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# Assessment of male football players' physical fitness levels based on certain gene (*AGT* rs699 & *IL-6* rs1800795) polymorphisms

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## Abstract

**Background**: The present investigation aims to elucidate the physical fitness attributes inherent in male football players about the Angiotensinogen (*AGT*) rs699 and Interleukin-6 (*IL-6*) rs1800795 gene polymorphisms. **Methods**: Twenty-two male football players, aged 18 to 35 years, voluntarily enrolled in the study conducted within the North Macedonian Super League. Genomic DNA was extracted from oral epithelial cells. Genotyping procedures were then executed using real-time polymerase chain reaction (RT-PCR). All participants were actively involved in an intensive training program six days a week throughout the six-week pre-season preparation phase. The male football players underwent physical assessments both before and after the training program. Statistical analysis involved the use of the Paired-Sample *t*-Test to discern differences between the pre-test and post-test measurements of the male football players. **Results**: When stratifying the outcomes according to the *IL-6* genotype and *AGT* genotype variables, statistically significant differences were not observed in Squat Jump (SJ), 5 m sprint, 30 m sprint, Counter Movement Jump (CMJ), Drop Jump (DJ) evaluations, and body fat percentage ($p > 0.05$). In contrast, statistically significant differences were observed in the Yo-Yo Intermittent Recovery Test Level 2 (Yo-Yo IRT 2), 10 m sprint, and One Repetition Maximum (1RM) bench press variables (Yo-Yo IRT 2: CC and CT $p = 0.005$, $<0.001$; 10 m sprint: CT $p = 0.024$; and 1RM bench press: CC, CT and TT $p < 0.001$, $<0.001$, 0.045, respectively). Significant differences were also identified in the Yo-Yo IRT 2, 10 m sprint, and 1RM bench press measurements (Yo-Yo IRT 2: CC, CG and GG $p = 0.002$, 0.021, 0.001; 10 m sprint: CC and GG $p = 0.020$, 0.028; and 1RM bench press: CC, GG $p = 0.001$, 0.001, respectively). **Conclusions**: In summary, the *AGT* rs699 and *IL-6* rs1800795 gene polymorphisms may play a role in the adaptations induced by training in male football players.

## Keywords

Football; Physical fitness; Sprint; Jump ability; Strength; *AGT*; *IL-6*

## 1. Introduction

Research has shown that genetic variation is significantly associated with athletic performance, with peak performance often dependent on specific base pair configurations [1–3]. However, it is important to emphasize that genetics is not the only determinant of athletic performance. Factors such as environmental conditions, epigenetic interactions, lifestyle choices, dietary habits, and changes in motivational dynamics play a crucial role in shaping athletic outcomes and exert a significant influence on an athlete's performance in their respective discipline [4–8]. In addition, complex traits that constitute an essential aspect of physical performance, such as endurance, muscular strength, power, speed, and agility, have been reported to require a very specific genetic combination [5, 9, 10]. The corresponding matches in DNA sequences have a positive effect on adaptation to physiological changes in metabolism caused by athletic stress and the development of peak performance [11, 12].

A previous investigation identified over 250 genetic variations connected to athletic prowess. Of these, 128 variants have shown a positive correlation in several studies; in particular, 41 are associated with endurance, 45 with power, and 42 with strength [1]. The angiotensin (*AGT*) gene and its polymorphisms, including rs699, which is associated with power sports performance, and the interleukin 6 (*IL-6*) gene and its variants, such as rs1800795, which affects general physical fitness, are of particular importance in the develop-

ment of athletic performance [1, 13, 14]. The *AGT* gene, which plays a role in the maintenance of physical performance, consists of a 1455-nucleotide sequence translated into 485 amino acids and is located on chromosome 1 at locus 1q42.2. The *AGT* Met235Thr (T > C) variation has been associated with increased speed, power, and strength in elite athletes [10]. Furthermore, *AGT* is recognized as a genetic factor that is advantageous for exercise or physical activities, particularly regarding skeletal muscles, peripheral blood flow, and blood pressure regulation [15, 16].

The role of the renin-angiotensin system (RAS) is crucial when considering *AGT* in the context of hypertension and cardiovascular, renal, and salt-sensitive diseases. AGT, a protein synthesized in the liver, is a key element of the RAS. Renin converts AGT into angiotensin I, which is a precursor of angiotensin II. Angiotensin II is instrumental in controlling vascular resistance and maintaining sodium balance, primarily through vasoconstriction [17]. Elevated AGT levels lead to increased production of angiotensin II, which in turn can cause an increase in blood pressure. The Met235Thr (T > C) variant in the *AGT* gene, in which methionine is replaced by threonine at the 235th position of the protein, has been associated with notable changes in blood pressure control, increased risk of hypertension, and elevated plasma AGT levels [18–20].

The *IL-6* rs1800795 gene polymorphism is another genetic variant that plays a significant role in the development of physical performance levels, including conditioning, muscle repair, and hypertrophy. *IL-6* functions as both a cytokine and a myokine and is located at position 7p15.3 [21]. Its primary biological effects, such as cell survival, proliferation, differentiation, immune response, and apoptosis, are mediated by its interaction with the interleukin-6 receptor alpha, which is predominantly found in inflamed tissue. IL-6 is not only crucial for immune functions but also influences various aspects of athletic performance [22–24].

The production of IL-6 is influenced by a specific genetic variation, where a guanine base at position 174 is replaced by cytosine. This C/G polymorphism (rs1800795), located in the 5′flanking region of the gene, has functional implications. Studies have shown that the C allele is linked to lower plasma levels of IL-6, whereas the G allele is associated with enhanced power-based physical attributes like strength and speed. In addition, the C allele is frequently found in individuals with a predisposition to endurance, which is attributed to its role in reducing endogenous glucose synthesis and increasing lipid oxidation [25, 26]. Research in the field of athletic performance is increasingly focusing on the exploration of genetic variations and their significant effects on individual performance capabilities [8, 24].

Genetic markers, including *AGT* and *IL-6*, have been identified as influential in athletic performance in different ethnic groups [15, 18, 19, 26]. Nevertheless, there is a paucity of literature on the pre- and post-test results of various athletic performance measures in male football players. The main aim of this study is to investigate the associations between the *AGT* and *IL-6* gene polymorphisms and the improvement of athletic performance in elite male football players after a six-week training intervention. To achieve this goal, a series of tests focusing on athletic ability were conducted.

## 2. Materials and methods

### 2.1 Participants

This research followed a within-subjects design, in which two or more measurements were collected from a sample of subjects and groups. A total of volunteer twenty-two (n = 22; Goalkeeper = 3, Defender = 6, Midfielder = 11, Forward = 2) male football players from the North Macedonian Super League participated in this study, with the following descriptive characteristics: minimum and maximum age: 18–35 years, mean age (±standard deviation): 24.79 ± 4.56 years, height: 180.62 ± 4.88 cm, and body weight: 74.42 ± 5.42 kg. It was stated that, over three generations, the ancestry of all male football players is traced back to the Macedonian Caucasian region.

The selection criteria established by the researchers for the inclusion of participants were as follows:

(a) Individuals formally contracted as male football players within the primary team of the football club.

(b) Requirement for active involvement in both training sessions and competitive matches throughout the entirety of the respective football season while maintaining continuity within the same football club.

