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Research article

Angiotensin-converting enzyme genotype affects skeletal muscle strength in elite athletes

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Abstract

Previous studies have associated angiotensin-converting enzyme (ACE) D allele with variability in the skeletal muscle baseline strength, though conclusions have been inconsistent across investigations. The purpose of this study was to examine the possible association between ACE genotype and skeletal muscle baseline strength in elite male and female athletes involved in different event expertise. A group of 58 elite athletes, designated as Olympic candidates, were studied: 35 swimmers (19 males and 16 females, 18.8 ± 3.2 years) and 23 triathletes (15 males and 8 females, 18.7 ± 3.0 years). The athletes were classified as: short (≤ 200m) and middle (400m to 1500m) distance athletes, respectively. For each subject the grip strength in both hands was measure using an adjustable mechanical hand dynamometer. The maximum height in both squat jump (SJ) and counter movement jump (CMJ) were also assessed, using a trigonometric carpet (Ergojump Digitime 1000; Digitest, Jyvaskyla, Finland). DNA extraction was obtained with Chelex 100® and genotype determination by PCR-RFLP methods. Both males and females showed significantly higher right grip strength in D allele carriers compared to II homozygote's. We found that allelic frequency differs significantly by event distance specialization in both genders ($p < 0.05$). In fact, sprinter D allele carriers showed the superior scores in nearly all strength measurements ($p < 0.05$), in both genders. Among endurance athletes, the results also demonstrated that female D allele carriers exhibited the higher performance right grip and CMJ scores ($p < 0.05$). In conclusion, the ACE D allele seems associated with skeletal muscle baseline strength in elite athletes, being easily identified in females.

Key words: swimming; triathlon; genetic polymorphism; sport performance.

Introduction

Numerous studies have attempted to quantify the genetic contribution of physical phenotypes to skeletal muscle strength (Beunen and Thomis, 2004). Based on simple differences of muscle mass (Seeman et al., 1996) or by other factors (Narici et al., 1989), a strong influence of genetic variation in muscle function has been recognized (Beunen and Thomis, 2004). However, few specific candidate genes have been identified as being significant to the response of muscle phenotypes (Rankinen et al., 2006). One gene that has emerged as a candidate is angiotensin-converting enzyme (ACE gene). The ACE gene performs a key role in the regulation of the renin-angiotensin-aldosterone system (RAS). ACE catalyzes the conversion of angiotensin I to angiotensin II and has an important role on electrolyte balance and systemic blood pressure (Rieder et al., 1999).

Most of the published data focuses on a polymorphism (Rigat et al., 1990), which describes the presence (insertion, I allele) or absence (deletion, D allele) of a 287-bp sequence in intron 16, resulting in three genotypes: II and DD, homozygote's, and ID, heterozygous. Although this polymorphism occurs in an intron it is an exceptionally strong and consistent marker for ACE activity in serum and tissues (Rigat et al., 1990) in different Caucasian populations.

Skeletal muscle has substantial ACE activity owing to local RAS activity (Reneland and Lithell, 1994). Investigators have linked high levels of angiotensin II to overload-induced cardiac hypertrophy (Sadoshima et al., 1993; Montgomery et al., 1997; McEwan et al., 1998; Myerson et al., 2001; Silva et al., 2006) and smooth muscle hypertrophy (Berk et al., 1989; Gray et al., 1998). Other studies provide evidence of the potential importance of the RAS and ACE gene to skeletal muscle hypertrophy in response to overload (Gordon et al., 2001; Werterkamp and Gordon, 2005; McBride, 2006). However, studies investigating the effects of ACE genotype on skeletal muscle strength and mass in response to strength training have yielded inconsistent results.

In respect to skeletal muscle baseline strength, Zhang et al. (2003) showed a linear trend between decreases in type I fibers and increases in type IIb fibers from ACE II to ID and to DD genotypes. These findings have been proposed as a potential mechanism for the association between the ACE D allele and power-oriented athletic performance (Woods et al., 2001; Nazarov et al., 2001; Tsianos et al., 2004; Costa et al., 2008). In fact, Hopkinson et al. (2004) and Williams et al. (2005) reported these positive associations between the D allele and muscle strength. However, other authors (Thomis et al., 2004; Pescatello et al., 2006; Moran et al., 2004) failed to support such findings.

