Insulin action on heart and skeletal muscle glucose uptake in weight lifters and endurance athletes

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Departments of 1Medicine and 3Clinical Physiology, 2Turku Positron Emission Tomography Centre, University of Turku, FIN-20521 Turku; and 4Division of Endocrinology and Diabetology, Department of Medicine, University of Helsinki, FIN-00029 HYKS Helsinki, Finland

Takala, Teemu O., Pirjo Nuutila, Juhani Knuuti, Matti Luotolahti, and Hannele Yki-Järvinen. Insulin action on heart and skeletal muscle glucose uptake in weight lifters and endurance athletes. Am. J. Physiol. 276 (Endocrinol. Metab. 39): E706–E711, 1999.—There are no studies comparing myocardial metabolism between endurance- and resistance-trained athletes. We used 2-deoxy-2-[18F]fluoro-D-glucose and positron emission tomography combined with the euglycemic hyperinsulinemic clamp technique to compare the ability of insulin to stimulate myocardial, skeletal muscle, and whole body glucose uptake between weight lifters (n = 8), endurance athletes (n = 8), and sedentary men (n = 9). Maximal aerobic power (ml·kg−1·min−1) was higher in the endurance athletes (71 ± 2, P < 0.001) than the weight lifters (42 ± 2) and the sedentary men (42 ± 2). Skeletal muscle glucose uptake (µmol·kg muscle−1·min−1) was enhanced in the endurance athletes (125 ± 16, P < 0.01) but was similar in weight lifters (59 ± 12) and sedentary (63 ± 7) men. The rate of glucose uptake per unit mass of myocardium (µmol·kg−1·min−1) was similarly decreased in endurance athletes (544 ± 50) and weight lifters (651 ± 45) compared with sedentary men (1,041 ± 78, P < 0.001 vs. endurance athletes and weight lifters). Both groups of athletes had increased left ventricular mass. Consequently, total left ventricular glucose uptake was comparable in all groups. These data demonstrate that aerobic but not resistance training is associated with enhanced insulin sensitivity in skeletal muscle. Despite this, cardiac changes are remarkably similar in weight lifters and endurance athletes and are characterized by an increase in left ventricular mass and diminished insulin-stimulated glucose uptake per heart mass.

METHODS

Subjects. Eight male endurance athletes (runners, cross-country skiers, triathletes), eight weight lifters (power lifters), and nine sedentary healthy men participated in the study (Table 1). All athletes were competing at the national level and trained 4–6 times per week. The control group did not exercise regularly. The subjects were healthy as judged by history, physical examination, and routine laboratory tests and were not taking any medications. The nature, purpose, and potential risks of the study were explained to all subjects before written informed consent was obtained. The experimental protocol was reviewed and approved by the Commission of Ethics of Turku University and Turku University Central Hospital.

Study design. All subjects were studied after a 10- to 12-h overnight fast. The subjects had not exercised for 2 days before the study. Two catheters were inserted, one in an antecubital vein for infusion of glucose and insulin and
Table 1. Characteristics of the subjects

<table>
<thead>
<tr>
<th></th>
<th>Endurance Athletes</th>
<th>Weight Lifters</th>
<th>Sedentary Men</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of subjects</td>
<td>8</td>
<td>8</td>
<td>9</td>
</tr>
<tr>
<td>Age, yr</td>
<td>28 ± 1</td>
<td>29 ± 2</td>
<td>29 ± 1</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>75 ± 2</td>
<td>86 ± 5*</td>
<td>78 ± 3</td>
</tr>
<tr>
<td>Height, cm</td>
<td>186 ± 1</td>
<td>178 ± 3</td>
<td>182 ± 2</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>22.0 ± 0.3</td>
<td>27.0 ± 0.9</td>
<td>23.4 ± 0.7</td>
</tr>
<tr>
<td>Percent fat, %</td>
<td>9 ± 1*</td>
<td>13 ± 1*</td>
<td>17 ± 1</td>
</tr>
<tr>
<td>VO₂max, ml·kg⁻¹·min⁻¹</td>
<td>71 ± 2*</td>
<td>42 ± 2</td>
<td>42 ± 2</td>
</tr>
<tr>
<td>Body surface area, m²</td>
<td>1.99 ± 0.03</td>
<td>2.05 ± 0.07</td>
<td>1.98 ± 0.05</td>
</tr>
<tr>
<td>Fasting plasma glucose, mmol/l</td>
<td>5.3 ± 0.1</td>
<td>5.4 ± 0.1</td>
<td>5.2 ± 0.1</td>
</tr>
<tr>
<td>Fasting serum insulin, mU/l</td>
<td>5 ± 1</td>
<td>6 ± 1</td>
<td>7 ± 1</td>
</tr>
</tbody>
</table>

