Turkish Journal of Sport and Exercise /Türk Spor ve Egzersiz Dergisi
http://dergipark.gov.tr/tsed
Year: 2021 - Volume: 23 - Issue: 2 - Pages: 185-189
DOI: 10.15314/tsed.905202

Turkish Journal of Sport and Exercise
Türk Spor ve Egzersiz Dergisi
ISSN: 2147-5652
https://dergipark.org.tr/tr/pub/tsed

Distribution of Dopamine Receptor 2 DRD2 rs1800497 Polymorphisms in Professional Football Players: A pilot study

Beste TACAL ASLAN[1A], Özlem Özge YILMAZ[1B], Tolga POLAT[1C], Çisem ŞILAR[1D], Başak Funda EKEN[1E], Canan Sercan DOĞAN[2F], Korkut ULUCAN[1G]

[1] *Department of Medical Biology and Genetics, Faculty of Dentistry, Marmara University, Istanbul, Turkey*
[2] *Laboratory of Medical Genetics and Molecular Diagnostics, Üsküdar University, Istanbul, Turkey*
Address Correspondence to B.Tacal Aslan : e-mail: btacal@gmail.com

(Received): 29/03/2020/ (Accepted): 31.08.2021

A:Orcid ID: 0000-0001-5271-7917 B:Orcid ID: 0000-0002-4085-6159 C:Orcid ID: 0000-0002-2064-6613 D:Orcid ID: 0000-0002-1909-9122
E:Orcid ID: 0000-0002-2690-8071 F:Orcid ID: 0000-0002-2218-2234 G:Orcid ID: 0000-0002-1304-9386

Abstract

Previous studies have identified that genetic variation is a significant determinant of physical activity-related behaviors and for sport enthusiasm. Dopamine receptor genes have been linked to a higher degree of overall physical activity. The dopamine receptor D2 (DRD2) rs1800497 polymorphism affects the brain's dopaminergic system and athletic performance. However, little research has been done on the connection between DRD2 and sports participation, and the few studies that have been published are contradictory. This study aimed to determine the genotype and allele distributions of the DRD2 rs1800497 polymorphism in football players and compare them with the control group. For this purpose, 21 football players and 52 participants for control group were enrolled in our study. Genotyping was performed by PCR after DNAs were isolated from buccal epithelial cells. When we examined the genotype distributions, the AG and GG were found as 5 (24%) and 16 (76%), respectively. No AA genotype was found for DRD2. When allelic distributions were examined in the athlete group, the A allele was counted as 5 (12%) and the G allele as 37 (88%). In the control group, allelic distributions for A allele and G allele were 36 (%35), 68 (%65), in respectively. As we expected, in our study cohort, the DRD2 rs1800497 polymorphism was found to be dominated by the GG genotype and the G allele. However, we found no statistically significant differences between athlete and control group. Despite the limited sample size, the findings of this study may serve as a foundation for a larger study and point the way for future studies. Therefore, further studies with athletes from different branches and with larger study group are needed to reveal the effect of DRD2 rs1800497 polymorphism on athletic performance and physical activity-related behaviours.

Key words: Sports, Genetics, Polymorphism, DRD2, Football

Profesyonel Futbolcularda Dopamin Reseptörü 2 DRD2 rs1800497 Polimorfizmlerinin Dağılımı : Pilot çalışma

