Genetic basis of elite combat sports athletes: a systematic review

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ABSTRACT: Each athlete’s innate talent is widely recognized as one of the important contributors to achievement in athletic performance, and genetic factors determine a significant portion of talent or traits. Advances in DNA sequencing technology allow us to discover specific genetic variants contributing to these traits in sports performance. The objective of this systematic review is to identify genes that may play a significant role in the performance of elite-level combat sports athletes. Through the review of 18 full-text articles, a total of 109 different polymorphisms were investigated in 14,313 participants (2,786 combat sports athletes, 8,969 non-athlete controls, 2,558 other sports athletes). Thirteen polymorphisms showed a significant difference between elite combat athletes and the control group, and consist of 8 (PPARA rs4253778, ACTN3 rs1815739, ACE rs4646994, CKM rs8111989, MCT1 rs1049434, FTO rs9393609, GABP1 rs7181866 and rs8031031) oriented to athletic performance and 5 (COMT rs4680, FEV rs860573, SLC6A2 rs2242446, HTR1B rs11568817, ADRA2A rs521674) focused on psychological traits including emotional and mental traits in combat sports athletes. In addition, a recent whole genome sequencing study identified 4 polymorphisms (KIF27 rs10125715, APC rs518013, TMEM229A rs7783359, LRRN3 rs80054135) associated with reaction time in wrestlers. However, it is not clearly identified which genes are linked explicitly with elite combat sports athletes and how they affect the elite athlete’s status or performance in combat sports. Hence, a greater number of candidate genes should be included in future studies to practically utilize the genetic information.

INTRODUCTION

Some individuals are naturally talented and show excellent performance in specific sports, even with similar physical condition and training to others. It is widely recognized that the innate talent of each athlete is one of the significant contributors to success in sports, and a significant portion of an individual’s talent or traits is determined by genetic factors [1–3]. With recent advances in DNA sequencing technology, understanding the specific genetic variants contributing to these traits in sports performance has grown, and the research field ‘sports genomics’ has developed [1–3]. Through active research in the field of sports genomics, 185 genetic markers have been identified to be linked with elite athlete status over the past 20 years. Of the 185 genetic markers, 100 were endurance-related, 69 were power/strength-related, and 16 were psychogenetic-specific genetic markers [1–3].

Combat sports, including judo, wrestling, and mixed martial arts (MMA), are competitive contact sports characterized by explosive movement with high-intensity and endurance activities with low intensity [4]. Combat sports require various techniques and mixed power or strength and endurance performance [4]. In addition, combat sports require agility in shifting attention to different stimulation from the opponent as well as a strong desire to subdue the opponent [4]. It suggests that complex physical and psychological phenotypes are associated with combat sports.

This objective of this study is to systematically review previous studies identifying genes that may play a significant role in the performance of elite-level combat sports athletes, investigate genotype-phenotype relationships in combat sports, and suggest insight into the usefulness of genetic testing in identifying athletes’ traits.

MATERIALS AND METHODS

Search strategy

A published literature search that investigated the association between genes and combat sports was conducted from April 2010 to January
A literature search was performed on systematic databases for publications indexed in PubMed and Google Scholar using combinations of the following search items: “genes” OR “genetic” AND “combat sports” OR “judo” OR “martial arts” OR “Taekwondo” OR “wrestling.” Furthermore, additional search was conducted using other items: “polymorphism” OR “genotype” AND “wrestlers, and “polymorphism” OR “genotype” AND “combat sports”.

**Study selection**

All publications retrieved were screened by title, and any duplicates or those irrelevant to the research topic were excluded. The papers written in a language other than English were removed. Abstracts of the remaining studies were screened, and 38 studies were selected for full-text assessment with predetermined inclusion and exclusion criteria described below.

**Inclusion and exclusion criteria**

This review included case-control, cohort, and genome-wide associated studies. The studies were required to provide data on the genotypes associated with elite combat sports athlete performance and/or traits. Those studies identified as ‘elite’ were based on participants having been international competitors and/or national representatives in combat sports. There were no restrictions applied regarding the gender or ethnicity of the participants. Studies were excluded if they were review articles, congress abstracts, editorials, or other non-original articles. Finally, 18 studies were included in the qualitative synthesis. The study selection process is illustrated in Figure 1.

Studies were assessed for inclusion by two independent reviewers, with disagreements resolved by discussion. The final decision for inclusion and exclusion was made from the full text.

