

Review Article

Genetics and Artistic Gymnastics: 2014 Update

M Massidda^{1*}, S Toselli² and CM Calo¹¹Department of Life and Environmental Sciences, University of Cagliari, Italy²Department of Biomedical and Neuromotor Sciences, University of Bologna, Italy

*Corresponding author: Massidda M, Department of Life and Environmental Sciences, University of Cagliari, Italy SS 554 Km 4.500 – 09042 Monserrato (CA), Italy, Tel: +390706754154; Email: myosotis.massidda@unica.it

Received: November 17, 2014; Accepted: January 26, 2015; Published: February 02, 2015

Abstract

Purpose: Much evidence has been provided to support the relationship between single nucleotide polymorphisms and athletic performance and the susceptibility to develop injuries participating in sports. We report an up-to-date review of the genetic factors involved in artistic gymnastics.

Methods: We conducted a search in PubMed using specific keywords and a date range of 1990 to the present.

Results: Genetic predisposition to artistic gymnastics has been analyzed using candidate gene studies. To date, seven genetic polymorphisms (ACE I/D; ACTN3R577X; VDR FokI, BsmI, and TaqI; and ADRB3 Trp64Arg) have been associated with artistic gymnastics performance, while one polymorphism (COL11A1 4603C/T) has been correlated to artistic gymnastics injuries.

Conclusion: Recently, several individual genetic variations contributing to athletic performance have been identified, and various polymorphisms have been indicated as risk factors for sports injuries. However, genetic studies related to artistic gymnastics remain few in number and are somewhat contradictory. Further studies are needed to establish the influence and interaction of genes across a range of artistic gymnastics parameters.

Keywords: Artistic gymnastics; Athletic performance; Genetics; Genes; Single nucleotide polymorphisms; Sport injuries

Abbreviations

ACE: Angiotensin-Converting Enzyme; ACTN-3: alpha-actinin 3 protein gene; ADRB3: Beta 3 adrenergic receptor; AR: Adrenergic Receptor; BDNF: Brain-Derived Neurotrophic; BM: Body Mass; CI: Confidence Interval; COL11A1: type XI collagen alpha-1 chain gene; COL11A2: type XI collagen alpha-2 chain gene; COL2A1: type II collagen alpha-1 chain gene; h: hours; HR: Heart Rate; L_{max} : peak blood lactate concentrations; min: minute; mmol: millimolar; OR: Odds Ratio; RAS: Renin-Angiotensin System; SNPs: Single Nucleotide Polymorphisms; VDR: Vitamin D Receptor; VO_2 : Oxygen consumption; VO_{2max} : Maximal oxygen consumption; wk: week.

Introduction

Artistic gymnastics is one of the most popular and oldest sports in the world. Although it has been a part of every Olympic Games, women first competed in 1928 [1]. The sport comprises several activities in which female athletes perform routines on four apparatuses (vault, uneven bars, balance beam, and floor), while male gymnasts perform routines on six apparatuses (floor, pommel horse, rings, vault, parallel bars, and high bar) [2]. Elite female and male gymnasts may initiate training for their sport as early as age 6 and 9 years, respectively, and peak performance is reached at least 10 years later.

The primary determinant of success is the ability to perform a high-difficulty exercise with a high execution score. During a high-level competition, the performance scores on uneven bars and balance beam for women and on pommel horse for men have been shown to be the strongest predictors of final standing in the competition [3]. Successful performance in artistic gymnastics is the result of

the interaction of many factors that are difficult to distinguish [4]. Performance requires a combination of explosive and quasi-maximal contractions to face many difficulties together with sprinting, jumping, pushing, and pulling skills. The Heart Rate (HR) has been reported to be generally high, peaking around 170 to 190 beats·min⁻¹ in senior males after routines [5,6] and around 150 to 180 beats·min⁻¹ in females gymnasts [7]. Peak blood lactate concentrations (L_{max}) of 8 to 11 mmol·L⁻¹ [5] or 3 to 6 mmol·L⁻¹ [6] have been found in adult male gymnasts. A recent study of young female gymnasts showed that their peak HR was 183 to 199 beats·min⁻¹, peak oxygen consumption/Body Mass (VO_2/BM) was 33 to 44 mL·kg⁻¹·min⁻¹, and peak L_{max} was 7 to 9 mmol·L⁻¹ during the floor and uneven bars exercises. The vault was the event that raised HR and L_{max} the least, to 154 to 166 beats·min⁻¹ and 2.4 to 2.6 mmol·L⁻¹, respectively, and the balance beam created the lowest VO_2/BM (27-35 mL·kg⁻¹·min⁻¹) [8].

The complexity of the skills of elite gymnasts is increasing because of changes in performance requirements that have arisen from regulations imposed by the Code of Points combined with the development of more complex routines on each apparatus [9]. Accordingly, the practice of artistic gymnastics is becoming more an elitist sport in which the achievement of a high performance level is to the advantage of those who have a particular physical structure [10-13] and likely specific genetic variants as well.

Despite the numerous short-term and long-term health benefits of gymnastics participation [14-16], the combination of the youth of the participants and the long hours of physical training that increases through the competitive levels gives rise to a concern for the risk of injury [17,18]. Indeed, most gymnasts do not complete their years of training and competition without incurring injuries

[18]. Moreover, because of these physical demands, a wide variety of injuries occur. In fact, gymnastics continues to be one of the most popular yet injury-prone sports in the United States, and it is second only to spring football in its rate of injury during practice [19]. The lower back is the most frequently injured body part in the spine/trunk region of female gymnasts, and common injury sites reported for males and females include the vertebral bodies, intervertebral discs, and pars interarticularis [20]. Several researchers have noted higher frequencies of radiological abnormalities such as intervertebral disc degeneration, vertebral ring apophysis injury, and Schmorl's nodes among gymnasts [21-24].

The second most frequently-injured body region is the upper extremities. In this region, among females, the wrist is the most frequently injured, followed by the elbow. Among males, the shoulder is the most frequently injured, followed by the wrist [20]. The lower extremities also experience tremendous physical loads in gymnastics, yet surprisingly, there are no published prevalence data on lower extremity injuries affecting female or male gymnasts [20]. Genetics can contribute to an explanation of why one gymnast develops more injuries than another in the same environment. Therefore, the gymnasts' injuries may be caused not only by well-known environmental factors, but also by less-studied genetic factors. Few research papers associate genetic elements with gymnastics injuries and their performances.

