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ASSOCIATING GENETIC POLYMORPHISM AND PHYSICAL FITNESS OF AEROBIC AND STRENGTH CAPABILITY IN CHILDREN AND TEENAGERS: A SYSTEMATIC REVIEW

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Abstract: The evaluation of the genetic profile for predisposition of physical capacities combined with performance tests has been increasingly used in the search for sports talents. However, studies diverge regarding the investigated polymorphisms, characteristics of the subjects, and applied tests. Therefore, understanding how to search for the best variables for investigation can help studies to reduce the gaps in this theme. Through a systematic review to find an association of genetic polymorphisms and the physical performance of children and adolescents. Research on studies published in journals indexed in the PubMed and SciELO. databases was carried out until June 2020. The search strategy used the following descriptors and terms "polymorphism" [Title / Abstract] OR "polymorphisms" [Title / Abstract] AND "performance" [Title / Abstract]. 13 studies were found that showed an association of genes related to aerobic capacity (PPARD, PPARA, PPARGC1A, ECA, ACTN3, CKMM, and NRC4), strength (ECA, ACTN3, CKMM, PPARA, AMPD1, and NRC4), and balance (PPARD) with better results of the tests applied for the respective capacities. The tests most used for these associations were those of shuttle run to assess the capacity of aerobic resistance; and handgrip tests and jumps for strength assessment. The determination of the genetic profile combined with the application of physical performance tests seem to be tools that are associated and can help in the detection of talents. However, to evaluate the tests, it is necessary to adopt a performance score that better stratify the results of excellence.

Keywords: genetics; performance; aerobic resistance; strength; athletic performance.

INTRODUCTION

The physical capacities are indicators that reveal characteristics that potentially uncover an individual's predisposition to playing and succeeding in a sport. According to (1), the evaluations in athletics, such as vertical jump, 20-meter sprint, and endurance time tests, are often used in the process of identifying talents by distinguishing athletes with inclining potential to specific sports. In this context, the results of these tests show the ability level of the athlete and provide information for the planning of the individual work needed to elevate the athlete's ability to a higher level.

The challenge in this battery of tests is to conceive valid and trustworthy test projects for specific sports to delimit the physical capabilities of a young athlete, accelerate his improvement, and provide a predictive value for future performance and success (2). However, it is clear that the precision of those results is not satisfactory, so it is necessary to combine them with gene analysis, said genes are called candidates, to obtain a possible more precise conclusion (2).

On this topic, the authors (3) enumerated and described 69 genetic variants related to physical performance, among them the angiotensin-converting enzyme (ACE I / D) and the production of the α-actin-3 enzyme (ACTN3 R / X) are the most promising since they are the most studied and show a correlation of their genotypes with the resistance-power and force-power capacities, respectively. Therefore, most of the investigations on the subject seek an association between the polymorphisms with physical capacities, though they study adult athletes (4, 5, 6, 7) and only a few young athletes (8, 9, 10). Regarding the latter population, the concern in drawing an effective preparation for maximum and specific physical development is tackled by providing training and/or genetic factors' analysis (2, 11).

Therefore, the anticipation for the associated use of these indicators seems to bring

more effective results for the elite preparation, to perfect and plan the training according to the individual needs, as well as direct the athlete to the sport in which he has the potential to act as an elite athlete. However, as long as we know, there is not a systematic review that surveys the state of the art on the polymorphisms involved in aerobic and strength capacities in children and teenagers.

Thus, this systematic review has as a goal identifying, then, the possible genetic polymorphisms that associate with physical capacities in children and teenagers.

MATERIALS AND METHODS

SEARCH STRATEGY

We searched for papers systematically on PUBMED/Medline (Medical Literature Analysis and Retrieval System Online), Embase, Scorpus and Scielo (Scientific Electronic Library Online) online databases without any restrictions on publication dates before July 2021 The selection of terms and descriptors was based on the key-words available in previous studies. The terms we found in the literature were: "polymorphism" [Title/Abstract] OR "polymorphisms" [Title/Abstract] AND "performance" [Title/Abstract]. The similarity between the key-words, "polymorphism" or "polymorphisms", was necessary due to the previous search render a considerable difference in the number of articles presented when only one of the terms is used. On PUBMED and Embase we added a species (only humans' category) and age filter (children between six and 12 years old and teenagers between 13 and 18 years old). We added words "teens" [Title / Abstract] OR "young" [Title / Abstract] AND "child" [Title / Abstract] OR "preschool child" [Title / Abstract] to the Scopus database. On SiELO, the only filters in the research were the keywords. The research counted on two researchers.

