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ORIGINAL ARTICLE

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ACE Genotype May Have an Effect on Single versus Multiple Set Preferences in Strength Training

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Abstract A polymorphic variant of the human angiotensin converting enzyme (*ACE*) gene was identified. The 'D' (rather than 'I') variant was associated with improvements in strength related to physical training. We set out to determine whether the response to different patterns of strength training might also differ. Ninty-nine Caucasian male non-elite athletes were randomly allocated into one of three groups: 31 non-training/control (CG: 31), single-set (SSG: 35) and multiple-set (MSG: 33). SSG and MSG trained three times a week for 6 weeks. Both training groups were underwent a strength-training program with two mesocycles (12–15 repetition maximum (RM) and 8–12 RM mesocycles). One RM loads in half squat and bench press were assessed before training and after the first and second mesocycles. *ACE* polymorphisms analysed by polymerase chain reaction (PCR) methods. Subjects with *ACE* II genotype in the MST group had improved strength development in 12–15 RM, while SST and MST groups had similar gains in 8–12 RM. Subjects with *ACE* DD genotype in both the SSG and the MSG had similar benefits from both 12–15 RM and 8–12 RM. Strength gains for subjects with *ACE* ID genotype in the SSG were similar to MSG gains in response to 8–12 RM loads but not with 12–15 RM loads. Additionally, subjects with DD genotype had superior strength gains in both strength training groups. Tailoring strength training programmes (single-set vs. multiple set) according to the athlete's *ACE* genotype may be advantageous.

Keywords Resistance training systems · Training volume · Training intensity · *ACE* polymorphism · Genetics

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Introduction

In the circulating renin-angiotensin system (RAS), angiotensin-converting enzyme (ACE) cleaves vasodilator kinins to yield vasopressor angiotensin II. A polymorphism of the *ACE* gene exists in which deletion (D) of a 287 bp fragment is associated with higher ACE expression than its presence (Insertion, I). These systems also exist in diverse tissues, where *ACE* genotype seems to exert a similar effect (Costerousse et al. 1997; Danser et al. 1995). In particular, ACE is expressed in human muscle, and may here regulate muscle growth responses. Angiotensin II is known to cause hyperplasia (Daemen et al. 1991) and hypertrophy (Griffin et al. 1991) of vascular smooth muscle and cardiac muscle (Baker and Aceto, 1990), with the *ACE* D-allele associated with physiological (Montgomery et al. 1997; 2002; Myerson et al. 2001) and pathological (Lechin et al. 1995; Prasad et al. 1994) cardiac hypertrophy. In skeletal muscle, angiotensin II is a necessary mediator of the hypertrophic response to mechanical loading (Gordon et al. 2001).

One might thus expect the *ACE* D-allele to be associated with a greater hypertrophic response (and thus a greater increase in strength) in response to a strength-training programme. Indeed, data from Folland et al. (2000) support this notion. Similarly, Hopkinson et al. (2004) have shown the D-allele to be associated with quadriceps muscle strength in untrained COPD patients. In addition, the D-allele was associated with elite sprinting status (Myerson et al. 1999; Nazarov et al.

2001), elite short-distance swimmer status (Myerson et al. 1999; Woods et al. 2001), and a higher fast twitch muscle fibre ratio (Zhang et al. 2003). Thus, *ACE* DD genotype may be related with better response to low-volume high-intensity strength training regimens.

ACE I-allele is shown to be overrepresented amongst elite endurance athletes (Alvarez et al. 2000; Gayagay et al. 1998; Myerson et al. 1999; Nazarov et al. 2001; Tsianos et al. 2004). *ACE* II genotype is related with better muscular endurance (Montgomery et al. 1998), improved running economy (Woods et al. 2002), higher adaptation to hypoxia (Montgomery et al. 1998; Pahsa et al. 2001; Woods et al. 2002) and higher slow-twitch muscle fibre ratio (Zhang et al. 2003). This genotype may therefore be advantageous in response to high-volume and low-intensity strength training (muscular endurance training).

