

IS THE BALANCE BETWEEN SKELETAL MUSCULAR
METABOLIC CAPACITY AND OXYGEN SUPPLY
CAPACITY THE SAME IN ENDURANCE TRAINED AND
UNTRAINED SUBJECTS?

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Running head: Exercise capacity in endurance trained subjects

Abstract

We attempted to test whether the balance between muscular metabolic capacity and oxygen supply capacity in endurance-trained athletes (ET) differs from that in a control group of normal physically active subjects by using exercises with different muscle masses. Methods: We compared maximal exercise in 9 ET subjects (Maximal oxygen uptake [VO_2max] $64 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1} \pm \text{SD } 4$) and 8 controls (VO_2max $46 \pm 4 \text{ ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$) during one-legged knee extensions (1-KE), two-legged knee extensions (2-KE) and bicycling. Maximal values for power output (P), VO_2max , concentration of blood lactate ($[\text{La}^-]$), ventilation (VE), heart rate (HR), and arterial oxygen saturation of haemoglobin (SpO_2) were registered. Results: P was 43 (2), 89 (3) and 298 (7) W (mean \pm SE); and VO_2max : 1387 (80), 2234, (113) and 4115 (150) $\text{ml}\cdot\text{min}^{-1}$) for controls in 1-KE, 2-KE and bicycling, respectively. The ET subjects achieved 126%, 121% and 126% of the P of controls ($p < 0.05$) and 127%, 124% and 117% of their VO_2max ($p < 0.05$). HR and $[\text{La}^-]$ were similar for both groups during all modes of exercise, while VE in ET was 147% and 114% of controls during 1-KE and bicycling, respectively. For mass-specific VO_2max (VO_2max divided by the calculated active muscle mass) during the different exercises, ET achieved 148%, 141% and 150% of the controls' values, respectively ($p < 0.05$). During bicycling, both groups achieved 37% of their mass-specific VO_2 during 1-KE. Conclusion: ET subjects have the same utilization of the muscular metabolic capacity during whole body exercise as active control subjects.

Introduction

For nearly 100 years physiologists have been discussing what limits maximal exercise capacity, particularly maximal aerobic power. In the last 40 years, two opposing camps have evolved, one arguing that the limiting step is in the periphery (i.e., muscle mitochondrial volume) with the other group arguing that it is the limits of the cardiorespiratory system that set the maximal oxygen uptake. Then, in 1981, Taylor and Weibel introduced the hypothesis of “symmorphosis”, which states that “Structural design is a limiting factor for oxygen flow at each level of the respiratory system”. The hypothesis predicts that humans (and animals) are built in reasonable manner and that all parts of the O₂ pathway are matched to the functional capacity of the organism. If parts of the pathway were overbuilt this would be waste of energy. Therefore, depending on the exercise conditions, the “bottleneck” may shift from one level to another (Hoppeler & Weibel, 2000b). The most powerful demonstration of this phenomenon is seen when comparing the single-legged knee-extension exercise with whole body exercise, such as bicycling. While maximal heart rate is not reached during single-legged exercise, muscle energy turnover per unit of muscle mass during bicycling is far below that reached during single-legged exercise (Andersen & Saltin, 1985h).

Endurance training increases both stroke volume and mitochondrial volume in trained muscles. Wagner (2000d) postulated that untrained subjects are less O₂-supply limited than trained individuals since myoplasmic PO₂ is higher in untrained subjects. The implication is that training increases the peripheral factors, like mitochondrial capacity, more than the oxygen supply capacity of the cardiorespiratory system. This again may be caused by the fact that the adaptive range is larger in the skeletal muscles than in the heart.

