

Association of COMT rs4680 Polymorphism with High-Level Performance in Track & Field Athletes

Celal Bulgay¹, Veli Ozan Çakır², Işık Bayraktar³ and Mehmet Ali Ergün⁴

Abstract

The catechol-O-methyltransferase (COMT) gene rs4680 polymorphism, primarily linked to psychological traits, has been limitedly studied in the key athletic abilities including endurance, speed, and power. Thus, the current investigation sought to explore any possible connections between the rs4680 polymorphism in the COMT gene and competitive performance among Turkish high-level track & field athletes. As a part of an ongoing project, this study engaged 60 elite athletes, categorized into two distinct groups based on their specialty (31 sprint/power athletes and 29 endurance athletes). To provide a comparative baseline, a control group consisting of twenty sedentary individuals aged between 18 and 35 was also incorporated. The assessment of participants' performance levels is conducted using the methodology established by the International Association of Track & Field Federations (IAAF), which is based on personal bests (PBs). Whole exome sequencing (WES) was used in the research to analyze genomic DNA that was taken out of participant blood samples. The objective was to use linear regression models for the analysis of many variables, including gender, PBs, and the category of sport. These models facilitated comparisons both within and between the athletic groups and controls. Comparisons between and between the athletic groups and controls were made easier by these models. The distribution of the COMT gene rs4680 polymorphism in terms of genotypes (AA, GA, and GG) did not change significantly between the athlete and the control group or within the athletic groups, according to the research ($p > 0.05$). In a similar vein, the research did not discover any connections of note between athletes' PBs in the sprint/power or endurance categories and the rs4680 polymorphism. Based on these findings, the research concludes that there is no meaningful relationship between the COMT gene's rs4680 polymorphism and the competitive performance of the Turkish high-level track and field athletes under investigation. To have a clearer understanding of the influence of this polymorphism on athletic performances, future study with larger numbers of participants is recommended.

Keywords: Track and Field, Endurance Athletes, Sprint/Power Athletes, Athletics, COMT, Polymorphism, Rs4680

INTRODUCTION

Over the years, several aspects have been closely examined to enhance the performance of athletes. The parameters included in this list are training at high altitudes, the variety of muscle fibers, nutrition customized for certain sports, methods for recovery, maximal oxygen consumption (MaxVO₂), biomechanical and physical fitness. Coaches and scientists extensively study these factors, making them highly studied issues (Maciejewski-Skrendo et al., 2019; Ahmetov et al., 2022; Bulgay et al., 2023). However, over the past twenty years, in addition to environmental influences, progress in genetics has started to emphasize the significance of hereditary determinants in athletic performance. These advancements have established genetics as a vital field of study in relation to its influence on an athlete's performance. Each year, scientists are increasingly focusing their study on identifying specific genes that influence athletic ability (Ahmetov et al., 2015; Bojarczuk et al., 2022; Kumagai et al., 2023; Semenova et al., 2022). Recent studies have linked 251 genes—roughly 20 of which are associated with extraordinary performance in elite athletes—to various aspects of sports. This group includes 41 genes linked to strength, 45 genes linked to power, and 42 genes linked to endurance (Semenova et al., 2023).

Research suggests that an athlete's performance is not exclusively determined by their physical and physiological abilities but is also greatly affected by psychological elements such as motivation, stress, anxiety, and addiction. This highlights the significance of mental well-being in addition to physical training for athletes striving to attain peak performance (Voelcker-Rehage et al., 2015; Abe et al., 2017; Çetin et al., 2021). The

¹ Bingol University, Sports Science Faculty, Bingol, Türkiye. E-mail: cbulgay@bingol.edu.tr

² Gazi University, Sports Science Faculty, Ankara, Türkiye. E-mail: veliozancakir@gazi.edu.tr

³ Alanya Alaaddin Keykubat University, Sports Science Faculty, Alanya, Türkiye. E-mail: isik.bayraktar@alanya.edu.tr

⁴ Gazi University, Department of Medical Genetics, Faculty of Medicine, 06560 Ankara, Türkiye E-mail: aliergun@gazi.edu.tr

