Associations of Brain-Derived Neurotropic Factor rs6265 Gene Polymorphism with Personality Dimensions among Athletes

Kinga Humińska-Lisowska 1*, Jolanta Chmielowiec 2*, Krzysztof Chmielowiec 2*, Marta Niewczas 3, Milena Lachowicz 4, Paweł Cięszczyk 1, Jolanta Masiak 5, Aleksandra Strońska-Pluta 6, Monika Michałowska-Sawczyn 1, Ewelina Maculewicz 7, and Anna Grzywacz 1*

Abstract: Brain-Derived Neurotropic Factor (BDNF) is one of the essential mediating factors of exercise-induced neuroplasticity, but the underlying molecular mechanisms of exercise-induced neuroplasticity are still largely unknown. Personality dimensions differentiate individuals and depend on genes and environmental factors. The dimensions of openness to experience, emotional stability, extraversion and conscientiousness have been reported to be positively related to performance; considering agreeableness, a negative relation with sports performance was emphasized. However, not enough effort has been put into investigating the relationship between genetic polymorphisms affecting psychological abilities and competitive power sports. The aim of this study was to investigate the association of the rs6265 polymorphism of BDNF with personality dimensions in martial arts athletes. The study was conducted among martial arts athletes. The study group included 258 volunteers (martial arts athletes (n = 106) and controls (n = 152). BDNF polymorphism testing was performed using the real-time PCR method; personality dimensions were assessed using standardized NEO-FFI questionnaires. All analyses were performed using STATISTICA 13. We observed that martial arts athletes’ G/G genotypes compared to the control group G/G genotypes presented significantly higher severity of personality dimension “conscientiousness”. In comparison with the controls, the case group subjects had significantly higher scores in the dimension extraversion and conscientiousness compared to the control group with G/G genotypes. The combination of the analysis of the rs6265 polymorphism of BDNF and personality dimensions in martial arts athletes suggests that this polymorphism is associated with the development of personality traits in athletes, which may contribute to the success in competitive sports. Further studies are needed to confirm these findings and explore the underlying molecular mechanisms.
1. Introduction

“Athletic phenotype” is complex and depends on a combination of many elements, such as environmental variables and experience (training and diet) and biological and genetic factors. In recent decades, “sports genomics” has played an important role, showing that some DNA Single Nucleotide Polymorphisms (SNPs) can be linked to athlete performance and championship level, having an impact on physical activity behavior, endurance, speed, strength, flexibility, power, neuromuscular coordination, energetic expenditure, metabolic and cardiorespiratory fitness, as well as personality traits [1,2].

Personality is defined as consistent patterns of thoughts, emotions, and behaviors that characterize a person across a lifetime [3]. The NEO Five-Factor Personality Inventory (NEO FFI) is a questionnaire that measures a comprehensive model of general personality traits. The Five-Factor Model, or “Big Five”, defines the five dimensions of personality: extraversion, neuroticism, openness to experience, conscientiousness, and agreeableness. They depend on genes and environmental factors. They are stable over time and across cultures [4]. Personality traits appeared to be associated with the psychological characteristics of athletes [5,6]. Conscientiousness, openness, and agreeableness were found to be significant predictors of sports performance [7].

Previous studies looked at personality traits in various sports disciplines and found differences among different types of sports, race, gender, experience, and skill level [8–10]. Furthermore, regarding the personality traits of martial arts practitioners, it was found that openness to experience, extraversion, emotional stability, and conscientiousness are positively related to performance. At the same time, agreeableness displays a negative relation to performance. At the same time, agreeableness displays a negative relation to performance [11].

Numerous studies indicate that physical exercise improves brain function and structure [12–16]. In the last decades, Brain-Derived Neurotropic Factor (BDNF) has been extensively studied in neuroscience as one of the essential mediators of exercise-induced neuroplasticity. However, the underlying molecular mechanisms of exercise-induced neuroplasticity are still barely known [17]. Proposed mechanisms of exercise-induced neuroplasticity are increased expression, secretion, and downstream signaling of neurotrophic factors (among them BDNF), reduced stress levels [18], reduced inflammation [19,20], and improved metabolic and cardiovascular parameters. BDNF promotes neuronal survival and differentiation, as well as regulates synaptic transmission and plasticity (synaptogenesis, neurogenesis, long-term potentiation) of the adult brain in many regions of the Central Nervous System (CNS) [21]. First, a positive correlation between physical activity and BDNF expression was observed in rodents [22]. Pharmacological blocking of BDNF signaling in the rodent hippocampus reduced the neuroplastic effects of exercise. Similar to rodents, physical activity (chronic and acute) increases peripheral BDNF levels in healthy humans [23–26].