During one-legged knee-extension when only about 2 kg of muscle is working, neither trained nor untrained individuals are O₂-supply limited since end capillary PO₂ is high compared with whole body exercise (Andersen & Saltin, 1985g;Richardson *et al.*, 1993d;Magnusson *et al.*, 1997;Richardson *et al.*, 1999c). During bicycling, O₂ supply may be limiting because end capillary PO₂ is low and training tends to reduce it (Saltin, 1977). If Wagner (2000) is correct, endurance-trained subjects should be less able to use their metabolic capacity during whole body exercise. The ratio between one-legged knee-extension VO₂max and bicycling VO₂max should therefore be higher for trained than untrained individuals, since in single-legged exercise the muscles are free from oxygen supply limitations, with muscular metabolic capacity limiting the oxygen uptake. The present study tests this hypothesis by measuring maximal O₂ uptake during one-legged knee-extension exercise, two-legged knee-extension exercise and bicycling.

Methods

Subjects

Eight controls with normal physical activity level and nine endurance-trained subjects gave informed consent to participate in the study, which was approved by the Regional Ethics Committee and performed according to the Declaration of Helsinki. Physical characteristics of the subjects are presented in table 1. The subjects were included based on their history of physical activity and their VO_2 max achieved on an incremental treadmill test until exhaustion. Table 1.

Experimental protocol

Prior to test day, all 17 subjects reported to the laboratory on three different days to familiarize themselves with the ergometers. On the third familiarization day the subjects performed incremental workload tests on the ergometers to find the highest workload they could sustain for 2-3 minutes. This value would be used to determine initial workload for the actual tests. On test day the subjects reported to the laboratory at three different times to perform three exercise tests: single-legged knee extension exercise (1-KE), two-legged knee extension exercise (2-KE) and bicycling. Subjects initially sat still at the ergometer for 10 minutes to obtain resting values of the parameters to be tested. Subjects then performed a 5-min exercise-specific warmup with a workload of 20W per leg before the KE exercise tests, and 100W bicycling before the bicycling test. The tests were performed in stepwise workload increments where a step is defined as 5W per leg during knee extensions and 20W/25W (women/men) during bicycling. The initial workload for the test was set to three steps below the workload determined during familiarization, with the goal of achieving test length of 6-12 min. After the test began, workload was increased by one step every 3 min until exhaustion,

defined as inability to maintain a cycling frequency of 60 rpm. Subjects were given visual feedback on a PC monitor (knee extensions) or a gauge (bicycling) to control their cycling frequency. All tests were performed in one day with at least 2 hour's rest between tests. The order of the knee extensor exercises was counterbalanced, while bicycling which was assumed to be the most fatiguing exercise, was the final test. The 1-KE exercise was counterbalanced between right and left leg. Pulmonary oxygen uptake (VO_2), heart rate (HR) and the oxygen saturation of haemoglobin (SpO_2) were measured continuously before (10 min) and during exercise. Blood samples were taken from a fingertip immediately before warmup and at exhaustion, and analyzed for lactate concentration ($[\text{bLa}^-]$).

Measuring procedures

The knee extension exercises were performed on a modified model of an electromagnetically-braked knee-extension ergometer as reported by Hallén et al. (1996), which isolates leg muscle contractions to quadriceps during knee extensions (Andersen & Saltin, 1985f; Richardson *et al.*, 1998d; Radegran *et al.*, 1999e). To minimize engagement of muscle mass used to stabilize the body during the knee extensions, subjects were fastened tightly with a four-point seat belt and trained to keep their non-exercising extremities as relaxed as possible. Still, some subjects exhibited a more elevated oxygen uptake at exhaustion than expected from the increases in work load during 1-KE. In accordance to Andersen et al (1985b) we therefore extrapolated the final oxygen uptake from submaximal values for all subjects. This reduced the mean VO_2max during 1-KE by 0.4% and 1.3% in controls and ET, respectively (Correlation P and VO_2 ; $R \geq 0.992$).

Bicycling was performed on a mechanically-braked cycle ergometer (Monark 839E, Monark Exercise AB, Sweden). Cycle frequency was controlled with visual feedback to the subjects.

Pulmonary gas exchange was measured with an Oxycon Pro (Eric Jaeger, Hoechberg, Germany). Subjects breathed through a mouthpiece while the nose was sealed with a nose clip. The gas analyzer was routinely calibrated against certified calibration gases of known concentrations and a flow turbine (Triple V, Erich Jaeger) was calibrated with a 3 l calibration syringe (5530 series, Hans Rudolph, Kansas City, USA).