**Data extraction and quality assessment**

For all selected studies, the following data were extracted: (1) first author name; (2) publication date; (3) participant characteristics; (4) study design; (5) genetic markers were analysed. Their outcomes were extracted for the narrative review.

**RESULTS**

**Summary of studies reviewed**

The search strategy identified a total of 61 studies, of which, following exclusions, 18 full-text articles were reviewed.

The characteristics of the 18 studies are summarized in Table 1. A total of 109 different polymorphisms were investigated in 14,313 participants, of whom 2,786 were combat sports athletes, and 8,969 were non-athlete controls or 2,558 other sports athletes. The research focus of the 18 studies can be divided into three groups: athletic performance (10) [6–16], pain perception (1) [17], and psychological traits including emotional or mental trait (6) [18–23] in combat sports.
| References               | Participants                                      | Study design | Genes and SNPs | Results                                                                                                                                 |
|-------------------------|---------------------------------------------------|--------------|----------------|-----------------------------------------------------------------------------------------------------------------------------------------|
| Cieszczyk et al. 2011.  | Polish combat athletes (n = 60) and sedentary     | Case-        | PPARA rs4253778 | Higher frequency of the PPARA intron 7 G allele and GG genotype in a group of elite Polish combat athletes.                          |
|                         | controls (n = 181)                                 | Control      |                |                                                                                                                                         |
| Kikuchi et al. 2012.    | Japanese elite wrestlers (n = 135) and college    | Case-        | ACTN3 R577X    | The combination of the ACTN3 R allele + ACE DD genotype is associated with the athletic status of elite Japanese wrestlers.        |
|                         | students (n = 333)                                 | Control      | (rs1815739)    | (odds ratio of ACTN3 R577X R allele + ACE DD genotype being international or national was 3.85 or 1.37)                         |
|                         |                                                    |              | ACE I/D (rs4646994) |                                                                                                                                         |
| Rodriguez-Romo et al.   | Spanish Judo athletes (n = 108) and nonathletic   | Case-        | ACTN3 R577X    | No between-groups difference in allele                                                                                                |
|                         | men (n = 343)                                      | Control      |                |                                                                                                                                         |
| Kikuchi et al. 2013.    | Japanese wrestlers (n = 135) and healthy controls | Case-        | ACTN3 R577X    | Lower frequency of the ACTN3 XX genotype in the elite group and inverse linear correlation between the frequency the ACTN3 XX genotype and level of athletic status |
|                         | (n = 243)                                          | Control      |                |                                                                                                                                         |
| Olga et al. 2013.       | Polish and Russian combat athletes (n = 159) and  | Case-        | CKM rs8111989  | AA genotype of the MCT1 rs1049434 polymorphism is over-represented in wrestlers and associated with lower blood lactate concentration after 30 s anaerobic test and during intermittent sprint tests |
|                         | sedentary individuals (n = 1512)                   | Control      |                |                                                                                                                                         |
| Kikuchi et al. 2017.    | Wrestlers (n = 199) and controls (n = 649)        | Case-        | MCT1 rs1049434 | GG+GA genotype of the IGF2 gene higher in international-level athletes. Inverse correlation between the frequency of the IGF2 AA genotype and level of judo performance. Back muscle strength relative to height and weight higher in subjects with GG+GA genotype |
|                         |                                                    | control      |                |                                                                                                                                         |
| Ribas et al. 2017.      | Brazilian combat athletes (n = 37)                | Cohort       | ACTN3 R577X    | No difference between athletes and controls                                                                                           |
|                         |                                                    |              | ACE I/D        |                                                                                                                                         |
| Itaka et al. 2016.      | Japanese judo athletes (n = 156) and controls     | Case-        | IGF2 Apal rs680| GG+GA genotype of the IGF2 gene higher in international-level athletes. Inverse correlation between the frequency of the IGF2 AA genotype and level of judo performance. Back muscle strength relative to height and weight higher in subjects with GG+GA genotype |
|                         | (n = 167)                                          | Control      | ACTN3 R577X    |                                                                                                                                         |
| Guilherme et al. 2017.  | Brazilian athletes (n = 908; 328 endurance, 415   | Case-        | CNDP1 rs733686 | The power and combat groups showed an inverse genotype distribution for CNDP1 rs2887                                                                 |
|                         | power, 165 combat) and non-athletes (n = 967)     | Control      | rs2887         |                                                                                                                                         |
|                         |                                                    |              | CNDP2 rs12964619, rs6566810, rs3764509, rs734559, rs7577 CNDP1; CNDP2 rs2346061 |                                                                                                                                         |
| Guilherme et al. 2019.  | Brazilian athletes (n = 677; 323 endurance, 192    | Case-        | FTO rs9939609  | No differences were found between Russian combat sports athletes and matched non-athletes; Increased frequency of A-allele carriers in the Brazilian combat group. |
|                         | power, 162 combat) and non-athletes (n = 652)     | Control      |                |                                                                                                                                         |
|                         | Russian athletes (n = 920; 347 endurance, 228     |              |                |                                                                                                                                         |
|                         | power, 254 game, 91 combat) and non-athletes (n   |              |                |                                                                                                                                         |
|                         | = 754)                                            |              |                |                                                                                                                                         |
| Guilherme et al. 2020.  | Brazilian combat athletes (n = 164) and controls   | Case-        | GABPI1 rs7181866 | G-allele in rs7181866 in 4% of the controls compared to 8% of the athletes group or 10.9% of world-class competitors; T-allele in rs8031031 in 4% of the controls compared to 9.5% of the athletes group or 11.9% of world-class competitors |
|                         | (n = 965)                                          | Control      | rs8031031      |                                                                                                                                         |
|                         |                                                    |              | (among 23 polymorphisms in 20 genes) |                                                                                                                                         |
| Leźnicka et al. 2017.   | Combat athletes (n = 214) and healthy controls     | Case-        | COMT rs4680    | No difference between athletes and controls.                                                                                           |
|                         | (n = 395)                                          | Control      | OPRM1 rs1799971|                                                                                                                                         |
TABLE 1. Continue

