J Physiol Sci (2012) 62:115–121
DOI 10.1007/s12576-011-0189-0

ORIGINAL PAPER

ACE I/D, *ACTN3 R577X*, *PPARD T294C* and *PPARGC1A Gly482Ser* polymorphisms and physical fitness in Taiwanese late adolescent girls

Li-Ling Chiu · Tzu-Wen Chen · Sandy S. Hsieh · Ling-Ling Hsieh

Received: 5 May 2011 / Accepted: 19 December 2011 / Published online: 14 January 2012

Abstract Physical performance of youth is influenced by various factors, including body composition, biological maturity status, level of habitual physical activity, and muscular strength. Muscular strength has been largely attributed to genetic effects. To exclude possible confounding effects from various acquired factors, this study examined the relationships between polymorphisms of the angiotensin-converting enzyme (*ACE*), α-actinin-3 (*ACTN3*), peroxisome proliferator-activated receptor delta (*PPARD*), and peroxisome proliferator-activated receptor gamma coactivator-1 alpha (*PPARGC1A*) genes and performance as measured by six fitness tests (handgrip strength of dominant hand, 30- and 60-s sit-ups, standing long jump, 60-m dash, and 800-m run) in 170 sedentary adolescent girls with the adjustment of anthropometric characteristics. We found that subjects with the *ACE DD* genotype were significantly heavier than those with *I* allele, while those with the *ACTN3 RR* genotype had higher fat-free mass percentage (FFM%) than those with the *XX* genotype. In addition, those with the *PPARD TT* genotype were significantly taller, heavier, and had a greater FFM than those with the *CC* genotype. Subjects with the *ACE DD*, *ACTN3 RR* and *PPARD TC* genotype had better performance in handgrip strength, 30- and 60-s sit-up tests, and standing long jump, respectively, when individual gene was analyzed independently after adjusting anthropometric characteristics. In the gene combination analysis, subjects with *ACE DD, ACTN3 RR* and *PPARD TT* genotype had significantly greater performance in handgrip strength. Overall, the results indicate that the genes studied have a modest influence on individual performance as assessed by specific fitness and strength tests in female late adolescents.

Keywords Polygenic trait · Adolescence · Body composition · FFMI · Handgrip strength

Electronic supplementary material The online version of this article (doi:10.1007/s12576-011-0189-0) contains supplementary material, which is available to authorized users.

L.-L. Chiu
Graduate Institute of Biomedical Sciences, Chang Gung University, Tao-Yuan, Taiwan

L.-L. Chiu
Department of Nutrition and Health Sciences, Chang Gung University of Science and Technology, Tao-Yuan, Taiwan

T.-W. Chen
Department of Physical Education, National Taiwan Normal University, Taipei, Taiwan

S. S. Hsieh
Graduate Institute of Exercise and Sport Science, National Taiwan Normal University, Taipei, Taiwan

L.-L. Hsieh (✉)
Department of Public Health, Chang Gung University, 259 Wen-Hwa 1 Road, Kwei-San, Tao-Yuan 333, Taiwan
e-mail: llhsieh@mail.cgu.edu.tw

Introduction

It has been reported that the physical performance of youth is influenced by a variety of factors, including age, sex, body size, and composition, biological maturity status, level of habitual physical activity and muscular strength [1, 2]. Among them, muscular strength can be attributed to genetic effects varying from 0.27 to 0.58 based on family studies and between 0.14 and 0.83 based on twin studies [3]. Recently, the development of technology for rapid DNA sequencing and genotyping has allowed the identification of some individual genetic variations that contribute to physical performance. Bray et al. [4] has comprehensively reviewed

genes and markers that show evidence of association with performance or fitness phenotypes in sedentary or active people, in responses to acute exercise, and in terms of training-induced adaptation. Among the 214 listed autosomal genes, angiotensin-converting enzyme (*ACE*) and α-actinin-3 (*ACTN3*) are the genes with the highest number of positive findings. Most studies have linked the *ACE I* allele to endurance performance [5] and the *D* allele to muscle strength and power-oriented performance [6–8]. The *ACTN3 R* allele is prevalent among sprint athletes and the *X* allele is less common among sprinters, particularly in the homozygous form (*XX*) [9–13].

