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Characteristics of the BDNF Val^{66}Met polymorphism in competitive swimmers and judo athletes

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Studies have demonstrated that motivation, aggression, excitation intensity, competitive spirit, and tolerance to psychological stress are included in major psychological factors affecting the performance of athletes. However, to date, there have not been sufficient scientific studies on the relationship between genetic polymorphisms affecting psychological abilities and competitive strength/sport. In this study, we compared the distribution of the brain-derived neurotrophic factor (BDNF) gene polymorphism (Val66Met) in athletes between competitive swimming, which needs closed skill without opponents, and judo, which needs open skill with opponents, in order to investigate the genetic basis of sports performance and related psychological factors. The results showed that the prevalence of Met carriers of the BDNF polymorphism associated with vulnerability to psychological stress was lower in judo players, suggesting that judo athletes had a higher stress tolerance. In addition, the prevalence of the BDNF heterozygous group was higher in competitive swimmers, supporting the hypothesis that closed skill sports without opponents receive less stress than open skill sports with opponents, furthre suggesting that they are excellent in motor control and motor learning.

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Key words: BDNF Val66Met, competitive swimmers, judo athletes, psychological stress, motor control, motor learning

Introduction

Studies on exercise physiology and sport biomechanics have contributed to the improvement of performance in sports. For example, the results of studies on training and operating analysis have been utilized in practice. Recently, the relationship between competitive strength and genetic polymorphisms have been studied and more than 200 genes associated with athletic performance and health have been identified[1]. The *ACTN3* gene polymorphism is a representative genetic polymorphism that affects the physical ability of athletes. *ACTN3* codes for α-actinin-3, which affects the muscle phenotype, and its polymorphisms are associated with changes in the instantaneous force and endurance of muscles. It has been reported that the physical ability of explosive-type polymorphism carriers, among those with *ACTN3* gene polymorphisms, is significantly higher in several sports, including swimming and wrestling[2]. In addition, a study has suggested that insulin-like growth factor polymorphism may affect athletic performance in

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power-type sports[3].

It has been demonstrated that major psychological factors affecting the performance of athletes include motivation, aggression, excitation intensity, competitive spirit, and tolerance to psychological stress[4]. These findings suggest a relationship between genetic polymorphisms and competitive strength/sports. However, to date, there have not been sufficient scientific studies on the relationship between genetic polymorphisms affecting psychological abilities and competitive power/sports.

Among the polymorphisms affecting psychological change, the brain-derived neurotrophic factor (BDNF) polymorphism is supposed to increase the vulnerability for depression and anxiety disorder. *BDNF* is a neurotropic factor widely distributed in the central nervous system that is vital for the generation, growth, maintenance, and restoration of neurons, and enhancement of synaptic activity[5]. In addition, many animal studies have demonstrated that *BDNF* exhibits diverse physiological actions related to memory and learning, control of emotion and eating behavior, and glucose metabolism, among others. Moreover, clinical studies have shown that *BDNF* is decreased in the brain of patients with depression and those with Alzheimer's disease[6,7,8,9,10]. These findings indicate that *BDNF* plays a crucial role in controlling emotion and cognition, including stress tolerance. The single nucleotide polymorphism of the *BDNF* gene resulting in a substitution of valine (Val) for methionine (Met) in the amino-acid sequence (Val66Met) has been reported to be associated not only with decreased neural plasticity in brain regions, including the human hippocampus, but also with vulnerability to psychological stress[11]. This is thought to be because the discharge evoked by depolarizing stimuli is lower in *BDNF* Met carriers than in *BDNF* Val carriers[12].

Studies of the associations between psychological factors and athletic performance in athletes have shown that higher motivation is associated with better athletic performance. In contrast, changes (either high or low) in aggression, excitation intensity, and anxiety during the game lead to decreased athletic performance. The amygdala in the cerebral limbic system is the center for aggression, excitation, and anxiety[13]. On the other hand, the reward system centered in the basal ganglia produces motivation for individuals to satisfy their desires[14]. The activities of the amygdala and reward system are regulated by the executive function system centered in the dorsolateral prefrontal area through which adaptive behaviors are produced. These findings raise a possibility that athletes with superior athletic performance exhibit superiority in the activities of the amygdala, reward system, and executive function system. There is also a possibility that they are less likely to be the *BDNF* Met carriers, which is associated with an increased vulnerability to psychological stress.

