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ORIGINAL ARTICLE

The polymorphism T1470A of the SLC16A1 gene is associated with the lactate and ventilatory thresholds but not with fat oxidation capacity in young men

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Abstract

Purpose To examine the association of the single nucleotide polymorphism A1470T in the SLC16A1 gene with blood lactate accumulation during a graded exercise test and its associated metaboreflex.

Methods Forty-six Latin-American men (Age: 27 ± 6 years; Body fat: 17.5 ± 4.7%) performed a graded exercise test on a treadmill for the assessment of maximal oxygen uptake (VO_{2max}), lactate threshold (LT), ventilatory threshold (VT) and the exercise intensity corresponding to maximal fat oxidation rate (FATmax), via capillary blood samples and indirect calorimetry. Genomic DNA was extracted from a peripheral blood sample. Genotyping assay was carried out by real-time polymerase chain reaction to identify the A1470T polymorphism (rs1049434).

Results Genotypes distribution were in Hardy–Weinberg equilibrium ($X^2 = 5.6$, $p > 0.05$), observing allele frequencies of 0.47 and 0.53 for the A and T alleles, respectively. No difference in VO_{2max}, body composition nor FATmax were observed across genotypes, whereas carriers of the TT genotype showed a higher LT (24.5 ± 2.2 vs. 15.6 ± 1.7 mL kg^{-1} min^{-1}, $p < 0.01$) and VT in comparison to carriers of the AA + AT genotypes (32.5 ± 3.3 vs. 21.7 ± 1.5 mL kg^{-1} min^{-1}, $p < 0.01$). Both, VO_{2max} and the A1470T polymorphism were positively associated to the LT ($R^2 = 0.50$, $p < 0.01$) and VT ($R^2 = 0.55$, $p < 0.01$). Only VO_{2max} was associated to FATmax ($R^2 = 0.39$, $p < 0.01$).

Conclusion Independently of cardiorespiratory fitness, the A1470T polymorphism is associated to blood lactate accumulation and its associated ventilatory response during submaximal intensity exercise. However, the A1470 polymorphism does not influence fat oxidation capacity during exercise in young men.

Keywords Energy metabolism · Human genetics · Indirect calorimetry · Physical endurance · Sports medicine

Abbreviations

BLa	Blood lactate
CRF	Cardiorespiratory fitness
LT	Lactate threshold
VT	Ventilatory threshold

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FATmax	Exercise intensity that elicits maximal fat oxidation
VO_{2max}	Maximal oxygen uptake

Introduction

During a graded exercise test, the gradual increment of glycolytic flux within skeletal muscle is mirrored by the formation of lactate and H^+ due to progressive activation of lactate dehydrogenase (Howlett et al. 1998; Spriet et al. 2000; Poole et al. 2021). When exercise is performed at moderate exercise intensity, lactate formation is compensated by lactate clearance through the conversion of lactate to glucose into the liver and the oxidation of lactate within cardiac and skeletal muscle (Brooks et al. 2022; Poole et al. 2021). When moving toward vigorous intensity exercise, nonetheless, lactate production surpasses lactate clearance, resulting in lactate accumulation within the muscle fibers and the bloodstream (Poole et al. 2021). This process contributes to the so called "metaboreflex", triggering an exponential rise in pulmonary ventilation and heart rate that optimize muscle blood flow for the shuttle of monocarboxylic acids across the liver, the skeletal muscle, and the heart (Ducrocq and Kaufman 2020; Torres-Torrelo et al. 2021). Such rise in pulmonary ventilation, however, diminish oxygen uptake efficiency (Sun et al. 2012), elevates the fraction of O_2 in the expired air (Keir et al. 2022), and reduces skeletal muscle oxygen saturation levels (Feldmann et al. 2022). In complement, lactate accumulation contributes to fat oxidation rate and adipose tissue lipolysis downregulation by inhibiting carnitine palmitoyl transferase 1 and adenylyl cyclase, respectively (Spriet 2014; Rooney and Trayhurn 2011). The aforementioned metabolic modifications dramatically raise glycolytic flux for ATP resynthesis, exacerbating lactate accumulation (Wackerhage et al. 2022).