(c) Mandatory adherence to a rigorous training program, characterized by a training schedule spanning six days a week.

(d) Ancestry of Macedonian Caucasian origin for at least two successive generations was established as an essential criterion for participant inclusion. These rigorously defined inclusion criteria collectively formed the basis upon which the twenty-two male football players were meticulously selected to participate in the study.

### 2.2 Procedure

During the six-week pre-season preparation period, all participants adhered to an intensive training schedule that spanned six days per week. Training sessions varied in length, lasting anywhere from 35 to 150 minutes each. The training was carefully organized into two microcycles per week, with each microcycle comprising three unique training sessions. Notably, these training sessions were held twice daily, once in the morning and once in the evening, leading to a total weekly training time of around 900 minutes. The program was thoughtfully designed to include a variety of exercises aimed at improving both anaerobic and aerobic fitness, enhancing both intermuscular and intramuscular coordination, and increasing speed and plyometric training intensity. Further specifics of this program can be found in Table 1.

**TABLE 1. The training program for 1 microcycle in the pre-season.**

| Week 1 | Monday | Tuesday | Wednesday | Thursday | Friday | Saturday | Sunday |
|---|---|---|---|---|---|---|---|
| Morning | Strength training session | Coordination and basic plyometrics | Strength training session | Regeneration | Strength training session | Coordination and basic plyometrics | Strength training session |
| Evening | Football training and aerobic endurance training | Football training and aerobic endurance training | Preparation of match/compensation training for nonstarters and less-minuted players | Free | Football training and aerobic endurance training | Football training and aerobic endurance training | Preparation of match/compensation training for nonstarters and less-minuted players |
| Volume | 65 + 85 min | 75 + 70 min | 40 + 90 min | 35–40 min | 65 + 85 min | 75 + 70 min | 40 + 90 min |
| Intensity | Moderate-high | High | Moderate-high | Low | Moderate-high | High | Moderate-High |
| Metabolic load | 75–90% MHR | 95% MHR | 75–90% MHR | 50–60% MHR | 75–90% MHR | 90% MHR | 75–90% MHR |
| Mechanical load | <5000–6000 m | 6000–7000 m | 9000–13000 m | 1000–2000 m | <5000–6000 m | 6000–7000 m | 9000–13000 m |

*MHR: Maximum Heart Rate.*

### 2.2.1 Sample collection

Before and after the six-week training program, the male football players were subjected to physical evaluations. The same testing protocols were applied for both initial and final assessments. Given their experience in training and testing, the athletes were familiar with the procedures. A general warm-up phase, including light jogging and stretching exercises for both upper and lower limbs, preceded the actual tests. This was followed by submaximal efforts to prepare the athletes for the upcoming tests. Physical jump tests were conducted using the Optojump system (Optojump; version, 1.14.0, Microgate, Italy), with each jump test performed five times. The best performance out of these was recorded for later analysis, adhering to standard evaluation practices. Body fat percentage was measured using the Jackson Pollock method, which involves taking skinfold readings from seven different body areas using the Harpenden Caliper to calculate fat percentages.

The athletes underwent a comprehensive set of performance tests designed to measure various aspects of physical fitness. These included the Squat Jump (SJ) and Counter Movement Jump Test (CMJ) for assessing leg strength and vertical jump ability, and the Drop Jump Test (DJ) for evaluating reactive and explosive strength, using the Optojump device. The testing also included the Yo-Yo Intermittent Recovery Test Level 2 (Yo-Yo IRT 2) for recovery assessment and a One Repetition Maximum (1RM) test for maximal muscle strength in bench pressing. Sprinting skills over 5 m, 10 m and 30 m were measured using the Witty photosensor system. The entire testing process spanned two days, with a day's break in between. The first day involved the Body Fat Percentage, CMJ, DJ, and Yo-Yo IRT 2 tests, while after a two-day rest, the second phase included the 1RM test and the 5 m, 10 m and 30 m sprints. The sprint tests were conducted on a football field, while the other assessments took place in a gym setting.

### 2.2.2 Vertical jump testing

In the SJ test, participants placed their hands on their hips, bent their knees to 90°, and performed five jumps with 15-second breaks. The best jump was recorded. For the CMJ, participants were instructed to fully extend their legs after a downward movement, with the extent of the countermovement left to their choice. They kept their hands on their hips throughout. Both SJ and CMJ involved five jumps with 15-second intervals. An Infrared Contact Platform (Optojump) measured the flight time of each jump, allowing the calculation of jump height using the formula $h = gt^2/8$ ($g = 9.81$ m/s$^2$). Consistency in take-off and landing was required for a jump to be valid. The highest jump from each test was used for data analysis [27].

### 2.2.3 Yo-Yo IRT 2 test

The Yo-Yo IR 2 test is a key tool in sports science for assessing an athlete's fitness, particularly in team sports. It measures the ability to perform repeated high-intensity exercises, tapping into both aerobic and anaerobic energy systems. The test involves shuttle runs of 40 meters (two 20-meter segments) with increasing speed, interspersed with 10-second active recovery periods, guided by audio cues. Athletes continue until they cannot keep up with the increasing pace, with the test ending if they fail to reach the marker twice in a row. Typically lasting 5 to 15 minutes, it evaluates an individual's capacity for high-intensity exercise with significant anaerobic energy use [28].

### 2.2.4 1RM of bench press

The One Repetition Maximum (1RM) test is a method used to assess the maximum weight an individual can lift in a single repetition of an exercise. The test begins with a warm-up phase where participants engage in submaximal repetitions to prepare their muscles for the exertion. This is followed by the testing phase, which starts at 50–70% of the participant's estimated capacity. The weight is gradually increased in increments of 2.5 kg, up to 20 kg, until the participant is unable to complete a repetition. A specific example of the 1RM test is the bench press technique. This involves the participant lying down on the bench with their feet flat on the ground and maintaining contact at five points: the feet, calves, upper, back, and head. The participant grips the barbell at shoulder width and lifts it in a controlled manner. The determination of the 1RM is a critical part of the test. After completing the warm-up sets, the participant attempts the maximal lift. The weight is increased in subsequent attempts, with three-minute rest intervals between each attempt. This process continues until the participant is unable to complete a repetition. The weight lifted in the last successful attempt is recorded as 1RM. This value is significant as it represents the maximum strength capacity of the individual for that particular exercise [29, 30].

### 2.2.5 Sprint tests

Before starting the speed tests, six pairs of Witty Speed photocells from Microgate Equipment were set up at 0, 5, 10, 20 and 30 meters along a track. Male football players then performed two sprints each, starting 0.5 meters behind the line, in an indoor facility to avoid weather effects. Times for each distance were recorded to calculate sprint velocity and assess acceleration at different intervals (0–5 m, 5–10 m, 10–20 m and 20–30 m). A 5-minute rest between sprints ensured recovery and consistent performance. The fastest time from the two sprints was used for analysis.

### 2.2.6 Body fat (%)

The measurements were meticulously conducted, employing a Harpenden Skinfold Caliper, manufactured by Habdirect UK, at seven body sites, and body density and body fat percentage were calculated using the equations of Jackson and Pollock [31].