Our research has concentrated on the case-control analysis of athletes’ groups in the aspect of their personality traits in association with rs6265 BDNF gene polymorphism. This common G196A nonsynonymous polymorphism rs6265 that produces a valine (Val) to methionine (Met) substitution at codon 66 (Val66Met), is present in about 20% of the total world population, with strong differences among different ethnicities (e.g., 22% in Caucasians, 2% in African Americans) (IGSR: The International Genome Sample Resource, 2021). Rs6265 polymorphism is shown to modulate BDNF secretion and its distribution within a cell, synaptic plasticity, and negative influence on memory, cognitive function, and vulnerability to psychological stress [27–29]. This is probably because the discharge induced by depolarizing stimuli is lower in BDNF AA carriers than in BDNF GG carriers [30]. Additionally, it was already observed that BDNF rs6265 polymorphism increases the risk for depression. However, this genetic risk factor for suicidal ideation and major depression may be reduced by physical activity [31,32]. This is why there is an assumption that athletes with superior athletic performance are less likely to be BDNF AA carriers, which is also associated with an increased vulnerability to psychological stress. BDNF seems to be one...
of the most crucial neurotrophins engaged in sports performance. Several research groups have already confirmed such observations [29,33–40].

In our study, we investigate the association of the rs6265 polymorphism of *BDNF* with personality dimensions in martial arts athletes. We decided to explore martial arts genotypes compared to the control group and the severity of personality dimensions.

### 2. Materials and Methods

#### 2.1. Subjects

The study group consisted of 258 volunteers: martial arts (*n* = 106; mean age = 23.33 SD = 5.76, Minimum 17.00, Maximum 35.00, men 79%, judo, *n* = 25; boxing, *n* = 10; kickboxing, *n* = 14; Ju-jitsu, *n* = 35; wrestling, *n* = 22) and healthy, non-athlete controls (*n* = 152; mean age = 22.23, SD = 4.55, Minimum 17.00, Maximum 50.00, men 85%, women 15%). A total of 38% of the martial arts group achieved the championship level. The research was conducted in 2018–2019, before the COVID-19 pandemic. The study was conducted in accordance with the Declaration of Helsinki principles and approved by the Bioethics Committee for Clinical Research of the Regional Medical Society in Szczecin (protocol nr 13/KB/VI/2016, 8 December 2016). All subjects provided signed informed consent for participating in the research. There was no financial or other compensation for being part of the study sample. Martial arts and control subjects were examined by the NEO Five-Factor Personality Inventory (NEO-FFI).

The NEO-FFI includes six dimensions for each of the five traits—extraversion (positive emotion, warmth, gregariousness, activity, excitement seeking, assertiveness), agreeableness (tendermindedness, trust, altruism, straightforwardness, compliance, modesty), openness to experience (fantasy, feelings, aesthetics, actions, values, ideas), conscientiousness (deliberation, competence, dutifulness, order, achievement striving, self-discipline), neuroticism (anxiety, vulnerability to stress, hostility, self-consciousness, impulsiveness, depression) [41].

The results of NEO-FFI inventories were given as sten scores. The conversion of the raw score into the sten scale was performed according to Polish norms for adults; it was assumed that: stens: 1–2—very low scores; 3–4—low scores, 5–6—average scores; 7–8—high scores, 9–10—very high scores.

#### 2.2. Genotyping

Using standard procedures, the genomic DNA was extracted using the High Pure PCR Template Preparation Kit (Roche, Basel, Switzerland) from venous blood. Rs6265 polymorphism was conducted using TaqMan SNP Genotyping Assay C__11592758_10 (ThermoFisher Scientific, Waltham, MA, USA) with the real-time PCR method.