The monocarboxylate transporter 1 (MCT-1) expresses ubiquitously in the hepatocytes and oxidative fibers of cardiac and skeletal muscle, contributing to lactate clearance during exercise through a pH-dependent cotransport of lactate and H^+ (Kobayashi et al. 2021). This transmembrane protein shows a high affinity for lactate (K_M = 3.5–8.3 mM) and is upregulated in skeletal muscle after endurance training (Kitaoka et al. 2012; Thomas et al. 2012). In fact, lactate clearance is superior in trained vs. untrained individuals, whereas the lactate threshold (LT) is located at a higher exercise intensity in endurance athletes when compared to sedentary individuals and subjects with metabolic syndrome (Bircher and Knechtle 2004; Messonnier et al. 2013; San-Millán and Brooks 2022). These adaptations are linked to enhanced fat oxidation capacity and improved ventilatory regulation during exercise, observing that exercise intensity corresponding to LT, the ventilatory threshold (VT) and maximal fat oxidation (FATmax) are higher in trained vs. untrained individuals (Bircher and Knechtle 2004; San-Millán and Brooks 2022; Zurbuchen et al. 2020).

Recently, Sasaki et al., (2015) identified a single nucleotide polymorphism in the SLC16A1 gene (A1470T; rs1049434) that enhances the activity of MCT-1 via increasing its lactate transport capacity by ~39%. This polymorphism has been also associated with lower blood lactate accumulation (BLa) after a graded exercise test and a single circuit resistance training session in endurance athletes and trained individuals, respectively (Cupeiro et al. 2012; Guilherme et al. 2021). Therefore, it seems that carriers of the A1470T polymorphism may show a superior capacity for regulating lactate metabolism during exercise. Such hypothesis, nevertheless, has been challenged by other studies in elite endurance athletes and professional soccer players where carriers of the A1470T polymorphism exhibited higher BLa after a graded exercise test (Fedotovskaya et al. 2014; Massidda et al. 2021).

At present, the association of the A1470T polymorphism with BLa accumulation during submaximal intensity and its consequential effects on fat oxidation and pulmonary ventilation remain unexplored. The present study thus aimed to examine the interaction between cardiorespiratory fitness (CRF) and the A1470T polymorphism over the LT, VT and FATmax assessed during a graded exercise test. We hypothesized that exercise workload corresponding to LT, VT and FATmax will be higher in carriers of the A1470T polymorphism due to a delayed BLa accumulation.

Methods

Participants

Forty-six Latin-American men volunteered to participate in this study and were selected based on the following criteria: (I) body mass index (BMI) ≤ 25 kg m^2; (II) body fat percentage ≤25%; (III) fat mass index ≤6.6 kg m^2; (IV) resting heart rate ≤80 beats min^{-1}; (V) blood pressure ≤120/80 mmHg; (VI) fasting glucose levels between 70 and 110 mg dL^{-1}. All the participants were healthy adults and did not report a clinical background of cardiovascular, metabolic, or respiratory diseases that would impede exercise performance. For this study, only males were considered given that the A1470T polymorphism was associated to exercise BLa in men but not in women (Cupeiro et al. 2012; Fedotovskaya et al. 2014). The sample size was established in accordance to (1) the global minor allele frequency reported for the Latin-American population (A: 0.46; T: 0.54), and (2) the number of participants (N: 23–66) and large effect sizes in exercise BLa reported among genotypes in previous studies (Effect size >1.0) (Cupeiro et al. 2012; Fedotovskaya et al.

2014; Guilherme et al. 2021; Massidda et al. 2021). The general details of the study were provided to all the individuals who signed a written informed consent after acceptance. Furthermore, the study protocol was reviewed and approved by the Ethics Committee of the Autonomous University of Ciudad Juarez (CEI-2020-2-60).

Study protocol

In their first laboratory visit, the participants underwent an initial assessment of body composition, cardiovascular function, glucose levels, physical activity and resting metabolic rate. Seven days apart, they returned to the laboratory and performed an incremental-load exercise test on a treadmill for the assessment of metabolic thresholds, CRF and exercise fat oxidation capacity. The fasting levels of glucose and lactate, resting heart rate and resting metabolic rate were measured again prior to the exercise trial in order to verify the cardio-metabolic status of the participants. All the measurements were performed in the morning after an overnight fast (8–10 h) and the laboratory environmental temperature was kept constant between 22 and 24 °C. In addition, the participants were instructed to maintain their habitual diet and physical activity during the entire study, whereas alcohol and caffeine consumption was restricted at least 24 h prior to all the metabolic evaluations.

Measurements

Body mass and height were measured to the nearest 0.1 kg or cm, respectively, using a calibrated electronic scale (DETECTO, US) and a stadiometer (BAME 425, MX). In addition, fat mass and lean mass were determined through bioelectrical impedance by using a multi-frequency tetrapolar device (BodyStat Quadscan 4000, IM). Physical activity levels were subjectively assessed by using the short version of the International Questionnaire of Physical Activity (Craig et al. 2003).

