


Lactate recovery kinetics in response to high-intensity exercises

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Abstract

Purpose The aim of this study was to investigate lactate recovery kinetics after high-intensity exercises.

Methods Six competitive middle-distance runners performed 500-, 1000-, and 1500-m trials at 90 % of their current maximal speed over 1500 m. Each event was followed by a passive recovery to obtain blood lactate recovery curves (BLRC). BLRC were fitted by the bi-exponential time function: $La(t) = La(0) + A_1(1 - e^{-\gamma_1 t}) + A_2(1 - e^{-\gamma_2 t})$, where $La(0)$ is the blood lactate concentration at exercise completion, and γ_1 and γ_2 enlighten the lactate exchange ability between the previously active muscles and the blood and the overall lactate removal ability, respectively. Applications of the model provided parameters related to lactate release, removal and accumulation rates at exercise completion, and net amount of lactate released during recovery.

Results The increase of running distance was accompanied by (1) a continuous decrease in γ_1 ($p < 0.05$), (2) a primary decrease ($p < 0.05$) and then a stabilization of γ_2 , and (3) a constant increase in blood concentrations ($p < 0.05$) and whole body accumulation of lactate ($p < 0.05$). Estimated net lactate release, removal and accumulation rates at exercise completion, as well as the net amount of lactate released during recovery were not significantly altered by distance.

Conclusion Alterations of lactate exchange and removal abilities have presumably been compensated by an increase in muscle-to-blood lactate gradient and blood lactate concentrations, respectively, so that estimated lactate release, removal and accumulation rates remained almost stable as distance increased.

Keywords Middle-distance running · Bi-compartmental model · Lactate exchanges · Lactate removal

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Abbreviations

A_1 and A_2	Concentration parameters (amplitudes of the exponential functions)
BLRC	Blood lactate recovery curves
$La(0)$	Blood lactate concentration at exercise completion
$La(t)$	Blood lactate concentration at time t
La_{peak}	Maximal blood lactate concentration during recovery
$La_{warm-up}$	Blood lactate concentration at the end of the warm-up
LAR	Lactate accumulation rate
LRR	Lactate removal rate
MCR	Metabolic clearance rate of lactate
MCR _R	Metabolic clearance rate of lactate during recovery

NALR	Net amount of lactate released
NLRR	Net lactate release rate
QLaA	Amount of lactate accumulated in the body at exercise completion
QLaR	Amount of lactate removed from the end of exercise to La_{peak}
R_dR	Lactate disappearance rate
tLa_{peak}	Time to reach the maximal lactate concentration during recovery
V_M	Lactate distribution volume of muscles previously involved in exercise
$\dot{V}O_{2max}$	Maximal oxygen uptake
V_S	Volume of compartment S ($V_{TLS} - V_M$)
V_{TLS}	Volume of the total lactate distribution space
γ_1	Velocity constant enlighten lactate exchange ability
γ_2	Velocity constant enlighten lactate removal ability

Introduction

During high-intensity exercise, glycogenolysis and glycolysis are greatly activated, leading to concomitant lactate accumulation and pH decrease in active muscles and subsequently in blood (Marcinek et al. 2010; Osnes and Hermansen 1972). However, several studies suggest that at high concentrations, lactate and H^+ may potentially impair muscle function and energetics (Bangsbo et al. 1996; Costa Leite et al. 2007; Favero et al. 1997; Hollidge-Horvat et al. 1999; Jubrias et al. 2003; Nelson and Fitts 2014). Therefore, it may appear crucial for the exercising muscles to delay lactate accumulation and intracellular pH decline to preserve muscle function, although this point remains controversial (Allen and Westerblad 2004; Nielsen et al. 2001; Pedersen et al. 2004).

The possible deleterious effect of important lactate and proton accumulations has provided support for the idea that lactate and H^+ extrusion from myocytes might be determinant in delaying muscle dysfunction. In accordance with this line of reasoning, previous studies have shown that the ability to exchange lactate from muscles to blood was related to performance during high-intensity exercise (Messonnier et al. 2002, 2007).

Lactate removal constitutes an alternate and complementary way to delay muscle, and more generally, body lactate accumulation. It is well-established that lactate can be used as fuel by skeletal muscles (Bergman et al. 1999; Brooks 1986, 2000, 2002, 2009; Donovan and Brooks 1983; Emhoff et al. 2013; Messonnier et al. 2013; Miller et al. 2002; Stanley et al. 1986). Interestingly, previous studies have suggested that performance during high-intensity exercise may be related to the subject's overall ability

to remove lactate (Messonnier et al. 1997, 2002; Thomas et al. 2005). In agreement with these studies and the lactate shuttle concept (Brooks 2002), Thomas et al. (2004) underlined that the ability to remove lactate was related to muscle oxidative capacity and fatigue index, suggesting that oxidation might play an important role in the lactate removal processes, even in the context of high-intensity exercise.

High-intensity exercises have been described to induce unsteady state conditions: muscle and blood lactate concentrations and pH are constantly changing (Marcinek et al. 2010; Osnes and Hermansen 1972). However, lactate transport and removal may be affected by these alterations of *milieu intérieur*. For instance, the changes in muscle and blood lactate concentrations (Juel 1997; Roth and Brooks 1990) as well as local blood flow (Pilegaard et al. 1995) may affect lactate transport. Besides, mitochondrial respiration, which is the ultimate step of lactate removal by oxidation, has been shown to be inhibited by acidosis (Jubrias et al. 2003). Taken together, these latter results suggest that the lactate exchange and removal abilities may decrease during short high-intensity exercise and/or during subsequent recovery. In accordance with this latter inference, Freund et al. (1989) observed lower lactate exchange and removal abilities after 6 min than after 3 min of high-intensity exercise. However, no study has investigated, to date and to our knowledge, the alterations of lactate kinetics parameters measured during recovery after high-intensity exercises of various distances. Furthermore, beside to the classic lactate exchange and removal abilities, the lactate release, removal, and whole body accumulation rates estimated at exercise completion by applications of the bi-compartmental model of the lactate distribution space have never been considered. In the present study, they will be reported and discussed for the first time.