Since there is a wide variety of sports, including individual and team sports, it is presumed that the required abilities differ between sports. Individual sports can be divided into sports performed against opponents, such as martial arts, and sports without opponents, such as track and field and competitive swimming, in which the athlete is expected to achieve his/her best performance. In addition, sport skills can be classified into closed skills and open skills. Closed skills are not affected by the environment, whereas open skills are affected by the environment[15]. Closed skill sports, such as competitive swimming and track and field, are not influenced by others; consequently, athletes can concentrate on their personal performance. On the other hand, open skill sports, such as martial arts and ball games, are influenced by others, in which the athletes have to respond to the movement of their opponents and need to have skills to judge the conditions instantly. As a result, athletes in martial arts may experience higher levels of stress because the outcome is directly related to their personal performance. It is, therefore, believed that they have a lower frequency of *BDNF* Met carriers than that of athletes in other sports.

The *BDNF* gene is also reported to be associated with autism spectrum disorder (ASD), a neurodevelopmental disorder. ASD is associated with the function of the medial prefrontal area and amygdala (associated with emotion)[16] and is associated not only with genetic factors but also environmental factors[17]. In addition, the empathizing quotient (EQ) and systemizing quotient (SQ) are also associated with ASD; it has been demonstrated that ASD is associated with a particular brain function, including emotion recognition, nonverbal communication, mathematics, and spatial recognition ability[18]. The SQ is reported to be higher in males than in females[19] and it is evident that the SQ is extremely high in individuals with ASD[20]. There are similar findings that individuals with ASD are superior in numerical and calendrical calculation and computer programming ability[21,22]. In accordance with these observations, Mottron L has reported that individuals with ASD have great concentration ability[23]. It is usual that athletes in closed skill sports use imagery rehearsal to enhance concentration before games. In order to concentrate on the game through blocking the information from others, athletes need to have great concentration ability. It is therefore assumed that the performance on brain function tests in athletes may differ between sports.

In this study, we examined the relationship between *BDNF* gene polymorphisms and sports, focusing on competitive swimming and judo, in order to verify the genetic basis for sports performance and related psychological factors.

Methods

1. Subjects

The subjects were 105 male competitive swimmers (20.79 ± 5.19 years), 74 male judo athletes (19.91 ± 1.16 years) (both continued until university), and 87 male healthy non-athletes (20.39 ± 1.50 years). Of them, nine competitive swimmers and eight judo athletes had experience of taking part in world-class competition. The difference in age between the three group was analyzed using a one-way analysis of variance, and there was no significant difference in age between the three groups. This study was approved by the ethical committee of Nagasaki University (application no. 11072748).

2. DNA extraction and gene polymorphism analysis

Samples were collected from the buccal mucosa and DNA extraction was carried out using the QIAamp DNA mini extraction kit (Qiagen, Inc).

Gene polymorphism analysis was performed using the TaqMan probe. Single nucleotide polymorphism analysis was performed using a TaqMan probe specific for *BDNF* Val^{66}Met (rs 6265). The analysis was performed using real-time polymerase chain reaction with a Light Cycler (Light Cycler 480, Roche, Inc).

3. Brain function tests

Brain function tests including the Autism Spectrum Quotient (AQ) test[24], EQ test, and the SQ test[18] were performed. The Japanese version of each test (for adults) was used, and the AQ, EQ, and SQ score were calculated.

4. Statistical analysis

Data were analyzed using cross-tabulation and the statistical significance was analyzed using the chi-squared test among competitive swimmers, judo athletes and healthy non-athletes (3 x 3). When statistical significance was found, residual analysis was performed as a post-hoc test to examine the differences between groups. The unpaired t-test was used to compare the results of the brain function tests. For all analyses, statistical significance was set at $p < 0.05$.

