Baltic Journal of Health and Physical Activity

Volume 16 | Issue 2 Article 13

2024

# Association analysis of the OPRM1 polymorphism gene and personality traits among a cohort of professional athletes.

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## Recommended Citation

Reclaw R, Boron A, Chmielowiec K, Chmielowiec J, Prabucka K, Lachowicz M, Zadroga L, Gula L, Brozyna M, Grzywacz A. Association analysis of the OPRM1 polymorphism gene and personality traits among a cohort of professional athletes. Balt J Health Phys Act. 2024;16(2):Article13. DOI: 10.29359/BJHPA.16.2.13

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## Abstract

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## Keywords

OPRM1, polymorphism, personality traits, professional athletes



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This article is available in Baltic Journal of Health and Physical Activity: https://www.balticsportscience.com/journal/vol16/iss2/13

Baltic Journal
of Health and Physical Activity
e-ISSN 2080-9999

*Article*

# Association analysis of the OPRM1 polymorphism gene and personality traits among a cohort of professional athletes

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**Citation:** Reclaw R, Boron A, Chmielowiec K, Chmielowiec J, Prabucka K, Lachowicz M, Zadroga L, Gula L, Brozyna M, Grzywacz A. Association analysis of the OPRM1 polymorphism gene and personality traits among a cohort of professional athletes. Balt J Health Phys Act. 2024;16(2):Article13.
DOI: 10.29359/BJHPA.16.2.13

Academic Editor:
Agnieszka Maciejewska-Skrendo

Received: May 2024
Accepted: May 2024
Published: June 2024

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**Abstract:** Introduction: In sports research, genetic studies linked to the traits of the temperament, in addition to medical examinations and other physiological and biochemical tests, would enrich the scope of possibilities and successes that a competitor can accomplish. This could be beneficial for the protection of both mental and physical health. The aim of the study is to determine the association between the OPRM1 rs1799971 gene polymorphism and traits determined using the Temperament and Character Inventory (TCI-R) scores and sports subjects. Material and methods: The study group comprised 391 male volunteers. Out of these, 222 sports subjects and 186 were non-addicted (alcohol, drugs) and not practicing competitive sports. The temperament and character questionnaire (TCI-R) was used to determine personality traits such as novelty seeking, harm avoidance, reward addiction and perseverance, as well as self-direction, cooperation and self-transcendence. Genotyping OPRM1 rs1799971 was carried out with the real-time PCR method. Results: In the present study polymorphic variants of selected genotypes were associated with self-direction - A/A genotypes in the study group. Higher values were observed compared to the control group ($p = 0.045$). Similarly, the A/G genotype occurred statistically significantly more frequently in the study group compared to the control group. The G/G genetic variant was less common in the study group compared to the controls. Conclusions: The study reveals the validity of analyzing connections between personality traits and selected gene polymorphisms in athletes, a relatively new field. The presence of the OPRM1 rs1799971 AA genotype is associated with higher self-management scores, indicating genetic predispositions in the study group for better results in sports.

**Keywords:** OPRM1, polymorphism, personality traits, professional athletes.

## 1. Introduction

Certain athletes seem to be gifted by nature and excel at particular sports disciplines, even though their physical fitness and training regime does not differ from other athletes. It is generally believed that the inborn aptitude of each sportsperson is one of the key factors for top achievements in sports, and genetic factors play a crucial role in determining an individual's capability and specific characteristics [1–3]. Due to current developments in DNA sequencing technology, knowledge of the distinct genetic variants conducing to these characteristics in sports achievements has increased, and the field of study 'sports genomics' has evolved [1–3]. Throughout intensive research in the area of sports genomics, over the last 20 years, 185 genetic markers have been determined as correlated with the highest level of athletic performance. Among 185 genetic markers, 100 are stamina-related, 69 are power/potency-related, and 16 are psychogenetic-unique genetic markers [1–3]. Combat disciplines (such as judo, wrestling, and mixed martial arts MMA) are competitive fighting sports characterized by rapid movements with intense cardio workout alternated with low-intensity stamina exercises [4]. Combat sports rely on a variety of techniques and combine power/energy and endurance performance [4]. Furthermore, martial arts demand proficiency in maintaining constant attention to the opponent's actions along with a deep desire to overpower the opponent [4]. It indicates that intricate physical and psychological phenotypes are linked with combat sports. m-Opioid receptor stimulation promotes a reward based on social relations and other different experiences, as well as the abuse liability of exogenous opiate narcotics [5–7]. Agonists with high m-opioid receptor affinity enhance visual attention to faces in humans and improve cooperative play behavior in juvenile rodents as well as marmosets, whereas pharmacological blockade of opioid receptors results in deficits in these behaviors [8–10]. m-Opioid receptor availability in the human nucleus accumbens is adjusted by a range of social situations [11, 12], and intra-accumbal manipulations of m-opioid receptor activation can bidirectionally modify social behavior in rodents [13–15]. These results are concordant with a general function of m-opioid receptor activation within the nucleus accumbens in motivated behavior [16–18].

