ORIGINAL ARTICLE

Anthropometrical, Cardiovascular, and Biochemical Responses to Short-term Endurance Training among Untrained Individuals with Different *Ace I/D* Genotypes

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ABSTRACT

Introduction: *ACE I/D* variant and short-term endurance workout performance, glycemic, anthropometrical, and biochemical responses are unknown. Thus, this study investigated how *ACE I/D* gene polymorphism affects physiological performance after four weeks of endurance training. **Materials and methods:** Seventeen *ACE I/D* genotype-screened volunteers trained three times a week for four weeks at 45 minutes per session, equivalent to their 60% VO_2max in the first two weeks, 70% in the third, and 75% in the fourth and final week. The oral glucose tolerance test examined anthropometric, cardiovascular, lipid, and blood glucose before and after four weeks of endurance training. The dominant model groups (*II/ ID*) (n = 10) and recessive model groups (*DD/ ID*) (n = 14) were compared using the paired samples t-test. **Results:** The training significantly reduced total cholesterol in the recessive model group (-0.4 ± 0.6 mmol/l, p = 0.035). Both dominant and recessive groups showed increased maximal oxygen consumption (Dominant: 0.2 ± 0.3 l/min, p = 0.036; Recessive: 0.2 ± 0.2 l/min, p = 0.007) and peak power output (Dominant: 23.2 ± 18.6 l/min, p = 0.003; Recessive: 24.0 ± 14.6 l/min, p = 0.000). After training, the dominant model group had lower blood glucose than the recessive model group, however the difference was minor. **Conclusion:** In conclusion, the positive trend on the *I allele* on examined variables supports its beneficial influence on endurance exercise and glucose tolerance.
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INTRODUCTION

While some studies reported a link between the *I* allele of *ACE I/D* gene polymorphism's presence and endurance performance enhancement following endurance training (1,2), other study failed to replicate similar findings (3). The inconsistent finding in these studies may be attributed to the inclusion of populations that have a longer training effect, such as athletes and army recruits, which were found to have no connection. Hence, to reduce gene-environment interaction that could adversely affect training responses, further research is necessary to confirm the impact of the *ACE I/D* gene polymorphism on improved training results in individuals who have not received prior training. In addition to its connection with endurance performance, the *ACE I/D* gene variation has also been found to be linked to glucose tolerance. The *ACE I/D* gene polymorphism is suggested as one of the genetic risk factors for diabetic nephropathy and glucose intolerance due to elevated plasma ACE activity has been observed in certain individuals with diabetes. (4). In comparison with the *I* allele carrier, the subjects with the *D* allele were found to have higher blood glucose levels in the oral glucose tolerance test than those with the other genotypes (5). Numerous studies have demonstrated that exercise training increases glucose tolerance, particularly among diabetes patients (6,7). Nevertheless, a few studies have examined how the effect of exercise training on glucose tolerance can be modulated by *ACE I/D* gene variant (8,9). Although previous research has used a long-term intervention programme, there is limited information on the relationship between the *ACE I/D* gene variant and glycemic response to short-term endurance exercise. The data from this association can assist in identifying individuals who are most likely to have an improvement in glucose tolerance through short-term endurance exercise.

A study by Luptáková et al. (10) showed that the *D* allele carriers exhibited a worse lipid profile than the *I* allele carrier. Although exercise training has been shown to improve body composition and lipid profile (11),

the individual response to training is highly variable. Hence, this study aimed to investigate the potential correlation between the *ACE I/D* gene variant and the anthropometrical, cardiovascular, and metabolic responses to a brief period of endurance exercise. We hypothesized that anthropometrical, cardiovascular, and biochemical parameters in response to a short-term endurance training program would be improved in the *I* allele carrier compared to the *D* allele carrier.

MATERIALS AND METHODS

Study Design

This study used repeated measurements. Anthropometric, cardiovascular, lipid, and oral glucose tolerance test data were collected prior to and following four weeks of endurance exercise.

Ethical Clearance

This study was approved by Research Ethics Committee of University of Sydney (2013/894).