In this context, the aim of the present study was to investigate lactate recovery kinetics in response to high-intensity 500-, 1000-, and 1500-m running trials. Concisely, we hypothesized significant lactate accumulation and consistent alterations of lactate exchange and removal abilities during recovery when running distance increased.

Methods

Subjects

Six male middle-distance runners volunteered to participate in this study. Their mean age, body mass, and height (\pm standard error) were 21 ± 1 years, 62.1 ± 3.7 kg, and 177 ± 3 cm, respectively. Their current best performance over 1500 m (measured during a competition during the last month before the experiments) was $246 \text{ s} \pm 7 \text{ s}$

(4'06" \pm 7", average speed of 22.0 ± 0.6 km h⁻¹) that corresponded to 84 % of the world record over the distance 3'26" (26.2 km h⁻¹). The experiment was conducted in accordance with the Declaration of Helsinki regarding the use of human subjects and was approved by the Local Ethics Committee (no. 20146). Subjects were fully informed about the nature, the potential risks involved and the potential benefits of the study and gave their written consent to participate.

Study design

The experimental protocol consisted of three exercise sessions performed on a treadmill (Gymrol super 2500, HEF-Techmachine, Andrézieux-Bouthéon, France). Sessions 1 and 2 were separated by at least 1 week, whereas sessions 2 and 3 were separated by at least 2 days. Subjects were asked to refrain from any intense physical exercise 36 h prior to each exercise session but to continue their habitual daily living activities.

Session 1: incremental exercise up to exhaustion

At rest, 20 μ L of blood was sampled from the fingertip for the determination of blood lactate concentration. Thereafter, the subjects performed an incremental exercise test until volitional exhaustion. This test consisted of 3-min exercise stages interspersed by 0.5-min rest periods. Initial speed was set at 10.5 km h⁻¹. Running speed was subsequently increased by 1.5 km h⁻¹ every stage. Expired gases were collected during the last 30 s of exercise at each stage and the rest periods allowed blood sampling. Heart rate was recorded continuously throughout exercise session. This session was used for individual determination of maximal oxygen uptake, maximal aerobic speed, maximal heart rate, and blood lactate concentration (vs. running velocity) curve.

Sessions 2 and 3: 500-, 1000-, and 1500-m running trials

At their arrival, a heart rate monitor was placed on subjects' chest to record heart rate throughout the session. A resting blood lactate sample was then withdrawn from the earlobe. After a self-selected warm-up (~30 to 40 min) followed by a resting period (~10 min), another blood lactate sample was taken. Then, subjects performed 500 or 1000 m at the same speed corresponding to 90 % of their current best performance over 1500 m obtained in official competition. The 1500-m test was performed the same day 2 h after the 500 m. This procedure (the 500 m performed 2 h before the 1500 m) allowed the use of the 500-m test as a preparation for the subsequent intense exercise (1500 m). The same procedure of warm-up was used before 1500 m than before

500 and 1000 m. The 1000- and 500/1500-m tests were performed at least 2 days apart. The order of the exercise sessions between the 1000 m on the one hand, and the 500 and 1500 m on the other hand, was randomly determined. Exercises were followed by a seated passive recovery of 70, 80, or 90 min for the 500-, 1000-, and 1500-m events, respectively. During recovery, 20 μ L blood samples were taken from the earlobe at the following times: 0 (exercise completion), 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 4.5, 5, 6, 8, 10, 12, 15, 20, 30, 40, 50, 60, and 70 min and also at 80 and 90 min when applicable. These sessions allowed to obtain individual blood lactate recovery curves.

Ventilatory and metabolic measurements

After passing through a two-way low resistance mouth-piece (model 2700, Hans Rudolph, Kansas City, MO), and a low dead-space mixing chamber, the expired gases were collected in Douglas bags (HP Production, Saint-Etienne, France). The O₂ and CO₂ fractions were measured in ambient air and in Douglas bags by a gas analyzer (Transtrack type 2240) pre-calibrated on precision-analyzed gas mixtures. The expired air volumes, measured using a Tissot spirometer (Gymrol, Roche-la-Molière, France), and the O₂ and CO₂ fractions were recorded to calculate $\dot{V}O_2$. Maximal oxygen uptake ($\dot{V}O_{2max}$) was reached when $\dot{V}O_2$ displayed a plateau as speed continued to increase. If the plateau in $\dot{V}O_2$ was not observed, the highest $\dot{V}O_2$ recorded was considered to be $\dot{V}O_{2max}$ if two of the three following criteria were fulfilled: a respiratory exchange ratio exceeding 1.1, a blood lactate concentration higher than 9 mmol L⁻¹, and the achievement of a theoretical maximal heart rate ($220 - \text{age} \pm 10$ beats min⁻¹).

Maximal aerobic speed

Maximal aerobic speed corresponded to the speed at which $\dot{V}O_{2max}$ was reached. It was determined by linear interpolation from the $\dot{V}O_2$ vs. running speed curve.