Disruption of m-opioid receptor signaling may result in deficits in social interaction and other motivated behaviors which are characteristic features of neuropsychiatric disorders [19–23].

The behavior alteration caused by the dopamine and norepinephrine neurotransmitter release differs from the under-activation in the dorsolateral prefrontal cortex and deregulation of various pathways involved in the attention and impulse control processes [24, 25]. Cloninger's study on personalities [26] regarding four dimensions of human behavior (harm avoidance, reward dependence, novelty seeking, and perseverance) greatly contributed to assessing the personality structures of extreme sports athletes.

In sports research, genetic studies linked to the traits of the temperament, in addition to medical examinations and other physiological and biochemical tests, would enrich the scope of possibilities and successes that a competitor can accomplish. This could be beneficial for the protection of both mental and physical health. The aim of the study is to determine the association between the *OPRM1* rs1799971 gene polymorphism and traits determined using the Temperament and Character Inventory (TCI-R) scores and sports subjects.

## 2. Material and methods

### *2.1. Materials*

The study group comprised 391 male volunteers. Out of these, 222 sports subjects no prior history of substance dependency or psychosis (mean age = 26.23, SD = 8.18; F = 27%, M = 73%, Table 1) and 186 were non-addicted alcohol, drugs and not practicing competitive sports (mean age = 23.98, SD = 6.16; F = 40%, M = 60%). The study was completely

anonymized, in compliance with the principles of personal data protection. Athletes were recruited as people involved in sports at a professional level. The control group was selected according to age and gender. All sports subjects and controls were European to reduce the possibility of racial bias and overcome any potential problems resulting from population stratification The Bioethics Committee of the Pomeranian Medical University in Szczecin (KB-0012/106/16) had approved the study. All participants submitted their written consent to partake in the study, and the studies were conducted in the Independent Health Promotion Laboratory. The control subjects control subjects were recruited and were subsequently examined by a psychiatrist.

The associations between personality traits and polymorphisms in the *OPRM1* rs1799971 gene were investigated in a group of sports subjects and controls subjects.

*2.2. Measures*

The MINI-International Neuropsychiatric Interview is a structured diagnostic interview designed to evaluate the diagnoses of psychiatric patients according to the DSM-IV and ICD-10 criteria. This tool was used to exclude from further research proceedings people with mental disorders and problems with addiction to psychoactive substances.

*2.3. Psychological tests*

Temperament and Character Inventory-Revised (TCI-R) is a self-perception survey designed to establish personality traits with the usage of 240 items based on Cloninger's multidimensional model and structured into seven factors [four for temperament (novelty seeking, harm avoidance, reward dependence, and persistence), and three for character (self-directedness, cooperation, and self-transcendence)]. Adequate adaptations were made to obtain the Polish-language psychometrical research instrument [26, 27].

*2.4. Genotyping*

The genomic DNA was isolated from venous blood by using standard procedures. Genotyping was carried out with the real-time PCR method. A LightCycler® 480 II system (Roche Diagnostic, Basel, Switzerland) was used to perform fluorescence resonance energy in the genotype data. PCR was performed with 50 ng of DNA from each sample in a final volume of 20 μl containing 2 μl of reaction mixture, 0.5 mM of each primer, 0.2 mM of each hybridization probe, and 2 mM MgCl2, according to the manufacturer's instructions. After amplification, a melting curve was generated. The fluorescence signal was plotted against temperature to obtain melting curves for each sample. The fluorescence signal was plotted as a function of temperature to provide melting curves for each sample. *OPRM1* rs1799971 gene peaks are read (1800498), 56.64 ° C for the C allele and 62.85 ° C for the (-) allele.