Özet

Daha önce yapılan çalışmalar, genetik varyasyonun fiziksel aktivite ile ilgili davranışların ve spor yapma isteğinin önemli bir belirleyicisi olduğunu belirlemiştir. Dopamin reseptör genleri, daha yüksek seviyede bir fiziksel aktivite derecesi ile ilişkilendirilmiştir. Dopamin reseptörü D2 (DRD2) rs1800497 polimorfizmi, beynin dopaminerjik sistemini ve atletik performansı etkiler. Bununla birlikte, DRD2 ile spor katılımı arasındaki bağlantı üzerine çok az araştırma yapılmıştır ve yayınlanan çalışmalar birbiriyle çelişkilidir. Bu çalışmada DRD2 rs1800497 polimorfizminin futbolcularda genotip ve allel dağılımlarının belirlenmesi ve kontrol grubu ile karşılaştırılması amaçlanmıştır. Bu amaçla 21 futbolcu ve kontrol grubu için 56 katılımcı çalışmamıza alınmıştır. Bukkal epitel hücrelerinden izole edilen DNA'lardan PCR yöntemi ile genotipleme gerçekleştirildi. Genotip dağılımlarını incelediğimizde AG ve GG sırasıyla 5 (% 24) ve 16 (% 76) olarak bulundu. DRD2 için AA genotipi bulunamadı. Atlet grubunda allelik dağılımlar incelendiğinde, A alleli 5 (% 12) ve G alleli 37 (% 88) olarak sayıldı. Kontrol grubunda ise A alleli ve G alleli sırasıyla 36 (%35), 68 (%65) olarak bulunmuştur. Çalışma kohortumuzda, beklediğimiz gibi, profesyonel futbolcularda DRD2 rs1800497 polimorfizminin GG genotipi ve G alelinin baskın olduğunu tespit ettik. Bununla birlikte, sporcu ve kontrol grubu arasında anlamlı bir farklılık bulamadık. Sınırlı örneklem büyüklüğüne rağmen, çalışmamızın bulguları daha kapsamlı bir çalışma için temel oluşturabilir ve gelecekteki çalışmalara yol gösterebilir. Bu nedenle, DRD2 rs1800497 polimorfizminin atletik performans ve fiziksel aktivite ile ilgili davranışlar üzerindeki etkisini ortaya çıkarmak için farklı branşlardan sporculardan oluşan ve örneklem sayısı daha yüksek olan çalışmalara ihtiyaç vardır.

Anahtar kelimeler: Spor, Genetik, Polimorfizm, DRD2, Futbol

INTRODUCTION

Athletic performance is a combination of various environmental factors, including nutritional and psychological factors, as well as inherent genetic factors and is an important component of athletes (5). Sports genetics, which studies the functioning and regulation of genes that affect athletic performance, has been accepted as a new branch of science (25). The aim of sports genetics studies includes the determination of gene polymorphisms that affect athletic performance, determination of molecular mechanisms regulated by these genes, such as ACE, ACTN3, COL1A1, and determination of predispositions to enhanced athletic performance (24,2).

Neurotransmitter substances such as serotonin, dopamine, and the genes that metabolize them are important in determining the effect of psychological factors on athletes (8).

In the late 1950s, dopamine was defined as a neurotransmitter of the dopaminergic system (12). Dopamine is a neurotransmitter of the Central Nervous System (CNS) that plays a crucial role in regulating various processes such as motor control, cognition, emotion, reward, and cardiovascular regulation (9, 13). Dopamine has emotional, cognitive and sensory-motor functions as it includes the limbic system. Consequently, dopamine is associated with the control of pleasant emotions, reward, and drug addiction (16). The dopaminergic reward system is associated with obesity as well as alcohol, sex, and gambling addictions. In addition, the dopaminergic reward system plays a critical role in neuropsychiatric disorders such as schizophrenia and attention deficit hyperactivity disorder (ADHD) (3, 21).

Dopamine is the primary endogenous ligand for dopamine receptors. There are five different types of dopamine receptors, DRD1, DRD2, DRD3, DRD4 and DRD5 (10). The dopamine D2 receptor gene (DRD2) is a candidate gene for the level of physical activity due to its role in motion control as well as reward mechanisms (7, 22). The rs1800497 polymorphism G>A conversion is also known as TaqIA (or Taq1A). The G allele in the DRD2 rs1800497 polymorphism is considered the wild type, while the A allele is considered the polymorphic allele. The A allele is associated with fewer dopamine binding sites in the brain and is thought to play a role in alcohol dependence, smoking, and some neuropsychiatric disorders (23). In animal study showed that in comparison to wild-type mice, D2 dopamine receptor (DRD2) knockout mice had lower locomotor activity (15). In different animal study also presented that DRD2 expression was higher in mice for high levels of activity compared to the control group (4). In humans, De Moor et al. revealed that there was no connection between DRD2 and leisure-time physical activity (6). Another research group found no significant differences between physical performance and DRD2 gene (14).

However, little research has been done on the connection between DRD2 and sports participation and eagerness, and the few studies that have been published are contradictory. This study aimed to determine the distribution of the dopamine receptor 2 (DRD2) rs1800497 polymorphism in professional football players and to compare the results with sedentary individuals. Therefore, we hypothesized that sports enthusiasm and athletic performance are related to the mechanism of addiction.