### 2.2.7 Genotyping

The epithelial cell samples were collected after obtaining signed consent forms from all participants. The working procedures were conducted following the principles of the Helsinki Declaration. DNA isolation was performed using the commercially available Canvax DNA Isolation Kit (Canvax Reagents S.L., AN0036, C. Luis de Mercado, Boecillo, Valladolid, Spain), following the manufacturer's instructions. All genotyping procedures were conducted using Real-Time PCR (StepOne Plus, USA). For the genotyping process, *AGT* rs699 and IL-6 rs1800795 TaqMan Single Nucleotide Polymorphism (SNP) Genotyping Assays (Thermo Fisher,

USA) were utilized as per the manufacturer's guidelines. Genotyping was completed using 5 $\mu$L of master mix, 3.75 $\mu$L of $H_2O$, 0.25 $\mu$L of the assay, and 1 $\mu$L (10 ng) of DNA, totaling 10 $\mu$L. The TaqMan Probe sequences used for genotyping are presented in Table 2. The C allele for the 5-Carboxyfluorescein (5-FAM) primer and the T allele for the 2′-chloro-7′-phenyl-1,4. dichloro-6-carboxyfluorescein (VIC) primer, used in the *AGT* TaqMan SNP Genotyping Assay, were identified (Fig. 1). Similarly, the G allele for the FAM primer and the C allele for the VIC primer, used in the *IL-6* TaqMan SNP Genotyping Assay, were identified (Fig. 2).

### 2.3 Statistical analysis

The minimum sample size for this study was determined using G*power Software 3.1.9.7 (Heinrich Heine University Düsseldorf, Düsseldorf, NRW, Germany). An a priori power analysis, employing *t*-tests based on the study's design, was conducted. This design included a Paired Sample *t*-test analysis with a single group measured at two different time points. The significance level ($\alpha$) was set at 0.05, and the minimum effect size was established at 0.60 [32]. To achieve a power (1 − $\beta$ error probability) of 0.80, the required sample size for statistical significance was calculated to be 19 participants, resulting in an actual power of 80.0%.

The statistical analysis of the collected data was performed using SPSS 25.0 (Statistical Package for the Social Sciences, Armonk, NY, USA: IBM Corp.). Descriptive statistics, including percentages, means, and standard deviations, were used to evaluate the dataset. The results of the Shapiro-Wilk & Kolmogorov-Smirnov tests, along with skewness and kurtosis values, confirmed that the data followed a normal distribution [33]. Therefore, to identify differences between the pre-test and post-test measurements among male football players, the Paired Sample *t*-test was appropriately used. Additionally, to determine the effect sizes (ES) for the pairwise comparisons of the pre- and post-test measurements, Cohen's *d* was calculated. This provided a quantification of the magnitude of these comparisons. The categorization of effect sizes was as follows: less than 0.2 indicated a trivial effect, 0.2 to 0.6 a small effect, greater than 0.6 up to 1.2 a moderate effect, above 1.2 but not exceeding 2.0 a large effect, and over 2.0 a very large effect, as outlined by [34]. Hypothesis testing was conducted with a 95% confidence interval, and a significance threshold of $p < 0.05$ was adopted, in line with standard conventions of statistical significance.

## 3. Results

The present study investigated the possible association between certain aspects of athletic performance and *AGT* and *IL-6* gene polymorphisms. A cohort of twenty-two football players was selected for this study.

The training program for a single microcycle during the preseason preparation phase is outlined in Table 1. The results shown in Table 3 come from using the paired-sample *t*-test on the group of football players, depending on how their *AGT* genotype variable was categorized. The comprehensive analysis elucidated a lack of statistically significant differences across various variables, including SJ, 5 m, 30 m, CMJ, DJ evaluations, and body fat percentage ($p > 0.005$). Nevertheless, the present study unveiled that the outcomes from the Yo-Yo IRT 2, 10 m, and 1RM tests exhibited statistically significant differences (Yo-Yo IRT 2: CC and CT $p = 0.005$, $<0.001$; 10 m: CT $p = 0.024$; 1RM: CC, CT and TT $p \leq 0.001$, $<0.001$ and 0.045, respectively) (Fig. 1).

Based on the *IL-6* genotype variable, Table 4 shows that there were no statistically significant differences ($p > 0.05$) between the variables that were looked at in this study for SJ, 5 m, 30 m, CMJ, DJ tests, and body fat percentage. Still, there was a statistically significant difference between the results of the Yo-Yo IRT 2, 10 m and 1RM tests (Fig. 2). More specifically, there was a significant difference in the Yo-Yo IRT 2 performance depending on the allelic permutations of CC, CG and GG, with *p*-values of 0.002, 0.021 and $<0.001$, respectively. In a similar vein, during the 10 m sprint test, the CC and GG genotypes displayed a lack of significant difference, registering a *p*-value of 0.020 and 0.028, respectively. The results of the 1RM test revealed significant differences linked to the CC and GG genotypes, yielding corresponding *p*-values of $< 0.001$ and $< 0.001$, respectively. The effect sizes (Cohen's *d*) corresponding to the statistically significant outcomes are reported in Tables 3 and 4.

## 4. Discussion

The emergence of sports genomics in scholarly research gained momentum following the groundbreaking discovery of the human DNA structure and the identification of initial DNA polymorphisms Angiotensin-Converting Enzyme (*ACE*) & Alpha-Actinin-3 (*ACTN3*) linked to athletic prowess [13, 35, 36]. Factors such as speed, strength, endurance, agility, recuperation speed, susceptibility to injuries, and the propensity for using performance-enhancing substances in elite athletes are shaped by the precise arrangement of nucleotides in the billions of base pairs in human DNA [37, 38]. Current research is increasingly concentrating on

**TABLE 2. Sequences of the TaqMan probe used for genotyping *AGT* rs699 and *IL-6* rs1800795 polymorphisms.**

| qPCR | Genes | Sequence, 5′-3′ |
|---|---|---|
| | *AGT* | CAGGGTGCTGTCCACACTGGCTCCC[A/G] TCAGGGAG CAGCCAGTCTTCCATCC |
| | *IL-6* | ACTTTTCCCCCTAGTTGTGTCTTGC[C/G] ATGCTAAAG GACGTCACATTGCACA |

*qPCR: Quantitative Polymerase Chain Reaction; AGT: Angiotensinogen; IL-6: Interleukin 6.*