Strength training programmes utilize 'single set' system (SST): the performance of each exercise as one set and/or multiple set systems (MST): the performance of each exercise as several sets—e.g. Bulk system, DeLorme, Oxford, Triangle, Super Set, Tri-Set systems, etc. (Fleck and Kraemer 2004). During shorter training periods, evidence suggests that strength gains in response to SST are similar to those seen with MST (Carpinelli 2002; Wolfe et al. 2004). Later on, however, sustained improvement seems better when MST is used (Wolfe et al. 2004).

We thus hypothesized that the relative responses to MST or SST might similarly be associated with *ACE* genotype. We tested this hypothesis.

Materials and methods

Ninety-nine subjects were randomly assigned to three groups: a single-set group (SSG), a multiple-set group (MSG) and a control group (CG). In the SSG and the MSG, a periodization programme with two mesocycles was applied in order to create variations in volume and intensity. 12–15 repetition maximum (RM) loads (approximately 60–70% of 1 RM) were used in the first 3-week period (first mesocycle). In the second 3 week period (second mesocycle), the load was upgraded to 8–12 RM (approximately 70–80% of 1 RM). Frequency of training sessions was three times per week during the entire 6-week study period for both strength training groups. Nine to eleven muscle groups were trained in each individual session. The SSG used one set for each exercise for the entire training programme. The MSG used the Bulk system in the first mesocycle and used the Super-set systems with 20 to 30-s rest intervals between sets in the second mesocycle. The bulk system refers specifically to a multiple set system of three sets per exercise using the same load. Super setting has two distinct but similar types of programmes. One of them uses several sets of two exercises for the same body part but two groups of antogonistic muscles in rapid succession and the second type uses one set of several exercises for the same muscle group in rapid succession (Fleck and Kraemer, 2004). These particular training systems were used by the MSG in the second mesocycle to produce higher local tissue hypoxia. Both groups used similar exercise drills in their training programmes. Exercise programmes of the SSG and the MSG are summarized in the Table 1.

All subjects were Caucasian from the same geographic origin and were students in the School of Physical Education and Sports. They all had minimal experience in weight training and had not participated in weight training programmes during the previous 6 months. Control group was included in the study in order to monitor strength alterations resulting from Physical Education class participations and other possible factors.

All tests and weight training sessions were monitored by experienced instructors. Four training sessions were provided to familiarize students with the exercises and drill techniques to be used in the study. Changes in maximum weight for bench press (BP) and half squat (SQ) 1 RM were calculated as percentages.

Written consent was received from all subjects. The study was approved by the ethics committee of the Faculty of Medicine.

One repetition maximum tests

Width between grips in BP test and knee flexion angle in SQ test were standardized for each subject in order to ensure exercise position precision between trials. A standardized warm-up program preceded the 1 RM tests. The Brzycki formula (Brzycki 1993) was used to calculate 1 RM scores.

ACE genotyping

Genomic DNA was extracted from 200 μl of EDTA-anticoagulated peripheral blood leucocytes using the QIAmp Blood Kit (QIAGEN, Cat. No. 51106, Mississauga, ON, Canada). *ACE* genotype was determined by polymerase chain reaction (PCR) (Rigat et al. 1992). Each DD genotype was confirmed through a second PCR with primers specific for the insertion sequence (Shanmugam et al. 1993). The samples with II and DD homozygote genotypes and ID heterozygote genotype were selected at random. These samples were then purified by PCR products purified system (Genomics, Montage PCR, Millipore, Billerica, MA, USA) and directly sequenced by the ABI 310 Genetic Analyzer (ABI Prisma PE Applied Biosystems, Foster City, CA, USA).

Statistical analysis

Statistical analyses were performed using SPSS for Windows version 11.0 (SPSS Inc., Chicago, IL, USA).