| Study                     | Sport                          | Number of athletes | Controls          | Genomic data | Genes                                                                 | SNP                  | Findings                                                                 |
|---------------------------|--------------------------------|--------------------|-------------------|--------------|----------------------------------------------------------------------|----------------------|-------------------------------------------------------------------------|
| Tartar et al. 2020. [18]   | Martial arts fighters (n = 21), athletes (n = 21), and control (n = 41) |                    |                   |              |                                                                     | COMT rs4680          | Greater GG genotype frequency in martial arts fighters                  |
| Leźnicka et al. 2018. [19]| Combat athletes (n = 199) and healthy controls (n = 165) |                    |                   |              |                                                                     | COMT rs4680, OPRM1 rs1799971 | homozygous athletes with the G allele (GG) of COMT were characterized by lower sensitivity. |
| Cherepkova et al. 2019. [20]| MMA fighters (n = 107), Criminals (n = 214), controls (n = 425 for DRD4 gene, n = 941 for DAT gene) |                    |                   |              |                                                                     | DRD4 Ex3 VNTR, DAT VNTR | Combination of the DRD4 genotype 4/7 and DAT genotype 10/10 higher in the violent criminals and MMA fighters |
| Michalowska-Sawczyn et al. 2019. [21] | Polish combat athletes (n = 200) and healthy controls (n = 102) |                    |                   |              |                                                                     | DRD4 Ex3 VNTR          | No differences of genotype between cases and controls, but associated with openness and conscientiousness |
| Peplonska et al. 2019. [22] | Elite athletes (n = 621; 212 endurance, 183 power, 226 combat and sedentary controls (n = 672) |                    |                   |              |                                                                     | FEV rs860573, SLC6A2 rs2242446, HTR1B rs11568817, ADRA2A rs521674 | AG genotype in FEV rs860573 was markedly frequent in the control (combat sports 3.18%, p = 0.025). CC genotype in SLC6A2 rs2242446 was underrepresented, C allele in HTR1B rs11568817 and TT+AT genotypes in ADRA2A rs521674 were overrepresented in combat sports |
| Boulygina et al. 2020. [23] | Tatar wrestlers (n = 20), athletes (n = 283; 101 boxing, 82 wrestling, 21 karate, 24 taekwondo, 45 volleyball, 10 table tennis), controls (n = 189) |                    |                   |              |                                                                     | Whole genome sequencing | 4 alleles (KIF27 rs10125715 A, APC rs518013 A, TMEM229A rs7783359 T, LRRN3 rs80054135 T) were found to be independently associated with the best reaction time in wrestlers |