The gas exchange at rest and during the exercise trial was measured by indirect calorimetry using a breath-by-breath gas analyzer (Cortex MetaLyzer 3B, DE) that was calibrated before each test by using a certified gas mixture of known concentrations (5% CO_2, 16% O_2, and balance of N2; Cortex-Medical, DE). In addition, the flow sensor was calibrated with a 3-L syringe (Hans Rudolph, US).

The resting metabolic rate was continuously measured during 20–25 min while the participants remained in Fowlers position over a reclining chair. Then, 5-min steady-state values (RQ < 5%) were used to calculate energy expenditure from the Weir equation (Weir 1949), and macronutrient oxidation with Frayn's stoichiometric equations (Frayn 1983). Prior to the incremental exercise test on the treadmill (Quinton TM55, US), a brief walking warmup (5 min) was carried out at 4 km h^{-1} with no inclination. Then, the test started at 3 km h^{-1} for individuals with a low physical activity level (<600 Mets min^{-1} sem^{-1}) or 5 km h^{-1} in subjects with moderate to high physical activity level (>600 Mets min^{-1} sem^{-1}), sustaining a gradient of 1%. Afterward, the speed was increased every 3 min (1 km h^{-1}) until a respiratory exchange ratio of 1.0 was sustained during 30 s. Thereafter, both speed (1 km h^{-1}) and gradient (1%) were increased simultaneously every minute until volitional exhaustion. The participants' heart rate was measured under resting conditions and during the entire exercise trial by using a wireless heart rate monitor (Polar Electro F6, FI). In addition, capillary blood samples (50 µl) were taken at rest for the assessment of glucose (ReliOn Prime, US) and lactate concentration (Nova Biomedical, US), while additional blood samples were collected 30 s before the ending of each test stage for the assessment of BLa kinetics and the increment in BLa levels from rest to maximal effort.

The maximal oxygen uptake (VO_{2max}) was validated by the following criteria: (1) a plateau in oxygen uptake kinetics, defined as an increment ≤2 mL during the last two stages of the exercise test; (2) a heart rate ≥90% of age-predicted maximum maximal heart rate (220-age (years)); (3) a respiratory exchange ratio ≥1.1; (4) maximal BLa ≥ 8 mM (Howley et al. 1995). Furthermore, sex and age guidelines provided by the American College of Sport Medicine were considered for definition of the CRF level (Dumke 2018). The LT was computed through the log–log approach, whereas the VT was manually determined by a trained physiologist through the ventilatory equivalents of oxygen approach (Binder et al. 2008). The gas exchange values recorded during the last 2-min of each stage were averaged to calculate fat oxidation rates from the stoichiometric equations provided by Jeukendrup and Wallis (Jeukendrup and Wallis 2005). Then, fat oxidation rates were depicted against exercise intensity for definition of FATmax and maximal fat oxidation rate (MFO) through a third-degree polynomial regression analysis (Amaro-Gahete et al. 2019).

For the genotyping analysis, genomic DNA was extracted from a peripheral blood sample (4 ml) using the Master Pure DNA purification kit from Epicentre (Illumina Inc., US). Thereafter, a real-time polymerase chain reaction (real-time PCR) was performed in the QuantStudio™ 3 Real-Time PCR System (Thermo Fisher Scientific, US) to analyze the A1470T polymorphism in the SLC16A1 gene (rs1049434; chr8:37966280). The real-time PCR reaction was performed using a total volume of 5 µl that contained: (1) 2.65 µl of the rhAmp Genotyping Master Mix (Integrated DNA Technologies, US), (2) 0.25 µl of the rhAmp Reporter Mix containing the FAM/VIC probes (Context: TGGGCCCTCC[A/T]TCT GTGTCTT) (Integrated DNA Technologies, US), (3) 1.1 µl of DNase free water (Thermo Fisher Scientific, US), and (4) 1 µl of genomic DNA previously diluted to a concentration

of 5 ng μl^{-1}. A total of 40 cycles were used for the genotyping analysis, including an initial phase for enzymatic activation (95 °C, 10 min), followed by denaturation (95 °C, 10 s), annealing (60 °C, 30 s), extension (68 °C, 20 s) and deactivation (95 °C, 15 min). The results retrieved from the real-time PCR were analyzed in QuantStudio ™ Design and Analysis Software v.1.4.3.