In addition to *ACE* and *ACTN3*, there is emerging evidence that the peroxisome proliferator-activated receptor delta (*PPARD*) [14, 15] and peroxisome proliferator-activated receptor gamma coactivator-1 alpha (*PPARGC1A*) [16] gene may play an important role in physical performance. Recently, Eynon et al. [17] found that the *PPARD T294C* polymorphism together with peroxisome proliferator-activated receptor γ coactivator-1α (*PPARGC1A*) play an important role in endurance-type performance.

There are few data available on the combined influence of polymorphisms of *ACE*, *ACTN3* and other genes on physical capability phenotypes, especially in non-athletic populations [18–21]. Furthermore, physical performance is also determined by a range of acquired factors such as age, body composition, and physical training. To exclude possible confounding effects from these factors, the present study was carried out to examine the relationships between the *ACE*, *ACTN3*, *PPARD*, and *PPARGC1A* genotypes and performance in fitness tests by sedentary female adolescents (16–18 years).

Methods

Subjects

This study was conducted according to the Harriss and Atkinson Statement [22] and approved by the Institutional Review Board of Chang Gung Memorial Hospital. To exclude the possible influences of menstrual and disease status on physical performances, we first surveyed the disease history as well as the menstrual cycle length and the first day of the latest menstrual bleeding for all the 11th grade (16–18 years old) female students. Only those students with a regular menstrual cycle length of 28–30 days and the first day of their latest menstrual bleeding were within just 3 days were asked to participate the present study. Finally, a total of 170 sedentary female students without cardiovascular, metabolic, or musculoskeletal diseases were included for the present analysis. All parents gave written consent and each girl also provided individual written assent. Body mass index (BMI) was calculated as weight (kg) divided by square of the height (m^2). The percentage of body fat was estimated by bioelectrical impedance analysis using an OMRON (HBF-355) hand-to-foot body composition monitor (Omron Healthcare, Kyoto, Japan) [23] and was used to calculate the fat-free mass FFM (kg) and the fat-free mass percentage (FFM%). The fat-free mass index (FFMI) was calculated as the FFM (kg) divided by the square of the height (m^2).

According to the Taiwan physical fitness test manual [24], six fitness tests were carried out without any prior training. They were (1) handgrip strength of the dominant hand, (2) 30- and 60-s sit-ups, (3) a standing long jump, (4) a 60-m dash, and (5) a 800-m endurance run. All the tests were executed in the morning and all the subjects completed the same test on the same day. In addition, 5 mL of saliva was collected from each participant and centrifuged at 800*g* for 10 min at room temperature to obtain oral mucosa cells for genotyping.

Genotyping

Genomic DNA was purified from oral mucosa cells by digestion with proteinase K and then extracted using a conventional phenol/chloroform procedure. Genotyping of the *ACE I/D* (rs1799752) was performed using polymerase chain reaction (PCR) as previously described [25]. The genotypes *ACTN3 R577X* (rs1815739) and *PPARD T294C* (rs2016520) were determined by PCR restriction fragment length polymorphism (RFLP) as described by Mills et al. [26] and Ahmetov et al. [14], respectively. The conditions for PCR were as shown in Table 1. Since it has been reported that amplification of the *ACE I* allele is sometimes suppressed in *ID* heterozygotes and mistyped as the *DD* genotype [27], all the samples classified as *DD* genotype were checked with a second PCR reaction using an I-specific primer pair: 5′-TGGGACCACAGCGCCCGCCACT AC-3′ (forward) and 5′-TCGCCAGCCCTCCCATGCCCA TAA-3′ (reverse) [28]. The *ACTN3* and *PPARD* genotypes were determined by enzymatic digestion of their amplicons with Dde I and Bsc4I, respectively. The *PPARGC1A* Gly482Ser (rs8192678) genotype was determined as described previously [29] using TaqMan-based allelic discrimination assay on a 7500 Real-Time PCR System (Applied Biosystems, Foster City, CA, USA).