In the last two decades, much evidence has been provided to support the relationship between Single Nucleotide Polymorphisms (SNPs) and many phenotypic traits related to elite athletic status [25]. Recently, 21 SNPs were identified as candidates for capturing the heritable component (approximately 50% of total inter-individual variability) of the response of $VO_{2\max}$ to endurance training [26]. Genetic factors account for approximately 50% to 80% of inter-individual variation in lean body mass, and effects on both 'training-naive' muscle mass and its growth response have been found [27].

Psychology plays an important role in training, competition, tolerance of pain, and motivation. However, the role of genetic variations in determining one's psychological state and responses remains poorly understood. Only recently have some authors identified a polymorphism (BDNF, Val66Met polymorphism) that affects the psychological response to stress and also the motivation to exercise. In particular, the authors found it has marked effects on the individual's positive or negative thinking during intense exercise and competition [28,29].

Finally, much evidence has also been provided to support the relationship between SNPs and the susceptibility to developing injuries while participating in sports and performances related to sports activities [27,30]. Accordingly, the performance of professional gymnasts and their individual susceptibilities to developing injuries could be influenced, at least partly, by genetic components. In this concept review, we report up-to-date studies on the genetic factors involved in artistic gymnastics. Studies addressing relationships between genetic polymorphisms, artistic gymnastics performance, and injuries were identified by searching for original articles in PubMed that were published from 1990 through October 31, 2014. Combinations of the key words, "gymnastics injuries" and "genetics" were used to screen for potentially relevant studies that focused on

the genetic susceptibility to gymnastics injuries. Combinations of the key words "artistic gymnastics" or "gymnastics" or "gymnasts" and "genetics" were used to screen for potentially relevant studies that focused on the genetic aspects of artistic gymnastics performance. Additional studies were also identified by cross-referencing.

Candidate genes associated with artistic gymnastics performance

Most of the currently established or putative loci related to artistic gymnastics performance were found using candidate gene studies. In detail, seven polymorphisms (ACE I/D, ACTN3R577X, VDR ApaI, VDR FokI, VDR TaqI, ADRB3 Trp64Arg) related to gymnasts were found. Identifying genetic predisposition to artistic gymnastics performance could be useful to coaches and trainers for predicting the genetic potential of their gymnasts. Personalized and individualized performance improvement strategies to enhance and exploit genetic advantages or overcome genetic barriers can be implemented to optimize the physical fitness and performance phenotype. The general hypothesis is that an inheritance component affects physical and athletic fitness and is able to interact with environmental factors, particularly with gymnastics training.

α -actin-3 protein gene

The α -actin-3 (ACTN3) gene, called the "speed gene" [31], has recently received the most attention for its association with sports performance and elite athlete status. It codifies for the actin binding α -actinin-3 protein, a component of the contractile machinery in mammalian fast skeletal muscle fibers [32].

The R577X SNP, associated with a complete absence of α -actinin-3 protein [33], has been identified in exon 16 of the ACTN3 gene (11q13-q14). The protein is almost exclusively expressed in fast, glycolytic, type IIx fibers that are responsible for the generation of rapid forceful contractions during activities such as sprinting [34,35]. It is also involved in the regulation of metabolic and signaling pathways, contractile properties, and fiber-type specification of the muscle fibers. A deficiency in α -actinin-3 results in increased calcineurin activity in mouse and human skeletal muscle and enhanced adaptive responses to endurance training [36]. This SNP is a C-to-T transversion in position 1747 and converts an arginine residue to a premature stop codon at residue 577 [33]. The homozygous condition for the stop codon, which results in no ACTN3 protein detectable in muscle fibers [33], occurs in about 18% of the European population and has a global incidence of around 16% [34,37]. A complete deficiency of the α -actinin-3 in 577X homozygotes does not result in a disease phenotype [33] because in this situation, the ACTN2 gene, expressed in both type I and II myofibers, can compensate for the loss of the ACTN3 protein in type II fibers. Meta-analyses [38,39], and a recent review [40] of the published literature regarding the influence of ACTN3 on athletic performance suggest that the ACTN3 577RR genotype is associated with sprint/power athletic status in Caucasians, while the ACTN3 577XX genotype is assumed to preclude top-level athletic performance in power and sprint sports [41-43].

Two studies focused on the role of ACTN3 R577X polymorphisms on artistic gymnastics performance [44,45]. We conducted the first study associating the ACTN3 R577X polymorphism with elite artistic gymnastics status [44] aiming to test whether the postulated advantage of the 577R allele for elite sprinting and power performance

was also valid for artistic gymnastics performance. The study sample comprised 35 top-level gymnasts from the Italian national junior and senior artistic gymnastics team (17 male) who were competitive at the international and Olympic levels during the years 2005–2007. The athletes were gymnasts for an average of 10.4 years (male, 12.5 ± 5.12 years; female, 8.4 ± 1.8 years), and they trained for 29.6 ± 6.2 h·wk⁻¹. The results showed that ACTN3 XX genotype was underrepresented in female and male gymnasts compared to controls (one gymnast carried the 577XX genotype), but was significant only among males (male, 0% vs. 16.1%, $p < 0.04$; female, 5.5% vs. 22.7%, $p = 0.39$). We thus hypothesized that the differences between male and female gymnasts versus controls could be the result of a greater advantage conferred by the α -actinin-3 protein to male gymnasts because their routines require a greater degree of muscular strength than those performed by females. However, the frequency distributions among female gymnasts, despite not being significantly different from the sedentary control group, were similar to those found in elite female sprinters [43]. We concluded that the role of the α -actinin-3 protein in enhancing sprint and power performance [43,46] could be the same for male artistic gymnasts, and we cannot exclude the possibility that the α -actinin-3 protein could also provide a less evident advantage for female gymnasts.