GREY LITERATURE

We searched through original papers and publications in conferences/congresses, books, or book chapters in the clinicaltrials.gov database.

STUDIES SELECTION AND QUALITY ASSESSMENT

The only included original articles were the ones that intended to identify the possible genetic polymorphisms associated with the physical capabilities of strength, aerobic resistance, flexibility, agility, and balance in children and teenagers, independent of physical activity and the applied tests. We discarded any articles based on animal models or adult subjects and reviews. The results were downloaded into the EndNote site to identify and remove duplicates.

To assess the quality of the studies, (12) the scale was used for observational studies. Scores range from 0 to 8 points. A score of 0–3 is considered to be of low quality, a score of 4-6 for moderate quality and a score of 7-8 for high quality. A detailed assessment of trial quality is included in Table 1. Any disagreement between reviewers was resolved by consensus.

RESULTS

Figure 1 displays the flowchart with the phases of our search and selection of included articles. We have identified 2094 articles using the search mechanism from PubMED (n = 853), EMBASE (n = 538), Scorpus (n = 703) and Scientific Electronic Library (SciELO) (n = 47). After the duplicate's exclusion phase, we found 1791 papers but discarded 1752 because they did not comply with the selection criteria set by reading the title and abstract. The selected for complete reading were 39, considering that only 13 were in the final analysis and inclusion. We settled any possible misunderstandings that arose by a consensus between reviewers. Since the studies showed either correlation and association, we did not define any methodological score.

Autores	Are the study methods valid?						Parcial (0 a 6)	What is the interpretation of the results?	What is applicability of the results	Total (0 a 8)
	1	2	3	4	5	6		7	8	
MORAN20 *et al.* (2006)	1	0	1	1	0	1	4	1	1	6
MORAN21 *et al.* 2007	1	0	1	1	0	1	4	1	1	6
Micheli19 *et al.* (2011)	1	0	1	1	1	1	5	1	1	7
Chiu18 *et al.* (2012)	1	0	1	1	1	1	5	1	1	7
Ahmetov27 *et al.* (2013)	1	0	1	1	1	1	4	1	1	7
Orysiak28 *et al.* (2014)	1	0	0	1	1	1	4	1	1	6
Dionísio17 *et al.* (2017)	1	0	0	1	1	1	4	1	1	6
García16 *et al.* (2017)	1	1	1	1	1	1	6	1	1	8
Orysiak46 *et al.* (2018)	1	0	1	1	1	1	5	1	1	7
Zehsaz15 *et al.* (2018)	1	1	1	1	1	1	6	1	1	8
Cao22 *et al.* (2019)	1	0	1	1	1	1	5	1	1	7
Jeremic14 *et al.*, 2019	1	0	1	1	1	1	5	1	1	7
Zehsaz13 *et al.* (2019)	1	1	1	1	1	1	6	1	1	8

Table 1. Analysis of the methodological quality of the included studies

Are the study methods valid?: 1 = Are the study design and sampling method appropriate for the research question?; 2 = Is the sampling frame appropriate?; 3 = Is the sample size adequate?; 4 = Are objective, suitable and standard criteria used for measurement of the health outcome?; 5 = Is the health outcome measured in an unbiased fashion?; 6 = Is the response rate adequate? Are the refusers described? What is the interpretation of the results?: 7 = Are the estimates of prevalence or incidence given with confidence intervals and in detail by subgroup, if appropriate? What is the applicability of the results?: 8 = Are the study subjects and the setting described in detail and similar to those of interest to you?

