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Original article

Does MCT1-T1470A Polymorphism Modify Lactate Kinetics and Training Status?

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Abstract. *Study Objectives:* The (*MCT1*-T1470A) polymorphism related to monocarboxylate transporters 1 (MCTs) which transport lactate (LA) may affect LA kinetics and training status, which is unclear. *Methods:* Participants in the athletic group (AG; 42 anaerobic athletes; 21.8 ± 2.7 years) and the control group (CG; 39 sedentary men; 23.0 ± 3.3 years) performed the Yoyo recovery level 1 test. LA elimination speeds were calculated by dividing the difference between LA5, LA15, and LA30 values of passive recovery corresponding to the 5th, 15th, and 30th minutes following the Yoyo test by the elapsed time. *MCT1* polymorphism was determined from genomic DNA samples by next-generation sequencing. *Results:* The LA5, LA15, and LA30 values of the control group were significantly higher than those of the athlete group (p=0.053, p=0.042, and p=0.028, respectively), but not for LA elimination speeds. There was no significant difference for these parameters between genotype groups. Although the VO_{2max} of the AA control group was significantly greater than that of the T carrier (Tc) control group, there was no significant difference for VO_{2max} between the athletic genotype groups (AA and Tc). *Conclusions: MCT1*-T1470A polymorphism did not have a significant effect on LA kinetics in athletes. However, the AA group was negatively affected for VO_{2max} compared to the Tc group. This may be due to extreme sensitivity of the AA group to the training caused by this polymorphism. Further studies are needed to shed light on this entity.

Key words: MCT1-T1470A, Polymorphism, Lactate transporters, Anaerobic exercise, Lactate elimination

Introduction

The physical and physiological demands of sports involving intense intermittent anaerobic exercises (such as basketball, handball and volleyball) are high due to covering multiple short intense activities like high-speed running and sprinting (1). In this type of sports, the subsequent recovery interval takes a few seconds and less than a few minutes. Thus, anaerobic glycolysis becomes the dominant energy pathway. Then H^+ ions increase with lactate (LA) concentration and pH decreases (2). These conditions can impair both the ATP/CP production and sport performance due to the decreased pH (1,2). Most of the LA produced in muscles undergoes aerobic oxidation in mitochondria, the rest is converted to glucose and/or glycogen by gluconeogenesis in livers and kidneys, which increases by endurance training (Tomlin & Wenger, 2001). Therefore, LA (removal) elimination speed (LES) and LA accumulation capacity (lactate tolerance, LT) in the

mentioned anaerobic sports (3) are important for performance (1,2,4). For example, athletes with more LT can change the score at any time as they have more balls towards the end of the match. Despite metabolic acidosis, they can transport lactate with protons from muscle to blood faster and with less pain sensation, and from there to other organs (3). Therefore, although team sports need a dominantly anerobic energy pathway, they need a good aerobic endurance capacity to recover faster (1–4). Mostly, the removal of LA is performed via the membrane bound proton-linked monocarboxylate transporters (MCTs), depending on pH and lactate gradient (in symport with H^+) by a cell–cell LA shuttle, which allows faster transportation of monocarboxylates like LA, pyruvate and ketone bodies (4–6). The most common isoforms in skeletal muscle are MCT1 and MCT4. MCT4 plays a role in the transport of lactate from type 2 muscle fibers to blood, MCT1 transports it from blood to other tissues and organs (5,6). MCT1 protein is mostly found in type 1 fibers, which have a greater affinity to LA than MCT4 (6).