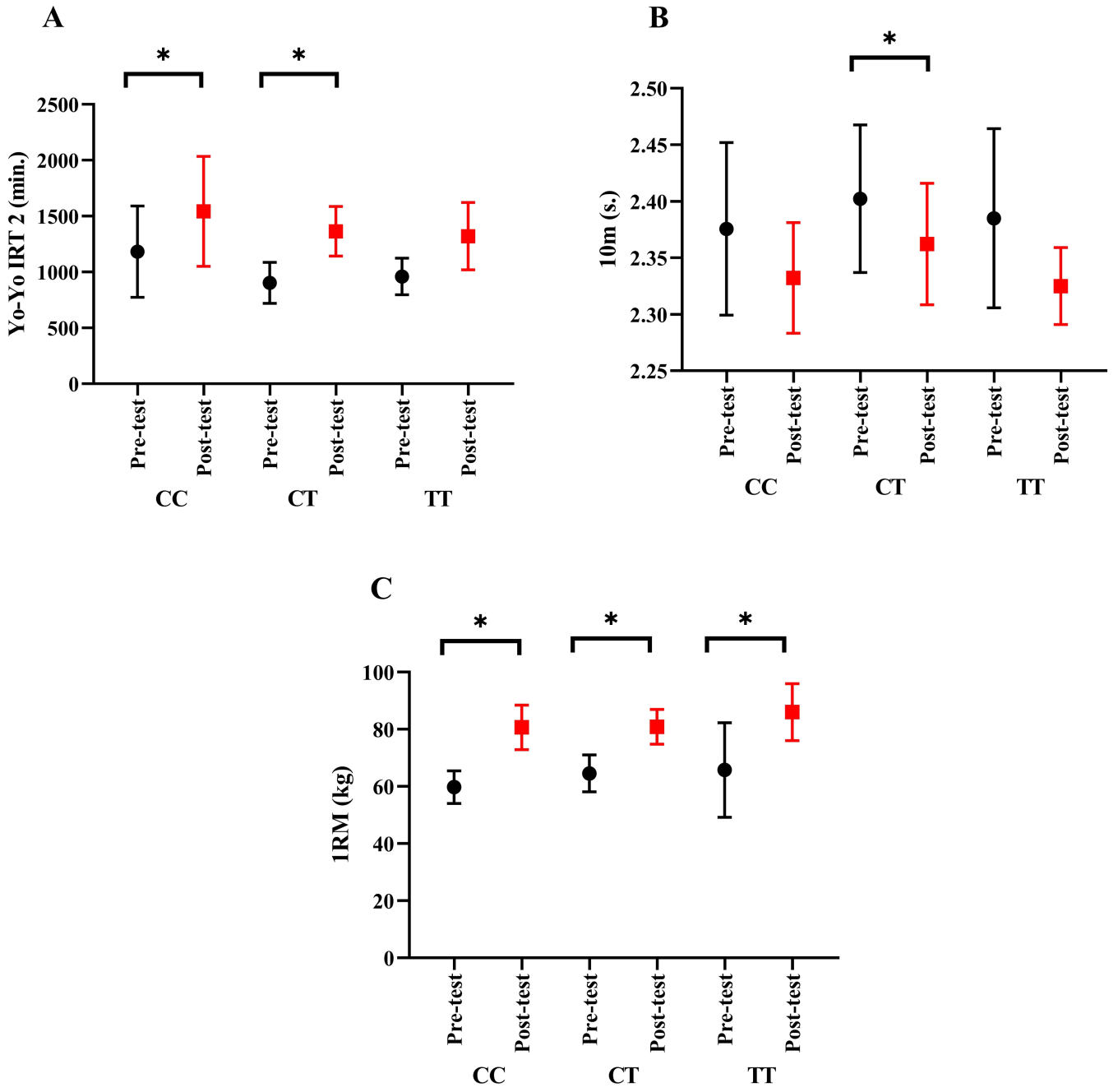


**FIGURE 1. The relationship between (A) Yo-Yo IRT-2, (B) 10 m sprint, 1RM (C) and *AGT* (rs699) gene polymorphism (CC, CT, and TT).** *: $p < 0.05$. IRT: Intermittent Recovery Test; 1RM: One Repetition Maximum.

examining either individual or combined gene effects to understand how genetic variations influence various athletic attributes like speed, strength, endurance, and recovery in both professional and non-professional athletes [1, 39–41].

The present study reveals that there were no statistically significant differences in variables such as SJ, 5 m, 30 m, CMJ, DJ, and body fat percentage values based on both *AGT* and *IL-6* genotypes. However, it was observed that for both gene polymorphisms, the results obtained from the Yo-Yo IRT 2, 10 m, and 1RM tests for specific genotype groups demonstrated significant and noteworthy variations. This study underscores the impact of genotype categorization on performance, particularly emphasizing the pivotal role played by the Yo-Yo IRT 2, 10 m, and 1RM tests, where statistically significant disparities were evident.

Prior studies have identified genes like *AGT* and *IL-6* as potential influencers of individual athletic performance, particularly in competitive team sports such as football, basketball, and rugby, focusing on the development of physical abilities [13, 19, 42–45]. Research in this area has shown that different genetic variants, including the *AGT* gene, can distinguish short-distance runners from endurance athletes and the general population [46]. In a remarkable study, it was found that people with the Met235Thr C allele of the *AGT* gene had significantly increased AGT levels in their blood. This allele is associated with higher levels of angiotensin II, which promotes skeletal muscle growth, which can be beneficial for sports that require power and strength. This can be seen in strength