Table 1 Exercise drills, loads (RM), set and repetition numbers used for the first and second mesocycles in SSG and MSGs

Single set group	First mesocycle - load: 12–15 RM			Second mesocycle - load: 8–12 RM		
	Mondays Load: 12 RM 1 set × 12 reps	Wednesdays Load: 15 RM 1 set × 15 reps	Fridays Load: 13–14 RM 1 set × 13–14 reps	Mondays Load: 8 RM 1 set × 8 reps	Wednesdays Load: 12 RM 1 set × 12 reps	Fridays Load: 10 RM 1 set × 10 reps
Knee extensors	KE	SQ	LP	SQ/LC[b]	FL/LC[b]	LP/LC[b]
Knee flexors	LC	LC	LC			
Shoulders	URR	ShP	LR	SP	URR	LR
Upper back	SR	LPD	SR	BP/SR[b]	BP/LPD[b]	BP/SR[b]
Chest muscles	BP	IP	CP			
Hip flexors	–	HF	HF	–	HF/HE[b]	HF/HE[b]
Hip extensors	HE	–	–	–		
Triceps brachii	TPD	TPD	TPD	FC/SC[b]	TPD/SBC[b]	TPD/SBC[b]
Biceps brachii	SBC	SBC	SBC			
Lower back	HyE	TR	TR	TR/RCS[b]	–	HyE/ Cr[b]
Abdominals	Cr	RCS	Cr			
Multiple set group	Mondays Load: 12 RM 3set × 12 reps[a]	Wednesdays Load: 15 RM 3 set × 15 reps[a]	Fridays Load: 13–14 RM 3 set × 13–14 reps[a]	Mondays Load: 8 RM 8 reps	Wednesdays Load: 12 RM 12 reps	Fridays Load: 10 RM 10 reps
Knee extensors	KE	SQ	LP	4 sets × SQ/ LC[b]	4 sets × FL/LC[b]	5 sets × LP/LC[b]
Knee flexors	LC	LC	LC			
Shoulders	URR	ShP	LR	1 set × SP/URR/ LR/IR[c]	4 sets × SP/LPD[b]	1 set × SP/URR/LR/IR[c]
Upper back	SR	LPD	SR	4 sets × BP/SR[b]		2 sets × BP/SR/IP/LPD[c]
Chest muscles	BP	IP	CP		1 set × BP/IP/DF/DP[c]	
Hip flexors	–	HF	HF	–	2 sets × HF/HE[b]	2 sets × HF/HE[b]
Hip extensors	HE	–	–	–		
Triceps brachii	TPD	TPD	TPD	1 set × TPD/ TC/FC[c]	3 sets × FC/SBC[b]	3 sets × TPD/SC[b]
Biceps brachii	SBC	SBC	SBC	1 set × SBC/ADC/SC[c]		
Lower back	HyE	TR	TR	3 sets × TR/Cr[b]	3 sets × TR/Cr[b]	HyE/RCS[b]
Abdominals	Cr	RCS	Cr			

[a]Bulk system

[b]Super set system with several sets of two exercises for two groups of antogonistic muscles in rapid succession

[c]Super set system with one set of several exercises for the same muscle group in rapid succession. *KE* knee extention; *LC* leg curl; *URR* upright row; *SR* seated row; *BP* bench press; *HE* hip extention; *TPD* triceps press down; *SBC* standing barbell curl; *HyE* hyper extention; *Cr* crunches; *SQ* 1/2 squat; *ShP* shoulder press; *LPD* lat pull down; *IP* incline press; *HF* hip flexion; *TR* trunk rotation; *RCS* roman chair sit-ups; *LP* leg press; *LR* lateral raise; *CP* chest press; *SP* seated press; *FC* french curl; *SC* scott curl; *TC* triceps curl; *ADC* alternating dumbell curl; *IR* infront raise

Frequencies, descriptive statistics, and means were analysed. Statistical significance was set at the $P < 0.05$ level. The Finetti $\chi 2$ statistics program was used to confirm that the observed genotype frequencies were in Hardy-Weinberg equilibrium. Differences between baseline and post-training values for all parameters of each group were analysed using the Wilcoxon test. Kruskal-Wallis and ANOVA tests and post hoc Bonferroni correction, Tukey HSD and LSD tests were used to analyse differences between groups. Genotype distribution across strength gain levels was compared by chi-square for linear trend in the SSG and the MSG for both BP and SQ.

Results

Ninety-nine male subjects (age: 19.4 ± 1.4, height: 180.3 ± 4.0 cm, weight: 70.9 ± 4.0 kg) took part in this study. Subject demographics were similar in all regards between the different groups (31 controls, 35 SSG subjects and 33 MSG subjects). Genotype distributions of subjects are listed in Table 2. Baseline performance measures were 111.4 ± 9.8 kg for SQ and 63.4 ± 4.6 kg for BP in the group overall ($n = 99$) and did not differ by genotype, nor by training group (Table 3).