These two MCTs increase with exercise, whereas muscle inactivity reduces MCT1 expression (7–9). This improvement can delay the onset of fatigue (3,9). But, the other important factor affecting MCT1 expression is also variations in *MCT1* gene (10). For example, A1470T (rs1049434) polymorphism (MCT1P) leads to an aspartic acid to-glutamic acid change in codon 490 of the SLC16A1 gene, which caused a reduction of 35–40% in the erythrocytes lactate transport rate of the patients carrying T allele of MCT1P. Therefore, it was revealed shown that T allele cariers had higher LA accumulation capacity, wheras A allele carrier have higher aerobic endurance (11). Similarly, in another study conducted with a small number of elite field hockey male athletes without a control group, it was shown that the decrease in blood lactate levels were lower in T allele carriers than that the A group during active recovery after a maximal exercise, but not during passive recovery (12) which is was not the first and only study in the literature examining the LES. Unlikely, it was found that the AA genotype have greater blood lactate levels than the other genotype groups during different exercise protocols in men (13). In another study, it was not different between these two genotype groups after a maximal exercise (14). As seen in the results of the above studies, they are contradictory and do not provide sufficient information on how lactate kinetics (including LES) behave during recovery after a maximal exercise in non-elite athletes and sedentary individuals. Furthermore, it was reported that MCT1P is associated with the incidence of muscle injuries in elite football players (15) and that deficiency in MCT1 in mice is related with the regeneration of peripheral nerves (16). Therefore, the present study may provide useful information on explaining the reasons why MCT1 is associated with sports injuries. Thus knowing the athletes' genetic predisposition to sports-related performance components and injuries can be important for both sports performance and individualizing training programs. Therefore, we designed a study by isolating as much as possible confounding factors such as LA measurement methods, presence of sedentary group and participant number and exercise protocol. We used the Yoyo IR-1 test as the protocol (17) because Yoyo intermittent recovery level 1 (Yoyo IR-1) tests are frequently used to measure both aerobic fitness levels and recovery capacity of none-elite players and team sports (18).

Therefore, the aim of the present study was to investigate the effects of Yoyo IR-1 exercise test on LA kinetics (LA concentrations and LESs) during passive recovery and the role of MCT1P on these possible effects in trained young male Turkish team players such as, basketball and handball. To our knowledge, it is the first study performed in regard to those parameters.

Materials and Methods

Participants

The study group consisted of 42 healthy males as athletic group (AG) whose ages were between 18-35 years and had been practicing an anaerobic sport (such as soccer, basketball, handball and volleyball) regularly for at least 3-4 months (21.78±2.67 years, 182.16±9.65 cm, 81.75±15.49 kg, BMI; 24.51±3.41) and 39 healthy sedentary individuals as control group (CG) of similar age and physical characteristics (23.02±3.28 years, 176.97±6.04 cm, BW; 75.65±7.95 kg, BMI;

24.13±2.05). The male individuals who were non-obese (body mass index, BMI<30), did not have any disease, and were not regularly using cigarettes participated in the present study. The sedentary volunteers were the individuals who weren't doing any exercise regularly for at least 3–4 months. For this purpose, a total of 100 participants were enrolled in the study. Initially, medical history were taken in terms of general health and they were examined by sports medicine doctors. Then, 81 participants who were found healthy and met our criteria were accepted to the present study. First, the anamnesis of the individuals participating in the study were taken in terms of health and they were examined by sports medicine doctors. Then, 81 participants who were found healthy and met our criteria accepted to the present study. The athletes did regular training at least 3 days a week and they had an experience of at least 3-4 years. Sedentary group, meeting the criteria was made up of students at Ege University. All individuals had the same ethnicity. The participants were informed about the purpose of the study, the benefits, the tests to be performed, as well as possible risks, and an informed consent was taken. Ege University Faculty of Medicine Scientific Research Ethics Committee approved the project, which is in compliance with the "Helsinki Declaration of Ethical Principles in Medical Research on Humans".

Design and Procedures

The Yoyo IR-1 test is an incremental shuttle run test. In this test, participants run 2x20 meter shuttle runs and each shuttle run has a 10 second recovery period. The recovery test is completed in about 10-30 minutes (18). The participants were adequately familiarized prior to actual testing in the present study and performed Yoyo test. Blood samples were taken from the fingertips to determine the lactate concentrations at LESs were calculated by dividing the elapsed time of the differences between LA5, LA15, and LA30 values corresponding to 5th, 15th, and 30th minutes during passive recovery after the Yoyo IR-1 test. The blood lactate taken in the 5th minute of the recovery was accepted as maximal LA. The test distances (m) obtained after the test were converted to indirect VO_{2max} values by the following formula (17). LA elimination speeds (LES15 and LES30) at LA15 and LA30 points were calculated by dividing the lactate differences between LA5 with LA15 and LA30 by the elapsed time (10 and 25 minutes).

$$VO_2max(ml/kg/min) = YoyoIR\text{-}1distance(m) \times 0.0084 + 36.4$$

(Eq.1)

Measurements

An electronic medical weighing instrument (Seca 769, Germany) was used for height and weight (BW) measurements. BMI calculated from height and body weight.