Statistical analyses

Data distribution for all the variables was analyzed using the Shapiro–Wilk test, Q–Q plots, and box plots. In addition, the homoscedasticity was verified by the Levene's test. Alleles and genotypes frequencies were determined by counting whereas a Chi-square test was used to evaluate the Hardy–Weinberg equilibrium. The influence of the A1470T polymorphism on the body composition and cardio-metabolic parameters (i.e., VO_{2max}, LT, VT and FATmax) was explored under the additive (one-way analysis of variance or Krustal–Wallis), codominant and recessive models (unpaired t-tests or Mann–Whitney U). Furthermore, the association of the CRF (VO_{2max}) and the A1470T polymorphism with the LT, VT and FATmax was analyzed by multiple linear regression analysis, and a simple bootstrapping procedure was used to verify the retrieved statistical models (500 resamples). The relationship between metabolic thresholds was investigated by performing a partial correlation analysis (adjusting for VO_{2max} and genotype).

All the statistical analyses were performed in Jamovi version 2.3.13., and the figures were elaborated in GraphPad Prism v.8.1 (GraphPad Software, US). The data are reported as mean ± standard error (SE) and the level of significance was set at $p < 0.05$.

Results

The participants' characteristics are reported in Table 1. Genotype distribution was in agreement with the Hardy–Weinberg equilibrium ($X^2 = 5.6$, $p > 0.05$), with allele frequencies of 0.47 for the A allele and 0.53 for the T allele. Genotypes frequencies were 13% (6), 67% (31) and 20% (9) for the AA, AT, and TT genotypes, respectively. A poor-to-fair CRF level was observed in 59% (27) of the participants whereas 41% (19) of them showed an excellent to superior CRF level. No difference in CRF or body composition parameters were observed across genotypes under any of the evaluated models (Table 1). Only a significant difference in glucose levels and maximal speed values was observed under the codominant and recessive models, respectively.

Table 1 Characteristics of the participants

	Genotypes (*n*)			Statistical models (*p* values)		
	AA (6)	AT (31)	TT (9)	Additive	Codominant	Recessive
Age	33 ± 5	25 ± 1	28 ± 1	0.13	0.05	0.20
BMI (kg m^{-2})	25.5 ± 1.0	24.8 ± 0.5	24.6 ± 0.6	0.58	0.84	0.89
Body fat (%)	17.9 ± 2.4	16.9 ± 0.7	19.3 ± 1.7	0.41	0.22	0.21
FMI (kg m^{-2})	4.6 ± 0.7	4.2 ± 0.2	4.7 ± 0.7	0.68	0.35	0.42
Lean mass (%)	82.1 ± 2.4	83.1 ± 0.7	80.7 ± 1.7	0.41	0.22	0.21
PA (Mets min^{-1} $week^{-1}$)	1550 ± 611	2443 ± 517	3647 ± 867	0.16	0.31	0.07
Glucose (mg dl^{-1})	95 ± 5	89 ± 2	95 ± 2	0.10	**0.02**	0.16
RMR (kcal d^{-1})	2007 ± 89	2107 ± 53	2143 ± 70	0.63	0.83	0.61
RHR (beats min^{-1})	64 ± 4	63 ± 2	62 ± 3	0.98	0.89	0.75
BLa rest (mmol l^{-1})	1.6 ± 0.3	1.8 ± 0.2	1.4 ± 0.2	0.77	0.31	0.48
VO_{2max} (ml kg^{-1} min^{-1})	48.5 ± 3.3	48.8 ± 1.8	53.3 ± 2.3	0.43	0.39	0.19
RER_{max}	1.33 ± 0.06	1.31 ± 0.02	1.28 ± 0.01	0.72	0.46	0.54
HR_{max} (beats min^{-1})	178 ± 3	184 ± 2	179 ± 3	0.20	0.09	0.34
V_{max} (km h^{-1})	11.8 ± 0.6	12.2 ± 0.3	13.6 ± 0.3	0.10	0.29	**0.04**

Differences among genotypes are highlighted in bold

Data is reported as mean ± SE

BLa blood lactate levels, *BMI* body mass index, *FMI* fat mass index, HR_{max} maximal heart rate, *PA* physical activity, RER_{max} maximal respiratory exchange ratio, *RHR* resting heart rate, *RMR* resting metabolic rate, VO_{2max} maximal oxygen uptake, V_{max} maximal speed