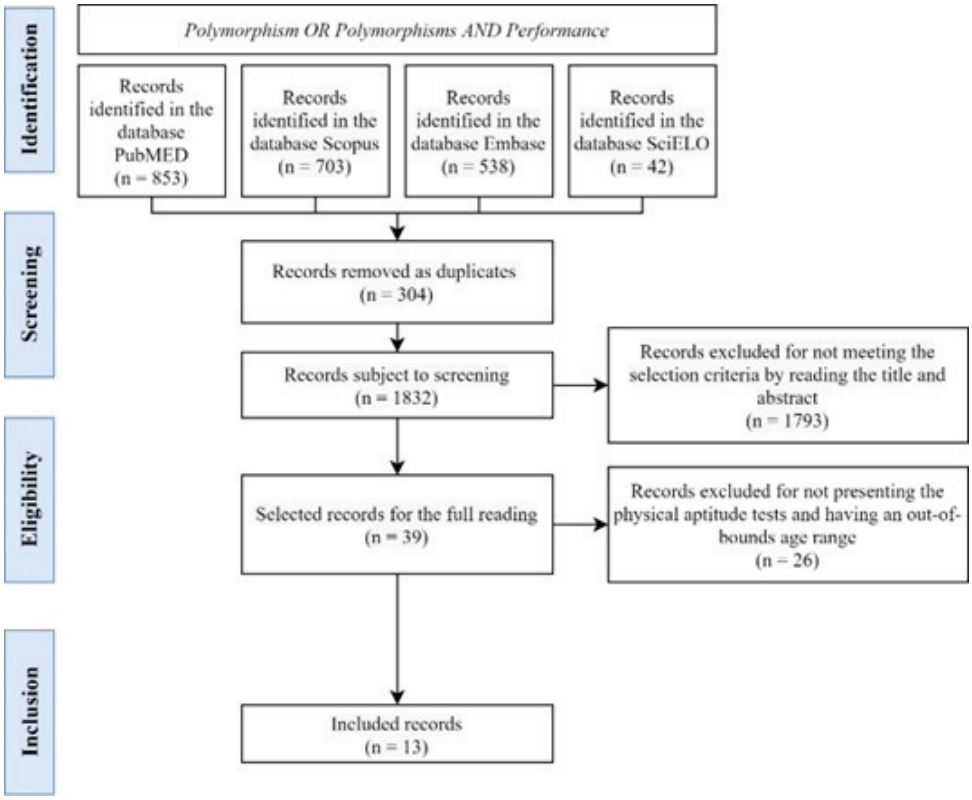

Figure 1. Flowchart of the article selection process. 1: Central Register of Controlled Trials, 2: Scientific Electronic Library

SUBJECT CHARACTERIZATION

In general, we observed a total sample size of 7911 subjects, 4006 boys and 1661 girls, with an age range from 5- to 18-year-olds. The body mass index (BMI) was the body composition evaluation chosen, which is the most common parameter to evaluate nutritional state in children and teenagers. In the studies based on this parameter, the BMI values ranged from 16.1 and 23.3Kg/m^2, which associate with the "below ideal weight" and "normal weight" classification. We were not allowed to separate age groups because some of the reviewed studies aggregated children and teenagers. The sport modalities studied were volleyball, swimming, ice hockey, canoeing, athletics, and soccer distributed in five studies, showing a bias from the eight studies for subjects who had yet to undergo a sports initiation, potentially influencing physical tests.

STUDY CHARACTERIZATION

We found ten genes that took part in the investigation throughout the reviewed studies. The genes of the family of receptors activated by peroxisome proliferators (PPARs): PPAR-alpha rs54253778 (PPARa), PPAR-beta T294C rs2016520 (PPARb), or PPARA and PPARD, respectively, were featured along with ECA I/D (rs1799752) and ACTN3 R/X (rs1815739), which are the most investigated in the literature when studying physical performance. Table 2 summarized the data for the study characterization.

All studies evaluated strength capacities; nine of them, velocity capacities (13, 14, 15, 16, 17, 18, 19, 20, 21); and eight, aerobic resistance capacities (20, 21, 18, 17, 16, 14, 15, 13). On the other side, more than half of the studies neglected other important capacities in sports, such as flexibility (20), agility (14, 20, 21), localized muscle resistance (14, 16, 18, 22), and balance (23), evidencing that future work should opt for evaluating protocols that encompass all cited capabilities. (20, 14) stood out for investigating genetic associations with five of the six attributes above-mentioned. In statistics, to evaluate the interactions between genotypes and the phenotypes, the studies used mainly Pearson's chi-squared test. The unilateral analysis of variance (ANOVA) or Kruskal-Wallis tests were the preferred tool to treat anthropometrics variables and the analysis of covariance (ANCOVA) to observe the iterations between physical performance and studied genotypes.