interconnectedness of mental resilience, emotional stability, and physical prowess suggests the need for a comprehensive approach to sports training. Sports psychogenetics is the scientific discipline that investigates the interaction between psychological elements and genetic components in sports (van Breda et al., 2015; Valeeva et al., 2019). This field underscores the importance of maintaining a harmonious emphasis on both mental and physical aspects to attain exceptional performance in athletes. It emphasizes that mental resilience is a crucial element for obtaining success. Research in this field examines the degree to which psychological traits (such as cognitive ability, memory capacity, reaction time, and personality) of athletes are influenced by genetics. It also explores how these traits may be connected to athletic success, as well as the genetic variations in the nervous system that can be linked to an individual's athletic status and personality traits (Voelcker-Rehage et al., 2015; Abe et al., 2017; Valeeva et al., 2019). Recent studies have identified genetic polymorphisms responsible for individual differences in cognitive abilities. Based on these findings, it is believed that genetic variations linked to variations in cognitive ability may also impact the competitive performance of athletes (van Breda et al., 2015; Voelcker-Rehage et al., 2015; Abe et al., 2017; Valeeva et al., 2019). However, there absence of a lot of studies that examine the connection between athletic performance and genetic variants associated with cognitive capacities.

One of the genes studied in the field of sports psychogenetics is the catechol-O-methyltransferase (*COMT*). The *COMT* gene is localized on 22q11.2 and is responsible for the breakdown of catecholamine compounds, including dopamine, noradrenaline, and adrenaline. The Val158Met or rs4680 is the most well researched single nucleotide polymorphism (SNP) in the *COMT* gene. This genetic variation in the *COMT* gene results in alterations in the functionality of the *COMT* enzyme, which is accountable for controlling the breakdown of dopamine (van Breda et al., 2015; Voelcker-Rehage et al., 2015; Abe et al., 2017; Humińska-Lisowska et al., 2023). Research has established that these alterations had a role in the onset of certain illnesses, such as schizophrenia, bipolar disorder, obsessive-compulsive disorder, and migraines. Additionally, they are also associated with the manifestation of aggressive, emotional reactions, motivation, and antisocial behaviors (Malhotra et al., 2002; Bilder et al., 2002; Handoko et al., 2005; Bertolino et al., 2006; Bosia et al., 2007; Mata et al., 2008; Stroth et al., 2010; Huang et al., 2016; Valeeva et al., 2020; Varma et al., 2011; Zmijewski et al., 2021; Lee et al., 2022).

Upon reviewing the pertinent literature, it becomes evident that there are just a few research that have examined the correlation between the *COMT* gene rs4680 polymorphism and athletic performances. The aim of this study is to investigate the genetic variations, particularly in the rs4680 polymorphism, among top sprint/power and endurance athletes, with sedentary individuals as the control group. Furthermore, this study aims to investigate the potential association between the rs4680 polymorphism and personal bests (PBs) of the athletes. To the knowledge of the current study, this is the first investigation into the connection between the rs4680 polymorphism and high-level Turkish track and field athletes. It is hypothesized that there will be significant differences in the genotype and allele frequencies of the rs4680 polymorphism between sprint/power athletes and endurance athletes. Moreover, the research anticipates that individuals with the AA genotype will exhibit superior athletic performance.

METHODS

Ethical Approval

The study was conducted in compliance with the Declaration of Helsinki and received clearance from the Gazi University Non-Interventional Clinical Research Ethics Committee on April 05, 2021, with decision number 09.

Participants

Before the initiation of the trial, individuals from both the athlete and control groups were required to provide consent forms and demographic information. This study included a cohort of 60 high-level track and field athletes, who were divided into two primary groups: sprint/power athletes (sprinters, throwers, and jumpers) and endurance athletes (long-distance runners).

Among the sprinter/power athlete category, there were 11 female participants, accounting for 35.5% of the total, and 20 male athletes, making up 64.5% of the whole. The endurance athlete section consisted of 10 female competitors, accounting for 34.5% of the total, and 19 male athletes, accounting for 65.5% of the total.

The study also involved 20 control participants, who were sedentary individuals and volunteered for the study. All athletes were affiliated with the Turkish Track & field Federation, held licenses in their respective sporting disciplines, and adhered to a strict training regime, engaging in their sport for at least six days a week. All participants were Caucasians.

The participants were classified into two categories: sprint/power athletes or endurance athletes, based on the distance, length, and energy demands of their respective sports. All athletes achieved a national ranking within the top 10 in their respective sports. The members of the elite group have taken part in prestigious international tournaments including the European Championships, Universiade, Mediterranean Games, and Balkan Championship. The sprint/power group consisted of competitors specializing in disciplines that primarily need anaerobic energy generation. The individuals in this cohort consisted of athletes specializing in 100–400-meter sprints, jumping events, and throwing events. The endurance athlete group consisted of athletes that mostly participated in long-distance events that heavily relied on aerobic energy generation. This group consisted of runners participating in the 3000m, 5000m, 10000m, and marathon events.

Athletic Performance

The research evaluated the performance of the athletes by utilizing the scoring system developed by the International Association of Track & Field Federations (IAAF), currently known as World Athletics, as outlined by Spiriev (Spiriev, 2014).

