Elite athletes and the gene for angiotensin-converting enzyme

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1Departments of Cardiology and Medicine, Royal Perth Hospital and The University of Western Australia, Perth, Western Australia 6001; 2Department of Biochemistry, Royal Perth Hospital, Perth, Western Australia 6001; 3Australian Institute of Sport, Belconnen, Australian Capital Territory 2616; and 4Department of Pathology, The University of Western Australia, Nedlands, Western Australia 6009, Australia

Taylor, Roger R., Cyril D. S. Mamotte, Kieran Fallon, and Frank M. van Bockxmeer. Elite athletes and the gene for angiotensin-converting enzyme. J. Appl. Physiol. 87(3): 1035–1037, 1999.—The deletion (D) allele of the gene for angiotensin-converting enzyme (ACE) is associated with higher plasma and tissue levels of the enzyme and has also been related to a variety of cardiovascular complications, particularly myocardial infarction. On the basis of indirect evidence, we hypothesized that inheritance of the D allele would contribute to elite athletic ability. Over a period of 4 yr, 120 Caucasian athletes who were national (Australian) representatives in sports demanding a high level of aerobic fitness were recruited. Their ACE genotypes were compared with those of a community control group recruited randomly from the electoral roll. There was no difference in ACE genotype frequencies between the two groups. The DD genotype frequency was 30% in athletes and 29% in the control group, and the II genotype frequency was 22.5 and 22%, respectively. The results do not exclude the possibility that ACE genotype could be related to some attribute relating to a specific type of elite athletic ability or that there may be a difference between genders. Larger studies are desirable.

deletion allele; insertion allele; inheritance; physical performance

METHODS

The study group of 81 men and 39 women, aged 30±14 (SD) yr, recruited from 1994 to the present, was restricted to those who were, or had been, national (Australian) representatives in highly aerobic sports (hockey, 26; cycling, 25; skiing, 21; track and field, 15; swimming, 13; rowing, 7; gymnastics, 5; other, 8). That is, participants in sports in which a high level of physical performance was not required, such as archery and pistol shooting, or those, such as weight lifting, requiring primarily muscular strength, were not included. Their results were compared with those of a community control group of healthy subjects, aged 40±6 yr, recruited from the electoral roll (347 men, 338 women). ACE genotyping was carried out as previously described (17).

RESULTS

Figure 1 illustrates the distribution of genotypes in the athletes and control subjects and the close agreement between the two groups, in which the genotypes were, respectively, DD, 30 and 29%; ID, 47.5 and 49%; and II, 22.5 and 22%. The odds ratio for athletes to have the DD genotype was 1.06 (95% confidence interval 0.69–1.62) and the II genotype 1.02 (95% confidence interval 0.64–1.62). Allele frequencies in the athlete and control groups were, respectively, D, 54 and 53%; and I, 46 and 47%, the odds ratio for the D allele in athletes being 1.02 (95% confidence interval 0.77–1.34).

Five of the athletes included in the above analysis were gymnasts, and eight others competed in sports that possibly did not require an excellent level of aerobic fitness. Excluding those from the analysis did not alter the interpretation, the genotypes in the remaining 107 athletes being DD, 34 (32%), ID, 49 (46%), and II, 24 (22.4%); the odds ratio for athletes to have the DD genotype was 1.15 (95% confidence interval 0.74–1.79), and that for the II genotype was 1.01 (95% confidence interval 0.62–1.65). The numbers studied would have detected, with 90% power, a difference
of 15% in the frequency of DD and 14% in that of II genotypes between the two groups; that is, for the DD genotype a frequency of 29 plus 15%, or 44%, would have been detected, and, for the II genotype, 36% would have been detected.

The numbers and proportion of female athletes were smaller than those for men and probably too small for valid comparison with the female control group or the athletic men. There were 75 male athletes among the 107 described above: DD, 30 (40%); ID, 29 (39%); II, 16 (21%); the odds ratio of DD for athleticism was 1.50 (95% confidence interval 0.89–2.50) and of II genotype was 0.98 (95% confidence interval 0.54–1.81). Although 8 of 32 female athletes had the II genotype, it is interesting and provocative that only 4 had the DD genotype.

**DISCUSSION**

Montgomery et al. (6) recently reported that the I, rather than the D, allele was significantly associated with the ability of mountaineers to ascend to 7,000 m without oxygen. This particular observation could be related to the specific attribute studied. As reviewed by Cargill and Lipworth (2), the renin-angiotensin system has an important influence on the pulmonary vasculature. It has been subsequently found that exposure to hypoxia increases the expression of ACE in the small pulmonary arteries of the rat and that the pulmonary hypertensive response to hypoxia is reduced by ACE inhibition (7, 8) and specific angiotensin II type 1 receptor inhibition (8, 19). It might be postulated that subjects with the DD genotype have more pulmonary ACE, a more active pulmonary renin-angiotensin system, and greater pulmonary vasoconstriction in response to hypoxia, whereas those with the II genotype are selected for the ability to withstand hypoxia. This hypothesis could be consistent with another recent observation (H. Montgomery, S. Myerson, R. Budget, H. Hemingway, and S. Humphries, personal communication) that the I allele frequency is directly related to the distance over which elite runners compete, suggesting a relationship with some aspect of endurance. However, this proposal is quite contrary to a recent preliminary finding that susceptibility to high-altitude pulmonary hypertension is greater in those with the II genotype (9). That result seems to contradict the finding in mountaineers (6) and was also surprising to the authors, who postulated linkage disequilibrium with some other gene; clearly, the whole question requires further examination, and in larger numbers of subjects.

The finding quoted above on the mountaineers (6) was complemented by a further finding that, after 10 wk of physical training of male army recruits, the ability to perform elbow flexion against resistance was significantly enhanced by inheritance of the I allele (6). However, the results of training of such a community group would not necessarily extrapolate to elite athletic performance, which is likely to depend on complex interactions among musculoskeletal adaptations, cardiovascular and pulmonary variables, tissue repair, and metabolic (5) and psychological factors. Montgomery et al. (5) have subsequently reported that, among the 81 male army recruits studied, those having the II genotype tended to gain total and nonfat mass during training, whereas D carriers tended to lose fat mass, the results being significantly different between these genotypes. This suggests metabolic dependence on ACE genotype, and the implications are unclear but would almost certainly differ among sports.

Our study would have detected an incidence of the II genotype of 40%, which was the incidence of that genotype in the very small group of high-altitude mountaineers (6). However, although we included over 100 athletes, we still did not have sufficient power to detect a smaller, and possibly important, ACE genotype influence on elite athleticism. However, there was no suggestion that the II genotype conferred elite athletic ability and, in men, there was a trend toward the DD genotype. The trend was the opposite in women, but the numbers were too small to draw conclusions. We also had to include athletes involved in a range of sports to obtain sufficient numbers at a truly elite level of physical performance. Our results must, therefore, be regarded as preliminary, but they, and other recent studies (5, 6; H. Montgomery, S. Myerson, R. Budget, H. Hemingway, and S. Humphries, personal communication), emphasize the importance of carrying out very large studies, together with observations on physiological mechanisms, on both male and female athletes involved in various types of sporting activities.

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