SNP, single nucleotide polymorphism
It is widely accepted that athletes’ mental features, including mental strength, persistence, and the ability to control stress or impulsivity, play an important role in achieving success in sports. When it comes to the genetic polymorphisms related to the emotional or mental traits, Peplonska et al. assessed that genetic variants in genes coding for protein modulate the activity of brain emotion centres in a group of 621 elite athletes [22]. Of ten identified variants, FEV rs860573, coding for a transcription factor exclusively expressed in neurons of the central serotonin system, was the only differentiating variant common to all of the sports groups [22]. The frequency of AG genotype was markedly higher in the control group than among the variant common to all of the sports groups [22]. Of ten identified variants, coding for protein modulate the activity of brain emotion centres in mental traits, Peplonska et al. assessed that genetic variants in genes it comes to the genetic polymorphisms related to the emotional or pulsivity, play an important role in achieving success in sports. When it comes to the genetic polymorphisms related to athletic performance, eight polymorphisms (rs4253778, rs521674, rs11568817, and ADRA2A rs521674), encoding components of the serotonergic and catecholaminergic systems [22]. The CC genotype in SLC6A2 rs2242446 was underrepresented in combat sports (p = 0.0113), while the C allele in HTR1B rs11568817 (p = 0.028) and TT+AT genotypes in ADRA2A rs521674 were overrepresented in combat sports (p = 0.0397) [22].

The COMT gene plays a role in degrading catecholamine. It is associated with genotypes related to dopamine availability in the brain, leading to COMT variants involved in several psychological functions, including cognition, anxiety, and response to stress [24]. Notably, the results for the COMT gene were contrasting. Leżnicka et al. found no significant association (p = 0.286 and p = 0.43) between COMT rs4680 GG genotype and elite combat sports athletes, suggesting that there was no difference between combat athletes and the control group in the aspect of pain perception [17, 19]. On the other hand, Tartar et al. found that the MMA group showed a significantly greater GG (warrior) phenotype frequency than the control group (p = 0.003), suggesting that the warrior genotype may play a participation role in combat sports (Table 2) [18]. However, their study’s sample size was too small, so the interpretation of the results needs to be cautious.

When it comes to the genetic polymorphisms related to athletic performance, eight polymorphisms (PPARA rs4253778, ACTN3 rs1815739, ACE rs4646994, CKM rs8111989, MCT1 rs1049434, FTO rs99939609, GABBP1 rs7181866 and rs8031031) were identified as genetic variants linked to elite combat sports status [6, 7, 9–11, 15, 16].

PPARs regulate the transcription of several genes involved in lipid metabolism, energy utilization and storage, and genes for glucose metabolism, carcinogenesis, and inflammation [25]. PPAR, one of three PPARs, regulates the expression of genes encoding several key muscle enzymes involved in fatty acid oxidation [6, 25]. Cieszczyk et al. compared 60 elite Polish combat athletes to 181 sedentary controls to analyse the distribution of the PPARA gene polymorphism [6]. Their study revealed that frequencies of the PPARA intron 7 G allele (82.50% vs. 70.17%; p = 0.01) and GG genotype (73.33% vs. 54.70%; p = 0.04) were significantly higher in the combat athletes and suggested the PPARA gene as a useful genetic marker in combat athletes, suggesting that the variant might be connected to metabolism regulation and energy production during a competition [6].

Kikuchi et al. published three studies comparing Japanese wrestlers with non-athlete controls [7, 9, 11]. One concerns ACTN3 R577X (rs1815739) and ACE I/D genotype (rs4646994), the second concerns ACTN3 R577X, and the third concerns MCT1 T1470A polymorphism (rs1049434). The ACTN3 gene encodes the protein α-actinin-3, which is almost exclusively expressed in sarcomeres of the fast glycolytic type II fibres responsible for the generation of rapid, forceful contraction activities [26]. ACE is a vital component of the renin-angiotensin-aldosterone system, generating the vasoconstrictor hormone angiotensin II and degrading the vasodilator kinins, and playing a metabolic role during exercise [7, 27].

The second case-control study of 135 Japanese elite wrestlers and 333 college students showed that the ACE I/D genotype distribution and allele frequency of all elite wrestlers significantly differed from those of the controls (p < 0.001) [7]. Furthermore, they demonstrated that the odds ratio of ACTN3 R577X R allele + ACE DD genotype being international or national was 3.85 or 1.37, suggesting that the combination of the ACTN3 R allele + ACE DD genotype was associated with the athletic status of elite Japanese wrestlers [7].