METHOD

Study subjects

21 football players participated in the study with 52 sedentary individuals acting as a control group. Physical characteristics of the participants are represented in Table 1. None of the volunteers had transmitted genetic anomalies. The study protocol was approved by the Uskudar University Ethical Committee and performed following the principles of the Declaration of Helsinki II (26). Before the study, all the football players signed consent forms

Containing relevant information such as the study protocol and the intended use and evaluation of the results.

Physical activity level of the participants

Football players cohort had a four times/week at least each with 100-110 min. training sections and needless to say every weekend they had game day performance. For the sedantery group they had an average of two days /week, with 30 min. walking activity.

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Table 1. Physical characteristics of study participants

	N	AGE (Year)		HEIGHT (cm)		WEIGHT (Kg)		BMI (Kg/m2)	
		AVG	SD	AVG	SD	AVG	SD	AVG	SD
Study Group	21	20,14	±1,424	173,1	±5,440	66,95	±5,454	22,40	±2,191
Control Group	52	27,23	±5,29	169,8	±10,69	73,92	±15,07	26,04	±6,057

Genotyping

DNA isolations from the buccal cells of the athletes participating in the study were performed with a commercially obtained PureLink DNA isolation kit (Invitrogen, Thermo Fisher Scientific, Inc.). Genotyping of the DRD2 rs1800497 polymorphism was performed using Real-Time PCR on a StepOnePlus (Thermo Fisher Scientific, Inc.) device and Taqman SNP Genotyping Assays genotyping kits according to the manufacturers' protocols (cat. no. 4362691, Thermo Fisher Scientific, Inc.). G and A alleles were determined using VIC and FAM primers, respectively (Fig. 1). For a total volume of 10 µl reaction, 5 µl of Genotyping Master Mix (Applied Biosystems, Foster City, CA), 3.5 µl of nuclease-free H2O (Thermofisher, USA), 0.5 µl of genotyping test (Applied Biosystems), and 1 µl of DNA were used. The sequences of the TaqMan Probe used for genotyping are listed in Figure 2.

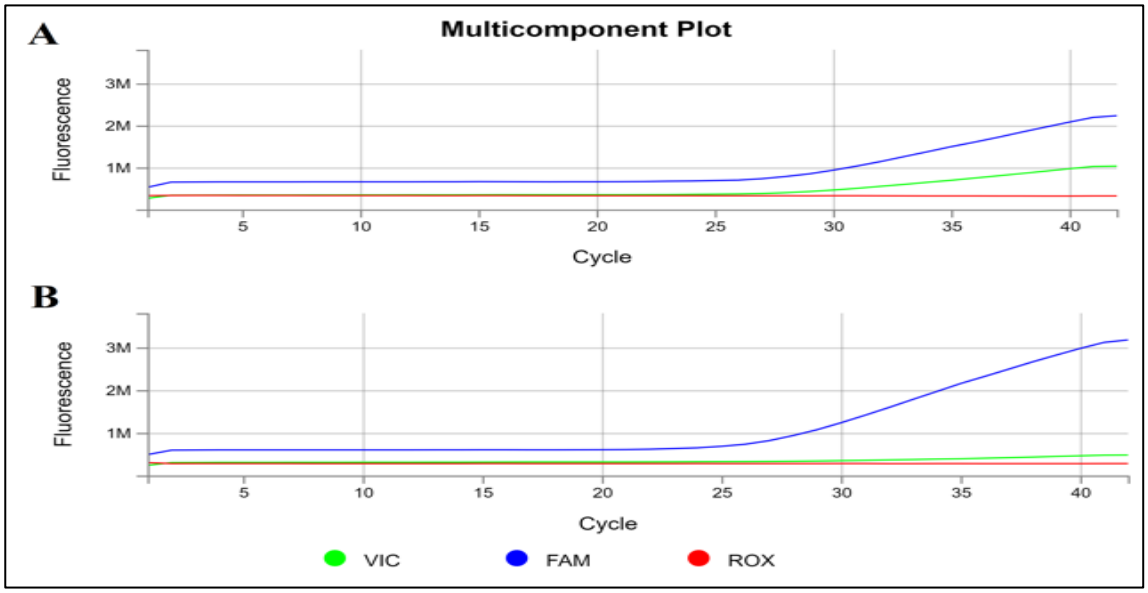

Figure 1. Quantitative PCR amplification of the AG genotype and GG genotype of DRD2 rs1800497 polymorphism. FAM indicates the G allele (blue curve), whereas VIC (green curve) indicates the A allele. (A) The single blue curve indicates the homozygous genotype of GG, whereas (B) the blue and green curves indicate the heterozygous genotype of AG.