A LightCycler® 480 II System (Roche Diagnostic, Basel, Switzerland) was applied to perform the fluorescence resonance energy in the genotypic data. The data relating to the *BDNF* gene polymorphism were obtained under the following conditions: PCR was performed with 50 ng DNA of each sample in a final volume of 20 µL containing 2 µL reaction mix, 0.5 mM of each primer, 0.2 mM of each hybridization probe, and 2 mM MgCl2, according to the manufacturer’s instructions, with initial denaturation (95 °C for 10 min) and then 35 cycles of denaturation (95 °C for 10 s), annealing (60 °C for 10 s), and extension (72 °C for 15 s). After amplification, a melting curve was generated by holding the reaction at 40 °C for 20 s and then heating slowly to 95 °C. The fluorescence signal was plotted against temperature to provide melting curves for each sample.

#### 2.3. Statistical Analysis

Concordance between the genotype frequency distribution and Hardy–Weinberg equilibrium (HWE) was tested with the HWE software (https://wpcalc.com/en/equilibriumhardyweinberg/ (accessed on 10 May 2022)). The relationships between *BDNF* rs6265, martial arts and control subjects and NEO Five-Factor Inventory were analyzed in a multivariate analysis of Factor effects ANOVA (NEO-FFI/ × genetic feature × control and
martial arts \times (genetic feature \times control and martial arts)). The homogeneity of variance was satisfied (Levene test \( p > 0.05 \)). The distribution of the analyzed variables did not present a normal distribution. The NEO-FFI (neuroticism, extraversion, openness, agreeability, and conscientiousness) was measured and compared using the Mann–Whitney U test. \( BDNF \) rs6265 genotype frequencies between healthy control subjects and martial arts subjects were tested with the chi-square test. For these variables, the Bonferroni multiple comparisons correction was applied, and the accepted level of significance was 0.01 (0.05/5) and 0.0083 (0.05/6). All computations were performed with the usage of STATISTICA 13 (Tibco Software Inc, Palo Alto, CA, USA) for Windows (Microsoft Corporation, Redmond, WA, USA).

3. Results

The frequency distributions accorded with the HWE. There was no statistical difference between martial arts participants and people from the control group (Table 1).

Table 1. Frequency of genotypes and alleles of the \( BDNF \) rs6265 in a group of martial arts subjects and controls.

| BDNF rs6265 | Martial Arts \( n = 106 \) | Controls \( n = 152 \) | \( \chi^2 \) (\( p \)-Value) |
|-------------|-----------------------------|------------------------|-----------------------------|
| G/G         | 76 (71.7%)                  | 100 (65.8%)             | 1.009 (0.6039)              |
| A/G         | 27 (25.5%)                  | 47 (30.9%)              |                             |
| A/A         | 3 (2.8%)                    | 5 (3.3%)                |                             |
| G           | 179 (84.4%)                 | 247 (81.2%)             | 0.880 (0.3484)              |
| A           | 33 (15.6%)                  | 57 (18.8%)              |                             |

Hardy-Weinberg equilibrium

\[ \chi^2 (p-value) = 0.102 (0.7498) \]

\[ \chi^2 (p-value) = 0.033 (0.8548) \]

\( p \)—statistical significance, \( \chi^2 \)—Chi\^2 test result, \( n \)—number of subjects, G/G and A/A—genotypes (homozygotes), A/G—genotype (heterozygote), G and A—alleles.

The \( BDNF \) rs6265 genotypes and alleles frequencies in the studied sample do not differ in the analyzed groups of subjects (Table 1).

The means and standard deviations for NEO Five-Factor Inventory results in groups of martial arts subjects and control subjects are presented in Table 2. In comparison with the controls, the case group subjects had significantly higher scores on the extraversion/scale (M 6.89 vs. M 6.43, \( p = 0.0405 \)) and conscientiousness/scale (M 7.23 vs. M 5.89, \( p < 0.0001 \)).