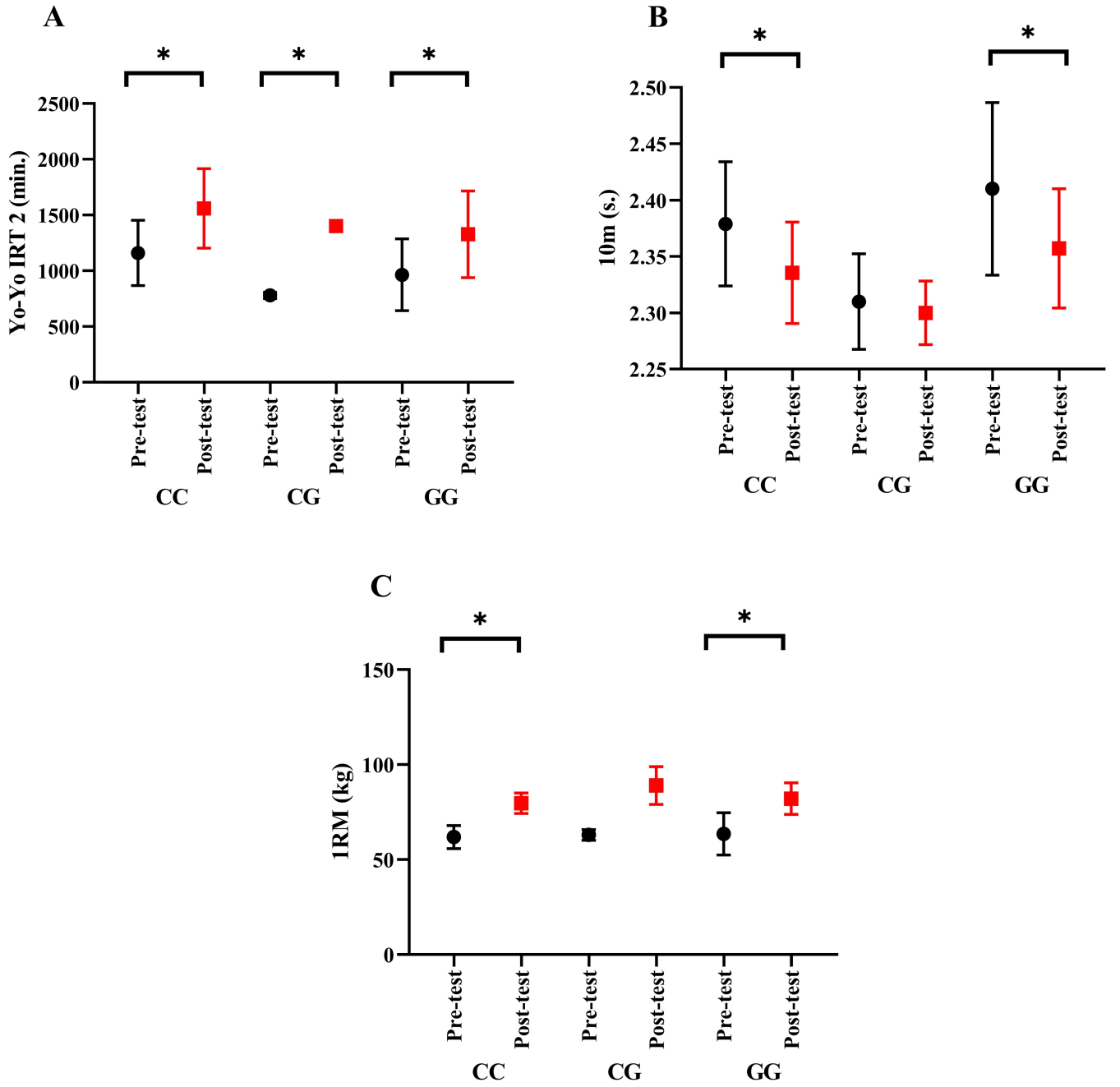


**FIGURE 2. The relationship between (A) Yo-Yo IRT-2, (B) 10 m sprint, 1RM (C) and *IL-6* (rs1800795) gene polymorphism (CC, CG, and GG).** *$p < 0.005$; $< 0.001$. IRT: Intermittent Recovery Test; 1RM: One Repetition Maximum.

athletes such as throwers, sprinters, and jumpers who show the benefits of this genetic trait [14].

In a study by Aleksandra *et al.* [15], the impact of the *AGT* M235T genotype on the response to a 12-week aerobic dance training program was examined, with a focus on strength-related variables like SJ and CMJ. The study found that the C allele led to greater improvements in these variables compared to TT homozygotes, suggesting that the *AGT* M235T polymorphism could be a significant genetic marker for predicting training response and for traits related to power and strength. However, a study by Bulgay *et al.* [47], which examined the *AGT* rs699 gene polymorphism in professional male football players and sedentary individuals, found no significant differences in *AGT* polymorphisms and alleles between the two groups, although a higher proportion of CT genotypes and C allele carriers was observed in both groups.

In the current study, no significant differences were found in SJ, 5 m, 30 m, CMJ, DJ, or body fat percentage in male football players based on the *AGT* gene variations ($p > 0.05$). However, significant differences were observed in the 10 m sprint tests in favor of the CT genotype and the Yo-Yo IRT 2 and 1RM tests in favor of both CC and CT genotypes ($p < 0.05$) (Table 3; Fig. 1). These findings suggest that while *AGT* gene polymorphism may not influence all aspects of athletic performance, it could have a notable impact on specific performance traits such as sprinting ability and response to certain types of training.

The *IL-6* rs1800795 polymorphism, identified as another

**TABLE 3. Comparison of Physical Fitness Parameters Based on *AGT* (rs699 Polymorphism) Genotypes.**

| Parameters | Genotype | n | Pre-test M ± S.D. | Post-test M ± S.D. | *T* | *p* | ES |
|---|---|---|---|---|---|---|---|
| SJ (cm) | | | | | | | |
| | CC | 9 | 41.58 ± 3.06 | 41.45 ± 4.44 | 0.199 | 0.953 | 0.03 |
| | CT | 9 | 37.23 ± 4.81 | 37.49 ± 3.70 | −0.303 | 0.770 | −0.06 |
| | TT | 4 | 38.83 ± 3.38 | 38.38 ± 3.55 | 0.375 | 0.715 | 0.12 |
| Yo-Yo IRT 2 (min) | | | | | | | |
| | CC | 9 | 1182.22 ± 407.97 | 1542.22 ± 491.57 | −3.828 | 0.005* | −0.79 |
| | CT | 9 | 903.22 ± 182.46 | 1364 ± 222.21 | −8.615 | <0.001* | −2.26 |
| | TT | 4 | 960.00 ± 163.29 | 1320.00 ± 301.10 | −3.057 | 0.055 | −1.48 |
| 5 m (s) | | | | | | | |
| | CC | 9 | 0.67 ± 0.01 | 0.70 ± 0.03 | −2.186 | 0.060 | −1.34 |
| | CT | 9 | 0.68 ± 0.03 | 0.70 ± 0.35 | −1.029 | 0.334 | −0.08 |
| | TT | 4 | 0.68 ± 0.02 | 0.71 ± 0.42 | −1.890 | 0.155 | −0.10 |
| 10 m (s) | | | | | | | |
| | CC | 9 | 2.37 ± 0.07 | 2.33 ± 0.04 | 1.938 | 0.089 | 0.70 |
| | CT | 9 | 2.40 ± 0.06 | 2.36 ± 0.53 | 2.771 | 0.024* | 0.10 |
| | TT | 4 | 2.38 ± 0.07 | 2.32 ± 0.03 | 1.604 | 0.170 | 1.11 |
| 30 m (s) | | | | | | | |
| | CC | 9 | 4.07 ± 0.10 | 4.03 ± 0.08 | 1.596 | 0.149 | 0.44 |
| | CT | 9 | 4.11 ± 0.11 | 4.08 ± 0.11 | 1.464 | 0.181 | 0.27 |
| | TT | 4 | 4.14 ± 0.04 | 4.13 ± 0.05 | 0.577 | 0.604 | 0.22 |
| CMJ (cm) | | | | | | | |
| | CC | 9 | 42.18 ± 3.17 | 42.84 ± 4.81 | −0.820 | 0.436 | 0.16 |
| | CT | 9 | 38.76 ± 5.13 | 38.11 ± 3.81 | 0.746 | 0.477 | 0.14 |
| | TT | 4 | 39.05 ± 2.35 | 38.90 ± 4.89 | 0.111 | 0.919 | 0.03 |
| DJ (cm) | | | | | | | |
| | CC | 9 | 41.28 ± 3.94 | 41.43 ± 4.78 | −0.185 | 0.858 | 0.03 |
| | CT | 9 | 38.07 ± 4.97 | 37.23 ± 4.10 | 0.687 | 0.511 | 0.18 |
| | TT | 4 | 36.15 ± 3.00 | 36.05 ± 3.96 | 0.104 | 0.924 | 0.02 |
| 1RM (kg) | | | | | | | |
| | CC | 9 | 59.77 ± 5.71 | 80.66 ± 7.76 | −7.635 | <0.001* | −3.06 |
| | CT | 9 | 64.55 ± 6.46 | 80.88 ± 6.07 | −6.198 | <0.001* | −2.60 |
| | TT | 4 | 65.75 ± 16.52 | 86.00 ± 9.96 | −1.826 | 0.045* | −1.48 |
| Body Fat (%) | | | | | | | |
| | CC | 9 | 8.67 ± 2.07 | 8.44 ± 1.72 | 1.038 | 0.334 | 0.32 |
| | CT | 9 | 8.50 ± 2.95 | 8.89 ± 1.94 | 0.723 | 0.490 | 0.24 |
| | TT | 4 | 8.92 ± 1.94 | 8.92 ± 1.81 | −0.067 | 0.951 | −0.03 |

**p < 0.005; < 0.001. SJ: Squat Jump; CMJ: Countermovement Jump; DJ: Drop Jump; Yo-Yo IRT 2: Yo-Yo Intermittent Recovery Test Level 2; 1RM: 1 Repetition Maximum; ES: Effect Size; M: Mean; S.D.: Standard Deviation.*