Additive: AA vs. AT vs. TT

Codominant: AT vs. AA + TT

Recessive: AA + AT vs. TT

The fat oxidation and BLa kinetics observed during the incremental-load exercise test are shown in Fig. 1 whilst the exercise intensity corresponding to metabolic thresholds is shown in Fig. 2. When analyzed under the additive model, a borderline difference in the LT was observed between carriers of the AT vs. TT genotypes (15.8 ± 1.9 vs. 24.6 ± 2.2 mL kg^{-1} min^{-1}, $p = 0.05$). In addition, the VT was located at a higher exercise intensity in carriers of the TT genotype in comparison to carriers of the AT genotype (32.6 ± 3.3 vs. 21.9 ± 1.9 mL kg^{-1} min^{-1}, $p < 0.05$). In a similar way, the recessive model showed that both the LT and VT were superior in carriers of the TT genotype in comparison to carriers of the AA + AT genotypes (LT: 24.5 ± 2.2 vs. 15.6 ± 1.7 mL kg^{-1} min^{-1}, $p < 0.01$; VT: 32.5 ± 3.3 vs. 21.7 ± 1.5 mL kg^{-1} min^{-1}, $p < 0.01$). Neither the FATmax, the MFO nor the increment in BLa from rest to exercise were associated to the A1470T polymorphism for any of the analyzed models.

The multiple regression analysis showed that both VO_{2max} and the A1470T polymorphism (recessive model) explained 50 and 55% of LT and VT variation, respectively. On the other hand, only the VO_{2max} was associated to FATmax (Fig. 3). The bootstrapping analysis validated the retrieved statistical models as non-significant bias was observed for the obtained β coefficients (Supplementary file 1). Additionally, the partial correlation analysis revealed that LT, VT and FATmax were moderately correlated (r: 0.38–0.63, $p < 0.05$), independently of CRF and SLC16A1 genotype.

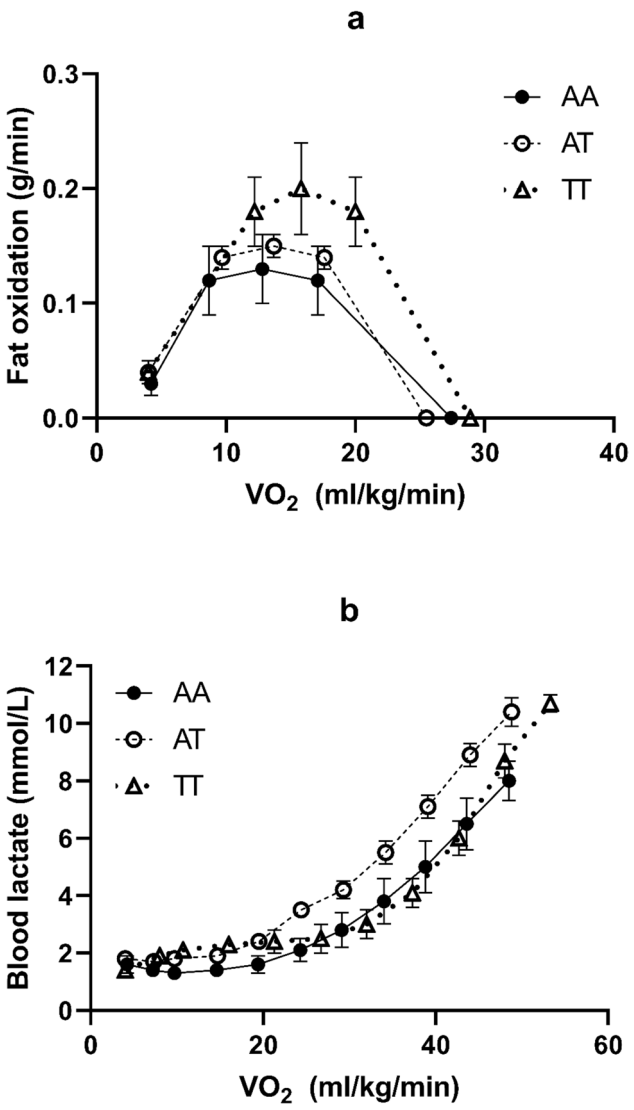

Fig. 1 Fat oxidation and blood lactate kinetics measured during the graded exercise test. VO_2, oxygen uptake

Discussion

In the present study, we investigated the role of CRF and the A1470T polymorphism on BLa accumulation during exercise and its associated metaboreflex. In this regard, we observed that both CRF and the A1470T polymorphism were positively associated to the LT and the VT, explaining around 50% of its intra-individual variation. On the contrary, only VO_{2max} was associated to FATmax, discarding an influence of the SLC16A1 polymorphism over fat oxidation capacity.