Lactate analysis: Whole blood samples were taken from the fingertips into two heparinized hematocrit capillary tubes (150-200µL). These samples were transferred into special YSI 2315 blood lactate preservative tubes which has anti-coagulant and anti-glycolytic substances and mixed and stored at 4^0C until the analysis was performed by the YSI 1500 Sport Lactate Analyzer (YSI Corp. Incorp., Yellow Springs, Ohio, USA) The analyzer measures total LA levels in both plasma and erythrocytes lysing with YSI 1515 cell lysing kits by an electro enzymatic (lactate oxidase) membrane method. It is known that erythrocytes (RBC), which are a significant lactate producer, also have an important role in LA transport. Therefore, RBC's LA levels were different in the genotype groups of MCT1P due to lactate transporter defects inskeletal muscle and red cells during resting (i.e.passive state) (10). Therefore, we measured total (within plasma + RBC) LA concentrations in the present study, which can better reflect the arterialized blood LA concentration. We used Yoyo IR-1 test protocol to examine LA kinetics because exercise protocols are confounding factors (13) and in addition it is the most commonly used test in team sports (17). This protocol can give the opportunity to examine the recovery and aerobic fitness levels obtained at the end of the same test and LA kinetics simultaneously together with phenotypic characteristics according to MCT1P.

Genotyping: *MCT1*-T1470A polymorphism (MCT1P) was performed from genomic DNA samples isolated from peripheral blood. Blood samples with

EDTA in the hemogram tubes were isolated with an auto-analyzer (Promega Maxwell RSC-AS4500, USA) using a DNA isolation kit (Maxwell RSC Blood DNA Kit-AS1400, USA). After PCR, MCT1P polymorphisms were determined by next-generation sequence (NGS) analysis in the laboratory of the department of medical genetics of Ege University Medical Faculty, in Turkey. The primers (PRZ Biotech, Turkey) used for NGS analysis are as follows: MCT1P forward: 5'-ACA CATACTGGGCATGTGGC-3', MCT1P reverse: 5'-AATCCCATCAATGAACAACTG GTAT-3'. Samples were categorized based on MCT1 genotyping results: TT homozygous group, TA heterozygous group, and AA homozygous group. Accordingly, the athletic TT homozygous group was named ATT and the athletic TA heterozygous group was named AAT, the control TT homozygous group was named CTT and the control TA heterozygous group was CAT. TT homozygous group and TA heterozygous group were combined due to lack of numbers and named as T carrier (Tc) group. Accordingly, the athletic group was named as ATc and AAA, and the control group was named as CTc and CAA. The discussion was performed according to last-named genotype groups. Genotype and allele frequencies were not significantly different between athletes and sedentary groups for *MCT1*-T1470A polymorphism ($\chi2$=5.384, p= 0.068; $\chi2$= 0.851, p= 0.356) (Table 1).

Statistical Analysis

Significance was based on p<0.05. The data obtained was applied in independent groups for the analysis of differences. The Shapiro-Wilk normality test was used to determine whether the distribution was homogeneous or not. "T-Test" was used for parametric data, and the "Mann Whitney U Test" was used for nonparametric data to find if there was a significant difference between athlete group (AG) and control group (CG). The relationships between the biochemical parameters and physical measurements of both groups were determined by "Spearman Correlation Analysis" and "Pearson Correlation Analysis". "Hardy-Weinberg equation" was taken into consideration in determining genotype and allele frequencies. Differences between the genotype frequencies of the groups were calculated by the chi-square test. Interactions between genotype and exercise for dependent variables were found by 2x2 (main group x genotype subgroups) factorial test (ANOVA). According to the literature review, in a study of two groups of approximately 38 people power analysis with (G * Power) test should have 80% accuracy (p= 0.80) to achieve a significant difference with an effect size of approximately (d= 0.70) (19). Therefore, the design of this study may be considered statistically appropriate.

Results

The allele frequencies and genotype distributions

In the present study, the frequencies of distributions of T allele and genotypes in the athletes and the controls were 42% and 35% (Table 1) and these data were similar to the previous literature (13,20,21).