DISCUSSION

GENETIC INFLUENCE IN AEROBIC CAPACITY

The adopted instruments to evaluate aerobic resistance capacity were shuttle run (20, 21, 16, 13, 15) yoyo test (14, 17), and the 800-meter run (18). From the nine studies that applied aerobic resistance capacity, only three found an association between the better results on the tests and investigated polymorphisms, they also used a shuttle run in sedentary male (13, 15) and physically active female (16) Iranian teenagers. In the present review, we found seven genes associated with aerobic capacity in children and teenagers. Those genes are PPARA, PPARGC1A, ECA, ACTN3, CKMM, and NRC4, presented in table 3. From the genes investigated by the reviewed studies, the ones that associated aerobic resistance capacity with only ECA (20, 19, 14, 13) and ACTN3 (21, 18, 14) were investigated by more than one study. These are the most studied on elite performance, as it is shown in multiple reviews (1, 24, 25), also showing a relationship to the performance of children and teenagers.

Authors	Genes	Sample	BMI (kg/m²)	Tests						
				aerobic resistance	muscular resistance	Velocity	Strength	Flexibility	Agility	Balance
MORAN20 *et al.*, 2006	ECA	Greek Sedentary Teenagers (11-18 anos); H: NA; N: 543 M/ F 484	NA	*Shuttle run*	NA	40 m*	Handgrip*/ Seated basketball throw / Vertical jump*/ Throw and catch	Seat and reach	*Shuttle run test*	NA
MORAN21 *et al.*, 2007	ACTN3	Greek Sedentary and Physically Active Teenagers (11-18 year-olds); H: NA N: 525 M /467	M: 23,3 F:22,06	*Shuttle run*	NA	40 m	Handgrip/ Seated basketball throw / Vertical jump	NA	*Shuttle run test*	NA
Micheli19 *et al.*, 2011	ECA VDR	Medium and high level soccer players(up to 17 year-olds); H: NA; N: 125	NA	NA	NA	10 m 20 m	*Medicine ball*/ Horizontal jump*/ Countermovement jump*	NA	NA	NA
Chiu18 *et al.*, 2012	ECA ACTN3 PPARD PPARGC1A	Female Sedentary Teenagers (16-18 year-olds); H:1,59m; N: 170	21,6	800 m	30 s sit-ups*/ 60 s sit-ups*	60 m	Handgrip*/ Vertical jump*	NA	NA	NA
Ahmetov27 *et al.*, 2013	ECA ACTN3 PPARA	Physically active Children (10-11 year-olds); H: 145,7 M / 147,7 F; N: 219 M / 238 F	M:17,11 F: 17,21	NA	NA	NA	Handgrip*/ Horizontal jump*	NA	NA	NA
Orysiak28 *et al.*, 2014	ACTN3	Male Voleyball, swimming, ice Hockey and Canoeing players (15-18 year-olds); H: 184,1; N: 200	22,8	NA	NA	NA	Countermovement jump *Akimbo*/ Countermovement jump* /*Spike* jump	NA	NA	NA
Dionísio17 *et al.*, 2017	ECA ACTN3 AGT AMPD1	Male Teenage Soccer Players (14-17 year-olds); H: NA; N: 164	NA	Yo-yo *test*	NA	*Sprint test* (10 m)*	*Squat Jump**/ Countermovement jump with help of hands*	NA	NA	NA
García16 *et al.*, 2017	NRC4	Physically active Children (7-13 year-olds); H: 147,9 M/ 138,4 F; N: 152 M/ 116 F	M: 19,04 F: 19,11	*Shuttle run**	300 m*	30 m	*Squat Jump*/ Countermovement jump	NA	NA	NA
Orysiak46 *et al.*, 2018	ECA ACTN3	Teenage voleyball, swimming, ice Hockey and canoeing players (16,7 M year-olds / 15,8 F year-olds); H: 1, 83 M / 1, 74 F; N: 266 M / 132 F	M: 22,78 F: 21,11	NA	NA	NA	Countermovement jump/ *Spike jump*/ Maximum joint torque	NA	NA	NA
Zehsaz15 *et al.*, 2018	PPARa PPARGC1A	Male Sedentary Teenagers (13,2 year-olds); H: 1,45m; N: 586	18,9	*Shuttle run**	NA	*Sprint test*	Horizontal jump	NA	NA	NA
Cao22 *et al.*, 2019	PPARD	Chinese children (5,36 year-olds); N: 1155 M / 1089 F	16,1	NA	NA	NA	Vertical jump	NA	NA	Walking velocity in a 3 m balance beam*
Jeremic14*et al.*, 2019	ECA ACTN3	Female Teenage Soccer Players (16-18 year-olds); N:27	NA	Yo-yo *test*	Seven Continuous jumps*	20m*	*Squat Jump*	NA	Zig-zag *test*	NA
Zehsaz13 *et al.*, 2019	ECA CKMM	Male Sedentary Teenagers (13,2 year-olds); H: 1,45m; N: 613	18,8	*Shuttle run**	NA	30 m 60 m	Vertical jump/ Jumping tests in *Abalakov*	NA	NA	NA

Table 2. Study Characterization.