Heart rate

Heart rate was recorded using a three-lead electrocardiogram (session 1) and a heart rate monitor (Polar RS 400, Polar Electro, Kempe, Finland) (sessions 2 and 3).

Blood lactate concentration

Arterialized capillary blood (20 μ L) sampled from fingertips (session 1) or earlobes (sessions 2 and 3) was immediately placed in tubes containing saponin (for hemolysis) and 180 μ L of dilution liquid. Tubes were then stored at 4 °C until analysis. Lactate concentration was determined

enzymatically in the whole blood using a YSI 2300 analyzer (YSI Inc., Yellow Springs, OH, USA).

Lactate kinetics after 500, 1000, and 1500 m

Tracer studies constitute the reference method to determine lactate kinetics parameters during exercise [e.g., (Brooks et al. 1991; Messonnier et al. 2013; Miller et al. 2002)]. However, to be fully applicable and reliable, tracer techniques require almost steady states in blood lactate and tracer concentrations, a near equilibrium in concentrations between the compartments of the body (e.g., between active muscles and blood) and several blood samples during exercise. These requirements are not fulfilled during high-intensity exercise. Therefore, for the present study, we have chosen to use the bi-compartmental model of lactate distribution space following high-intensity exercise (Freund and Zouloumian 1981a, b) which is appropriate for studying unsteady state conditions. In that model, lactate accumulated in the body at exercise completion is used as its own tracer for studying its kinetics during the subsequent recovery. Hence, individual blood lactate recovery curves were fitted to the bi-exponential time function:

$$La(t) = La(0) + A_1(1 - e^{-\gamma_1 t}) + A_2(1 - e^{-\gamma_2 t}), \quad (1)$$

where $La(0)$ and $La(t)$ (mmol L^{-1}) are blood lactate concentrations measured at exercise completion and at a given time into recovery, respectively. Concentration parameters A_1 and A_2 (mmol L^{-1}) are the amplitudes of the exponential functions. A_1 describes the amplitude of concentration variations due to the appearance of lactate in blood during recovery, so that the A_1 value depends directly on the muscle-to-blood lactate gradient. The velocity constants γ_1 (min^{-1}) represent the ability to exchange lactate between the previously active muscles and the blood, and γ_2 (min^{-1}) denotes the overall ability to remove lactate from the body (Freund et al. 1986; Freund and Zouloumian 1981a). The blood lactate recovery curves were fitted to Eq. (1) by iterative non-linear regression on the KaleidaGraph 4.0 software (Synergy Software, Reading, PA, USA) to determine the values of A_1 , A_2 , γ_1 , and γ_2 , $La(0)$ being an experimental measurement. Although determined during recovery, it is important to note that the alterations in γ_1 and γ_2 reflect very closely the adjustments of the lactate kinetic parameters implemented during exercise. Interestingly, the values of γ_2 have been shown to be very close to and to follow the same pattern in function of work rate and in response to endurance training than those of the fractional lactate turnover rate measured during low- to moderate-intensity exercises using tracers (Freund et al. 1989; Messonnier et al. 2001). Moreover, the values of γ_1 are consistent with the values of rate constants of lactate efflux from sarcolemmal vesicles obtained from human skeletal muscles (Juel 1997).

Applications of the bi-compartmental model of lactate distribution space allow predictions of the net lactate release rate during recovery (NLRR, mmol min^{-1}), the net amount of lactate released during recovery (NALR, mmol), the amount of lactate accumulated in the body at exercise completion (QLaA, mmol), the lactate removal rate at exercise completion [LRR(0), mmol min^{-1}], and the lactate accumulation rate during each fraction of 500 m (LAR, mmol min^{-1}). The metabolic clearance rate of lactate during recovery (MCRR, $\text{mL kg}^{-1} \text{min}^{-1}$) and the lactate disappearance rate at exercise completion [$R_dR(0)$, $\text{mg kg}^{-1} \text{min}^{-1}$] were also estimated. Methods and equations are detailed in the Appendix (vide infra).

Statistics

Means (\pm standard errors) were calculated by standard methods. The Kolmogorov–Smirnov test was used to refute the assumption of normality. Significant differences between the three distances were identified using Friedman's two-way ANOVA. The Wilcoxon rank test allowed us to determine the differences. Correlations between variables were studied by means of simple linear regression techniques. The statistical significance threshold was set at $p < 0.05$.

Results

Incremental exercise up to exhaustion

Maximal heart rate and oxygen uptake measured at exhaustion were 191 ± 3 beats min^{-1} and 4.13 ± 0.19 L min^{-1} (65.7 ± 2.3 $\text{mL min}^{-1} \text{kg}^{-1}$), respectively. Maximal aerobic speed was 21.8 ± 0.4 km h^{-1} . At exhaustion, blood lactate concentrations reached 12.1 ± 1.1 mmol L^{-1} .

Lactate recovery kinetics after 500, 1000, and 1500 m

The different distances were run at 93 ± 1 % of maximal aerobic speed. The 500-, 1000-, and 1500-m trials lasted 91 ± 2 s ($1'31'' \pm 2''$), 182 ± 5 s ($3'02'' \pm 5''$), and 273 ± 7 s ($4'33'' \pm 7''$), respectively. Blood lactate concentrations at rest before each trial were not significantly different (1.53 ± 0.14 , 1.43 ± 0.13 , and 1.37 ± 0.09 mmol L^{-1} for 500, 1000, and 1500 m, respectively). Blood lactate concentrations at the end of the warm-up were not significantly different (1.68 ± 0.09 , 1.54 ± 0.26 , and 1.65 ± 0.18 mmol L^{-1} for 500, 1000, and 1500 m, respectively). Figure 1 shows the time courses of blood lactate concentrations during recovery following 500, 1000, and 1500 m at 90 % of the current personal record. After all trials, blood lactate concentrations

displayed the classic biphasic pattern (Fig. 1) and were very well fitted by the bi-exponential model ($r^2 > 0.99$). Blood lactate levels were significantly different between the three distances from the end of exercise until the 12th minute of recovery (Fig. 1).

