**Association of *ANKK1* and *DRD2* Gene Polymorphisms with Exercise Addiction Among Elite Athletes**

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**Abstract**

Exercise addiction is a behavior that may dysregulate athletic performance as well as social and professional interactions of athletes. Whereas environmental factors such as training routines and personal traits could contribute to exercise addiction, recent studies have emphasized the importance of genetic predisposition, leading to the development of a subfield known as sports psychogenetics. Within this field of study, the ankyrin repeat and kinase domain containing 1 (*ANKK1*) and dopamine receptor D2 (*DRD2*) genes, which are located on chromosome 11 in a close proximity, have attracted research interest due to their involvement in dopaminergic signaling that plays a crucial role in reward processing, motivation, cognition and behavior. Therefore, the present study aimed to investigate potential associations between 14 polymorphisms in *ANKK1*/*DRD2* and exercise addiction among elite badminton players (n=39) and wrestlers (n=68). Exercise addiction was assessed using a psychometric screening instrument and allele frequencies of the selected polymorphisms were analyzed through genotyping with a single nucleotide polymorphism (SNP) microarray. Results indicated that two SNPs *ANKK1* rs7118900 (a missense variant) and *DRD2* rs4436578 (an intronic variant) were significantly and independently associated with exercise addiction among athletes. Of these, the *ANKK1* rs7118900 polymorphism has previously been associated with an increased risk of drug addiction, neuroticism, and depressed effect whereas the *DRD2* rs4436578 polymorphism has been associated with neuroticism. In addition to those SNPS, rs2283265 and rs1125394 SNPs were also linked to exercise addiction in a branch-independent manner. Thus, it is proposed that these SNPs could serve as genetic markers for identifying individuals at high risk of exercise addiction among athletes. However, further research is needed to understand the involvement of these SNPs in exercise addiction more comprehensively.

**Keywords:** Athletes, Badminton, Wrestling, Exercise addiction, Genetics, ANKK1, DRD2

## Introduction

Physical exercise is an individually performed and systematic activity aiming to improve health status and to enhance one or more components of physical fitness (Caspersen et al., 1985). Regular exercise triggers adaptive processes by regulating various metabolic changes. These adaptive processes contribute both to maintaining an individual's health and advancing the performance levels of elite athletes (Casuso and Huertas, 2021). Moreover, regular exercise leads to reduced body weight (Dixon et al., 2021), improved quality of life (Diz et al., 2021), recovery of cardiovascular functions (Cillekens et al., 2022), increased muscle mass (Hauben et al., 2022), accelerated metabolism (Hyvarinen et al., 2022), a lower risk of diabetes (Kanaley et al., 2022) and reduced levels of stress and anxiety (Weinstein and Weinstein, 2014; Singh et al., 2023). Additionally, it promotes regulation of sleep patterns (Wang and Boros, 2021) and cognitive functions (Bliss et al., 2021).

Although regular exercise is generally beneficial, excessive exercise may have some adverse effects. Excessive exercise can lead to, for instance, muscle injury (Markus et al., 2021), increase the risk of inflammation (Brolinson and Elliott, 2007) and cause damage to the cardiovascular system (Sharalaya and Phelan, 2019). Additionally, excessive and uncontrolled exercise may induce a psychological condition that has been termed as 'exercise addiction' (Vansteene et al., 2022). Exercise addiction is a behavioral condition in which individuals are unable to control their exercise routines and require more challenging exercise styles. As a result, exercise addiction negatively affects physical health of individuals as well as their social and professional interactions (Berczik et al., 2014; Bladon and Lindner, 2002; Szabo et al., 2015)

Unlike other addictions, exercise addiction involves high levels of physical effort and energy consumption (Egorov and Szabo, 2013). Even though there are associations between exercise addiction and drug abuse in terms of neurological mechanisms (Leeman and Potenza, 2013), exercise addiction has not formally been recognized as a psychiatric disorder in either the Diagnostic and Statistical Manual of Mental Disorders (DSM-5; American Psychiatric Association, 2013) or the International Classification of Diseases (ICD-11; World Health Organization, 2019).