Blood samples for [bLa⁻] were taken from a fingertip and immediately analyzed with a lactate analyzer (YSI 1500 Sport, Yellow Springs Instruments, Ohio, USA). The lactate analyzer was calibrated according to the instruction manual.

Heart rate was measured continuously with a Polar HR monitor (Polar Electro Oy, Kempele, Finland) and SpO₂ was determined by a pulse oximeter probe placed on the forehead (Nellcor N-395, Nellcor Puritan Bennet Inc.).

Muscle mass calculations

The knee-extensor muscle mass was estimated from anthropometrical measurements. The thigh volume (V), excluding subcutaneous fat, was calculated using the formula: $V = L \cdot (12\pi)^{-1} (O_1^2 + O_2^2 + O_3^2) - (S - 0.4) \cdot 2^{-1} \cdot L \cdot (O_1^2 + O_2^2 + O_3^2) \cdot 3^{-1}$ where L is the thigh length estimated from the top of patella to spina iliaca anterior superior, O₁, O₂ and O₃ are the circumferences at the points 1/4, 1/2 and 3/4 between the patella and the spina iliaca anterior superior and S is the mean skinfold thickness measured posteriorly and anteriorly at the middle measuring point (Jones & Pearson, 1969; Andersen & Saltin, 1985e; Raadegran *et al.*, 1999d). Skinfold thickness was measured using a Harpenden skin-fold calliper. Knee-extensor muscle mass was then calculated as: $Mass = 0.307 \cdot V + 0.353$ and then corrected as suggested by Raadegran *et al.* (1999c): $Mass_{corr} = 0.792 \cdot Mass - 0.382$. The active muscle mass during bicycling was estimated from gender and weight and corrected for age in accordance with Gallagher *et al.*

(1997): Women: Active muscle mass = $(Mb \cdot 0.26 - (Age - 20) \cdot 0.03_{mr})$; Men: Active muscle mass = $(Mb \cdot 0.29 - ((Age - 20) \cdot 0.05_{mr}))$ where Mb is the total body mass and “mr” is a factor of annual muscle mass reduction.

Data and statistical analyses

From each exercise test the maximal oxygen uptake and ventilation were calculated as the mean value over 1 minute (measured at the highest workload the subjects could perform for at least 1 minute). The other variables presented correspond to the same time periods. Resting values were taken 2 minutes prior to the start of exercise while subjects sat at the ergometers. Rest values taken prior to 1-KE and 2-KE were averaged to a single value for each parameter and used for knee extensor exercises, while values sitting at the bicycle were used as rest values for bicycling. Variables were tested for a significant difference between the groups by homoscedastic t-tests. Significance level was set at $P < 0.05$ (2-tailed). Results are presented as mean \pm S.E.M (SE).

Results

Peak power

Peak power for the control group during 1-KE, 2-KE and bicycling was 43 (2) W, 89 (3) W and 298 (7) W, respectively. The corresponding values for the ET were 126%, 121% and 126% of the controls' values ($p < 0.05$) (Fig.1).

Oxygen uptake

Resting VO_2 was similar for controls and ET. Maximal oxygen uptake ($\text{VO}_{2\text{max}}$) in controls was 1387 (76), 2234 (113) and 4115 (150) $\text{ml}\cdot\text{min}^{-1}$ during 1-KE, 2-KE and bicycling, respectively. The ET achieved 127, 124 and 117% of the VO_2 of controls, respectively ($p < 0.05$) (Fig.2A). Net VO_2 ($\text{VO}_{2\text{max}} - \text{VO}_2$ at rest) during 2-KE was 181% (6) of the 1-KE for controls, while it was 171% (7) of the 1-KE for ET (ns). Net VO_2 during bicycling was 343% (20) and 306% (17) of the 1-KE values for controls and ET, respectively (ns).

