Regulation of PDH in human arm and leg muscles at rest and during intense exercise

Kiilerich K, Birk JB, Damsgaard R, Wojtaszewski JP, Pilegaard H. Regulation of PDH in human arm and leg muscles at rest and during intense exercise. Am J Physiol Endocrinol Metab 294: E36–E42, 2008. First published October 23, 2007; doi:10.1152/ajpendo.00352.2007.—To test the hypothesis that pyruvate dehydrogenase (PDH) is differentially regulated in specific human muscles, regulation of PDH was examined in triceps, deltoid, and vastus lateralis at rest and during intense exercise. To elicit considerable glycogen use, subjects performed 30 min of exhaustive arm cycling on two occasions and leg cycling exercise on a third day. Muscle biopsies were obtained from deltoid or triceps on the arm exercise days and from vastus lateralis on the leg cycling day. Resting PDH protein content and phosphorylation on PDH-E1α sites 1 and 2 were higher (P ≤ 0.05) in vastus lateralis than in triceps and deltoid as was the activity of oxidative enzymes. Net muscle glycogen utilization was similar in vastus lateralis and triceps (≈50%) but less in deltoid (likely reflecting less recruitment of deltoid), while muscle lactate accumulation was ≈55% higher (P ≤ 0.05) in triceps than vastus lateralis. Exercise induced (P ≤ 0.05) dephosphorylation of both PDH-E1α site 1 and site 2 in all three muscles, but it was more pronounced at PDH-E1α site 1 in triceps than in vastus lateralis (P ≤ 0.05). The increase in activity of the active form of PDH (PDHe) after 10 min of exercise was more marked in vastus lateralis (≈246%) than in triceps (≈160%), but when it was related to total PDH-E1α protein content, no difference was evident. In conclusion, PDH protein content seems to be related to metabolic enzyme profile, rather than myosin heavy chain composition, and less PDH capacity in triceps is a likely contributing factor to higher lactate accumulation in triceps than in vastus lateralis.

Regulation of PDH in human arm and leg muscles at rest

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Regulation of PDH in human arm and leg muscles at rest and during intense exercise

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dehydrogenase phosphatase (PDP). The E1 subunit, pyruvate dehydrogenase (PDH), is responsible for catalyzing the decarboxylation of pyruvate. Therefore, regulation of this PDH component of the enzyme complex could be important for the mitochondrial choice of substrate at rest and during exercise.

Thus, to provide information on mechanisms underlying differences in carbohydrate metabolism in human muscles, the aim of the present study was to test the hypothesis that differences in exercise-induced activation of PDH in part can explain the dissimilarity in carbohydrate dependency between arm and leg skeletal muscles during exercise. This is examined by investigating PDH regulation in human arm and leg muscles characterized by different metabolic and MHC profiles.

**MATERIALS AND METHODS**

**Subjects.** Eight healthy male subjects with normal physical activity level, an average age of 26 yr (range: 23–30 yr), weight 85 kg (range: 71–96 kg), and height 185 cm (range: 179–192 cm) participated in the study. The maximum power (wattmax) was 121 ± 5 and 303 ± 12 W (average ± SE) for arm and leg, respectively.

The subjects were given both written and oral information about the experimental protocol and procedures and were informed about any discomfort that might be associated with the experiment before they gave their written consent. The study was performed according to the Declaration of Helsinki and was approved by the Copenhagen and Frederiksberg Ethics Committee, Denmark.

**Experimental protocol.** Approximately 1 wk before the first trial, the subjects performed preexperimental tests to determine wattmax for arm and leg exercise separately. The wattmax was determined for arm cycling and leg cycling separately using incremental tests where the resistance was increased (arm, 12 W; leg, 30 W) every second minute until exhaustion. Wattmax was estimated from the time to exhaustion and workload. Each subject completed three experimental days, one day with leg cycling using an electronic ergometer (Monark 839E) and two days with arm cycling using an arm crank ergometer (Monark 891E), which was adjusted so that the shoulder of the subject leveled the crank. The day before each experimental trial, the subjects refrained from exercise. On the experimental day, the subjects arrived at the laboratory 2.5 h after consuming a standardized breakfast [77% percent energy (E%) carbohydrate; 11 E% protein; 12 E% fat], regulated for bodyweight and activity level (34). Muscle biopsies were obtained from either deltoid or triceps on the arm exercise days.