Physical and physiological parameters of the groups

Heart rate (HR) levels for the participants after the Yoyo IR-1 test were around 190 bpm. This

Table 1. Genotype and allelic frequencies of *MCT1*-T1470A polymorphism

Frequencies	Groups	Athlete	Control	Total
Genotype frequencies	AA	16 (38.1%)	14 (35.9%)	30 (37.0%)
	AT	17 (40.5%)	23 (59.0%)	40 (49.4%)
	TT	9 (21.4%)	2 (5.1%)	11 (13.6%)
Allele frequencies	A	0.583	0.654	0.617
	T	0.417	0.346	0.383

A: A allele, T: T allele, AA: AA homozygous group, AT: AT heterozygous group, TT: TT homozygous group

Table 2. Physical, physiological parameters, lactate accumulation and lactate elimination rate values of the groups following Yoyo Test (Mean ± SD)

Variables	AG (n=42)	CG (n=39)	p value AG-CG
Age (years)	21.78 ± 2.67	23.02 ± 3.28	0.053
Height (cm)	182.16 ± 9.65	176.97 ± 6.04	0.005
BW (kg)	81.75 ± 15.49	75.65 ± 7.95	0.040
BMI (kg/m^2)	24.51 ± 3.41	24.13 ± 2.05	0.940
HR (beats/min)	190.66 ± 9.43	190.76 ± 10.17	0.963
VO_{2max} (ml/kg/min)	47.40 ± 3.16	44.27 ± 2.99	<0.001
LA5 (mM)	13.12 ± 3.18*	14.24 ± 3.43*	0.130
LA15 (mM)	9.19 ± 3.26†	10.32 ± 3.51†	0.247
LA30 (mM)	5.2 ± 1.91	6.22 ± 2.57	0.092
LES15 (mM/min)	0.392 ± 0.179$^{\Delta}$	0.391 ± 0.175$^{\Delta}$	0.979
LES30 (mM/min)	0.316 ± 0.08	0.320 ± 0.07	0.828

AG: athlete group, BMI: body mass index, BW: body weight, CG: control group, Distance: the distance during Yoyo IR-1 test, HR: heart rate, VO_{2max}: maximal oxygen consumption, LA5: lactate value in 5th minute, LA15: lactate value in 15th minute, LA30: lactate value in 30th minute, LES15: lactate elimination speed between 5th and 15th minutes, LES30: lactate elimination speed between 5th and 30th minutes. *: higher than that of LA15 and LA30 (p<0.001); †: higher than that of LA30 (p<0.001); $^{\Delta}$: higher than that of LES30 (p<0.01, in athlete group, p<0.05 in control group).

Table 3. Physical and physiological parameters of the genotype groups (Mean± SD)

Groups	ATc	AAA	CTc	CAA
Age (years)	21.61 ± 2.56	22.06 ± 2.90	23.52 ± 3.48	22.14 ± 2.79
Height (cm)	183.03 ± 10.61**	180.75 ± 7.97	175.54 ± 6.30$^{\#}$	179.53 ± 4.72
BW (kg)	83.10 ± 16.94	79.55 ± 13.00	75.10 ± 9.00	76.65 ± 5.79
BMI (kg/m^2)	24.64 ± 3.33	24.31 ± 3.65	24.34 ± 2.29	23.77 ± 1.52
HR (beats/min)	190.80 ± 10.54	190.43 ± 7.62	188.36 ± 10.75$^{\#}$	195.07 ± 7.59
VO_{2max}(ml/kg/m.min)	47.33 ± 3.04***	47.52 ± 3.46	43.44 ± 2.89$^{\#}$	45.76 ± 2.64

ATc: athlete T carrier group, AAA: athlete AA homozygous group, CTc: control T carrier group, CAA: control AA homozygous group, BMI: body mass index, BW: body weight, distance: the distance during Yoyo IR-1 test, HR: heart rate, VO2max: maximal oxygen consumption; *p<0.05, **p<0.01, ***p<0.001, compared with their control genotype groups, #p < 0.05, comparison of within group.

finding present that the Yoyo test was maximally performed. AG's VO_{2max} value was significantly higher than the CG (Table 2). VO_{2max} value of CAA group was significantly higher than in those of CTc (p=0.018). VO_{2max} value of the athletic ATc group was higher than CTc (p<0.001). But there were no significant differences found between the athletic genotype groups (AAA and ATc) for the other parameters (Table 3). These findings show that the athletes were trained.

