Year: 2020
Volume: 7
Issue Number: 3
Doi : 10.4103/jnbs.jnbs_28_20

Received 22.10.2020
Accepted 14.11.2020
JNBS, 2020, 7(3):147-151

Tolga Polat: {ORCID: 0000-0002-2064-6613}
Canan Sercan Doğan: {ORCID: 0000-0002-2218-2234}
Başak Eken: {ORCID: 0000-0002-2064-6613}
Özlem Özge Yılmaz: {ORCID: 0000-0002-4085-6159}
Çisem Şılar: {ORCID: 0000-0002-1909-9122}
Gözdem Karapınar: {ORCID: 0000-0003-0601-4473}
Begüm Su Baltacıoglu: {ORCID: 0000-0002-7493-5760}
Rıdvan Ekmekci: {ORCID: 0000-0001-5085-5988}
Korkut Ulucan: {ORCID: 0000-0002-1304-9386}

THE DISTRIBUTION OF BRAIN-DERIVED NEUROTROPHIC FACTOR (BDNF) RS6265 POLYMORPHISM IN TURKISH VOLLEYBALL PLAYERS

Tolga Polat[1], Canan Sercan Doğan[2], Başak Funda Eken[1], Özlem Özge Yılmaz[1], Çisem Şılar[1], Gözdem Karapınar[2], Begümsu Baltacıoğlu[2], Rıdvan Ekmekçi[3], Korkut Ulucan*[1,2]

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

Athletic performance is associated with many environmental factors such as inborn genetic factors, nutrition, psychological factors, and education. We aimed to analyze the brain derived neurotrophic factor (BDNF) rs6265 polymorphism, which is an important genetic marker related to psychological factors, in 21 professional female volleyball players and compare it with the control group. Genotyping was assessed by Real-time PCR technique. BDNF rs6265 polymorphism genotypes were calculated as 72% and 28% for GG and GA in volleyball players, respectively. No AA genotype was detected. In the control group, the GG, GA and AA genotype percentages were calculated as 57.8, 36.3 and 5.9, respectively. In the allelic distribution, the percentages in the athlete group were calculated as 86% (36) for the G allele and 14% (6) for the A allele, respectively. In the control group, for the G and A alleles, respectively; it was 76.25% and 23.75%. No statistical significance was found in terms of both genotype distribution (p = 0.407) and allelic frequency distribution (p = 0.218). Our results were in line with data indicating the stress and anxiety-related nature of professional volleyball players. More studies with more athletes and more groups of athletes are needed to understand the effect of these parameters on volleyball players.

Keywords: BDNF, sport genetics, volleyball, brain, polymorphism

[1] Marmara University, Faculty of Dentistry, Basic Medical Sciences, Medical Biology and Genetics Department, Istanbul, Turkey

[2] Uskudar University of Medical Genetics and Molecular Diagnostic Laboratory, Istanbul, Turkey

[3] Pamukkale University, Faculty of Sports Science, Sports Management Department, Denizli, Turkey

* Corresponding Author: [1,2,] Marmara University, Faculty of Dentistry, Basic Medical Sciences, Medical Biology and Genetics Department, Istanbul, Turkey, Uskudar University of Medical Genetics and Molecular Diagnostic Laboratory, Istanbul, Turkey. E-mail: korkutulucan@hotmail.com

1. Introduction

Environmental factors such as nutrition of athletes, training, coaching, family support, proper training conditions have important effects on the formation and development of athletic performance in sports. In addition to these effects, athletes' response to appropriate training models, susceptibility to appropriate sports branch, resistance to stress and ability to control the emotional and psychological pressure on them are very important. All these traits include, in part of genetic factors. The studies in the field of sports genetics include the analysis of genetic factors that affect sports activity, which are related to sports nutrition, and which determine our psychological emotional state such as serotonergic and dopaminergic. Studies in this area have begun in a large cohort, including single and double twins, and have continued to this day rapidly (Eken et al., 2018).

Among the sports genetics studies, athletic performance, as well as the determination of genes that affect mental performance, determine the mechanisms of these genes are involved. These studies have an important role not only in individual sports but also in the provision of psychological, mental programs suitable for genetic predispositions in team sports.

Volleyball, an advanced form of team play, needs a long-term low-density aerobic exercise. It requires special physical structure and motor characteristics with individual and team play types. Volleyball players, like other athletes, require a high degree of physical and physiological parameters to achieve high performance (Ulucan et al., 2017; Yüksel et al., 2017).

