Estimation of endurance performance markers using a metabolic model in cycling: a pilot study

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Abstract

Introduction: Metabolic models can be used to simulate dose-time responses in physiological parameters like blood lactate concentration. Likewise, these models can be applied to observed data from graded exercise tests to estimate endurance performance markers like maximal oxygen consumption ($\dot{V}O_2max$) and maximal lactate accumulation rate (ċLamax). Currently, this method is not explained in the literature. The aim of this pilot study is 1) to transparently report an algorithm for estimation, 2) to compare the theoretical and practical maximal lactate steady-state (MLSS), and 3) to inform a rigorous study design to optimize and validate this approach.

Methods: Ten Participants from two labs participated in this non-experimental study. Body composition, a submaximal ergometer test, and a 30-minute one-trial MLSS test at the intensity of the theoretical MLSS were conducted on two separate days. Maximal post-lactate values were fitted to the metabolic model from Mader & Heck (1986) to estimate $\dot{V}O_2max$ and ċLamax, which consequently determined the theoretical MLSS. The increase in blood lactate concentration from minute 10 to 30 was analyzed and a sensitivity analysis was conducted, using the advanced model from Mader (2003).

Results: The average blood lactate concentration increase in the one-trial MLSS test from minute 10 to 30 was 1.38 ± 1.27 mmol/L. The sensitivity analysis shows that for 50 % of the measurements the actual difference between the power at the theoretical and practical MLSS is less than 1.8%.

Conclusion: This study provides a proof-of-concept for using metabolic simulations to derive estimates for endurance performance markers that determine the metabolic profile of an athlete. This study can inform the design of future validation studies on this approach.

Keywords: cycling; endurance performance; blood lactate concentration; V̇o2max; exercise physiology

Introduction

Lactate thresholds (LT) are commonly used to evaluate endurance performance and to inform training methods[1,2]. Graded exercise tests with blood lactate measurement are used to derive a lactate-power curve and, consequently, derive estimates for LTs. A plethora of methods exist to estimate the anaerobic lactate threshold (also called LT2), which are surrogates of the maximal lactate steady-state (MLSS) determined by the uneconomical gold standard testing procedure over several days [2–4].

Mader & Heck (1986)[5] suggested a theoretical approach to the metabolic origin of the anaerobic threshold by using a metabolic simulation model [6]. The authors suggested that the metabolic profile can be modeled by a set of equations, where the maximal oxygen consumption ($\dot{V}O_2max$) and the maximal rate of lactate/pyruvate production (ċLamax) determines the MLSS. The activation of anaerobic glycolysis and oxidative phosphorylation are described by Hill-Equations with ċLamax and $\dot{V}O_2max$ as determinants (further determinants are [ADP], [AMP], pH and Hill-coefficients), respectively. Consequently, the point of equivalence between lactate production and removal is considered the metabolic origin of the MLSS. This model can also be used to calculate steady-state lactate concentrations below the anaerobic threshold, lactate accumulation above the anaerobic threshold as well as macronutrient utilization as a function of oxygen utilization, which we will now refer to as the *metabolic profile*. This theoretical approach was refined in future publications by considering the exchange between an active and a passive compartment and the influences of the biochemical environment [7,8]. So far, the model has been used to explain real-life phenomena theoretically but was rarely calibrated with real data. The results of two studies showing an acceptable agreement between experiments and the models' predictions [9,10] of the power at the anaerobic threshold were recently questioned [11]. Nevertheless, the model is used by practitioners as it is implemented in commercial software.

Generally, the model can be implemented by practitioners in two ways. First, $\dot{V}O_2max$ and ċLamax can be measured and used as input parameters to calculate the metabolic profile [9,10]. Although the measurement of ċLamax seems to be reliable [12], the validity has not been determined [13] which introduces a possible source of error. Second, multiple exercise bouts can be performed and model simulations can be used to estimate $\dot{V}O_2max$ and ċLamax and, consequently, the metabolic profile. A recent paper claimed very strong correlations between calculated and experimentally determined parameters ($\dot{V}O_2max$, MLSS) using this approach [14]. Regrettably, the authors did not demonstrate how the model was used to obtain $\dot{V}O_2max$, ċLamax and MLSS.