PPARA: alpha delta peroxisome proliferator activated receptor; PPARGC1A: peroxisome proliferator-activated receptor gamma 1 coactivator; PPARD: peroxisome proliferator-activated receptor delta; ECA: angiotensin converting enzyme; ACTN3: alpha-actinine-3; CKMM: creatine kinase; VDR: vitamin D receptor; AMPD1: adenosine monophosphate deaminase; AGT: angiotensinogen; NRC4: nuclear receptor subfamily 3, group c, member 4; H: Height; F: Female; M: male; N: Sample size; NA: Not applicable. *Used for association with capacity and polymorphism in the study.

METABOLIC AND ENERGETIC FACTORS

Among the investigated genes, three of them, known as PPARA, PPARD, and PPARG, codify three proteins: PPARα, PPARβ / δ, and PPARγ, respectively, and the receptors activated by peroxisome proliferators (PPARs). These receptors have as a characteristic the action in the body on metabolic pathways and metabolism of nutrients (26), and a recent review (27) showed that the found polymorphisms in PPARs relate to the capacity to obtain elite sports status in endurance athletes. Also, corroborating the data in this review, the papers observed, in elite athletes, the frequent presence of the alleles: G PPARA rs4253778 and C PPARD rs2016520. In fact, S, (10) studied young athletes, ages between 14- and 15-year-olds, evaluating the success of medium to long test transition. This study showed that the subjects that presented greater polymorphisms related to aerobic capacities had higher success rates in the transition, among the investigated genes were PPARA to allele G and PPARD to allele C. The studies with children and teenagers using these genes are few, and though they are promising, they are yet inconclusive on their effect on aerobic performance.

Another gene related to aerobic resistance capacity is PPARGC1A that presented an association with the Vo_2max value in one study (15). This gene is a co-activator of genes regulating the oxidative phosphorylation pathway for the generation of Adenosine Triphosphate (ATP), performing a link between its transcription factor — which is a transcriptional receptor γ co-activator 1 (PGC1) — and the physiological indicators of the mitochondrial energetic and cellular metabolism (27). In reviews that corroborates the finds of the present, in male teenagers, the authors show that PPARGC1A related to the elite athlete status in aerobic endurance sports (28) through, mainly, the Gly482 allele from PPARGC1A, which benefits prolonged activities due to the improvement in the ATP generation mechanism, which is the main energy source for this type of capacity (29).

Another investigated gene was the muscle-specific creatine kinase enzyme (CKMM) that has a function in the energetic homeostasis in the muscle cells catalyzing the conversion of creatine, consuming adenosine triphosphate (ATP) to create phosphocreatine and adenosine diphosphate (ADP) (30), where high levels of ADP in the bloodstream could indicate muscle damage. Moderate to intense physical exercise is already enough to induce muscle damage, moreover, researchers (31) showed that creatine kinase is, almost completely, found in the skeletal muscle. There is evidence that this gene was involved in the skeletal muscle performance in humans, especially during aerobic resistance training, which influences the response in maximum oxygen (Vo2max) consumption by AA genotype, according to Fedotovskaya's findings, which found an association of this genotype with high values of Vo_2 max in athletes (32). That corroborates with the result of a study found by this review, showing an association with aerobic performance in sedentary male children (13).

ANATOMICAL AND HORMONAL FACTORS

Another polymorphism that is well-established in the literature and showed association with the aerobic capacity found in one study in this review (13) was the renin-angiotensin system (ECA) polymorphism. The deletion (allele D) and insertion (allele I) of 287 pairs of nitrogenous bases compose ECA's polymorphic alleles (33,34). The homozygote II associates with low production of the angiotensin converter enzyme (35) and the aerobic resistance (36,34), showing the prediction potential of athletic capacities in endurance sports (1). In fact, we found a study that presented an association between allele I and the development of aerobic resistance capacity (15).

The alpha-actinin gene (ACTN3), responsible for coding the alpha-actinin-3 protein, belongs to the structural component of the skeletal muscle in the truncated and non-functional form of alpha-actinin-3. We found three studies in this review that investigated ACTN3. This polymorphism is called R577X and, in subjects who are homozygotes for allele X, is related to the resistance capacity in adults and elite athletes (37, 25). However, the three studies did not find a relationship between the polymorphism with the aerobic resistance capacity in sedentary and active subjects aging between 11 and 18, inviting more investigation on the ACTN3 predisposition in children and teenagers.