BDNF is a neurotrophin that affects the survival, growth, and function of neurons in the central and peripheral nervous system stabilizes synapses, regulates synaptic function, axon, and dendrite branches (Ulucan, 2016). This protein bolsters the survival of nerve cells (neurons) by playing a role in the growth, maturation (differentiation), and maintenance of these cells. In the brain, the BDNF protein is active at the connections between nerve cells (synapses), where cell-to-cell communication happens. The synapses can change and adapt over time in reply to experience, a characteristic called synaptic plasticity. In recent studies, it has been observed that, contrary to the above studies, exercise increases the serum level of BDNF, and even different types of exercise can affect the level of this increase. Studies investigating the effect of different types and loads of exercises on BDNF levels in sedentary individuals were examined (Bulğay et al., 2020). The BDNF protein helps regulate synaptic plasticity, which is important for learning and memory (Sears et al., 2011). The BDNF gene is localized at 11p13. BDNF, which is the neurotrophin in the brain, is synthesized as proBDNF because of progenitor cell proliferation and differentiation. A functional single nucleotide polymorphism rs6265 found in this gene causes the Val66Met transformation (Eken et al., 2018). According to studies in the literature, the G allele codes for Val, while the A allele codes for Met.

This transformation in BDNF polymorphism affects the motivation by causing stress during exercise and causes psychological problems in individuals (Hashimoto, 2007). In the present study, we aimed to determine the effects of BDNF polymorphisms on volleyball players.

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:

21 volleyball players volunteered to support our study. 26 sedentary individuals also participated as a control group. All the volunteers had no transmitted genetic anomalies. The study protocol was approved by Uskudar University Ethical Committee and was in line with the principles of the Declaration of Helsinki II. All the bodybuilder was informed by showing the experimental steps and ethical results and the consent form was signed.

2.2. Genotyping: DNA isolation from buccal cells was performed using a commercially available DNA Isolation kit (Invitrogen; Thermo Fisher Scientific, Inc.) according to the manufacturer's protocol. A mean total of 20 ng of the DNA was isolated from each sample, and the purity of the isolates were assessed based on the OD260/280 spectrophotometric ratio (Implen NanoPhotometer, München, Germany).

Genotyping of the BDNF rs6265 polymorphism was performed using real time-quantitative PCR on a StepOnePlus (Thermo Fisher Scientific, Inc.) using a TaqMan Genotyping assay according to the manufacturer's protocol (cat. no. 4362691; Thermo Fisher Scientific, Inc.). 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 postPCR 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.

2.3. Statistical analysis: Genotype distribution and allele frequencies between groups of athletes and controls were then compared by χ^2 testing using the GraphPad InStat statistical package. p values of $p<0.05$ were considered statistically significant

Table 1. Sequences of the TaqMan probe used for genotyping BDNF rs6265 polymorphism

qPCR	Sequence, 5'-3'
VIC/FAM	TCCTCATCCAACAGCTCTTCTATCA**[C/T]**GTGTTCGAAAGTG TCAGCCAATGAT

3. Results

BDNF was examined, it was found that 6 of 21 volleyball players (28%) were GA and 15 (72%) were GG genotypes. For BDNF there were no volleyball players in the AA genotype. Allele distributions are 14% A, 86% G. Table 2 lists the genotype and allelic frequencies of the BDNF rs6265 polymorphism in volleyball players. Also, Table 3 list the genotype and allelic frequencies of the BDNF rs6265 polymorphism in control group.