To the best of our knowledge, this is the first study that report a positive association between the A1470T polymorphism and the LT in healthy men. Specifically, we observed that carriers of the TT genotype maintain steady-state BLa levels throughout a wider range of metabolic rates, suggesting a superior capacity for lactate shuttling across different cell tissues in this population. These findings support the observations of Sasaki et al. (2015) who informed that the A1470T polymorphism enhances the lactate transport capacity of MCT-1. However, it must be noted that a significant association between the A1470T polymorphism and LT was only observed under the recessive model. Therefore, our data suggest that A > T substitution must occur in both alleles in order to upregulate lactate shuttling capacity during exercise. Further studies are deemed necessary to verify if carriers of the TT genotype show a superior lactate clearance capacity (rate of lactate appearance minus rate of lactate disappearance) during submaximal intensity exercise.

In addition to a higher LT, carriers of the TT genotype also exhibited a superior VT. From a physiological point of view, delaying the BLa accumulation and its associated ventilatory response would provide positive benefits for endurance performance since the exponential rise in pulmonary ventilation diminish oxygen uptake efficiency (Sun et al. 2012), elevates the fraction of O_2 in the expired air (Keir et al. 2022), and reduces skeletal muscle oxygen saturation levels (Feldmann et al. 2022). In fact, is well supported that