Table 2. Analysis of NEO Five-Factor Inventory results in martial arts subjects and controls.

| NEO Five-Factor Inventory/ | Martial Arts \( n = 106 \) | Control \( n = 152 \) | U Mann–Whitney Z | \( p \)-Value |
|---------------------------|-----------------------------|------------------------|------------------|-------------|
| M \pm SD                  | M \pm SD                    |                        |                  |             |
| Neuroticism/scale         | 4.75 \pm 2.24               | 4.65 \pm 1.92          | −0.128           | 0.8981      |
| Extraversion/scale        | 7.12 \pm 1.92               | 6.43 \pm 1.85          | 2.834            | 0.0045 *#   |
| Openness/scale            | 5.01 \pm 1.84               | 4.56 \pm 1.55          | 2.117            | 0.0342 *    |
| Agreeability/scale        | 6.00 \pm 2.36               | 5.71 \pm 2.06          | 1.038            | 0.2993      |
| Conscientiousness/scale   | 7.26 \pm 2.17               | 5.89 \pm 1.99          | 5.165            | 0.0000 *#   |

M—mean, SD—standard deviation, G/G and A/A—genotypes (homozygotes), A/G—genotype (heterozygote), G and A—alleles, U Mann-Whitney Z-test. *—significant statistical differences. # Bonferroni correction was used, and the \( p \)-value was reduced to 0.01 (\( p = 0.05/5 \) (number of statistical tests conducted)).
Neuroticism/scale and BDNF rs6265.

The results of $2 \times 3$ factorial ANOVA noticed statistically significant effect (without Bonferroni correction) of combined factor $BDNF$ rs6265 genotype of martial arts/control ($F_{2,252} = 3.11, p = 0.0465, \eta^2 = 0.024$) (Table 3, Figure 1). Power calculation—our sample had more than 59% power to detect the combined factor of martial arts/control $\times$ $BDNF$ rs6265 and their interaction effect (about 2.4% of the phenotype variance).

$$F_{2, 252} = 3.1051; p = 0.04654$$

Figure 1. Interaction between martial arts/-Control and $BDNF$ rs6265 and Neuroticism scale. # Bonferroni correction was used, and the $p$-value was reduced to 0.0083 ($p = 0.05/6$ (number of statistical tests conducted)). G/G and A/A—genotypes (homozygotes), A/G—genotype (heterozygote), G and A—alleles, 1—G/G, 2—A/G, 3—A/A, 4—G/G, 5—A/G, 6—A/A., * significant result

Table 3. The results of $2 \times 3$ factorial ANOVA for martial arts subjects and controls, NEO Five-Factor Inventory scale, and $BDNF$ rs6265.

| NEO Five-Factor Inventory | $BDNF$ Gene rs6265 | ANOVA |
|---------------------------|-------------------|-------|
|                           | $G/G$ $n = 74$ $M \pm SD$ | $A/G$ $n = 74$ $M \pm SD$ | $A/A$ $n = 8$ $M \pm SD$ | Factor | $F$ ($p$-Value) | $\eta^2$ | Power (Alfa = 0.05) |
| **Neuroticism/scale**     |                   |       |     |       |       |       |                  |
| Martial Arts (MA); $n = 106$ | 4.29 ± 2.02 | 5.85 ± 2.43 | 6.67 ± 2.31 | intercept | $F_{1,252} = 385.18 (p < 0.0001)$ *# | 0.604 | 1.000 |
| Control; $n = 152$        | 4.55 ± 2.06 | 4.85 ± 1.60 | 4.80 ± 1.92 | MA/control $BDNF$ | $F_{2,252} = 3.11 (p = 0.0465)^*$ | 0.024 | 0.594 |
Table 3. Cont.

| NEO Five-Factor Inventory | Group | BDNF Gene rs6265 | ANOVA |
|---------------------------|-------|------------------|-------|
|                            |       | G/G              |       | A/G              |       | A/A              |       |
|                            |       | n = 176 M ± SD   |       | n = 74 M ± SD   |       | n = 8 M ± SD    |       |
| Extraversion/ scale        |       | 7.39 ± 1.83      |       | 6.48 ± 2.04     |       | 6.00 ± 1.73     |       |
| Control; n = 152           |       | 6.38 ± 1.92      |       | 6.53 ± 1.72     |       | 6.60 ± 1.82     |       |
| Openness/ scale            |       | 4.95 ± 1.85      |       | 5.00 ± 1.84     |       | 6.67 ± 1.15     |       |
| Control; n = 152           |       | 4.61 ± 1.56      |       | 4.55 ± 1.56     |       | 3.60 ± 1.14     |       |
| Agreeableness/ scale       |       | 6.25 ± 2.37      |       | 5.55 ± 2.26     |       | 3.67 ± 1.15     |       |
| Control; n = 152           |       | 5.81 ± 2.10      |       | 5.51 ± 1.67     |       | 5.60 ± 3.21     |       |
| Conscientiousness/ scale   |       | 7.54 ± 2.04      |       | 6.67 ± 2.20     |       | 5.67 ± 4.16     |       |
| Control; n = 152           |       | 5.57 ± 1.98      |       | 6.47 ± 1.91     |       | 6.80 ± 1.64     |       |