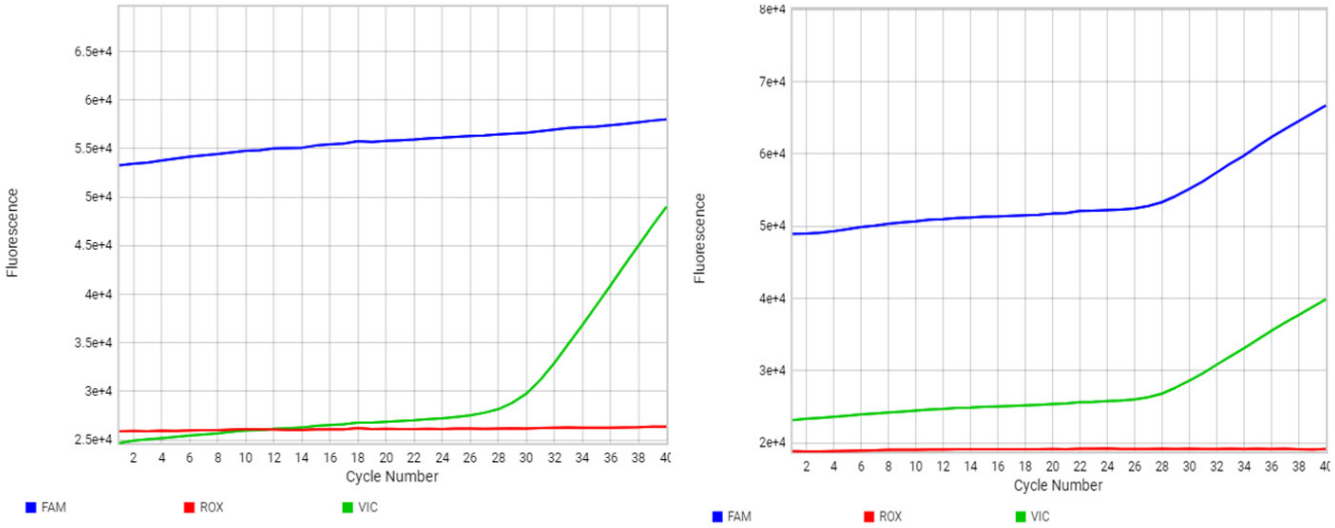

Figure 1. Quantitative PCR amplification of the GG genotype (on the left) and GA genotype (on the right) of BDNF rs6265 polymorphism. FAM indicates the A allele, whereas VIC indicates the G allele). The single blue curve indicates the homozygous genotype of GG on the left, whereas the blue and green curves indicate the heterozygous genotype of GA (CT), on the right.

Table 2. Genotypic and allelic distribution of the BDNF rs6265 polymorphism in volleyball players.

		GENOTYPES			p Value	ALLELES		p Value
		GG	GA	AA		G	A	
BDNF (n=21)	Number	15	6	-	0.407	36	6	0.218
	Percentage (%)	72	28	-		86	14	

* p,0.05, statistically significant differences. Comparison with controls using x2 test.

Table 3. Genotypic and allelic distribution of the *BDNF* rs6265 polymorphism in the control group.

		GENOTYPES			ALLELES	
		GG	GA	AA	G	A
BDNF (n=40)	Number	23	15	2	61	19
	Percentage (%)	57.8	36.3	5.9	76.25	23.75

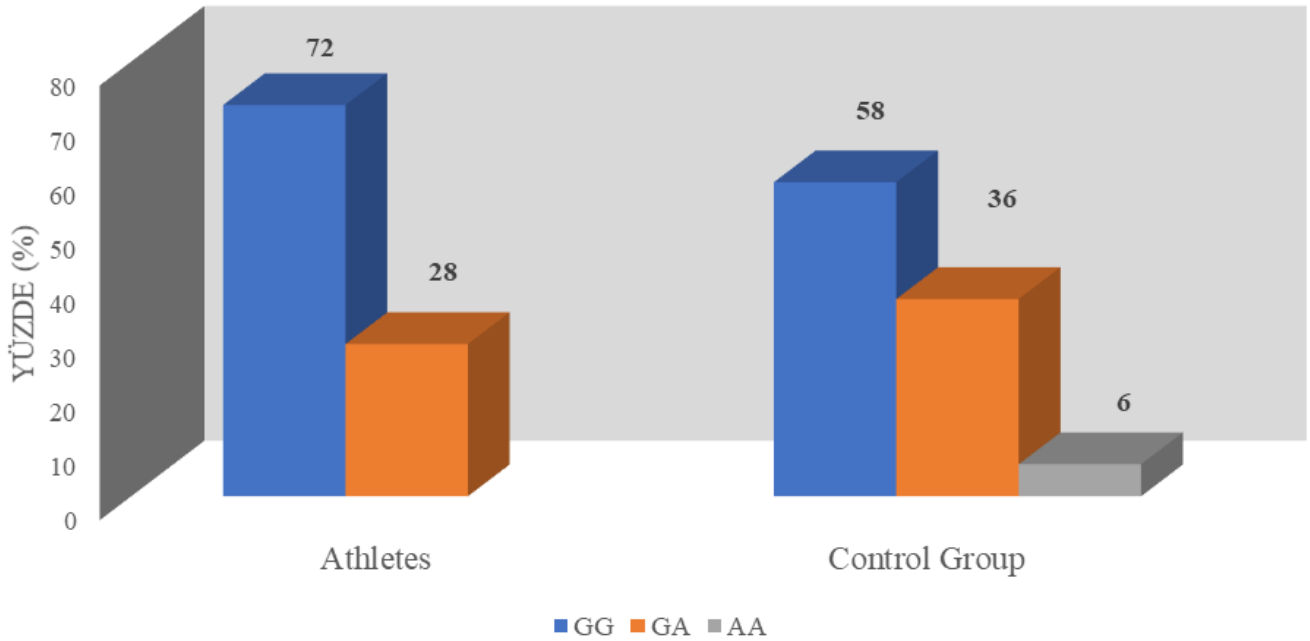

Figure 2. BDNF rs6265 genotype distributions by groups.