**TABLE 4. Comparison of Physical Fitness Parameters Based on *IL-6* (rs1800795 polymorphism) Genotypes.**

| Variable | Genotype | n | Pre-test M ± S.D. | Post-test M ± S.D. | *T* | *p* | ES |
|---|---|---|---|---|---|---|---|
| SJ (cm) | | | | | | | |
| | CC | 9 | 38.92 ± 5.03 | 38.31 ± 4.98 | 0.669 | 0.522 | 0.12 |
| | CG | 2 | 41.95 ± 3.46 | 38.85 ± 4.17 | 4.400 | 0.142 | 0.80 |
| | GG | 11 | 39.30 ± 3.97 | 40.13 ± 3.83 | −1.906 | 0.086 | 0.21 |
| Yo-Yo IRT 2 (min) | | | | | | | |
| | CC | 9 | 1160.00 ± 292.57 | 1560.00 ± 356.08 | −4.671 | 0.002* | 1.22 |
| | CG | 2 | 780.00 ± 28.28 | 1400.00 ± 0.00 | −31.000 | 0.021* | 1.22 |
| | GG | 11 | 964.45 ± 322.60 | 1327.27 ± 389.38 | −5.849 | <0.001* | 1.01 |
| 5 m (s) | | | | | | | |
| | CC | 9 | 0.68 ± 0.01 | 0.70 ± 0.03 | −2.234 | 0.056 | 0.89 |
| | CG | 2 | 0.66 ± 0.28 | 0.67 ± 0.42 | −1.000 | 0.500 | 0.02 |
| | GG | 11 | 0.69 ± 0.27 | 0.70 ± 0.35 | −1.576 | 0.146 | 0.03 |
| 10 m (s) | | | | | | | |
| | CC | 9 | 2.37 ± 0.05 | 2.33 ± 0.04 | 2.889 | 0.020* | 0.88 |
| | CG | 2 | 2.31 ± 0.04 | 2.30 ± 0.20 | 1.000 | 0.500 | 0.06 |
| | GG | 11 | 2.41 ± 0.76 | 2.35 ± 0.05 | 2.578 | 0.028* | 0.11 |
| 30 m (s) | | | | | | | |
| | CC | 9 | 4.10 ± 0.10 | 4.07 ± 0.10 | 1.246 | 0.248 | 0.30 |
| | CG | 2 | 4.06 ± 0.11 | 4.05 ± 0.20 | 0.077 | 0.951 | 0.06 |
| | GG | 11 | 4.11 ± 0.11 | 4.07 ± 0.09 | 2.221 | 0.051 | 0.39 |
| CMJ (cm) | | | | | | | |
| | CC | 9 | 40.62 ± 5.27 | 39.82 ± 5.72 | 0.668 | 0.523 | 0.14 |
| | CG | 2 | 39.85 ± 3.32 | 41.20 ± 4.66 | −1.421 | 0.390 | 0.33 |
| | GG | 11 | 39.95 ± 3.61 | 40.30 ± 4.41 | −.947 | 0.366 | 0.08 |
| DJ (cm) | | | | | | | |
| | CC | 9 | 40.04 ± 6.18 | 39.54 ± 6.38 | 0.362 | 0.767 | 0.07 |
| | CG | 2 | 38.05 ± 3.04 | 37.75 ± 2.89 | 3.000 | 0.214 | 0.10 |
| | GG | 11 | 38.40 ± 3.26 | 38.25 ± 3.66 | 0.277 | 1.000 | 0.04 |
| 1RM (kg) | | | | | | | |
| | CC | 9 | 61.88 ± 6.03 | 79.66 ± 5.36 | −7.933 | <0.001* | 3.11 |
| | CG | 2 | 63.00 ± 2.82 | 89.00 ± 9.89 | −5.200 | 0.121 | 3.57 |
| | GG | 11 | 63.54 ± 11.16 | 82.09 ± 8.31 | −5.972 | <0.001* | 1.88 |
| Body Fat (%) | | | | | | | |
| | CC | 9 | 9.19 ± 2.66 | 8.92 ± 2.00 | 0.897 | 0.396 | 0.29 |
| | CG | 2 | 6.21 ± 0.26 | 7.40 ± 0.26 | - | - | - |
| | GG | 11 | 8.63 ± 2.11 | 8.19 ± 2.30 | −1.514 | 0.164 | 0.48 |

**p < 0.005; < 0.001. SJ: Squat Jump; CMJ: Countermovement Jump; DJ: Drop Jump; Yo-Yo IRT 2: Yo-Yo Intermittent Recovery Test Level 2; 1RM: One Repetition Maximum; ES: Effect Size; M: Mean; S.D.: Standard Deviation.*

key genetic marker, is believed to influence the development of power-based physical performance, particularly in individuals with the G allele [25]. Research by Eynon *et al.* [48] showed a higher frequency of the GG genotype and G allele in national/international-level athletes engaged in strength and endurance sports. In another study with strength athletes (n = 158) and non-athletic volunteers (n = 254), a higher incidence of the GG genotype and the G allele was also found in the group of athletes [21]. Studies focusing on the status of athletes have shown that the polymorphism of the *IL-6* gene GG is a common variant in athletes who specialize in strength and performance [26]. Tuna *et al.* [49] observed that professional swimmers (n = 45) had higher rates of the GG genotype and G allele compared to a control group (n = 30), but no significant difference was found in the *IL-6* rs1800795 polymorphism between swimmers and the control group, nor was there a correlation between swimming styles/distances and genotypes. Ruiz *et al.* [46] found that endurance and power athletes had significantly higher frequencies of the GG genotype and G allele compared to other groups. Ulucan *et al.* [50] investigated the *IL-6* rs1800795 polymorphism in ski athletes and found an equal distribution of GG and GC genotypes, with the CC genotype absent (75% G allele, 25% C allele). Cenikli *et al.* [51] reported no significant difference in the IL-6 G174C variant frequencies between elite athletes and control groups.

In this study, the *IL-6* polymorphism in male football players was more commonly found in the GG variants compared to CG and CC (Table 3). No significant differences were observed in physical fitness tests (SJ, 5 m, 30 m, CMJ, DJ) and body fat percentage based on *IL-6* genotype in these players ($p > 0.005$). However, the Yo-Yo IRT 2, 10 m, and 1RM test results showed significant differences favoring the CC, CG, and GG genotypes ($p < 0.005$; Table 3). This contrasts with Huuskonen *et al.* [52], who found the greatest improvement in $VO_2$ max performance in participants with the CG genotype after an eight-week training program. It can be said that while the *IL-6* rs1800795 polymorphism appears to be a prevalent genetic variant among athletes, particularly those in power and endurance sports, its impact on specific physical performance measures can vary. This study's findings suggest that while certain *IL-6* genotypes (CC, CG, GG) may confer advantages in specific fitness tests, they do not uniformly affect all aspects of physical performance in male football players. Additionally, the role of *IL-6* in immune system regulation and its potential link to pro-inflammatory responses highlights the complexity of its influence on athletic performance.