Mass-specific oxygen uptake is calculated by dividing the net oxygen uptake by the active muscle mass during exercise (Table 1). The mass-specific oxygen uptake in controls was 386 (27), 347 (28) and 138 (6) $\text{ml}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ during 1-KE, 2-KE and bicycling, respectively. The mass-specific oxygen uptake for ET was 148, 141 and 150% of that for the controls, respectively ($p < 0.05$) (Fig.3). The mass-specific oxygen uptake during 2-KE was 90% (9) and 87% (10) of the 1-KE values for controls and ET, respectively (ns). During bicycling the corresponding values were 37% (2) and 37% (4) of the 1-KE values for controls and ET, respectively (ns).

Lactate, HR, VE and SpO₂

No group differences were found for [bLa⁻] or HR at rest or during any of the exercises (Fig.2B and 2C).

Ventilation was similar for controls and ET at rest. During 1-KE, 2-KE and bicycling the ventilation for ET was 147% (p<0.05), 118% (ns) and 114% (p<0.05) of the ventilation in controls (Fig.2D).

The SpO₂ was similar in both groups at rest, during 1-KE and 2-KE. During bicycling the SpO₂ was 4% higher for ET (p<0.05) (Fig.2E).

Discussion

This study suggests that the balance between muscular metabolic capacity and cardiorespiratory capacity of oxygen supply is similar in endurance-trained and normal physically active individuals. Therefore, the data doesn't support a switch hypothesis as suggested by Wagner (2000c). This conclusion is based on our finding of similar utilization of the muscular metabolic capacity during whole body exercise in both groups.

VO₂max increases as the exercising muscle mass increases from 1-KE to 2-KE and bicycling (Fig. 4). When we divide the oxygen uptake during the different exercises by the respective size of the active muscle mass we get the mass-specific VO₂ (Andersen & Saltin, 1985d). As expressed in figure 3, the mass-specific VO₂max decreases as the muscle mass increases from knee extension exercises to bicycling. This is a demonstration of reduced muscular perfusion that results in an oxygen delivery insufficient to support the muscular metabolic capacity during whole body exercise. The mechanism behind this is a systemic vasoconstriction of the arterial vessels feeding the exercising muscles during bicycling that is necessary to maintain blood pressure (Secher *et al.*, 1977; Secher & Volianitis, 2006). The highest mass-specific bloodflow and VO₂ in humans is probably achieved during 1-KE (Andersen *et al.*, 1985a; Richardson *et al.*, 1995b). Due to overperfusion, and therefore a short capillary mean transit time of the blood cells, the muscles would probably not reach higher mass-specific VO₂ without increasing the arterial PO₂ (Richardson *et al.*, 1995a; Richardson *et al.*, 1999b; Richardson *et al.*, 1993c). 1-KE exercise is therefore a widely accepted method of quantifying the muscular metabolic capacity in vivo in healthy subjects. We can compare the mass-specific VO₂ of exercise involving greater muscle mass with the 1-KE mass-specific

VO₂ to evaluate how much of the muscular metabolic capacity the oxygen delivery can support. If oxygen supply could increase without limits we would expect no reduction in mass-specific VO₂ as the muscle mass increases. However, this is not the case and indeed, as the study by Andersen & Saltin (1985c) was the first to reveal, the mass-specific VO₂ during whole body exercise is less than half of the mass-specific VO₂ during exercise with a small muscle mass.

During 1-KE, the net VO₂max in controls was 1.06 l·min⁻¹, giving a muscular mass-specific oxygen uptake of 386 ml·kg⁻¹·min⁻¹ (1.06 l·min⁻¹ / 2.8 kg). The mass-specific oxygen uptake during bicycling was only 37% of this value (Fig.5). The respective muscular metabolic capacity data for ET was considerably higher than that of controls, at 570 ml·kg⁻¹·min⁻¹ during 1-KE. However, the relative utilization of this capacity during bicycling was the same (37%), indicating that oxygen supply limitations during bicycling are relatively similar for the two groups (Fig 5). The calculated utilization of the muscular metabolic capacity during 2-KE was similar for the two groups as well: 90% and 87% of the 1-KE values for controls and ET, respectively (Fig. 5).