Subjects

PS programme determined sample size. The study has 0.80 power and 0.05 types I error probability for testing the null hypothesis. The pre-testing evaluation included 35 healthy, untrained male and female cyclists who could exhaust themselves. In the initial sample of 35, only 17 subjects (22.7 ± 2.8 years old, 4 females, 13 men) completed the endurance training programme and post-training evaluation due to individual reasons. The genotyping study yielded 3 *II*, 7 *ID*, and 7 *DD* genotypes. Due to the low number of *II* genotypes, the individuals were assigned to two *ACE I/D* gene polymorphism model groups: dominant (*II/ ID*) (n=10) and recessive (*DD/ ID*) (n=14).

ACE I/D genotyping determination

All subjects provide a 5 ml blood sample to ascertain their *ACE I/D* genotype. Following the manufacturer's instructions, the Wizard® Genomic DNA Purification Kit isolated genomic DNA from blood samples. PCR was performed in a 25 µl volume with 2.5 µl of 10 X standard reaction buffer (GeneAllBiotechnologyCo. Ltd, Korea) (25 mM Mg2+, 50 mMTris-HCl, 50 mMKCl, 0.1 mM EDTA, 1 mM DTT, 0.5 mM PMSF, 50% glycerol), 2.0 µl of 200 µM dNTP mix, and 0.8 µl of dNTP mix. The target fragment was amplified for 7 minutes at 95 °C, followed by 25 cycles of 30 seconds at 95, 30 seconds at 62, and 1 minute at 72, and a final step of 7 minutes at 72. The amplified products were electrophoresed on a 1.5% agarose gel pre-stained with ethidium bromide for 1 hour at 70 volts. *ACE I* and *D* alleles have 490 and 190 base pair bands, respectively.

Pre- and Post-training tests

Participants reported to the lab in the morning after fasting overnight. Before the oral glucose tolerance test, weight, height, BMI, waist and hip circumference, heart rate, blood pressure, glucose, cholesterol, HDL, and LDL were measured. Waist and hip circumference measurements were obtained using a flexible tape measure, with participants instructed to stand upright while the narrowest point of the waist and the widest point of the hips were identified and recorded in centimeters. Heart rate (HR) was monitored using a digital heart rate monitor, with participants instructed to remain seated and calm during measurement and beats per minute (BPM) were recorded. Blood pressure (BP) was measured using an automated blood pressure monitor, with participants seated comfortably and the cuff placed around the upper arm at heart level; systolic and diastolic pressure readings were recorded in millimeters of mercury (mmHg). Blood samples were collected after an overnight fast, and cholesterol levels, including total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), and triglycerides, were analyzed using standard laboratory procedures. HDL and LDL levels were specifically quantified as part of the lipid profile analysis, and all cholesterol measurements were recorded in milligrams per deciliter (mg/dL). The individuals drank 75g glucose in 200 ml water in 2 minutes. After the glucose load (0, 10, 20, 30, 60, 90, and 120 min), 7 finger pricks collected 1.0 ml blood. VO_2max was measured on a cycle ergometer after the oral glucose tolerance test (OGTT). Three sub-maximal exercise workloads of 7 minutes each are followed by 5 minutes of extremely low-intensity recovery cycling on the cycle ergometer before the VO_2max test. Starting at 100 watts, the ergometer power was increased by 15 watts every 30 seconds until the subjects could no longer cycle despite the researcher's encouragement.

Endurance training

The pre-training VO_2max test was used to personalize cycle ergometer training to each participant's aerobic capability. The endurance training consisted of three 45-minute riding sessions each week for four weeks. The first two weeks of the intervention, individuals cycled at 60% of their VO_2max, then 70% and 75% in the third and fourth weeks. The training protocol used in this study was based on previously published protocols by Reardon et al. (12).

Statistical analysis

IBM SPSS version 28.0 was used for all statistical evaluations, with a significance level of $p < 0.05$. The descriptive data is shown as mean ± SD. Pairwise t-tests compared each group's pre- and post-training values for all parameters.