The insights gained from studying the *AGT* and *IL-6* gene polymorphisms, particularly their impact on training adaptations among male football players, hold considerable practical value. Understanding the link between these genetic variations and the body's response to training can be highly beneficial for coaches and sports professionals. This knowledge paves the way for creating customized training plans that consider the unique genetic makeup of each athlete. Coaches, by recognizing players with these specific gene polymorphisms, can tailor training methods to maximize their potential for improved adaptability and performance. Furthermore, the categorization of genotypes can play a crucial role in assessing physical fitness. Tests like the Yo-Yo IRT 2, 10 m, and 1RM, which are indicative of muscle power and inflammation responses, can be more effectively utilized to monitor an athlete's development, factoring in their genetic predispositions. This genetic information is also invaluable for sports medicine experts and coaches in devising strategies for injury prevention. Athletes with certain genotypes, for instance, might be more susceptible to inflammation-related issues, necessitating adjusted recovery plans or workload management to reduce injury risks and enhance preventive measures. Moreover, tailoring training programs to align with the genetic profiles of professional athletes and adjusting training loads on an individual basis could lead to improvements in both individual and team performances. A key consideration is the extent to which these candidate genes can predict specific abilities or performance outcomes in sports. This approach represents a significant shift towards more personalized and effective training methodologies in sports, particularly in football.

## 5. Conclusions

In conclusion, the study suggests that *AGT* and *IL-6* genetic variations may influence training adaptations in male football players, with notable performance differences observed in Yo-Yo IRT 2, 10 m and 1RM tests based on genotypes. This insight could be pivotal in shaping training programs that are more aligned with athletes' genetic predispositions, potentially aiding coaches in steering athletes towards sports disciplines where they are most likely to excel.

## 6. Limitations and future research

The study's limitations include limited sample sizes, the impact of football players' intense training schedules, the need for long-term research to understand the relationship between genetics and training adaptation, the importance of examining a broader range of genetic variations, and the necessity of conducting research across various sports disciplines. Additionally, the ethical issues associated with genetic testing should also be considered.

Further research is needed to address limitations and fully explore the link between *AGT* and *IL-6* polymorphisms in male football players. Future studies should use multigenetic analysis in larger, diverse groups (including female/male athletes of different age groups and sports disciplines) and consider epigenetic factors. Additionally, considering the physical and physiological differences among football players based on their positions could be a further research question, as it would be beneficial to assess genetic polymorphisms in a broad sample group, categorized by playing positions.

### AVAILABILITY OF DATA AND MATERIALS

Data are available for research purposes upon reasonable request to the corresponding authors.

## AUTHOR CONTRIBUTIONS

CB, MD, and MC—designed the research study. CB, MC, HİC and MD—wrote the manuscript. OG, NLB, SYT and TP—performed the research. VOÇ, MSK and KU—analyzed the data. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

## ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Before the study commenced, the athletes signed consent forms containing all information such as the study protocol and use of the data. Tetowa University Ethics Committee approved the study protocol (2022/02-1474/1), and the study procedure was conducted following the principles of the Helsinki Declaration.

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## CONFLICT OF INTEREST

The authors declare no conflict of interest.

## REFERENCES

[1] Semenova EA, Hall ECR, Ahmetov II. Genes and athletic performance: the 2023 update. Genes. 2023; 14: 1235.

[2] Furrer R, Hawley JA, Handschin C. Themolecular athlete: exercise physiology frommechanisms to medals. Physiological Reviews. 2023; 103: 1693–1787.

[3] Leońska-Duniec A, Borczyk M, Piechota M, Korostyński M, Brodkiewicz A, Cięszczyk P. TTN variants are associated with physical performance and provide potential markers for sport-related phenotypes. International Journal of Environmental Research and Public Health. 2022; 19: 10173.

[4] Wackerhage H, Miah A, Harris RC, Montgomery HE, Williams AG. Genetic research and testing in sport and exercise science: a review of the issues. Taylor & Francis. 2009; 27: 1109–1116.

[5] Bulgay C, Kasakolu A, Kazan HH, Mijaica R, Zorba E, Akman O, *et al*. Exome-wide association study of competitive performance in elite athletes. Genes. 2023; 14: 660.

[6] Hudson AL, Gandevia SC, Butler JE. A principle of neuromechanical matching for motor unit recruitment in human movement. Exercise and Sport Sciences Reviews. 2019; 47: 157–168.

[7] Kumagai H, Kaneko T, Shintake Y, Miyamoto-Mikami E, Tomita H, Fukuo M, *et al*. Genetic polymorphisms related to muscular strength and flexibility are associated with artistic gymnastic performance in the Japanese population. European Journal of Sport Science. 2023; 23: 955–963.

[8] Konopka MJ, van den Bunder JCML, Rietjens G, Sperlich B, Zeegers MP. Genetics of long-distance runners and road cyclists—a systematic review with meta-analysis. Scandinavian Journal of Medicine and Science in Sports. 2022; 32: 1414–1429.

[9] Bouchard C, Rankinen T, Timmons JA. Genomics and genetics in the biology of adaptation to exercise. Comprehensive Physiology. 2011; 1: 1603–1648.

[10] Varillas-Delgado D, Del Coso J, Gutiérrez-Hellín J, Aguilar-Navarro M, Muñoz A, Maestro A, *et al*. Genetics and sports performance: the present and future in the identification of talent for sports based on DNA testing. European Journal of Applied Physiology. 2022; 122: 1811–1830.

[11] Guth LM, Roth SM. Genetic influence on athletic performance. Current Opinion in Pediatrics. 2013; 25: 653–658.

[12] Mann TN, Lamberts RP, Lambert MI. High responders and low responders: factors associated with individual variation in response to standardized training. Sports Medicine. 2014; 44: 1113–1124.

[13] Ahmetov II, Hall ECR, Semenova EA, Pranckevičienė E, Ginevičienė V. Advances in sports genomics. Advances in Clinical Chemistry. 2022; 107: 215–263

[14] Gomez-Gallego F, Santiago C, González-Freire M, Yvert T, Muniesa CA, Serratosa L, *et al*. The C allele of the AGT Met235Thr polymorphism is associated with power sports performance. Applied Physiology, Nutrition, and Metabolism. 2009; 34: 1108–1111.

[15] Aleksandra Z, Zbigniew J, Waldemar M, Agata LD, Mariusz K, Marek S, *et al*. The AGT gene M235T polymorphism and response of power-related variables to aerobic training. Journal of Sports Science and Medicine. 2016; 15: 616–624.

[16] De Cavanagh EMV, Inserra F, Ferder L. Angiotensin II blockade: a strategy to slow ageing by protecting mitochondria? Cardiovascular Research. 2011; 89: 31–40.

[17] Zhuo JL. Augmented intratubular renin and prorenin expression in the medullary collecting ducts of the kidney as a novel mechanism of angiotensin II-induced hypertension. American Journal of Physiology-Renal Physiology. 2011; 301: F1193–1194.

[18] Zarębska A, Sawczyn S, Kaczmarczyk M, Ficek K, Maciejewska-Karłowska A, Sawczuk M, *et al*. Association of rs699 (m235t) polymorphism in the agt gene with power but not endurance athlete status. The Journal of Strength & Conditioning Research. 2013; 27: 2898–2903.

[19] Aleksandra Z, Zbigniew J, Waldemar M, Agata LD, Mariusz K, Marek S, *et al*. The AGT gene M235T polymorphism and response of power-related variables to aerobic training. Journal of Sports Science and Medicine. 2016; 15: 616–624.

[20] Southward K, Rutherfurd-Markwick K, Badenhorst C, Ali A. The role of genetics in moderating the inter-individual differences in the ergogenicity of caffeine. Nutrients. 2018; 10: 1352.