The influence of genes on phenotypes relevant to sports performance varies, in its significance, in response

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Table 1. Subject characteristics by gender and event distance expertise. Data presented as means (± standard deviation).

		AO (athletes overall)	(n)	SDA (≤200m)	(n)	MDA (≥400m)	(n)
Age (years)	**Male**	19.8 (3.1)	34	21.1 (2.9)	14	18.9 (3.0)	20
	Female	17.2 (2.3)	24	17.5 (2.9)	8	17.1 (2.1)	16
Height (m)	**Male**	1.78 (.07)	34	1.82 (.06)	14	1.75 (5.5)	20
	Female	164.7 (4.5)	24	1.65 (.04)	8	1.65 (4.7)	16
Mass (kg)	**Male**	71.0 (8.3)	34	77.4 (5.4)	14	66.5 (6.9)	20
	Female	56.2 (4.7)	24	56.7 (4.5)	8	56.0 (4.9)	16

AO = athletes overall; SDA = short distance athletes; MDA = medium distance athletes.

to several factors, particularly age. In this regard, studies in twins have shown that the hereditary influence is higher in younger groups, where the environment may be more homogeneous and less time to have any significant effects. Consequently, in adult athletes the effect of training specialization since puberty may difficult the recognition of an interaction between a candidate gene and phenotypic variability. The authors consider this an important issue that warrants consideration. Therefore, it is unclear whether similar findings regarding the ACE D allele effects on baseline muscle strength capacity (Thomis et al., 2004; Pescatello et al., 2006; Moran et al., 2004) can apply to elite athletes and whether these results can be reproducible in both genders or in different event expertise.

Given the data indicating a possible role for ACE in muscle strength and the findings of some studies that ACE genotype is associated with muscle phenotypes, the aim of this study was to investigate the association between ACE genotype and skeletal muscle strength in elite male and female athletes involved in different duration swimming events.

Methods

Subjects

58 elite Portuguese athletes from both genders were selected. The study sample groups included 35 swimmers (19 males and 16 females, 18.8 ± 3.2 years) and 23 triathletes (15 males and 8 females, 18.7 ± 3.0 years), representing over than 80% of the Olympic candidates by their sport Federation.

Accordingly to the characterization survey these elite athletes trained 9.3 ± 0.4 sessions per week including 3.2 ± 0.8 strength training units. All strength measurements were made immediately before main international or national competitions to ensure that all athletes would be in a state of good overall performance.

The athletes were stratified by gender and, additionally, into two homogeneous groups, based on their current distance event of expertise: short distance athletes (SDA), between 50 and 200m (mainly anaerobic events) and middle distance athletes (MDA), 400 to 1500m (mixed anaerobic and aerobic events). Thus, the SDA group includes only sprint elite swimmers. Even though all known elite endurance Portuguese swimmers were included for analysis, it was necessary to enlarge this middle/long distance group (particularly in males). Therefore, we included in this MDA group the elite Portuguese triathletes, being almost all ex-middle/long distance swimmers (Table 1 and Figure 1).

All subjects and their parents (in the under 18 years old subjects) were informed, in advance, about the procedures and asked to sign a term of consent that had been approved by local health sciences research ethics committee and carried out according to the Helsinki Declaration.

Experimental approach to the problem

The D allele is associated with power-oriented performance, and has been found in excess in swimmers overall (Woods et al., 2001) and particularly in short-distance swimmers (Nazarov et al., 2001; Tsianos et al., 2004). It is accepted that considerable human variation exists in the