The research aim of this pilot study was threefold: First, to provide a proof-of-concept of the algorithms used to derive the model-based metabolic profile (including $\dot{V}O_2max$, ċLamax and MLSS) from graded exercise tests. Second, to compare the model-based MLSS to a practical one-trial MLSS test. Lastly, to inform a rigorous study that aims to optimize and validate the model-based approach outlined in this study.

Methods

Participants

A convenience sample of ten healthy male and female recreational athletes volunteered to participate in this non-experimental, cross-sectional pilot study. The measurements took place in two different locations (A & B). The sample constitutes of sports science students (n=5, Lab B) and recreational cyclists and triathletes (n=5, Lab A). The participants had no known medical conditions that would inhibit their ability to perform strenuous exercise or cause them any harm while doing so. In addition, the experimental procedures and potential risks were fully explained.

Procedures

The participants visited the labs on two different days. On the first day, a body composition (only Lab B) and a submaximal ergometer test were conducted. On the second day, the 30-minute MLSS trial was carried out.

Equipment

Before each test in lab B, vertical and horizontal positions of the saddle, handlebar height, and stem length were modified to match the most comfortable position of the participants for the sport science students. Participants tested at lab A brought their own bike that was fitted onto the Cyclus 2. Blood samples were hemolyzed in 2-mL microtest tubes and analyzed enzymatic amperometrically by the Biosen C-Line Sport (EKF-Diagnostik, Barleben, Germany). Lab A used the same method for measuring the blood lactate concentration.

Body Composition Testing

The body composition measurement is needed to determine the La_{space}. At lab B, body composition was measured with a biometrical impedance analysis system (BIA; InBody 770, JP Global Markets GmbH, Eschborn, Germany). Participants were instructed to follow their normal diet without any restriction 24h before the measurement. The La_{space} can be calculated based on the total body water [5]. At lab B the La_{space} was calculated based on the body fat percentage (bf) from previous measurements. The following equation was used based on commercially available software:

$$La_{space} = \frac{(-0.5 \times bf + 55.13)}{100}$$

Submaximal bike ergometer test

This test consisted of four different exercise bouts with varying intensity and duration. First, an eight-minute exercise bout was performed at an intensity around the estimated maximal fat combustion (fatmax). The second exercise bout was 6 min long and at an intensity between fatmax and the estimated anaerobic threshold. A four-minute lasting exercise bout at an intensity close to the anaerobic threshold followed. Lastly, a two-minute exercise bout was performed aiming to produce a maximal post-lactate beyond 5 mmol/L. All exercise bouts were interspersed by a short resting phase to achieve lactate concentration < 2.5 mmol/L. The intensities of the test were determined based on the individual characteristics of each participant and adapted during the test if needed.

To measure capillary blood lactate concentration, 20 mL capillary blood samples were taken from the earlobe after each block. In total 20 lactate samples were collected per participant. Specific time points of sample collection are provided in figure 1.

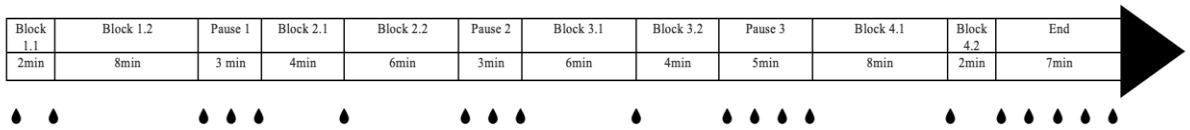

Figure 1: Blood Sampling. Each drop represents a time point when blood samples were collected. The Horizontal lengths of the boxes are proportional to the duration of the phases.

MLSS trial

A 30-minute trial at the intensity of the theoretical anaerobic threshold (see paragraph *metabolic model*) was conducted. A 14-minute warm-up with 2 intervals below the anaerobic threshold was performed on a bike ergometer before testing. After one minute of rest, the official 30-minute protocol started. Capillary blood samples were collected at 5-minute intervals during the test as well as one and three minutes after the test. Lactate concentration was measured using the same devices compared to the submaximal testing.