The second of the two studies, performed by Morucci et al., considered the role of ACTN3 R577X polymorphism in artistic gymnastics performance [45]. It aimed to test the association between gymnastics performance and ACE ID polymorphism, ACTN3 R577X polymorphisms, and Vitamin D Receptor (VDR) gene. Between 2009 and 2011, data was collected from eighty white male gymnasts (aged 14.5 ± 4.2 years; average training time 31 ± 1 h·wk⁻¹) from the Italian gymnastics team participating in international competitions. Analysis indicated that gymnasts with ACTN3 RR or RX genotypes showed lesser athletic performances (volume, intensity, and density) compared to those gymnasts with the XX genotype. More specifically, mean values for volume were higher among parallel bars and high bar gymnasts with the XX genotype ($n = 13$) than those with other ACTN3 genotypes (RX genotype, $n = 46$; RR genotype, $n = 2$; parallel bars, XX vs. RR, $p = 0.02$; XX vs. RX, $p = 0.005$; horizontal bar, XX vs. RR, $p = 0.04$; XX vs. RX, $p = 0.03$). Similarly, mean values for intensity were higher among parallel bars and vault gymnasts with the XX genotype than those with other genotypes (parallel bars, XX vs. RR, $p = 0.01$; XX vs. RX, $p = 0.008$; vault, XX vs. RR, $p = 0.02$; XX vs. RX, $p = 0.05$). Finally, mean values for density were higher among pommel horse, parallel bars, and high bar gymnasts with the XX genotype than those with other genotypes (pommel horse, XX vs. RR, $p = 0.05$; parallel bars, XX vs. RR, $p = 0.05$; XX vs. RX, $p = 0.05$; horizontal bar, XX vs. RR, $p = 0.04$; XX vs. RX, $p = 0.03$). No comparisons of allele and genotype frequencies between gymnasts and controls were given.

An additional study included gymnasts when determining the role of ACTN3 R577X polymorphisms on athletic performance [47]. Four hundred and eighty-six male and female Russian athletes that competed regionally or nationally included 44 gymnasts. The data suggested that the ACTN3 RR and RX genotypes were associated with predisposition to power sports, in which artistic gymnastics are included and positively correlated with elite power athlete status among Russian athletes.

ACE gene insertion/deletion polymorphism

The Renin-Angiotensin System (RAS) plays a homeostatic role in human circulation and in left ventricular remodelling. Angiotensin Converting Enzyme (ACE) is a key component in the RAS, generating the vasoconstrictor angiotensin II and degrading the vasodilator kinins [48]. Angiotensin II affects metabolism [49], blood pressure, and tissue growth [50] and is a recognized growth factor necessary for hypertrophy of skeletal muscle in response to mechanical loads [51]. In 1998, a polymorphism of the ACE gene became the first genetic element shown to substantially impact human physical performance [52]. The functional polymorphism of the ACE gene has been identified: the presence or Insertion (I) allele of a 287-bp fragment rather than the absence or Deletion (D) allele is associated with low ACE activity in both serum and tissues [53,54]. Higher ACE activity results in increased production of angiotensin II and aldosterone and decreased half-life of bradykinin [55,56]. However, the literature is currently equivocal about the association between the ACE ID polymorphism and athletic performance. The ACE genotype is associated with differences in athletic performance in part through modulation of kinin levels (although a role for altered Ang II activity at its receptors cannot be excluded). Moreover, the ACE genotype may also influence human skeletal muscle growth [57] and the mechanical/metabolic efficiency of skeletal muscle [58]. In general, the I allele seems associated with endurance-orientated events, while the D allele seems associated with strength- and power-orientated performance [27]. A recent meta-analysis [39] of 366 articles on ACE showed that, with respect to sport discipline, the II genotype was found to be associated with performance in endurance athletes (OR, 1.35; 95% CI, 1.17–1.55) but not in power athletes (OR, 0.93; 95% CI, 0.64–1.34).

Two studies focused on the role of ACE ID polymorphism in artistic gymnastics performance [45,59]. We conducted the first study associating ACE ID polymorphism and elite artistic gymnast status [59]. We assessed 33 (17 male) top-level Italian gymnasts against a control group of 53 (31 male) unrelated sedentary individuals. All gymnasts were from the Italian national junior and senior artistic gymnastics team (2005–2007) from continental Italy. Male and female athletes practiced gymnastics for 12.52 ± 5.12 years and 8.1 ± 1.8 years, respectively, and their training consisted of 29.3 ± 6.33 h·wk⁻¹. The purpose of the study was to determine the association between ACE genotypes and sprint athlete status among elite Italian gymnasts. We found an absence of significant differences in the distribution of genotype and allele frequencies of the ACE ID polymorphism in both gymnasts and controls. We attributed this result to the higher frequency of the D allele and DD genotype in the Italian population with respect to those of other Caucasian populations, as reported in similar studies of ACE polymorphisms in elite athletes. In fact, the genotype and allele frequencies of the control group, as with other Italian samples [60,61] and other European populations [62,63], were different than those found in the published data [64–67]. Moreover, the genotype and allele frequencies of the control group were quite similar to those of elite sprint athletes and short-distance swimmers, as reported by Myerson et al. ($p = 0.73$) [64], Nazarov et al. ($p = 0.46$) [65], Woods et al. ($p = 0.91$) [67], and Tsianos et al. ($p = 0.67$) [66]. We concluded that there was no association between the ACE ID polymorphism and elite gymnastics performance in Italians. Our

study agreed with those of Oh et al. [68], who analyzed a group of 139 Korean male elite athletes, including 12 gymnasts. The authors did not find differences in the distribution of the ACE ID genotype and allele frequencies between athletes and controls.

The second of the two studies considering the role of ACE ID polymorphism and artistic gymnastics performance was conducted by Morucci et al. [45]. The results indicated that gymnasts with ACE II genotypes showed decreased athletic performances (volume, intensity, and density) compared to those gymnasts who carried the ID or DD genotype. More specifically, volume was lower among gymnasts training for floor exercise, pommel horse, and parallel bars with the II genotype ($n = 10$) than those with other ACE genotypes (floor, II vs. ID, $p = 0.02$; pommel horse, II vs. ID, $p = 0.002$; II vs. DD, $p = 0.02$; parallel bars, II vs. ID, $p = 0.03$). Similarly, intensity was lower among gymnasts training for pommel horse with the II genotype than those with other genotypes (II vs. ID, $p = 0.03$; II vs. DD, $p = 0.02$). Finally, density was lower among gymnasts training for floor exercise, pommel horse, and rings with the II genotype than those with other genotypes (Among floor gymnasts, $p = 0.01$ between both II and ID genotypes and II and DD genotypes; among pommel horse gymnasts, $p = 0.001$ between II and ID genotypes, and $p = 0.006$ between II and DD genotypes; and among rings gymnasts, $p = 0.02$ between II and ID genotypes). No comparisons of allele and genotype frequencies between gymnasts and controls were given. The authors concluded that their results should drive gymnastics trainers to carefully plan new specific individual training programs for gymnasts with the ACE II genotype to improve their power abilities in areas where they are less genetically predisposed.