Whole Exome Sequencing

A commercial DNA isolation kit (DNeasy Blood and Tissue Kit; Qiagen, Germany) was used to obtain genomic DNA from the blood samples of the participants. After isolation, a NanoDrop (NanoDrop 1000 Spectrophotometer; Thermo Scientific, USA) was used for the determination of the concentrations and purity of the DNAs.

For Whole Exome Sequencing (WES), DNAs were processed as libraries using Twist Human Comprehensive Exome Panel (Twist Biosciences, USA) in which DNA was fragmented, barcoded, size-selected, hybridized to the Twist Hybridization probes and PCR amplified according to the supplier's instructions. After determination of concentrations using Qubit fluorometer (Thermo Scientific, USA), the libraries were run in Illumina NextSeq500 (Illumina Inc., USA) according to the standard protocol of the manufacturer.

Genome Analysis Toolkit (GATK) was first preferred for raw data processing (Van der Auwera et al., 2013). Alignments and variant calls were carried out using HaplotypeCaller program using GRCh38/hg38 human reference genome. ANNOVAR (Wang et al., 2010) was used for the variant annotations.

Analysis

In the current research, the statistical analyses were conducted using SPSS statistical package version 25.0 for Mac. A power analysis, carried out with the G*Power 3.1 software, was used to determine the necessary number of study participants. Effect sizes were defined as 0.10 for small, 0.30 for medium, and 0.50 for large, in line with Cohen's recommendations (Cohen, 1988). The research aimed at a large effect size of 0.50. Seeking a 95% power and an alpha level of 0.05, the analysis indicated that a minimum of 80 participants was required according to the χ^2 tests: Goodness-of-Fit test for the Contingency model.

The study determined the frequencies of genotypes and alleles for the polymorphism and evaluated whether they followed the Hardy-Weinberg equilibrium. This was done using either the chi-square test or Fisher's exact test, depending on the adequacy of the data. A one-way ANCOVA was conducted to investigate the relationship between the rs4680 polymorphism of the *COMT* gene and personal best performances in athletes. The analysis included adjustments for variables such as sex and years of experience in sports. To validate the robustness of these connections, linear regression models were utilized across a range of genetic frameworks, encompassing

co-dominant, dominant, recessive, over-dominant, and additive models. The linear regression analysis yielded 95% confidence intervals for each connection. The SNPStats software (Sole et al., 2006) was used to validate the results, assisting in the examination of allele and genotype frequencies and the implementation of association studies. P -value < 0.05 were considered statistically significant.

FINDINGS

The objective of this study is to investigate any potential correlation between the *COMT* rs4680 polymorphism and the performance of a group of elite Turkish athletes in PB/competitive events, compared to a control group.

Firstly, the frequencies of genotypes and alleles were determined. Based on the findings, there were no statistically significant variations seen between the AA, GA, and GG genotypes within and across the groups ($p > 0.05$). In terms of allele frequencies, although the count of allele A was greater than that of allele G, there were no statistically significant differences seen within or between the groups ($p > 0.05$; Table 1).

Table 1. Genotype and allele frequencies of rs4680 polymorphism in elite athletes and controls

Disciplines	Genotype			p -value	Allele		p -value
	AA	GA	GG		A	G	
Sprint/power	16(45.2%)	11(35.5%)	6(19.4%)	0.33	43(65.2%)	23(34.8%)	0.45
Endurance	11(37.9%)	13(44.8%)	5(17.2%)		35(60.3%)	23(39.7%)	
Controls	4(20.0%)	13(65.0%)	3(15.0%)		21(52.5%)	19(47.5%)	

Finally, the study examined the potential correlation between the *COMT* rs4680 polymorphism and personal bests (PBs) in sprint/power and endurance athletes. Various genetic models, including codominant, dominant, recessive, and over-dominant, were used for the analysis. The results indicated that there were no significant associations between the rs4680 polymorphism and PBs in both the sprint/power ($p > 0.05$; Table 2) and endurance ($p > 0.05$; Table 3) athlete categories.