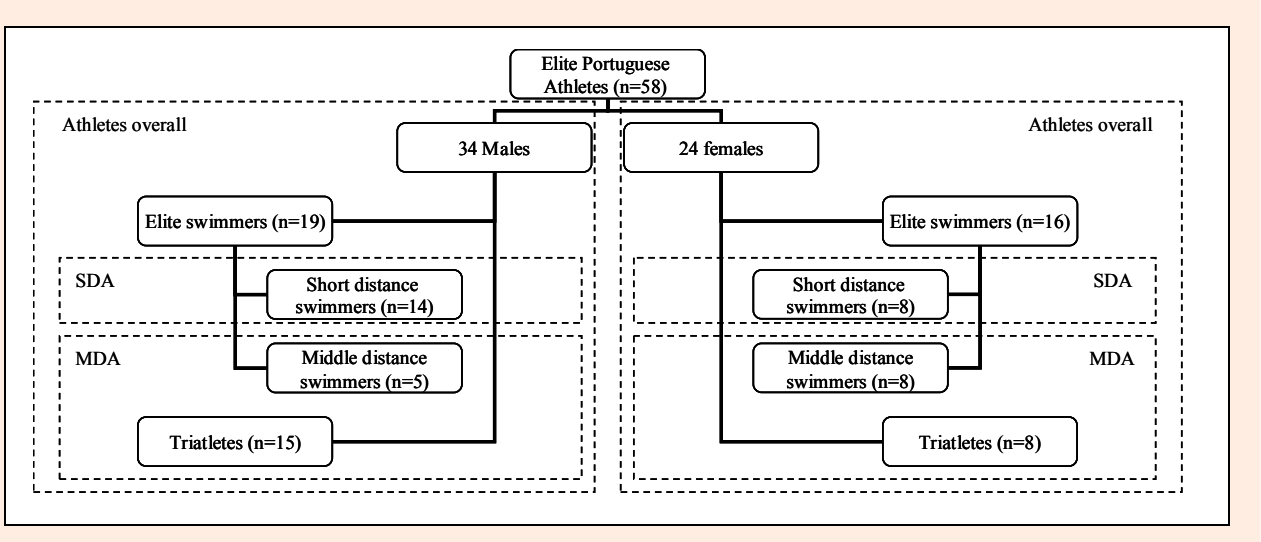

Figure 1. Study sample stratification.

capacity to perform physical tasks maximally over a short period of time. Elite sprint athletes of a given sport are able to accomplish more work during maximal exercise of short duration than age and sex matched athletes involved in endurance tasks (Serresse et al., 1989). Competitive swimming is not an exception. In this way, the authors intended to study if ACE genotype is associated with strength in elite male and female athletes and, when studied by their event distance of specialization.

The relevance of strength and power in short distance events is unquestionable. However, the importance of strength effects in combination with endurance training remains vague. The study of Millet et al. (2002) is one of the few recent studies that have sought to establish this relationship, particularly in triathletes. The results showed that additional heavy weight training led to improve maximal strength and running economy, with no significant effects on the O2 kinetics pattern in heavy exercise (Millet et al., 2002).

The ability to measure phenotypes that reflect physical function with relatively high heritability and which can be measured in large samples has attracted considerable interest (Frederiksen et al., 2002). Additionally, phenotypes focused on one muscle group may give partial information about the heritability of muscle strength in the whole body (Tiainen et al., 2004). Also, regarding to ACE gene, it is not known if there is a general simultaneous influence on strength in multiple muscle groups or if the lack of association reported by several studies is due to differently degree of ACE gene contribution in varied muscle groups.

An evaluation process requires reliability and facility of application, especially when elite athletes spend much time competing and traveling between training and competition events. Consequently, the following tests were select to minimize possible interference with the competition schedule and that could be rapidly administered: (i) hand grip isometric strength, long used as a measure of total body strength (Carmelli and Reed, 2000; Foo, 2007) and, recently, associated with swimming performance in young (Geladas, Nassis e Pavlicevic, 2005) and elite master swimmers (Zampagni et al., 2008); (ii) maximum vertical jump, as a good estimate of lower extremity power output (Markovic et al., 2004; Marques et al., 2008) and possibly associated with the skill to perform a stronger impulse and less time contact with the wall during swimming turns (Chow et al., 1984; Blanksby, Gathercole and Marshall, 1995). Furthermore, both strength parameters have been long included in some specific batteries of swimmers evaluation (Silva et al., 2007).

