Bölüm 6

Doping and Genetic Impact in Sports

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Abstract

The aim of this study was to examine the problems caused by doping and genetic tests in sports. Studies registered in Web of Science, Pubmed, Pubmed-Central and Google Scholar internet search engines were examined in the current research. The use of doping in sports is becoming an increasingly important issue. Doping is the process of artificially enhancing performance once or continuously. These practices are performed with traditional and genetic origin nowadays. The doping substances may cause irreversible health problems for athletes. Despite the great harms caused by the use of doping, there are serious increases in the use of these substances. This may have been the result of the sport becoming a major industry over time. The Human Genome Project has undertaken an important mission in the diagnosis and treatment of diseases. However, this may have led to some abuses. These are gene doping, the prevalence of which has increased recently, and genetic tests to determine the sports branch. Although genetic testing provides many benefits to human health, it may cause an important problem such as genetic discrimination. However, the correct use of genetic tests may make serious contributions to athlete health. Interest in both doping use and genetic testing is increasing nowadays. The consequences of being the best in sports on athlete health are also concerned. As a result, raising awareness of sports stakeholders and thinking of sports for health may be an important step in solving the problem. On the contrary, sports will turn into a phenomenon that serves different purposes and will be used as a means of superiority among people.

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Introduction

Sports are physical activities including both mental and psychological health. It is far from the aim of health and is expressed in the superiority today. Unfortunately, the superiority has increased the interest in sports. Since sports are a financial sector, the achievements of athletes has been expressed in material values over time. As a result, this causes serious pressure on athletes. Due to this pressure, athletes focus on continually winning in the competition. Therefore, the use of doping in sports has significiantly raise (Kahya, 2023).

HGP (Human Genom Project), completed in 2003, revealed approximately 3 billion base double nucleotide sequences of humans and the presence of an estimated 29,000 to 36,000 genes (Ulutin, 2005). *HGP* was initially used effectively in the diagnosis and treatment of diseases (Karabulut et al., 2019). The data obtained from *HGP* have been used to improve sports performance. This development has added a new dimension to sports performance and revealed the importance of genetic tests in the selection of elite level athletes. However, the use of genetic testing may cause some problems. The researchs provide that genetic tests include many risks. For this purpose, in the study by Williams et al. (2016) it was found that genetic testing on humans may raise a number of problems. In another study, Demir (2013) found that genetic manipulations may endanger people's freedom by instrumentalizing them. The health risks of doping substances and the ethical subjects arising from genetic test are important problems that must solve.

The aim of this study was to examine the problems caused by doping practices and genetic tests in sports from many aspects. The results of the research are expected to guide scientists serving this field.

Material & Method

The study included problems caused by the use of doping substances in sports and genetic manipulation. The current research is designed to summarize the studies on the subject within the literature. The research included the examination of data registered in Web of Science, Pubmed, Pubmed-Central and Google Scholar search engines. The keywords "sports and doping and risks", "gene doping and health risks", "sports and genetics", "sports and genetic tests", "sports and ethic issues", and "sport and the future" into internet search engines were written. Experimental, meta-analysis, systematic review and traditional and comprehensive review articles were involved in the research. A total of 170 study were included in

the research. This researchs were evaluated and were record. Publications that are not related to the research subject and do not comply with scientific theories were excluded from the scope. As a result, 54 studies suitable for the research aim were determined according to the *PRISMA* technique developed by Moher et al. (2009). The desing of research is presented in Figure 1.