This study questions whether the central limitations to VO₂max are more evident in trained subjects (Wagner; 2000) compared to normal physically active controls. The present data do not support this hypothesis; however, this analysis is heavily reliant on the accuracy and validity of the estimates of active muscle mass (Richardson *et al.*, 1998c). In addition, pulmonary VO₂, which reflects whole body VO₂, adds uncertainty as to how much of the VO₂ can be attributed to the estimated exercising muscle mass. However, the muscles involved in knee extensions are well defined (Andersen & Saltin, 1985b; Richardson *et al.*, 1998b; Radegran *et al.*, 1999b) and the challenge is therefore to distinguish the VO₂ in

quadriceps from that in other tissues, especially during maximal effort when muscles are potentially engaged for stabilization (Andersen & Saltin, 1985a; Richardson *et al.*, 1993b). Previous studies have found the 1-KE mass-specific O₂ uptake, measured by invasive methods, to range from 350 to 602 ml·kg⁻¹·min⁻¹ (Andersen & Saltin, 1985i; Rowell *et al.*, 1986; Richardson *et al.*, 1993a; Radegran *et al.*, 1999a; Richardson *et al.*, 1999a; Mourtzakis *et al.*, 2004). The mass specific O₂ uptake found in the present study of 386 and 570 ml·kg⁻¹·min⁻¹ for controls and ET, closely agree with this range. During bicycling on the other hand, the challenge is to identify the extent of muscle activation in the lower body, which is considered more heterogeneous (Richardson *et al.*, 1998a). Our calculations are based on formulas that state that during bicycling a certain percentage of the body is muscles and that a certain part of the body's muscles are involved in bicycling. In addition, there are small corrections for age and sex. The validity of the formulas used to estimate active muscle mass from anthropometric measurements in the present study is difficult to verify. However, the subjects in both groups in this study were lean physical education students, therefore, we assume that any uncertainties would apply to the same extent for both groups.

A study by Roca *et al.* (Roca *et al.*, 1992b) reported a greater increase in muscle O₂ diffusing capacity than in oxygen delivery after 9 weeks of endurance training, thus increasing the extraction 10%. This finding challenges our conclusion. Those authors speculated that the subjects in their study were not oxygen supply-limited before training but were after training (later described by Wagner (2000b) as the switch hypothesis). The activity levels were likely lower in the subjects investigated by Roca *et al.* (1992a) compared to those in the present study (based on VO₂max during bicycling; 37 and 46 ml·min⁻¹·kg⁻¹, respectively). This could indicate that our control subjects have passed the point at which VO₂ limitations switch from muscular metabolic to oxygen supply, thus explaining the finding of an equal balance in

muscular metabolic and oxygen supply capacity for controls and ET. However, when comparing the data from a previous study from our group (paper in press) with the same protocol performed on COPD patients and a control group (age 59 yr; VO_2max during bicycling $32 \text{ ml}\cdot\text{min}^{-1}\cdot\text{kg}^{-1}$) and the ET subjects in the present study, the ET achieved 180, 188 and 195% of their VO_2max during 1-KE, 2-KE and bicycling, respectively.

A broader approach to the ratio between bicycling and 1-KE is to calculate on the absolute VO_2max without corrections for active muscle mass. This ratio is 2.7 and 3.0 in ET and controls, respectively ($p=0.13$). Given the limited number of subjects, we can not exclude that this is a type II error and that there exist a difference between the groups. If so, this is in line with Wagner (2000a) and indicates that ET is more oxygen supply limited during bicycling than the controls. However, this broad analysis does not take into account that the controls have a larger muscle mass in the quadriceps than ET. This support the approach used here to apply correction factors in an attempt to account for the differences in muscle mass between the groups. Application of these corrections removes the difference in the ratios observed between the groups. However, in a previous study from our group healthy sedentary sedate subjects (Rud et al; age 59 yr; VO_2max during bicycling $32 \text{ ml}\cdot\text{min}^{-1}\cdot\text{kg}^{-1}$) showed a low ratio (2.5) between absolute VO_2max during bicycling and 1-KE; a value which also tended to be lower than ET ($p=0.09$). Therefore, whether correcting for muscle mass or not, this approach indicates that ET subjects are no more oxygen supply limited than controls. Hence, we think that the present data indicate that the balance between muscular metabolic capacity and cardiorespiratory capacity of oxygen delivery is rather equal in endurance-trained and normal physically active, as well as sedate individuals.