**MUSCLE BIOPSY.** Muscle biopsies were taken after 10 and 30 min of exercise. The biopsies were taken from the subject on exertion level. Whereas the two arm exercise trials needed to ensure exhaustion after 30 min of exercise, based on reports from the subject on exertion level. The two arm exercise trials increased the heart rate to 155 ± 6 and 156 ± 4 beats/min at the end of exercise. The day before each experimental trial, the subjects underwent a standardized breakfast [77 E% carbohydrate; 11 E% protein; 12 E% fat], regulated for bodyweight and activity level (34). Muscle biopsies were obtained from either deltoid or triceps on the arm exercise days.

Muscle glycoenzymes, lactate, and enzyme activity. Muscle specimens were freeze-dried and dissected free of blood, fat, and connective tissue under the microscope, and muscle glycoenzymes were determined as glycose units after acid hydrolysis using an automatic spectrophotometer as previously described (16).

Muscle lactate concentrations of freeze-dried samples were determined fluorometrically (16).

The activity of CS, HAD, lactate dehydrogenase (LDH), and PFK was analyzed spectrophotometrically as previously described (11).

**Muscle lystate.** Muscle pieces were homogenized in an ice-cold buffer (10% glycerol, 20 mM Na-pyrophosphate, 150 mM NaCl, 50 mM HEPES, 1% NP-40, 20 mM β-glycerophosphate, 10 mM NaF, 1 mM EDTA, 1 mM EGTA, 2 mM PMSF, 10 µg/ml aprotinin, 10 µg/ml leupeptin, 2 mM Na3VO4, 3 mM benzamidine, pH 7.5) for 20 s using a homogenizer (PT 3100, Kinematica). Homogenates were rotated end over end for 1 h at 4°C. Lysates were generated by centrifugation (17,500 g) for 20 min at 4°C. Protein content in lysates was measured by the bicinchoninic acid method (Pierce Chemical).

**SDS-PAGE and Western blotting.** The protein expression and phosphorylation of sites 1 and 2 were measured in muscle lysate by SDS-PAGE (Tris·HCl) 10% gel, Bio-Rad) and Western blotting using polyvinylidene difluoride (PVDF) membrane and semi-dry-transfer technique, followed by incubation with primary antibody overnight at 4°C (TBST + 2% skim milk), followed by incubation with primary antibody overnight at 4°C (TBST + 2% skim milk).

The following day, the membrane was incubated with horseradish peroxidase-conjugated secondary antibody (Dako) for 1 h at room temperature (TBST + 2% skim milk). Immobilon Western (Millipore) was used as a detection system. Bands were visualized using an Eastman Kodak Image Station 2000MM. Bands were quantified using Kodak Molecular Imaging Software v.4.0.3, and protein content was expressed in units relative to control samples loaded on each gel.

**Protein levels of the PDH-E1α subunit and phosphorylation of site 1 (Ser305) and site 2 (Ser309) of PDH-E1α were determined using antibodies generated in sheep as previously described (22).**

**Activity of the active form of PDH.** The activity of the active form of PDH (PDHα) was determined as previously described (9, 10, 26) after homogenizing ~10 mg of muscle tissue for 50 s in the modified glycogen synthase kinase-3 buffer given above, using a glass homogenizer (Kontes), and quickly (10–15 s) freezing the samples in liquid nitrogen.

**Statistics.** Values presented are means ± SE. Two-way ANOVA for repeated measures was applied to evaluate the effect of muscle type and time. One-way ANOVA for repeated measures was used to test for differences in fiber type distribution and enzyme activity between muscle types. The Student-Newman-Keuls post hoc test was used to locate differences. Differences were considered significant at P ≤ 0.05, and a tendency is reported when 0.05 ≤ P ≤ 0.1. Statistical calculations were performed using SigmaStat v.2.03.

**RESULTS**

**Muscle fiber composition.** The percent occurrence of type I fibers was similar in vastus lateralis (52%) and deltoid (54%), whereas triceps (32%) contained less type I fibers than vastus and deltoid (P ≤ 0.05; Table 1).

**Enzyme activity.** The activity of CS was ~50% higher in vastus lateralis (31.3 mmol·min⁻¹·kg dry wt⁻¹) than in both triceps (18.8 mmol·min⁻¹·kg dry wt⁻¹) and deltoid (17.1...
mmol·min⁻¹·kg dry wt⁻¹) (P ≤ 0.05) (Table 1). The HAD activity was ∼20% higher in deltoid (29.9 mmol·min⁻¹·kg dry wt⁻¹) than in triceps (25.8 mmol·min⁻¹·kg dry wt⁻¹) (P ≤ 0.05) and ∼50% and ∼30% higher in vastus lateralis (39.5 mmol·min⁻¹·kg dry wt⁻¹) than in triceps and deltoid, respectively (P ≤ 0.05) (Table 1). There were no differences in total LDH (752–1,023 mmol·min⁻¹·kg dry wt⁻¹) or PFK (370–411 mmol·min⁻¹·kg wet wt⁻¹) activity among the three muscles (Table 1).