LA kinetics

Although the recovery LA5, LA15, and LA30 values of CG were markedly higher than those of AG (8.0%, 11% and 16.4%, respectively) (Table 2), it was not found to be statistically. The recovery LA (LA5, LA15, and LA30) values of CTc group (9.4%, 12.7%, and 24.1%, p>0.05) and those of ATc group (9.4%, 12.7%, and 24.1%, respectively) were also unsignificantly higher than those of their athletic genotype

groups, but not for LESs, p>0.05 (Table 5). Because most of the recovery LAs of the groups were related with BW in both the CG and AG including the genotype groups (Table 6), LA kinetics were compared by dividing their body weight (correction by BW). Then LA5, LA15, and LA30 values of CG were higher than those of AG (p=0.053, p=0.042, and p=0.028), respectively), but not for LESs (Table 4). Since LA amount produced in the muscles during exercise is distributed throughout the body by circulation, it is an expected finding to be lower in the blood in proportion to the size of the body cavity and active muscle mass (due to increased LA consumption) (4) furthermore adipose tissue is also significant because it contributes to systemic lactate turnover (22).

However, when we also made a similar application for LA kinetics between the genotype groups, a significant difference was not found for any parameter. When the athletes and control groups (including genotype groups) were evaluated within themselves; significant differences were found among LA5 and LA15 and LA30 and between LA15 and LA30 values (p< 0.001) and also between LES15 and LES30 (at least p< 0.05 level) in the same groups (Table 2,3,4).

The Correlations in the Athletic Group

Negative correlation found between BMI and LA5 (r= -0.354, p=0.021). Additionally, BMI correlated with LES15 (r=-0.343, p=0.026) and LES30 (r=-0.403, p=0.008). Similarly, BW correlated with LA5 (r=-0.424, p=0.005) and LES30 (r=-0.432, p=0.004). There were positive correlations between LA5 and LA15 (r=0.844, p=0.000); between LA5 and LA30 (r=0.749, p=0.001); between LA5 and LES30 (r=0.808, p=0.001); between LA15 and LA30

Table 4. The comparisions of lactate (LA) and lactate elimination rate (LES) values of the groups following Yoyo Test (Mean ± SD) when LA kinetics were divided by BW

Variables	AG (n=42)	CG (n=39)	P values
LA5/BW ratio (mM/kg)	0.1686 ± 0.062	0.1921 ± 0.057	0.053
LA15/BW ratio (mM/kg)	0.1186 ± 0.057	0.1395 ± 0.065	0.042
LA30/BW ratio (mM/kg)	0.0667 ± 0.031	0.0843 ± 0.039	0.028
LES15/BW ratio (mM/kg.min)	0.0045 ± 0.0025	0.0050 ± 0.002	0.626
LES30/BW ratio (mM/kg.min)	0.0041 ± 0.0015	0.0040 ± 0.001	0.444

AG: athlete group, BMI: body mass index, BW: body weight, CG: control group, Distance: the distance during Yoyo IR-1 test, HR: heart rate, VO_{2max}: maximal oxygen consumption, LA5: lactate value in 5th minute, LA15: lactate value in 15th minute, LA30: lactate value in 30th minute, LES15: lactate elimination speed between 5th and 15th minutes, LES30: lactate elimination speed between 5th and 30th minutes.

Table 5. Lactate concentrations and lactate elimination rate values of the groups following Yoyo Test (Mean± SD).

Group	LA5 (mM)	LA15 (mM)	LA30 (mM)	LES15 (mM/min)	LES30 (mM/min)
ATc (n=26)	13.37±3.51*	9.48±3.05†	5.28±1.89	0.388±0.180$^{\Delta}$	0.323±0.094
AAA (n=16)	12.71±2.59*	8.71±3.62†	5.05±2.01	0.399±0.184$^{\Delta}$	0.306±0.073
CTc (n=25)	14.64±3.75*	10.69±3.93†	6.55±2.87	0.395±0.160$^{\Delta}$	0.323±0.081
CAA (n=14)	13.52±2.73*	9.67±2.62†	5.63±1.86	0.385±0.205	0.315±0.068

