

1 Article

2 **Bypass of Respiratory Complex I and its relation to**  
3 **different lactate landmarks – a pilot study**

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1 **1. Introduction**

2 The controversy about a valid  
3 demarcation of different exercise intensity  
4 domains is an ongoing discussion in sports  
5 and exercise physiology. To-date, thresholds  
6 are mostly determined by concentration  
7 changes of molecules and biomarkers  
8 determining energy-yielding pathways in  
9 the blood (i.e., lactate) or by exchange of  
10 pulmonary gases (Poole, Rossiter, Brooks, &  
11 Gladden, 2020). Besides that, critical power  
12 has recently been demonstrated to more  
13 accurately reflect a maximal metabolic  
14 steady-state than other measures using blood  
15 lactate concentration or respiratory gases  
16 (Jones, Burnley, Black, Poole, & Vanhatalo,  
17 2019). However, none of these  
18 aforementioned estimates of thresholds  
19 intensity takes into account what  
20 perturbations occur inside a muscle cell or a  
21 mitochondrion where ATP (i.e., the energy  
22 currency of the human body) are re-  
23 phosphorylated using oxidative pathways.

24 Lately, Nilsson, Bjornson, Flockhart,  
25 Larsen, and Nielsen (2019) demonstrated in a  
26 model that respiratory Complex I is bypassed  
27 during high intensity exercise using oxygen  
28 uptake ( $\dot{V}O_2$ ) data derived from an  
29 incremental exercise test. Complex I is one of  
30 four enzyme complexes that is involved in  
31 the electron transport chain that transport  
32 protons across the inner mitochondrial  
33 membrane in order to create a proton motive  
34 force that is used to generate ATP from ADP  
35 and inorganic phosphate in Complex V (also

36 known as the enzyme ATPase). The bypass of  
37 Complex I is suggested to be based on a  
38 trade-off between maximizing power output  
39 (i.e., higher flow rate) and maximizing  
40 substrate efficiency (i.e., lower flow rate).  
41 Complex I max ( $CI_{max}$ ) refers to this  
42 threshold where Complex I is bypassed.

43 The aim of this study is therefore to  
44 provide a potential study design for a  
45 physiological validation of  $CI_{max}$ , i.e., the  
46 relation of  $CI_{max}$  to the intensity associated  
47 with lactate threshold (LT) and the onset of  
48 blood lactate accumulation (OBLA).

49 **2. Materials and Methods**

50 In this pilot work five male and well-  
51 trained cyclists and triathletes volunteered to  
52 participate. Participants were required to  
53 visit the laboratory once to determine (a)  
54  $CI_{max}$ , (b) LT, and (c) OBLA during a high-  
55 resolution graded exercise test (GXT). Tests  
56 were conducted on an electromagnetically  
57 braked cycle ergometer (Lode Excalibur  
58 Sport, Groningen, The Netherlands). During  
59 the GXT respiratory gases were measured  
60 breath-by-breath using a portable gas  
61 analyser (MetaMax3B, Cortex Biophysik  
62 GmbH, Leipzig, Germany). To determine  
63 blood lactate ( $BLa^-$ ) concentration capillary  
64 blood sample were obtained from the  
65 earlobe, diluted in 1000  $\mu$ L glucose solution  
66 and were subsequently analysed using an  
67 automated analyser (Biosen C\_Line; EKF-  
68 diagnostic GmbH, Barleben, Germany).

69 The GXT commenced at 40 W and work  
70 rate was increased by 5 W according to the



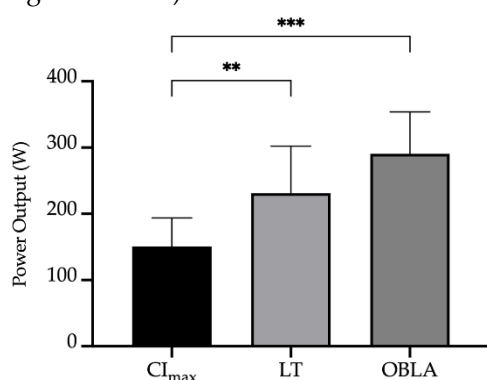
71 recommendations of Nilsson et al. (2019).  
 72 When  $[BLa^-]$  reached a concentration of  $>4.0$   
 73 mmol/L the GXT was terminated. The mean  
 74 duration  $\pm$  standard deviation (SD) of the  
 75 GXT was  $83.3 \pm 18.3$  min.

76  $CI_{max}$  was determined using a Matlab  
 77 code provided in Nilsson et al. (2019) using  
 78  $\dot{V}O_2$  and  $\dot{V}CO_2$  data that were averaged to 30-  
 79 s intervals. LT was determined as the first  
 80 increase of  $[BLa^-]$  above baseline (Yoshida,  
 81 Chida, Ichioka, & Suda, 1987) and OBLA was  
 82 set at a fixed 4 mmol/L  $BLa^-$  concentration  
 83 (Sjödín & Jacobs, 1981).

84 A paired-samples *t*-test was conducted  
 85 to assess differences between  $CI_{max}$  and LT,  
 86 and between  $CI_{max}$  and OBLA. The strength  
 87 of an association between parameters was  
 88 assessed using Pearson product moment  
 89 correlation. Data is presented as mean  $\pm$  SD.  
 90 Statistical significance was accepted at *P* <  
 91 0.05.