Table 2. rs4680 association with the PBs within the sprint/power athletes

Model	Genotype	n	Mean score (PB)	Difference (95% CI)	p -value
Codominant	AA	14	998.36	0.00	0.69
	GA	11	961.36	-15.44 (-99.21 – 68.34)	
	GG	6	1030.67	33.02 (-65.78 – 131.82)	
Dominant	AA	14	988.36	0.00	0.93
	GA-GG	17	985.82	3.37 (-68.20 – 74.93)	
Recessive	AA-GA	25	976.48	0.00	0.43
	GG	6	1030.67	37.99 (-55.50 – 131.49)	
Over-dominant	AA-GG	20	1001.05	0.00	0.57
	GA	11	961.36	-23.09 (-102.82 – 56.64)	

Table 3. rs4680 association with the PBs within the endurance athletes

Model	Genotype	n	Mean score (PB)	Difference (95% CI)	p -value
Codominant	AA	11	1015.09	0.00	0.64
	GA	13	1038.38	23.56 (-42.02 – 89.13)	
	GG	5	995.4	-9.80 (-93.03 – 73.43)	
Dominant	AA	11	1015.09	0.00	0.65
	GA-GG	18	1026.44	14.28 (-47.36 – 75.92)	
Recessive	AA-GA	24	1027.71	0.00	0.51
	GG	5	995.4	-24.33 (-96.33 – 47.66)	
Over-dominant	AA-GG	16	1008.94	0.00	0.35
	GA	13	1038.38	27.31 (-28.90 – 83.52)	

DISCUSSION

To date, numerous studies have shown that athletic performance in high-level track & field athletes is the result of a complex interaction among various factors such as environmental, nutritional, physical, physiological, biomechanical, sociocultural, and genetic elements (Eynon, et al., 2013; Joyner, 2019; Varillas-Delgado et al., 2022). Research in track & field as additionally highlighted the importance of phenotypes such as endurance and sprint/power for athletes to achieve excellence (Buxens et al., 2011; Eynon, et al., 2013; Bulgay et al., 2023).

When the relevant literature is examined, most studies investigating the relationship between genetic factors and athletic performance in high-level athletes have explored different genes and/or polymorphisms in these genes (Eynon et al., 2011; Pitsiladis et al., 2013; Salinero et al., 2017; Maciejewska-Skrendo et al., 2019; Kikuchi et al., 2021). Nonetheless, there is a scarcity of studies that specifically investigate the correlation between the *COMT* gene rs4680 polymorphism and athletic performance in elite track and field athletes. The aim of this study was to investigate the genetic differences between persons who lead a sedentary lifestyle and those who are highly trained in sprint/power and endurance training, with a specific focus on the rs4680 polymorphism. Moreover, this study aimed to investigate the potential link between the rs4680 polymorphism and personal bests (PBs) of the athletes. To our best knowledge, the current study is the first investigation to determine whether the rs4680 polymorphism associates the athletic performance of high-level track & field athletes in Turkish population in a perspective of the cognitive ability associated gene, *COMT*. Upon examining the findings of the current study, no significant differences in genotype and allele frequencies between groups were identified. Furthermore, no relationship was found between the rs4680 polymorphism and PBs of the athletes within each athletic group. Therefore, the research hypothesis was not supported, and it was concluded that the rs4680 polymorphism was not an effective indicator for distinguishing differences between the specified athlete groups in Turkish population.

The *COMT* gene is responsible for the production of an enzyme that is key in breaking down neurotransmitters, including dopamine, primarily in the midbrain region (Humińska-Lisowska et al., 2023). The Val158Met variant, also referred to as the rs4680 polymorphism within the *COMT* gene, can lead to notable variations in the enzyme's functioning based on the genotype (Voelcker-Rehage et al., 2015). The AA genotype is linked to reduced enzyme activity, heightened enzyme sensitivity to temperature (thermolability), and raised dopamine levels. These traits can result in a range of physiological consequences. In contrast, the GG genotype is associated with increased enzyme activity, normal susceptibility to heat, and decreased dopamine levels, which can also impact other physiological functions (Zmijewski et al., 2021).

Multiple studies have indicated that the *COMT* rs4680 polymorphism is a genetic variant that impacts cognitive performance (Valeeva et al., 2020; Lee et al., 2022). These studies have found that the *COMT* Val/Met polymorphism is involved in the development of schizophrenia and impacts the functioning of the prefrontal cortex (PFC) and hippocampus. Individuals who carry the Met allele, which has reduced enzyme activity, tend to have superior cognitive performance (Bilder et al., 2002; Handoko et al., 2005; Bosia et al., 2007). According to Malhotra et al. (2002), their research revealed that those who carry the Met allele demonstrated superior performance in executive tasks, even among those who were considered healthy volunteers. Bertolino et al. (2006) found that those who carry the Met allele showed a more favorable clinical response to antipsychotic medications and experienced cognitive improvement (Bertolino et al., 2006). In contrast to these observations, some researchers have found no correlation between *COMT* Val/Met polymorphisms and vulnerability to schizophrenia or cognitive functions (Mata et al., 2008; Huang et al., 2016).