The third case-control study of 199 Japanese elite wrestlers and 649 controls suggested that the AA genotype of the ACTN3 R577X polymorphism was significantly over-represented in wrestlers [11]. MCT is known to mediate lactate transport across the sarcolemma of skeletal muscle, and the MCT1 isoform depresses net muscle lactate release by facilitating intramuscular lactate exchange oxidation [28]. Interestingly, the authors investigated the change of blood lactate concentration during and after anaerobic performance tests and suggested that AA genotype was associated with lower blood lactate concentration after a 30 s anaerobic test and repeated sprint tests [11]. They indicated that the MCT1 T1470A polymorphism was associated with lactate metabolism during multiple bouts of high-intensity intermittent exercise as well as after a single bout of exercise effort [11].

Olga et al. investigated the association between the CKM A/G polymorphism (rs8111989) and combat athlete status, comparing 159 elite combat athletes with 1,512 sedentary controls from Poland and Russia [10]. CKM is an essential enzyme for maintaining energy in the muscle cell during muscle contraction, and CKM A/G polymorphism has been demonstrated to correlate with physical performance [29]. Olga et al. found that the CKM G allele frequency
was significantly higher in athletes than in controls (41.2% vs. 35.6%; \( p = 0.047 \)) and suggested that the CKM gene was associated with combat athlete status [10]. However, the authors did not evaluate how the CKM A/G polymorphism influences the physical performance.

Genome-wide association studies have reported that polymorphisms in the FTO gene are strongly associated with enhanced susceptibility to excess body mass [30, 31], and there was a relationship between a common T > A polymorphism (FTO rs9939609) and body mass–related traits in non-athletes; the A allele was associated with greater weight, waist circumference, and subcutaneous fat mass [31]. Guilherme et al. evaluated the frequency of the FTO rs9939609 polymorphism in elite athletes from two cohorts of a Brazilian cohort (677 athletes and 652 controls) and a Russian cohort (920 athletes and 754 controls) [15]. There were no differences between Russian combat sports athletes and matched controls regarding combat sports, but an increased frequency of A-allele carriers was found in the Brazilian combat group [15]. According to weight categories, A/A genotype was found in 23.7% of combat sports athletes of heavier weight categories compared with only 4.3% of combat sports athletes of lighter weight categories in the combined data of the Brazilian and Russian cohorts, suggesting that heavy-weights have heavier body mass and higher body fat percentage [15].

The same Brazilian research group analysed 23 performance-related polymorphisms in 164 Brazilian combat-sport athletes and 965 non-athletic controls. They found that the GABP\( \beta \)1 gene was associated with athletic status, with the minor G (rs7181866) and T (rs8031031) alleles overrepresented in athletes (\( p \leq 0.003 \)), especially among world-class competitors (\( p \leq 0.0002 \)) [16]. They suggested that deacetylation of GABP\( \beta \)1 involves promoting proper mitochondrial function, and single nucleotide polymorphisms within the GABP\( \beta \)1 gene may contribute to a greater innate predisposition to intermittent efforts in combat sport athletes [16]. Because this study was conducted on one cohort and had a small sample size of combat sport athletes, further research is needed.

### TABLE 2. Allele frequencies of the single nucleotide polymorphism identified by comparison between elite combat sports athletes and controls.