Metabolic profile

The metabolic profile was calculated according to Mader and Heck (1986)[5]. The metabolic profile is defined as a combination of performance indicators ($\dot{V}O_2max$, ċLamax, La_{space}) and physiological responses (e.g., lactate). For each athlete, varying values of $\dot{V}O_2max$ and ċLamax were used to simulate several metabolic profiles. By comparing simulated to measured lactate values, the best fit was determined by visual inspection of lactate responses and the sum of squared errors (χ2). Thus, the performance indicators ($\dot{V}O_2max$ and ċLamax) were extracted for further usage. Detailed documentation of the application of the model in the programming language python is provided as an interactive notebook. The following provides the rationale that allows the calculation of the lactate kinetics based on the model.

Lactate concentration <u>below</u> the anaerobic threshold

Theoretical lactate steady-states can be calculated assuming infinite time (see the purple line in Figure 2), whereas the theoretical anaerobic threshold is supposed to be the vertical asymptote. However, to account for time-dependent physiological lactate responses, the lactate concentration was calculated as a function of time. For this purpose, the following modified equations [8] were used:

Eq. 1: $$La(t) = La_{ss}\left(1 - e^{t/T}\right)$$

Eq. 2: $$T = 1.6886\ La_{ss} - 0.519$$

Consequently, the time-dependent lactate concentrations for the 8-, 6- and 4-minute stages were calculated (see dots in Figure 2). For further processing, the calculated values are fitted to a second-order polynomial with a fixed resting lactate of 1.25 mmol/L.

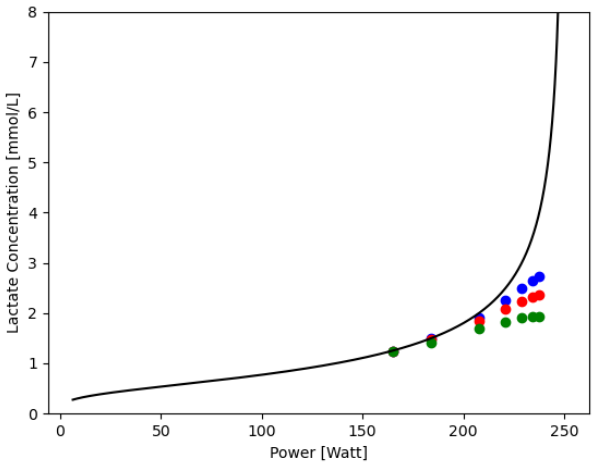

Figure 2: Theoretical, model-based lactate concentrations and the corresponding intensity in cyclists (measured in Watts). The black line indicates values reached upon an infinite time. Dots indicate time-dependent lactate concentration in the 8- (blue), 6- (red) and 4-minute (green) stages.

Lactate concentration <u>above</u> the anaerobic threshold

The anaerobic threshold is described as the equilibrium between lactate removal and production. Figure 3 shows the difference between both, where the orange line indicates higher lactate removal and the golden line indicates higher production. As higher lactate removal than production is impossible under steady-state conditions, the orange line resembles the possible use of fatty acids as substrates. The golden line indicates the net lactate accumulation rate for intensities above the anaerobic threshold. Consequently, the lactate concentrations above the anaerobic threshold were calculated by multiplying the net lactate accumulation rate for a given power by the duration of the exercise bout.

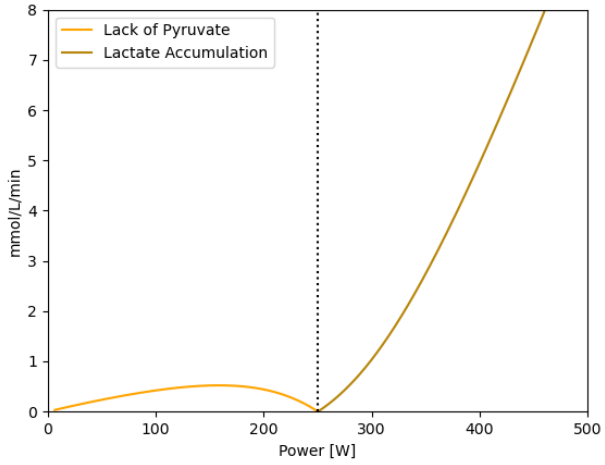

Figure 3: Difference between lactate production and removal. The orange line indicates higher lactate removal (lack of pyruvate); the golden line indicates higher lactate production (net lactate accumulation rate) and the dotted line indicates the anaerobic threshold.