*2.5. Statistical analysis*

A concordance between the genotype frequency distribution and Psychological Tests Temperament and Character Inventory-Revised (TCI-R) was established. Hardy-Weinberg equilibrium (HWE) was tested using the HWE software (https://wpcalc.com/en/equilibrium-hardy-weinberg/ (05 April 2023). The relations between *OPRM1 rs1799971* variants: Sports Subjects and control subjects and the TCI-R were analyzed using a multivariate analysis of factor effects ANOVA [TCI-R scale × genetic feature × control and Sports Subjects × (genetic feature × control and Sports Subjects)]. The condition of homogeneity of variance was fulfilled (Levene test $p > 0.05$). The analyzed variables were not distributed normally. The TCI-R was applied and compared using the U Mann–Whitney test. *OPRM1 rs1799971* genotype frequencies between healthy control subjects and Sports Subjects were tested using the chi-square test. All computations were performed using STATISTICA 13 (Tibco Software Inc, Palo Alto, CA, USA) for Windows (Microsoft Corporation, Redmond, WA, USA).

**Table 1.** The percentages of surveyed athletes practicing specific sports

| | n | % |
|---|---|---|
| box | 32 | 14.41% |
| judo | 35 | 15.77% |
| MMA | 63 | 28.38% |
| kickboxing | 11 | 4.95% |
| karate | 9 | 4.05% |
| ice-hockey | 24 | 10.81% |
| triathlon | 1 | 0.45% |
| basketball | 2 | 0.90% |
| handball | 4 | 1.80% |
| volleyball | 2 | 0.90% |
| swimming | 4 | 1.80% |
| skiing | 2 | 0.90% |
| jujitsu | 7 | 3.15% |
| gym workouts | 10 | 4.50% |
| football | 16 | 7.21% |

## 3. Results

These frequency distributions accorded with the HWE both in the sports subjects and the control subjects are presented in Table 2.

**Table 2.** Hardy-Weinberg's law for sports subjects and control subjects.

| Hardy-Weinberg equilibrium calculator including analysis for ascertainment bias | | Observed (Expected) | allele freq | $\chi^2$ ($p$ value) |
|---|---|---|---|---|
| *OPRM1* rs1799971 | | | | |
| Sports Subjects n = 222 | A/A | 160 (156.7) | p (A)= 0.84 q (G)= 0.16 | 2.756 (0.097) |
| | A/G | 53 (59.6) | | |
| | G/G | 9 (5.7) | | |
| Control N = 186 | A/A | 159 (157.2) | p (A)= 0.92 q (G)= 0.08 | 3.135 (0.077) |
| | A/G | 24 (27.6) | | |
| | G/G | 3 (1.2) | | |

$p$–statistical significance $\chi^2$ test.

Statistically significant differences were found in the frequency of *OPRM1* rs1799971 genotypes in the tested sports subjects compared to the control group. *OPRM1* rs1799971 (A / A 0.72 vs A / A 0.85; G / G 0.04 vs G / G 0.02; A / G 0.24 vs A / G 0.13, $\chi^2 = 10.833$, $p < 0.0044$). Similarly, statistically significant differences in the frequency of *OPRM1* rs1799971 gene alleles were found the *OPRM1* rs1799971 between sports subjects and the control group (A 0.84 vs. A 0.92; G 0.16 vs. G 0.08, $\chi^2 = 12.710$, $p = 0.0004$) (Table 3).

The means and standard deviations for all the TCI-R results for the sports subjects and control subjects are presented in Table 4.

The test sports subjects compared to the control group obtained higher scores in the assessment of the Temperament and Character Inventory Self-directedness scale (27.13 vs. 24.10; Z = 6.259; $p < 0.0001$) and the Temperament and Character Inventory Cooperation scale (21.17 vs. 20.19; Z = 1.984; $p = 0.0472$).

The results of the factorial ANOVA of the Temperament and Character Inventory (TCI-R) scales are summarized in Table 5.

