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The Effect of Dopamine D2 Receptor TAQ A1 Allele on Sprinter and Endurance Athlete

Öznur Özge Özcan, Canan Sercan, Hamza Kulaksız, Mesut Karahan, Korkut Ulucan

***Abstract*—**Genetic structure is very important to understand the brain dopamine system which is related to athletic performance. Hopefully, there will be enough studies about athletics performance in the terms of addiction-related genetic markers in the future. In the present study, we intended to investigate the Receptor-2 Gene (*DRD2*) rs1800497, which is related to brain dopaminergic system. 10 sprinter and 10 endurance athletes were enrolled in the study. Real-Time Polymerase Chain Reaction method was used for genotyping. According to results, A1A1, A1A2 and A2A2 genotypes in athletes were 0 (%0), 3 (%15) and 17 (%85). A1A1 genotype was not found and A2 allele was counted as the dominating allele in our cohort. These findings show that dopaminergic mechanism effects on sport genetic may be explained by the polygenic and multifactorial view.

***Keywords*—**Addiction, athletic performance, genotype, polymorphism, sport genetics.

I. Introduction

ATHLETIC performance is a significant part of the athletes and genetic factors contributing to athletic performance without doubt [1], [2]. Genotyping provides us to obtain information about genomic research, including sports medicine and exercise science and also muscle strength, cardiopulmonary capacity, body weight, adiposity, insulin and glucose metabolism [3]. Additional components of athletic performance include physical and mental factors with the combination of genetic variants [4]. Therefore, the question is not about performance-related features are heritable, but 'which' genetic variants remain substantial to athletic performance, and we are able to use these variants to identify future athletes [5].

Brachial slices were separated by Falck Hillarp method. By this method, monoamines are localized in the neuronal bodies of Substantia Nigra (SN) and Striatum with visualization of monoamines [6]. These regions are the medial hypothalamus branching through Ventral Tegmental Area (VTA), SN and the arcuate nucleus. There are four pathways that have been discovered as nigrostriatal, mesolimbic, mesocortical and tuberoinfundibular, which carry DA to other brain regions. The fifth, the thalamic pathway, is still researched by the scientists [7]. Dopamine (DA) has been identified a neurotransmitter of the dopaminergic system by the end of the 1950s [8]. DA is a neurotransmitter of Central Nervous System (CNS) and leads the motivation, motor control and reward system [9]. DA is a key to brain's processing and mesolimbic pathway, which extends from VTA to the striatum ventral, including amygdala, hippocampus, and orbitofrontal cortex. Because it involves the limbic system, it has emotional, cognitive, and sensorimotor functions, and consequently pleasant feelings are associated in the control of reward and drug addiction [10]. The dopaminergic reward system plays a critical role in sex addiction, obesity, gambling as well as in neuropsychiatric disorders including schizophrenia, attention deficit hyperactivity disorder (ADHD) [11], [12]. During exercise, DA was shown to increase in the direction of release in the midbrain, hypothalamus and striatum [13]. Sensory perception and sensory-motor integration is more effective when DA is released by the physical activity [14]. Especially, anaerobic exercise like athleticism is important for the treatment of addiction, ADHD and neurodegenerative disorders like Parkinson Disease (PD) [15]-[18]. Physical exercise can also be a treatment for depression [19]. Physical exercise may protect people from depression disease [20].

The rs1800497 on chromosome 11q23.2 is located in exon 8 of the ankyrin repeat domain containing one gene downstream of DRD2 [21]. Most of DA 2 receptors are intensively distributed on the postsynaptic, non-dopaminergic neurons in the striatum where D2 signaling modulates a variety of functional domains, including reward processing [22], [23]. In past years, numerous genetic association studies have focused on the single-nucleotide polymorphism (SNP) rs1800497 (also known as Taq1A).

In the present study, we aimed to analyze the distribution of *DRD2* rs1800497 polymorphism in sprinter and endurance athletes. This polymorphism is firstly related with addiction, and therefore we hypothesized that sports willingness and athletic performance is related with addiction mechanism.

II. Materials and Methods

A. Subjects

10 sprinter and 10 endurance athletes were enrolled for the study. Üsküdar University Ethics Committee approved the study protocol, which was in accordance with the principles of the Declaration of Helsinki II. All subjects read, understood and confirmed the study by signing the informed consents explaining the study steps.

B. DNA Sample Collection and Genotyping

DNA samples were collected by DNA collector swap and isolated with DNA purification kit (Thermofisher Invitrogen),

Korkut Ulucan is an academician in Molecular Biology and Genetic Department, University of Uskudar, Altunizade Mahallesi, Haluk Turksoy Sk. No:14, 34662 Üsküdar/İstanbul/ Turkey (phone: +9021640022-2409; e-mail: korkut.ulucan@uskudar.edu.tr).

by following manufacturer's instructions. The rs1800497 genotyping was carried out by Real-Time Polymerase Chain Reaction (RT-PCR) by using commercially provided Taqman Genotyping Assay (Catolog no: #4351379 Thermofisher, USA), by using specific primers (Table I).