RESULTS

Table I shows pre- and post-training anthropometric, cardiovascular, and lipid characteristics in dominant (*ACE II/ID*) and recessive (*ACE DD/ID*) models. All factors

did not alter significantly between pre- and post-training between the two groups ($p < 0.05$). After analyzing pre- and post-training data for each group, endurance training significantly reduced total cholesterol in the recessive model group (-0.4 ± 0.6 mmol/l, $p = 0.035$). After four weeks of endurance training, the maximal oxygen consumption and total power output were significantly changed in both groups. The dominant model and recessive model groups had a 0.2 ± 0.3 l/min ($p = 0.036$) and 0.2 ± 0.2 l/min ($p = 0.007$) increase in the VO^2max after the endurance training program, respectively. Likewise, with endurance training, the peak power output was significantly increased in both groups; dominant model (23.2 ± 18.6 l/min, $p = 0.003$) and recessive model (24.0 ± 14.6 l/min, $p < 0.001$. Table II shows the dominant and recessive model groups' pre- and post-training blood glucose readings. Before training, dominant model group blood glucose readings at fasting, 30 min, and 120 min were marginally lower than recessive model group. The recessive model group had higher blood glucose readings at 60 and 90 min than the dominant model group. The differences were not statistically significant (all $p > 0.05$). After training, both groups had similar fasting blood glucose. Though not statistically significant (all $p > 0.05$), the dominant model group had lower 2-hour blood glucose readings than the recessive model group. There was no significant change between pre- and post-training data in either group (all $p > 0.05$). After endurance training, both groups raised their area under the glucose curve value, but the recessive model group had a greater value. The comparison was not statistically significant (all $p > 0.05$).

Table I: Anthropometric, cardiovascular, and lipid parameters in the dominant and recessive model *ACE I/D* genotype groups

Variables		Dominant model *ACE II/ ID* (n = 10)	Recessive model *ACE DD/ ID* (n = 14)	p-value (Dominant-Recessive)
Body weight (kg)	**Pre-training**	74.1 ± 12.4	73.6 ± 13.2	0.921
	Post-training	74.6 ± 12.8	70.8 ± 16.2	0.540
	Response (change)	0.5 ± 2.5	-2.8 ± 8.4	0.247
	p-value (Pre-Post)	0.557	0.235	
Body mass index (kg/m²)	**Pre-training**	23.7 ± 2.4	24.0 ± 2.9	0.787
	Post-training	23.8 ± 2.3	23.1 ± 4.1	0.614
	Response (change)	0.1 ± 0.7	-0.9 ± 2.7	0.248
	p-value (Pre-Post)	0.622	0.221	
Waist circumference (cm)	**Pre-training**	80.1 ± 7.6	79.6 ± 8.6	0.863
	Post- training	79.5 ± 7.7	78.6 ± 10.0	0.818
	Response (change)	-0.6 ± 2.4	-1.0 ± 2.6	0.783
	p-value (Pre-Post)	0.382	0.180	
Hip circumference (cm)	**Pre-training**	98.3 ± 4.8	98.3 ± 6.3	0.986
	Post-training	98.4 ± 5.0	96.7 ± 7.2	0.534
	Response (change)	0.1 ± 1.8	-1.6 ± 3.0	0.118
	p-value (Pre-Post)	0.823	0.066	
Waist hip ratio	**Pre-training**	0.82 ± 0.05	0.81 ± 0.04	0.739
	Post-training	0.81 ± 0.05	0.81 ± 0.06	0.860
	Response (change)	-0.01 ± 0.01	0.00 ± 0.03	0.343
	p-value (Pre-Post)	0.081	0.868	
Body fat (%)	**Pre-training**	19.2 ± 6.4	19.9 ± 7.6	0.822
	Post-training	19.9 ± 7.2	19.9 ± 7.9	0.982
	Response (change)	0.7 ± 2.1	0.0 ± 2.6	0.561
	p-value (Pre-Post)	0.349	0.921	
Systolic blood pressure (mmHg)	**Pre-training**	120.5 ± 6.1	120.1 ± 5.7	0.885
	Post-training	119.5 ± 7.0	118.9 ± 5.2	0.819
	Response (change)	-1.0 ± 5.5	-1.2 ± 4.7	0.919
	p-value (Pre-Post)	0.578	0.347	
Diastolic blood pressure (mmHg)	**Pre-training**	73.6 ± 5.5	74.1 ± 7.7	0.870
	Post-training	75.1 ± 6.7	76.8 ± 6.9	0.559
	Response(change)	1.5 ± 10.1	2.7 ± 8.8	0.756
	p-value(Pre-Post)	0.648	0.268	

CONTINUE

Table I: Anthropometric, cardiovascular, and lipid parameters in the dominant and recessive model *ACE I/D* genotype groups (CONT')