DNA analysis

Blood was collected in regular filter paper by finger blood spot (Albet, DP 400200) and the samples were dried at room temperature and stored in separate plastic bags at 4ºC until DNA extraction. DNA was extracted by Chelex 100® (BioRad Laboratories, Hercules, CA) protocol (Walsh et al., 1991). To evaluate the extraction technique, a negative control was always used.

ACE genotyping

The ACE I/D polymorphism was genotyped using conditions previously described (Tiret et al., 1992). Reaction products were visualized by electrophoresis on 2% agarose gel and identified by ethidium bromide staining. Based on gel visualization against UV light, three ACE ID genotypes were identified: II – a 490 bp band; DD – a 190 bp band; and heterozygote ID – the presence of both 490 and 190 bp bands.

Anthropometric measurements

The anthropometric measures were registered according to the International Working Group on Kinanthropometry methodology described by Ross and Marfell-Jones (1991).To evaluate height (cm) a stadiometer (SECA, model 225, Germany) with a range scale of 0.10 cm was used and body mass (kg) was measured to the nearest 0.1 kg using a digital scale (Philips, type HF 351/00).

Strength measurement protocols and variables:

Grip strength was measured with an adjustable mechanical hand dynamometer (Lafayette Instrument, Lafayette, IN) and expressed in kilograms (kg). The American Society of Hand Therapists recommendations for testing grip strength were followed (Mathiowetz et al., 1984). Subjects were encouraged to exert their maximal grip in three trials, with brief pauses, for each hand alternately. The average result was chosen for analysis (Haidar et al., 2004).

A trigonometric carpet (Ergojump Digitime 1000; Digitest, Jyvaskyla, Finland) was used to access maximum height in both squat jump (SJ) and countermovement jump (CMJ), according to Bosco (1994) procedures. For each type of jump was allowed three attempts, with two minutes of recovery. The average maximum height of three trials was considered and expressed in centimeters (cm).

Due to the high correlation between the vertical jump and the body weight mentioned in literature (Weiss et al., 1997), the authors decided to present both jump measurements (SJ and CMJ) in their absolute value (m) and when normalized to the body mass of each subject: SJn (m.kg-1) and CMJn ($m \cdot kg^{-1}$).

Prior to baseline tests, each subject underwent one familiarization session and was counseled on proper exercise technique, as well as stretching and an appropriate warm up. This familiarization served to validate particularly the measured SJ and the CMJ by preventing the large gains that tend to occur as the subjects learn the testing procedure.

Statistical analyses

All data for this study were analyzed using SPSS computer software for Windows (version 12.0). Allele frequencies were estimated by gene-counting method. Genotype distribution and allele frequencies between groups were compared by Chi-Square test. Statistical analysis for this investigation used Mann Whitney's U to compare the means among ACE D-allele carriers and non-carriers (II genotype vs. ID+DD genotypes). D allele carriers were grouped together to allow for easy comparison with other

Table 2. ACE genotype distribution and allele frequencies of the athletes.

Subjects		N	ACE genotype			Allele frequency	
			DD	ID	II	D	I
AO (athletes overall)	Male	34	15 (.54)	14 (.41)	5 (.15)	.65	.35
	Female	24	10 (.42)	9 (.37)	5 (.21)	.60	.40
SDA (≤200m)	Male	14	9 (.64)	5 (.36)	0 (.00)	.82	.18
	Female	8	4 (.50)	4 (.50)	0 (.00)	.75	.25
MDA (≥400m)	Male	20	6 (.30)	9 (.45)	5 (.25)	.53	.47
	Female	16	6 (.38)	5 (.31)	5 (.31)	.53	.47

studies that performed similar analyses. Furthermore, analyses of the data across the three genotype groups were done by Kruskal Wallis Tests. Male and female subjects were analyzed separately given known gender-specific influences of ACE genotype on phenotypic measures (O'Donnell et al., 1998; Crawford et al., 2000).

All other data are presented as least squared means ± standard error. Statistical significance for all analyses was as accepted at $p \leq 0.05$.

Results

A total sample of 58 subjects was studied and their characteristics are presented in Table 1; no significant differences were observed among groups ($p > 0.05$).