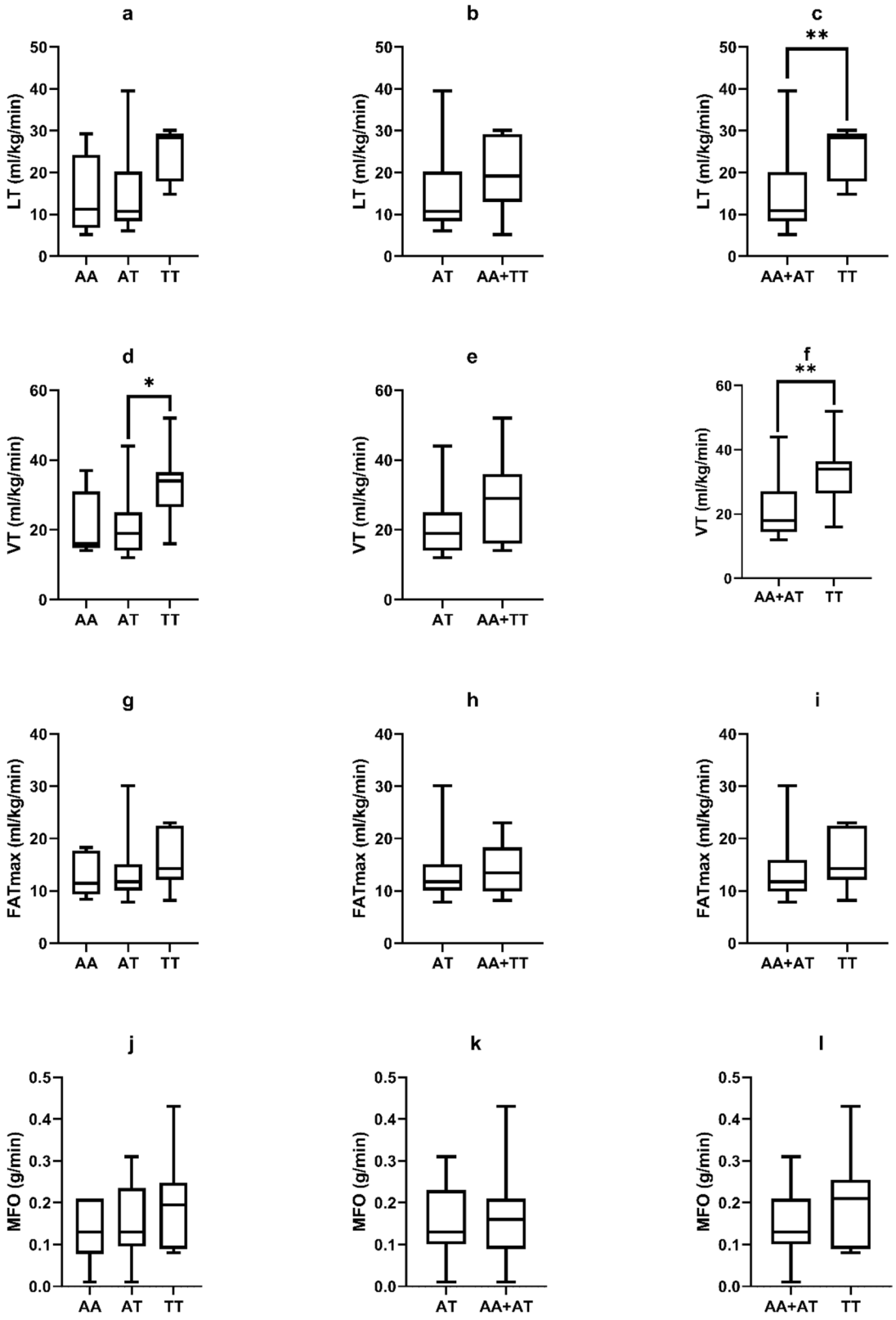

Fig. 2 Differences among metabolic thresholds assessed during the graded exercise test. The data is reported as mean ± interquartile range, and represents the results retrieved from the additive (**a**, **d**, **g**, **j**), codominant (**b**, **e**, **h**, **k**) and recessive models (**c**, **f**, **i**, **l**). *LT* lactate threshold, *VT* ventilatory threshold, FAT_{max} exercise intensity that elicited maximal fat oxidation (MFO). $^{**}p < 0.01$