*—significant result p = 0.05; MA—Martial Arts; M ± SD—mean ± standard deviation, G/G and A/A—genotypes (homozygotes), A/G—genotype (heterozygote), G and A—alleles, BDNF—Brain-Derived Neurotropic Factor, F—F ratio score, η²—effect size # Bonferroni correction was used, and the p-value was reduced to 0.01 (p = 0.05/5 (number of statistical tests conducted)).

Conscientiousness/scale and BDNF rs6265.

The results of 2 × 3 factorial ANOVA noticed a statistically significant effect (with Bonferroni correction) of combined factor BDNF rs6265 genotype of martial arts/control (F2,252 = 6.16, p = 0.0024, η² = 0.047) (Table 3, Figure 2). Our sample had more than 89% power to detect the combined factor of martial arts/control × BDNF rs6265 and their interaction effect (about 4.7% of the phenotype variance). The post-hoc analysis is shown in Table 4.

Table 4. Post-hoc LSD (least significant difference) analysis of interactions between martial arts/- Control and BDNF rs6265 and neuroticism scale and conscientiousness scale.

| BDNF rs6265 and NEO FF Neuroticism Scale | [1] | [2] | [3] | [4] | [5] | [6] |
|-----------------------------------------|----|----|----|----|----|----|
| M = 4.29                                |    |    |    |    |    |    |
| Martial arts BDNF G/G [1]               | 0.0006 *# | 0.0461 * | 0.3963 | 0.1344 | 0.5837 |
| Martial arts BDNF A/G [2]               | 0.5070 | 0.0032 *# | 0.0407 * | 0.2847 |
| Martial arts BDNF A/A [3]               | 0.0742 | 0.1315 | 0.0013 | 0.2058 |
| Control BDNF G/G [4]                    | 0.3990 | 0.7868 |
| Control BDNF A/G [5]                    | 0.9571 |
| Control BDNF A/A [6]                    | 0.888 |

| BDNF rs6265 and NEO FF conscientiousness scale | [1] | [2] | [3] | [4] | [5] | [6] |
|------------------------------------------------|----|----|----|----|----|----|
| M = 7.34                                      |    |    |    |    |    |    |
| Martial arts BDNF G/G [1]                    | 0.0561 | 0.1183 | 0.0000 *# | 0.0048 *# | 0.4309 |
| Martial arts BDNF A/G [2]                    | 0.4190 | 0.0134 * | 0.6858 | 0.8928 |
| Martial arts BDNF A/A [3]                    | 0.9353 | 0.5680 | 0.4453 |
| Control BDNF G/G [4]                         | 0.0130 * | 0.1873 |
| Control BDNF A/G [5]                         | 0.7284 |
| Control BDNF A/A [6]                         | 0.888 |

*—significant statistical differences, M—mean. For these variables, G/G and A/A—genotypes (homozygotes), A/G—genotype (heterozygote), G and A—alleles, BDNF—Brain-Derived Neurotropic Factor, # Bonferroni correction was used, and the p-value was reduced to 0.0083 (p = 0.05/6 (number of statistical tests conducted)).
In our study, we investigate the association of the rs6265 polymorphism of BDNF with personality dimensions in martial arts athletes. We decided to explore martial arts genotypes compared to the control group and the severity of personality dimensions.

Studies have shown that there is a possibility to predict future success in sport, based on psychological factors, relatively successfully, even in an early stage of engagement in sports [42]. The latest Genome-Wide Association Study (GWAS) [43] showed a very low significant p-value of rs6265 BDNF with general risk tolerance in the general population.

Asai et al. 2020 presented the results concerning the group of 74 male judo athletes and 87 healthy male non-athletes. In the study [27], the relationship between BDNF gene polymorphism and sports (the main focus was on judo) was the concern. This study indicated that judo athletes, who need open skills and higher stress tolerance, presented a higher frequency of the GG genotype and a lower frequency of the AA genotype, which can strongly implicate the relationship between the BDNF gene polymorphism and sports. Moreover, they also emphasized that the ratio of A carriers was elevated in the group of athletes who continued sporting activity to the university level than in healthy non-athletes [44].