ATc: Athlete T carrier group, AAA: Athlete AA homozygous group, CTc: Control T carrier group, CAA: Control AA homozygous group, LA5: lactate concentration in 5th minute, LA15: lactate concentration in 15th minute, LA30: lactate concentration in 30th minute, LES15: lactate elimination rate between 5th and 15thminutes, LES30: lactate elimination rate between 5th and 30th minutes. *: higher than that of LA15 and LA30 (p<0.001), †: higher than ATc, AAA and CTc of LA30 (p<0.001), and CAA (p<0.01); $^{\Delta}$:higher than that of LES30 (p<0.05).

(r=0.867, p=0.001); negative relationship was found between LA15 and LES15 (r=-0.320, p=0.039) differently from the control group (there was no found any relationship at the control group; betweenLA15 and LES30 (r=0.473, p=0.002); between LES15 and LES30 (r=0.571, p=0.001).

The Correlations in the Control Group

Negative correlation was observed between BMI and LES15 (r=-0.343, p=0.026). Additionally, BMI correlated with LES30 (r=-0.403, p=0.008). Similarly, BW correlated with LA5 (r=-0.321, p=0.046), LA15 (r=-0.317, p=0.049) and LES30 (r=-0.432, p=0.004); LA5 correlated with heightand BW (r=-0.417, p=0.008). However, there were positive correlations between LES15 and LES30 (r=0.446, p=0.003); between LA5 and LA15 (r=0.862, p=0.001); between LA5 andLA30 (r=0.799, p=0.001);between LA5 and LES30 (r=0.701, p=0.001); between LA15 and LA30 (r=0.797, p=0.001); between LA15and LES 30 (r=0.504, p=0.001).

Correlations of athletic and control genotype groups are given in Table 6. These correlations were similar to those in the AG and CG groups.

Table 6. The important correlations in the genotype groups during passive recovery following Yoyo Test

Groups	Variables	**r**	**P**
ATc	LA5 vs. BW	-0.593	0.001
	LA5 vs. BMI	-0.441	0.024
	LA5 vs. LA15	0.859	0.000
	LA5 vs. LA30	0.781	0.000
	LA5 vs. LES15	0.497	0.010
	LA5 vs. LES30	0.865	0.000
	LA15 vs. BW	-0.432	0.028
	LA15 vs. LA30	0.857	0.000
	LA15 vs. LES30	0.593	0.001
	LES30 vs. BW	-0.510	0.008
	LES30 vs. BMI	-0.468	0.016
	LES15 vs. LES30	0.683	0.000
AAA	LA5 vs. LA15	0.875	0.000
	LA5 vs. LA30	0.713	0.002
	LA5 vs. LES30	0.633	0.008
	LA15 vs. LA30	0.884	0.000
	LA 15 vs. LES15	-0.733	0.001
	LA30 vs. LES15	-0.733	0.001
CTc	LA5 vs. BW	-0.402	0.046
	LA5 vs. LA15	0.913	0.000
	LA5 vs. LA30	0.845	0.000
	LA5 vs. LES30	0.655	0.000
	LA15 vs. BW	-0.49	0.013
	LA15 vs LA30	0.917	0.000
	LES15 vs. LES30	0.567	0.003
CAA	LA5 vs LA15	0.733	0.003
	LA5 vs LA30	0.783	0.001
	LA15 vs. LA30	0.684	0.007
	LA5 vs. LES30	0.718	0.004

ATc: athlete T carrier group, AAA: athlete AA homozygous group, CTc: control T carrier group, CAA: control AA homozygous group, BMI: body mass index, BW: body weight, LA5: lactate accumulation in 5th minute, LA15: lactate accumulation in 15th minute, LA30: lactate accumulation in 30th minute, LES15: lactate elimination rate between 5th and 15th minutes, LES30: lactate elimination rate between 5th and 30th minutes.

Discussion

One of the main findings of the present study was that the recovery LA (LA5, LA15, and LA30) values (the corrected by BW) of the CG were significantly higher than those of the AG (not for LES). Additionally, there was no significant difference for these parameters between genotype groups (Table 4). Endurance (VO_{2max}) levels of all athletic groups, including the genotype groups, were significantly greater than those of the control groups, but, the VO_{2max} values were not significantly different between the athletic groups despite the AA group has higher VO_{2max} compared to the Tc group. These findings indicate that the AA athletic group was negativelly affected for VO_{2max} from the training according to Tc group. Furthermore, there was a negative relationship between LA15 and LES15 in the AA group.