Over the past decade, the number of studies on exercise addiction has significantly increased (Godoy-Izquierdo et al., 2021; Szabo and Demetrovics, 2022). These studies have frequently examined psychosocial factors such as perfectionism (Cakin et al., 2021; Gonzalez-Hernandez et al., 2023), narcissism (Zeigler-Hill et al., 2021; Krol et al., 2022), anxiety (Colledge et al., 2020; Zhang et al., 2024) and motivation (Kovacsik et al., 2021). However, these studies have sparked debates about the definition of exercise addiction. Different methods and measurement approaches have led to conflicting results. Therefore, a comprehensive approach is needed, and genetic studies could provide more appropriate objectivity. Evaluating psychological parameters associated with genetic background has given rise to a novel field called sports psychogenetics (Valeeva et al., 2019).

In sport psychogenetics, several genes have been identified as potential markers for various psychological traits (Abrahams et al., 2019; Humiska-Lisowska et al., 2022; 2023; 2024; Chmielowiec et al., 2021; McAuley et al., 2022; McFie et al., 2018; Michalowska-Sawczyn et al., 2019; 2021; 2025; Niewczas et al., 2021; Stroth et al., 2010; Tartar et al., 2020; Thomson et al., 2013; van Breda et al., 2015). Nevertheless, by single gene approach, the integration of psychogenetics into sports science remains limited. Recently, a genome-wide association study (GWAS) among athletes identified six SNPs (rs74345126, rs72652685, rs6745226, rs17614860, rs1025542, rs4841662, rs7599488 and rs1551336) associated with exercise addiction (Bulgay et al., 2025). However, further research is needed with a larger cohort to elucidate potential association markers for exercise addiction more fully.

Beyond the GWAS approach, focusing on addiction-related loci in terms of genetic associations in a large cohort would be informative. The q22-q23 loci on chromosome 11 have been highlighted in literature for their association with addiction phenotypes. This region contains two critical genes, ankyrin repeat, and kinase domain-containing 1 (*ANKK1*) and dopamine receptor D2 (*DRD2*), whose protein counterparts are involved in dopaminergic signaling and neurological processes and are associated with various addiction profiles (Li and Li, 2018; Ma et al., 2015). Hence, the study assessed possible associations between SNPs in these loci (on these genes) and exercise addiction among Turkish elite badminton players and wrestlers.

It was hypothesized that the 11q22-q23 loci and the genes *ANKK1* and *DRD2* would link to addiction phenotypes and allele frequencies of specific SNPs in these genes may vary across different sports disciplines. Moreover, it was investigated whether these SNPs were associated with exercise addiction profiles among elite athletes. The present study aimed to better understand the etiology of exercise addiction among elite athletes.

## Methodology

### *Ethics*

The study was approved by the Clinical Research Ethics Committee of Gazi University (approval number: 642; April 2021) for research involving wrestlers and by the Ethics Committee of XXX University (approval number: 24/01; July 2024) for research involving badminton players. The study adhered to the Declaration of Helsinki (World Medical Association, 2013) and the ethical standards of sport and exercise sciences. Both verbal and written informed consent were obtained from all participants before data collection.

### *Participants*

In the first part of the study, 68 wrestlers (all males; mean age = 23.40 years [SD = 5.04]; height = 175.70 cm [SD = 7.21]; weight = 78.81 kg [SD = 14.64]; sports experience = 12.58 years [SD = 4.70]) affiliated within the Turkish Wrestling Federation were involved. All wrestlers were elite-level athletes who competed in international events including the Olympic Games, European Championship and Balkan Championship. The second athlete group comprised 39 badminton players (16 females and 23 males; mean age = 25.48 years [SD = 5.39]; height = 175.05 cm [SD = 7.60]; weight = 72.50 kg [SD = 10.80]; sports experience = 14.28 years [SD = 4.22]) affiliated within the Turkish Badminton Federation. All athletes participated in international competitions such as the BWF World Junior Championship, Yonex International Championship, European Junior Championship and European Championship and were classified as having national elite status.

### *Exercise addiction profiling*

The exercise addiction profiles of the athletes were assessed using the 17-item Exercise Addiction Scale (Tekkursun Demir et al., 2018). In this scale, items 1 to 7 assess emotional distress and excessive focus, items 8 to 13 assess the postponement and conflict of individual and social necessities, and items 14 to 17 assess passion and tolerance. All items are rated on a five-point Likert scale ranging from 1 (strongly disagree) to 5 (strongly agree). Using this scoring approach, scoring 17 is no risk, 18-34 is low-risk, 35-51 is moderate risk, 52-69 is addiction and 70-85 is high addiction. Nevertheless, in the present study, this strategy caused heterogenicities in which the sample sizes were remarkably deviated. Thus, for association analyses, exercise addiction levels were evaluated by direct calculation scores (17-85).

