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DISTRIBUTION OF DOPAMINE RECEPTOR 2 (DRD2) RS1800497 POLYMORPHISMS IN PROFESSIONAL CYCLIST

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Ethics committee approval: The protocol used in the present study was approved by the Üsküdar University Ethics Committee and was performed in accordance with the principles of the Declaration of Helsinki II. All participants signed consent forms containing all the information such as the study protocol, results and evaluation of the results.

Abstract

Genetic and environmental factors are important determinants of the athletic performance. Sports genetic determines certain the alleles for the identification of the genes that affect athletic performance. Comprehensive researches, including the biology of mental properties are accumulating due to the improvement of the information of molecular biology. Dopamine is an important neurotransmitter of the dopaminergic system that affects the athlete mentally and psychologically. In this study, our goal is to determine the genotype and allele distributions of the DRD2 rs180047 polymorphism in the cyclists. 19 cyclists and 52 sedentary individuals (controls) participated in our study. Genotyping was carried out by real time PCR (rt-PCR) after DNA was isolated from buccal epithelial cells. In our cohort, AG and GG genotypes were detected as 6 (32%) and 13 (68%), respectively. In the control group, the respective AA, AG and GG genotypes were detected as 9 (17%), 18 (35%) and 25 (48%). No statistically significant difference was detected in terms of genotype distribution between the two groups (p= 0,1107). When allelic distributions were examined, in athlete cohort. A and G allele numbers were counted as 6 (16%) and 32 (84%), respectively. In the control group, same alleles were count as 36 (35%) and 68 (65%). There was no significant difference in the terms of alleles in our study cohort (p=0,0295). In our cohort, GG genotype and the G allele of the DRD2 rs1800497 polymorphism were dominant. Recent studies showed the association of the A allele with addiction. Therefore we hypothesized the association of the related allele and sucess in cyclists. Although we were unable to find statistically significant difference, we suggest to analyse the same polymorphism in athletes with different sport branches to fulfill the role of the given polymorphism.

Keywords: sports, genetics, polymorphism, DRD2, cyclist

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1. Introduction

The need for research in athletic performance is increasing due to the development of technology and science in sports. There are many factors determining success in sports. Training types and diversity, genetic factors, epigenetics, diet patterns, motivation, equipment and other environmental factors are some of them. Mental and physical factors make up the overall athletic performance and increases with the progress in environmental factors such as training and nutrition. Having information about the genetic structure in athletes is important to have certain functions and personal training programs in both individual and team sports.

Cycling activities that requires long-term endurance and strength. Muscle volume and muscle fiber types affect many biomechanical variables like pedal force in cyclists. Therefore, it effects the cycling performance. There are also many different types of cycling and the performance in these types varies accordingly.

Dopamine is an important neurotransmitter that significantly effects the dopaminergic system and physical activities that we face in daily routine. Apart from these activities, it affects exercise and athletic performance to a great extent. It provides regulation of neurological functions and communication between neurons, that are crucial in motor activities. Factors affecting the central nervous system are directly related to psychology. Therefore, dopamine affects mentally athletic performance (Ulucan et al.,2014).

There are five different types of dopamine receptors; DRD1, DRD2, DRD3, DRD4 and DRD5 (Gingrich et al., 1993). DRD2 gene that encoding dopamine metabolism is localized at 11q22-q23. Some polymorphisms have been identified in the gene, one of which is rs1800497 (G/A transition). The G allele in the DRD2 rs1800497 polymorphism is considered wild type and related with the high numbers of the receptor moleculed on the cell membrane. The A allele is considered to be polymorphic allele and studies to date have linked the A allele with lower receptor numbers and lower dopamine levels (Turner et al., 1992). Dopaminergic neurons and regions in the brain also appear to play a role in addiction and with some neuropsychiatric disorders (Pohjalainen et al., 1998).

In the present study, we aimed to examine the distribution of receptor 2 (DRD2) rs1800497 in cyclists, and compare the results with the sedentary individuals. This report, according to the best of our knowledge, is the first which is carried out in cyclists.

2. Materials and Methods

The protocol used in the present study was approved by the Üsküdar University Ethics Committee and was performed in accordance with the principles of the Declaration of Helsinki II. All participants signed consent forms containing all the information such as the study protocol, results and evaluation of the results.