Several research have indicated that the *COMT* rs4680 polymorphism is one of the genetic variations that affects athletic performance, in addition to cognitive ability. In a study conducted by Abe et al. (2017) on swimmers, it was found that competitive swimmers who had the Met amino acid (allele A) of the Val158Met polymorphism performed better in competitions compared to those who had the Val/Val amino acid combinations (allele G). The researchers proposed that individuals harboring the Met allele may have improved competitive performance due to stronger emotional and self-regulation abilities, which are boosted by increased dopamine levels in the prefrontal cortex (PFC). Furthermore, researchers suggests that swimmers with the Val/Val genotype may enhance their athletic performance by engaging in rigorous training regimens designed to boost their aerobic capacity. A study conducted with 75 participants who participated in a 17-week running program discovered that individuals with the Val/Val genotype shown improved executive skills after completing their aerobic exercise routine, in comparison to those who had the Met allele. The results indicate that enhancements in physical fitness resulted in enhanced cognitive function, most likely by influencing the regulation of dopamine pathways (Stroth et al., 2010). Although the current study did not find any statistically significant differences in endurance sports depending on genotype, it did discover that athletes with the AA

genotype had higher average performance scores compared to those with other genotypes. These results are consistent with the findings of the current investigation and the existing literature.

In the present investigation, although there were no statistically significant differences in genotype and allele frequencies, it was noticed that the number of persons with the A allele was consistently larger across all groups. A drawback of this study was the lack of psychological phenotypic data, which limits the ability to analyze and understand the results from both a genetic and psychological standpoint. Previous study indicates that individuals with the A gene may demonstrate enhanced cognitive and athletic abilities (Voelcker-Rehage et al., 2015; Valeeva et al., 2020; Zmijewski et al., 2021; Lee et al., 2022). However, additional research is needed to confirm these views. However, relevant literature and the current study finding suggests that hereditary structures may have a crucial impact on comprehending the psychological and athletic characteristics of athletes.

There are several limitations in the current study. Its small sample size, which could potentially weaken the statistical significance of the findings. Moreover, the athlete participants exhibit a significant lack of variability in their phenotypic features. This is further exacerbated by the omission of psychological phenotypic data, which could offer more profound understanding of athlete performance and resilience. In addition, the study fails to address epigenetic variables, disregarding the possible influence of environmental factors on the regulation of gene expression over a period. Conversely, the homogeneity among the groups of athletes can be viewed as an advantageous component of this study because it enables more precise comparisons under controlled conditions.

CONCLUSION

The study's findings indicate that there is no substantial correlation between the rs4680 polymorphism in the *COMT* gene and competitive performance among the group of Turkish high-level track & field athletes that were evaluated. Nevertheless, it is recommended that additional study with a bigger sample size be conducted to have a more conclusive understanding of the influence of this polymorphism on athletic performance. This advice emphasizes the necessity for more extensive investigations to potentially reveal nuanced genetic factors that can impact sports performance, which may not be identifiable in smaller sample groups.