Total genotype score (TGS) determination

The combined influence of the four studied polymorphisms was determined in a similar manner to the previous study by Ruiz et al. [20]. A genotype score (GS) for the 'optimal' or preferable endurance genotype in each polymorphism was assigned as 2, whereas a GS of 0 was assigned to the

Table 1 Forward/reverse primers and PCR conditions for *ACE*, *ACTN3*, and *PPARD* genotyping

Gene	Forward primer (5′–3′)	Reverse primer (5′–3′)	PCR reaction conditions		
			Denaturation	Annealing and cycles	Final extension
ACE	CTGGAGACCACTC CCATCCTTTCT	GATGTGGCCATCA CATTCGTCAGAT	95°C for 5 min	35 cycles of 95°C for 1 min, 58°C for 30 s, 72°C for 40 s	72°C for 10 min
ACTN3 (exon 16)	CTGTTGCCTGT GGTAAGTGGG	TGGTCACAGTAT GCAGGAGGG	95°C for 5 min	35 cycles of 95°C for 1 min, 58°C for 30 s, 72°C for 40 s	72°C for 10 min
PPARD (exon 4)	CATGGTATAGCAC TGCAGGAA	CTTCCTCCTGTG GCTGCTC	95°C for 5 min	35 cycles of 95°C for 1 min, 60°C for 30 s, 72°C for 40 s	72°C for 10 min

Table 2 Genotype score (GS) and frequency distribution of *ACE*, *ACTN3*, *PPARD*, and *PPARGC1A* studied in Taiwanese female late adolescents

Gene	Polymorphism	Genotype score (GS)	Frequency (%)
ACE	287-bp Ins(I)/Del(D)	0 = DD, 1 = ID, 2 = II	7, 44, 49
ACTN3	Arg(R)577Ter(X)	0 = RR, 1 = RX, 2 = XX	27, 53, 20
PPARD	T294C	0 = TT, 1 = TC, 2 = CC	38, 45, 17
PPARGC1A	Gly482Ser	0 = Ser/Ser, 1 = Gly/Ser, 2 = Gly/Gly	18, 58, 24

Genotype score: 0 = "optimal" sprint/power genotype

ACE Angiotensin-converting enzyme gene, *ACTN3* α-actinin-3 gene, *PPARD* peroxisome proliferator-activated receptor delta gene, *PPARGC1A* peroxisome proliferator-activated receptor gamma coactivator-1 alpha gene

least optimal genotype (Table 2). The sum of the GS from the genes studied (i.e. $GS_{ACE} + GS_{ACTN3} + GS_{PPARD}$) was designated as the $TGS_{ACE+ACTN3+PPARD}$.

Statistical analysis

All statistical analyses were performed using SPSS v.13.0 (SPSS, Chicago, IL, USA). The distribution of genotypes studied was tested for the fulfilment of Hardy–Weinberg equilibrium status by using a Chi-square test with one degree of freedom. The differences in anthropometric characteristics among the different genotypes were compared by one-way analysis of variance (ANOVA) or the Kruskal–Wallis test depending on the normality of the variables. The differences in physical performance among the different genotypes were compared by analysis of covariance (ANCOVA) adjusted for height, body weight, BMI, FFM%, FFM, and FFMI. The level of significance was set at 0.05. All reported p values are 2-sided.