Results

In order to evaluate the relationship between the *BDNF* gene polymorphism (Val66Met) and sports, we investigated the *BDNF* gene polymorphisms in 105 male competitive swimmers and 74 male judo athletes (both continued until university), and 87 healthy non-athletes. Table 1 shows the distribution of *BDNF* gene polymorphism (Val66Met). The distributions were compared using the chi-squared test and a significant difference was found ($\chi^2 = 16.46$, df = 4, $p < 0.01$). The distribution of the gene polymorphisms in healthy non-athletes was what we had expected. In the competitive swimmers requiring closed skills, the frequency of the Val/Val type was significantly lower than the expected value, while the frequency of the Val/Met type was significantly higher than the expected value. There was no significant difference in the Met/Met type. Table2 shows that the distribution of gene polymorphisms in the nine competitive swimmers who had experience of taking part in world-class competition was one with the Val/Val type, six with the Val/Met type, and two with the Met/Met type; the distribution was similar to that in the competitive swimmers without experience of taking part in world-class competition.

On the other hand, in the judo athletes requiring open skills, the frequency of the Val/Val type was significantly higher than the expected value, while the frequency of the Met/Met type was significantly lower than the expected value (Table1). There was no significant difference in the Val/Met type. Interestingly, all eight judo athletes with experience of taking part in world-class competition had Val-containing genotypes (Table2): five with the Val/Val type and three with the Val/Met type. Results of statistical analyses using athletes with experience of taking part in world-class competition were similar to the those using all athletes, high Val/Val type in judo athletes (Table2). Intriguingly, the ratio of the athletes with experience of taking part in world-class competition among those with the Val/Met type was 8.8% (3/34) and that among those with the Val/Val type was 14.7% (5/34), supporting the idea that Val/Val type is more in top judo athletes who require a higher stress tolerance.

Taken all results together, our current study showed that judo athletes, who require open skills and a higher stress tolerance, had a higher frequency of the Val/Val type and a lower frequency of the Met/Met type, strongly suggesting the relationship between *BDNF* gene polymorphism (Val66Met) and sports. In addition to above finding, we also revealed that the ratio of individuals with Val-carriers was higher in athletes who continued sporting activity until

Table 1. Comparison of BDNF gene polymorphism (Val66Met)

BDNF Genotype		Val/Val	Val/Met	Met/Met	Total
Competitive swimmers	Count	22	65	18	105
	Adjusted residual	-3.011*	2.544*	0.35	
Judo athletes	Count	34	34	6	74
	Adjusted residual	3.13**	-1.279	-2.216*	
Non-athletes	Count	28	40	19	87
	Adjusted residual	0.148	-1.429	1.752	
Total	Count	84	139	43	266

*p<0.05, **p<0.01

Table 2. Comparison of BDNF gene polymorphism (Val66Met) in athletes with experience of taking part in world-class competition

BDNF Genotype		Val/Val	Val/Met	Met/Met	Total
Competitive swimmers	Count	1	6	2	9
	Adjusted residual	-2.213*	1,203	1,419	
Judo athletes	Count	5	3	0	8
	Adjusted residual	2.213*	-1.203	-1.419	
Total	Count	6	9	2	17

*p<0.05

university (both competitive swimmers and judo athletes) than in healthy non-athletes.

Athletes try to enhance their concentration before a game in order to improve their athletic performance. It has been reported that the *BDNF* gene is associated with ASD, a neurodevelopmental disorder, and that individuals with ASD have great concentration[24]. In addition, it has also been demonstrated that the SQ, which is related to brain functions such as spatial recognition ability, is extremely high in individuals with ASD[20]. Therefore, we used the AQ and EQ/SQ tests in order to evaluate brain function in competitive swimmers and judo athletes. The results of the AQ and EQ/SQ tests are shown in Figures 1, 2, and 3, respectively. There were no significant differences in any of the results of the brain function tests between the two groups. In addition, the scores of the athletes were similar to those of the healthy non-athletes[18,24]. We further evaluated AQ and EQ/SQ tests in each group in terms of *BDNF* Val^{66}Met polymorphism. Again, there were significant differences in none of the results of the brain function tests among *BDNF* polymorphism in each group (Figs.1, 2, 3).