VDR Apal, FokI, and TaqI polymorphisms

The VDR gene is located on human chromosome 12 (12q12–q14) and has a length of 100 kb with more than 100 restriction endonuclease cutting site polymorphisms [69]. It is a member of the steroid super family of nuclear receptors which plays a key role in the regulation of the transcriptional activity of the vitamin D metabolite 1α , 25-dihydroxyvitamin D₃. Vitamin D has a well-described role in calcium metabolism, increasing the absorption of calcium and phosphate from the intestine and increasing renal calcium reabsorption. It has been suggested to also have an important role in influencing skeletal muscle function, and vitamin D receptors have been identified in this tissue. It has been hypothesized to act on myocytes via VDR, with effects on myocyte proliferation, differentiation, growth, and inflammation [70].

The gene encoding the VDR is known to contain a large number of polymorphisms. A polymorphic start codon at the 5' end of the gene is identified by the restriction enzyme FokI. At the 3' end of the gene, there are 3 additional polymorphisms, generating BsmI, ApaI, and TaqI restriction sites [71]. Some of these polymorphisms were related to differences in strength and changes in bone mineral density in response to physical training [27], but very few studies have investigated the direct relationship between VDR gene polymorphisms and sport performance. These functional genetic polymorphisms in the VDR could be involved in other tissues that respond to vitamin D, such as muscle cells and adipocytes. It has been demonstrated that vitamin D targets skeletal muscle and its metabolites directly affect muscle cell metabolism through various pathways [72]. Also, vitamin D deficiency is associated with muscle weakness [72,73].

Associations between vitamin D status and muscle strength, body sway, and physical performance have been investigated in a large number of cohort and cross-sectional studies with most [74] but not all [75] studies showing the beneficial effect of vitamin D status on measured indices. To date, only the study by Morucci et al. [45] analyzed the role of VDR polymorphisms (BsmI, FokI, and ApaI) on artistic gymnastics performance, and the authors did not find associations between the VDR genotypes and athletic performance of the gymnasts.

Trp64Arg polymorphism

A T-to-C transition in codon 64 of exon 1 of the gene encoding β 3-Adrenergic Receptor (ADRB3) on chromosome 8 results in a tryptophan to arginine (Trp64Arg) variation. The Adrenergic Receptor (AR) is linked to G-protein which uses catecholamines, such as epinephrine or norepinephrine, as ligands, and it is known that it has subtypes such as the β 1-AR, β 2-AR, and β 3-AR [76]. In particular, the β 3-AR is distributed in brown adipose tissue and white adipose tissue. When it is stimulated by catecholamines, lipolysis and thermogenesis are promoted and play a critical role in energy expenditure [77].

The Trp64Arg polymorphism in ADRB3 is associated with reduced lipolytic activity compared to the T genotype (Trp-containing protein) [78,79]. This polymorphism has also been associated with hypertension in males with type 2 diabetes [80]. However, some studies indicate that it is not associated with the risk for cardiovascular disease [77,81–84]. Moreover, the β -AR also has an emerging role as a candidate that influences physical performance [85], even though very few studies have examined the distribution of the β 3-AR gene polymorphism in athletes [86–88].

To date, two studies that included gymnasts have analyzed the role of the β 3-AR gene on athletic performance [86,88]. The first study has examined the genotypic and allelic frequencies of the Trp64Arg polymorphism in Korean rugby, basketball, soccer, handball, field hockey, volleyball, badminton, and taekwondo players as well as gymnasts. It reported that the Arg allele was most frequently found among volleyball players (38%) and basketball players (35%) [86].

The second study examined eighty-one athletes (8 long-distance runners, 17 soccer players, 8 baseball players, 10 basketball players, 8 volleyball players, 8 ice hockey players, 8 judo players, 6 taekwondo players, and 8 gymnasts) and 33 healthy controls [88]. The data suggested that genotype and allele distribution of the Trp64Arg polymorphism in the β 3-AR gene was significantly different between the disciplines, and the highest Arg allele frequency was found among volleyball players and gymnasts ($p < 0.05$). Moreover, this polymorphism was significantly associated with serum HDL-cholesterol and glucose level in athletes ($p < 0.05$), including the gymnasts.

Candidate genes associated with susceptibility to artistic gymnastics injuries

The loci associated with susceptibility to developing artistic gymnastics injuries were analyzed using candidate gene studies. Specifically, only one polymorphism (COL11A1 4603C/T) was correlated with artistic gymnastics injuries. Identification of these loci could lead to customized exercise recommendations for specific

gymnastic populations. Personalized performance improvement strategies could be useful for coaches and trainers to safeguard the health of a gymnast. Moreover, prevention strategies such as avoiding weight-bearing and high-impact movements could be used for gymnasts who have higher-risk genotypes.

COL11A1 4603C/T polymorphism

Mutations in the type XI collagen α -1 chain gene (COL11A1) cause a change in protein structure that alters its interactions with collagens II and V, resulting in abnormalities in cartilage [89]. The COL11A1 codifies, together with COL11A2 and COL2A1, for type XI collagen [90,91]. Specifically, heterozygous mutations in COL11A1 typically result in a mild autosomal dominant phenotype, such as Stickler or Marshall Syndrome, while homozygous and compound heterozygous mutations result in a more severe autosomal recessive skeletal dysplasia, such as fibrochondrogenesis. These disorders are collectively named “type XI collagenopathies” [92], and all are complicated by abnormalities of the spine, including narrowing of the intervertebral discs.