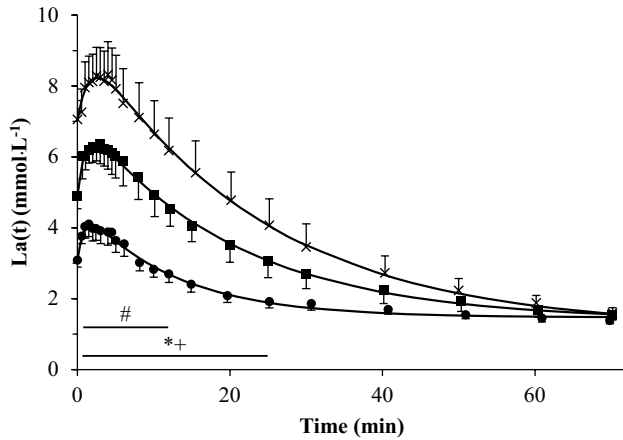
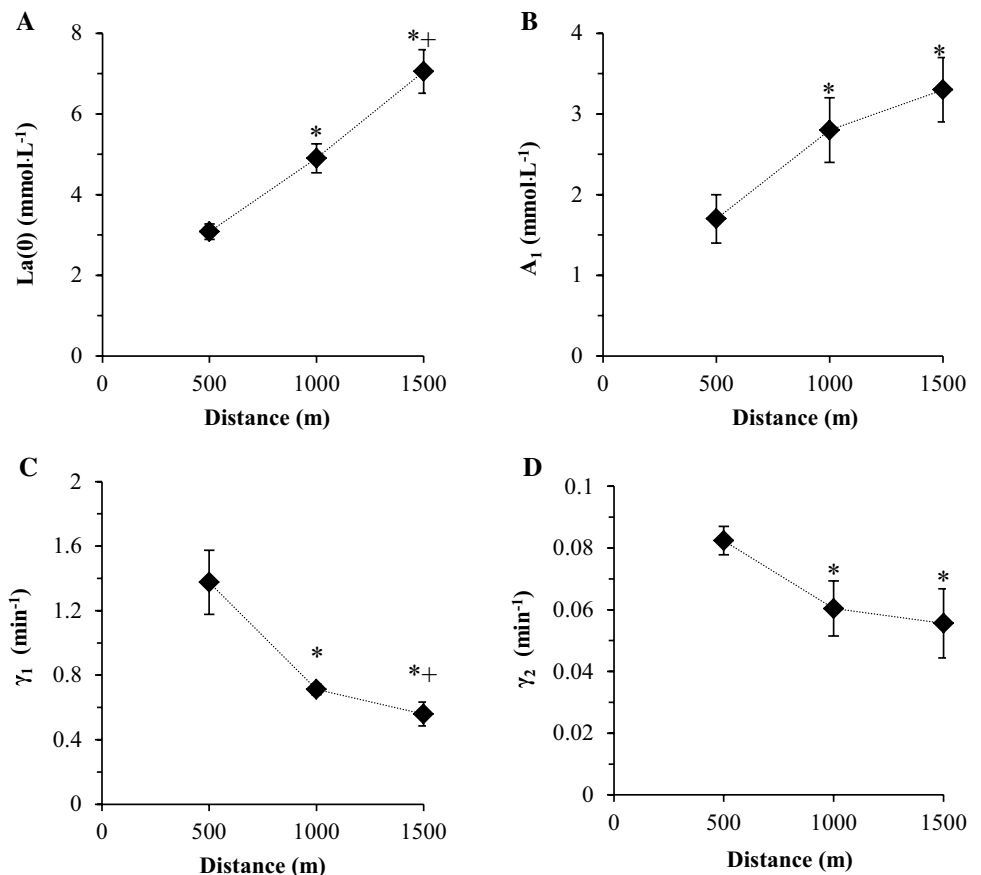


Fig. 1 Time courses of blood lactate concentrations during recovery after 500 m (circle), 1000 m (square), and 1500 m (cross). *Significantly different between 500 and 1000 m ($p < 0.05$), +significantly different between 500 and 1500 m ($p < 0.05$), and #significantly different between 1000 and 1500 m ($p < 0.05$)

Fig. 2 **a** $La(0)$: the blood lactate concentration at the end of exercise, **b** A_1 : the concentration parameter representing the amplitude of the first exponential term, **c** γ_1 : the velocity constant representing the ability to exchange lactate from the previously active muscle to the blood, and **d** γ_2 : the velocity constant representing the ability to remove lactate from the body after 500-, 1000-, and 1500-m running, *significantly different from 500 m ($p < 0.05$). +Significantly different from 1000 m ($p < 0.05$)