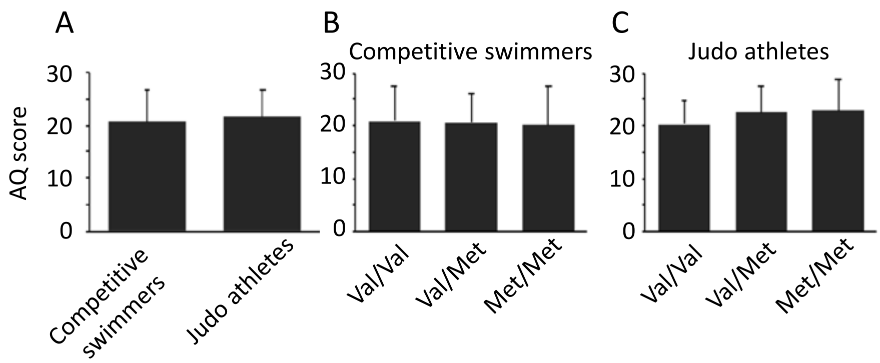

Figure 1. Comparison of the Autism Spectrum Quotient (AQ) scores
AQ scores were compared between competitive swimmers and judo athletes (A), among BDNF gene polymorphisms in competitive swimmers (B) or judo athletes (C). 105 competitive swimmers and 74 judo athletes performed AQ test. The unpaired t-test was performed and there were no statistical difference between any groups.

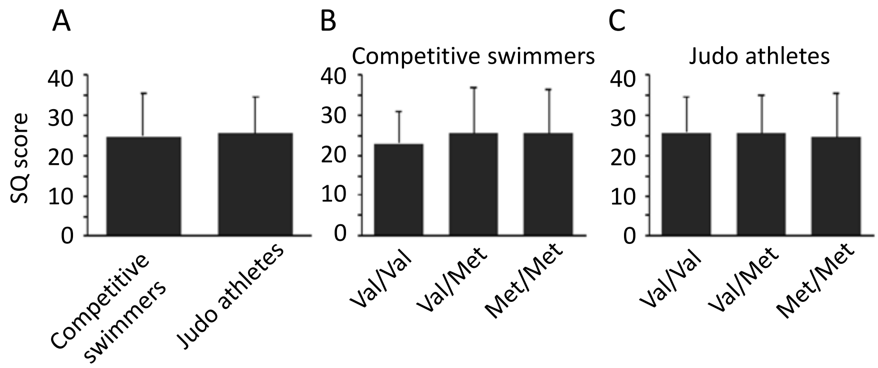

Figure 2. Comparison of the systemizing quotient (SQ) scores
SQ scores were compared between competitive swimmers and judo athletes (A), among BDNF gene polymorphisms in competitive swimmers (B) or judo athletes (C). 105 competitive swimmers and 74 judo athletes performed SQ test. The unpaired t-test was performed and there were no statistical difference between any groups.

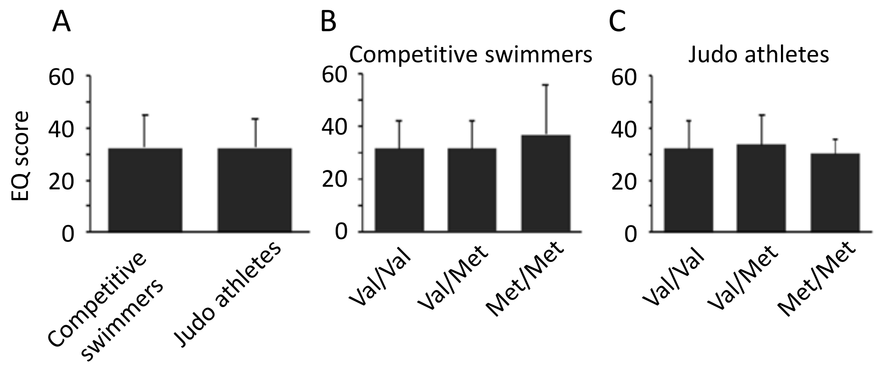

Figure 3. Comparison of the empathizing quotient (EQ) scores
EQ scores were compared between competitive swimmers and judo athletes (A), among BDNF gene polymorphisms in competitive swimmers (B) or judo athletes (C). 105 competitive swimmers and 74 judo athletes performed EQ test. The unpaired t-test was performed and there were no statistical difference between any groups.

Discussion

This study investigated the relationship between a gene polymorphism that influences the vulnerability to psychological stress and the characteristics of the sports of competitive swimming and judo. The results showed a significant difference in *BDNF* gene polymorphisms between the two sports. Met-type *BDNF* is a risk factor for developing depression[11] because it is thought to enhance the vulnerability to psychological stress. The results show that the judo athletes had a higher frequency of Val homozygous carriers and a lower frequency of Met carriers, suggesting that they have a greater tolerance to psychological stress. The competition in judo is mostly held in a tournament form, in which losing once means elimination from the tournament. The pressure to win becomes higher when the athletes remain in the competition, especially in larger-scale competitions; therefore, they have to play games under strong psychological pressure. In addition, even high-level judo athletes may lose by accident because judo is a combat sport. In order to survive in domestic and international competitions, judo athletes need to have good stress tolerance so that they can perform optimally.