Effects of SST and MST on muscular strength performance

Subjects in the SSG and the MSG obtained significant strength gains in the first and the second mesocycles and for the entire training period as compared to controls for both SQ and BP (all P values < 0.001). Strength gains in the MSG were higher than in the SSG for the 12–15 RM and for the entire training period ($P < 0.001$) and also for the 8–12 RM period ($P < 0.005$) in SQ and BP (Tables 4 and 5).

Effects of ACE genotypes on strength gains in SSG and MSG

Single-set group showed linear trends by genotype distribution across strength gain ratios in SQ and BP for the first and the second mesocycle and for the entire study period except first mesocycle gains in BP as strength gains in DD > ID > II (P values ≤ 0.001 for all). In MSG, linear trends in strength gains existed as DD > ID > II for the second mesocycle in both BP and SQ (P values ≤ 0.001) and for the entire period in BP ($P < 0.01$), but there were no linear trends in the first mesocycle (Table 6).

After the first mesocycle, strength gains were significantly higher in the MSG than in the SSG ($P < 0.05$) for both SQ and BP in *ACE* II subjects and for only SQ in *ACE* ID subjects ($P < 0.05$) (Tables 4 and 5). However, in subjects with *ACE* DD genotype, there were no statistically significant strength gain differences between SST and MST groups (Tables 4 and 5).

There was no difference between 1 RM variation ratio of MSG and SSG in each *ACE* genotype subgroup in the second mesocycle (Table 5).

Strength improvements between baseline and after sixth week of training period in the MSGs were significantly higher than in the SSGs for *ACE* II and ID genotypes ($P < 0.001$ and $P < 0.01$, respectively), while there were no 1 RM differences between the SSG and the MSG in subjects with DD genotype (Table 5).

All *ACE* genotype subgroups of MSG and SSG groups obtained significantly increased 1 RM values compared to CG subjects in the first and second mesocycles and for the entire study period ($P < 0.0001$; Tables 4 and 5).

Differences in strength gains between mesocycles

Strength gain ratios did not vary between mesocycles in the subjects with DD genotype in either SST or MST groups. The BP and SQ 1 RM improvement ratios for the MST groups significantly decreased in second mesocycle compared to the first mesocycle in *ACE* II ($P < 0.01$) and ID genotypes ($P < 0.05$). However, in the SSG, only SQ 1 RM values decreased significantly between mesocycles in *ACE* II and ID genotypes ($P < 0.01$

Table 2 Distributions of *ACE* genotypes in all groups

	n	*ACE* Genotype					
		II		ID		DD	
		n	Percent	*n*	Percent	*n*	Percent
SSG	35	10	28.6	11	31.4	14	40.0
MSG	33	10	30.3	10	30.3	13	39.4
CG	31	10	32.3	9	29.0	12	38.7
All	99	30	30.3	30	30.3	39	39.4

Table 3 Baseline strength values of all groups (in kg)

		SSG	MSG	CG	
ACE II genotype		(*n* = 10)	(*n* = 10)	(*n* = 10)	P^a
	SQ	107.1 ± 10.7	107.6 ± 5.7	105.5 ± 4.6	0.685
	BP	62.3 ± 5.0	61.6 ± 3.6	63.6 ± 4.1	0.512
ACE ID genotype		(*n* = 11)	(*n* = 10)	(*n* = 9)	P^a
	SQ	113.0 ± 11.4	114.8 ± 11.4	106.4 ± 5.5	0.432
	BP	62.7 ± 3.9	65.6 ± 4.9	62.0 ± 4.0	1.166
ACE DD genotype		(*n* = 14)	(*n* = 13)	(*n* = 12)	P^a
	SQ	119.2 ± 10.4	113.3 ± 9.2	110.3 ± 4.8	0.59
	BP	63.9 ± 4.7	66.3 ± 4.8	61.8 ± 4.9	0.88
All (*N* = 99)		(*n* = 35)	(*n* = 33)	(*n* = 31)	$P^{a\ b}$
	SQ	113.8 ± 11.6	112.0 ± 9.3	108.1 ± 7.0	0.056
	BP	63.1 ± 4.5	64.7 ± 4.8	62.4 ± 4.3	0.129