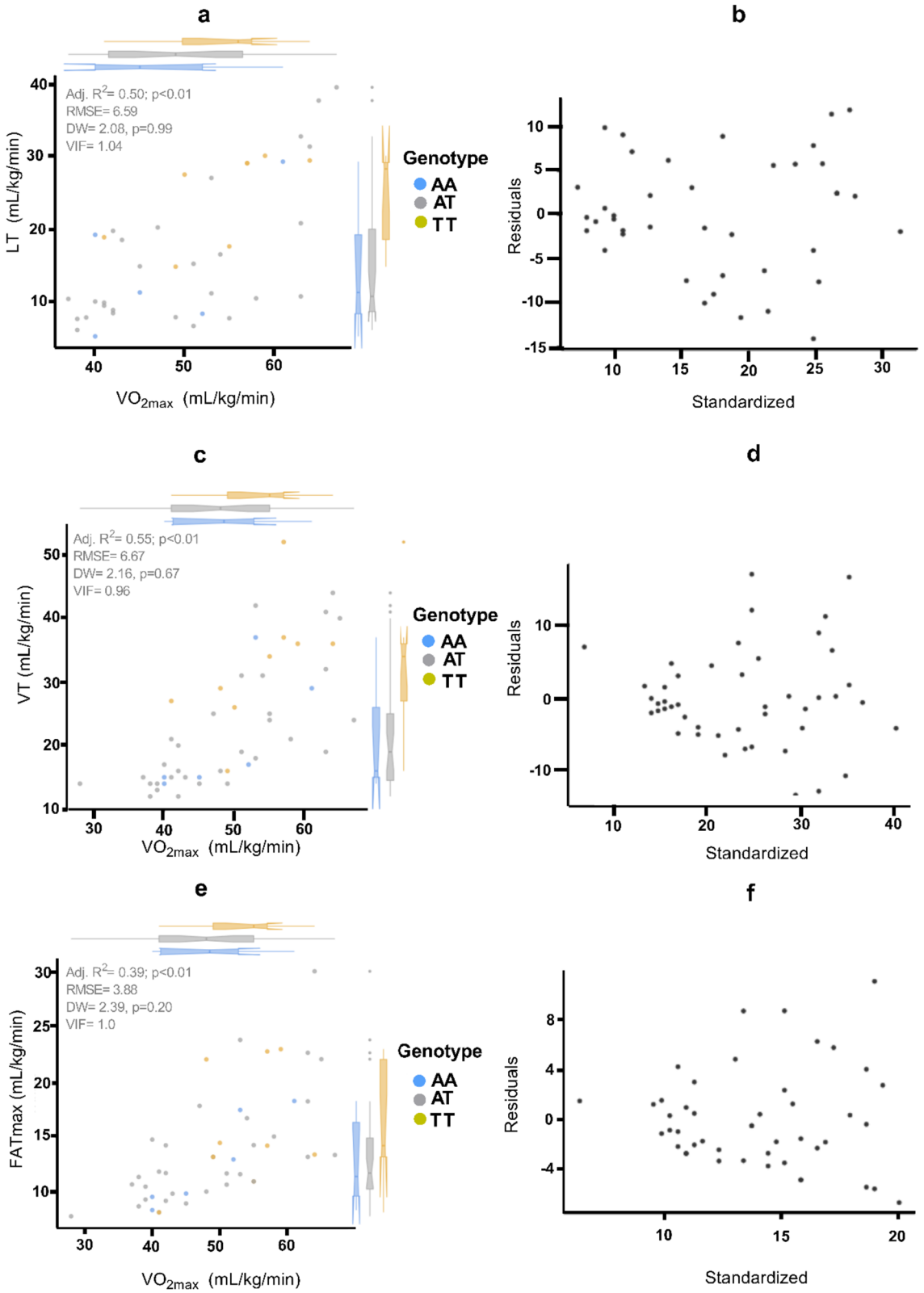

Fig. 3 Linear regression models that represent the association of the cardiorespiratory fitness and the A1470T polymorphism with the lactate threshold (LT; **A**, **B**), the ventilatory threshold (VT; **B**, **C**) and the exercise intensity that elicited maximal fat oxidation rate (FATmax; **D**, **E**). All the statistical models met the assumptions of normality (Shapiro–Wilk), heteroscedasticity (Breusch-Pagan), residuals autocorrelation (Durbin-Watson) and non-collinearity (VIF). The *box plots* represent the mean ± interquartile rank

LT is positively correlated to maximal aerobic power and endurance performance in long and middle-distance cyclists and runners (Faude et al. 2009; Ghosh 2004). Further studies, however, are necessary to verify that fatigue resistance, aerobic efficiency and metabolic power are superior in carriers of the TT genotype.

On the other hand, although an elevated lactate clearance capacity has been associated with a superior fat oxidation rate during exercise, the A1470T polymorphism in the SLC16A1 gene was not related to FATmax or MFO. In fact, a deficient fat oxidation capacity was observed on all genotypes, considering normative MFO and FATmax values previously reported for recreationally trained lean men (MFO: 0.13–0.20 g min^{-1}; FATmax: 25–30%VO_{2max}; both lower than 20th percentile) (Maunder et al. 2018). It must be noted that FATmax was moderately correlated to the LT ($r = 0.38$, $p < 0.05$) and VT ($r = 0.63$, $p < 0.01$) even after adjusting for CRF and SLC16A1 genotype. Therefore, we cannot discard that a superior lactate clearance capacity may enhance fat oxidation rate, possibly by elevating oxygen efficiency uptake during exercise as before mentioned.

Controversial results concerning the association between the A1470T polymorphism and BLa accumulation during exercise have been previously reported in the literature, with some studies observing a superior BLa accumulation after a graded exercise test in carriers of the T allele while others report a lower BLa accumulation (Cupeiro et al. 2012; Fedotovskaya et al. 2014; Guilherme et al. 2021; Massidda et al. 2021). Noteworthy, BLa levels at rest prior to initiation of the exercise test were not considered in these studies, a point that may bias their conclusions. Therefore, we compared the increment in BLa from rest to maximal intensity exercise for an accurate representation of BLa accumulation stimulated by exercise. Interestingly, we did not find a significant association between the A1470T polymorphism and BLa increment. This result suggests that both resting and maximal BLa levels must be considered to avoid equivocal conclusions. In the present study, we did not find any correlation between the LT and BLa increment from rest to exercise. However, to the best of our knowledge, the connection between these biomarkers of lactate metabolism has not been deeply investigated and deserve further research.

In this study, we examined the association of the A1470T polymorphism in the SLC16A1 gene with several cardiometabolic biomarkers in 46 Latin-American men, a sample size that is comparable to previous investigations that evaluated the association of the A1470T polymorphism with BLa levels (sample size: 23–66 participants). Nonetheless, since the prevalence of the A1470T polymorphism differs among European, Latin-American, and Afro-descendant individuals (Guilherme et al. 2021), future studies need to replicate our analyses in other populations. Moreover, as fat oxidation, BLa kinetics and the ventilatory response to exercise differ among exercise modalities (i.e., running vs. cycling) and protocols (i.e., short-graded vs. long duration steady-state) (Amaro-Gahete et al. 2019; Binder et al. 2008; Faude et al. 2009), further studies need to verify the here reported associations under additional exercise models.

In conclusion, the A1470T polymorphism is positively associated to the LT and VT in healthy men, independently of CRF. Therefore, carriers of this genetic variant may show a superior endurance performance due to delayed BLa accumulation during exercise and its associated rise in pulmonary ventilation.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s00421-023-05407-w.

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Author contributions Investigation, IACG; conceptualization and methodology: IACG, VMB, JAPL; resources and data curation: IACG, EGR, MTT; formal analysis: IACG, FJAM, ARJ; supervision and project administration, ARJ, EGR. All the authors have read, edited and approved the final version of the manuscript and agreed with the order of presentation of the authors.

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Data availability The dataset supporting the findings reported in this study is available upon request from the leading author.

Declarations

Conflict of interest The authors report there are no competing interests to declare.

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