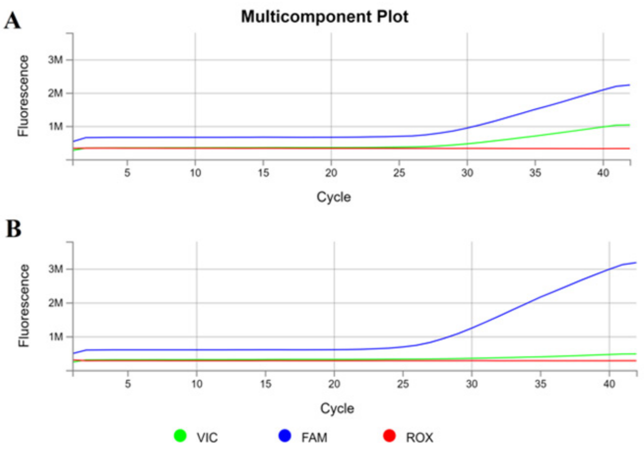
2.1. Study subjects

19 cyclist were participated in our study. 52 sedentary individuals also participated as a control group. All the volunteers had no transmitted genetic anomalies. The study protocol was approved by Üsküdar University Ethical Committee and was in line with the principles of the Declaration of Helsinki II. Before the study, all participants signed consent forms containing all the information such as the study protocol, results and evaluation of the results.

2.2. Genotyping:

DNA isolations from buccal epithelial cells of the athletes were carried by the commercially obtained PureLink DNA isolation kit (Invitrogen, Van Allen Way, Carlsbad, CA, USA). Genotyping of the DRD2 rs1800497 polymorphism was performed using quantitative real- time PCR (StepOnePlus, Thermo Fisher Scientific, Inc.), using a TaqMan Genotyping assay (cat. no. 4362691; Thermo Fisher Scientific, Inc.). Manufacturer's protocols were followed for the genotyping processes. PCR conditions were 60 °C for 30 s and 95 °C for 10 min, followed by 40 cycles of 15 s at 95 °C for and 1 min at 60 °C. Finally, 60 °C for 30 s was applied for post PCR reading. The fluorescent signal was detected at the prePCR, amplification at the end of each cycle, and postPCR reading steps. G and A alleles were determined using VIC and FAM primers, respectively (Fig. 1). The sequences of the TaqMan Probe used for genotyping are listed in Table 1.

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. The blue and green curves indicate the heterozygous genotype of AG (A) whereas the single blue curve indicates the homozygous genotype of GG (B).



2.3. Statistical analysis

Genotype distribution and allele frequencies between groups of athletes and controls were compared by χ^2 test, using the SPSS (version 18.0 for Windows, SPSS, Chicago, IL, USA) program. $p<0.05$ value was accepted as statistically significant.

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

qPCR	Sequence, 5'-3'
VIC/FAM	CACAGCCATCCTCAAAGTGCTGGTC**[A/G]**AGGCAGGCGCC-CAGCTGGACGTCCA

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3. Results

In our cohort, 13 (68%) of 19 players had GG and 6 (32%) of them had AG genotypes. No AA genotype was detected. When allele distributions were examined, it was observed that the percentage of A allele was 16% and the G allele was 84%. In the control group (n = 52), 9 individuals had AA, 18 individuals had AG and 25 individuals had GG genotype. 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 1. Genotypic and allelic distribution of the DRD2 rs1800497 polymorphism in the study cohort.

	Genotype			p Value	Allelic Frequency		p Value
	AA	AG	GG		A	G	
Cyclist (19)	-	6	13	0,1107	6	32	0,0295
Percentage	0%	32%	68%		16%	84%	
Control (52)	9	18	25		36	68	
Percentage	17%	35%	48%		35%	65%	

Significance was assessed at the $p < 0.05$ level. Comparison with the control group was made using the x^2 test.

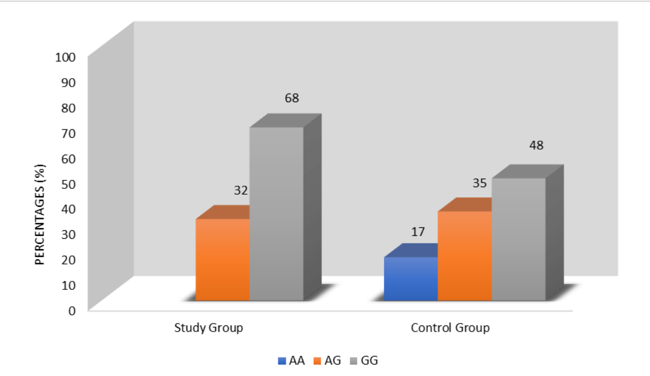

Figure 3. Percentage of the genotype distributions of DRD2 rs1800497 polymorphism.