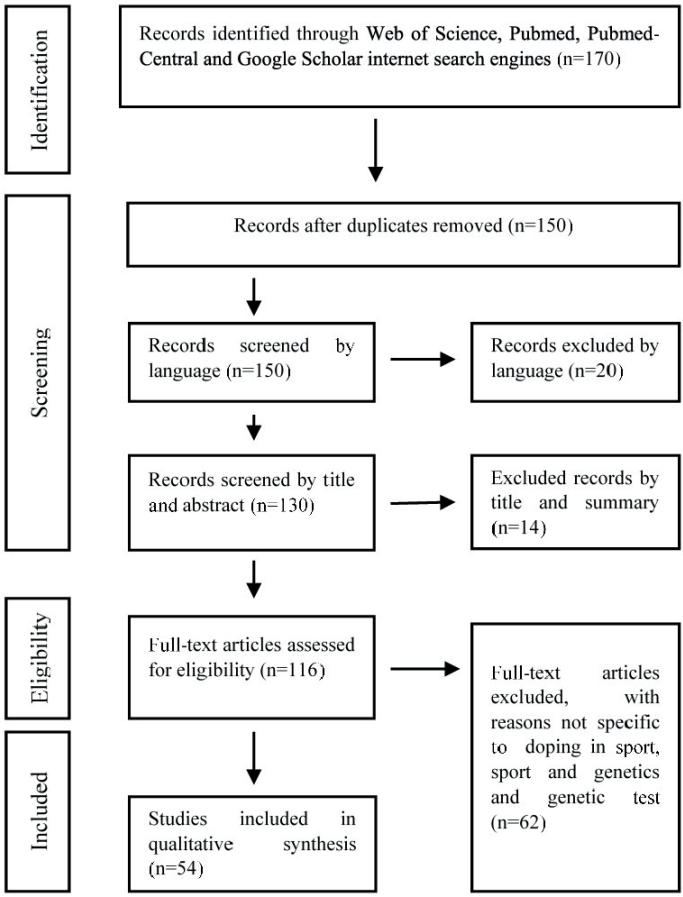

Figure 1. Design of the studies used in the research according to the PRISMA

Use of Doping in Sports

It was clear that athletes consumed mushrooms to increase their performance, in the BC, and Roman warriors used stimulants (Songün et al., 2015). Doping is the excessive use of substances that are not in the metabolism to artificially increase performance once or continuously (Öngel,

1997). Doping, which dates back to the 8th century BC, is based on the beverage consumed by the South African natives to be durable in hunting and religious ceremonies. The doping word gets its name from the drink called "Dope". This word has been translated into English as Doping over time and has become the common definition of performance-enhancing substances and methods (Ünal and Ünal, 2003). Due to the death of a British cyclist from an overdose of trimethyl in 1886, the *IOC* (International Olympic Committe) banned the use of doping in sports with its decision in 1967. After this decision, the World Anti-Doping Agency (*WADA*) was established in 1999 under the leadership of the *IOC*. Since its establishment, *WADA* has been fighting against doping substances. To this aim, *WADA* updates its list of doping substances every year (Karataş et al., 2012).

The use of doping substances can cause irreversible health problems for athletes and even serious cases that may result in death (Akarsu, 2021). Some information on traditional doping is presented in Table 1 (Ertin and Bardakçı, 2020).

Table 1. Traditional doping with metabolic functions and health-related conditions

Doping	**Function**	**Health Risks**
Anabolic Androgenic Steroids	Increase the level of testosterone in the body and stimulates muscle growth.	Dysfunctions of the liver, hormonal and reproductive system.
Stimulants	Provide endurance capacity and concentration through activation of anaerobic energy pathways	Hypertension, stroke, insomnia, psychological disorders and palpitations.
Growth Hormone	Stimulates muscle hypertrophy and reduction in fat mass.	Cancer and some degenerative disorders in the brain.
Erythropoietin	Has positive effects on increasing the number of red blood cells and endurance capacity.	Stroke, pulmonary embolism, hypertension, increase in blood viscosity.
Beta Blockers	Lower the heart rate and reduces anxiety about sports performance.	Low pulse, increased respiratory resistance, and decrease in endurance performance.

Except for Table 1, there are pharmacological, chemical and physical manipulations for blood doping (Dallı et al., 2015). The change of sports performance with traditional doping substances has turned into a different situation with the emergence of genes. Gene doping, which is an application beyond traditional doping practices, is the best instance of this. Gene doping is the non-therapeutic use of genes to improve the performance of athletes (Wells, 2009). Gene doping has added a different dimension to traditional

doping practices overtime. Some genes that may be candidates for gene doping and their locations and performance functions are presented in Table 2 (Ulucan et al., 2015; Lopez et al., 2020).