### *Genotyping*

Genotyping of genetic variants was performed using genomic DNA extracted from peripheral blood samples of the participants with a commercial DNA isolation kit (QIAamp Blood Mini Kit; Qiagen, Switzerland). For the wrestling group, variants were genotyped using the Infinium Global Screening Array (Illumina Inc., USA) according to the supplier's standard protocol. The Axiom Precision Medicine Diversity Array Kit (Thermo Fisher Scientific, USA) was used to genotype DNA from badminton players. Local service providers conducted the genotyping processes, and genotypes were obtained in variant call format (VCF).

The VCF for each participant underwent quality control. Minor allele frequencies (MAFs) were set at >0.01 to detect SNPs. Statistical analyses focused on SNPs located in the 11q22-q23 region, where 14 SNPs (rs7118900, rs1800497, rs2587550, rs2734842, rs1124493, rs6277, rs6275, rs2283265, rs2440390, rs2734833, rs1125394, rs4436578, rs4460839 and rs4648317) were screened.

### *Statistical analysis*

Candidate gene approaches were used to investigate associations between polymorphisms in the 11q22-q23 region and exercise addiction levels. Generalized linear models were applied to determine addiction scores and relevant SNPs, with sports experience, height, weight, sports branch and sex (only for badminton players) included as fixed effects in the model. The models assessed both additive effects and dominance deviations of relevant variants. Fisher's exact test was conducted to evaluate differences in allele frequencies. For association analyses, exercise addiction levels were based on direct calculations and beta values were used to estimate the average effect of gene substitutions in the additive model and full dominance in the dominant model, depending on the A1 allele count in both models. The models were implemented using Plink 1.9 software (Chang et al., 2015). Additionally, the candidate SNPs were screened in the Turkish Genome Project (TGP) database (https://tgd.tuseb.gov.tr/en; accessed on February 15, 2025) and allele frequencies were compared with those obtained in the present study. Statistical significance for the candidate gene approach was set at $p < 0.05$ for each model.

## Results

First, allele frequencies of the 14 SNPs were compared between badminton players and wrestlers. The results showed no statistically significant deviations in allele frequencies for

SNPs between the two sports groups ($p > 0.05$; Table 1). Next, exercise addiction was assessed within each sport branch. For this aim, without classifying participants as addicted or non-addicted, direct calculations of exercise addiction scores (ranging from 17 to 85) were tested for associations with the selected SNPs. In the badminton group, the association of the *ANKK1* rs7118900 polymorphism (a missense variant) with exercise addiction was statistically significant in both additive and dominant models ($p < 0.05$; Table 2). However, none of the SNPs were significantly associated with exercise addiction in the wrestling group ($p > 0.05$; Table 3).

Beyond the within-group analyses, both branches were combined into a single group to increase sample size, and the data were re-analyzed for exercise addiction. After adjusting for age, sex and sports experience, SNPs located in the introns of the *DRD2* gene (rs2283265, rs1125394 and rs4436578) were significantly associated with exercise addiction in the combined athlete group ($p < 0.05$; Table 4). The *DRD2* rs2283265 and rs1125394 polymorphisms were in linkage disequilibrium (LD; $r^2 > 0.6$) with *ANKK1* rs7118900. In contrast, *DRD2* rs4436578 was independent of the aforementioned SNPs (rs7118900, rs2283265 and rs1125394).

Finally, the selected SNPs were cross-referenced with the TGP database, which includes sequencing data from 557 samples, allowing access to allele frequencies among healthy Turkish individuals. The allele frequencies (alternative allele frequencies in Table 1) were 0.837 for rs7118900, 0.829 for rs1800497, 0.681 for rs2587550, 0.682 for rs2734842, 0.879 for rs2283265, 0.850 for rs2440390, 0.607 for rs2734833, 0.865 for rs4436578, 0.943 for rs4460839 and 0.853 for rs4648317. Frequencies for rs1124493, rs6277, rs6275 and rs1125394 were not reported. Differences in allele frequencies between athletes and healthy individuals were not analyzed due to the lack of data for four SNPs.