Competitive swimmers had a higher frequency of Val/Met *BDNF* individuals. Competitive swimming is a closed skill. Swimmers are expected to achieve their optimal performance in competitions. As in judo, losing once means the end of participation in competitive swimming; however, competitive swimmers are supposed to experience a lower level of psychological stress compared with judo athletes because they can concentrate on their personal performance without distractions from others and this may have influenced the results.

Interestingly, it has been reported that the volumes of the gray matter of supplementary motor area in the cerebellum are greater in Val/Met *BDNF* carriers than in the Val/Val or Met/Met carriers[25], suggesting that Val/Met carriers are superior in motor control and motor learning. Swimming is performed in water, in the absence of any form of support; therefore, in addition to providing a driving force and floating, the maintenance of balance is important. Fumoto et al. stated that having a sense of one's own body and motor control based on sensory information are important in competitive swimming, suggesting that balance is especially important in competitive swimming[26]. This may be the reason for the higher frequency of Val/Met carriers in competitive swimmers.

It is easy to imagine that top athletes receive severe stress before and during matches. It is reported that BDNF receptor, TrkB, interacts with glucocorticoid receptor, GR[27], moreover, chronic administration of glucocorticoid, which is secreted by stress exposure, suppresses BDNF-induced glutamate release by reducing TrkB-GR interaction in cultured cortical neurons[27]. It is interesting, although BDNF polymorphism does not seem to modify the affinity of TrkB-GR interaction, it has been reported that stress at work reduce serum BDNF levels and plasma BDNF is less in BDNF Met-carrier[28,29], suggesting that Met carriers suppress BDNF-induced glutamate release more, which might weaken synaptic plasticity.

There were no significant differences in the results of the brain function tests (AQ, EQ, and SQ) between the two groups and among BDNF polymorphism in each sport. ASD is a neurodevelopmental disorder (multifactorial genetic disorder)[16] that is related to the function of the medial prefrontal area and amygdala (associated with emotion) in the brain. ASD is associated not only with genetic factors but also with environmental factors[17]. In addition, the EQ and SQ are also associated with brain function and it has been demonstrated that ASD is associated with particular brain functions, including emotion recognition, nonverbal communication, mathematics, and spatial recognition ability[18]. In this study, we found that there were no significant differences in the results of the brain function tests between the different groups. Both competitive swimming and judo are individual sports and different from team sports, such as ball games. Although competitive swimmers require closed skills while judo athletes require open skills, both of them may need to have greater concentration before games. In addition, the subjects in this study were all male and this may have influenced the results of brain function tests. In this study, a difference was found in the *BDNF* gene polymorphism but not in brain function. The results suggest a relationship between the gene polymorphism and sports. These findings suggest that the distribution of the *BDNF* gene polymorphism differs between sports and this difference reflects the characteristics of the sport. Since this study investigated only elite athletes in university, further investigations will be important to understand when and how preference of sports is established. As is the case that the subjects in this study were all male, many investigations have performed gene polymorphisms in male athletes. As far as we know, the only one report has analyzed ESR1 gene polymorphism in female athletes[30]. Therefore, further investigations of BDNF gene polymorphisms in female athletes or between sex might acquire useful information about common and sex-specific characteristics.

Summary

In this study, we compared the distribution of BDNF gene polymorphisms in competitive swimmers and judo players in order to evaluate the genetic basis for understanding the characteristics of sports and related psychological factors. The results showed that the frequency of carriers of the Met BDNF polymorphism, which is associated with vulnerability to psychological stress, was lower in judo athletes, suggesting that judo athletes had stronger stress resistance. In addition, competitive swimmers had a higher frequency of Val/Met *BDNF* polymorphism, suggesting that they are superior in motor control and motor learning.

The subjects in the present study were elite athletes who continued sporting activity until university. Further studies including a wide range of athletes with different levels of performance may be useful for further understanding the characteristics of sports.

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