Table 2. Candidate genes for gene doping and their characteristics

Gene	Target tissue	Physiological response	Chromosome location	Performance feature
ACTN3	Skeletal muscles	Regulates myofiber contraction.	11q13.1	Speed-Endurance
ACE	Skeletal muscles	Stimulates the development in endurance performance.	17q23.3	Speed-Endurance
eNOS	Blood vessels	Stimulates the endothelium on the inner surface of the vessels.	7q36	Speed-Endurance
EPO	Hematopoietic	Increases the need of cells for oxygen.	7q22	Endurance
VEGFA	Vascular endothelium	Enhances the development of blood vessels.	6p12	Endurance
HIF1A	Hematological and immune system	Provides an increase in red blood cells with the use of cell energy.	14q23.2	Endurance
MSTN	Skeletal muscles	Inhibits the development of muscle tissues.	2q32.2	Strength
IGF1	Skeletal muscles	Increases muscle development.	12q23.2	Strength

Abbreviations: *ACTN3:* Alpha-actinin 3, *ACE:* Angiotensin converting enzyme, *eNOS* : Nitric oxide synthase 3, *EPO:* Erythropoietin, *VEGFA:* Vascular Endothelial Growth Factor-A, *HIF1A:* Hypoxia inducible factor 1 alpha, *MSTN*: Myostatin, *IGF1:* Insulin growth factor

Gene doping is an illegal practice that poses many health risks to athletes (Boer et al., 2019). For instance, *EPO* affects the viscosity of the blood by increasing the proliferation of red blood cells. Fatal health risks such as heart attack and stroke may occur (Unal and Unal, 2004). For this reason, the use of *EPO* as a gene transfer may cause vulnerable to many unknown health risks of athletes.

The development of gene therapies and the increase in treatment opportunities show that practices for gene doping may continue (Cantelmo et al., 2020). Due to this development, many unknown aspects of gene doping will be revealed by scientists. However, there will encounter some difficulties in determining gene doping. Although *WADA* provides all kinds

of support to laboratories that perform tests to detect gene doping, it has serious difficulty in detecting these substances (Sugasawa et al., 2021).

The Ethical Dimension of Doping

Due to the increasing economics of sports, athletes have applied unethical behaviors in competitions (Çelebi et al., 2017). Doping, which is one of these behaviors, is an undesirable practice in sports (Lu et al., 2023). This substances seriously affects both physiological and mental health. Despite the many physiological and mental negativities of doping, the use of these substances is importantly increasing. Although the information and warning are provided by *WADA*, athletes regard these substances as a routine of their sports life and use intensively.

There are many problems caused by the use of doping in sports. Doping is a substance that affects athletes not only physiologically but also ethically. Sport is a phenomenon that has ethical values (Gençtürk et al., 2009). Despite to this ethical values, athletes use intensively this illegal substances in their sport branchs. These substances, which are used by the athlete to reach a high level of performance, are not an appropriate behavior in sports ethics (Vlahovich et al., 2017).

The Relationship Between Genetics and Sports

Human's chromosomes, localized in the cell nucleus, store all the information of the genome. The information is converted into proteins, which are necessary for metabolism, by genes. Thus, the genetics has a very important in human's life in terms of heredity (Doğgün, 2022). Genetic examines genome structure, gene function, recombination rate, and the relationship of mutations with disease (Karayılan et al., 2013).

