LETTER

Increased frequency of the homozygous II ACE genotype in Italian Olympic endurance athletes

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Angiotensin-converting enzyme (ACE, EC 3.4.15.1) plays an important role in the circulatory homeostasis by generating the potent vasoconstrictor angiotensin II and degrading the vasodilator bradykinin.¹ An insertion polymorphism in the gene coding for ACE² has been reported to be associated with decreased ACE activity³ as well as with improved physical performance.⁴ The insertion (I) allele turned out to be over-represented among high-altitude mountaineers⁴ and carriage of at least one I allele was associated with improved endurance among males recruited in the UK army.⁴ Among elite endurance athletes, a significantly higher frequency of the I allele was reported in 64 Australian rowers,⁵ 79 British Olympic-standard runners selected as potential Olympic competitors⁶ and 60 Spanish athletes,⁷ as compared with controls. Conversely, an excess of the deletion (D) allele has been reported among elite athletes competing in more power-oriented sports such as short distance swimming^{6,8} and sprinting.⁶

Therefore, recruitment of athletes from mixed disciplines may result in lack of association between the ACE polymorphism and physical performance,^{9,10} as recently pointed out by Nazarov *et al.*¹¹ In that study, the ACE genotype/allele distribution of all athletes was not different from that of controls, but an excess of the D allele was observed among sprinters (short distance athletes) and an excess of

the I allele among athletes competing over 1 to 20 min (middle distance athletes).¹¹

We have investigated the distribution of ACE genotypes in 126 Italian athletes (101 males and 25 females aged between 18 and 35 years) designated as 'candidate Olympic athletes' by their own Sport Federations. The ACE genotype frequency distribution of all athletes did not differ from that of 152 healthy Italian subjects aged between 16 and 40 years. The study group included 71 'aerobic' athletes (26 road cyclists, 17 track and field endurance athletes, 28 cross-country skiers), who can be classified as 'long distance athletes',¹¹ and 55 'anaerobic' flat-water kayak athletes (racing times between 30 and 210 s). Genotype and allele frequencies of aerobic and anaerobic athletes did not differ from those of the control group. Comparison between the athlete groups showed a significant difference for genotypes ($P=0.03$) but not for alleles (Table 1).

Among the 126 athletes we further selected an elite group of 52 (33 aerobic and 19 anaerobic), based on actual participation in the Olympic Games (14 Olympic Medalists, six of which won the gold medal; nine World Champions) and top aerobic performance ($VO_{2\max}$ values between 65 and 80 ml/Kg for aerobic athletes, and between 40 and 55 for anaerobic athletes). The selection was made by a person (GM) that was unaware of the athletes' ACE

Table 1 ACE genotypes in Italian athletes

		DD		ID		II	
		<i>n</i>	%	<i>n</i>	%	<i>n</i>	%
Aerobic athletes							
All aerobic athletes	<i>n</i>	71	39.4	28 [#]	39.4	15 [#]	21.1
Olympic aerobic athletes	<i>n</i>	33	39.4	10 ^{§*}	30.3	10 ^{§*}	30.3
Road cyclists	<i>n</i>	10	40.0	4	40.0	2	20.0
Track and field runners	<i>n</i>	7	28.6	2	28.6	3	42.8
Cross-country skiers	<i>n</i>	16	43.7	4	25.0	5	31.3
Anaerobic athletes							
All flat-water kayakers	<i>n</i>	55	38.2	31 [#]	56.4	3 [#]	5.5
Olympic flat-water kayakers	<i>n</i>	19	36.8	11 [*]	57.9	1 [*]	5.3
Healthy population							
	<i>n</i>	152	44.1	66 [§]	43.4	19 [§]	12.5

The I/D ACE gene polymorphism was investigated as described² and confirmed by means of a second PCR amplification that selectively detects the I allele.¹⁴ DD, homozygotes for the deletion allele; II, homozygotes for the insertion allele; ID, heterozygotes. [#] $\chi^2=7.238$, exact $P=0.03$ for genotype frequencies in all kayakers vs all aerobic athletes. [§] $\chi^2=6.755$, exact $P=0.03$ for genotype frequencies in aerobic Olympic athletes vs healthy population. ^{*} $\chi^2=5.867$, exact $P=0.05$ for genotype frequencies in Olympic kayakers vs Olympic aerobic athletes.

genotypes. The II genotype was more frequent in the 33 Olympic aerobic athletes than in the 19 Olympic anaerobic athletes (Table 1). In addition, the genotype distribution in the aerobic group differed significantly from that of controls, whose distribution was very similar to that observed in 1307 normal Italian subjects.¹²

These findings, obtained by selecting subjects with top endurance characteristics, confirm the association of the II genotype with improved aerobic performance, and extend the results of Nazarov *et al.*¹¹ to long distance athletes.

Although it has been suggested that the higher ACE II genotype frequency in endurance athletes could reflect the selection of individuals with a 'healthier' cardiovascular system and improved aerobic capacity,⁹ a physiological explanation for the association between ACE genotype and endurance phenotypes is not available at present.⁹ Increased O₂ or substrate availability as well as improved mitochondrial metabolism,^{4,13} are plausible candidates to explain the positive selection of this genotype among elite athletes.

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