

PREVALENCE OF ACSL (RS6552828) POLYMORPHISM AMONG RUNNERS

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ABSTRACT

The ACSL A/G polymorphism is associated with endurance trainability. Previous studies have demonstrated that homozygotes of the minor AA allele had a reduced maximal oxygen consumption response to training compared to the common GG allele homozygotes, and that the ACSL A/G single nucleotide polymorphism explained 6.1% of the variance in the VO₂max response to endurance training. The contribution of ACSL single nucleotide polymorphism to endurance trainability was shown in non-athletes, however, its potential role in professional athletes is not clear. Moreover, the genetic basis to anaerobic trainability is even less studied. Therefore, the aim of the present study was to examine the prevalence of ACSL single nucleotide polymorphism among professional Israeli long distance runners (n=59), middle distance runners (n=31), sprinters and jumpers (n=48) and non-athletic controls (n=60). The main finding of the present study was that the ACSL1 AA genotype, previously shown to be associated with reduced *endurance* trainability, was not higher among sprinters and jumpers (15%) compared to middle- (16%) and long-distance runners (15%). This suggests that in contrast to previous studies indicating that the ACSL1 single nucleotide polymorphism may influence endurance trainability among non-athletic individuals, the role of this polymorphism among professional athletes is still not clear.

Keywords: *sprinters, long distance runners, genetic polymorphism, ACSL*

INTRODUCTION

Long-chain-fatty-acid – CoA ligase 1 is an enzyme that in humans is encoded by the ACSL1 gene [12, 13]. ACSL1 exhibits an important potential relevance to the adaptation to regular exercise. ACSL1 contributes most of the acyl-CoA synthetase activity in adipose tissue and is highly expressed also in skeletal muscles and in the heart. ACSL1 encodes for an enzyme that is involved in the partitioning of fatty acids and the control of lipid influx but, even more importantly, the control of carbohydrate efflux [8]. It plays a key role in normal insulin metabolism and fatty acid-induced insulin resistance. A SNP in ACSL1 has been associated with fasting glucose, insulin resistance, and the presence of metabolic syndrome, particularly in the presence of a high-fat diet [10]. Besides its possible relevance to habitual physical activity and exercise, studies have shown that homozygotes of the rs6552828 minor allele (A/A) had 125 ml/min (28%) and 63 ml/min (17%) lower VO_2max responses to endurance exercise training than the common allele homozygotes (G/G) and heterozygotes (A/G), respectively. In a single-SNP analyses, rs6552828 explained 6.1% of the variance in the VO_2max response to training [3]. Therefore, the potential contributing role of the ACSL1 gene in aerobic metabolism at the adipocyte, cardiomyocyte, liver and skeletal muscle fiber level [4, 5–7, 9, 11] highlights its potential to explain individual variability in endurance performance, as well as in some health-related phenotypes.

While the contribution of ACSL1 single nucleotide polymorphism to endurance trainability was shown in non-athletes, its potential role in professional athletes is less studied. Moreover, the genetic basis to anaerobic trainability is even less studied. Therefore, the aim of the present study was to examine the prevalence of ACSL1 SNP among professional Israeli long distance runners, middle distance runners, sprinters and jumpers. We hypothesized that the ACSL1 AA genotype associated with reduced endurance trainability would be higher among sprinters and jumpers.

MATERIALS AND METHODS

Subjects

One hundred and thirty-eight male athletes [59 long distance runners (LDR), 31 middle distance runners (MDR), 48 sprinters and jumpers (S/J)], and 60 non-athletic controls participated in the study. All athletes competed in national and/or international level meets on a regular basis. Athletes' data are presented in Table 1.

Table 1. Athletes' data.

Group	N	Main even	Age (Mean±SD, Range)
LDR	59	5000m–marathon	32.4±9.5 (20–50)
MDR	31	800–1500m	32.3±15.0 (17–55)
S/J	48	100–200m, jumps	30.5±13.7 (17–49)
Control	60	nr	26.4±5.8 (19–29)

LDR – long distance runners; MDR – middle distance runners; S/J – sprinters and jumpers

The study was approved by the Institutional Review Board of the Hillel Yaffe Medical Center, Hadera, Israel, according to the Declaration of Helsinki. A written informed consent was obtained from all participants.

Genotyping

Genomic DNA was extracted from samples of peripheral venous blood or buccal cells according to the salting-out procedure. Genotypes were determined using the Taqman allelic discrimination assay. The Assay-by-Design service (<https://www.thermofisher.com/il/en/home.html>) was used to set up a Taqman allelic discrimination assay for the ACSL (rs6552828 A/G), Primers and probe sequences are given in Table 2.

Table 2. Primers and probe sequences for ACSL (rs6552828 A/G) Taqman allelic discrimination assays.

Primer sequences		Probe sequences	
Forward	Reverse	Forward: VIC	Reverse: FAM
pdUGpdUApdCpd	pdCpdUGpdUApdC	CGGCTGCATCTA	TGCATAAACTTT
UpdUpdUpdCpdUp	pdUpdUpdUpdCpd	GGATCTCAA	AAACCAACCAC
dCpdUpdCpdCAAp	UpdUpdUpdCpdCA		CA
dCA	ApdCA		

The Polymerase Chain Reaction (PCR) mixture included 5ng genomic DNA, 0.125µl TaqMan assay (40*, ABI), 2.5µl Master mix (ABI) and 2.375µl water. PCR was performed in 96 well PCR plates in an ABI 7300 PCR system (Applied Biosystems Inc., Foster City, CA, USA) and consisted of initial denaturation for 5min at 95 °C, and 40 cycles with denaturation of 15s at 95 °C and annealing and extension for 60s at 63 °C. Results were analyzed by the ABI Taqman 7900HT using the sequence detection system 2.22 software (Applied Biosystems Inc., Foster City, CA, USA).