Due to the developments in omics technologies, many features of the human genome are revealed by the researchs. In parallel with these developments, the relationship between sports and genetics has begun to be examined in detail. For this purpose, the relationship between sports and genetics focus on the genetic diversity of exercise and differences in the expression of gene variations (Akgül et al., 2018; Eken et al., 2021). The first studies on the relationship between sports and genetics started on twin, identical twin and fraternal twin, individuals. These studies were included in the field of sports genetics as a source of sports genomics over time (Eken et al., 2018). Sports genomics is a concept that includes basic motor skills such as endurance, strength, sprinting, flexibility, neuromuscular coordination, etc (Vancini et al., 2014; Bragazzi et al., 2020). 250 gene variants have

identified for the relationship between sports performance and genes so far (Tarakçıoğlu and Doğan, 2013; Süel and Pehlivan, 2015; Dinç and Gökmen, 2019). Some candidate genes are presented in Table 3 (Maffulli et al., 2013; Jacob et al., 2018; Balberova et al., 2021; Semenova et al., 2023).

Table 3. Characteristics of candidate genes related to sports performance

Gene	Choromosome location	Effect on sports performance
ADRB1	10q25.3	Provides increases in endurance exercises, especially MaxVO2.
AMPD1	1p13.2	Catalyzes the deamination of adenosine monophosphate to inosine monophosphate and produces *ATP*.
CKM	19q13.32	Plays a key role in the rapid and powerful contraction of muscles in a short time.
COL1A1	17q21.33	Arranges the lenght of soft tissues such as tendons and ligments.
COL5A1	9q34.3	Determines sensitivity to tendon and anterior cruciate ligament and muscle-tendon flexibility.
IGF1	12q23.2	Stimulates the growth of tissues such as muscles, bones, cartilage, etc.
MCT1	1q12	Increases muscle endurance related to lactic acid in exercise.
NOS3	7q36	Provides an increase in endurance and power capacity in sports.
PPARA	22q13.31	Maintains the breakdown of fatty acids in long-term exercises.
mtDNA loci	mtDNA	Makes increase in aerobic endurance capacity.
TFAM	10q21	Supports the development of endurance capacity increasing mitochondrial biogenesis.
VEGFA	6q12	Improves endurance performance by affecting the vascular mechanism.

Abbreviations: *ADRB1:* Beta-1 adrenergic receptor, *AMPD1:* Adenosine monophosphate deaminase type 1, *CKM:* Creatinekinase, M-type, *COL1A1:* Collagen type 1 alpha 1, *COL5A1:* Collagen type 5 alpha 1, *IGF1:* Insulin growth factor 1, *MCT1:* Monocarboxylate transporter 1, *NOS3:* Nitric oxide synthase 3, *PPARA:* Peroxisome proliferator-activated receptor alpha, *mtDNA loci:* Mitochondrial DNA, *TFAM:* Transcription factor A mitochondrial, *VEGFA:* Vascular endothelial growth alpha.

It is believed that genes that have an effect on sports performance may be associated with many physical parameters. For this reason, 66% of sports performance is explained by genetic factors (Subak et al., 2017). On the

other hand, this still is a controversial issue because of some uncertainty. Although the inheritance of skeletal-muscle phenotypes are well known, the mechanisms underlying them are not clearly (Pratt et al., 2020). However, obesity, which is considered as the source of most health problems, is a disease that may be explained by genetic factors (Tunçbilek, 2005). Additionally, genetic factors may be also associated with increased risk of soft tissue diseases. EDS (Ehlers Danlos Syndrome) is characterized by hypermobility of joints and skin hyperelasticity.

Genetic Discrimination and Its Reflection on Sports

Thanks to the instrumentalization of the human body for scientific purposes, many genetic-based researches have been conducted on human health. However, these researches have led to some abuses, over time (Bulut, 2019). As a result, the use of genetic research for individual health insurance and employment purposes has caused some ethical problems (Çetin, 2017). One of these problems is genetic discrimination, in which people are classified according to their genetic structure (Tuğ et al., 2002). UNESCO, which conducts serious studies on genetic discrimination, prepared a new declaration in 2003. In 2005, this declaration was included into bioethics and human rights (Gökçümen and Gültekin, 2009).