Data obtained for both genotype and allele distributions analysis is showed in Table 2.

The results obtained for the genotype distributions and allelic frequencies showed that there were no statistical differences between male and female athletes ($p > 0.05$) among the samples groups consider. However, we were able to verify that allelic frequencies of elite SDA were significant different towards MDA in males ($p = < 0.001$) and females ($p = 0.002$).

As noted in Table 3, the right and left grip strength in males differed significantly among swimming event expertise (SDA vs. MDA, $p = 0.000$ and $p = 0.009$, respectively). In females, none of the strength parameters (assuming the normalized SJn and CMJn as preferential for analysis) differed significantly by event specialization. Nevertheless, when we exclude the II homozygote's, the differences between athletic specialties became entirely obvious (particularly in females); in fact, the SDA D allele carriers and the DD homozygote's in males and females (respectively) showed superior scores in nearly all strength measurements ($p < 0.05$).

Given the lack of II homozygote's (see Table 2) in the SDA, further inferential analysis on this sub-group was not practicable. Consequently, in both genders the analysis was only considered for: (i) the athletes overall group (AO) and, (ii) the middle distance athletes (MDA, > 400 m) sub-group.

As noted in Table 4, analysis of the male cohort by genotype group pointed out no significant differences ($P \geq 0.05$) for all strength measurements.

In females (Table 5), there were significant differences found between genotype groups (DD, ID, II) for right grip, however just for middle distance athletes (MDA, $P = 0.026$).

Table 6 shows the statistical differences analysis for all strength measurements between the two separate genotype groups (II homozygote's and D allele carriers) and among ACE homozygote's (DD vs. II), separated by males and females.

In both genders, right grip strength was significantly ($p \leq 0.05$) higher in DD homozygote's and even in D allele carriers than II homozygote's. This trend remains significant between the D allele carriers and II homozygotes in female endurance athletes (MDA) as well ($p = 0.032$). Furthermore, the female D allele carriers jump significantly higher in CMJ than the II homozygotes ($p = 0.048$), though not found when adjusted for body mass (CMJn, $p = 0.136$) or amongst the endurance specialists (MDA).

Discussion

We raise the hypothesis that the D allele of the ACE gene may contribute to higher levels of strength between athletes of the same age, gender, status and sporting discipline. This hypothesis was partially supported, by the association between grip strength with D allele carriers in both genders. Though, only in females this strength parameter varied significantly across genotype ($p = 0.026$). The results also revealed a tendency for female carriers of the D allele to have greater lower extremity power, although limited to AO group and to CMJ in their absolute value ($p = 0.048$).

The conflicting association results between ACE genotype and muscle phenotypes in several studies could be due to the heterogeneity of the study cohorts (Woods et al., 2000; Macarthur and North, 2005). In this respect, we first certified if all strength measurements not differed significantly between the two swimming distance

Table 3. Statistical differences between SDA and MDA for strength measurements in males and females by ACE genotype.

	Males			Females		
SDA vs. MDA	DD+ID+II	DD+ID	DD	DD+ID+II	DD+ID	DD
Right grip (kg)	.000 *	.001 *	.015 *	.400	.954	1.000
Left grip (kg)	.009 *	.044 *	.238	.365	.656	.268
SJ (m)	.002 *	.001 *	.011 *	.042 *	.091	.027 *
SJn ($m \cdot kg^{-1}$)	.489	.358	.045 *	.107	.155	.050 *
CMJ (m)	.005 *	.002 *	.045 *	.003 *	.011 *	.027 *
CMJn ($m \cdot kg^{-1}$)	.716	.550	.157	.020 *	.051	.050 *

SDA = short distance athletes; MDA = medium distance athletes. * $p \leq 0.05$.

Table 4. Muscle strength in males grouped by ACE genotype. Data presented as means (± standard deviation).