[21] Eider J, Cieszczyk P, Leońska-Duniec A, Maciejewska A, Sawczuk M, Ficek K, *et al*. Association of the 174 G/C polymorphism of the IL6 gene in polish power-orientated athletes. The Journal of Sports Medicine and Physical Fitness. 2013; 53: 88–92.

[22] Tanaka T, Narazaki M, Kishimoto T. *IL*-6 in inflammation, immunity, and disease. Cold Spring Harb Perspect Biol. 2014; 6: a016295.

[23] Kotowska J, Jówko E, Cieśliński I, Gromisz W, Sadowski J. *IL*-6 and HSPA1A gene polymorphisms may influence the levels of the inflammatory and oxidative stress parameters and their response to a chronic swimming training. International Journal of Environmental Research and Public Health. 2022; 19: 8127.

[24] MacDonald C, Wojtaszewski JF, Pedersen BK, Kiens B, Richter EA. Interleukin-6 release from human skeletal muscle during exercise: relation to AMPK activity. Journal of Applied Physiology. 2003; 95: 2273–2277.

[25] Robson-Ansley PJ, de Milander L, Collins M, Noakes TD. Acute interleukin-6 administration impairs athletic performance in healthy, trained male runners. Canadian Journal of Applied Physiology. 2004; 29: 411–418.

[26] González-Estrada GD, Berrio GB, Gómez-Ríos D. Association between ACE, ACTN3, AGT, BDKRB2, and IL-6 gene polymorphisms and elite status in Colombian athletes. Journal of Physical Education and Sport. 2023; 23: 1036–1043.

[27] Mandic R, Jakovljevic S, Jaric S. Effects of countermovement depth on kinematic and kinetic patterns of maximum vertical jumps. Journal of Electromyography and Kinesiology. 2015; 25: 265–272.

[28] Mayhew SR, Wenger HA. Time motion analysis of professional soccer. Journal of Human Movement Studies. 1985; 11: 49–52.

[29] ACSM. American College of Sports Medicine-Guidelines for exercise testing and prescription. 11th edn. ACSM: USA. 2021.

[30] Edward TH, Dixie LT. Fitness professional's handbook. 6th edn. Human Kinetics: USA. 2012.
[31] Jackson AS, Pollock ML. Generalized equations for predicting body density of men. British Journal of Nutrition. 1978; 40: 497–504.
[32] Cohen J. Statistical power analysis for the behavioral sciences. 2nd edn. Erbbaum: Hillsdale, NJ. 1988.
[33] Kline RB. Principles and practice of structural equation modeling. 3rd edn. Guilford Press: New York, NY. 2011.
[34] Hopkins WG, Marshall SW, Batterham AM, Hanin J. Progressive statistics for studies in sports medicine and exercise science. Medicine & Science in Sports & Exercise. 2009; 41: 3.
[35] Demirci B, Bulgay C, Ceylan Hİ, Öztürk ME, Öztürk D, Kazan HH, *et al*. Association of ACTN3 R577X polymorphism with elite basketball player status and training responses. Genes. 2023; 14: 1190.
[36] Eroğlu O, Zileli R. The effect of genetic factors on sportive performance. International Journal of Sports, Exercise & Training Science. 2015; 1: 63–76.
[37] Grgic J. Effects of caffeine on resistance exercise: a review of recent research. Sports Medicine. 2021; 51: 2281–2298.
[38] McAuley ABT, Hughes DC, Tsaprouni LG, Varley I, Suraci B, Roos TR, *et al*. Genetic association research in football: a systematic review. European Journal of Sport Science. 2021; 21: 714–752.
[39] Massidda M, Voisin S, Culigioni C, Piras F, Cugia P, Yan X, *et al*. ACTN3 R577X polymorphism is associated with the incidence and severity of injuries in professional football players. Clinical Journal of Sport Medicine. 2019; 29: 57–61.
[40] Massidda M, Bachis V, Corrias L, Piras F, Scorcu M, Culigioni C, *et al*. ACTN3 R577X polymorphism is not associated with team sport athletic status in Italians. Sports Medicine-Open. 2015; 1: 6.
[41] Varillas-Delgado D, Gutierrez-Hellin J, Maestro A. Genetic profile in genes associated with sports injuries in elite endurance athletes. International Journal of Sports Medicine. 2023; 44: 64–71.
[42] Maciejewska-Skrendo A, Sawczuk M, Cieszczyk P, Ahmetov I. Genes and power athlete status: genes and power athlete status. In Barh D, Ahmetov I (eds.) Sports, exercise, and nutritional genomics (pp. 41–72). Academic press: Cambridge, UK. 2019.
[43] González-Estrada GD, Berrio GB, Gómez-Ríos D. Association between ACE, ACTN3, AGT, BDKRB2, and *IL*-6 gene polymorphisms and elite status in Colombian athletes. Journal of Physical Education and Sport. 2023; 23: 1036–1043.
[44] Ben-Zaken S, Meckel Y, Nemet D, Pantanowitz M, Eliakim A. The AGT M235T (RS699, 4072T>C) polymorphism is not associated with elite weightlifting performance. Acta Kinesiologiae Universitatis Tartuensis. 2018; 23: 34.
[45] Gomez-Gallego F, Santiago C, González-Freire M, Yvert T, Muniesa CA, Serratosa L, *et al*. The C allele of the *AGT* Met235Thr polymorphism is associated with power sports performance. Applied Physiology, Nutrition and Metabolism. 2009; 34: 1108–1111.
[46] Ruiz JR, Arteta D, Buxens A, Artieda M, Gómez-Gallego F, Santiago C, *et al*. Can we identify a power-oriented polygenic profile? Journal of Applied Physiology. 2010; 108: 561–566.
[47] Bulgay C, Polat T, Yılmaz OÖ, Tacal Aslanet B, Ali Ergün M, Ulucan K. Determination of Angiotensinogen (*AGT*) rs699 Polymorphism Distribution in Football Players. Kilis 7 Aralık University Journal of Physical Education and Sports Sciences. 2021; 5: 145–153.
[48] Eynon N, Ruiz JR, Oliveira J, Duarte JA, Birk R, Lucia A. Genes and elite athletes: a roadmap for future research. Journal of Physiology. 2011; 589: 3063–3070.
[49] Tuna G, Polat T, Yılmaz ÖÖ, Savaşan M, Erdil NG, Ulucan K, *et al*. The relationship between swimming styles and Il-6 Rs1800795 polymorphism in professional swimmers. Pakistan Journal of Medical & Health Sciences. 2022; 16: 444–445.
[50] Ulucan K, Yuksel I, Doğan CS, Kaynaret Ö. Interleukin-6 rs1800795 polymorphism is not considered as a genetic biomarker in Turkish national skiing running athlete cohort. Fresenius Environ Bull. 2020; 3: 1–5.
[51] Cenikli A, Nursal A, Tural E, Polat Y, Tasmektepligil MY, Yigit S. The correlation between rs1800795 variant of *IL*-6 and sports performance among Turkish elite athletes. International Journal of Humanities Social Sciences and Education. 2016; 1: 3–11.
[52] Huuskonen A, Tanskanen M, Lappalainen J, Oksala N, Kyröläinen H, Atalay M. A common variation in the promoter region of interleukin-6 gene shows association with exercise performance. Journal of Sports Science and Medicine. 2009; 8: 271–277.

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