### 92 3. Results

93 Average power output associated with  
 94  $CI_{max}$ , LT, and OBLA were  $151 \pm 43$  W,  $231 \pm$   
 95  $71$  W, and  $290 \pm 64$  W, respectively (Figure 1).  
 96  $CI_{max}$  was significantly lower compared to LT  
 97 ( $t_4 = 3.73$ ;  $P = 0.020$ ) as well as OBLA ( $t_4 = 7.73$ ;  
 98  $P = 0.002$ ) and both lactate landmarks were  
 99 not significantly correlated with  $CI_{max}$  (LT:  $r =$   
 100  $0.749$ ,  $P = 0.146$ ; OBLA:  $r = 0.780$ ;  $P = 0.120$ ;  
 101 Figure 2 and 3).

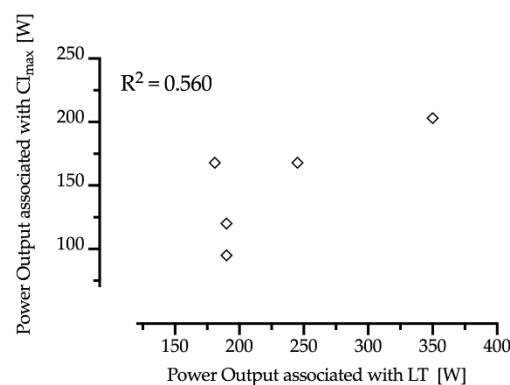


102  
 103 **Figure 1.** Mean  $\pm$  SD for the power outputs  
 104 associated with  $CI_{max}$ , LT and OBLA.

### 105 4. Discussion

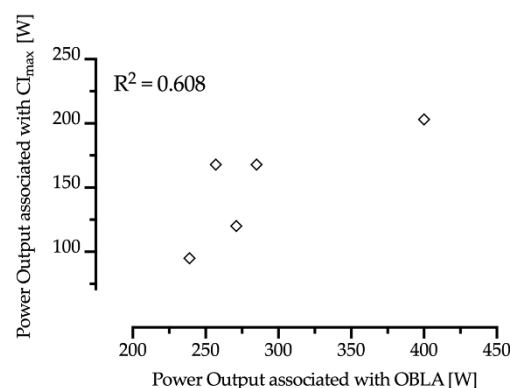
106 The findings of this pilot work suggest  
 107 that  $CI_{max}$  is significantly lower than  
 108 commonly used lactate landmarks like LT or

109 OBLA. This suggests that  $CI_{max}$  cannot be  
 110 used as a surrogate for LT that mostly serves  
 111 as a boundary between the moderate and  
 112 heavy exercise intensity domain. Therefore,  
 113 the physiological underpinnings for a bypass  
 114 of Complex I are not similar to those of LT  
 115 since  $CI_{max}$  is occurring at a significantly  
 116 lower power output. Moreover, results  
 117 suggest that  $CI_{max}$  occurs at  $[BLa^-]$  that are  
 118 generally lower than 4 mmol/L. It is  
 119 commonly accepted that LT as well as OBLA  
 120 serve as an indicator of aerobic fitness. A  
 121 tendency towards a strong relation between  
 122  $CI_{max}$  and both lactate landmarks suggests  
 123 that power output at  $CI_{max}$  is positively  
 124 associated with the aerobic capacity of an  
 125 athlete.



126

127 **Figure 2.** Scatter plot of LT and  $CI_{max}$ .



128

129 **Figure 3.** Scatter plot of OBLA and  $CI_{max}$ .

### 130 5. Practical Applications.

131  $CI_{max}$  might have the potential to serve  
 132 as a new (low intensity) parameter assessing  
 133 aerobic fitness as well as reflecting an

134 'efficient' substrate usage of the  
135 mitochondrion which might be related to  
136 gross efficiency during cycling and running  
137 economy. Moreover,  $CI_{max}$  has probably a  
138 usefulness as a new indicator of assessing  
139 aerobic fitness. Future studies should focus  
140 on reliability of  $CI_{max}$  determination as well  
141 as a physiological validation of  $CI_{max}$ .

## 142 References

143 Jones, A. M., Burnley, M., Black, M. I., Poole,  
144 D. C., & Vanhatalo, A. (2019). The  
145 maximal metabolic steady state:  
146 redefining the 'gold standard'.  
147 *Physiological Reports*, 7(10), e14098.  
148 doi:10.14814/phy2.14098  
149 Nilsson, A., Bjornson, E., Flockhart, M.,  
150 Larsen, F. J., & Nielsen, J. (2019).  
151 Complex I is bypassed during high  
152 intensity exercise. *Nature*

153 *Communications*, 10(1), 5072.  
154 doi:10.1038/s41467-019-12934-8  
155 Poole, D. C., Rossiter, H. B., Brooks, G. A., &  
156 Gladden, L. B. (2020). The anaerobic  
157 threshold: 50+ years of controversy.  
158 *Journal of Physiology*.  
159 doi:10.1113/JP279963  
160 Sjödín, B., & Jacobs, I. (1981). Onset of blood  
161 lactate accumulation and marathon  
162 running performance. *International*  
163 *Journal of Sports Medicine*, 2(1), 23-26.  
164 doi:10.1055/s-2008-1034579  
165 Yoshida, T., Chida, M., Ichioka, M., & Suda,  
166 Y. (1987). Blood lactate parameters  
167 related to aerobic capacity and  
168 endurance performance. *European*  
169 *Journal of Applied Physiology and*  
170 *Occupational Physiology*, 56(1), 7-11.  
171 doi:10.1007/bf00696368  
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