**Table 3.** Frequency of genotypes of the *OPRM1 rs1799971*gene polymorphisms in the sports subjects and control subjects

| | *OPRM1 rs1799971* | | | | |
|---|---|---|---|---|---|
| | Genotypes | | | Alleles | |
| | A/A n(%) | A/G n(%) | G/G n(%) | A n(%) | G n(%) |
| Sports Subjects n = 222 | 160 (72.07%) | 53 (23.87%) | 9 (4.05%) | 373 (83.63%) | 73 (16.37%) |
| Control n = 186 | 159 (85.48%) | 24 (12.90%) | 3 (1.61%) | 342 (91.93%) | 30 (8.06%) |
| $\chi^2$ (p value) | | 10.833 (0.0044)* | | 12.710 (0.0004)* | |

*n*–number of subjects. *–significant statistical differences.

**Table 4.** Tests Temperament and Character Inventory (TCI-R) scores between controls and sports subjects

| TCI-R | Sports Subjects (n = 222) | Control (n = 186) | Mann–Whitney U-test Z | (p-Value) |
|---|---|---|---|---|
| Novelty seeking /scale | 20.36±4.69 | 20.09±4.76 | 0.712 | 0.4763 |
| Harm avoidance /scale | 10.02±4.55 | 10.59±4.90 | -1.213 | 0.2250 |
| Reward dependance /scale | 10.06±2.97 | 10.33±3.00 | -0.529 | 0.5971 |
| Self-directedness /scale | 27.13±4.17 | 24.10±4.89 | 6.259 | <0.0001* |
| Cooperation/ scale | 21.17±4.26 | 20.19±4.82 | 1.984 | 0.0472* |
| Self-transcendence /scale | 6.87±3.59 | 7.13±3.51 | -0.7603 | 0.4471 |

*p,* statistical significance with Mann–Whitney U-test; *n,* number of subjects; M ± SD, mean ± standard deviation; * statistically significant differences.

*Self-directedness scale*

There was a statistically significant effect of *OPRM1* rs1799971 genotype interaction and sports subjects or control group on the Self-directedness scale ($F_{2, 402} = 5.47$, $p = 0.0045$; $\eta^2 = 0.026$; Figure 1). The power observed for this factor was 85%, and approximately 3% was explained by the polymorphism rs1799971 in sports subjects or lack thereof on the Self-directedness scale score variance. Table 6 shows the results of the post hoc test. Sports subjects with A/A genotypes have significantly higher Self-directedness scale scores compared to controls with A/A and A/G genotypes. Sport subjects with the A/G genotype also had significantly higher Self-directedness scale scores compared to controls with the A/A and A/G genotype. Sports subjects with A/A and A/G genotypes have significantly lower Self-directedness scale scores compared to sports subjects with G/G genotypes. Sports subjects with G/G genotypes have significantly lower Self-directedness scale scores compared to controls subjects with G/G genotypes. Controls subjects with A/G genotypes have significantly lower Self-directedness scale scores compared to controls subjects with G/G genotypes.