| References                | Candidate allele or genotype | Frequency in elite combat athletes | Frequency in controls | \( P \)-value |
|---------------------------|-----------------------------|----------------------------------|-----------------------|--------------|
| Cieszczyk et al. 2011. [6]| PPPARA rs4253778 G allele   | 82.50%                           | 70.17%                | 0.01*        |
| Kikuchi et al. 2012. [7]  | ACTN3 R577X R allele        | 53%                              | 49%                   | 0.346        |
|                          | ACE DD genotype             | 65%                              | 48%                   | < 0.01*      |
| Rodriguez-Romo et al. 2013. [8]| ACTN3 R577X R allele   | 49.6%                            | 56.4%                 | 0.077        |
| Kikuchi et al. 2013. [9] | ACTN3 R577X XX genotype    | 11%                              | 29%                   | 0.019*       |
| Olga et al. 2013. [10]   | CKM rs8111989 G allele      | 41.2%                            | 35.6%                 | 0.047*       |
| Kikuchi et al. 2017. [11]| MCT1 rs1049434 AA genotype | 53%                              | 45%                   | 0.037*       |
| Itaka et al. 2016. [13]  | IGF2 Apal rs680 G allele   | 87.2%                            | 81.4%                 | 0.16         |
|                          | ACTN3 rs1815739 R allele   | 66.7%                            | 73.7%                 | 0.06         |
| Guilherme et al. 2019. [15]| FTO rs9939609 A allele     | 44.1%                            | 37.2%                 | 0.025*       |
| Guilherme et al. 2020. [16]| GABP\( \beta \)1 rs7181866 G allele | 8%                           | 4%                    | 0.003*       |
|                          | GABP\( \beta \)1 rs8031031 T allele | 9.5%                           | 4%                    | 0.002*       |
| Leźnicka et al. 2017. [17] | COMT rs4680 G allele      | 51.9%                            | 48.1%                 | 0.286        |
|                          | OPRM1 rs1799971 A allele   | 91.1%                            | 91.2%                 | 0.984        |
| Tartar et al. 2020. [18] | COMT rs4680 GG genotype    | 52.4%                            | 19.5%                 | 0.003*       |
| Leźnicka et al. 2018. [19] | COMT rs4680 G allele      | 52.01%                           | 49.09%                | 0.43         |
|                          | OPRM1 rs1799971 A allele   | 91.46%                           | 91.21%                | 0.91         |
| Michalowska-Sawczyn et al. 2019. [21] | DRD4 Ex3 VNTR S allele | 78%                              | 80%                   | 0.413        |
| Peplońska et al. 2019. [22] | FEV rs860573 A allele     | 3.18%                            | 7.44%                 | 0.025*       |
|                          | SLC6A2 rs2242446 C allele | 27.43%                           | 31.34%                | 0.011*       |
|                          | HTR1B rs11568817 C allele | 46.02%                           | 40.13%                | 0.028*       |
|                          | ADRA2A rs521674 T allele  | 25.11%                           | 20.94%                | 0.0397*      |

*\( P \)-value < 0.05
DISCUSSION

This review finally analysed a total of 18 papers and obtained data from 2,786 elite combat sports athletes, including judo, wrestling, and MMA, and 8,969 non-athlete controls or 2,558 other sports athletes to identify polymorphisms and genes contributing to athletic performance or traits to differentiate elite combat sports athletes from controls. There were thirteen identified polymorphisms with a significant difference between elite combat athletes and controls: PPARA rs4253778, ACTN3 R577X (rs1815739), ACE I/D (rs4646994), CCM rs8111989, MCT1 rs1049434, FTO rs9399609, GABP1 rs7181866 and rs8031031, CMOT rs4680, FEV rs860573, SLC6A2 rs2242446, HTR1B rs11568817, and ADRA2A rs521674 [5, 6, 8–10, 14, 16, 20]. The candidate alleles or genotypes were as follows: 1) ten were significantly overrepresented in elite combat sports athletes – PPARA rs4253778 G allele, ACE DD genotype, CCM rs8111989 G allele, MCT1 rs1049434 AA genotype, FTO rs9399609 A allele, GABP1 rs7181866 G allele, GABP1 rs8031031 T allele, CMOT rs4680 GG genotype, HTR1B rs11568817 C allele, ADRA2A rs521674 T allele [6, 7, 10, 11, 15, 16, 18, 22], 2) three were significantly underrepresented in athletes – ACTN3 R577X XX genotype, FEV rs860573 A allele, SLC6A2 rs2242446 C allele [9, 22], 3) four (KIF27 rs10125715 A allele, APC rs518013 A allele, TMEM229A rs7783359 T allele, LRRN3 rs80054135 T allele) were found to be favourable through WGS [23].

First, most studies focused on discovering genetic markers involving the athletic performance of combat sports [5–16]. Research on the genes affecting skeletal muscle structure and function has been mostly actively conducted. Among these genes, ACTN3 would be representative. Two studies by Kikuchi et al. suggested that ACTN3 RR or RX genotypes are strongly correlated with elite combat athletes [7, 9]. A previous animal study also showed that ACTN3-knockout mice, the animal model of α-actinin-3 deficiency, had lower grip strength and lower muscle weights than the wild-type mice [32]. A study on muscle fibre composition in speed skaters suggested that ACTN3 XX genotype carriers exhibited a higher proportion of slow-twitch muscle fibres [33]. Therefore, an individualized training strategy may be needed distinguishing between athletes with ACTN3 RR or RX genotypes and those with ACTN3 XX, completely deficient in α-actinin-3 protein.