**Table 1.** Allele frequencies of *ANKK1/DRD2* polymorphisms among elite badminton players and wrestlers.

| Gene | Locus 11q22-q23 | SNP | A1 | A2 | Badminton (A1 Allele Freq.) | Wrestling (A1 Allele Freq.) | *p* | OR | SE |
|---|---|---|---|---|---|---|---|---|---|
| *ANKK1/DRD2* | Chr11_113396099 | rs7118900 | A | G | 0.102 | 0.125 | 0.277 | 1.25 | 0.454 |
| | Chr11_113400106 | rs1800497 | A | G | 0.166 | 0.125 | 0.742 | 0.714 | 0.399 |
| | Chr11_113402203 | rs2587550 | G | A | 0.355 | 0.345 | 0.893 | 0.958 | 0.299 |
| | Chr11_113409552 | rs2734842 | G | C | 0.346 | 0.350 | 0.692 | 1.02 | 0.299 |
| | Chr11_113411573 | rs1124493 | T | G | 0.359 | 0.345 | 0.895 | 0.943 | 0.297 |
| | Chr11_113412737 | rs6277 | G | A | 0.421 | 0.426 | 0.243 | 1.022 | 0.289 |
| | Chr11_113412755 | rs6275 | A | G | 0.359 | 0.345 | 1.00 | 0.943 | 0.297 |
| | Chr11_113414814 | rs2283265 | A | C | 0.076 | 0.088 | 0.409 | 1.161 | 0.521 |
| | Chr11_113416156 | rs2440390 | T | C | 0.179 | 0.191 | 0.595 | 1.081 | 0.366 |
| | Chr11_113422198 | rs2734833 | G | A | 0.359 | 0.419 | 0.242 | 1.288 | 0.293 |
| | Chr11_113426463 | rs1125394 | C | T | 0.081 | 0.088 | 0.411 | 1.097 | 0.522 |
| | Chr11_113436043 | rs4436578 | C | T | 0.153 | 0.154 | 0.509 | 1.004 | 0.393 |
| | Chr11_113451074 | rs4460839 | C | T | 0.076 | 0.051 | 0.798 | 0.651 | 0.575 |
| | Chr11_113460810 | rs4648317 | A | G | 0.153 | 0.213 | 0.616 | 1.491 | 0.377 |

**Table 2.** Association analysis of *ANKK1*/*DRD2* polymorphisms with exercise addiction among badminton players.

| Gene | Locus 11q22-q23 | Polymorphism | Allele Information | | | Additive | | | Dominant | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | REF | ALT | A1 | BETA | SE | *p* | BETA | SE | *p* |
| *ANKK1/DRD2* | Chr11_113396099 | rs7118900 | G | A | A | 5.667 | 2.605 | **0.036*** | 7.355 | 3.097 | **0.023*** |
| | Chr11_113400106 | rs1800497 | G | A | A | 4.018 | 2.552 | 0.124 | 4.575 | 2.923 | 0.127 |
| | Chr11_113402203 | rs2587550 | G | A | G | -1.139 | 1.810 | 0.533 | -3.588 | 2.442 | 0.151 |
| | Chr11_113409552 | rs2734842 | G | C | G | -0.948 | 1.857 | 0.612 | -3.443 | 2.382 | 0.157 |
| | Chr11_113411573 | rs1124493 | T | G | T | -1.102 | 1.776 | 0.539 | -3.443 | 2.382 | 0.157 |
| | Chr11_113412737 | rs6277 | G | A | G | 0.925 | 1.872 | 0.624 | -0.899 | 2.692 | 0.740 |
| | Chr11_113412755 | rs6275 | A | G | A | -1.102 | 1.776 | 0.539 | -3.443 | 2.382 | 0.157 |
| | Chr11_113414814 | rs2283265 | C | A | A | 4.640 | 2.857 | 0.113 | 6.390 | 3.597 | 0.084 |
| | Chr11_113416156 | rs2440390 | T | C | T | -0.467 | 2.111 | 0.826 | -1.531 | 2.668 | 0.569 |
| | Chr11_113422198 | rs2734833 | G | A | G | 2.131 | 1.894 | 0.268 | 1.176 | 2.526 | 0.644 |
| | Chr11_113426463 | rs1125394 | T | C | C | 4.521 | 2.911 | 0.130 | 6.188 | 3.670 | 0.101 |
| | Chr11_113436043 | rs4436578 | C | T | C | -0.557 | 2.585 | 0.830 | -1.587 | 2.922 | 0.590 |
| | Chr11_113451074 | rs4460839 | C | T | C | -6.465 | 3.397 | 0.065 | -6.465 | 3.397 | 0.065 |
| | Chr11_113460810 | rs4648317 | G | A | A | 1.078 | 1.983 | 0.590 | 2.242 | 2.825 | 0.433 |

*$p < 0.05$.