The present data therefore supports the symmorphosis hypothesis (Taylor & Weibel, 1981; Weibel *et al.*, 1991; Hoppeler & Weibel, 2000a). Weibel (2000) expressed it this way: “...It does not make sense for the body to build and maintain, at some metabolic cost, structures of a fundamental and vital functional system that will never be used.” The interpreted muscular metabolic reserve capacity during whole body exercise, as discussed above, is undoubtedly a challenge to this hypothesis. However, we should keep in mind that the significance of the apparent huge muscular metabolic capacity seen during 1-KE is not completely understood, and multiple mechanisms could possibly explain its presence. For example the muscular metabolic capacity is not superfluous during strenuous exercise with a small muscle mass. In addition, the homogeneousness of muscle and fibre recruitment during strenuous whole body exercise is uncertain (Armstrong & Taylor, 1982; Richardson *et al.*, 1998e). This suggests that even during exercise where the muscular metabolic capacity in an active muscle group is significantly higher than the oxygen supply, some part of the active muscle mass may actually utilize 100% of its metabolic capacity. However, we assume these uncertainties apply to the same extent for both groups in the present study. In addition, because the study was designed such that each subject served as his or her own control, muscle activation uncertainty should not disqualify the conclusions.

Summary/Conclusion

Endurance-trained subjects had both a higher muscular metabolic capacity and maximal oxygen uptake than subjects with a normal physical activity level. The data suggests that endurance-trained individuals utilize the same percentage of their muscular metabolic capacity during whole body exercise as the untrained individuals. This indicates that the muscular metabolic capacity and oxygen supply capacity are more in balance than previously suggested by Wagner (2000e).

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Table 1: Subjects characteristics

	Subjects with normal physical	Endurance trained subjects
n	8 (7 men)	9 (8 men)
Age (years)	27.3 (3.5)	24.6 (3.2)
Height (cm)	181 (9)	180 (9)
Mass (kg)	90 (12)	76 (9)*
$\dot{V} O_{2max}$ (ml kg ⁻¹ min ⁻¹)	46.3 (4.1)	64.4 (3.6)*
$\dot{V} E_{max}$ (l min ⁻¹)	158 (25)	180 (17)*
HR _{max} (beats min ⁻¹)	190 (12)	187 (8)
Muscle mass 1-KE (kg)	2.8 (0.3)	2.5 (0.3)
Muscle mass 2-KE (kg)	5.6 (0.7)	5.1 (0.7)
Muscle mass bicycling (kg)	26 (4)	21 (3)*

Values are mean \pm SD. See text for calculation details of muscle masses. Asterisks indicate p-values less than 0.05 between groups.

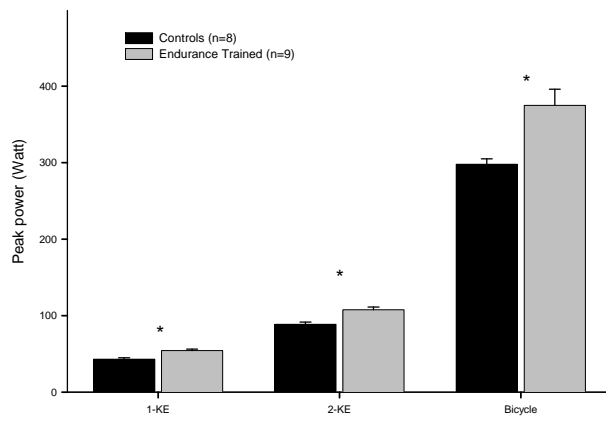


Fig. 1. Maximal power output during one-legged knee extensor exercise (1-KE), two-legged knee extensor exercise (2-KE) and bicycling. Asterisks indicate p-values less than 0.05 between groups.