All P values > 0.05
[a] Kruskal Wallis test
[b] ANOVA

Table 4 Strength development ratios in groups ({[last value/ previous value]-1}*100)

		SSG	MSG	CG		
ACE II genotype		($n=10$)	($n=10$)	($n=10$)	$\chi 2$	*P*
12–15 RM	SQ	11.7 ± 1.2	14.9 ± 1.1	1.2 ± 3.6	25.061	0.0001[a]
(I.mesocycle)	BP	10.9 ± 2.0	13.6 ± 0.8	0.7 ± 3.3	23.494	0.0001[a]
8–12 RM	SQ	9.7 ± 1.3	11.4 ± 0.8	1.9 ± 4.6	18.014	0.0001[a]
(II.mesocycle)	BP	9.9 ± 1.1	10.9 ± 0.7	1.3 ± 1.2	21.392	0.0001[a]
1–6 weeks	SQ	22.6 ± 2.4	27.9 ± 0.8	3.0 ± 3.1	25.824	0.0001[a]
(Entire period)	BP	21.9 ± 1.7	26.0 ± 1.5	2.1 ± 2.7	25.812	0.0001[a]
ACE ID genotype		($n=11$)	($n=10$)	($n=9$)	$\chi 2$	*P*
12–15 RM	SQ	13.0 ± 0.8	14.3 ± 0.8	1.3 ± 1.7	22.237	0.0001[a]
(I.mesocycle)	BP	11.7 ± 1.9	13.1 ± 1.4	2.4 ± 1.1	19.197	0.0001[a]
8–12 RM	SQ	11.3 ± 1.3	12.8 ± 0.7	2.7 ± 2.1	21.313	0.0001[a]
(II.mesocycle)	BP	10.6 ± 0.9	11.9 ± 1.0	1.9 ± 1.8	19.197	0.0001[a]
1–6 weeks	SQ	25.9 ± 1.8	29.3 ± 1.8	4.1 ± 2.6	23.742	0.0001[a]
(Entire period)	BP	23.2 ± 2.7	26.6 ± 1.6	4.3 ± 1.7	22.042	0.0001[a]
ACE DD genotype		($n=14$)	($n=13$)	($n=12$)	$\chi 2$	*P*
12–15 RM	SQ	13.3 ± 0.6	14.1 ± 1.0	1.8 ± 1.2	27.758	0.0001[a]
(I.mesocycle)	BP	12.3 ± 1.5	13.0 ± 0.8	2.3 ± 2.0	24.615	0.0001[a]
8–12 RM	SQ	13.5 ± 0.6	14.0 ± 1.2	2.3 ± 1.0	24.806	0.0001[a]
(II.mesocycle)	BP	11.8 ± 1.5	12.6 ± 1.3	0.6 ± 1.3	25.114	0.0001[a]
1–6 weeks	SQ	28.6 ± 1.2	30.1 ± 1.8	3.7 ± 2.1	26.826	0.0001[a]
(Entire period)	BP	25.5 ± 2.6	27.3 ± 2.0	2.9 ± 1. 8	25.265	0.0001[a]
All ($N=99$)		($n=35$)	($n=33$)	($n=31$)	$\chi 2$	*P*
12–15 RM	SQ	12.8 ± 1.1	14.4 ± 1.0	1.5 ± 2.3	654.170	0.001[a]
(I.mesocycle)	BP	11.7 ± 1.8	13.2 ± 1.0	1.8 ± 2.4	242.345	0.001[a]
8–12 RM	SQ	11.8 ± 1.9	12.8 ± 1.4	2.3 ± 2.8	968.139	0.001[a]
(II.mesocycle)	BP	10.9 ± 1.4	11.9 ± 1.3	1.2 ± 1.5	378.642	0.001[a]
1–6 weeks	SQ	26.6 ± 3.0	29.2 ± 1.8	3.6 ± 2.6	567.550	0.001[a]
(Entire period)	BP	23.8 ± 2.8	26.7 ± 1.7	3.1 ± 2.2	988.306	0.001[a]

[a] $P < 0.001$ (Kruskal Wallis test)

and $P < 0.05$, respectively). Variation ratios for BP and SQ 1 RMs for each mesocycle may be found in Table 4.