Model fitting

An example of the calculated post-lactate values for a single simulation in one athlete is presented in Figure 4. The lines represent the expected maximal post-lactate concentrations for each stage. The data collected during the test is visualized as dots. Several simulations were compared by adjusting the values for maximal aerobic ($\dot{V}O_2max$) and glycolytic power (ċLamax) as independent variables. The best fit was determined by visual inspection and $\chi 2$ as the fitting index. Hence, $\dot{V}O_2max$, ċLamax and the anaerobic threshold from the best-fitting model were used.

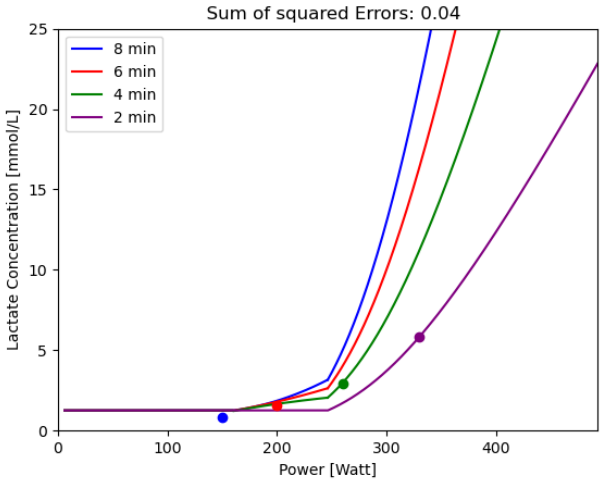

Figure 4: Maximal expected post-lactate values (y-axis) for varying intensities (x-axis) and varying stage lengths (colors). Lines indicate theoretical, model-based predictions; dots indicate measured maximal post-lactate concentrations. Input parameters ($\dot{V}O_2max$, ċLamax) were varied to find the best fit.

Sensitivity Analysis

As only one MLSS-Trial was performed in this pilot study the sensitivity analysis allows us to make an informed decision about the difference between calculated and true power at the MLSS. The sensitivity analysis was performed with the two-compartment model [7]. Multiple constant 30-minute exercise bouts were simulated with intensities around the MLSS. The calculated lactate kinetics were further analyzed to make an informed decision about the accuracy of the performed MLSS-Trial in comparison to the actual MLSS.

Statistical analysis

A descriptive comparison between the modeled anaerobic threshold and the one-trial MLSS result was carried out. The difference in blood lactate concentration between minutes 10 and 30 was the outcome parameter. Values close to 1 indicate an optimal agreement [15]. Further, a sensitivity analysis was conducted to evaluate discrepancies between the practical and theoretical anaerobic threshold. The outcomes of modeling the submaximal test ($\dot{V}O_2max$, ċLamax and anaerobic threshold) are presented descriptively. The model fit was evaluated using $\chi 2$.

Results

Nine of the participants (body mass: 79.7 ± 14.6 kg) were included in the statistical analysis. One participant was excluded because of extremely high baseline lactate concentrations. The determined physiological parameters based on the stage test are summarized in table 1. Participants 1 – 5 were examined at lab A, whereas the remaining participants visited lab B. The explicit data for every participant's stage test is provided in our online-repository https://osf.io/yeq3t/ [16].

Table 1: Model-based endurance performance indicators for each athlete.