Variables		Dominant model *ACE II/ ID* (n = 10)	Recessive model *ACE DD/ ID* (n = 14)	p-value (Dominant-Recessive)
Mean arterial pressure (mmHg)	**Pre-training**	89.2 ± 4.4	89.4 ± 5.7	0.924
	Post-training	89.9 ± 5.5	90.8 ± 5.5	0.686
	Response (change)	0.7 ± 7.3	1.4 ± 5.8	0.788
	p-value (Pre-Post)	0.775	0.383	
Resting heart rate (bpm)	**Pre-training**	55.5 ± 7.5	56.1 ± 7.1	0.851
	Post-training	54.4 ± 9.2	53.4 ± 8.3	0.774
	Response (change)	-1.1 ± 6.6	-2.7 ± 6.6	0.561
	p-value (Pre-Post)	0.613	0.147	
Total cholesterol (mmol/l)	**Pre-training**	4.0 ± 0.6	4.1 ± 0.7	0.698
	Post-training	3.8 ± 0.6	3.7 ± 0.6	0.716
	Response (change)	-0.2 ± 0.6	-0.4 ± 0.6	0.412
	p-value (Pre-Post)	0.398	0.035*	
High-density lipoprotein cholesterol (mmol/l)	**Pre-training**	1.4 ± 0.4	1.3 ± 0.4	0.758
	Post-training	1.3 ± 0.3	1.3 ± 0.3	0.981
	Response (change)	-0.1 ± 0.2	0.0 ± 0.2	0.503
	p-value (Pre-Post)	0.297	0.895	
Low-density lipoprotein cholesterol (mmol/l)	**Pre-training**	2.1 ± 0.7	2.2 ± 0.6	0.573
	Post-training	2.1 ± 0.7	2.0 ± 0.6	0.644
	Response (change)	0.0 ± 0.6	-0.2 ± 0.7	0.309
	p-value (Pre-Post)	0.877	0.194	
Maximal oxygen consumption (l/min)	**Pre-training**	3.2 ± 0.8	3.1 ± 0.7	0.769
	Post-training	3.4 ± 0.8	3.3 ± 0.8	0.644
	Response (change)	0.2 ± 0.3	0.2 ± 0.2	0.539
	p-value (Pre-Post)	0.036*	0.007*	
Peak power output (watts)	**Pre-training**	275.6 ± 71.0	260.0 ± 62.8	0.575
	Post-training	298.8 ± 72.2	284.0 ± 63.3	0.600
	Response (change)	23.2 ± 18.6	24.0 ± 14.6	0.907
	p-value (Pre-Post)	0.003*	0.000*	

* Significant at $p < 0.05$

Table II: Oral glucose tolerance test in the dominant and recessive model *ACE I/D* genotype groups

Variables		Dominant model *ACE II/ ID* (n = 10)	Recessive model *ACE DD/ ID* (n = 14)	p-value (Dominant-Recessive)
Fasting blood glucose	**Pre-training**	4.8 ± 0.5	4.9 ± 0.3	0.591
	Post-training	4.9 ± 0.4	4.9 ± 0.4	0.934
	Response (change)	0.1 ± 0.7	0.0 ± 0.5	0.687
	p-value (Pre-Post)	0.800	0.759	
Blood glucose 30 min	**Pre-training**	8.2 ± 1.4	8.5 ± 1.6	0.648
	Post-training	8.0 ± 2.6	8.1 ± 2.2	0.892
	Response (change)	-0.2 ± 3.1	-0.4 ± 2.6	0.897
	p-value (Pre-Post)	0.777	0.534	
Blood glucose 60 min	**Pre-training**	7.3 ± 1.5	7.0 ± 1.2	0.562
	Post-training	7.5 ± 1.2	7.6 ± 1.4	0.758
	Response (change)	0.2 ± 1.2	0.6 ± 1.5	0.389
	p-value (Pre-Post)	0.733	0.136	
Blood glucose 90 min	**Pre-training**	6.8 ± 1.0	6.6 ± 0.7	0.520
	Post-training	6.5 ± 0.9	6.6 ± 0.8	0.728

CONTINUE

Table II: Oral glucose tolerance test in the dominant and recessive model *ACE I/D* genotype groups (CONT')