TABLE I
PRIMERS USED FOR THE GENOTYPING OF RS 1800497

	DNA sequence (5'→3')
DRD2 (Exon 9)	5'-primer: 5'-CACAGCCATCCTCAAAGTGCTGGTC -3' (VIC)
	3'-primer: 5'-AGGCAGGCGCCCAGCTGGACGTCCA' (FAM)

III. RESULTS

20 athletes participated in our study. 10 of those athletes were sprinter athletes, and the others were endurance athletes. 3 of the athletes (15%) had AG (A1A2) and 17 (85%) had GG (A2A2) Genotypes (Fig. 1). Primer used for the genotyping of rs 1800497 is shown in Table I. We detected no A1A1 Genotypes in our cohort. (A) Allele was counted as 3 (7.5%) and (G) Allele as 37 (92.5%). Genotype and allele distributions of *DRD2* rs1800497 polymorphism in athletes are shown in Table II.

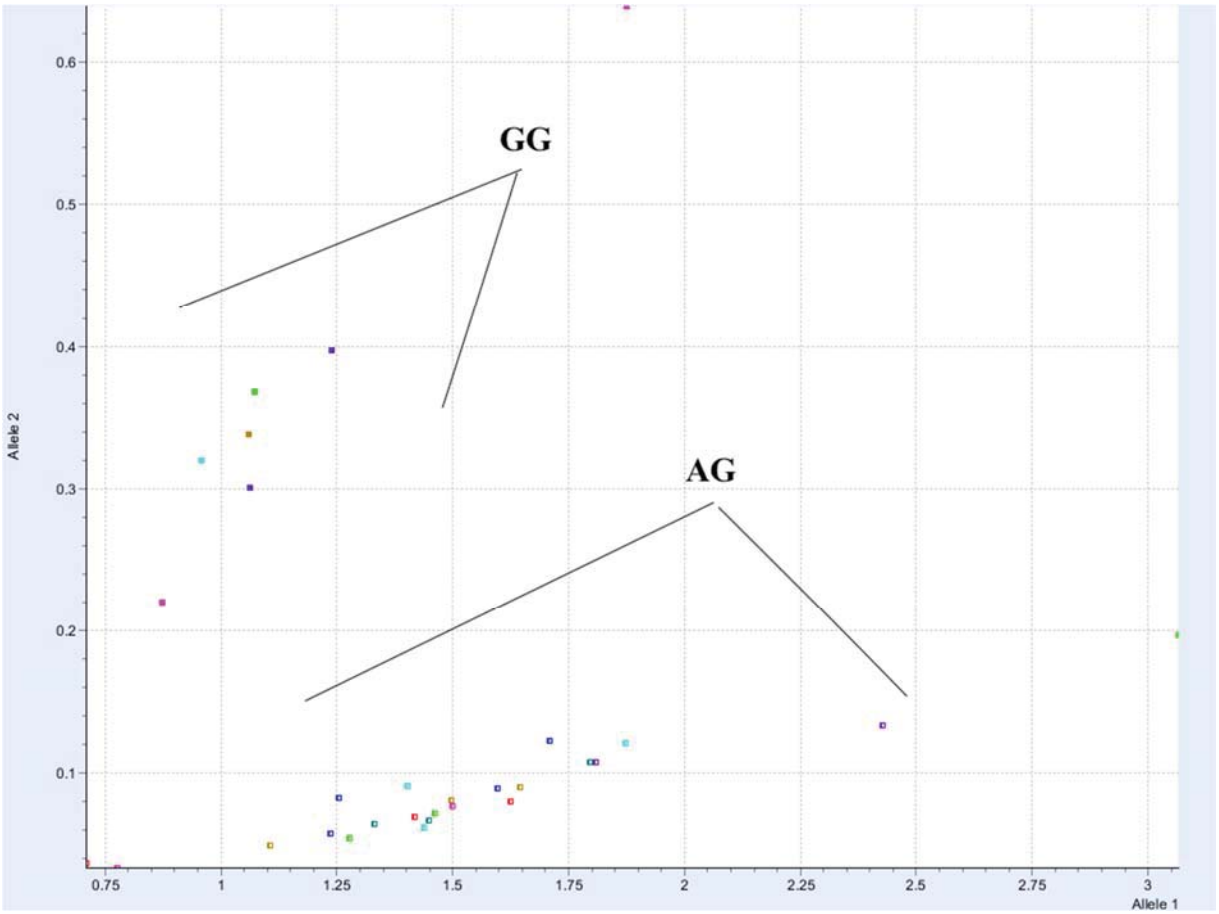

Fig. 1 Genotype results of the athletes

TABLE II
GENOTYPES AND ALLELS

	Genotypes			Alleles	
Alleles	**A_1A_1**	**A_1A_2**	**A_2A_2**	**A_1**	**A_2**
Number of Athletes (%)	0	3	17	3	37
	% 0	% 15	% 85	% 7.5	% 92.5