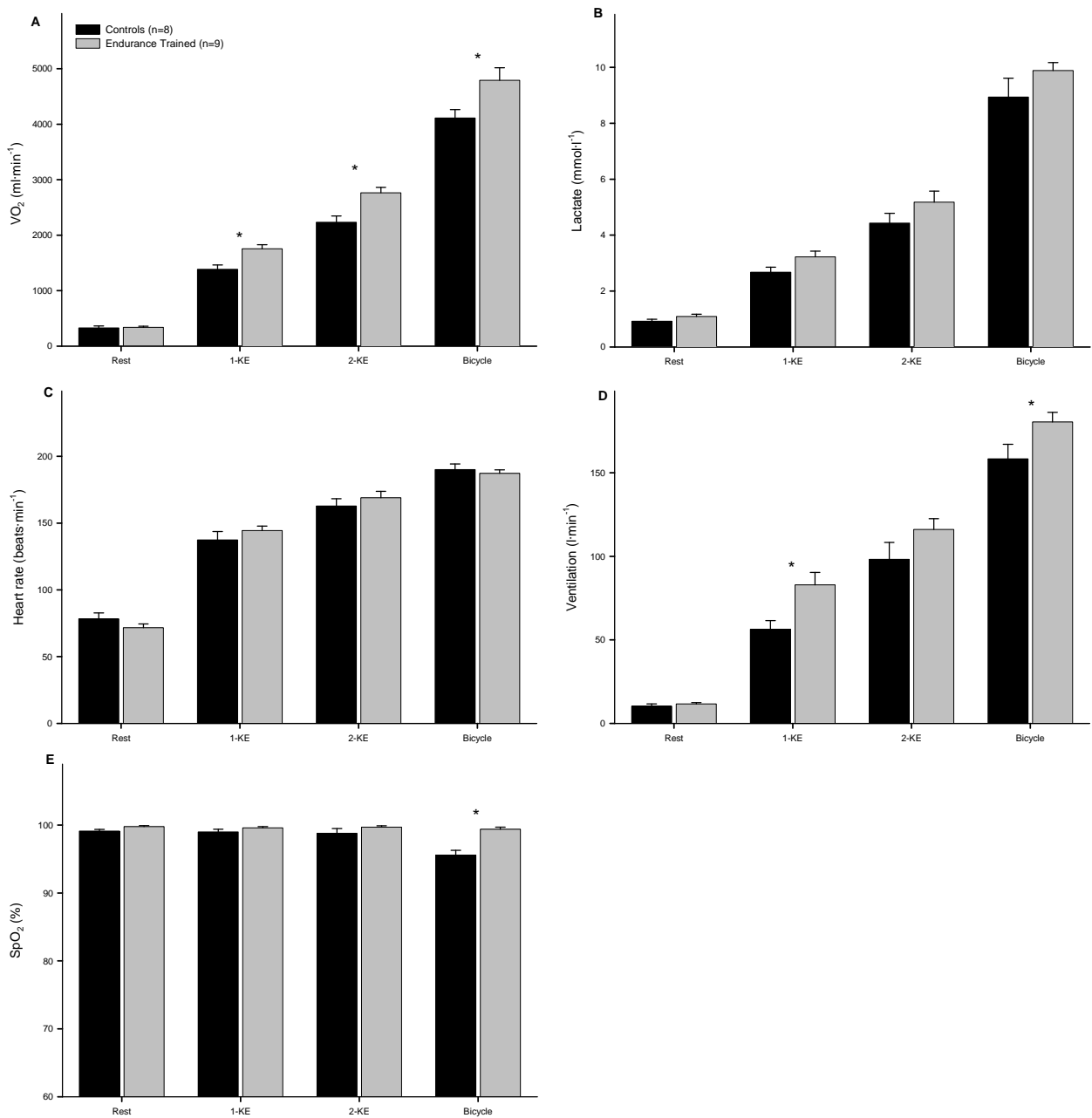


Fig. 2. VO₂max (A), Lactate (B), Heart rate (C), Ventilation (D) and SpO₂ (D) during one-legged knee extensor exercise (1-KE), two-legged knee extensor exercise (2-KE) and bicycling. Asterisks indicate p-values less than 0.05 between groups.