Muscle glycogen. The glycogen concentration at rest was lower in deltoid (366 mmol/kg dry wt) than in triceps (457 mmol/kg dry wt) and vastus lateralis (454 mmol/kg dry wt) (Table 2). Net glycogen utilization during exercise was similar in vastus (205 mmol/kg dry wt) and triceps (269 mmol/kg dry wt) but lower (P ≤ 0.05) in deltoid (90 mmol/kg dry wt). The average net glycogen utilization rate from onset of exercise to 10 min of exercise was 11.4 and 8.4 mmol·kg dry wt⁻¹·min⁻¹ in triceps and vastus lateralis, respectively, and for the last 20 min of exercise was 7.2 mmol·kg dry wt⁻¹·min⁻¹ in both muscles.

On the basis of these findings, it is concluded that both triceps and vastus lateralis were intensely activated during the full 30 min of exercise, and a direct comparison on PDH regulation during this exercise protocol is only reasonable for these two muscles, assuming that net muscle glycogen use is a reflection of muscle recruitment. Therefore, the exercise data below are only statistically analyzed for vastus lateralis and triceps.

Muscle lactate. There was at rest no difference in the lactate concentration in triceps (18.5 mmol/kg dry wt), vastus (12.6 mmol/kg dry wt), and deltoid (17.3 mmol/kg dry wt) (Table 2). Exercise increased muscle lactate concentration after both 10 (∼315% increase) and 30 min (∼380% increase) of exercise compared with rest for triceps and vastus (P ≤ 0.05) (Table 2). The level of muscle lactate was higher in triceps than in vastus lateralis after both 10 and 30 min of exercise (P ≤ 0.05) (Table 2).

PDH-E1α protein and phosphorylation state. PDH-E1α protein content was higher in vastus lateralis than in triceps and deltoid (P ≤ 0.05) (Table 1). Phosphorylation of the PDH-E1α subunit at sites 1 and 2 was higher in vastus lateralis than in triceps and deltoid at rest (P ≤ 0.05) (Table 1). Considering the relative phosphorylation (normalized to PDH-E1α content) of sites 1 and 2, there was no difference between vastus lateralis and deltoid, but a more marked phosphorylation of the two sites was still evident in vastus relative to triceps (P ≤ 0.05) (Table 1).

Exercise induced a pronounced dephosphorylation of sites 1 and 2 in both triceps and vastus lateralis (P ≤ 0.05). After 10 and 30 min of exercise, phosphorylation of site 1 was 21 and 14% of the resting level in triceps and 29 and 24% in vastus lateralis, respectively (Fig. 1C). A more pronounced phosphorylation of the PDH-E1α subunit on site 1 was present in vastus lateralis compared with triceps during exercise (P ≤ 0.05) (Fig. 1B).

Relative to the level at rest, the phosphorylation level of site 2 was reduced (P ≤ 0.05) in triceps to 6 and 4% and in vastus lateralis to 19 and 16% after 10 and 30 min of exercise.