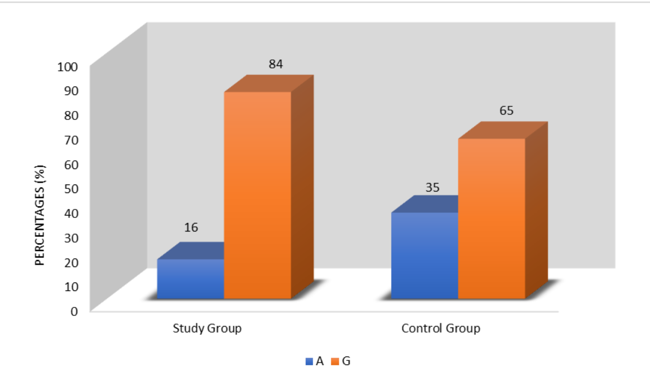

Figure 4. Percentage of the allelic distributions of DRD2 rs1800497 polymorphism.

4. Discussion and Conclusion

Variations in the DRD2 gene can affect athletic performance. Low dopamine level due to DRD2 polymorphisms may be a parameter that prevents success in sports. Low dopamine levels are associated with neurological diseases and hyperactivity as well as sports performance. Apart from that, high dopamine levels are also associated with abnormal brain function (Ndamanisha et al., 2009). There are studies in which polymorphism is associated with sports addiction (Munafo et al., 2007).

Dopamine shows its biological effects by binding to its receptors (DRDs). DRD1, DRD2, DRD3, DRD4 and DRD5 are the known five different dopamine receptors. Studies shows that DRD2 receptors in neuronal membranes are higher in numbers who have the GG genotypes than in the AA genotypes (Grandy et al. 1989).

In our cohort, AG and GG genotypes were detected as 6 (32%) and 13 (68%), respectively. A and G allele numbers and percentages were respectively 6 (16%) and 32 (84%). There were no statistically significant difference between athletes and controls.

There are few studies investigating the relationship between the DRD2 rs1800497 polymorphism and sports performance. Yüksel et al. (2017) investigated the rs1800497 polymorphism in volleyball players. In their study, all the genotypes of all players were found as GG. Before, a allele has been poorly associated with addiction in sports. Özcan et al. (2018) anaylsed DRD2 rs1800497 polymorphism in sprinter and endurance athletes and reported that GG genotype and G allele were superior in the study cohort. Abe et al. (2017) examined the COMT, DRD2 and DRD3 polymorphisms which have effect on dopaminergic nerve functions, and reported that AA genotype of DRD2 rs1800497 polymorphism was lower when compared to AG and GG genotypes.

In our study with 19 cyclists, the GG genotype was found higher than the AG genotype. There were no athletes with the AA genotype. At the same time, when we compare the G allele with the A allele, G allele is higher than the A allele. The results of our study were in agreement with the previous studies. Our results are similar to the findings of previous studies. The DRD2 A Allele has been found to be associated with addiction. Studies have shown that the same allele is associated with sports addiction and athletic performance. Our study will contribute to the literature and support other studies in this field. It can help prevent early psychological disorders encountered in athletes.

Patient informed consent: Informed consent was obtained.
Ethics committee approval: The protocol used in the present study was approved by the Üskdar University Ethics Committee and was performed in accordance with the principles of the Declaration of Helsinki II. All participants signed consent forms containing all the information such as the study protocol, results and evaluation of the results.
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Author contribution subject and rate:
Çisem Şılar (20%): data collection, formation of the article
Esra Karagöz (20%): data collection, formation of the article
Tolga Polat (10%): data collection, statistics 10%
Özlem Özge Yılmaz (10%): laboratory assistance
Begüm Su Baltacıoğlu(10%): laboratory assistance
Beste Tacal Aslan(10%): laboratory assistance
Canan Sercan Doğan(5%): data collection
Tuğba Kaman(5%): data collection

References:

Berridge, K. C. (2017). Is Addiction a Brain Disease? Neuroethics, 10(1), 29–33. https://doi.org/10.1007/s12152-016-9286-3

Banting, L.K., Pushkarev, V.P., Cieszczyk, P. et al. (2015). Elite athletes' genetic predisposition for altered risk of complex metabolic traits. BMC Genomics 16, 25 https://doi.org/10.1186/s12864-014-1199-0