IV. DISCUSSION

The neurotransmitters of the CNS have many functional regulations such as learning, memory, motivation, reward and behavior [24]. In addition to enhancing the activity of the CNS which also affects the physiological mechanisms in the brain, it is also effective in stress response and motor control generally also the levels of the brain are increasing in the CNS due to endurance exercise [25]-[27]. The detection of DA levels in the brain has provided us to examine addiction and diseases mechanism. There are different 5 types of DA receptors; D1, D2, D3, D4 and D5 [28]. One of these types of receptor is the D2 receptor. DA receptors show different distributions with respect to brain localization [29]. D1 receptor is quite abundant

in the striatum; D5 receptor is in hippocampus and the Entorhinal Cortex. The D2 receptor is observed in the striatum, hippocampus, amygdala and thalamus. D2 receptor is lower in the prefrontal cortex. D3 receptor, like other receptors, is in the striatum and considerable amount in the ventral striatum. D4 receptor is separated from the prefrontal cortex, found in the hippocampus, while the other is absent in the striatum [30]. The D2 receptor that has been proven to increase long-term release from the VTA that was cloned in 1988 [31] and other D1, D3, D4 and D5 receptors were later described.

There are two alleles of the rs1800497: A1 and A2 and Taq1A polymorphism is the most widely studied polymorphism in psychiatry [32]. In particular, genotyping based on allele distribution frequencies of genes involved in the secretion of monoamines as neurotransmitters; plays an important role in the analysis of SNP results of the susceptibility to psychiatric and neurological diseases such as schizophrenia, bipolar disorder and major depression [33], [34]. In recent years, focusing on behavior and nutritional demand, the desire to stimulate areas that seek to find taste in drug rewards such as drugs has led to various gene polymorphisms. Drug addiction has been associated with the association of the A1 allele of the DA D2 gene with cocaine, alcohol and opioid. Making such polymorphisms is important for solving the predisposition of the individual to addiction [35]-[37]. A1 Alleles carriers have a reduced number of receptor binders in the cellular membrane compared to carriers with A2 Alleles [38], [39]. There are many different mechanisms underlying the physiological and biological pathways of physical exercise and physical inactivity, and these are related to our obtaining health benefits [40]-[42]. It has been determined that exercise and allele frequencies are protective effects of depression genotyping in athletes. Genotyping studies in sport and regular physical exercise indicate that there is a protective aspect of the disease [43]. Most exercise epidemiology research suggests that different models and theories that compare with the psychosocial and environmental factors and physical inactivity phenotypes of different types of exercise are aware of the confusion of its variations [44]. Therefore, as shown in our study, we are thinking that DRD2 research in sports should open the way for knowledge of physical activity on many other genetic and environmental factors. For instance, Peripheral DA release is increased after exercise in highly effective anaerobic sprinter athlete. In addition to enhancing the activity of the nervous system which also affects the physiological mechanisms in the DA, it is also effective in stress response and motor control, and in general, the levels of the brain are increasing in the CNS due to endurance exercise. It has been reported that low membrane activity of the A1 Allele of *D2* receptor plays a role in drug addiction [45]-[47].

In our study, RT-PCR was applied as a result of isolation process of the swap samples taken from the endurance and sprinter athletes and an image of the results was obtained. According to the results, 20 (15%) were AG (A1 / A2) and 17 (85%) were GG (A2 / A2) Genotypes and Allelic frequency distributions, A Allele 3 (7.5%) and G Allele 37 (92.5%), respectively. G Allele (A2) is accepted to be the wild type, whereas A Allele (A1) is accepted as the polymorphic allele. Addiction or having tendency to addiction may be effective in athletic performance. In our cohort, none of the athletes carried the A1 Allele, which is related to addiction, when compared to A2 Allele. These results were in agreement with our results, in the terms of A2 Allele superiority.

DRD2 A1 Allele was found to be associated with addiction, and we hypothesized the same allele to be associated with sports addiction and by this way it is related with athletic performance. In our study, the frequency of A1 Allele was found to be lower than A1 Allele. Although we expected A1A1 homozygotes genotype founded, low sample size may be the reason for our results. Today, the results of the studies show that A1A2 Genotype are the highest number in individual.

There are not enough literature including rs1800497 polymorphism and athletes before body builders and volleyball players. In their cohort, A1A1, A1A2 and A2A2 Genotypes in bodybuilders were founded to be as 2 (13%), 1 (7%) and 12 (80%), respectively [48]. All the volleyball players had A2A2 Genotypes in their cohort. This study is in agreement with our, indicating the overrepresented of A1A2 and A2A2 Genotypes, and A2 Allele.

A comparison of the athletes from different sports to a control group can be important from the aspect of researchers being able to draw better defined conclusions. The type of genetic background can be important for being successful athlete to be able to have same performance at a high level and, but may not be that essential in every sport. Genotyping is related to SNP in successful athletes genome is important for sport medicine to find out the optimal alleles of the related genes. One of the restrictions of the present study is the small sample size. According to results for our writing, we are planning to replicate the study in different athletes. We could not find another study to compare our results; this is the second limitation of our discussion. We hope this first experiment will lead further studies in the terms of psychological and genetic factors.

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