Statistics

The SPSS statistical package, version 20.0, was used to perform all statistical evaluations (SPSS, Chicago, IL, USA). A χ^2 -test was used to confirm that the observed genotype frequencies were within the Hardy-Weinberg equilibrium, and to compare allele and genotype frequencies between athletes and controls, as well as between athletes from different competitive levels. If observed or expected values included a cell with a value of 5, we used Fisher's exact test to compare alleles and genotype frequencies.

RESULTS

The complete data on allele and genotype frequencies are presented in Table 3. The genotype subtype did not differ by age or sex. *ACSL* genotypes were in agreement with the Hardy-Weinberg equilibrium for all groups ($p = 0.917$ for Controls, $p = 0.843$ for S/J, $p = 0.856$ for MDR; $p = 0.930$ for LDR).

Table 3. *ACSL* A/G (rs6552828) Genotype and allele frequencies (%).

	Control	S/J	MDR	LDR
n	60	48	31	59
AA	7(12)	7(15)	5(16)	9(15)
AG	24(40)	23(48)	11(35)	30(51)
GG	29(48)	18(38)	15(48)	20(34)
A allele	38(32)	37(39)	21(34)	48(41)
G allele	82(68)	59(61)	41(66)	70(59)

S/J – sprinters and jumpers; MDR – middle distance runners; LDR – long distance runners

The frequency of the *ACSL* AA genotype carriers, which is related to reduced VO_2max response to training, was not significantly different among LDR, MDR, S/J and controls (Figure 1).

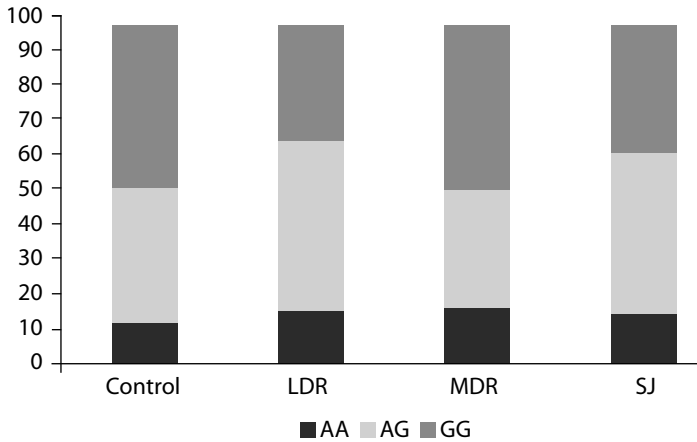


Figure 1. ACSL A/G genotype frequencies among S/J, MDR, LDR, and controls.

DISCUSSION

The present study examined the prevalence of ACSL1 SNP among professional Israeli long distance runners, middle distance runners, sprinters and jumpers. The main finding of the study was that in contrast to our hypothesis, the ACSL1 AA genotype, previously shown to be associated with reduced *endurance* trainability, was not higher among sprinters and jumpers compared to long-distance runners.

The ACSL A/G polymorphism is associated with endurance trainability. It was previously demonstrated that homozygotes of the minor AA allele had a reduced VO_2 max response to training compared to the common GG allele homozygotes, and that the ACSL A/G single nucleotide polymorphism explained 6.1% of the variance in the VO_2 max response to endurance training [3]. However, while this association was found in non-athletic individuals, the linkage between the ACSL1 single nucleotide polymorphism and endurance trainability among professional athletes, and in particular, among a homogeneous group of long-distance runners, is much less clear.

The ACSL SNP may vary among different populations of long-distance runners. Consistent with that the frequency of the AA genotype (associated with reduced endurance trainability) among native Israeli long-distance runners was higher (24%) than the frequencies reported among Spanish endurance athletes (17.1%) and lower compared to Chinese (31.3%) endurance athletes [14]. Moreover, we recently studied the frequency of the ACSL genotype among Israeli long-distance runners of Ethiopian and non-Ethiopian origin. The Ethiopian Beta Israel community consist only about

1.7% of the overall Israeli population, but their dominance in Israeli long-distance record table is dramatic (e.g. between 50–66% of the 30 all-time best male results in the marathon and half-marathon). We found that the frequency of the AA genotype carriers among Israeli long-distance runners of Ethiopian origin was significantly lower (8%) compared to the non-Ethiopian Origin Israeli runners (24%) [2]. Thus, fewer long-distance runners of Ethiopian origin had a genetic predisposition for reduced response to aerobic training. Interestingly, among the non-Ethiopian origin runners the frequency of AA carriers was significantly lower among elite compared to national levels runners suggesting the potential role of the ACSL genotype for endurance excellence in this population as well.

We hypothesized that since endurance trainability is less important for short-distances athletic events, the frequency of the ACSL1 single nucleotide polymorphism would be lower among sprinters and jumpers. However, in contrast to our hypothesis no significant difference was found in the ACSL AA genotype between professional Israeli long-distance runners, middle-distance runners, sprinters and jumpers. The potential contribution of many potential genes for excellence in endurance and anaerobic-power type sports were studied in recent years, and several favoring endurance and anaerobic-power single nucleotide polymorphism profiles were proposed [1]. The present study suggests that the ACSL1 single nucleotide polymorphism cannot distinguish between these two ends of the endurance to sprint

The potential use of genetic polymorphisms, and in particular the single nucleotide polymorphism (SNP) of hormone genes, as a tool to assist in predicting future athletic performance is currently an extremely challenging topic, mainly because each possible gene makes only a small contribution to the overall heritability. Previous results and the results of the present study suggest that while the ACSL1 single nucleotide polymorphism may influence endurance trainability among non-athletic individuals, its role among professional athletes is still not clear.

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