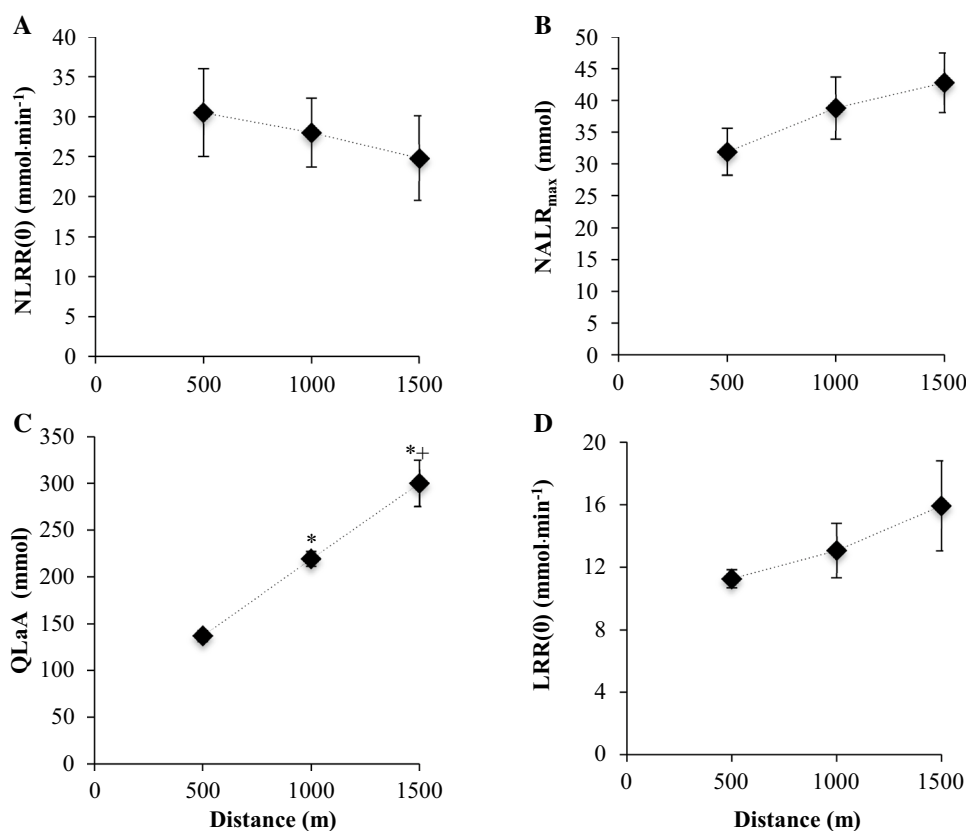


$La(0)$ raised as distance increased. From $3.08 \pm 0.19 \text{ mmol L}^{-1}$ at the end of the 500-m trial, $La(0)$ increased to $4.90 \pm 0.36 \text{ mmol L}^{-1}$ after 1000 m ($p < 0.05$) and further to $7.05 \pm 0.54 \text{ mmol L}^{-1}$ ($p < 0.05$) after 1500 m (Fig. 2a). La_{peak} followed the same pattern as $La(0)$: it increased significantly with distance (4.12 ± 0.34 , 6.43 ± 0.52 , and $8.51 \pm 0.86 \text{ mmol L}^{-1}$ for 500, 1000, and 1500 m, respectively; $p < 0.05$). Moreover, the time at which La_{peak} was reached (tLa_{peak}) increased with distance (1.3 ± 0.1 , 2.3 ± 0.2 , and $3.3 \pm 0.4 \text{ min}$ for 500, 1000, and 1500 m, respectively; $p < 0.05$).

A_1 increased with running distance. From $1.7 \pm 0.3 \text{ mmol L}^{-1}$ after 500 m, it increased to $2.8 \pm 0.4 \text{ mmol L}^{-1}$ after 1000 m ($p < 0.05$) and further (although not significantly) to $3.3 \pm 0.4 \text{ mmol L}^{-1}$ after 1500 m (Fig. 2b). A_2 decreased as distance increased. From $-3.3 \pm 0.4 \text{ mmol L}^{-1}$ at the end of the 500-m trial, A_2 decreased to $-6.4 \pm 0.7 \text{ mmol L}^{-1}$ after 1000 m ($p < 0.05$) and further to $-9.3 \pm 0.9 \text{ mmol L}^{-1}$ after 1500 m ($p < 0.05$).

γ_1 decreased non-linearly from $1.376 \pm 0.199 \text{ min}^{-1}$ after 500 m to $0.712 \pm 0.033 \text{ min}^{-1}$ after 1000 m ($p < 0.05$) and further to $0.559 \pm 0.074 \text{ min}^{-1}$ after 1500 m ($p < 0.05$; Fig. 2c). γ_2 significantly decreased ($p < 0.05$) between 500 m ($0.0824 \pm 0.0046 \text{ min}^{-1}$)

Fig. 3 **a** NLRR(0): the net lactate release rate at the end of exercise, **b** NALR_{max}: the maximal net amount of lactate released, **c** QL_{aA}: the amount of lactate accumulated at the end of exercise, and **d** LRR(0): the lactate removal rate at the end of exercise after 500-, 1000-, and 1500-m running. *Significantly different from 500 m ($p < 0.05$). +Significantly different from 1000 m ($p < 0.05$)



and 1000 m ($0.0604 \pm 0.0089 \text{ min}^{-1}$). However, the 8 % decrease of γ_2 between the 1000- and 1500-m trials ($0.0556 \pm 0.0112 \text{ min}^{-1}$) was not statistically significant (Fig. 2d).

NLRR(0) was not different after 500 m ($30.5 \pm 5.5 \text{ mmol min}^{-1}$), 1000 m ($28.0 \pm 4.3 \text{ mmol min}^{-1}$), or 1500 m ($24.8 \pm 5.3 \text{ mmol min}^{-1}$; NS; Fig. 3a). NALR_{max} was not different among trials (31.9 ± 3.7 , 38.8 ± 4.9 , and $42.8 \pm 4.7 \text{ mmol}$ after 500, 1000, and 1500 m, respectively; Fig. 3b). The amount of lactate accumulated (QL_{aA}) calculated at the end of exercise increased almost linearly with distance (137 ± 6 , 219 ± 8 , and $300 \pm 25 \text{ mmol}$ for 500, 1000, and 1500 m, respectively; Fig. 3c).