Type XI collagen is a cartilage-specific extracellular matrix protein, and it has an important role in regulating fibrillogenesis and in organizing the extracellular matrix [93]. The COL11A1 4603C/T gene polymorphism was associated with lumbar disc herniation in a Japanese population [94], and it has also been shown to be a risk factor for limbus vertebra in Japanese collegiate gymnasts [95]. The study by Koyama et al. [95] analyzed 103 Japanese collegiate gymnasts (70 male) who were aged 19.7 ± 1.0 years, had 11.8 ± 3.6 years sporting experience, and included Olympic and World Champion medalists. The main finding was that the COL11A1 genotype and the years of sporting experience were risk factors for limbus vertebra. Moreover, the risk of limbus vertebra decreased with advancing age. Those with a TT genotype of COL11A1 were at a greater risk for limbus vertebra than those with a CT genotype. The authors concluded that the TT genotype of the COL11A1 polymorphism was associated with increased risk of limbus vertebra in Japanese collegiate gymnasts, and sporting experience was an important risk factor for limbus vertebra in the same population.

Conclusion

Several studies in recent years have suggested that genetic factors influence many phenotypic traits related to elite athletic status [25], to an individual's response to exercise training [96], and to a susceptibility to developing sport injuries [97]. In general, research has highlighted two major difficulties in this area. First, a clear phenotype definition is needed. This is important because of the specific nature of each sport and of the different physiopathology of injuries. Specifically, the artistic gymnastics phenotype is a complex trait that involves various physiological pathways used to achieve a high level of performance. Similarly, artistic gymnastics injuries are a wide variety of complex disorders that do not have a clear-cut pattern of inheritance. They are also difficult to study and treat because the specific factors that cause most of these disorders have not yet been well-identified.

Consequently, the second problem is that the effect of a single gene variant is generally too small to preclude the possibility of becoming an elite gymnast or to have a determinant role in the development

of a specific artistic gymnastics injury. Therefore, identifying the “optimum” genetic profile for an artistic gymnastics phenotype requires a more comprehensive approach, and it would be of extreme importance to recognize the maximum possible number of SNPs related to injuries in gymnastics. Each gene associated with artistic gymnastics performance and injuries may also have a different weight in explaining the variation of phenotypic traits related to artistic gymnastics [98]. Identifying a genetic predisposition to soft tissue injury in artistic gymnastics is an example of how genetic models can be used to effectively recognize risk and identify gymnasts who would benefit from injury prevention, treatment, and rehabilitation programs.

This review of the literature reveals that, to date, the genetic studies in the field of artistic gymnastics remain small in number and are, in part, contradictory. Further studies are needed to establish the influence and interaction of genes across a range of artistic gymnastics parameters. A polygenic profile must be identified that allows, at least in part, an accurate prediction of the variability of factors (phenotypic traits) involved in artistic gymnastics. Genetic analyses will be useful for coaches and trainers to know the genetic potential of their athletes and to identify young gymnasts with advantageous physiology, morphology, and psychology. Individualized training programs based on gymnasts' genetic profiles could help athletes with lower capacities to respond/adapt to training as well as those who have higher chances of incurring injuries.

References

1. Singh H. *Gymnastics*. Singh H, editor. In: 33 Olympic Games. New Delhi: Discovery Publishing House. 2004; 43-44.
2. Prassas S, Kwon YH, Sands WA. Biomechanical research in artistic gymnastics: a review. *Sports Biomech*. 2006; 5: 261-291.
3. Massidda M, Calo CM. Performance scores and standings during the 43rd Artistic Gymnastics World Championships, 2011. *J Sports Sci*. 2012; 30: 1415-1420.
4. Franks IM, Goodman D. A systematic approach to analysing sports performance. *J Sports Sci*. 1986; 4: 49-59.
5. Goswami A, Gupta S. Cardiovascular stress and lactate formation during gymnastic routines. *J Sports Med Phys Fitness*. 1998; 38: 317-322.
6. Jemni M, Friemel F, Lechevalier JM, Origas M. Heart rate and blood lactate concentration analysis during a high-level men's gymnastics competition. *J Strength Cond Res*. 2000; 14: 389-394.
7. Noble L. Heart rate and predicted Vo₂ during women's competitive gymnastic routines. *J Sports Med Phys Fitness*. 1975; 15: 151-157.
8. Marina M, Rodríguez FA. Physiological demands of young women's competitive gymnastic routines. *Biol Sport*. 2014; 31: 217-222.
9. Irwin G, Hanton S, Kerwin DG. The conceptual process of skill progression development in artistic gymnastics. *J Sports Sci*. 2005; 23: 1089-1099.
10. Malina RM. Physical growth and biological maturation of young athletes. *Exerc Sport Sci Rev*. 1994; 22: 389-433.
11. Malina RM. Growth and maturation of elite female gymnasts: is training a factor? Zemel B, Eveleth PB, Johnston FE, editors. In: *Human growth in context*. London: Smith-Gordon. 1999; 291-301.
12. Beunen GP, Malina RM, Thomis M. Physical growth and maturation of female gymnasts. Johnston FE, Zemel B, Eveleth PB, editors. In: *Human growth in context*. London: Smith-Gordon. 1999; 281-289.
13. Massidda M, Toselli S, Brasili P, Calo CM. Somatotype of elite Italian gymnasts. *Coll Antropol*. 2013; 37: 853-857.