		DD	n	ID	n	II	(n)	P-value
Right grip (kg)	AO	52.90 (7.45)	15	52.62 (6.05	14	43.80 (6.18)	5	.063
	SDA	56.72 (5.40)	9	56.80 (4.78	5	-	0	-
	MDA	47.17 (6.56)	6	50.00 (5.42	9	43.80 (6.18)	5	.350
Left grip (kg)	AO	50.40 (7.94)	15	49.19 (6.36	14	39.20 (5.85)	5	.052
	SDA	52.50 (6.88)	9	51.50 (6.20	5	-	0	-
	MDA	47.25 (9.00)	6	47.75 (6.41	9	39.20 (5.85)	5	.232
SJ (m)	AO	.340 (.064)	15	0.317 (.038	14	.312 (.070)	5	.386
	SDA	.375 (.047)	9	.336 (.019	5	-	0	-
	MDA	.287 (.049)	6	.305 (.043)	9	.312 (.070)	5	.870
SJn (m·kg^{-1})	AO	.0046 (.0009)	15	.0045 (.0006)	14	.0049 (.0010)	5	.874
	SDA	.0050 (.0008)	9	.0041 (.0002)	5	-	0	-
	MDA	.0040 (.0009)	6	.0047 (.0006)	9	.0049 (.0010)	5	.183
CMJ (m)	AO	.388 (.068)	15	.348 (.037)	14	.353 (.071)	5	.215
	SDA	.416 (.058)	9	.376 (.019)	5	-	0	-
	MDA	.347 (.064)	6	.330 (.034)	9	.353 (.071)	5	.634
CMJn (m·kg^{-1})	AO	.0053 (.0011)	15	.0049 (.0005)	14	.0056 (.0015)	5	.681
	SDA	.0055 (.0009)	9	.0047 (.0004)	5	-	0	-
	MDA	.0049 (.0014)	6	.0051 (.0006)	9	.0056 (.0015)	5	.558

AO = athletes overall; SDA = short distance athletes; MDA = medium distance athletes; N = number of subjects.

expertise groups (Table 3). In fact, only in males the right and left grip strength differed significantly among swimming event expertise; for that reason, its data should be treated with caution when viewed alone. However, when we compare the strength measurements (SDA vs. MDA) without the II homozygotes, these differences become quite evident in both genders (Table 3). Assuming that the SDA sub-group is much more stimulated with specific power-oriented training, these results might sustain an association of the ACE D allele with improved strength training response, as reported previously by other authors (Williams et al. 2005).

The sprinter's subgroup (≤200m) was removed from the analysis given the lack of II homozygotes. This restriction hinders our ability to conclude if the ACE gene is associated with baseline muscle strength in any case of swim event specialization (*intra-group analysis)*. Although, the excess of the D allele frequency observed (table 2) seem convergent with several studies in elite swimmers overall (Woods et al., 2001) but mostly in those who compete in shorter distances events (Nazarov et al., 2001). Even so, among our endurance female athletes (MDA), the D allele also appears to add same influence in grip strength ($p = 0.032$). This result highlight the effect of this polymorphism in muscular strength even under different environmental factors associated with training specialization. In fact, it would be really interesting if it had been possible for us to verify this influence in the SDA subgroup. In sprint athletes, the influence of the I/D polymorphism in baseline muscle strength would be much more difficult to determine, because rivals with the effects resulting from their training specialization (where the difference in strength will have substantially more impact on the athlete´ performance). Indubitably, this is an important limitation of the present study that warrants reflection. Nevertheless, we trust that our data are innovative and important as it sets, truly, the consequent need for studies to confirm our preliminary results.

Table 5. Muscle strength in females grouped by ACE genotype. Data presented as means (± standard deviation).