Genetic tests are important issues that are highly discussed. Genetic studies, which had initially used for the treatment of diseases, were later used in the selection of talent in sports. This tests have been associated with genetic superiority among humans, recently (Akçay and Tıngöy, 2021). Thus, genetic testing must use carefully in sports. If genetic tests is used correctly, it may benefit athletes. However, genetic testing in sports is a controversial issue, nowadays. Since genetic tests may not always be accurate (Pickering and Kiely, 2020). On the other hand, even if genetic testing data may determine an athlete's physiological superiority, ethical issues exist always in the field of sports (Webborn et al., 2015).

The Future of Sports Performance and Its Possible Risks

Data on athlete skills are provided directly to individuals today. For this purpose, genetic tests for skills in sports have become increasingly popular and have started to be provided as "Direct to Consumer" service (Du and Wang, 2020). The validity and reliability of this practice has brought along some discussions. Despite this, these tests may make serious contributions to athletes. For this reason, knowing the genetic predisposition of athletes to injuries is important for personalizing sports (Appel et al., 2021; Kahya, 2022). In the study by Rodas et al. (2019) it was found that some gene

polymorphisms, rs11154027, rs4362400, and rs10263021, may be an important risk factor for tendon injuries.

Sports technologies affect the development of performance. This is more complicated for elite-level athletes. Since athletes want to be the fastest, strongest and most durable. To this end, genetic developments could make it possible to transform from a supermouse model to a genetically modified human model (Tural et al., 2011). This result suggests that genetic improvements can often promote the advancement of genetic testing. Therefore, genetic testing is predicted to play a fatalistic role in sports in the coming years. As a result, many problems related to genetic tests may challenge people in the future (Miah, 2012).

Discussion

The study was conducted to examine the problems that arise as a result of the use of doping in sports and genetic tests from many perspectives. The use of doping in sports, included gene doping, and problems related to athletes' health tend to increase continuously. Unfortunately, the use of these substances by young athletes for early success in sports is a negative situation for the future of sports. Although *WADA* has taken the necessary measures regarding the use of doping in sports, some substances are still not on the banned list. This causes serious problems both in terms of athletes' health and ethical principles. For this purpose, in the study by Luigi et al. (2017) it was found that drugs containing *PDE5i* (Phosphodiesterase Type 5 Inhibitors) may cause many health problems which have cardiovascular, neurodegenerative, muscular, metabolic, etc. As a result of the same study, it was reported that healthy athletes who use these drugs may achieve unfair success in sports by winning races under unequal conditions. In another study by Møller and Dimeob (2014) found that athletes may encounter serious health problems by using doping substances. In a study by Fischetto and Bermon (2013) on gene doping it was found that doping may cause serious health problems because it causes uncontrolled production of specific proteins. Brzeziańska et al. (2014) concluded in their study that uncontrolled manipulation of genetic materials may cause some health risks in athletes. Although there are many suggestions to reduce the harms caused by the use of doping in sports, adhering to some human values can be an effective strategy to solve the problem. To this end, Altukhov et al. (2019) concluded in their study that the best defense against doping in sports is to take into account the purposes of being human.

Another issue as important as doping in sports is the directing of athletes to sports branches according to genetic test results. Genetic tests, which play an important role in some conditions, such as sports injuries, early detection of physiological damage, are applications that need to be interpreted carefully. On the contrary, genetic testing can cause social stigma and discrimination. For this reason, Tanisawa et al. (2020) reported that genetic applications in sports may cause genetic discrimination. When the findings obtained from the study and the results of the study in the literature were compared, it was concluded that similar data were obtained.

Conclusion

The current study has revealed that doping substances can cause great harm to human health. The raising popularity of the sport is to increase both the number of genetic tests and the use of doping substances. Scientific studies are used to excel in sports. The current study supports this results. Doping and genetic testing may pose serious dangers, especially for young athletes. As a result, raising awareness of sports stakeholders may be important for solving the problem. On the contrary, sports will turn into a phenomenon that serves different purposes and will be used as a means of superiority among people.

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