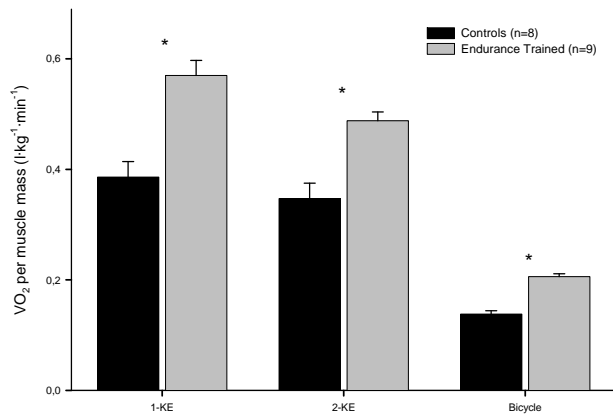


Fig. 3. Mass-specific VO₂ during one-legged knee extensor exercise (1-KE), two-legged knee extensor exercise (2-KE) and bicycling. Asterisks indicate p-values less than 0.05 between groups.

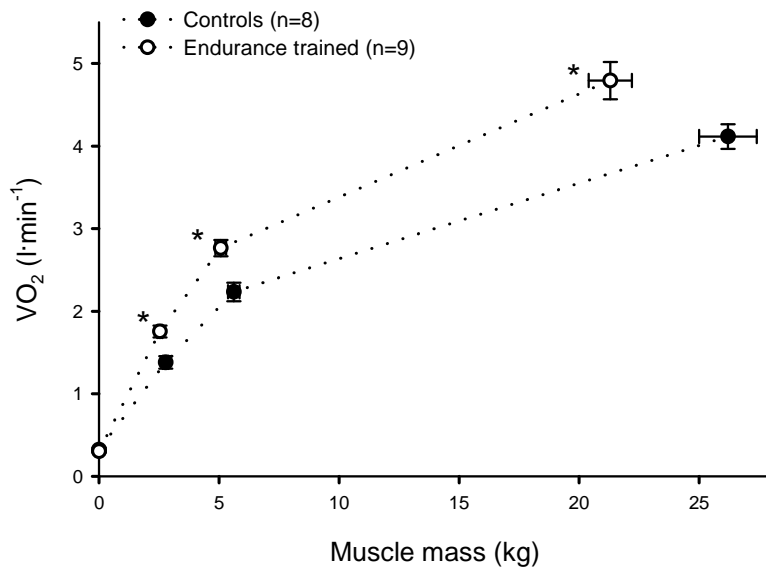


Fig.4: Oxygen uptake vs. muscle mass during single-leg knee extensor exercises during one-legged knee extensor exercise (1-KE), two-legged knee extensor exercise (2-KE) and bicycling. Asterisks indicate p-values less than 0.05 between groups.

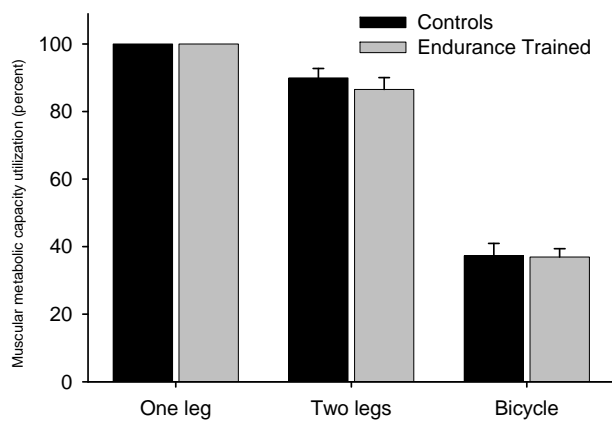


Fig.5: Utilization of the muscular metabolic capacity during one-legged knee extensor exercise (1-KE), two-legged knee extensor exercise (2-KE) and bicycling.