		DD	n	ID	n	II	(n)	P-value
Right grip (kg)	AO	38.44 (4.85)	10	34.28 (4.58)	9	29.80 (4.77)	5	.026 *
	SDA	39.25 (1.50)	4	33.63 (5.71)	4	-	0	-
	MDA	37.80 (6.65)	6	34.80 (4.09)	5	29.80 (4.77)	5	.098
Left grip (kg)	AO	35.28 (4.65)	10	31.56 (4.70)	9	29.60 (4.72)	5	.128
	SDA	36.38 (1.49)	4	30.75 (4.79)	4	-	0	-
	MDA	34.40 (6.27)	6	32.20 (5.07)	5	29.60 (4.72)	5	.440
SJ (m)	AO	.263 (.053)	10	.253 (.030)	9	.232 (.028)	5	.476
	SDA	.305 (.040)	4	.251 (.028)	4	-	0	-
	MDA	.229 (.035)	6	.256 (.034)	5	.232 (.028)	5	.461
SJn (m·kg^{-1})	AO	.0048 (.0010)	10	.0044 (.0006)	9	.0042 (.0008)	5	.624
	SDA	.0056 (.0008)	4	.0043 (.0007)		-	0	-
	MDA	.0041 (.0007)	6	.0045 (.0005)	5	.0042 (.0008)	5	.512
CMJ (m)	AO	.280 (.059)	10	.262 (.024)	9	.231 (.026)	5	.138
	SDA	.325 (.054)	4	.273 (.015)	4	-	0	-
	MDA	.244 (.033)	6	.253 (.027)	5	.231 (.026)	5	.505
CMJn (m·kg^{-1})	AO	.0051 (.0011)	10	.0046 (.0006)	9	.0042 (.0006)	5	.205
	SDA	.0059 (.0011)	4	.0047 (.0007)	4	-	0	-
	MDA	.0044 (.0006)	6	.0044 (.0005)	5	.0042 (.0006)	5	.733

AO = athletes overall; SDA = short distance athletes; MDA = medium distance athletes; N = number of subjects. * $p \leq 0.05$.

Table 6. Statistical differences for strength measurements in males and females by ACE genotype. Data presented as means (± standard deviation).

		Males		Females	
		DD vs. II	DD+ID vs. II	DD vs. II	DD+ID vs. II
Right grip (kg)	AO	.020 *	.021 *	.011 *	.021 *
	MDA	.272	.175	.059	.032 *
Left grip (kg)	AO	.023 *	.018 *	.082	.167
	MDA	.169	.088	.251	.244
SJ (m)	AO	.407	.514	.230	.233
	MDA	.584	.853	.834	.668
SJn (m·kg^{-1})	AO	.631	.616	.317	.412
	MDA	.201	.405	.917	.806
CMJ (m)	AO	.432	.940	.109	.048 *
	MDA	.715	.405	.530	.297
CMJn (m·kg^{-1})	AO	.896	.616	.162	.136
	MDA	.465	.517	.917	.462

AO = athletes overall; MDA = medium distance athletes. * $p \leq 0.05$.

Among men, this apparent steadiness of the D allele contribution in grip strength is not replicated: in MDA the left grip did not differ significantly ($p > 0.05$) among the three genotypes or between D allele carriers and II homozygote's. Additionally, none of vertical jumps differed significantly ($p > 0.05$) among males for all the considered genotype groups. This could sustain that the components of the skeletal muscle tissue-based RAS are markedly affected by gender (Fischer et al., 2002). This finding may be attributed to a down-regulation of renin (Danser et al., 1998; Schunkert et al., 1997) and ACE (Proudler et al., 1995; Schunkert et al., 1997) as well as the AT-1 receptor (Nickenig et al., 1998; Roesch et al., 2000) by the presence of estrogen found naturally in these young women and, in males, the linear relationship that seems to exist between the level of testosterone and the plasma renin activity (Ellison et al., 1989).

To the authors' knowledge, this is the first case report to describe an association between ACE gene and baseline strength in elite strength-trained athletes. The two previous studies that reported this positive association were done in healthy untrained subjects (Williams et al., 2005) and in Caucasian patients with a diagnosis of chronic obstructive pulmonary disease (Hopkinson et al., 2004), and only check for quadriceps muscle strength. Williams et al (2005) study, particularly, concluded that those with the most circulating ACE, DD homozygote's were the strongest, whereas those with lower ACE levels, II homozygote's, were the weakest. This results were significantly correlated with isokinetic ($r = 0.38$, $p < 0.0005$) but also isometric ($r = 0.25$-0.29, $p < 0.02$) quadriceps muscle strength.