**Table 5.** Differences in *OPRM1* rs1799971 and TCI-R Inventory between healthy Control subjects and Sports Subjects

| TCI-R | Group | *OPRM1* rs1799971 | | | ANOVA | | | |
|---|---|---|---|---|---|---|---|---|
| | | A/A n=319 M±SD | A/G n=77 M±SD | G/G n=12 M±SD | factor | F (p value) | $\eta^2$ | Power (alfa=0,05) |
| Novelty seeking scale | Sports Subjects (SpS); n= 222 | 4.76±0.38 | 19.89±4.07 | 20.22±6.83 | intercept | $F_{1,402} = 1206.52$ ($p < 0.0001$)* | 0.750 | 1.000 |
| | | | | | SpS /control | $F_{1,402} = 0.95$ ($p = 0.3867$) | 0.005 | 0.215 |
| | Control; n = 186 | 20.23±4.77 | 19.37±4.77 | 18.00±4.58 | rs1799971 | $F_{2,402} = 0.79$ ($p = 0.3746$) | 0.002 | 0.144 |
| | | | | | SpS /control x rs1799971 | $F_{2,402} = 0.19$ ($p = 0.8266$) | 0.001 | 0.080 |
| Harm avoidance scale | Sports Subjects (SpS); n= 222 | 10.00±4.73 | 9.91±4.14 | 11.00±3.84 | intercept | $F_{1,402} = 382.49$ ($p < 0.0001$)* | 0.488 | 1.000 |
| | | | | | SpS /control | $F_{1,402} = 1.09$ ($p = 0.3384$) | 0.005 | 0.241 |
| | Control; n = 186 | 10.41±4.98 | 11.42±4.25 | 13.67±4.62 | rs1799971 | $F_{2,402} = 1.83$ ($p = 0.1775$) | 0.005 | 0.271 |
| | | | | | SpS /control x rs1799971 | $F_{2,402} = 0.58$ ($p = 0.5579$) | 0.003 | 0.147 |
| Reward dependance scale | Sports Subjects (SpS); n= 222 | 10.29±3.07 | 9.58±2.55 | 8.89±3.02 | intercept | $F_{1,402} = 723.57$ ($p < 0.0001$)* | 0.643 | 1.000 |
| | | | | | SpS /control | $F_{1,402} = 1.94$ ($p = 0.1453$) | 0.010 | 0.401 |
| | Control; n = 186 | 10.36±3.03 | 10.46±2.84 | 8.00±2.65 | rs1799971 | $F_{2,402} = 0.001$ ($p = 0.9793$) | 0.00001 | 0.050 |
| | | | | | SpS /control x rs1799971 | $F_{2,402} = 0.65$ ($p = 0.5240$) | 0.003 | 0.158 |
| Self-directedness scale | Sports Subjects (SpS); n= 222 | 27.52±4.12 | 26.77±4.09 | 22.22±1.39 | intercept | $F_{1,402} = 2279.23$ ($p < 0.0001$)* | 0.850 | 1.000 |
| | | | | | SpS /control | $F_{1,402} = 1.25$ ($p = 0.2879$) | 0.006 | 0.272 |
| | Control; n = 186 | 24.18±4.92 | 23.04±4.68 | 28.67±1.53 | rs1799971 | $F_{2,402} = 0.04$ ($p = 0.8452$) | 0.0001 | 0.054 |
| | | | | | SpS /control x rs1799971 | $F_{2,402} = 5.47$ ($p = 0.0045$)* | 0.026 | 0.848 |
| Cooperation scale | Sports Subjects (SpS); n= 222 | 21.39±4.27 | 20.77±4.34 | 19.56±3.09 | intercept | $F_{1,402} = 1350.99$ ($p < 0.0001$)* | 0.771 | 1.000 |
| | | | | | SpS /control | $F_{1,402} = 1.44$ ($p = 0.2372$) | 0.007 | 0.309 |
| | Control; n = 186 | 20.32±4.94 | 19.58±4.09 | 18.00±4.00 | rs1799971 | $F_{2,402} = 1.38$ ($p = 0.2414$) | 0.003 | 0.216 |
| | | | | | SpS /control x rs1799971 | $F_{2,402} = 0.01$ ($p = 0.9840$) | 0.0001 | 0.052 |
| Self-transcendence scale | Sports Subjects (SpS); n= 222 | 7.19±3.67 | 6.19±3.39 | 5.22±2.73 | intercept | $F_{1,402} = 192.02$ ($p < 0.0001$)* | 0.323 | 1.000 |
| | | | | | SpS /control | $F_{1,402} = 6.84$ ($p = 0.0012$)* | 0.033 | 0.920 |
| | Control; n = 186 | 7.42±3.52 | 5.71±3.07 | 3.33±0.58 | rs1799971 | $F_{2,402} = 0.72$ ($p = 0.3964$) | 0.002 | 0.136 |
| | | | | | SpS /control x rs1799971 | $F_{2,402} = 0.62$ ($p = 0.5362$) | 0.003 | 0.154 |

*–significant result; SpS – Sports subjects; M±SD – mean ± standard deviation.