Results

The distribution of genotype for these four genes studied was not deviated from Hardy–Weinberg equilibrium (all p values >0.05). The association between anthropometric characteristics and *ACE*, *ACTN3*, *PPARD*, and *PPARGC1A* polymorphisms were shown in Table 3. Subjects with the *ACE DD* genotype (61.6 kg) were significantly heavier than those with the *ID* (54.9 kg) and the *II* (55.4 kg) genotype. Subjects with the *ACTN3 RR* genotype (71.0%) had higher FFM% values than those with the *XX* genotype (68.6%). In addition, those with the *PPARD TT* genotype were significantly taller (161.0 cm), heavier (57.1 kg), and had a greater FFM (39.3 kg) than those with the *CC* genotype (157.1 cm, 51.8 kg, and 36.2 kg). On the other hand, BMI and FFMI themselves were not significantly associated with the *ACE*, *ACTN3*, *PPARD*, and *PPARGC1A* polymorphisms.

After adjustment of anthropometric characteristics (height, weight, BMI, FFM%, FFM and FFMI), subjects with the *ACE DD* genotype had greater handgrip strength (28.3 kg) than those with the *ID* (25.0 kg) and the *II* (25.6 kg) genotype (Table 4). Individuals with the *ACTN3 RR* genotype performed better in the 30- and 60-s sit-up tests (18.7 and 34.1 counts) than those with the *RX* genotype (17.0 and 30.3 counts). Subjects with the *PPARD TC* genotype (150.1 cm) performed significantly better in the standing long jump test than those with the *CC* genotype (136.9 cm). Subjects with the *PPARGC1A Gly/Gly* genotype (34.4 counts) performed significantly better in the 60-s sit-up test than those with the *Gly/Ser* genotype (30.5 counts). However, there were no associations between the genotypes and either 60-m dash or 800-m endurance run test.

The combined gene influence on physical performance was further explored. As shown in Table S1 (supplementary)

Table 3 Association between anthropometric characteristics and *ACE*, *ACTN3*, *PPARD*, and *PPARGC1A* polymorphisms

Genotype	Height (cm)	Weight (kg)	BMI (kg m^{-2})	FFM%	FFM (kg)	FFMI (kg m^{-2})
ACE						
DD ($n = 12$)	163.3 ± 2.2	**61.6 ± 2.2**[b,c]	23.1 ± 0.8	67.5 ± 1.1	41.3 ± 1.0	41.3 ± 1.0
ID ($n = 74$)	160.5 ± 0.6	**54.9 ± 1.1**[b]	21.2 ± 0.4	70.0 ± 0.5	38.0 ± 0.5	38.0 ± 0.5
II ($n = 84$)	159.9 ± 0.6	**55.4 ± 1.1**[c]	21.6 ± 0.4	70.1 ± 0.4	38.1 ± 0.5	38.1 ± 0.5
p value	0.152	0.023	0.102	0.115	0.055	0.112
ACTN3						
RR ($n = 46$)	160.5 ± 0.8	54.3 ± 1.1	21.0 ± 0.4	**71.0 ± 0.6**[e]	38.6 ± 0.6	41.3 ± 1.0
RX ($n = 90$)	161.0 ± 0.7	56.0 ± 1.1	21.5 ± 0.4	69.8 ± 0.5	38.2 ± 0.5	38.0 ± 0.5
XX ($n = 34$)	158.7 ± 0.7	56.4 ± 1.7	22.3 ± 0.6	**68.6 ± 0.7**[e]	37.8 ± 0.8	38.1 ± 0.5
p value	0.126	0.766	0.296	0.04	0.735	0.514
PPARD						
TT ($n = 65$)	**161.0 ± 0.7**[a]	**57.1 ± 1.2**[d]	22.0 ± 0.4	69.4 ± 0.6	**39.3 ± 0.6**[f]	41.3 ± 1.0
TC ($n = 77$)	161.1 ± 0.6	55.8 ± 1.2	21.4 ± 0.4	70.2 ± 0.5	38.2 ± 0.5	38.0 ± 0.5
CC ($n = 28$)	**157.1 ± 0.9**[a]	**51.8 ± 1.3**[d]	21.0 ± 0.5	70.1 ± 0.7	**36.2 ± 0.7**[f]	38.1 ± 0.5
p value	0.002	0.025	0.166	0.454	0.009	0.130
PPARGC1A						
Ser/Ser ($n = 31$)	159.6 ± 0.9	56.5 ± 2.0	22.1 ± 0.7	69.0 ± 0.7	38.0 ± 1.0	14.9 ± 0.3
Gly/Ser ($n = 98$)	160.3 ± 0.6	54.5 ± 0.9	21.2 ± 0.3	70.2 ± 0.4	37.9 ± 0.5	14.7 ± 0.1
Gly/Gly ($n = 41$)	161.6 ± 0.8	57.5 ± 1.6	22.0 ± 0.5	70.1 ± 0.8	39.6 ± 0.6	15.1 ± 0.2
p value	0.259	0.197	0.234	0.361	0.149	0.269