Table 1. Resting values of triceps, vastus lateralis, and deltoid

<table>
<thead>
<tr>
<th></th>
<th>Triceps</th>
<th>Vastus</th>
<th>Deltoid</th>
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<tbody>
<tr>
<td>Muscle fiber, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type I</td>
<td>32±4.8</td>
<td>52±6.7*</td>
<td>54±6.9*</td>
</tr>
<tr>
<td>Type I/IIa</td>
<td>19±5.4</td>
<td>16±5.6</td>
<td>8±5.3</td>
</tr>
<tr>
<td>Type IIa</td>
<td>35±5.6</td>
<td>20±4.3</td>
<td>29±1.6</td>
</tr>
<tr>
<td>Type IIx</td>
<td>14±8.8</td>
<td>12±5.5</td>
<td>9±7.7</td>
</tr>
<tr>
<td>Enzyme activity, mmol·min⁻¹·kg dry wt⁻¹</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CS</td>
<td>18.8±3.2</td>
<td>31.3±2.3†</td>
<td>17.1±2.4</td>
</tr>
<tr>
<td>HAD</td>
<td>25.8±3.2</td>
<td>39.5±2.8†</td>
<td>29.9±4.8*</td>
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<td>LDH</td>
<td>924±91</td>
<td>752±109</td>
<td>1,023±132</td>
</tr>
<tr>
<td>PFK</td>
<td>411±49</td>
<td>375±17</td>
<td>370±13</td>
</tr>
<tr>
<td>PDH</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Protein content</td>
<td>1.2±0.2</td>
<td>1.8±0.1†</td>
<td>1.2±0.1</td>
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<tr>
<td>Absolute phosphorylation on site 1</td>
<td>0.7±0.2</td>
<td>1.5±0.2†</td>
<td>0.8±0.0</td>
</tr>
<tr>
<td>Absolute phosphorylation on site 2</td>
<td>0.6±0.2</td>
<td>1.3±0.2†</td>
<td>0.6±0.0</td>
</tr>
<tr>
<td>Relative phosphorylation on site 1</td>
<td>0.6±0.1</td>
<td>0.9±0.1†</td>
<td>0.7±0.1</td>
</tr>
<tr>
<td>Relative phosphorylation on site 2</td>
<td>0.5±0.1</td>
<td>0.8±0.1*</td>
<td>0.6±0.1</td>
</tr>
<tr>
<td>PDH, activity, mmol·min⁻¹·kg wet wt⁻¹</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Absolute</td>
<td>0.82±0.19</td>
<td>0.90±0.15</td>
<td>1.0±0.16</td>
</tr>
<tr>
<td>Relative</td>
<td>0.62±0.18</td>
<td>0.53±0.09</td>
<td>0.91±0.12</td>
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</tbody>
</table>

Values are means ± SE. For the enzyme activity and the pyruvate dehydrogenase (PDH) data: n = 6–8. For muscle fiber analysis: triceps and vastus, n = 4; deltoid, n = 5. CS, citrate synthase; HAD, 3-hydroxyacyl-CoA dehydrogenase; LDH, lactate dehydrogenase; PFK, phosphofructokinase; PDH, active form of PDH. *Different from triceps, P ≤ 0.05. †Different from deltoid, P ≤ 0.05. ‡Different from triceps with use of paired t-test, P ≤ 0.05.

Table 2. Muscle glycogen concentration and lactate accumulation in triceps, vastus lateralis, and deltoid

<table>
<thead>
<tr>
<th></th>
<th>Triceps</th>
<th>Vastus</th>
<th>Deltoid</th>
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<tbody>
<tr>
<td>Glycogen, mmol/kg dry wt</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rest</td>
<td>457±24</td>
<td>454±22</td>
<td>366±188§</td>
</tr>
<tr>
<td>10 min of exercise</td>
<td>349±29†</td>
<td>381±15†</td>
<td>304±13</td>
</tr>
<tr>
<td>30 min of exercise</td>
<td>188±23†</td>
<td>249±28†*</td>
<td>276±14</td>
</tr>
<tr>
<td>Lactate, mmol/kg dry wt</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rest</td>
<td>18.5±4.1</td>
<td>12.6±3.0</td>
<td>17.3±3.0</td>
</tr>
<tr>
<td>10 min of exercise</td>
<td>80.2±10.2†</td>
<td>50.4±6.8*</td>
<td>34.8±10.5</td>
</tr>
<tr>
<td>30 min of exercise</td>
<td>90.3±10.5†</td>
<td>60.4±12.0†*</td>
<td>42.9±7.3</td>
</tr>
</tbody>
</table>

Values are means ± SE; n = 7–8. During exercise, statistical analysis was performed only on triceps and vastus. †Different from preexercise within same muscle, P ≤ 0.05. ‡Different from 10 min of exercise within same muscle, P ≤ 0.05. *Different from triceps, P ≤ 0.05. §Different from vastus, P ≤ 0.05.
respectively (Fig. 1D). No difference was apparent between the muscles in site 2 phosphorylation during exercise (Fig. 1D).

When converting the absolute phosphorylation to the relative phosphorylation, no difference was evident between triceps and vastus lateralis during exercise.

**PDHa activity.** There was no difference in the PDHa activity among the three muscles at rest (0.82–1.0 mmol·min⁻¹·kg⁻¹ wet wt⁻¹) (Table 1). In triceps, an ≈160% increase in PDHa activity was evident after 10 min of exercise compared with the activity at rest (Fig. 1A) (P ≤ 0.05), with no significant difference between rest and 30 min of exercise (Fig. 1A). In vastus lateralis, the PDHa activity increased ≈246 and ≈170% after 10 and 30 min of exercise, respectively, relative to rest (Fig. 1A) (P ≤ 0.05).