LRR(0) (11.2 ± 0.6 , 13.1 ± 1.7 , and $15.9 \pm 2.9 \text{ mmol min}^{-1}$ after 500, 1000, and 1500 m, respectively; Fig. 3d) and LAR (56 ± 6 , 55 ± 6 , and $55 \pm 13 \text{ mmol min}^{-1}$ after 500, 1000, and 1500 m, respectively) were not significantly different among trials.

MCCR was significantly higher after 500 m ($41 \pm 2 \text{ mL kg}^{-1} \text{ min}^{-1}$) than after 1000 m ($p < 0.05$). No differences were observed in MCCR after 1000 and 1500 m (30 ± 4 and $28 \pm 6 \text{ mL kg}^{-1} \text{ min}^{-1}$, respectively, NS). R_dR at the end of exercise [$R_dR(0)$] was not different among trials (16.3 ± 0.9 , 18.7 ± 2.4 , and $22.3 \pm 2.9 \text{ mg kg}^{-1} \text{ min}^{-1}$ after 500, 1000, and 1500 m, respectively).

Discussion

The purpose of this study was to investigate alterations in parameters of lactate recovery kinetics in response to 500-, 1000-, and 1500-m high-intensity running trials. The main findings of the present study were that the increase of running distance induced (1) decrease of the lactate exchange ability, (2) decrease and then relative stabilization of the lactate removal ability during recovery, and (3) regular increases in the amount of lactate accumulated in the body and blood lactate concentrations at exercise completion. Estimated lactate release, removal and accumulation rates at exercise completion, and the net amount of lactate released during recovery were not significantly altered by running distance.

Lactate exchange ability

The decrease of γ_1 observed in the present study (Fig. 2c) testified to an important decline in the lactate exchange ability with running distance, particularly in response to the second 500 m. This decrease in γ_1 means that a smaller fraction of muscular lactate is released into the bloodstream per unit of time after 1000 m than after 500 m, and after 1500 m than after 1000 m. In other words, the

efficiency with which lactate is released from the previously active muscles into the blood diminished with the increase of running distance. The lactate exchange ability depends (1) on muscle perfusion which itself depends on capillary density (Messonnier et al. 2002) and recruitment (Coggins et al. 2001) and on local blood flow (Pilegaard et al. 1995) and (2) on lactate transport capacity (Dubouchaud et al. 1999; Eydoux et al. 2000; Juel 1997; Roth and Brooks 1990) which itself depends on sarcolemmal MCT1 and MCT4 (lactate/H⁺ co-transporters) content (Dubouchaud et al. 2000) as well as on the functionality of the carriers (Juel 1997). During high-intensity submaximal exercises, reduction in muscle perfusion (i.e., alterations in muscle blood flow and capillary recruitment) is unexpected (Mortensen et al. 2008). On the other hand, the drop of lactate exchange ability can be more likely attributed either to (1) a decrease in the carriers content, (2) alterations in the functionality of transporters, and (3) a combination of these possibilities. Consistent with a possible decrease in the sarcolemmal lactate carriers content, Bishop et al. (2007) have reported a decrease in lactate/H⁺ co-transporters MCT1 and MCT4 during short high-intensity exercise that could induce impairment in the lactate exchange ability. Consistent with the possible alteration in the functionality of the transporters, Juel (1997) reported that for a same muscle-to-blood lactate gradient, the net lactate efflux from giant sarcolemmal vesicles decreased when lactate concentrations increased, suggesting a deleterious role of the concentrations per se on the efficiency with which the transporters work. These data led him to the conclusion that lactate accumulated externally may affect lactate extrusion, probably due to a higher lactate/lactate exchange, resulting in fewer carriers transporting lactate out (Juel 1997). In accordance with the results of Juel and his interpretation, we observed in the present study an inverse relationship between La(0) and γ_1 , suggesting that blood lactate concentrations may contribute to dampen the lactate exchange ability (Fig. 4).

Net lactate release rate

A decrease of lactate exchange ability is expected to create a hindrance in lactate efflux during exercise. However, the estimated net lactate release rate at the end of exercise [i.e., NLRR(0)] was not significantly different after 500, 1000, or 1500 m (Fig. 3a). This lack of significant alteration in NLRR(0) might be explained by an increase during exercise of the muscle-to-blood lactate gradient which determines, in addition to the exchange ability, lactate flux between muscle and blood. In other words, the decrease in lactate exchange ability was compensated by an increase in muscle-to-blood lactate gradient, so that the estimated net lactate release rate remained almost constant after 500,

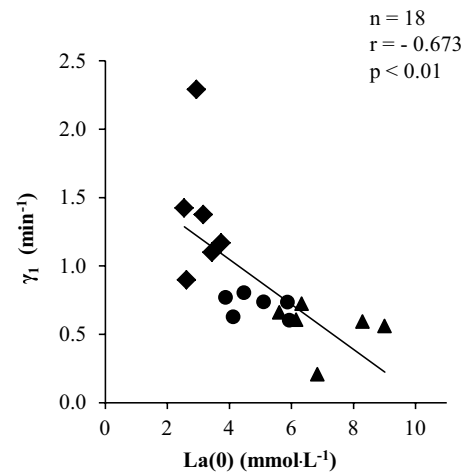


Fig. 4 Correlation between γ_1 and La(0), where γ_1 is the lactate exchange ability between the previously active muscles and the blood and La(0) is the blood lactate concentration at exercise completion. *Diamonds*, *circles*, and *triangles* refer to data obtained after 500-, 1000-, and 1500 m, respectively

1000, and 1500 m. In accordance with this inference, A_1 values, which depend on the muscle-to-blood lactate gradient, tended to increase with distance (Fig. 2b). The present results and the above line of reasoning are in accordance with the previous works showing that the net lactate release rate increased and then plateaued during high-intensity exercise, while the muscle-to-blood lactate gradient obviously increased, indicating disturbances in the lactate exchange ability (Juel et al. 1990).