ID	MLSS [Watt]	VO_2max [ml/min/kg]	ċLamax [mmol/L/s]	χ2
1	245	73.8	0.57	1.32
2	265	55.5	0.52	1.52
3	244	45.8	0.44	0.29
4	298	54.0	0.44	2.33
5	292	58.4	0.36	0.35
6	188	50.0	1.03	9.82
7	150	46.4	0.97	3.48
8	227	48.0	0.90	9.84
9	216	46.2	0.99	8.90
Mean ± SD	236 ± 45	53.1 ± 8.5	0.69 ± 0.26	4.21 ± 3.87

ID: subject identifier, MLSS: maximal lactate steady-state, $\dot{V}O_2max$: maximal oxygen consumption, ċLamax: maximal lactate production rate, χ2 : Sum of Squared Errors, SD: standard deviation

The determined anaerobic threshold (Table 1) was tested in a one-trial 30-minute MLSS test. The rise in lactate concentration from the 10th to the 30th minute was analyzed. The average lactate increase from minute 10 to 30 was 1.38 ± 1.27 mmol/L. Figure 5 provides an overview of the lactate kinetics during the test.

The virtually created athlete for the sensitivity analysis has its MLSS at 277 Watts (figure 6). Subsequently, the intensity of the exercise bouts was manipulated in either direction by 5 Watts (1.8%). The difference in lactate concentration difference between minutes 10 and 30 was reduced to 0.48 and increased to 1.63 mmol/L, respectively. In comparison to the experimentally performed MLSS-Trials, the analysis suggests that the entire interquartile range (figure 5) of the calculated MLSS is within a 1.8% deviation from the actual MLSS (figure 6).

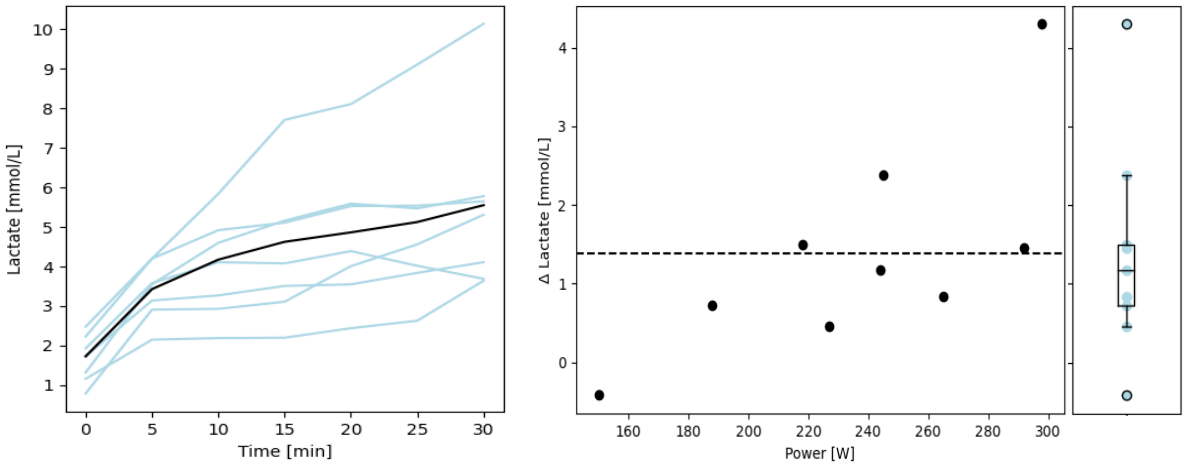

Figure 5: Blood Lactate response concentration during the MLSS trial (left) and difference of lactate concentration between minutes 10 and 30 (right). Left: Black line indicates the mean and blue lines individual data. Right: Dashed line indicates the mean difference and dots represent individual data.