Values expressed as mean ± SE

BMI Body mass index, *FFM%* far-free mass percentage, *FFM* fat-free mass, *FFMI* fat-free mass index

[a–f] The bold values indicate that there is a significant difference in the post hoc test using the [a,f] Scheffe and [b–e] Mann–Whitney *U* tests

and Table 5, $TGS_{ACE+ACTN3+PPARD+PPARGC1A}$ was only marginally associated with handgrip strength, while $TGS_{ACE+ACTN3+PPARD}$ was associated with handgrip strength and 60-s sit-up. Additionally, it is worth noting that the maximum handgrip strength (41.4 kg) found among all the subjects was an individual who did not have the "optimal" gene profile for the least endurance group, namely a TGS of 0.

Discussion

In this study, we found that performance in the handgrip strength, 30-/60-s sit-up, standing long jump, and 60-s sit-up test results were significantly associated with *ACE*, *ACTN3*, *PPARD*, and PPARGC1A polymorphisms, respectively, in sedentary female late adolescents after adjusting for anthropometric characteristics (Table 4). The *ACE D* allele is associated with higher ACE activity and thus an increased angiotensin II level [30]. Therefore, this allele would theoretically favor performance in power-oriented exercise tasks. Previous studies have reported a positive association of the *ACE D* allele and baseline grip strength in healthy untrained subjects [8], patients with chronic obstructive pulmonary disease [31], advanced cancer patients [32], and elite strength-trained athletes [33]. In contrast, some studies have failed to support such findings [28, 34]. Surprisingly, the Moran et al. [35] study of teenage Greeks reported that the homozygous I-allele individuals exhibited higher performance scores. In the present study, an association between *ACE* polymorphism and standing long jump was not observed. Similar phenomenon was also noted by Rodriguez-Romo et al. [36] in young non-athletic adults.

It has been reported that *ACTN3 XX* genotype precluded top-level athletic performance in ''pure'' power and sprint sports (sprinting, jumping, weightlifting, and throwing events), especially among women [13]. In the present study, we found that those with the *ACTN3 RR* genotype in combination with the *ACE DD* genotype performed significantly better in terms of handgrip strength than those with other genotype combinations (Tables S2 and S3). However, no effect on standing long jump was observed. Previous studies have also demonstrated that the *ACTN3* R577X polymorphism does not seem to influence explosive leg muscle power (jumping, sprinting) alone or in combination with the *ACE I/D* polymorphism in a young non-athletic population, irrespective of gender [36]. Clarkson et al. [37] and Walsh et al. [38] reported that women with the *ACTN3 XX* genotype have lower strength than those with the *RX* genotype. Chiu et al. [39] reported that

Table 4 Association between the fitness test results and *ACE*, *ACTN3*, *PPARD*, and *PPARGC1A* polymorphisms