Variables		Dominant model *ACE II/ ID* (n = 10)	Recessive model *ACE DD/ ID* (n = 14)	p-value (Dominant-Recessive)
Blood glucose 90 min	**Response (change)**	-0.3 ± 1.4	0.0 ± 1.1	0.504
	p-value (Pre-Post)	0.530	0.834	
Blood glucose 120 min	**Pre-training**	5.8 ± 0.7	6.1 ± 0.8	0.355
	Post-training	5.4 ± 0.9	5.7 ± 1.1	0.380
	Response (change)	-0.4 ± 0.9	-0.4 ± 1.1	0.833
	p-value (Pre-Post)	0.169	0.244	
Area under curve	**Pre-training**	13.9 ± 1.5	13.8 ± 1.2	0.939
	Post-training	14.0 ± 1.4	14.2 ± 1.3	0.759
	Response (change)	0.1 ± 1.3	0.4 ± 1.0	0.647
	p-value (Pre-post)	0.783	0.248	

DISCUSSION

This study shows that short-term endurance training enhances aerobic capacity in untrained persons with varied *ACE I/D* genotypes. In either *I* or *D* allele subjects, four weeks of endurance training increased VO_2max and peak power production. Although the two groups' maximal oxygen consumption values changed similarly, individuals with the *I* allele had a somewhat higher baseline value than those with the *D* allele. *I* allele carriers had a higher baseline peak power production than *D* allele carriers. These findings support earlier research (2,13) that the *I* allele improves endurance activities.

However, the *D* allele carrier had bigger peak power output improvements in response to endurance training, suggesting that it may improve physical function more in this carrier. The *D* allele may improve power performance, supporting the earlier study that found it improved short-duration aerobic performance (2). ANG II production in skeletal muscle may explain the *D* allele's beneficial influence on power performance in this study. Increased local ANG II production in skeletal muscle increases protein synthesis and cell growth, causing maximal power contraction (14). After endurance exercise, participants with the *I* or *D* allele had lower total cholesterol. Only *D* allele carriers showed a significant drop in this measure. Although the result was negligible, the dominant model group had a lower baseline total cholesterol value than the recessive group, like a prior finding that the *D* allele carrier had higher total cholesterol than the *I* allele carrier (11). This supports the idea that the *D* allele is more likely to develop cardiovascular disease because elevated cholesterol is the main risk factor (15). The larger change in total cholesterol in the *D* allele carrier than the *I* allele carrier suggests that endurance training can reduce cholesterol significantly in high-risk individuals.

Our glucose tolerance measurements showed that *I* allele carriers had lower glucose at fasting and 120 min than *D* allele carriers. This confirms the earlier work (16) showing a *D* allele raises fasting blood glucose. Our healthy subject findings matched the study that found increased blood glucose levels following an OGTT in diabetics with the *DD* genotype (5). Although not statistically significant, this shows that the *D* allele may increase the chance of glucose intolerance in non-diabetics. Genotype-dependent insulin tolerance mechanisms are obscure and poorly described. The *D* allele may enhance Angiotensin II production, which increases vasoconstriction and blood pressure and glucose absorption (17).

Even while our study had encouraging outcomes, the mixed and non-significant results for other metrics may have been owing to the small number of patients. Our sample group was healthy and mixed gender. Thus, it is unclear if the *ACE I/D* polymorphism affects gender differently. Diabetes and cardiovascular patients display training responses. The quantity of training sessions may explain this contentious result. This speculation needs further exploration because there is no concrete guideline on the number of training sessions needed to determine how this polymorphism affects training response. Even with these limitations, the current results are legitimate because the study participants were healthy and trained similarly. Participants standardised the intervention with the same trained investigator who trained them. To minimise beginning point measurement variability due to fear, subjects were familiarised. In this double-masked study, the participant's genotype was kept from them and the trained investigator who gave the training.

CONCLUSION

We conclude that the *ACE I/D* gene polymorphism may improve short-term endurance performance which suggest that genetic screening before enrolling in a health management exercise programme is crucial to maximise efficiency and benefits. Identification of *ACE I/D* genotype-specific responses to endurance training can help develop targeted training strategies. For instance, individuals with certain genotypes may benefit more from specific types or intensities of endurance training.

insights into genotype-specific training responses may assist coaches, trainers, and healthcare professionals in optimizing training adaptations and enhancing performance outcomes among athletes and fitness enthusiasts. This study found no association between the *ACE I/D* gene polymorphism and anthropometrical and biochemical responses to endurance training. Larger studies should investigate.

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