The androgen receptor (AR), also known by the acronym NRC4, is involved in the transcription of hormones, such as testosterone and dihydrotestosterone, which are involved in sexual and body development. Due to this function, some studies have tried to find an association of its activity with physical performance. In the present review, we found a review that presented an association between the best aerobic resistance performance results and the GGN_L allele in physically active girls (16). They also found an association between the CAG allele from NRC4 and the best responses to hypoxia training in Chinese men (38). However, (39) found no association between this allele with muscle mass and strength performance in young adults.

Given those premises, we observed that specific gene profiles influence the aerobic capacity, but we conjecture, following our findings in the literature for adults and elite athletes, a tendency of similar results in children and teenagers. In identifying talents, trainers must search those resources to get a more precise evaluation between children and teenagers. The research in this review shows that the polymorphisms in the PPRAs, PPARGC1A, ECA, CKMM, and NRC4 genes are agents that can help the identification of talent, especially in sedentary children.

GENETIC INFLUENCE IN STRENGTH CAPACITY

In evaluating strength capacity, the studies grouped the different tests into the ones for upper-body (handgrip, seated throw, medicine ball) and lower-body limbs (vertical, horizontal, countermovement, countermovement with the help of the hands or *Abalakov*, spike, akimbo, and squat jumps). The most common test for upper-body strength is the handgrip, present in four studies (20, 21, 18, 40), where three of them found an association between the best results of the test and the investigated polymorphisms (ECA, ACTN3, PPARA e PAPARD), in sedentary teenagers (20,18), as well as, active children (40). On the genes that might have an association with strength performance, we found ten studies that studied the relationship between that capacity with the ECA (14, 13, 41, 17, 19, 20), ACTN3 (14, 41 , 17, 40 , 18, 21), the vitamin D receptor (VDR) (19), CKMM (13), PPARA (40), AMPD1 (17), AGT (17), and NRC4 (16) genes. The most studied were ECA, with four investigations, and ACTN3, with three.

ACTN3 AND ECA

ECA and ACTN3 are the most popular in the number of mentions when the relationship is related to performance, including strength, and the genes from the PPARs family and AMPD1 that, in the current review, along with ECA and ACTN3, were the most popular for this approach in children and teenagers.

The polymorphism of the ACTN3 gene is the most popular in the literature, among the ones associated with strength performance and muscular resistance. We found three studies that related allele R with the best results of strength and muscular resistance in sedentary female teenagers (18) and physically active male teenagers (17) and children (40). Other two similar studies, which did not pass

Physical Capacity	Gene	Polymorphism	Allele Association	Study
Aerobic Resistence	*PPARD*	T294C (rs2016520)	C	Chiu 18*et al*., 2012
	PPARA	(rs54253778)	G	Zehsaz15 *et al*., 2018*
	PPARGC1A	Gly482Ser(rs8192678)	G	Chui *et al*., 2012; Zehsaz15 *et al*., 2018*
	ECA	I/D (rs1799752)	I	Chiu18 *et al*., 2012; Dionísio17 *et al*., 2017; Zehsaz13 *et al*., 2019*; Jeremic14 *et al*., 2019;
	ACTN3	R/X (rs1815739)	X	Moran *et al*., 2007; Chiu18 *et al*., 2012; Dionísio17 *et al*., 2017; Jeremic13 *et al*., 2019;
	CKMM	(rs 8111989)	A	Zehsaz13 *et al*., 2019*
	NRC4	GGN	GGN_L	Rodríguez-García16 *et al*., 2017*
Strength	*ECA*	I/D (rs1799752)	D	Ahmetov 27*et al*., 2013*; Kim18 *et al*., 2015; Dionísio17 *et al*., 2017*; Orysiak46 *et al*., 2018; Zehsaz13 *et al*., 2019; Jeremic14*et al*., 2019;
		I/D (rs442495; rs4311)	I	Moran *et al*., 2006*; Micheli19 *et al*., 2011*
	ACTN3	R/X (rs1815739)	R	Moran *et al*., 2007; Chiu18 *et al*. 2012*; Ahmetov27 *et al*., 2013*; Kim18 *et al*., 2015; Orysiak28 *et al*., 2014*; Dionísio17 *et al*., 2017*; Orysiak46 *et al*., 2018; Jeremic14 *et al*., 2019;
	VDR	*Fok I*	ff	Micheli19 *et al*., 2011
	CKMM	(rs 8111989)	G	Zehsaz13 *et al*., 2019
	PPARA	(rs54253778)	C	Ahmetov27 *et al*., 2013*
	AMPD1	C34T	C	Dionísio17 *et al*., 2017*
	AGT	M235T	T	Dionísio17 *et al*., 2017
	NRC4	CAG	CAG_S	Rodríguez-García16 *et al*., 2017**
Dinamic Balance	*PPARD*	(rs2016520)	C	Cao22 *et al*., 2019*
		(rs2267668)	G	
		(rs2299869)	-	
		(rs11571504)	-	