REFERENCES

- Abe, D., Doi, H., Asai, T., Kimura, M., Wada, T., Takahashi, Y., Matsumoto, T., & Shinohara, K. (2017). Association between *COMT* Val158Met polymorphism and competition results of competitive swimmers. *Journal of Sports Sciences*, 1–5. <https://doi.org/10.1080/02640414.2017.1309058>
- Ahmetov, I. I., Hall, E. C. R., Semenova, E. A., Prankevičienė, E., & Ginevičienė, V. (2022). *Advances in sports genomics* (pp. 215–263). <https://doi.org/10.1016/bs.acc.2021.07.004>
- Ahmetov, I. I., Kulemin, N. A., Popov, D. V., Naumov, V. A., Akimov, E. B., Bravy, Y. R., Egorova, E. S., Galeeva, A. A., Generozov, E. V., Kostryukova, E. S., Larin, A. K., Mustafina, L. J., Ospanova, E. A., Pavlenko, A. V., Starnes, L. M., Zmijewski, P., Alexeev, D. G., Vinogradova, O. L., & Govorun, V. M. (2015). Genome-wide association study identifies three novel genetic markers associated with elite endurance performance. *Biology of Sport*, 32(1), 3–9. <https://doi.org/10.5604/20831862.1124568>
- Bertolino, A., Rubino, V., Sambataro, F., Blasi, G., Latorre, V., Fazio, L., Caforio, G., Petruzzella, V., Kolachana, B., Hariri, A., Meyer-Lindenberg, A., Nardini, M., Weinberger, D. R., & Scarabino, T. (2006). Prefrontal-Hippocampal Coupling During Memory Processing Is Modulated by *COMT* Val158Met Genotype. *Biological Psychiatry*, 60(11), 1250–1258. <https://doi.org/10.1016/j.biopsych.2006.03.078>
- Bilder, R. M., Volavka, J., Czobor, P. ál, Malhotra, A. K., Kennedy, J. L., Ni, X., Goldman, R. S., Hoptman, M. J., Sheitman, B., Lindenmayer, J.-P., Citrome, L., McEvoy, J. P., Kunz, M., Chakos, M., Cooper, T. B., & Lieberman, J. A. (2002). Neurocognitive correlates of the *COMT* Val158Met polymorphism in chronic schizophrenia. *Biological Psychiatry*, 52(7), 701–707. [https://doi.org/10.1016/S0006-3223\(02\)01416-6](https://doi.org/10.1016/S0006-3223(02)01416-6)
- Bojarczuk, A., Boulygina, E. A., Dzitkowska-Zabielska, M., Łubkowska, B., Leońska-Duniec, A., Egorova, E. S., Semenova, E. A., Andryushchenko, L. B., Larin, A. K., Generozov, E. V., Cieszczyk, P., & Ahmetov, I. I. (2022). Genome-Wide Association Study of Exercise-Induced Fat Loss Efficiency. *Genes*, 13(11), 1975. <https://doi.org/10.3390/genes13111975>
- Bosia, M., Bechi, M., Marino, E., Anselmetti, S., Poletti, S., Cocchi, F., Smeraldi, E., & Cavallaro, R. (2007). Influence of catechol-O-methyltransferase Val158Met polymorphism on neuropsychological and functional outcomes of classical rehabilitation and cognitive remediation in schizophrenia. *Neuroscience Letters*, 417(3), 271–274. <https://doi.org/10.1016/j.neulet.2007.02.076>

