

Effects of genetic variability on running performance in professional runners

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ABSTRACT

Introduction: With the recent advancement in the field of genetics, researchers and general public are interested to know the effects of genetic variability on human body. A variety of studies can be found literature regarding the genetic variabilities on human body, however, there is a scarcity of data regarding systematic review on the topic. This review was conducted in order to systematically review the available literature on the effects of genetic variability on running performance in professional runners.

Material & Methods: A systematic review was conducted according to PRISMA guidelines. The literature search was performed in different databases using the terms genes OR genetic (variation, variability, polymorphism) OR genomics AND running (performance, status, success) OR elite runners OR competitive running. Research articles published in English language from inception of medical literature to August 2019 that reported the effects of genetic variability on running performance were included. Those studies were excluded which reported association of gene mutations with genetic disorders. Reviews, commentaries, letter to editors and conference papers were excluded.

Results: Out of total 8 included studies, 5 were case control and 3 were cohort studies. Six articles showed association between genetic variability and running performance while 2 reported no association between genetic variability and running performance in professional runners. Three studies investigated 'I' and 'D' allele of angiotensin-converting enzyme (ACE) gene, out of which two studies found association between 'D' allele of 'ACE' gene and running performance. Besides ACE, the included studies reported association between running performance and 'C' allele of aquaporin 1, Pro582 C allele of rs11549465 & 'A' allele of rs17099207 of HIF1A gene, bradykinin receptor B2, adrenergic receptor beta 2 & adenosine monophosphate deaminase 1 and Titin gene.

Conclusion: Genes such as 'ACE', 'HIF1A', aquaporin '1' and Titin may be associated with running performance in professional runners, however, there is limited evidence regarding it as only few articles have been published on this topic. Majority of the published articles are case control studies which clearly indicate a demand for conducting high quality research in this area.

Key Words: Athlete, Elite, Genes, Performance, Running, Variation

The authors declared no conflict of interest and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All authors contributed substantially to the planning of review, data collection and write-up of the systematic review.

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INTRODUCTION

With the recent advancement in the field of genetics, researchers and general public are interested to know the effects of genetic variability on human body.¹ In the past two decades, hundreds of genetic variations have been reported which can have effect on human physical performance.² Because physical performance is necessary for athletic activities that's why researchers and sport communities pay much attention to determine the association of genetic factors with athletes' status.³

Just like other athletic activities, running performance predominantly depends on runners' physique and other physiological characteristics which in turn depend on genetic makeup of the athlete. Some genes such as angiotensin-converting enzyme (ACE) gene, are consistently reported in the literature to be associated with physical performance.⁴⁻⁶ The genetic testing enables the sporting community to predict athletic performance on the basis of the genetic makeup of the athlete.¹

Despite the fact that quite a few studies have been conducted to report the association of genetic factors and physical performance,

still, literature regarding the effects of genetic variation on running performance is scarce. Therefore, the current study was designed to systematically review the available literature on the effects of genetic variability on running performance in professional

MATERIALS & METHODS

A systematic review was conducted according to Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) guidelines. Literature search was performed in databases MEDLINE, AMED, EMBASE, HMIC, BNI, PsycInfo, CINAHL (EBSCO), and HEALTH BUSINESS ELITE in September 2019. The literature search was performed using the terms genes OR genetic (variation, variability, polymorphism) OR genomics AND running (performance, status, success) OR elite runners OR competitive running. Search terms were combined using Boolean logic. Truncations were used where appropriate. Systematic reference list scanning was conducted to find out additional articles. Search results were imported into reference manager Endnote X7 in order to remove the duplicates. After

duplicate removal, two reviewers independently screened the titles and abstracts of the studies and divided the articles into 'relevant' and 'irrelevant' categories according to inclusion and exclusion criteria. All discrepancies were resolved by consensus meeting and discussion. Research articles published from inception of medical literature to August 2019 that reported the effects of genetic variability on running performance were included. Only peer-reviewed articles in English language were included. Those studies were excluded which reported association of gene mutations with genetic disorders. Similarly, views, commentaries, letter to editors and conference papers were excluded. From each included study, participants characteristics, genes under investigation and primary findings were extracted.

RESULTS

Initial searches identified 289 research articles. Following removal of the duplicates, 215 studies were left. Of these, 24 were excluded because they were published in languages other than English. Titles and abstracts of the remaining 191 articles were screened, and 183 were excluded because they did not fulfill the eligibility criteria. Finally, 8 studies were included in the current systematic review. Summary of the included studies is presented in table I.

Out of total 8 studies, 5 were case control⁷⁻¹¹ and 3 were cohort studies.¹²⁻¹⁴ Six articles determine association between genetic variability and running performance^{7-10, 12, 13} while 2 reported no significant association between genetic variability and running performance in professional runners.^{11, 14} Three studies investigated 'I' and 'D' allele of angiotensin-converting enzyme (ACE) gene^{7, 10, 14}, out of which two found association between 'D' allele of ACE gene and running performance^{7, 10} while one study reported no association of ACE gene with running performance.¹⁴

The other genes investigated in the included studies were aquaporin 'I' 'C' & 'G' allele, hypoxia-inducible factor 1-alpha (HIF1A) gene, Bradykinin receptor B2, adrenergic receptor beta 2, adenosine monophosphate deaminase 1, alpha-actinin-3, peroxisome proliferator activated receptor alpha, adrenergic receptor alpha 2A rs553668 C&T allele, alpha-actinin-3 and Titin gene.^{8, 9, 11-14} The studies reported association between running performance and 'C' allele of aquaporin 1⁸, Pro582 C allele of rs11549465 & 'A' allele of rs17099207 of HIF1A gene⁹, bradykinin receptor B2, adrenergic receptor beta 2 & adenosine monophosphate deaminase 112 and Titin rs10497520.¹²