Discussion

This is the first study that has examined the effect of an athlete's *ACE* genotype on strength development rate in response to single-set versus multiple-set weight training systems.

Table 5 Differences amongst groups in strength (p values)

		MSG ($n=33$)		
SQ 12–15 RM	SSG	0.0001 ***,[a]		
SQ 8–12 RM	SSG	0.087 a / 0.035 *,[b]		
SQ 1–6 weeks	SSG	0.0001 ***,[a]		
BP 12–15 RM	SSG	0.003 **,[a]		
BP 8–12 RM	SSG	0.012 [a]		
BP 1–6 weeks	SSG	0.0001 ***,[a]		
		ACE II MSG	*ACE* ID MSG	*ACE* DD MSG
SQ 12–15 RM	SSG	0.013*,[c]	0.047*,[c]	0.115
SQ 8–12 RM	SSG	0.523	0.103	0.642
SQ 1–6 weeks	SSG	0.0001***,[c]	0.002***,[c]	0.90
BP 12–15 RM	SSG	0.038*,[c]	0.152	0.719
BP 8–12 RM	SSG	0.146	0.076	0.377
BP 1–6 weeks	SSG	0.0001***,[c]	0.003***,[c]	0.142

[a] Tukey HSD
[b] LSD
[c] Bonferroni. SSG and MSG strength development ratios were significantly higher than CG in all variables ($P > 0.001$) (Bonferroni correction) * $P < 0.05$; ** $P < 0.01$; *** $P < 0.001$

Subjects with *ACE* II genotype had an advantage in strength gain while exercising with multiple-set systems than with single-set system in 12–15 RM loads. However, there was no difference in strength gains between single-set and multiple-set systems in 8–12 RM in this genotype group. When changes between baseline measurements and measurements after 6-weeks were considered, multiple-set systems seems to be advantageous for *ACE* II and ID genotypes for strength gain (Tables 4 and 5).

Subjects with *ACE* DD genotype had similar strength gains using both set systems for both loads. These subjects might not need to use multiple-set systems for 1 RM development, since single-set system strength development for both 12–15 RM and 8–12 RM loads was just as effective. *ACE* DD genotype groups obtained higher gains in strength than other genotype groups in both set systems and both loads (Tables 4 and 5).

ACE II and ID genotypes showed significant decreases in 1 RM development ratios in the second mesocycle than the first mesocycle. There might be a greater motor learning effect for all genotypes in the early phase of the study. However, there was no such difference in *ACE* DD genotype group. These findings might be interpreted as *ACE* DD genotype having an advantage in strength development when higher loads are used. In the second mesocycle, there were linear trends by genotype distribution across strength gain ratios in SQ and BP both for the SSG and MSG as strength gains in DD > ID > II. However, in the first mesocycle, the linear trend in strength gains by *ACE* genotype observed only for SQ of the SSG (Table 6).

Table 6 Linear trends in genotype distribution across strength gains ratios for SSG and MSG

		ACE II	*ACE* ID	*ACE* DD		
SSG (N = 35)		(*n* = 10)	(*n* = 11)	(*n* = 14)	$\chi 2$	*P*
12–15 RM	SQ	11.7 ± 1.2	13.0 ± 0.8	13.3 ± 0.6	11.410	0.001[b]
(I.mesocycle)	BP	10.9 ± 2.0	11.7 ± 1.9	12.3 ± 1.5	3.287	0.070
8–12 RM	SQ	9.7 ± 1.3	11.3 ± 1.3	13.5 ± 0.6	23.924	0.0001[a]
(II.mesocycle)	BP	9.9 ± 1.1	11.7 ± 1.9	11.8 ± 1.5	10.199	0.001[b]
1–6 weeks	SQ	22.6 ± 2.4	25.9 ± 1.8	28.6 ± 1.2	23.111	0.0001[a]
(Entire period)	BP	21.9 ± 1.7	23.2 ± 2.7	25.5 ± 2.6	10.465	0.001[b]
MSG (N = 33)		(*n* = 10)	(*n* = 10)	(*n* = 13)	$\chi 2$	*P*
12–15 RM	SQ	14.9 ± 1.1	14.3 ± 0.8	14.1 ± 1.0	3.584	0.058
(I.mesocycle)	BP	13.6 ± 0.8	13.1 ± 1.4	13.0 ± 0.8	2.253	0.133
8–12 RM	SQ	11.4 ± 0.8	12.8 ± 0.7	14.0 ± 1.2	18.444	0.0001[a]
(II.mesocycle)	BP	10.9 ± 0.7	11.9 ± 1.0	12.6 ± 1.3	10.496	0.001[b]
1–6 weeks	SQ	27.9 ± 0.8	29.3 ± 1.8	30.1 ± 1.8	8.813	0.003[b]
(Entire period)	BP	26.0 ± 1.5	26.6 ± 1.6	27.3 ± 2.0	2.861	0.091