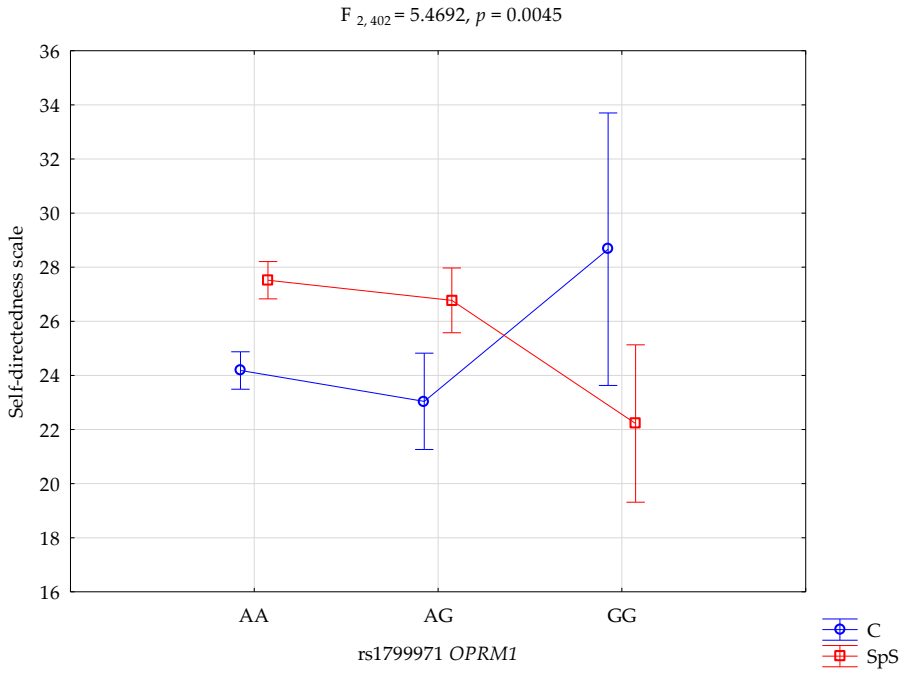


**Figure 1.** Interaction between the Sports Subjects (SpS) / Control (C) and *OPRM1 rs1799971* and Self-directedness scale.

**Table 6.** Post hoc test (Least Significant Difference) analysis of interactions between the Sports subjects/Control and *rs1799971* and Self-directedness scale.

| rs1799971 and Self-directedness scale | | | | | | |
|---|---|---|---|---|---|---|
| | {1} | {2} | {3} | {4} | {5} | {6} |
| | M=27.51 | M=24.18 | M=26.77 | M=23.04 | M=22.22 | M=28.67 |
| Sports Subjects A/A {1} | | 0.0000* | 0.2899 | 0.0000* | 0.0005* | 0.6573 |
| Control A/A {2} | | | 0.0003* | 0.2411 | 0.1981 | 0.0837 |
| Sports Subjects A/G {3} | | | | 0.0007* | 0.0047* | 0.4726 |
| Control A/G {4} | | | | | 0.6369 | 0.0391* |
| Sports Subjects G/G {5} | | | | | | 0.0300* |
| Control G/G {6} | | | | | | |

* – significant statistical differences, M – mean.

## 4. Discussion

The objective of the psychogenetics of sports is the fact that a polymorphism of the specific gene may influence cognitive traits (e.g. memory, way of thinking, reaction time, concentration) and character traits (e.g. aggression, motivation, temperament) of a sports-person. The understanding of how to seek polymorphisms of candidate genes most effectively, which may be reflected in the psychology of elite sports athletes, requires the knowledge of the central and peripheral nervous system molecular mechanisms. Genetic markers which facilitate the development of such personality traits as stress resilience, concentration, reaction time or adaptability are intrinsically connected in one way or another with the neurotransmitter system. Various stimulating and motivating behaviors are particularly linked to the serotoninergic, dopaminergic or opioid systems.

In the present study, we noted statistical significance. Polymorphic variants of selected genotypes were associated with self-direction - A/A genotypes in the study group. Higher values were observed compared to the control group ($p$ = 0.045, Tables 3, 5, 6). Similarly, the A/G genotype occurred statistically significantly more frequently in the study group com-pared to the control group. The G/G genetic variant was less common in the study group compared to the controls.