- Bulgay, C., Kasakolu, A., Kazan, H. H., Mijaica, R., Zorba, E., Akman, O., Bayraktar, I., Ekmekci, R., Koncagul, S., Ulucan, K., Semenova, E. A., Larin, A. K., Kulemin, N. A., Generozov, E. V., Balint, L., Badicu, G., Ahmetov, I. I., & Ergun, M. A. (2023). Exome-Wide Association Study of Competitive Performance in Elite Athletes. *Genes*, 14(3), 660. <https://doi.org/10.3390/genes14030660>
- Buxens, A., Ruiz, J. R., Arteta, D., Artieda, M., Santiago, C., González-Freire, M., Martínez, A., Tejedor, D., Lao, J. I., Gómez-Gallego, F., & Lucia, A. (2011). Can we predict top-level sports performance in power vs endurance events? A genetic approach. *Scandinavian Journal of Medicine & Science in Sports*, 21(4), 570–579. <https://doi.org/10.1111/j.1600-0838.2009.01079.x>
- Çetin, E., Bulğay, C., Tekkurşun Demir, Gönül, Cicioğlu, Hİ., Bayraktar, I., & Orhan, Ö. (2021). The examination of the relationship between exercise addiction and performance enhancement in elite athletes. *International Journal of Mental Health and Addiction*, 19(4), 1019–1030.
- Cohen, J. (1988). Statistical power analysis for the behavioral sciences. *Erbbaum*.
- Eynon, N., Hanson, E. D., Lucia, A., Houweling, P. J., Garton, F., North, K. N., and Bishop, D. J. (2013). Genes for elite power and sprint performance: ACTN3 leads the way. *Sports Medicine*, 43(9), 803–817.
- Eynon, N., Ruiz, J. R., Oliveira, J., Duarte, J. A., Birk, R., & Lucia, A. (2011). Genes and elite athletes: A roadmap for future research. In *Journal of Physiology* (Vol. 589, Issue 13, pp. 3063–3070). <https://doi.org/10.1113/jphysiol.2011.207035>
- Handoko, H. Y., Nyholt, D. R., Hayward, N. K., Nertney, D. A., Hannah, D. E., Windus, L. C., McCormack, C. M., Smith, H. J., Filippich, C., James, M. R., & Mowry, B. J. (2005). Separate and interacting effects within the catechol-O-methyltransferase (COMT) are associated with schizophrenia. *Molecular Psychiatry*, 10(6), 589–597. <https://doi.org/10.1038/sj.mp.4001606>
- Huang, E., Zai, C. C., Lisoway, A., Maciukiewicz, M., Felsky, D., Tiwari, A. K., Bishop, J. R., Ikeda, M., Molero, P., Ortuno, F., Porcelli, S., Samochowiec, J., Mierzejewski, P., Gao, S., Crespo-Facorro, B., Pelayo-Terán, J. M., Kaur, H., Kukreti, R., Meltzer, H. Y., ... Kennedy, J. L. (2016). Catechol-O-Methyltransferase Val158Met Polymorphism and Clinical Response to Antipsychotic Treatment in Schizophrenia and Schizo-Affective Disorder Patients: a Meta-Analysis. *International Journal of Neuropsychopharmacology*, 19(5), pyv132. <https://doi.org/10.1093/ijnp/pyv132>
- Humińska-Lisowska, K., Chmielowiec, K., Chmielowiec, J., Strońska – Pluta, A., Bojarczuk, A., Dzitkowska-Zabielska, M., Łubkowska, B., Spieszny, M., Surala, O., & Grzywacz, A. (2023). Association Between the rs4680 Polymorphism of the COMT Gene and Personality Traits among Combat Sports Athletes. *Journal of Human Kinetics*. <https://doi.org/10.5114/jhk/168789>
- Jamil, R. A., ul Hassan, S. R., Khan, T. I., Shah, R., & Nazir, S. (2024). Influence of personality on skepticism toward online services information, consumer stress, and health: an experimental investigation. *Management Research Review*, 47(1), 123–140.
- Joyner, M. J. (2019). Genetic Approaches for Sports Performance: How Far Away Are We? *Sports Medicine*, 49(S2), 199–204. <https://doi.org/10.1007/s40279-019-01164-z>
- Kikuchi, N., Moreland, E., Homma, H., Semenova, E. A., Saito, M., Larin, A. K., Kobatake, N., Yusupov, R. A., Okamoto, T., Nakazato, K., Williams, A. G., Generozov, E. V., & Ahmetov, I. I. (2021). Genes and Weightlifting Performance. *Genes*, 13(1), 25. <https://doi.org/10.3390/genes13010025>
- Kumagai, H., Kaneko, T., Shintake, Y., Miyamoto-Mikami, E., Tomita, H., Fukuo, M., Kawai, W., Harada, M., Kikuchi, N., Kamiya, N., Hirata, K., Zempo, H., Maeda, S., Miyamoto, N., & Fuku, N. (2023). Genetic polymorphisms related to muscular strength and flexibility are associated with artistic gymnastic performance in the Japanese population. *European Journal of Sport Science*, 23(6), 955–963. <https://doi.org/10.1080/17461391.2022.2078741>
- Lee, C. G., Moon, H., Kang, J., Choi, J. H., & Kwon, J. H. (2022). Long-term effects of adolescent sport experience, DRD2 and COMT genes, and their interaction on sport participation in adulthood. *Brain and Behavior*, 12(1). <https://doi.org/10.1002/brb3.2459>
- Maciejewska-Skrendo, A., Sawczuk, M., Cieszczyk, P., & Ahmetov, I. I. (2019). Genes and power athlete status: Genes and power athlete status. In *Sports, Exercise, and Nutritional Genomics*. Academic Press., 41–72. <https://www.sciencedirect.com/science/article/pii/B9780128161937000038>
- Malhotra, A. K., Kestler, L. J., Mazzanti, C., Bates, J. A., Goldberg, T., & Goldman, D. (2002). A Functional Polymorphism in the COMT Gene and Performance on a Test of Prefrontal Cognition. *American Journal of Psychiatry*, 159(4), 652–654. <https://doi.org/10.1176/appi.ajp.159.4.652>
- Mata, I., Pereziglesias, R., Pelayoteran, J., Rodriguezsanchez, J., Gonzalezblanch, C., Carrascomarin, E., Vazquezbarquero, J., & Crespofacorro, B. (2008). Lack of influence of COMT Val158Met genotype on cognition in first-episode non-affective psychosis. *Schizophrenia Research*, 102(1–3), 206–209. <https://doi.org/10.1016/j.schres.2008.02.011>
- Pitsiladis, Y., Wang, G., Wolfarth, B., Scott, R., Fuku, N., Mikami, E., He, Z., Fiuza-Luces, C., Eynon, N., & Lucia, A. (2013). Genomics of elite sporting performance: What little we know and necessary advances. In *British Journal of Sports Medicine* (Vol. 47, Issue 9, pp. 550–555). <https://doi.org/10.1136/bjsports-2013-092400>
- Salinero, J., Lara, B., Ruiz-Vicente, D., Areces, F., Puente-Torres, C., Gallo-Salazar, C., Pascual, T., & Del Coso, J. (2017). CYP1A2 Genotype Variations Do Not Modify the Benefits and Drawbacks of Caffeine during Exercise: A Pilot Study. *Nutrients*, 9(3), 269. <https://doi.org/10.3390/nu9030269>