The research by Joffe et al. analyzed 467 non-clinical Caucasian subjects of European ethnicity who participated in the Brain Resource International Database (BRID). The study examined relationships between the BDNF G196A polymorphism and five-factor personality dimensions in BDNF A carriers. Lower total hippocampal grey matter volume was...
associated with higher neuroticism. These specific relationships were not present in BDNF Val/Val homozygotes (G196G) [45]. The study mentioned [45] showed the differences between A carriers and the GG genotype group. The first group did not have an elevated level of neuroticism in direct comparison with the second one. Some studies identified a shortage of influence of BDNF polymorphism and neuroticism levels in healthy volunteers [46,47]. However, some also report a small but significant elevation of neuroticism in Met carriers [47]. When considering both BDNF A carrier and GG groups, the studies indicate the association of higher neuroticism and higher depression trait and related symptoms of anxiety and stress, which seems to be evidence of shared genetic risk among these dimensions [48,49]. However, not enough effort has been put into investigating the relationship between genetic polymorphisms affecting psychological abilities and competitive power sports.

Our study was focused on a particular group of martial arts practitioners, and we observed that martial arts athletes’ G/G genotypes (Val66), in comparison to the control group’s G/G (Val66) genotypes, presented significantly higher scores on personality dimension “conscientiousness”. In the NEO-FFI dimension, “conscientiousness” covers personality traits as: competence, order, dutifulness, achievement striving, self-discipline, and deliberation. Our research showed that there is a possibility that the athletes who perform martial arts and present with G/G genotypes are “neurobiologically” predisposed to those achievements. An interesting question is how participation in sports and competitions influences the development of those personality features? Therefore, our future research will focus on young martial arts athletes’ G/G genotypes compared to the control group’s G/G genotypes and NEO-FFI dimensions in longitudinal research.

In comparison with the controls, the case study subjects had significantly higher scores on the extraversion/scale (M 6.89 vs. M 6.43, \( p = 0.0405 \)) and conscientiousness/scale (M 7.23 vs. M 5.89, \( p < 0.0001 \)). We noticed differences in the NEO-FFI scale and the analysis of interactions connected with the status of an athlete and genes. The results of 2 × 3 factorial ANOVA noticed a statistically significant effect of combined factor BDNF rs6265 genotype of martial arts/control (\( F_{2,252} = 3.11, p = 0.0465, \eta^2 = 0.024 \)) (Table 3, Figure 1).

Additionally, we observed that the results of 2 × 3 factorial ANOVA showed a statistically significant influence of combined factor BDNF rs6265 on the martial arts/control genotype (\( F_{2,252} = 6.16, p = 0.0024, \eta^2 = 0.047 \)) (Table 3, Figure 2).

Human fitness is conditioned by several environmental and genetic factors [50]. Neuronal survival, neurogenesis, growth, and synaptic plasticity are regulated by BDNF, whereas BDNF rs6265 polymorphism is connected with serum BDNF concentration that changes in response to exercise [30].

In our previous research, we also presented the influence of BDNF on the group of athletes. In the group of individuals practicing martial arts, the statistically significant interaction between the occurrence of T/T and A/T genotypes in BDNF rs10767664 was noticed, as well as increased results of the NEO FFR sten and conscientiousness scales in comparison with the control group. When comparing martial arts athletes and the control group, we also observed a statistically significant interaction between the frequency of G/G genotypes and elevated results on the NEO-FFI and conscientiousness dimension [51].

We are aware of our research’s limitations. However, as it is the only polymorphism, we observe statistical significance there.

The combination of the analysis of personality dimensions with genetics—as in the case of the polymorphism of the BDNF gene related to neuroplasticity—indicates that neurobiology cannot be ignored in educating sports champions. We already know that this is related to genetics. However, little is still known about the influence of personality traits on sports performance.

5. Conclusions

In our research, we observed that martial arts athletes’ G/G genotypes compared to the control group’s G/G genotypes presented significantly higher severity of personality
dimension “conscientiousness”. This is worthy of further analysis, probably longitudinal studies on a more numerous group of athletes.

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