14. Zanker CL, Osborne C, Cooke CB, Oldroyd B, Truscott JG. Bone density, body composition and menstrual history of sedentary female former gymnasts, aged 20-32 years. *Osteoporos Int.* 2004; 15: 145-154.
15. Vuillerme N, Teasdale N, Nougier V. The effect of expertise in gymnastics on proprioceptive sensory integration in human subjects. *Neurosci Lett.* 2001; 311: 73-76.
16. Scerpella TA, Davenport M, Morganti CM, Kanaley JA, Johnson LM. Dose related association of impact activity and bone mineral density in pre-pubertal girls. *Calcif Tissue Int.* 2003; 72: 24-31.
17. Daly RM, Bass SL, Finch CF. Balancing the risk of injury to gymnasts: how effective are the counter measures? *Br J Sports Med.* 2001; 35: 8-18.
18. Caine DJ. Injury epidemiology. Sands WA, Caine DJ, Borms J, editors. In: *Scientific Aspects of Women's Gymnastics.* Med Sport Sci. Basel, Karger. 2003; 45: 72-109.
19. Overlin AJ, Chima B, Erickson S. Update on artistic gymnastics. *Curr Sports Med Rep.* 2011; 10: 304-309.
20. Caine DJ, Nassar L. Gymnastics injuries. *Med Sport Sci.* 2005; 48: 18-58.
21. Bennett DL, Nassar L, DeLano M. Lumbar spine MRI in the elite level gymnast. Paper presented at the 2003 USA Gymnastics National Congress: Science in Gymnastics Symposium, Anaheim, CA, August 23, 2003.
22. Goldstein JD, Berger PE, Windler GE, Jackson DW. Spine injuries in gymnasts and swimmers. An epidemiologic investigation. *Am J Sports Med.* 1991; 19: 463-468.
23. Hellstrom M, Jacobsson B, Sward L, Peterson L. Radiologic abnormalities of the thoraco-lumbar spine in athletes. *Acta Radiol* 1990; 31: 127-132.
24. Sward L, Hellstrom M, Jacobsson B, Peterson L. Back pain and radiologic changes in the thoraco-lumbar spine of athletes. *Spine (Phila Pa 1976).* 1990; 15: 124-129.
25. Eynon N, Ruiz JR, Oliveira J, Duarte JA, Birk R, Lucia A. Genes and elite athletes: a roadmap for future research. *J Physiol.* 2011; 589: 3063-3070.
26. Bouchard C, Sarzynski MA, Rice TK, Kraus WE, Church TS, Sung YJ, et al. Genomic predictors of the maximal O₂ uptake response to standardized exercise training programs. *J Appl Physiol (1985).* 2011; 110: 1160-1170.
27. Puthuchery Z, Skipworth JR, Rawal J, Loosemore M, Van Someren K, Montgomery HE. Genetic influences in sport and physical performance. *Sports Med.* 2011; 41: 845-859.
28. Bryan A, Hutchison KE, Seals DR, Allen DL. A transdisciplinary model integrating genetic, physiological, and psychological correlates of voluntary exercise. *Health Psychol.* 2007; 26: 30-39.
29. Chen ZY, Jing D, Bath KG, Ieraci A, Khan T, Siao CJ, et al. Genetic variant BDNF (Val66Met) polymorphism alters anxiety-related behavior. *Science.* 2006; 314: 140-143.
30. Lippi G, Longo UG, Maffulli N. Genetics and sports. *Br Med Bull.* 2010; 93: 27-47.
31. Chan S, Seto JT, MacArthur DG, Yang N, North KN, Head SI. A gene for speed: contractile properties of isolated whole EDL muscle from an alpha-actinin-3 knockout mouse. *Am J Physiol Cell Physiol.* 2008; 295: C897-904.
32. MacArthur DG, North KN. A gene for speed? The evolution and function of alpha-actinin-3. *Bioessays.* 2004; 26: 786-795.
33. North KN, Yang N, Wattanasirichaigoon D, Mills M, Easteal S, Beggs AH. A common nonsense mutation results in alpha-actinin-3 deficiency in the general population. *Nat Genet.* 1999; 21: 353-354.
34. Mills M, Yang N, Weinberger R, Vander Woude DL, Beggs AH, Easteal S, et al. Differential expression of the actin-binding proteins, alpha-actinin-2 and -3, in different species: implications for the evolution of functional redundancy. *Hum Mol Genet.* 2001; 10: 1335-1346.
35. Vincent B, De Bock K, Ramaekers M, Van den Eede E, Van Leemputte M, Hespel P, et al. ACTN3 (R577X) genotype is associated with fiber type distribution. *Physiol Genomics.* 2007; 32: 58-63.
36. Seto JT, Quinlan KG, Lek M, Zheng XF, Garton F, MacArthur DG, et al. ACTN3 genotype influences muscle performance through the regulation of calcineurin signaling. *J Clin Invest.* 2013; 123: 4255-4263.
37. Yang N, MacArthur DG, Wolde B, Onyewera VO, Boit MK, Lau SY, et al. The ACTN3 R577X polymorphism in East and West African athletes. *Med Sci Sports Exerc.* 2007; 39: 1985-1988.
38. Alfred T, Ben-Shlomo Y, Cooper R, Hardy R, Cooper C, Deary IJ, et al. ACTN3 genotype, athletic status, and life course physical capability: meta-analysis of the published literature and findings from nine studies. *Hum Mutat.* 2011; 32: 1008-1018.
39. Ma F, Yang Y, Li X, Zhou F, Gao C, Li M, et al. The association of sport performance with ACE and ACTN3 genetic polymorphisms: a systematic review and meta-analysis. *PLoS One.* 2013; 8: e54685.
40. Eynon N, Hanson ED, Lucia A, Houweling PJ, Garton F, North KN, et al. Genes for elite power and sprint performance: ACTN3 leads the way. *Sports Med.* 2013; 43: 803-817.
41. Ahmetov II, Rogozkin VA. Genes, athlete status and training -- An overview. *Med Sport Sci.* 2009; 54: 43-71.
42. MacArthur DG, North KN. ACTN3: A genetic influence on muscle function and athletic performance. *Exerc Sport Sci Rev.* 2007; 35: 30-34.
43. Yang N, MacArthur DG, Gulbin JP, Hahn AG, Beggs AH, Easteal S, et al. ACTN3 genotype is associated with human elite athletic performance. *Am J Hum Genet.* 2003; 73: 627-631.
44. Massidda M, Vona G, Calo CM. Association between the ACTN3 R577X polymorphism and artistic gymnastic performance in Italy. *Genet Test Mol Biomarkers.* 2009; 13: 377-380.
45. Morucci G, Punzi T, Innocenti G, Gulisano M, Ceroti M, Pacini S. New frontiers in sport training: genetics and artistic gymnastics. *J Strength Cond Res.* 2014; 28: 459-466.
46. Niemi AK, Majamaa K. Mitochondrial DNA and ACTN3 genotypes in Finnish elite endurance and sprint athletes. *Eur J Hum Genet.* 2005; 13: 965-969.
47. Druzhevskaya AM, Ahmetov II, Astratenkova IV, Rogozkin VA. Association of the ACTN3 R577X polymorphism with power athlete status in Russians. *Eur J Appl Physiol.* 2008; 103: 631-634.
48. Coates D. The angiotensin converting enzyme (ACE). *Int J Biochem Cell Biol.* 2003; 35: 769-773.
49. Brink M, Wellen J, Delafontaine P. Angiotensin II causes weight loss and decreases circulating insulin-like growth factor I in rats through a pressor-independent mechanism. *J Clin Invest.* 1996; 97: 2509-2516.
50. Collins M, Xenophontos SL, Cariolou MA, Mokone GG, Hudson DE, Anastasiades L, et al. The ACE gene and endurance performance during the South African Ironman Triathlons. *Med Sci Sports Exerc.* 2004; 36: 1314-1320.
51. Gordon SE, Davis BS, Carlson CJ, Booth FW. ANG II is required for optimal overload-induced skeletal muscle hypertrophy. *Am J Physiol Endocrinol Metab.* 2001; 280: E150-159.
52. Montgomery HE, Marshall R, Hemingway H, Myerson S, Clarkson P, Dollery C, et al. Human gene for physical performance. *Nature.* 1998; 393: 221-222.
53. Danser AH, Schalekamp MA, Bax WA, van den Brink AM, Saxena PR, Riegger GA, et al. Angiotensin-converting enzyme in the human heart. Effect of the deletion/insertion polymorphism. *Circulation.* 1995; 92: 1387-1388.
54. Rigat B, Hubert C, Alhenc-Gelas F, Cambien F, Corvol P, Soubrier F. An insertion/deletion polymorphism in the angiotensin I-converting enzyme gene accounting for half the variance of serum enzyme levels. *J Clin Invest.* 1990; 86: 1343-1346.
55. Baudin B. New aspects on angiotensin-converting enzyme: from gene to disease. *Clin Chem Lab Med.* 2002; 40: 256-265.
56. Williams AG, Dhamrait SS, Wootton PT, Day SH, Hawe E, Payne JR, et al. Bradykinin receptor gene variant and human physical performance. *J Appl Physiol (1985).* 2004; 96: 938-942.