Table 1: details of the studies included in the review

Study and participant information	Genes and SNPs under investigation	Genes and SNPs under investigation
Amir et al. conducted a case control study in 2007 in which 79 professional runners, 42 athletes and 247 controls participated.	Insertion (I) allele and deletion (D) allele of angiotensin-converting enzyme gene rs4646994	Deletion (D) allele of angiotensin-converting enzyme (ACE) gene was associated with running performance in professional runners. Moreover, SNP ACE D rs4646994 & ACE DD rs4646994 was significantly of higher percentage in professional runners as compared to controls.
Martinez et al. conducted a case control study in 2009 in which 1177 professional runners participated.	aquaporin 1 rs1049305 C&G allele	The C allele was reported to be associated with running performance in professional runners.
Döring et al. conducted a case control study in 2010 in which 316 professional athletes, out of which 39 were runner participated. There were 304 controls.	Hypoxia-inducible factor 1-alpha gene	The authors reported that Pro582 C allele of rs11549465 and A allele of rs17099207 were related to running performance. These SNPs were significantly of higher percentage in professional runners as compared to controls.
Tobina et al. conducted a case control study in 2010 in which 73 professional runners and 335 controls from general population participated.	Insertion (I) allele and deletion (D) allele of angiotensin-converting enzyme gene rs4646994	They concluded that D allele was responsible for fast running however angiotensin-converting enzyme gene I & D frequency was not too much higher in professional runners.
Tsianos et al. conducted a cohort study in 2010 in which 438 professional runners participated.	Bradykinin receptor B2, adrenergic receptor beta 2, adenosine monophosphate deaminase 1, alpha-actinin-3, peroxisome proliferator activated receptor alpha	Bradykinin receptor B2, adrenergic receptor beta 2 and adenosine monophosphate deaminase 1 were found to be associated with running performance.
Sawczuk et al. conducted a case control study in 2013 in which 123 athletes, out of which 12 were professional athletes participated. There were 228 controls.	adrenergic receptor alpha 2A rs553668 C & T allele	The authors failed to find association between running performance and genes under investigation.
Stebbins et al. conducted a cohort study in 2018 in which 141 professional runners and 137 controls participated.	Titin rs10497520	Titin is reported to be associated with faster running performance due to its effects on anatomy and physiology of muscle fascicle
Papadimitriou et al. conducted a cohort study in 2018 in which 698 professional runners participated.	alpha-actinin-3 R577X, Insertion (I) allele and deletion (D) allele of angiotensin-converting enzyme gene	The authors failed to find association between running performance and genes under investigation.

DISCUSSION

In the modern era of advancement and technology, genetic studies have received robust attention. A lot has been written and published about genomes and a huge amount of literature has been produced in the last two decades.¹⁵ Many mutations have been identified and many genetic disorders can be diagnosed on the basis of gene analysis.¹⁶ Besides disease identification, researchers investigated the effects of different gene sequencing on normal morphology and physiology.¹³ A huge bulk of literature is produced to discuss the effects of genetic variability on human performance. Despite all this, there is not enough evidence to support the argument that genetic variations contribute to running performance in professional runners.¹⁷ Therefore, the current systematic review was carried out to assimilate the available literature regarding the effects of genetic variability on running performance in professional runners.

The results of current study revealed that out of total 8 included studies, 6 studies concluded that different genes and SNP's are associated with running performance^{7-10, 12, 13} while two studies failed to show association between genes under investigation and running performance in professional runners.^{11, 14} Studies in humans and in other animals have revealed that a large number of genes are responsible for physical performance.¹⁸ The development of molecular genetics analyses enable the researcher to identify those specific genes which enhance the physical performance. Many high quality researches in the form of systematic reviews and meta-analysis provide evidence for the assumption that some genes are responsible for better performance in sports.^{19, 20} Because there is lack of high quality evidence regarding association of specific genes and running performance, that is the reason that many investigators are searching to determine whether those genes which enhance the physical performance also increases the running performance in professional runners.¹⁷

ACE gene is the most commonly discussed gene in literature which is supposed to be responsible for better athletic performance.^{1, 21} Results of the current study revealed that two studies supported the argument that it is associated with running performance in professional runners. Though there are some studies which reported that the ACE gene effects on physical performance is debatable,²²⁻²⁴ however, many researchers believe it to be the utmost gene involved in physical performance.^{8-10, 13} Besides ACE, other genes such as aquaporin 1, HIF1A gene and Titin gene are reported to be associated with physical performance.^{1, 3, 5} In accordance with the results of previous studies, the current systematic review also reported that these genes are responsible for better running performance in professional runners.

Despite the fact that current review assimilate published literature regarding the effects of genetic variability on running performance in professional runners, still, it has some limitations. Protocols of the current review were not registered and due to scarcity of literature about the effects of genetic variability on running performance, the current review only included 8 studies. It is recommended that large clinical trials and multi-centered prospective cohort studies should be conducted to truly determine the effects of genetic variability on running performance in professional runners.

CONCLUSION

Genetic variations exist in professional runners and general population. Certain genes such as ACE, HIF1A, aquaporin 1 and Titin genes may be associated with running performance in professional runners, however, there is limited evidence regarding it, as only few articles have been published on this topic. Majority of the published articles are case control studies which clearly indicate for a demand for conducting high quality research in this area.

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