Strength gain ratios was calculated as: {[last value/previous value]-1}*100
[a] $P < 0.001$; [b] $P < 0.01$ (chi-square test)

These data suggest that *ACE* I-allele might be responsible for better response to high volume—low intensity muscular endurance training while D-allele might be related to better strength development with higher intensity—lower volume resistance training. Resistance exercises with multiple sets and 12–15 RM loads last longer than single set and 8–12 RM loads, causing more tissue hypoxia. Thus, the advantage of *ACE* II genotype in strength gain as response to MST as compared to SST in 12–15 RM loads may result from the higher oxidative capacity and hypoxia adaptation properties of this genotype. *ACE* II genotype subject seem to lose this advantage in 8–12 RM because of diminished training volume.

In subjects with *ACE* II genotype, since increased half-life of bradykinin results in improved tissue oxygenation, contractile properties of cardiac and skeletal muscles may elevate (Jones et al. 2002). This greater peripheral tissue oxygenation and decreased rise in lactate, reflecting greater muscle efficiency, occurs more in *ACE* II compared to DD subjects during exercise in patients with COPD (Kanazawa et al. 2002).The inhibition of ACE may increase glucose uptake, glycogen concentration in skeletal muscle and adaptation of glycolytic enzymes (Henriksen and Jacob 1995; Jacob et al. 1996). Inhibition of ACE also enhances peak aerobic capacity, induces improvement in skeletal muscle perfusion (Drexler et al. 1989; Mancini et al. 1987), improves peripheral oxygen extraction and exercise performance greater than acute improvements in cardiac output (Drexler et al. 1991).

Subjects with higher *ACE* D allele ratio have higher anaerobic performance (Woods et al. 2001; Myerson et al. 1999; Nazarov et al. 2001) and have greater quadriceps muscle strength gains in response to isometric resistance training (Folland et al. 2000). DD genotype of the *ACE* gene, associated with increased bradykinin degradation, has also been associated with significant blunting of nitric oxide vasodilatory responses (Butler et al. 1999). Inhibition of vasodilatation restricts local blood flow and lipolysis in skeletal muscle tissue (Goossens et al. 2004) and glucose oxidation exceeds uptake (Townsend and DiPette, 1993) in those subjects. Elevated plasma and tissue angiotensin II levels in this genotype may facilitate the redirection of blood flow from type I muscle fibres to the type II fibres (Rattigan et al. 1996) that are favoured in power performance. Greater plasma and tissue angiotensin II causes a reduction in mitochondrial density (Drexler et al. 1992), reduces muscle oxidative capacity (Drexler et al. 1992; Mettauer et al. 2001) and increases the proportion of fatigue-sensitive fast type II fibres and consequently decreases proportion of slow-twitch, fatigue-resistant type I fibres (De Sousa et al. 2000). Findings on *ACE* DD genotype in this study may stem from these associations.

In conclusion, *ACE* DD genotype seems to have an advantage in strength development when compared to II and ID genotypes. Subjects with DD genotype benefit similarly from single- and multiple-set systems and therefore it is not necessary to use multiple-set systems to obtain optimum strength improvements for these subjects. For subjects with *ACE* II genotype, single-set training produces sufficient strength increases in 8–12 RM loads, but use of multiple-set systems is advised for optimum benefit.

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