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4. Discussion

Stress-related depressive and anxious behaviors have been found to be associated with decreasing BDNF levels, especially in the hippocampus (Duman & Monteggia,2006). It is reported that BDNF, one of the neurotrophic proteins in the brain, prevents cognitive diseases (such as Alzheimer's and Parkinson's) during physical exercise (Podewils et al., 2005). Since BDNF comes along to be related in activity-dependent synaptic plasticity, there is great interest in its activities in learning and memory (Yamada & Nabeshima, 2003). These characteristics are important factors that affect players activities.

Recent studies have shown that some genes are effective in determining the performance of athletes both physiologically and psychologically. Genetic models can be developed and used to find the optimal genetic hardware of a volleyball player to help build up scientists or to find their predisposition. These results will be very useful for sports genetics also athletic performance. This study researches the association between the BDNF rs6265 polymorphism psychological and learning mechanism properties in 21 volleyball players. In our study cohort, the GG genotype for BDNF genotype was higher than GA. The G allele considered to be the wild-type allele of the gene and associated with protective allele. The association of G alleles with neurodegenerative diseases was less than A allele.

Figueiredo et al. (2019) examined, in the long term, the modulation of BDNF and HDL-c concentrations may be a determining factor for protection against neurological and cardiovascular diseases. Physical activity was conceptualized as a protective factor; the interaction between BDNF and physical activity was hypothesized to be associated with lower levels of depressive symptoms. Central nervous system and peripheral nervous system BDNF levels have been reported to play a role in the pathophysiology of mood disorders. A negative correlation was found between the severity of depression and BDNF levels. Major depression is characterized by low serum BDNF concentration, which supports the hypothesis that BDNF plays a role in mood disorders (Kazak & Yarim, 2015).

Another study shown like that, a consistent finding from previous research is that higher lifetime educational attainment is associated with a lower risk of dementia, an effect often explained through the heightened resilience of brain networks indicative of higher cognitive reserve (Ward et al., 2020).

Thomas Seifert et al., (2010) showed that endurance training increased the expression of BDNF mRNA in mice hippocampus rather than in the cortex and the BDNF release from the human brain. Long-term regular exercise on BDNF values a significant difference was found in the direction of rising depending on ($P < 0.05$).

In one study, individuals who were in high daily physical activity were followed for 9 years. While cognitive decline was slower and gradual in individuals with the Val/Val (GG) genotype, this beneficial decline was not seen in individuals carrying the Met (A) allele (Thibeau et al., 2016)

5. Conclusion

In this study, we examined the distribution of BDNF polymorphisms in volleyball players for the first time. BDNF GG genotype and G allele dominated our cohort. In our study, the high ratio of G allele in the volleyball players group comes across with the studies in the literature. These results indicate that BDNF rs6265 polymorphism may be one of the determining factors of psychological susceptibility in sports. In our cohort, volleyball players, the G allele was expected to be high because the psychological study data gave us this information. These polymorphisms are well known, but few studies have been studied in different populations and in sports. According to our results, psychological and plasticity of volleyball players were parallel to cognitive tests. This polymorphism, alone or in combination with additional polymorphisms, should be considered when determining a genomic score profile for sport success. In order to make clearer interpretations, it is necessary to increase the studies in this direction and to analyze in larger groups of athletes. Since there are few and limited number of athletes, it is important to continue to examine how the BDNF rs6265 polymorphism affects the effects of regular exercise on attention and information processing speed. Such studies will be an important data source to make sense of sports genetics and BDNF rs6265 region.

Patient informed consent: Informed consent was obtained.
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.
Conflict of interest: There is no conflict of interest to declare.
Financial support and sponsorship: No funding was received.
Author contribution subject and rate:
Tolga Polat (40%): Data collection, formation of the article
Canan Sercan Doğan (10%): Data collection
Başak Funda Eken (10%): Data collection
Özlem Özge Yılmaz (10%): Data collection, statistics
Çisem Şılar(10%): Laboratory assistance
Gözdem Karapınar (5%): Laboratory assistance
Begüm Su Baltacıoğlu (5%): Laboratory assistance
Rıdvan Ekmekçi (%5): Interpretation of psychological results
Korkut Ulucan (5%): Formation of the article

We would like to thank Sarıyer Volleyball Sports Club, which provided us with the opportunity to analyze with its successful players in this work we carried out.

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