In a previous study (23), no significant difference was found between sedentary and trained male football players for recovery LA levels and LES value following Yoyo intermittent endurance (level 2) tests. These findings were substantially consistent with our LES findings, but not for LA values. The peak LA and

LES values of the trained and sedentary boys were not different after a 1-minute maximal exercise (24) similar to the present study.

It is well known that endurance training decreases LA production and accumulation, while increases its clearance (25) due to increased mitochondria volume and oxidation capacity as well as increased LA uptake and gluconeogenesis (4,8). Therefore, the differences for the LA between the athletic and the control groups during recovery in the present study can mainly be due to the training adaptations (8,26,27). Thus, these findings can indicate that the AG has a greater lactate elimination capacity (not LES), but not for the genotype groups. In the present study, the recovery LA values of Tc group were not significantly higher than AA genotype group differently from the literature (11,12). But the AA control group's value at LA30 point was markedly higher than that of the athletic group (24.1%, $p > 0.05$). In the present study, the VO_{2max} values of the athletic AA and Tc groups were not significantly different from each other, therefore, the important difference found at LA30 value between the two genotype groups may be due to polymorphism (MCT1P) rather than endurance capacity. Therefore, the significant LA differences found between CG and AG groups may be a reflection of that found at LA30 point in the AA genotype group, although not at a significant level.

As for the LES difference, the LESs of sportsmen and sedentary groups were higher during partial active recovery than in the passive recovery (24,28). Similarly, in a study composed of elite athletes (12), T allele carriers of MCT1P had a lower blood LA decline than the A allele carriers during the 10–20 min period of the active recovery (unlike the present study), but not for passive recovery similar to the present study. It is reported that resting muscles take less LA due to a lower metabolic rate, but this increases by active recovery (12). Therefore, LA and LES differences between active and passive recovery may mainly be due to accelerated metabolism with increased blood flow during active recovery. Because active recovery can activate highly MCTs, acid-base buffer capacity, gluconeogenesis, mitochondrial oxidative capacity. Therefore, in the present study, the main reason for the absence of a significant difference between the athletic and control genotype groups for LA and LES might be the above mentioned factors (1) as well as the MCT1P (12).

But, the following factors may also play an important role in these differences in the present study: It was reported that MCT1P is associated with endurance levels (higher in AA group than Tc) and blood LA level (higher in T allele than the other) (11,12). However, in the present study, contrary to the above studies, a significant difference between their athletic genotype groups (AAA and ATc) was not found for the endurance capacity (VO_{2max} values) despite the AA control group has higher for VO_{2max} according to the control Tc group. These findings can indicate that the AA group is different from the literature as endurance capacity and that this group is negativelly affected for VO_{2max} levels from the trainings according to the Tc group due to genetic disposition. These findings are the first in the literature for (training status) to the best of our knowledge. Therefore, these factors (including the training status) may also be a important reason for the lack of a significant LA difference between the athletic AA genotype group and its control group (CAA) (at least at LA30 point). Furthermore, the other reason forthe differences found in VO_{2max} and LA kinetics between the present and the other studies may be the differences in ethnicity for MCT1P. In a study, it was found that the frequency of the T allele was overrepresented in Polish climbers, but not in Japanese climbers (29). In the present study, although genotype and allele frequencies were not significantly different between athletes and sedentary groups (Table 1), the percentage of the T allele frequency (34.6%) was lower than that of the A allele in the control group, which was similar to the literature (10,20,30). However, in the athletic group, the frequencies for T vs A allele were (41.7 vs 58.3%) (Table 1), which was slightly different from control, although not significant. The cause of this difference could possibly be the role of selecting athletes from anaerobic athletes, because,it is known that the T allele frequency is higher in anaerobic athletes such as sprinters (11,29). In the present study, since the number of people with TT homozygous is very low, we made comparisons by creating a T carrier (Tc) group by combining those from AT and TT to get more reliable results. Therefore, the differences between the present study and the others may have a role in this. However, it was shown that ethnicity affected the results. For example, it was shown that African runners displayed lower blood lactate

concentrations than Caucasian counterparts after a 400-m track running. For these reasons, although the participants in the present study have the same ethnicity, it may have a role in the differences between this study and other studies conducted for this purpose.