Genotype	Handgrip strength (kg)	Standing long jump (cm)	30-s sit-up (counts)	60-s sit-up (counts)	60-m dash (s)	800-m run (s)
ACE						
DD ($n = 12$)	**28.3 ± 1.2**	152.6 ± 6.1	18.0 ± 1.2	32.3 ± 2.3	11.6 ± 0.4	290.1 ± 10.0
ID ($n = 74$)	**25.0 ± 0.5**	144.5 ± 2.5	17.5 ± 0.5	31.6 ± 1.0	11.9 ± 0.2	287.2 ± 4.1
II ($n = 84$)	25.7 ± 0.5	146.0 ± 2.3	18.0 ± 0.4	32.0 ± 0.9	11.8 ± 0.1	281.7 ± 3.8
p value	0.048	0.421	0.734	0.941	0.649	0.535
ACTN3						
RR ($n = 46$)	26.7 ± 0.6	143.8 ± 3.2	**18.7 ± 0.5**	**34.1 ± 1.2**	12.1 ± 0.2	285.2 ± 5.2
RX ($n = 90$)	25.1 ± 0.5	145.9 ± 2.2	**17.0 ± 0.4**	**30.3 ± 0.8**	11.7 ± 0.1	285.1 ± 3.7
XX ($n = 34$)	25.3 ± 0.8	147.5 ± 3.7	18.3 ± 0.7	32.8 ± 1.4	11.7 ± 0.2	282.8 ± 6.1
p value	0.141	0.751	0.048	0.029	0.355	0.940
PPARD						
TT ($n = 65$)	25.6 ± 0.5	144.5 ± 2.5	17.6 ± 0.5	31.7 ± 1.0	11.9 ± 0.2	281.6 ± 4.3
TC ($n = 77$)	25.6 ± 0.5	**150.1 ± 2.4**	17.8 ± 0.5	31.8 ± 0.9	11.6 ± 0.1	283.8 ± 4.0
CC ($n = 28$)	25.5 ± 0.8	**136.9 ± 4.0**	18.0 ± 0.8	32.2 ± 1.6	12.1 ± 0.2	294.4 ± 6.7
p value	0.996	0.018	0.930	0.969	0.158	0.274
PPARGC1A						
Ser/Ser ($n = 31$)	25.8 ± 0.8	146.9 ± 3.8	18.3 ± 0.7	32.9 ± 1.4	11.7 ± 0.2	288.6 ± 6.2
Gly/Ser ($n = 98$)	25.4 ± 0.4	146.4 ± 2.1	17.3 ± 0.4	**30.5 ± 0.8**	11.8 ± 0.1	284.9 ± 3.5
Gly/Gly ($n = 41$)	26.2 ± 0.7	144.1 ± 3.4	18.7 ± 0.6	**34.4 ± 1.3**	11.9 ± 0.2	281.2 ± 5.6
p value	0.589	0.825	0.126	0.026	0.652	0.675

Values expressed as mean ± SE adjusted for height, body weight, BMI, FFM%, FFM, and FFMI by ANCOVA

The bold values indicate that there is a significant difference in the Bonferroni post hoc test

pre-adolescents with the *ACTN3 RR* genotype exhibited the best performance across all phases (before, during, and after training) of 25-m swimming performance. However, in older women (64 years), knee extensor concentric peak power was found to be higher in X allele homozygote individuals compared with *RR* genotype individuals [40]. These discrepancies may reflect that there is an interaction between age and genotype [41].

There is compelling evidence indicating that a functional *T294C* polymorphism of *PPARD* influences human physical performance [15]. In the present study, we found that the subjects with the *TC* genotype demonstrated a better performance in the lower extremity explosive power standing long jump test than those with *CC* genotype. This finding supports the hypothesis that the *PPARD C* allele is associated with a predisposition to endurance performance [17].