Net amount of lactate released during recovery

NALR_{max} did not increase significantly with running distance. This means that despite an obvious increase in muscle lactate concentrations with distance, the quantity of lactate that left the previously active muscles during recovery did not change drastically. This suggests that a higher proportion of accumulated lactate remained inside the previously active muscles during the subsequent recovery.

Lactate removal

The results of the present study demonstrated that after an initial period of decrease, there is a relative maintenance of the removal ability. Specifically, γ_2 was lower after 1000 m than after 500 m, but was not further altered after 1500 m. A possible hypothesis to explain the decrease in the lactate removal ability would be that acidosis associated with lactate accumulation (Marcinek et al. 2010) had altered cellular respiration (Jubrias et al. 2003) and consequently lactate removal (Thomas et al. 2004). However, this hypothesis is not consistent with the fact that γ_2 decreased only between

the 500- and 1000-m trials when lactate levels were relatively modest. Furthermore, the lack of further decrease in γ_2 after 1500 m might indicate that lactate accumulation was not sufficient in the present study to alter substantially acid/base balance and, therefore, mitochondrial respiration. Thus, it appears clear that the underlying mechanisms that explain the observed changes in the lactate removal ability remain unknown and deserve to be specifically investigated in future studies.

We also estimated lactate removal rate at exercise completion. LRR(0) was not significantly different after 500, 1000, or 1500 m. The maintenance of LRR(0) with exercise duration, while γ_2 decreased, can be attributed to the concomitant elevation of blood lactate concentrations [i.e., La(0)] when running distance increased. Indeed, the effect of lactate concentrations per se on lactate disappearance rate had been clearly shown by experiments using a lactate clamp procedure which consistently demonstrated that the lactate disappearance rate increased when blood lactate concentrations were increased by the lactate clamp (Messonnier et al. 2013; Miller et al. 2002). In other words, the decrease of γ_2 observed in the present study has been compensated by an increase in blood lactate concentrations, thus maintaining LRR(0).

The lactate removal ability expresses the efficiency with which lactate is removed from the body. Therefore, the physiological meaning of γ_2 is very close to the one of the lactate metabolic clearance rate (MCR) obtained via tracer methods. Interestingly, an MCR during recovery (MCR_R, mL⁻¹ kg⁻¹ min⁻¹) can be derived from γ_2 (see Eq. 6). Remarkably, the MCR_R values obtained in the present study are in line with those of the literature (Freund et al. 1989; Messonnier et al. 2001) and with those of MCR when the relative exercise intensity is taken into account (Fig. 5). We can also estimate the lactate disappearance rate at exercise completion [R_dR(0), mg kg⁻¹ min⁻¹]. Interestingly, R_dR(0) values are very close to those obtained in the literature (Messonnier et al. 2013; Miller et al. 2002).

Blood and whole body lactate accumulation

Because at exercise completion, the net lactate release rate [NLRR(0)] was similar among trials and the lactate removal rate [LRR(0)] was (1) lower than NLRR(0) and (2) also not different among trials, it is, therefore, not surprising that La(0) increased almost linearly with running distance. Moreover, the fact that LAR was similar during each fraction of 500 m, while LRR(0) remained unchanged among trials, argue in favor of an almost constant lactate production rate. At first sight, it would seem that the levels of lactate and well-known concomitant decrease in pH were not strong enough in the present study to dampen significantly muscle energetics and especially lactate production during

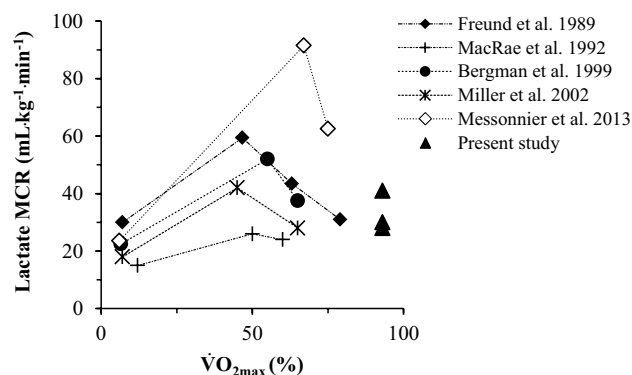


Fig. 5 Metabolic clearance rate of lactate as a function of relative rates ($\dot{V}O_{2\max}$) elicited in the present and previous studies. Redrawn from Messonnier et al. (2013)

exercise, as it has been experimentally demonstrated and modeled (Hollidge-Horvat et al. 1999; Korzeniewski and Zoladz 2015).

Limitations

We are aware that the present study involved a relatively low number of subjects. However, we do not believe that this constitutes a major limitation in the present case. Our position lies on the fact that (1) the trials were very different, so that the alterations in lactate concentrations and kinetics parameters among trials were important and much higher than the intra-individual variability and (2) each subject was compared to himself that also contributes to reduce a possible bias.