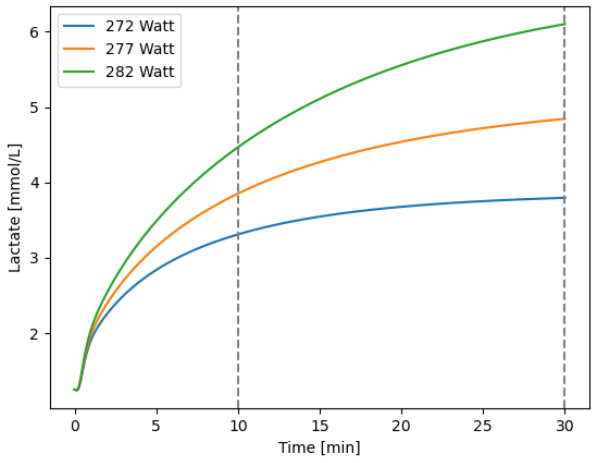

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Figure 6: Sensitivity Analysis for three MLSS-Trials. The difference between the 10th - to the 30th -minute was 0.48, 0.99, 1.63 mmol/L, respectively. Input parameters for the model were body weight = 70 kg, $\dot{V}O_2max$ = 60 ml/min/kg, ċLamax = 0.6 mmol/L/s, Kel = 2.5, La_{space} = 0.45, Active Muscle = 0.26.

Discussion

This pilot study provides the technical framework for deriving several endurance-related performance parameters (e.g. $\dot{V}O_2max$, ċLamax, MLSS, Fatmax) based on a single graded exercise test using metabolic simulation. This pilot study *does not* provide a firm validation of the described approach, though it is aimed to inform such a study. However, the sensitivity analysis let us conclude, that the procedure can possibly resemble the practically determined MLSS.

Comparison with the literature

The results of this study can be compared to an investigation performed by Podlogar et al. (2022) [14]. These authors used a similar graded exercise test protocol to assess MLSS and $\dot{V}O_2max$. Unfortunately,

the authors were not able to transparently describe the mathematical computations used to determine MLSS and $\dot{V}O_2$max. Therefore, it can only be speculated that a similar approach was used. Calculated MLSS and $\dot{V}O_2$max were subsequently validated using multiple 30-minute-MLSS trials and a $\dot{V}O_2$max-ramp-test. With a mean bias of 2W, it seems reasonable that the validity of the power at the MLSS in comparison to this study is of a similar magnitude. In addition, a similar spread including outliers in both directions around the intensity at the MLSS was reported.

Accuracy of the test

The study showed that for two participants the model was inaccurate by significantly overestimating and underestimating the MLSS, respectively. A source of error that was introduced is the rough method that was applied to measure La_{space}. However, it is unlikely that this large error exclusively stems from a wrongly estimated La_{space} as the influence of this parameter on the overall system does not allow such variance. It can be speculated that both participants have a high active muscle mass in relation to the overall La_{space}. This relationship, which largely influences the lactate kinetics in the body, is not accounted for in the applied one-compartment model. This is one of the multiple limitations of the applied model in comparison to the more sophisticated two-compartment model. Further limitations are outlined in a later part of the discussion.

The sensitivity analysis revealed a good agreement between calculated and actual MLSS. It must be pointed out that the sensitivity analysis can only be regarded as a valid mean under the assumption that the two-compartment model accurately describes the lactate kinetics. Nevertheless, the findings of the sensitivity analysis are of a comparable magnitude to experiments investigating the influence of power on lactate kinetics during MLSS-Trials [17]. Therefore, despite the lack of thorough validation of the two-compartment model, the results of the sensitivity analysis are regarded as accurate. Consequently, it is concluded that for most of the participants the MLSS was estimated with an accuracy of 1.8%.

$\dot{V}O_2$max and ċLamax

The calculated $\dot{V}O_2$max and ċLamax were not subject to validation in this study. Despite the power at MLSS being an informative parameter to assess an athlete's endurance capabilities the biological mechanism allowing this power is still masked. $\dot{V}O_2$max and ċLamax are used as parameters describing the interplay between aerobic and glycolytic metabolism. Consequently, these parameters are the target of a training intervention and therefore of great importance. The same power at MLSS may be subject to a different mixture of $\dot{V}O_2$max and ċLamax. Therefore, exclusively based on the accuracy of the power at MLSS it cannot be concluded that $\dot{V}O_2$max and ċLamax were accurately calculated.

Model assumptions

The one-compartment model by Mader & Heck (1986)[5] assumes steady-state conditions in all circumstances. This assumption holds untrue for the conducted test protocol regarding the oxidative [19] and glycolytic metabolism[17]. It was tried to correct the lactate kinetics accordingly using eq. 1 and eq 2. Similarly, the inhibitory effect of accumulating H^+ on the glycolytic metabolism was neglected. Future studies investigating the application of this model in a metabolic diagnostical setting should use the more sophisticated approach of the model, which can dynamically calculate the transition periods and respects the inhibitory effect of $[H^+]$ on the glycolytic metabolism [7].