Table 3. Relationship between genes and physical capacities.

PPARA: alpha delta peroxisome proliferator activated receptor; PPARGC1A: peroxisome proliferator-activated receptor gamma 1 coactivator; PPARD: peroxisome proliferator-activated receptor delta; ECA: angiotensin converting enzyme; ACTN3: alpha-actinine-3; CKMM: creatine kinase; VDR: vitamin D receptor; AMPD1: adenosine monophosphate deaminase; AGT: angiotensinogen; NRC4: nuclear receptor subfamily 3, group c, member 4

this review's selection criteria, showed similar results (42, 43). According to (25), allele 577R from the ACTN3 gene produces the ACTN3 active protein in the RR homozygotes and RX heterozygotes. The alpha-actinin-3 expression is almost exclusively restricted to type II fast muscle glycolytic fibers, which are responsible for generating strong high-velocity contractions. These genotypes are favorable for anaerobic activity, as shown by reviews (44, 28). The association between the genotype and the strength phenotype for anaerobic activity was the most common in this review, raising considerable evidence of the influence of ACTN3 on strength performance for talent detection. However, we need to consider that the studies that presented an association involved athletes and players, reducing the effect of the genotype when comparing with sedentary subjects.

About the ECA gene, in physically active male subjects (40) and male soccer players (17), we found that the best results in strength performance were related to the D allele

frequency of ECA. Also, for the strength capacity, the study by (19) with 17-year-old soccer players found an association with the ID heterozygotes and the one by (20) in 11 to 18-year-olds with II homozygotes (20). Those results can seem atypical, considering that, according to the literature, it shows an association between the strength capacity and allele D (33). One possible explanation is that the results with soccer players could be affected by the collectiveness nature of soccer, filled with *stop and go* cues, which helps with jumping performance, the test used to measure strength capacity in lower limbs. Their poor performance on upper limbs strength capacity further corroborates with the previous argument. Another source of influence induced by soccer is its bioenergetic aerobic and anaerobic variation that can cause a better response from the heterozygote. Additionally, children and teenagers suffer less environmental influence and present the genotypical function better (1). Therefore, the found results on the action of ECA show some caution on its effect on the phenotype.

MUSCLE BREAKDOWN

Another gene that can be an influence in the strength capacity is CKMM. About this potential, the literature shows a connection between CKMM and the breakdown of skeletal muscle fiber in response to physical exertion (45). In the paper (46), the authors hypothesize that allele G can protect against muscle breakdowns. The meta-analysis from (47) showed that strength athletes more frequently present allele G. In this review, one study (13) did not find an association between the best results in strength tests and the allele G from CKMM in sedentary male teenagers.

METABOLIC FACTORS

The Vitamin D receptor gene, VDR, is responsible for regulating the homeostasis of phosphate, calcium, and, consequently, bone metabolism, and it began to be studied due to results that reported that its variants would be involved in the strength of the lower limbs (48). One of these variants is Fok1 (which in endonuclease is 'F' due to the absence of the restriction site and in the presence 'f') that results in a C-to-T transition in exon II of the VDR gene, located on chromosome 12q. In our review, one study observed an association of the homozygote 'ff' in strength through the squat and counter-movement jump tests in 17-year-old soccer players (19). This finding corroborates the results found in men and women homozygotes 'ff' between 50 and 80 years old that answered better to resistive training (49). The information on those polymorphisms acting on muscle-building, improving the performance in resistive training is yet unknown and needs further investigation.