The combined effect of the *ACE*, *ACTN3*, *PPARD*, and *PPARGC1A* polymorphisms on performance across the six fitness tests was further evaluated using the TGS index as described previously [20]. In the present study, since there was no subject with homozygous *ACE DD*, *ACTN3 RR*, *PPARD TT*, and *PPARGC1A Ser/Ser* genotype, the greatest mean handgrip strength was observed in subjects with $TGS_{ACE+ACTN3+PPARD+PPARGC1A} = 1$ as expected (Table S1). Furthermore, subjects that were homozygous *ACE DD*, *ACTN3 RR*, and *PPARD TT* had the greatest handgrip strength, which suggests that these "strength/power" alleles do indeed confer a performance advantage (Table 5). However, it is also interesting to note that the subject with the best handgrip strength performance did not belong to the "optimal" (TGS = 0) power genotype group. These findings indicate that the relationships between the genetic traits and physical performance are quite complex and not yet completely understood [19, 21, 42].

Handgrip strength has been linked to premature mortality, disability, and other health-related complications in middle-aged and older people [43–45]. In the present study, we demonstrated an association between three genetic polymorphisms (*ACE I/D, ACTN3 R577X*, and *PPARD T294C*) and handgrip strength in sedentary female adolescents (16–18 years). These results may provide evidence that helps the development of recommendations such as early specific nutritional and/or functional interventions (e.g., resistance training activity) for those with a high TGS index. In the future, polygenic physical fitness profiling of a larger general population linked to specific nutritional/

Table 5 Association between total genotype score ($TGS_{ACE+ACTN3+PPARD}$) and performance in the fitness tests studied

Physical performance	Total genotype score							
	0	1	2	3	4	5	6	*p*
n	3	15	39	38	57	11	7	
Handgrip strength (kg)	32.7 ± 2.5 (33.1–36.0)	26.4 ± 1.0 (19.8–35.2)	25.8 ± 0.7 **(15.1–41.4)**	24.3 ± 0.7 (16.6–33.0)	25.9 ± 0.6 (16.3–37.9)	25.5 ± 1.3 (18.0–31.4)	25.1 ± 1.6 (18.6–31.6)	0.050
Standing long jump (cm)	168.6 ± 12.2	144.6 ± 5.2	143.6 ± 3.4	144.7 ± 3.4	149.5 ± 2.8	144.3 ± 6.4	133.9 ± 7.9	0.235
30-s sit-up (counts)	19.80 ± 2.3	17.2 ± 1.0	18.6 ± 0.6	16.6 ± 0.6	18.0 ± 0.5	17.6 ± 1.2	19.2 ± 1.5	0.329
60-s sit-up (counts)	35.4 ± 4.6	30.1 ± 2.0	34.4 ± 1.3	28.9 ± 1.3	32.3 ± 1.1	30.1 ± 2.4	34.5 ± 3.0	0.077
60-m dash (s)	11.9 ± 0.7	12.4 ± 0.3	11.6 ± 0.2	12.0 ± 0.2	11.6 ± 0.2	11.7 ± 0.4	12.2 ± 0.5	0.335
800-m run (s)	281.0 ± 20.0	292.8 ± 8.5	277.6 ± 5.6	292.3 ± 5.6	280.8 ± 4.6	293.0 ± 10.4	281.4 ± 14.0	0.457

All values indicate the mean ± SE adjusted for height, body weight, BMI, FFM%, FFM and FFMI by ANCOVA (with range, in handgrip strength performance); the bold numbers indicate the lowest and highest handgrip strength

functional intervention studies will be required to provide valid information on the true role of genetic factors on physical fitness and health.

In conclusion, the results indicate that the studied genes have a moderate influence on performance as measured by specific fitness tests and the effect of the *ACE* and *ACTN3* polymorphisms on the strength type of fitness is greater than the effect of *PPARD* and *PPARGC1A* polymorphism among Taiwanese female late adolescents.

Acknowledgment This study was supported by Grant NSC-96-2413-H-003-033 from the National Science Council, Taiwan.

Conflict of interest The authors declare no conflict of interest.

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