8; 10]. Endurance is a measure of an athlete's ability, strength, and speed to perform maximal exercise for 20 minutes or more. Endurance requires constant control of parameters such as the number of heart beats, speed and average blood pressure, which requires proper control of the optimal cardiovascular system. Long-distance runners, cyclists, and triathletes with maximal endurance can exhibit prolonged physiological activity using an enhanced aerobic phenotype.

Studies on ADRB gene polymorphisms and high scores are lacking, mostly in endurance athletes [18; 19]. The cardiovascular system's response to exercise is individual, which suggests that genetic variations in genes encoding receptors involved in the regulation of cardiovascular system activity may affect physical capacity [13]. Previously, the ADRB2 Gly16Arg polymorphism was associated with resistance, in which the Arg (A) allele had a positive effect [16]. ADRB2 and ADRB3 genes serve as informative markers in the correction of endurance and weight indicators in athletes [8; 20].

The human ADRB3 gene is located on chromosome 8 at position 8p11.1-p12 and encodes a polypeptide of 408 amino acids, including 2 exons and 1 intron. A mutational substitution of thymine to cytosine at position 190 of the gene results in the replacement of tryptophan (Trp) at amino acid position 64 with an arginine (Arg) residue in the first intracellular loop of the ADRB3 receptor. This mutation is associated with a tenfold decrease in sensitivity to external factors that control adipocyte function. The ADRB3 gene at position 190 has a mutation site that can detect the presence of thymine (T) or cytosine (C). One of the mutations in the ADRB3 gene results in the replacement of tryptophan with arginine at position 64 of the coding sequence, which may affect the ability of the receptor to interact with Gs proteins in adipocytes [11].

Central and peripheral physiological characteristics such as increased left ventricular contractility, greater proportion of type I muscle fibers with higher mitochondrial and capillary density, higher VO<sub>2</sub>max, higher lactate thresholds, increased fat oxidation, and ability to reflect greater control of acid-base homeostasis. Athletes with these characteristics differ from other athletes and the general population [10; 12; 13]. Exercise-induced increase in mitochondrial density in muscle promotes efficient utilization of oxygen and utilization substrate by working

muscles, resulting in a significantly delayed onset of muscle fatigue due to reduced substrate availability. Although this adaptation mechanism can be improved by long-term preparation for training, however, the results showing this performance in athletes have been shown to be much lower than the performance of athletes with the  $ADR\beta 2$  gene, which emphasizes that genetic characteristics can influence athletes' long-term training endurance [8; 9; 12; 13].  $\beta 2$ -adrenergic receptor ( $ADR\beta 2$ ) encodes a 2-adrenergic receptor mainly responsible for bronchodilation, increased ventricular function and vasodilation, all of which have direct effects on cardiovascular and cardiac exercise [144]. Studies have highlighted the importance of this gene for increasing endurance due to its expression in the cardiovascular, respiratory, metabolic and musculoskeletal systems, as well as its effect on lipid metabolism to regulate energy expenditure from adipose tissue. The cytogenetic location of the  $ADR\beta 2$  gene is between the q31 and q32 bands of the 5th chromosome [13; 17]. These polymorphisms are unique to Arg16Gly(Arg/Arg, Arg/Gly and Gly/Gly) and Gln27Glu(Gln/Gln; Gln/Glu and Glu/Glu variants) with increased lipolytic sensitivity, as well as regulation of vascular tone and signalling. related to the expression of features [18; 19]. A clinical study has shown that weight gain during adolescence, which gradually increases in adulthood, is more common in people with the Gly form, even if it is represented by a single allele (Arg/Gly). Identifying the potential impact of the  $ADR\beta 2$  single nucleotide polymorphism on the endurance of athletes, the receptor function of the cardiovascular, respiratory, metabolic and locomotor systems, as well as epigenetics and its interaction with the environment on the various complications that may develop during training adaptation for people with genetic polymorphisms need to be determined. Evidence is still insufficient to reliably determine the polymorphic effects of aerobic phenotypes on cardiovascular, respiratory, metabolic, and musculoskeletal  $ADRB2$  receptor systems. [11; 15; 19; 20; 21].

Aspects such as training intensity and volume allow the improvement of genetic polymorphisms to further enhance physiological characteristics and performance during endurance exercise. It also allows genotyping to be used as a talent identification tool. These data can assist in the development of physical training protocols and talent identification criteria, taking into account the specific demands of the sport. Exercise protocols aim to increase oxygen and substrate availability and stimulate efficient energy production from working muscles [16].

A proven method of increasing fatigue resistance is a form of interval training, in which a large number of exercises are combined with short rest intervals at a lower intensity. The goal is to improve lactate kinetics, stimulate neurological models of muscle fiber recruitment, and improve fatigue endurance and athletic performance [18; 19]. As mentioned earlier, epinephrine stimulation of  $\beta 2$ -receptors increases the activity of  $Na+K+ATPase$  enzyme. Evidence shows that endurance athletes have higher concentrations of the enzyme  $Na+K+ATPase$  in their blood plasma membrane. Activation of  $Na+K+ATPase$  enzyme by catecholamines is explained by stimulation of action potential and force production in skeletal muscles. Thus, exercise regimens can exploit the force-producing capacity of skeletal muscle by performing high-intensity sprint exercise to increase  $Na+K+ATPase$  concentrations and thereby increase the amount of force produced by muscle fibers during stimulation [8; 9; 14].

The polymorphism of subjects expressing homozygous Gly16 alleles showed greater capacity for exercise due to higher aerobic performance and increased exercise responses. Thus, healthy subjects expressing homozygous Gly16 alleles are more likely to have the greatest potential for strengthening endurance performance, as it is highly expressed in the cardiovascular, respiratory, and metabolic systems. However, there is also conflicting evidence showing that homozygous Gly16 allele carriers are negatively associated with endurance performance [7; 11; 13; 14; 15].

In conclusion, it can be said that molecular genetic studies allow to identify potentially important

markers of DNA polymorphism, which can provide a predisposition to success in a certain sport.

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