**Table 3.** Association analysis of *ANKK1*/*DRD2* polymorphisms with exercise addiction among wrestlers.

| Gene | Locus 11q22-q23 | Polymorphism | Allele Information | | | Additive | | | Dominant | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | REF | ALT | A1 | BETA | SE | *p* | BETA | SE | *p* |
| *ANKK1/DRD2* | Chr11_113396099 | rs7118900 | G | A | A | 0.314 | 3.308 | 0.924 | 0.314 | 3.308 | 0.924 |
| | Chr11_113400106 | rs1800497 | G | A | A | 0.314 | 3.308 | 0.924 | 0.314 | 3.308 | 0.924 |
| | Chr11_113402203 | rs2587550 | G | A | G | -2.903 | 2.182 | 0.188 | -1.770 | 2.941 | 0.549 |
| | Chr11_113409552 | rs2734842 | G | C | G | -3.114 | 2.210 | 0.163 | -2.045 | 2.988 | 0.496 |
| | Chr11_113411573 | rs1124493 | T | G | T | -2.903 | 2.182 | 0.188 | -1.770 | 2.941 | 0.549 |
| | Chr11_113412737 | rs6277 | G | A | G | -2.283 | 2.185 | 0.300 | -1.660 | 3.142 | 0.599 |
| | Chr11_113412755 | rs6275 | A | G | A | -2.903 | 2.182 | 0.188 | -1.770 | 2.941 | 0.549 |
| | Chr11_113414814 | rs2283265 | C | A | A | 5.104 | 3.752 | 0.178 | 5.104 | 3.752 | 0.178 |
| | Chr11_113416156 | rs2440390 | T | C | T | -0.409 | 3.051 | 0.893 | -0.409 | 3.051 | 0.893 |
| | Chr11_113422198 | rs2734833 | G | A | G | -0.200 | 2.307 | 0.930 | 2.545 | 3.172 | 0.425 |
| | Chr11_113426463 | rs1125394 | T | C | C | 5.104 | 3.752 | 0.178 | 5.104 | 3.752 | 0.178 |
| | Chr11_113436043 | rs4436578 | C | T | C | -3.712 | 2.632 | 0.163 | -5.358 | 3.041 | 0.083 |
| | Chr11_113451074 | rs4460839 | C | T | C | -0.440 | 5.210 | 0.932 | -0.440 | 5.210 | 0.932 |
| | Chr11_113460810 | rs4648317 | G | A | A | -2.001 | 2.700 | 0.461 | -3.762 | 3.127 | 0.233 |

**Table 4.** Association analysis of *ANKK1*/*DRD2* polymorphisms with exercise addiction among all athletes.

| Gene | Locus 11q22-q23 | Polymorphism | Allele Information | | | Additive | | | Dominant | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | REF | ALT | A1 | BETA | SE | *p* | BETA | SE | *p* |
| *ANKK1/DRD2* | Chr11_113396099 | rs7118900 | G | A | A | 2.024 | 2.317 | 0.384 | 2.147 | 2.471 | 0.387 |
| | Chr11_113400106 | rs1800497 | G | A | A | 1.337 | 2.228 | 0.549 | 1.351 | 2.353 | 0.567 |
| | Chr11_113402203 | rs2587550 | G | A | G | -2.726 | 1.514 | 0.074 | -3.375 | 2.041 | 0.101 |
| | Chr11_113409552 | rs2734842 | G | C | G | -2.865 | 1.546 | 0.066 | -3.529 | 2.044 | 0.087 |
| | Chr11_113411573 | rs1124493 | T | G | T | -2.719 | 1.505 | 0.073 | -3.348 | 2.023 | 0.101 |
| | Chr11_113412737 | rs6277 | G | A | G | -1.622 | 1.563 | 0.301 | -2.343 | 2.225 | 0.294 |
| | Chr11_113412755 | rs6275 | A | G | A | -2.719 | 1.505 | 0.073 | -3.348 | 2.023 | 0.101 |
| | Chr11_113414814 | rs2283265 | C | A | A | 5.049 | 2.574 | 0.052 | 5.778 | 2.797 | **0.041*** |
| | Chr11_113416156 | rs2440390 | T | C | T | -1.240 | 1.929 | 0.521 | -1.785 | 2.102 | 0.397 |
| | Chr11_113422198 | rs2734833 | G | A | G | -0.096 | 1.619 | 0.952 | 0.840 | 2.189 | 0.701 |
| | Chr11_113426463 | rs1125394 | T | C | C | 4.979 | 2.599 | 0.058 | 5.697 | 2.825 | **0.046*** |
| | Chr11_113436043 | rs4436578 | C | T | C | -2.959 | 1.930 | 0.128 | -4.488 | 2.207 | **0.044*** |
| | Chr11_113451074 | rs4460839 | C | T | C | 0.766 | 3.167 | 0.809 | -0.766 | 3.167 | 0.809 |
| | Chr11_113460810 | rs4648317 | G | A | A | -.393 | 1.805 | 0.442 | -2.837 | 2.240 | 0.208 |