Besides, we would like to underline that in the present study, we used the 500-, 1000-, and 1500-m trials at 90 % of maximal competition speed as a model to investigate the changes in lactate kinetics after high-intensity exercises and not in the purpose to understand what may happen during a 1500-m race. In other words, the present results cannot be extended to what happens during a 1500-m race, where speed is not constant and exercise is exhaustive.

Perspectives

Because the lactate exchange and removal abilities are related to performance (Bret et al. 2003; Messonnier et al. 1997, 2002) and since both γ_1 and γ_2 decline with running distance, this raises the question of knowing whether an optimal running strategy exists to delay or reduce these decreases, maintain work capacity and ultimately improve performance. Thus, in a near future, lactate recovery kinetics in response to high-intensity exercises using different running strategy would be warranted.

Conclusions

In summary, alterations in lactate kinetics occurred in response to high-intensity 500-, 1000-, and 1500-m running trials. These changes included: (1) a continued decrease in lactate exchange ability (γ_1) and (2) an initial decrease and then a stabilization of the lactate removal ability (γ_2). Despite these alterations, the net lactate release [NLRR(0)], removal [LRR(0)], and whole body accumulation (LAR) rates were not significantly modified by running distance, so that lactate concentration [La(0)] and whole body accumulation (QLaA) increased almost linearly with running distance. It was also deduced from these results that the lactate production rate remained approximately constant. Finally, the fact that the net amount of lactate released during subsequent recovery was unaltered by running distance, while an increase in muscle lactate concentrations was expected, suggested that a higher proportion of muscle lactate remained inside the previously active muscles during the subsequent recovery with the increase in running distance.

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Compliance with ethical standards

Conflict of interest No conflicts of interest, financial or otherwise, are declared by the authors.

Appendix

An application of the bi-compartmental model of lactate distribution space allows the prediction of the net lactate release rate (NLRR, mmol min⁻¹) during recovery using the following equation:

$$NLRR(t) = (\gamma_1 - d_2) \times V_S \times A_1 \times e^{-\gamma_1 t} + (\gamma_2 - d_2) \times V_S \times A_2 \times e^{-\gamma_2 t} + \mu, \quad (2)$$

where V_S is the volume of compartment S [i.e., 250 mL kg⁻¹ body mass; $V_S = V_{TLS}$ (volume of the total lactate distribution space) - V_M (lactate distribution volume of muscles previously involved in exercise)], μ is the net muscular release rate of lactate at $t \rightarrow \infty$ and was set at 0.12 mmol min⁻¹ (Bret et al. 2003; Freund and Zouloumian 1981b; Maciejewski et al. 2013), and d_2 is the efficiency of lactate utilization in compartment S . The application of the model gives realistic prediction when d_2 is close to γ_2 . Therefore, to approximate NLRR, we set, as previously

(Bret et al. 2003; Freund and Zouloumian 1981b; Maciejewski et al. 2013), $d_2 = \gamma_2 - 0.005$. The integral of Eq. (2) gives an estimation of the net amount of lactate released during recovery (NALR, mmol) from the previously active muscles to the blood (Bret et al. 2003). The maximal value (NALR_{max}) will be considered (Maciejewski et al. 2013).

Recently, Maciejewski et al. (2013) have developed a method to estimate the amount of lactate accumulated in the body at exercise completion (QLaA, mmol):

$$QLaA = QLaA \text{ at } La_{peak} + QLaR, \quad (3)$$

where QLaA at La_{peak} is the quantity of lactate accumulated at La_{peak} which is calculated as the following:

$$QLaA \text{ at } La_{peak} = La_{peak} \times V_{TLS}, \quad (4)$$

where La_{peak} represents the maximal blood lactate concentration during recovery, and V_{TLS} represents the volume of the total lactate distribution space (i.e., 500 mL kg⁻¹).

QLaR represents the amount of lactate removed from the end of exercise to La_{peak} , which is calculated as

$$QLaR = [(La_{peak} + La(0))/2] \times \gamma_2 \times tLa_{peak} \times V_{TLS}, \quad (5)$$

where tLa_{peak} is the time to reach the maximal lactate concentration during recovery. For more information about this method, we refer the reader to Maciejewski et al. (2013).

Lactate removal rate at the end of each exercise [LRR(0), mmol min⁻¹] was estimated from the following equation:

$$LRR(0) = \gamma_2 \times QLaA. \quad (6)$$

A calculation of the lactate accumulation rate (LAR, mmol min⁻¹) during each fraction of 500 m was derived from QLaA values according to the following equation:

$$LAR = \Delta QLaA / t, \quad (7)$$

where $\Delta QLaA$ is the difference in QLaA between two distances and t is the time to complete 500 m. For the first 500 m, $\Delta QLaA = QLaA - (La_{warm-up} \times V_{TLS})$, where $La_{warm-up}$ is the blood lactate concentration at the end of the warm-up.

As done in the past (Freund et al. 1986; Messonnier et al. 2001), a metabolic clearance rate of lactate during recovery (MCRR, mL kg⁻¹ min⁻¹) can be derived from γ_2 values according to the following equation:

$$MCRR = \gamma_2 \times V_{TLS}. \quad (8)$$

A calculation of the lactate disappearance rate at exercise completion ($R_dR(0)$, mg kg⁻¹ min⁻¹) can also be derived from Eq. (8) according to the following equation:

$$R_dR(0) = MCRR \cdot (QLaA / V_{TLS}) \cdot (89/1000). \quad (9)$$

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