After 10 min of exercise, the absolute PDHa activity was ≈45% higher in vastus lateralis than in triceps (P ≤ 0.05) (Fig. 1A), but after 30 min of exercise, there was no longer a difference between the two muscles (Fig. 1A). Normalizing the PDHa activity to PDH-E1α protein content resulted, however, in similar PDHa activity in vastus lateralis and triceps.

The relationship between phosphorylation on sites 1 and 2 and the PDHa activity shows that a high PDHa activity is associated with an extremely low phosphorylation on both site 1 and site 2 (Fig. 2, A and B). Within the lower level of PDHa activity, there was, however, a large range in phosphorylation and, therefore, not the same strong relation between activity and phosphorylation. Analyzing the data for phosphorylation and activity using a monoexponential model gives, for triceps, \( r^2 = 0.23 \) and \( r^2 = 0.34 \) for sites 1 and 2 and, for vastus, \( r^2 = 0.54 \) and \( r^2 = 0.67 \) for sites 1 and 2, respectively.

**DISCUSSION**

The main findings of the present study are that the PDH content follows the metabolic profile of the muscle rather than the MHC fiber type distribution, and that a smaller exercise-induced increase in PDHa activity in triceps than in vastus lateralis can be explained by a lower content of PDH in triceps rather than differences in activation of each PDH molecule. In addition, the lower PDHa activity in triceps

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**Fig. 1.** Effect of 30 min of arm [80% maximum power (wattmax)] or leg exercise (70% wattmax) in triceps, vastus lateralis, and deltoid. A: absolute PDHa activity (where PDHa is the active form of pyruvate dehydrogenase). B: detection by Western blot phosphorylation (phos). C and D: absolute phosphorylation of PDH-E1α site 1 (C) and PDH-E1α site 2 (D). Muscle samples were taken before exercise (pre) and after 10 (10') and 30 min (30') of exercise. Values are means ± SE. For triceps, n = 6–8. For vastus lateralis and deltoid, n = 7–8. Due to less recruitment of deltoid, statistical comparison during exercise is done only for triceps and vastus lateralis. *Different from triceps, P ≤ 0.05. †Different from preexercise within same muscle, P ≤ 0.05. §Tendency to differ from triceps, P = 0.085.
during exercise was associated with higher lactate accumulation in this muscle.

Because endurance training has been shown to increase oxidative capacity (2) as well as PDH-E1α protein content (15), it would be expected that the most endurance trained muscle had the largest amount of PDH-E1α protein. In accordance, PDH-E1α protein content and CS and HAD activity were higher in vastus lateralis than in the two arm muscles, and the linear correlation between PDH-E1α protein and CS ($r^2 = 0.70$) and HAD ($r^2 = 0.49$) activity further underlines that the PDH capacity follows the oxidative potential of the muscle. In contrast, the PDH-E1α protein content did not follow the MHC fiber type composition, as vastus lateralis and deltoid had similar MHC fiber type distribution, but vastus lateralis had higher PDH-E1α protein content than deltoid. A similar indication for divergence between metabolic characteristics and MHC fiber type has previously been reported for gene expression profile and MHC fiber type distribution in human skeletal muscle (25).

The present findings of lower PDHα activity and higher lactate accumulation in triceps than in vastus lateralis are in line with the possibility that limited PDHα activity can be at least a contributing factor for the larger lactate accumulation and release from arm than leg muscles during exercise (1). Moreover, the observation that the PDHα activity normalized to the PDH-E1α protein content was the same in triceps and vastus lateralis at each of the three time points indicates that each PDH molecule is activated to the same degree in triceps and vastus lateralis, meaning that the higher absolute PDHα activity and likely flux through PDH in vastus lateralis was due to greater PDH capacity in vastus lateralis than in triceps rather than differences at the molecule level. Thus it is suggested that, because of a lower capacity of PDH, the flux through the PDH complex is lower in triceps, resulting in the conversion of pyruvate to lactate. However, it may be noted that triceps showed a more marked dephosphorylation of site 1 than vastus lateralis during exercise, indicating that there may indeed be some differences in regulation of the phosphorylation state of PDH in triceps and vastus lateralis.