57. Folland J, Leach B, Little T, Hawker K, Myerson S, Montgomery H, et al. Angiotensin-converting enzyme genotype affects the response of human skeletal muscle to functional overload. *Exp Physiol*. 2000; 85: 575-579.
58. Wagner H, Thaller S, Dahse R, Sust M. Biomechanical muscle properties and angiotensin-converting enzyme gene polymorphism: a model-based study. *Eur J Appl Physiol*. 2006; 98: 507-515.
59. Massidda M, Vona G, Calo CM. Lack of association between ACE gene insertion/deletion polymorphism and elite artistic gymnastic performance of Italian gymnasts. *Eur J Sport Sci*. 2011; 11: 149-153.
60. Aucella F, Vigilante M, Margaglione M, Grandone E, del Popolo A, Forcella M, et al. Polymorphism of the angiotensin-converting enzyme gene in end-stage renal failure patients. *Nephron*. 2000; 85: 54-59.
61. Scanavini D, Bernardi F, Castoldi E, Conconi F, Mazzoni G. Increased frequency of the homozygous II ACE genotype in Italian Olympic endurance athletes. *Eur J Hum Genet*. 2002; 10: 576-577.
62. Mansoor A, Mazhar K, Khaliq S, Hameed A, Rehman S, Siddiqi S, et al. Investigation of the Greek ancestry of populations from northern Pakistan. *Hum Genet*. 2004; 114: 484-490.
63. Watkins WS, Ricker CE, Bamshad MJ, Carroll ML, Nguyen SV, Batzer MA, et al. Patterns of ancestral human diversity: an analysis of Alu-insertion and restriction-site polymorphisms. *Am J Hum Genet*. 2001; 68: 738-752.
64. Myerson S, Hemingway H, Budget R, Martin J, Humphries S, Montgomery H. Human angiotensin converting enzyme gene and endurance performance. *J Appl Physiol*. 1999; 87: 1313-1316.
65. Nazarov IB, Woods DR, Montgomery HE, Shneider OV, Kazakov VI, Tomilin NV, et al. The angiotensin converting enzyme I/D polymorphism in Russian athletes. *Eur J Hum Genet*. 2001; 9: 797-801.
66. Tsianos G, Sanders J, Dhamrait S, Humphries S, Grant S, Montgomery H. The ACE gene insertion/deletion polymorphism and elite endurance swimming. *Eur J Appl Physiol*. 2004; 92: 360-362.
67. Woods D, Hickman M, Jamshidi Y, Brull D, Vassiliou V, Jones A, et al. Elite swimmers and the D allele of the ACE I/D polymorphism. *Hum Genet*. 2001; 108: 230-232.
68. Oh SD. The distribution of I/D polymorphism in the ACE gene among Korean male elite athletes. *J Sports Med Phys Fitness*. 2007; 47: 250-254.
69. Taymans SE, Pack S, Pak E, Orban Z, Barsony J, Zhuang Z, et al. The human vitamin D receptor gene (VDR) is localized to region 12cen-q12 by fluorescent in situ hybridization and radiation hybrid mapping: genetic and physical VDR map. *J Bone Miner Res*. 1999; 14: 1163-1166.
70. Pojednic RM, Ceglia L. The emerging biomolecular role of vitamin D in skeletal muscle. *Exerc Sport Sci Rev*. 2014; 42: 76-81.
71. Habuchi T, Suzuki T, Sasaki R, Wang L, Sato K, Satoh S, et al. Association of vitamin D receptor gene polymorphism with prostate cancer and benign prostatic hyperplasia in a Japanese population. *Cancer Res*. 2000; 60: 305-308.
72. Janssen HC, Samson MM, Verhaar HJ. Vitamin D deficiency, muscle function, and falls in elderly people. *Am J Clin Nutr*. 2002; 75: 611-615.
73. Bischoff-Ferrari HA, Borchers M, Gudat F, Durmuller U, Stahelin HB, Dick W. Vitamin D receptor expression in human muscle tissue decreases with age. *J Bone Miner Res*. 2004; 19: 265-269.
74. Kuchuk NO, Pluijm SM, van Schoor NM, Looman CW, Smit JH, Lips P. Relationships of serum 25-hydroxyvitamin D to bone mineral density and serum parathyroid hormone and markers of bone turnover in older persons. *J Clin Endocrinol Metab*. 2009; 94: 1244-1250.
75. Annweiler C, Schott-Petelaz AM, Berrut G, Kressig RW, Bridenbaugh S, Herrmann FR, et al. Vitamin D deficiency-related quadriceps weakness: results of the Epidemiologie De l'Osteoporose cohort. *J Am Geriatr Soc*. 2009; 57: 368-369.
76. Naga Prasad SV, Nienaber J, Rockman HA. Beta-adrenergic axis and heart disease. *Trends Genet*. 2001; 17: S44-49.
77. Morrison AC, Brancati FL, Folsom AR, Smith L, Boerwinkle E. Beta3-adrenergic receptor Trp64Arg polymorphism does not predict incident CHD or carotid intima-media thickness in a community-based sample of whites: the ARIC study. *Atherosclerosis Risk in Communities*. *Hum Genet*. 1999; 105: 314-319.