- Semenova, E. A., Hall, E. C. R., & Ahmetov, I. I. (2023). Genes and Athletic Performance: The 2023 Update. *Genes*, 14(6), 1235. <https://doi.org/10.3390/genes14061235>
- Semenova, E. A., Zempo, H., Miyamoto-Mikami, E., Kumagai, H., Larin, A. K., Sultanov, R. I., Babalyan, K. A., Zhelankin, A. V., Tobina, T., Shiose, K., Kakigi, R., Tsuzuki, T., Ichinoseki-Sekine, N., Kobayashi, H., Naito, H., Burniston, J., Generozov, E. V., Fuku, N., & Ahmetov, I. I. (2022). Genome-Wide Association Study Identifies CDKN1A as a Novel Locus Associated with Muscle Fiber Composition. *Cells*, 11(23), 3910. <https://doi.org/10.3390/cells11233910>
- Sole, X., Guino, E., Valls, J., & Iniesta, R. (2006). SNPStats: a web tool for the analysis of association studies. *Bioinformatics*, 22(15), 1928–1929.
- Spiriev, B. (2014). IAAF Scoring Tables of Athletics. 368.
- Stroth, S., Reinhardt, R. K., Thöne, J., Hille, K., Schneider, M., Härtel, S., Weidemann, W., Bös, K., & Spitzer, M. (2010). Impact of aerobic exercise training on cognitive functions and affect associated to the COMT polymorphism in young adults. *Neurobiology of Learning and Memory*, 94(3), 364–372. <https://doi.org/10.1016/j.nlm.2010.08.003>
- Valeeva, E. V., Ahmetov, I. I., & Rees, T. (2019). Psychogenetics and sport. In *Sports, Exercise, and Nutritional Genomics* (pp. 147–165). Elsevier. <https://doi.org/10.1016/B978-0-12-816193-7.00007-5>
- Valeeva, E. V., Kashevarov, G. S., Kasimova, R. R., Ahmetov, I. I., & Kravtsova, O. A. (2020). Association of the Val158Met Polymorphism of the COMT Gene with Measures of Psychophysiological Status in Athletes. *Neuroscience and Behavioral Physiology*, 50(4), 485–492. <https://doi.org/10.1007/s11055-020-00924-z>
- van Breda, K., Collins, M., Stein, D. J., & Rauch, L. (2015). The COMT val158met polymorphism in ultra-endurance athletes. *Physiology & Behavior*, 151, 279–283. <https://doi.org/10.1016/j.physbeh.2015.07.039>
- Van der Auwera, G.A., Carneiro, M.O., Harl, C., Poplin, R., Del Angel, G., Levy-Moonshine, A. . . . , & DePristo, M.A. (2013). From FastQ Data to High-Confidence Variant Calls: The Genome Analysis Toolkit Best Practices Pipeline. *Curr. Protoc. Bioinform*, Wiley Online Library. <https://doi.org/10.1002/0471250953.bi1110s43>
- Varillas-Delgado, D., Del Coso, J., Gutiérrez-Hellín, J., Aguilar-Navarro, M., Muñoz, A., Maestro, A., & Morencos, E. (2022). Genetics and sports performance: the present and future in the identification of talent for sports based on DNA testing. In *European Journal of Applied Physiology* (Vol. 122, Issue 8, pp. 1811–1830). Springer Science and Business Media Deutschland GmbH. <https://doi.org/10.1007/s00421-022-04945-z>
- Varma, G. S., Karadağ, F., Emin Erdal, M., Ay, Ö. I., Levent, N., Tekkanat, Ç., Gökdoğan, E. T., & Herken, H. (2011). Effects of catechol-O-methyltransferase enzyme Val158Met polymorphism on cognitive functions in schizophrenic patients. *Klinik Psikofarmakoloji Bulteni*, 21(1), 24–32. <https://doi.org/10.5350/kpb-bcp201121105>
- Voelcker-Rehage, C., Jeltsch, A., Godde, B., Becker, S., & Staudinger, U. M. (2015). COMT gene polymorphisms, cognitive performance, and physical fitness in older adults. *Psychology of Sport and Exercise*, 20, 20–28. <https://doi.org/10.1016/j.psychsport.2015.04.001>
- Wang, K., Li, M., & Hakonarson, H. (2010). ANNOVAR: functional annotation of genetic variants from high-throughput sequencing data. *Nucleic Acids Research*, 38(16), e168.
- Zmijewski, P., Leońska-Duniec, A., Stula, A., & Sawczuk, M. (2021). Evaluation of the Association of COMT Rs4680 Polymorphism with Swimmers' Competitive Performance. *Genes*, 12(10), 1641. <https://doi.org/10.3390/genes12101641>.