*$p < 0.05$.

## Discussion

The present study is the first one investigating the potential associations between polymorphisms in the *ANKK1*/*DRD2* genes (11q22-q23) and exercise addiction among elite badminton players and wrestlers. The main findings indicated that two SNPs—*ANKK1* rs7118900 (a missense variant) and *DRD2* rs4436578 (an intronic variant)—were significantly and independently associated with exercise addiction among athletes.

In the present study, the allele frequencies of the selected SNPs did not significantly differ between badminton players and wrestlers. Similar findings have been reported in previous studies, where no statistically significant deviations were observed for one or more of the selected SNPs between study groups (Silar et al., 2020; Michałowska-Sawczyn et al., 2021; Bayraktar et al., 2023). However, genetic heterogeneity and sample size may influence these findings.

Regarding exercise addiction, rs7118900 was significantly associated with addiction profiles under both additive and dominant models among badminton players. Moreover, when all participants were analyzed as a single group, rs2283265, rs1125394 and rs4436578 were also significantly linked to exercise addiction in a dominant model analysis. Therefore, the A allele in rs7118900 and rs2283265, and the C allele in rs1125394 and rs4436578 could be considered as genetic markers associated with an increased risk of exercise addiction among athletes.

The selected polymorphisms are located in chromosome 11 (q22-q23), which encompasses two genes, *ANKK1* and *DRD2*. These genes have previously been associated with various addiction profiles (Noble et al., 1994; Li et al., 2006; Perez de los Cobos et al., 2007; Wei et al., 2012;

Ragia et al., 2013). Their close genomic localization suggests functional similarities. Therefore, 14 SNPs within these genes were collectively analyzed. The *DRD2* gene encodes the dopamine D2 receptor, which plays a role in synaptic dopamine signaling, motivation, motor control, reward processing and addiction (Blum et al., 1995, 2022; Berridge et al., 2016; Kibaly et al., 2021). Consequently, variations in *DRD2* may influence social behavior and addiction susceptibility (Chmielowiec et al., 2021). Similarly, the *ANKK1* gene encodes a protein with ankyrin repeats and a kinase domain involved in dopaminergic signaling and neuronal development (Koeneke et al., 2020). Both genes are regulated by the same transcription factor, which may overlap their function (Lucht et al., 2010). Due to their physical and functional similarities, *ANKK1* and *DRD2* have frequently been studied together (Ma et al., 2015; Lachowicz et al., 2020; Michałowska-Sawczyn et al., 2021).

One of the most extensively studied polymorphisms in *ANKK1* is rs1800497, which was in linkage disequilibrium with $r^2=0.93$ with rs7118900 in the present study, and also known as Taq1A. Initially mapped within the *DRD2* gene, it was later determined to be in the *ANKK1* gene (Neville et al., 2004). This polymorphism has been identified as a key genetic marker in addiction status due to its effects on the dopaminergic system (Noble et al., 1991; Hirvonen et al., 2009). Taq1A directly influences dopamine D2 receptor density and binding capacity (Montalban et al., 2022), potentially disrupting reward mechanisms and increasing addiction risk.