78. Clément K, Vaisse C, Manning BS, Basdevant A, Guy-Grand B, Ruiz J, et al. Genetic variation in the beta 3-adrenergic receptor and an increased capacity to gain weight in patients with morbid obesity. *N Engl J Med*. 1995; 333: 352-354.
79. Umekawa T, Yoshida T, Sakane N, Kogure A, Kondo M, Honjo H. Trp64Arg mutation of beta3-adrenoceptor gene deteriorates lipolysis induced by beta3-adrenoceptor agonist in human omental adipocytes. *Diabetes*. 1999; 48: 117-120.
80. Ringel J, Kreutz R, Distler A, Sharma AM. The Trp64Arg polymorphism of the beta3-adrenergic receptor gene is associated with hypertension in men with type 2 diabetes mellitus. *Am J Hypertens*. 2000; 13: 1027-1031.
81. Rissanen J, Kuopusjarvi J, Pihlajamaki J, Sipilainen R, Heikkinen S, Vanhala M, et al. The Trp64Arg polymorphism of the beta 3-Adrenergic receptor gene. Lack of association with NIDDM and features of insulin resistance syndrome. *Diabetes Care*. 1997; 20: 1319-1323.
82. Stangl K, Cascorbi I, Laule M, Stangl V, Meisel C, Wernecke KD, et al. The beta3-adrenergic receptor Trp64Arg mutation is not associated with coronary artery disease. *Metabolism*. 2001; 50: 184-188.
83. Tamaki S, Iwai N, Tsujita Y, Nakamura Y, Ohmichi N, Kinoshita M. Variant of the beta3-adrenergic receptor gene and coronary atherosclerosis in Japanese subjects. *Int J Cardiol*. 1999; 69: 309-311.
84. Zafarmand MH, van der Schouw YT, Grobbee DE, de Leeuw PW, Bots ML. T64A polymorphism in beta3-adrenergic receptor gene (ADRB3) and coronary heart disease: a case-cohort study and meta-analysis. *J Intern Med*. 2008; 263: 79-89.
85. Moore GE, Shuldiner AR, Zmuda JM, Ferrell RE, McCole SD, Hagberg JM. Obesity gene variant and elite endurance performance. *Metabolism*. 2001; 50: 1391-1392.
86. Lim BV, Choi KD, Chun GJ, et al. Comparison of relative frequencies of angiotensin-converting enzyme and b3-adrenergic receptor gene polymorphism of athletes in different events. *Kor J Exerc Nutr*. 2006; 10: 216-224.
87. Santiago C, Ruiz JR, Buxens A, Artieda M, Arteta D, Gonzalez-Freire M, Rodriguez-Romo G. Trp64Arg polymorphism in ADRB3 gene is associated with elite endurance performance. *Br J Sports Med*. 2011; 45: 147-149.
88. Kim SM, Oh SD, Jung IG, Lee J, Sim YJ, Lee JK, et al. Distribution of the Trp64Arg polymorphism in the β 3-adrenergic receptor gene in athletes and its influence on cardiovascular function. *Kardiol Pol*. 2010; 68: 920-926.
89. Vuoristo MM, Pihlajamaa T, Vandenberg P, Korkko J, Prockop DJ, Ala-Kokko L. Complete structure of the human COL11A2 gene: the exon sizes and other features indicate the gene has not evolved with genes for other fibrillar collagens. *Ann N Y Acad Sci*. 1996; 785: 343-344.
90. Burgeson RE, Hebda PA, Morris NP, Hollister DW. Human cartilage collagens. Comparison of cartilage collagens with human type V collagen. *J Biol Chem*. 1982; 257: 7852-7856.
91. Oxford JT, Doege KJ, Horton WE Jr, Morris NP. Characterization of type II and type XI collagen synthesis by an immortalized rat chondrocyte cell line (IRC) having a low level of type II collagen mRNA expression. *Exp Cell Res*. 1994; 213: 28-36.
92. Spranger J. The type XI collagenopathies. *Pediatr Radiol*. 1998; 28: 745-750.
93. Blaschke UK, Eikenberry EF, Hulmes DJ, Galla HJ, Bruckner P. Collagen XI nucleates self-assembly and limits lateral growth of cartilage fibrils. *J Biol Chem*. 2000; 275: 10370-10378.
94. Mio F, Chiba K, Hirose Y, Kawaguchi Y, Mikami Y, Oya T, et al. A functional polymorphism in COL11A1, which encodes the alpha 1 chain of type XI collagen, is associated with susceptibility to lumbar disc herniation. *Am J Hum Genet*. 2007; 81: 1271-1277.

95. Koyama K, Nakazato K, Min S, Gushiken K, Hatakeda Y, Seo K, et al. COL11A1 gene is associated with limbus vertebra in gymnasts. *Int J Sports Med.* 2012; 33: 586-590.
96. Roth SM, Rankinen T, Hagberg JM, Loos RJ, Perusse L, Sarzynski MA, et al. Advances in Exercise, Fitness, and Performance Genomics in 2011. *Med Sci Sports Exerc.* 2012; 44: 809-817.
97. Maffulli N, Margiotti K, Longo UG, Loppini M, Fazio VM, Denaro V. The genetics of sports injuries and athletic performance. *Muscles Ligaments Tendons J.* 2013; 3: 173-189.
98. Massidda M, Scorcu M, Calo CM. New genetic model for predicting phenotype traits in sports. *Int J Sports Physiol Perform.* 2014; 9: 554-560.