Unlike other sports, combat sports are designed to involve competition between similar stature and body mass athletes by categorizing them into a series of weight classes for fair competition. Therefore, it is essential for combat sports athletes to control their weight to be advantageous in the match they want to compete in and meet the eligibility criterion. Many athletes commonly achieve their target weight using various means, including severe food intake restriction and dehydration [34]. Because of combat sports’ characteristics requiring high-intensity muscle power, these athletes are trained to maximize their lean body mass while minimizing fat mass and total body mass. Therefore, when athletes control weight, the proportion of fat-free mass should be well maintained. When considering the reviewed papers’ results, FTO rs939609 polymorphism might play a crucial role in regulating body mass [15]. The MCT1 gene might also involve our body mass, considering the previous study, which suggested that the MCT1 T allele was associated with the percentage of fat-free mass [35]. Therefore, for combat sports athletes, more efficient training methods could be conceived according to the athlete’s polymorphism when determining the weight class of athletes or performing weight control.

Second, a few types of research have focused on genetic polymorphisms (COMT rs4680, FEV rs860573, SLC6A2 rs2242446, HTR1B rs11568817, ADRA2A rs521674) involving our serotoninergic and catecholaminergic pathways [18, 22]. In other words, there is a lack of research evaluating psychogenetic factors contributing to the mental or emotional strength of elite combat sports athletes. Although the genetic factors of the emotional and mental traits have not been investigated enough, the results of previous studies suggest that there might be genetic variants affecting various phenotypic traits related to elite athletic performance. The findings of the present review indicate that various genes influence athletic performance or traits, and that more genetic markers may be discovered in the future.

Studies included in this review article have identified several types of genetic markers in combat sports athletes. The greatest limitations of these types of studies are their small sample sizes and a lack of replicated studies that can support those studies’ reliability. Therefore, first of all, it is necessary to verify whether the results of these studies are false-positive. In addition, it should be carefully considered that there may be a bias since these studies were mainly conducted on the population of some countries, such as Russian, Polish, and Japanese, and especially on the male population. To reduce bias by gender and race, future research is needed for more diverse population groups.

To date, most of the studies assessing the genetic components in combat sports have focused on athletic or physical performance [6–16]; future research should focus on identifying genetic markers associated with other sport phenotypes such as stress tolerance, mental strength, and temperament.

Most of the reviewed studies focused on studying the effect of single genes [6, 8, 9–11, 15, 18, 21]. However, since elite athletic status is not determined by any one gene, but rather is a polygenic trait involving highly complex and multiple genes [1], one should avoid prematurely predicting or determining an athlete’s potential or talent with specific genes showing a significant association. A recent WGS study identified 4 polymorphisms (KIF27 rs10125715, APC rs518013, TMEM229A rs7783359, LRRN3 rs80054135) associated with reaction time in wrestlers [23]. It may give us a new direction which could detect a wide range of candidate alleles related to athletic success by using WGS.

Although inherited genetic components may significantly influence an athlete’s character or potential, it should not be overlooked that environmental factors are also important determinants of athlete success. Because various factors are involved in athletic performance,
it would be desirable to utilize genetic information to develop personalized training methods that improve athletes’ talent or traits and prevent potential injury, rather than identifying only elite athletes’ talent.

**CONCLUSIONS**

This is, to our knowledge, the first systemic review investigating the association between genetic markers and elite athletes’ performance in combat sports. This review identified that thirteen potential polymorphisms might influence the athletic performance or traits in elite combat sports. They consist of genetic markers involved in mental or emotional traits as well as an athlete’s physical status. The included studies suggested that candidate polymorphisms had a significant association. However, it is still unclear which genes are specifically linked with elite combat sports athletes and how they affect elite athletes’ status or performance in combat sports. Hence, a greater number of candidate genes should be included in future studies to practically utilize the genetic information.

**Disclosure statement**

No potential conflict of interest was reported by the authors.

**Conflict of Interest**

All authors declare having no conflict of interest.

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