In contrast, Thomis et al. (2004), Pescatello et al. (2006) failed to support such findings. These previous studies concluded that baseline isokinetic, isometric and isotonic muscle strength were not associated with ACE genotype in either the upper arm (Pescatello et al., 2006; Thomis et al., 2004) or the quadriceps. However, there are some important limitations in these studies. For the most part, small sample sizes were considered. The two studies that investigated leg training protocols (Williams et al., 2005) also had inconsistency between their testing protocols. In respect to the upper arm strength, the large-scale study by Pescatello et al., 2006 did not report separate analyses for sex- or race-based subgroup, and didn't referred to the hand grip strength, been shown to be a highly heritable phenotype (Reed et al., 1991).

Moran et al's (2004) study in teenage Greeks reported a strong association ($p < 0.001$) between the ACE I/D polymorphism and both handgrip strength and vertical jump in females. These gender specific differences observed appears to be consistent with our results, although were the homozygotes for the I-allele exhibiting the higher performance-related phenotype scores. Moran et al. (2004) interpreted handgrip strength and vertical jump as activities having many different components including strength/power (upper limb and lower body, respectively) and skill. Therefore, how easily I/D polymorphism effect strength will depend on the relative importance of given component to the specific performance-related test.

Based on our results, we add to this assumption that ACE genotype will influence strength in a different way depending also on the subject's physical activity level. In untrained subjects, general performance strength tests would be highly reliant on skill, besides strength itself. Conversely, in elite trained athletes, the component strength/power will contribute for the most part to phenotypic variance. Further research is necessary to clear of the involvement of the ACE gene in human performance.

The plausible mechanism through which ACE genotype affects skeletal muscle strength is through production of angiotensin II. Skeletal muscle hypertrophy has been shown in animal models to be correlated with angiotensin II in the presence of overload (Gordon et al., 2001; Westerkamp and Gordon, 2005), specifically through the AT1 receptors (McBride, 2006). These studies provide a biological rationale for explaining a potential role for ACE genotype in affecting muscle size.

However, as we know, the hypertrophy is not the only mechanism for improving muscle strength (Garfinkel and Cafarelli, 1992; Hakkinen et al., 1998). A significant share of responsibility in this matter must be endorsed to morphological and neuromuscular changes (Jones, 1992; Narici et al., 1989). In so doing, it is interesting to note that angiotensin II may also be important in the redirection of blood flow from type I muscle fibers to the type II fibers (Rattigan et al., 1996) that are favored in power performance. Greater local Ang II production would therefore facilitate muscle contraction for maximal power (Rattingan et al., 1996) while having potentially deleteri-

ous effects on efficiency and endurance (Montgomery et al., 1999; Williams et al., 2000). Other actions of Ang II that might influence performance include the facilitation of sympathetic transmission by enhancing noradrenaline release from peripheral sympathetic nerve terminals and the center nervous system (Saxena, 1992).

The lack of a measure of muscle volume restrict us to elucidate whether our results are due to relatively preserved regional muscle size and/or greater specific tension i.e. improved strength per unit of muscle. Arguments can be advanced for both mechanisms (Jones, 1992; Narici et al., 1989). Further research is necessary to clear of this limitation and to elucidate the molecular mechanisms explaining the involvement of the ACE gene in highly trained subject's performance.

Conclusion

We have hypothesized that ACE genotype would be associated with muscle strength in elite male and female athletes. Our data indicated significant higher grip strength in D allele carriers from both genders. The sprinter D allele carriers in both genders were the one's that showed the better scores in nearly all strength measurements ($p < 0.05$). Among endurance athletes, the results also showed that female D allele carriers exhibited the higher performance right grip ($p < 0.05$) and counter-movement jump scores. The ACE genotype effect in skeletal-muscle baseline strength appears to be supported by our data, being easily identified in females.

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Key points

- DD homozygote's and D allele carriers from both genders shows significantly higher right grip strength.
- Right grip strength remains significantly higher in the D allele carrier's female endurance group.
- Female's D allele carriers exhibited the higher performance counter-movement jump scores.
- ACE genotype effects in skeletal-muscle strength are diverse by gender, being easily identified in females.

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