Furthermore, in the present study, significant positive correlations were found between LESs and LAs in the genotype groups (except the athletic AA group) (Table 6). The observed relationships can confirm that lactate clearance are mainly dependent on the magnitude of the LA concentration and pH gradient (3,4) between intracellular and outer as well as MCT quantity (31). But, interestingly, unlike the other groups, there was a negative relationship between LES15 and LA15 only in the AA athletic group (also between LES15 and LA30). The LA concentration at LA15 point was 8.7 mM vs 5.1 mM at LA30.LA transport across the sarcolemma is not only an active process but is driven by LA concentration and pH difference across the membrane (3,4). Thus, this negative relationship may be due to a delay in the return of muscle pH to normal levels at LA15 point of the recovery due to metabolic acidosis (32), which may lead to a LES15 deficiency. Then, if this is a phenomenon for the AA genotype group, the repetitive severe exercises done during training may lead to proton accumulations and decreasing of pH at the LA15 point due to the insufficient LES15, which may prevent the effective working of MCT1s (3,4), and may decrease their number. Also under these conditions, the activity of aerobic enzymes (3) may decrease, which may also decrease VO_{2max} levels due to deficiency in LES15, in addition, this case may lead to excessive sensitivity to anaerobic training for the AA group at the end of the training. Consequently, this AA group could be adversely affected by training for endurance capacity, and this can also cause sports injuries in Turkish athletes. A study proving this idea has been published in the literature, in this study, it was shown that individuals with the AA genotype exhibit significantly higher muscle injury incidents according to the TT genotype in elite italian football players (15). Therefore, there may be a link between these two cases (injury incident and negative effect of training) and this possible association may result from insufficient LES15 at LA15 point due to MCT1P. In addition, the fact that the players of these two studies are also Caucasian increases the existence of this relationship. Then, the training in the AA group can also increase the risk of muscle injury due to insufficient recovery (15) and reduced MCT1 quantity (16). Therefore, it is possible that the AA genotype is genetically more sensitive to anaerobic training due to LES15 deficit. Thus, it can be necessary to determine anew recovery and training strategy considering these phenotypic features in the AA genotype group, which may improve performance and protect from sports injuries. This possible phenomenon (LES deficient) at the 15th minute of recovery after a maximal exercise seems worthy of further investigation, because this time point is a region where the elimination of lactadine is expected to be the fastest (12).

Although we didn't use active recovery in the present study, significant differences were found between the AG and the CG for the LA values during recovery. The protocol (Yoyo IR-1 test protocol) we used may lead to this findings. As this test is more aerobic than Yoyo IR-2 and it is activated with insufficient anaerobic energy reserves, a maximum oxygen consumption capacity is reached at the end of the test (17,18,33). Furthermore, it was reported that high-intensity training increases both MCT1 and MCT4 protein levels (8,9) and that it has been reported that MCT1 and MCT4 are also induced rapidly and maintained at elevated levels after an exercise stimulus (34). Thus, MCT1s and MCT4s may have been effectively worked during this short time-recovery in the present study. The second reason may be the recovery protocol, because, it was shown that a passive recovery lasting up to 30 minutes is as effective as an active recovery load performed at 40% of the lactate threshold for LA elimination (not LES) (28).

The limitations and practical importance of the present study

Although there were no expected significant correlations between LA kinetics (including LES) and VO_{2max}, the procedure we used could distinguish LA kinetics and performance parameters of sedentary and the athletes. Therefore, this procedure can be used for this purpose. It should be determined a new recovery and training strategy according to these phenotypic features in the AA genotype group, which may improve performance and protect from sports injuries.

Making it homogeneous and with a large number of participants from the same sports branch, including female athletes, can give more reliable results.

Conclusion

MCT1-T1470A polymorphism did not have a significant effect on LA kinetics in athletes. However, the AA group was negatively affected for VO_{2max} compared to the Tc group. This may be due to an extreme sensitivity of the AA group to the training caused by this polymorphism. Further studies are needed to light on this entity.

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