The A allele of Taq1A has been documented as a risk factor for addiction, including smoking (Noble et al., 1994; Reyes-Gibby et al., 2015), heroin use (Li et al., 2006; Perez de los Cobos et al., 2007), alcohol use (Yau et al., 2015) and opioid dependence (Najafabadi et al., 2005). Additionally, this allele has been associated with behavioral addictions, such as problematic media use (Emond et al., 2025), internet addiction (Rył et al., 2024), and physical activity and body weight regulation (Hojjati et al., 2020). By modulating D2 receptor expression, the A allele has also been linked to changes in cognitive behavioral capacity (Thompson et al., 1997; Lachowicz et al., 2020; Antrobus et al., 2022). Furthermore, A/A and G/A genotypes of Taq1A have been associated with schizophrenia, obesity and drug abuse (Aliasghari et al., 2021; Habibzadeh et al., 2021; Switała and Leonska-Duniec, 2021; Switała et al., 2022).

Despite its well-documented role in addiction, the present study found no association between Taq1A and exercise addiction among elite badminton players or wrestlers. However, an association was observed with rs7118900, which was strongly correlated ($r^2=0.93$) with Taq1A.

This finding may be attributable to population-specific factors. Similarly, a previous study among Turkish athletes found no association between this polymorphism and athletic parameters although a significant relationship emerged when considering the duration of elite sports experience (Bayraktar et al., 2023).

Among the SNPs associated with exercise addiction in the present study, rs7118900 is a missense variant that results in an amino acid change (p.Ala239Thr) in the ANKK1 protein. This polymorphism has been implicated in neurological processes related to addiction phenotypes. Garrido et al. (2011) suggested that rs7118900 plays a key role in addiction pathophysiology by increasing expression levels and altering responses to dopamine stimulation. Levran et al. (2013) demonstrated that rs7118900 was associated with methadone dosage, which is used to treat opioid addiction. The same research group later reported a significant association between rs7118900, and heroin and cocaine addiction. Interestingly, the A allele of the rs7118900 has been found to be associated with an increased risk of neuroticism, depressed affect and feelings of guilt in the UK Biobank cohort (Open Targets, 2025).

Another SNP, rs2283265 (in linkage disequilibrium with $r^2$=0.64 with rs7118900 in the present study), has also been highlighted in studies on genetic variations in the dopaminergic system. Stolf et al. (2019) found an association between this polymorphism and crack cocaine addiction. Other studies have also shown that rs2283265 has been linked to cocaine and heroin addiction (Moyer et al., 2011; Sullivan et al., 2013; Levran et al., 2015;) and general drug abuse (Al-Eitan et al., 2012). Similarly, rs1125394 (which was in linkage disequilibrium with $r^2$=0.63 with rs7118900 in the present study), which was significantly associated with exercise addiction in the present study, has been associated with heroin addiction (Wang et al., 2016) and drug abuse (Al-Eitan et al., 2012). Finally, the *DRD2* rs4436578 (which is independent of rs7118900, rs2283265 or rs1125394) has widely been reported in addiction-related studies, with the G allele showing associations with indoor tanning (Mays et al., 2020), heroin addiction (Gao et al., 2017), opioid addiction (Lambert et al., 2024) and neuroticism (Open Targets Genetics, 2025). Overall, the associations of these SNPs with various addiction phenotypes support the findings of the present study.

Although the present study reports significant associations with exercise addiction, several limitations should be acknowledged. First, the sample size was relatively small due to the limited number of elite athletes, which may affect the generalizability of the results. Hence, further studies with larger cohorts are needed. Second, the study focused on badminton players and wrestlers, and the findings may not be generalizable to other sports. Sport-specific investigations are necessary for broader generalization. Third, the study analyzed a limited number of SNPs, and genome-wide association studies may provide further insights. Lastly, the study focused solely on genetic associations without considering environmental factors, necessitating epigenetic studies.

## Conclusions

The present study evaluated multiple *ANKK1*/*DRD2* polymorphisms for potential associations with exercise addiction among elite Turkish athletes from two disciplines, badminton and wrestling. The findings suggested that four polymorphisms (rs7118900, rs2283265, rs1125394 and rs4436578) may significantly be associated with exercise addiction. Based on these findings, it is proposed that *ANKK1* rs7118900 allele A and *DRD2* rs4436578 allele G could be genetic markers for identifying individuals at high risk of exercise addiction among athletes. Nonetheless, further research is necessary to validate these findings and fully explore the genetic basis of exercise addiction.

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