The following is the abstract of the article discussed in the subsequent letter:

**Fuentes, Ricardo M., Markus Perola, Aulikki Nissinen, and Jaako Tuomilehto.** ACE gene and physical activity, blood pressure, and hypertension: a population study in Finland. *J Appl Physiol* 92: 2508–2512, 2002.—The study evaluated the association of the insertion/deletion polymorphism of the angiotensin-converting enzyme gene (ACE I/D) with self-reported moderate-intensity leisure time physical activity (MILTPA), arterial blood pressure (BP) and history of hypertension (HT). A representative population-based sample of 721 middle-aged adults (358 women) from two areas of Finland was genotyped for the ACE I/D. After exclusion criteria were applied, 455 subjects (288 women) were selected for the analysis. The distribution of the ACE I/D genotypes did not differ significantly among frequent vs. nonfrequent MILTPA groups (2 = 2.556; df = 2; P value = 0.279). The main predictors of BP were male gender, age, body mass index, and arterial pulse. Additionally, tobacco smoking and alcohol consumption also had a significant main effect on diastolic BP. HT was significantly more frequent in subjects with obesity, family history of cardiovascular disease, or lower educational level. As for BP, neither ACE I/D nor MILTPA was associated with HT. The study confirmed recent reports from population-based studies of no association between ACE I/D and physical fitness. The study also confirmed a lack of association between ACE I/D and BP or HT.

**ACE gene, physical activity, and physical fitness**

*To the Editor:* We read with interest the recent article on the topic of the angiotensin-converting enzyme (ACE) gene by Fuentes and colleagues (2). We see some value in aspects of their study, for example, as an investigation of the effect of the ACE insertion (I)/deletion (D) polymorphism on blood pressure in a specific population. However, we were disturbed at elements of both the introduction section and the discussion and conclusion.

An introduction section is traditionally used to outline the theoretical basis for the investigation being presented. In this case (2), a major focus of the study was the possible association of the ACE gene with self-reported moderate-intensity leisure time physical activity. The theoretical basis presented for such an association was weak in the extreme, for two reasons.

First, no literature was cited by Fuentes et al. (2) to support the premise that a greater fitness level and/or trainability will encourage greater physical activity in adulthood (regardless of any influences of specific genes). Yet this was the premise underpinning a major part of the study (see Table 2 in Ref. 2).

Second, even if appropriate literature supporting the premise that greater fitness and/or trainability produces greater activity in adulthood had been cited, there are strong reasons why seeking an effect of the ACE gene in this regard is likely to prove fruitless. Specifically, the research on the ACE gene has suggested possible beneficial effects of both alleles on the response to physical training. Growing evidence associates the D allele with the growth of muscle in humans (1, 6, 9) and elite performance in power events (8). Furthermore, evidence from a nonhuman model associates angiotensin II (the product of the action of ACE on angiotensin I) with skeletal muscle growth (4).

Thus evidence suggests that the D allele might predispose an individual to successful performance in particular sporting events. Although we acknowledge that there is some important contradictory evidence (10, 11), there is also considerable evidence associating the I allele with certain endurance phenotypes (5, 12, 13) and with elite endurance status (3, 7, 8). Hence, evidence suggests that the I allele, in addition to the D allele, might predispose an individual to successful performance in particular sporting events. Consequently, an effect of the ACE gene on activity in adulthood due to effects on fitness and/or the response to training is highly unlikely.

Even more importantly, the lack of association of the ACE I/D polymorphism with adulthood activity is used (2) to “confirm” reports of no association between ACE I/D and physical fitness in both the concluding paragraph of the article and the abstract. The lack of association reported by Fuentes et al. (2) does not confirm anything of the sort. Single-question self-reported moderate-intensity leisure time physical activity is not a recognized fitness phenotype suitable for investigating gene and environment effects. Thus the data presented by Fuentes et al. add nothing to the debate on the effect of the ACE gene on fitness phenotypes and should not be used to “confirm” results of one sort or another in that field.

**REFERENCES**


To the Editor: The aim of our study was to evaluate the association of the I/D ACE gene polymorphism with regular leisure time physical activity (LTPA) in a representative sample of the Finnish middle-aged adult population (2). The relevance of the study is based on the high cardiovascular disease risk associated with low levels of regular physical activity and on the association of the D allele of the ACE gene with both coronary heart disease risk and physical endurance. Both of these aspects are briefly introduced in the introduction section of the article (2).

Our working hypothesis was that “given an ACE I/D genotype, subjects might be more likely to become physically active during adulthood” (2). Our working hypothesis was not that “a greater fitness level and/or trainability will encourage greater physical activity in adulthood,” as has been suggested. We did not use the I/D ACE gene polymorphism as a surrogate of fitness and/or trainability, and we do not see the reason to do that. In a population survey, a subject will be found to have a certain level of regular physical activity and physical fitness (supposing it can be measured), and no causal relationship can be determined between them.

We acknowledge that we did not consider the association of the I allele of the ACE gene with physical endurance because the evidence for this association is contradictory.

We used a single question to assess behavior, LTPA, in the Finnish middle-aged adult population. As discussed in the article, the validity of few-question or single-question self-assessment of LTPA has been found acceptable to consider and recommend their use in population studies (1, 3, 4). We did not use single-question self-reported moderate-intensity LTPA as a surrogate of fitness.

Our study conclusion “we found no association between ACE I/D and LTPA in the Finnish middle-aged adult population. Although a single-question self-assessment of LTPA was used in our study, the result confirms recent negative reports in which physical fitness has been assessed more thoroughly” is a general comparative statement that precisely considers the fact that single-question self-assessment of LTPA is not a good surrogate of physical fitness (2).

REFERENCES


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