The PPARα protein codifying gene, which is PPARA with an intron 7 G/C polymorphism, has been associated with strength performance and allele C power. In the Wingate anaerobic test, the best results were associated with the frequency of allele C in hockey athletes (50). Also, a review about genes and their relationship with sports shows that strength-driven sports include athletes with a higher frequency of allele C (51). One possible explanation is that allele G was related to the frequency of the type I fiber (52) and the presence of allele C could increase type II fibers that are efficient to exert strength. We found in this review an association with allele C with the best strength performance in active male children (40). As far as we know, this is the first study that found the allele C association, and further investigation with the population of male children is needed.

The C34T polymorphism of AMP deaminase gene (AMPD1) is located at chromosome 1p13-p21 and also investigated. It acts, during intense activities, resetting the unbalance between ATP/ADP. The transition mutation of C to T nucleotide of the AMPD1 gene was shown to be a negative factor for athletic performance (53) due to the reduction of gene activity and, consequently, resulting in less production of the ATP/ADP energy pathway. In a study (17), allele C showed an association with the best results for strength capacity performance in male teenager soccer players. However, the results should be treated with caution due to the frequency of allele T showing association with smaller aerobic and power capacities (54).

OTHER FACTORS

Another investigate gene was the angiotensinogen (AGT), it is located in codon 235 at chromosome 1q42-43 and presents with the exchange of methionine (M) to threonine (T). Allele T showed an association with the biggest heart mass (55) and strength performance in athletes (56) and, in the study (17), they did not find an association between the strength capacity in male teenage soccer players, (17). Another review showed that AGT belongs to a possible polygenic profile for strength athletes (57). However, we are still on the first steps of the research line to determine this profile in children and teenagers (57).

The literature still lacks investigation on the action of the NRC4 gene on strength performance. In the present review, the physically active male children showed an association of the CAG allele with the best results of strength performance (16). The authors also showed that the subjects had a smaller frequency of the CAG and GGN polymorphisms when compared to the group with less strength performance. The lower repetition favors the androgenic action (58) and, consequently, to body development, but they did not observe differences in the muscle mass of the groups. Other studies sought to observe an association between the variations of the androgen receptor that can influence strength and muscle mass in adults, however, without success. Their findings suggest that the gene affects strength's features in infancy and loses that influence after maturation.

Regarding gene usage, on the genes cited in this review, ECA and ACTN3 stand out by presenting the biggest frequency among the association with the phenotypes, also due to being the most commonly investigated. The genes PPARA, AMPD1, and NRC4 showed promising results in their findings. Obviously (*) a range of gene candidates influences the strength capacity, increasing the need for further investigation on this perspective to explore how that capacity can be better observed and identified. Further investigation on the genetic profile can be influencing the predisposition of strength capacity in children and teenagers.

NEW PERSPECTIVE

In the present review, one study observed an association of allele G with gene PPARA in children (23). Investigations showed that the PPARD variants are involved in elite athlete statuses (59, 29). The authors of the study investigating the G allele of rs2267668 Polymorphism also found association with the best results of the balance capacity. However, the best performance in ski athletes, which relies greatly on dynamic balance, is related to the G allele (60).

Though the genes found in this review are related to physical capacities, ability acquisition capacity is also an investigation area that can bring further clarification about the talent detection process. Through this perspective, the gene variation of the dopamine receptor (DRD2), brain-derived neurotrophic factor (BDNF), and the catechol-O-methyltransferase (COMT) are very promising (1) and

could be included in future research on this topic, besides the genes covered in the present review. However, it is noteworthy that, besides the expressed genes and their combinations, the environmental factors that influence the results in the studies in this thematic should also be considered carefully. Stratifying samples in the research by maturation helps to reduce possible influences on the subjects that are far over or under the average body and nutritional developmental status. We propose new studies that apply tests in order to verify the maximum possible physical capacities, due to a high-level athlete being induced to develop all capacities to remain in an elite status. We also propose that the research done following this review trace profiles based on more than one polymorphism associated to a physical capacity, searching for references in test batteries that classify results in determining how close to predicted said result is or if that is in fact a possible motor talent.

However, the ethical features raised by those research areas require consideration. The stratification of elite athletes based on the genetic profile can be considered unethical. For a more qualitative process of that development and selection, suggest an athlete detection, identification, selection, and development.

When taken together, our findings shown that field performed easy-to-apply tests are tools to determine talent acquisition, especially those of aerobic resistance and strength. Sedentary populations seem to be more prone to correlations between the genetic profile and physical performance. The polymorphisms associated with aerobic capacity seem to introduce the answers to the phenotype when compared to strength polymorphisms. That may be due to the different types that the strength capacity can express, such as strength, maximum shape, and power.

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