The test protocol

The exercise protocol was chosen based on current practice and the application of this approach in commercial software, which should not remain undebated. Due to the not given possibility of modeling transition processes using the simplistic version of the model the protocol was designed to include four separate bouts of exercise ensuring sufficient rest in between. Modeling of the typically used step-test protocols would require the implementation of the more sophisticated model. This is thought to be investigated in a future study. A problematic aspect of using the computer simulation for such a testing protocol is the missing ability of the computer simulation to account for differences in the monocarboxyltransporter (MCT) content of individuals. MCT is known to positively correlate with the maximal oxygen consumption.[20] Therefore, an unindividualized mathematical description of the lactate diffusion process from the muscle to the blood introduces a new source of error. In order to circumvent this problem multiple capillary blood samples were taken after each exercise bout. The exercise was only resumed if the last collected lactate concentration was significantly lower than the previous sample. The highest lactate concentration was then used for this exercise bout for further data processing. Similar pitfalls of biological variability impede the accurate calculation of the activation of the oxidative and glycolytic metabolism, regardless of using the one – or two-compartment model.

In the here conducted study it was made sure that the participants' blood lactate concentration before each exercise bout was below 2.5 mmol/L to minimize the interference between the different exercise bouts. The intensity of the exercise bouts was set to cover almost the entire metabolic profile from intensities around the maximal fat combustion up to nearly the maximal oxygen consumption. However, in theory, exercise bouts with arbitrary intensities and duration are also possible to analyze. This flexibility theoretically allows the testing of athletes during a training session, keeping in mind that alterations to the protocol have not been investigated. Concerning the applied protocol, the implementation of stages with an outcome of low lactate concentrations must be criticized. Inspecting the Power-Lactate-Curve under the anaerobic threshold (figure 2), it becomes apparent that the curve runs flat and significant rises in lactate concentration also require a significantly increased power. Consequently, small errors in the measurement of blood lactate concentration result in a large shift on the power axis. To minimize the effect of measurement errors, lactate concentrations after each stage should at least exceed a value of 2.5 mmol/L. A further critical aspect of the test is the short duration of the last stage. It is unlikely to reach $\dot{V}O_2max$ within two minutes. Nevertheless, a spread of intensities across the metabolic profile will likely increase the quality criteria of the test results. Hence, the stage should be just long enough to reach $\dot{V}O_2max$ but also as short as possible to allow the highest possible power. These practical considerations are thought to be implemented in future studies.

Prospects

To overcome the methodological restrictions of this pilot study future studies should use the more complex two-compartment model. Consequently, a clear rationale is needed to properly calibrate the model (e.g.: determination of active muscle mass) to minimize the source of error. Furthermore, the mere comparison between the calculated and experimentally observed power at MLSS does not satisfyingly validate the model. Similarly, the measurement of $\dot{V}O_2max$ and ċLamax is needed. The lack of an accurate method to measure ċLamax poses a great challenge to the field. Moreover, it must be respected that the constants used in the model may be subject to biochemical variability questioning the applicability of this model in endurance diagnostical settings. The here outlined pitfalls must be overcome to validate the use of the model.

Conclusion

The study shows how the lactate kinetics of exercise bouts with varying intensity and duration can be compared to the metabolic simulation. To the authors' knowledge, this is the first study transparently describing an approach applying the model to graded exercise tests. Furthermore, the study investigated the validity of the calculated power at the MLSS based on a graded exercise test and the metabolic simulation. The experiment suggests a good agreement between calculated and experimental MLSS. Multiple methodological constraints must be respected in interpreting the results of the study and are thought to inform future studies.

Contributions

Conceptualization, Methodology – JS, RS; Formal Analysis, Visualization – JS, Investigation – JS, MT, AG; Supervision – RS; Writing – Original Draft & Review/Editing – JS, MT, AG, RS

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NA

Declaration of interest

The authors declare no conflict of interest.

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