Corak, A., Kapıcı, S., Sercan, C., et al. (2017). A pilot study for determination of anxiety related SLC6A4 promoter "S" and "L" alleles in healthy Turkish athletes. Cellular and Molecular Biology, 63 (5), 29-31. https://doi.org/10.14715/cmb/2017.63.5.6

Dopamin D2 Receptor TAQ A1 Allele on Sprinter and Endurance Athlete. International Journal of Medical, Medicine and Health Science, 11.0(9). http://doi.org/10.5281/zenodo.1474429

Drago J, Padungchaichot P, Accili D, Fuchs S. (1998). Dopamine receptors and dopamine transporter in brain function and addictive behaviors: insights from targeted Mouse mutants. Dev Neurosci 20:188 – 203. https://doi.org/10.1159/000017313

Eken, B., Akpınaroğlu, C., Arslan, K.S., et al. (2018). Genlerin Sporda Psikolojik Faktörlerle İlişkisi. The Journal of Neurobehavioral Sciences, 5 (1), 56-61. https://doi.org/10.5455/JNBS.1516796381

Gingrich, J.A., Caron, M.G., (1993). Recent advances in the molecular biology of Dopamine receptors. Annu Rev Neurosci, 16, 299-321. https://doi.org/10.1146/annurev.ne.16.030193.001503

Lanferdini F. J, Bin R. F, Cunha G. S, Lopes A. L, Castro FAS, Oliveira AR, et al. (2014). Relationship between physiological and biomechanical variables with aerobic power output in Cycling. Journal of Science and Cycling.;3(1):2-8. https://doi.org /10.3390/app10124112

Munafo, M. R., Matheson, I. J., Flint, J. (2007). Association of the DRD2 gene Taq1A polymorphism and alcoholism: a meta-analysis of case-control studies and evidence of publication bias. Mol Psychiatry. pp. 12:454-461 http://doi.org/10.1038/sj.mp.4001938

Noble, E. P. (2000). Addiction and its reward process through polymorphisms of the D2 dopamine receptor gene: a review, European Psychiatry, 15, 79– 89. https://doi.org/ 10.1016/s0924-9338(00)00208-x

Ndamanisha, J. C., Guo, L. (2009). Nonenzymatic glucose detection at ordered mesoporous carbon modified electrode, Biosens Bioelectron, 23, 60- 63. https://doi.org/10.1016/j.bioelechem.2009.05.003

Pohjalainen, T., Rinne, J., Någren, K. et al. (1998). The A1 allele of the human D 2 dopamine receptor gene predicts low D 2 receptor availability in healthy volunteers. Mol sychiatry 3, 256–260 https://doi.org/10.1038/sj.mp.4000350

Polat, T., Dogan, C. S., Dogan, M., Akçay, T., & Ulucan, K. (2020). Distribution of α- actinin - 3 rs1815739 and angiotensin - 1 converting enzyme InDel polymorphisms in Turkish bodybuilders. 1–5. https://doi.org/10.3892/br.2020.1374

Turner, E., Ewing, J., Shilling, P., Smith, T.L., Irwin, M., Schuckit, M., Kelsoe, J.R. (1992). Lack of association between an RFLP near the D2 dopamine receptor gene and severe alcoholism. Biol Psychiatry, 31(3), 285-290 https://doi.org/10.1016/0006-3223(92)90052-2

Ulucan, K. (2016). Spor genetiği açısından türk sporcuların ACTN3 R577X polimorfizm literatür özeti. Clinical and Experimental Health Sciences, 6, 44-47. https://doi.org/10.5152/clinexphealthsci.2016.059

Ulucan K, Yalcin S, Akbas B, Uyumaz F, Konuk M. (2014). Analysis of Solute Carrier Family 6 Member 4 Gene promoter polymorphism in young Turkish basketball players. The journal of Neurobehavioral Sciences.;1 (2):37-40. https://DOI:10.5455/JNBS.1403730925]

Ulucan K. (2016). Literature Review of Turkish Sportsmen in Terms of ACTN3 R577X Polymorphism. Clinical and Experimental Health Sciences. 6 (1):44-7. https:// doi.org/10.5152/clinexphealthsci.2016.059

Yüksel, İ., Kapıcı, S., Sercan, C., Kulaksız, H., Polat, T., Turan, G., & Ulucan, K. (2017). Addiction Related DRD2 gene rs 1800497 polymorphism distribution in volleyball players and bodybuilders. The Journal of Neurobehavioral Sciences, 1. https://doi.org/10.5455/jnbs.1502377893