The correlation between athletes' personalities and their success has been studied for many years. Beckmann and Kazen [28] observed that controlled type sports athletes whose demands connected with energy regulation were high (long-distance runners and rowers) were predisposed to suffering from failure-related state orientation or the shortage of motivation. Other studies found that people with higher novelty-seeking easily lose determination in the situation that does not meet their needs [29,30]. Morgan [31] observed that male distance runners declared lower stress, depression, anger, and tiredness in comparison to an average person. Egloff and Gruhn [32] proposed that in the case of endurance athletes, outgoingness and sociability are the features that greatly influence the choice of sport. Extraversion is characterized by sociability, controlled impulsiveness, and optimism [33]. Bäckmand [34] argued that endurance sport athletes had lower neuroticism scores than other sports athletes.

The μ-opioid receptor is a crucial receptor for endogenous and exogenous opioids analgesic substances, such as β-endorphin, enkephalin and morphine; thus, it is of high importance in the physiological and psychological response to stress, trauma and pain [35]. The A118G (A>G functional substitution at locus 118; rs1799971) polymorphism is one of the most frequently investigated single-nucleotide polymorphism (SNPs) in the OPRM1 gene. The variant affects a presumed glycosylation site and the protein stability of the μ-opioid receptor, and it also lowers receptor expression and receptor signaling efficacy [36, 37]. It has been demonstrated that the rs1799971 polymorphism is involved in the need for analgesia in chronic pain, and its significance in both pain sensation and pain management has been shown [38–40].

The studies on polymorphisms in the OPRM1 concerning pain have been conducted for many years and have been widely described. The behavior was linked to OPRIM genotypes back in 2018. The model of neurotransmission in the opioid system was then linked to personality traits. A similar model of connections in the animal model was created - as the one presented in our study. However, we have attempted to combine opioid receptor with personality traits. Interestingly, such findings have been scarce. The one worth noticing was the study on animals where researchers combined OPRM1 and other genotypic variants with personality traits [41]. Inoue-Murayama et al. studied personality, subjective well-being, and hair cortisol level, in common marmosets Callithrix jacchus, a small, cooperatively breeding New World monkey, by examining their associations with one another and genotypes. Personality and arbitrary well-being were evaluated by keeper ratings on two questionnaires; hair samples were collected to test cortisol level, and buccal swabs were used to assess AVPR1a, OPRM1 and DAT genotypes. Three personality domains – Dominance, Sociability, and Neuroticism – were identified. Sociability and Neuroticism were connected to higher and lower arbitrary well-being, correspondingly. Sociability was also linked with higher hair cortisol levels. The personality domains and hair cortisol levels were hereditary and affiliated with genotypes: the short form of AVPR1a was affiliated with lower Neuroticism, and the AA genotype of the A111T SNP of OPRM1 was related to lower Dominance, lower Neuroticism, and higher hair cortisol level [41]. The study by Inoue-Murayama et al. demonstrates the validity of the model linking polymorphisms in genes related to the opioid system to personality-related behaviors.

## 5. Conclusions

The study reveals the validity of analyzing connections between personality traits and selected gene polymorphisms in athletes, a relatively new field. The presence of the OPRM1 rs1799971 AA genotype is associated with higher self-management scores, indicating genetic predispositions in the study group for better results in sports. Despite limitations, such as limited analysis of polymorphic variants, the findings already demonstrate significant associations the OPRM1 rs1799971 AA genotype and Self-directedness scale in the Sports Subjects. Further research with larger participant groups and expanded gene analysis is needed to explore these relationships more comprehensively.

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**Author Contributions:** Study Design, RR and AG; Data Collection, RR, KC, JC, and AG; Statistical Analysis, RR, AB, KC, KP, and LZ; Data Interpretation, RR, KC, and AG; Manuscript Preparation, RR, AB, KC, JC, KP, ML, LZ, PG, MB, and AG; Literature Search, RR, AB, JC, ML, PG, MB, and AG; Funding Acquisition, RR and AG. All authors have read and agreed to the published version of the manuscript.

**Funding:** The research obtained no external funding.

**Institutional Review Board Statement:** The Bioethics Committee of the Pomeranian Medical University in Szczecin (KB-0012/106/16) had approved the study.

**Informed Consent Statement:** All participants submitted their written consent to partake in the study, and the studies were conducted in the Independent Health Promotion Laboratory.

**Data Availability Statement:** Data available from the corresponding author on request.

**Conflicts of Interest:** The authors declare no conflict of interest.