The present finding of more pronounced phosphorylation of sites 1 and 2 in vastus lateralis than in triceps at rest, as an absolute value as well as when normalized to PDH protein content, would be expected to cause a lower PDHα activity in vastus lateralis than in triceps. The fact that no differences in the PDHα activity were observed among the three muscles at rest indicates that the PDHα activity is not regulated only by these two phosphorylation sites, which is supported by previous findings (22) where intralipid infusion resulted in an increased phosphorylation of PDH without an effect on the PDHα activity. Because regulation of PDHα activity at site 3 usually is considered negligible in human skeletal muscle (20), these findings may indicate that other covalent regulations of PDH exist. While a discrepancy seems to exist between PDHα activity and the degree of phosphorylation at rest, a stronger correlation exists at higher PDHα activities, but still the decline in PDHα activity from 10 to 30 min of exercise was not associated with a stronger phosphorylation of sites 1 and 2. Thus the covalent regulation of PDHα activity in skeletal muscle during exercise also seems to be more complex and, perhaps, is not only explained by phosphorylation of sites 1 and 2.

The exercise-induced activation of PDHα activity corresponds well with previous human studies on vastus lateralis (18, 22, 26, 31, 32). In these studies, the intensity has in general been moderate [45–55% maximal oxygen consumption (VO₂ max) or wattmax], and only one study examined PDHα activity during intense exercise (6), where subjects performed graded 10-min sessions of exercise at 60 and 90% VO₂ max. Previous studies (32, 33) have reported a PDHα activity of ≈2.8 mmol·min⁻¹·kg wet wt⁻¹ after 10 min of exercise at 55% VO₂ max, corresponding to a 3-fold increase compared with rest, and an ≈3.5-fold increase in PDHα activity was found after 5 min of exercise at 55% VO₂ max (30). This is rather similar to the level obtained in the present study, where the PDHα activity in vastus lateralis was ≈3.1 mmol·min⁻¹·kg wet wt⁻¹ after 1 min of exercise at 70–80% Wmax, corresponding to an ≈3.5-fold increase relative to rest. Thus the PDHα activity and the relative increase in PDHα activity do not seem to be higher in the present study with more intense exercise than in protocols with low and intermediate exercise intensities. This observation can probably be explained by an upper limit of total PDH activity, which has been reported to be ≈3.6 mmol·min⁻¹·kg wet wt⁻¹ (17). This number is, however, sensitive to aerobic exercise training, as 8 wk of aerobic exercise was found to increase total PDH activity from ≈3.8 to ≈4.9 mmol·min⁻¹·kg wet wt⁻¹ (15). It may therefore be
regulation of PDH in human arm and leg muscles

speculated that the normally physically active subjects in the present study were close to the maximal PDH activity after 10 min of exercise. Furthermore, no study has reported PDH activities reaching total PDH activity during exercise. Studies with low-intensity exercise suggest that a high PDH activity found after 10 min of exercise (32) is sustained during the initial 2 h of exercise, followed by a decline toward resting level as exercise duration proceeds beyond 2 h (18, 22). In the present study with high-intensity exercise, the PDH activity was highest after 10 min of exercise, and for triceps, the PDH activity returned to resting level after 30 min of exercise. Thus it seems that the exercise-induced upregulation of PDH activity is rather independent of exercise intensity, while the intensity is important for the timing of the downregulation of PDH activity observed in both types of muscles investigated. The reduction in PDH activity may be related to decreasing glycogen levels in the exercising muscle, and, as high-intensity exercise consumes a great amount of muscle glycogen, this may contribute to the early downregulation of PDH activity observed in both vastus lateralis and triceps at 30 min of exercise in the present study.

As explained, the deltoid muscle was not included in the comparison of exercise-induced PDH regulation between muscles because of less marked net glycogen usage in deltoid and thus, most likely, less recruitment of deltoid. Interestingly, however, the smaller net glycogen utilization in deltoid was associated with less marked changes in PDH activity and PDH-E1α phosphorylation in response to arm cycling, indicating that local factors rather than systemic factors are critical in regulating PDH during this type of exercise. Whether the level of muscle glycogen itself could be a determining factor is presently not known.

In conclusion, the present findings show that, in humans, PDH protein content follows the metabolic profile of the muscle rather than MHC fiber type distribution. While PDH protein content and exercise-induced PDH activation are higher in vastus lateralis than in triceps, the PDH molecule seems to be regulated similarly in the two muscles. This suggests that a lower PDH capacity in triceps, rather than less PDH activation of the PDH molecule, is likely a contributing factor to differential carbohydrate metabolism in triceps vs. vastus lateralis.

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