Statistical analysis

In our study, all the athletes and sedentary individuals were compared in terms of both genotype and allelic distribution. Comparison processes were carried out using SPSS (version 18.0 for Windows, SPSS, Chicago, IL, USA) by χ^2 analysis. P <0.05 value was accepted as statistically significant

qPCR	Sequence, 5'-3'
VIC/FAM	CACAGCCATCCTCAAAGTGCTGGTC[A/G]AGGCAGGCGCCCAGCTGGACGTCCA

Figure 2. Sequences of the TaqMan probe used for genotyping DRD2 rs1800497 polymorphism.

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RESULT

In the DRD2 analysis, it was determined that 16 (76%) out of 21 players had GG, and 5 (24%) of them had the AG genotype. No AA genotype was found for DRD2. When allele distributions were examined, it was observed that the percentages were 12% for A allele and 88% for G allele. In the control group (n = 52), 9 individuals had AA, 18 individuals had AG and 25 individuals had GG genotypes. A allele was counted as 36 (35%) and G allele as 68 (35%). The genotype and allele number distributions of the athletes are summarized in Table 1.

Table 2. Genotypic and allelic distribution of the DRD2 rs1800497 in the examined football players.

	Genotype			p Value	Allelic Frequency		p Value
	AA	**AG**	**GG**		**A**	**G**	
Athlete (21)	-	5	16		5	37	
Percentage	0%	24%	76%		12%	88%	
Control (52)	9	18	25	0,0430	36	68	0,0057
Percentage	17%	35%	48%		35%	65%	

◎ Significance was assessed at least at the p <0.05 level. Comparison with the control group was made using the x2 test.

DISCUSSION

Addiction or addiction tendency can affect athletic performance. DRD2 deficiency may cause individuals to have higher risk of multiple addictive, impulsive, and compulsive behaviors (19). High dopamine levels can lead to mental disorders related to abnormal brain function (18). The A allele of the DRD2 rs1800497 polymorphism is thought to be associated with addiction (17).

Dopamine is the primary binding ligand for dopamine receptors and there are five different dopamine receptors, DRD1, DRD2, DRD3, DRD4, and DRD5. It has been reported that the number of DRD2 receptors in neuronal membranes is higher in the GG genotype, while it is lower in the AA genotype (11). In our cohort, AG and GG genotypes were found as 5 (24%) and 16 (76%), respectively. A and G allele numbers were 5 (12%) and 37 (88%) in our athlete group.

There are limited numbers of studies investigating the relationship between the DRD2 rs1800497 polymorphism and sports performance. Yüksel et al. investigated the DRD2 rs1800497 polymorphism in volleyball players and bodybuilders. All volleyball players in the study group were found to be in the GG genotype. It has been observed that the addiction-related A allele is less common in volleyball players and bodybuilders (27). Özcan et al. investigated the DRD2 rs1800497 polymorphism and found that the GG genotype and G allele were higher in sprinter and endurance athletes. None of the athletes carried the A Allele, which is related to addiction compared to the G Allele (20). Abe et al. examined COMT, DRD2, and DRD3 polymorphisms, which are thought to affect dopaminergic nerve functions, in swimmers. In their studies, the frequency of the AA genotype was lower than the other genotypes, and the AG genotype was higher than the GG genotype (1).

In our study, the GG genotype was higher than the GA genotype and no AA genotype was found in athletic group. At the same time, when we compared the G allele with the A allele, it was found that the G allele was higher in percentage terms. Our findings are similar to those of previous studies. According to our results G allele was dominant in the both study group. Therefore, we found no statistically significant differences between the professional football players and control group. We think that small sample study group could be the reason of similar allelic distribution of control and athletic groups . Despite the small number of participants, results of our study may be the preliminary report for a larger study in the future .

CONFLICT OF INTEREST

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article. No funding was received.

ACKNOWLEDGEMENTS

We would like to thank Altınordu Football Club, which provided us with the opportunity to

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analyze with its successful players in this work we carried out.

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