Values are expressed as means ± SE. *P < 0.05 compared with other groups.

Glucose uptake in weight lifters and endurance athletes

Injection of [18F]FDG and another retrogradely in a heated hand for sampling of arterialized venous blood. Whole body, skeletal, and heart muscle glucose uptake rates were thereafter determined by combining the euglycemic hyperinsulinenic clamp technique with [18F]FDG and PET, as we will describe in detail.

Whole body glucose uptake. Whole body glucose uptake was quantitated by use of the euglycemic hyperinsulinenic clamp technique (2). Serum insulin was increased for 120 min by a primed-continuous (1 mU·kg⁻¹·min⁻¹) infusion of insulin (Velosulin, Novo Nordisk, Bagsvaerd, Denmark). Normoglycemia was maintained using a variable rate infusion of 20% glucose based on plasma glucose measurements, which were performed every 5 min from arterialized venous blood. Whole body glucose uptake was calculated from the glucose infusion rate during the period of PET scanning (60–120 min). Serum free insulin, plasma lactate, and serum free fatty acid concentrations were measured every 30 min during hyperinsulinemia.

Heart and skeletal muscle glucose uptake. [18F]FDG was synthesized with an automatic apparatus (10). The [18F]FDG study was performed as previously described (18). [18F]FDG (6–7 mCi or 220–260 MBq) was injected intravenously over 2 min. A dynamic scan of the thoracic region was performed for 25 min. Plasma radioactivity was measured with an automatic gamma counter (Wizard 1480 3, Wallac, Turku, Finland). An eight-ring ECAT 931/08-tomograph (Siemens/CTI, Knoxville, TN) with an axial resolution of 6.7 mm and in-plane resolution of 6.5 mm was used. Before the emission scan, a transmission scan was performed. All data were corrected for deadtime, decay, and measured photon attenuation. Dynamic FDG scans were reconstructed into a 128 × 128 matrix using a Hann filter with a cut-off frequency of 0.5. Final in-plane resolution of the reconstructed images was 8 mm.

For determination of myocardial glucose uptake, three (lateral, anterior, septal) regions of interest (ROIs) were drawn on at least four representative midventricular slices, with care taken to avoid myocardial borders. All myocardial time-activity curves were corrected for partial volume effect and spillover from cavity (28). ROIs within femoral muscles were drawn as previously described (22). The three-compartment model of [18F]FDG kinetics (29) and graphical analysis according to Patlak and Blasberg (24) were used to quantitate the rates of glucose uptake as previously described (22).

Echocardiography. M-mode and two-dimensional echocardiography (model SSD-870, Aloka, Tokyo, Japan) was performed according to the recommendations of the American Society of Echocardiography (26). Left ventricular (LV) mass was calculated according to the Penn convention (3): LV mass = 1.04 [(end diastolic diameter + posterior wall thickness + septal thickness)² – end diastolic diameter²] – 13.6 g.

Maximal aerobic power and body composition. Maximal aerobic power (VO₂max) was determined using direct measurement of the rate of oxygen consumption and a cycle ergometer (model 800 S, Ergoline, Mijnhardt, The Netherlands) with a continuous incremental protocol. Body fat content was estimated from four skinfolds (subscapular, triceps brachii, biceps brachii, and crista iliaca) as measured with a caliper (4).

Other measurements. Blood pressure and heart rate were determined every 30 min throughout the study using an automatic oscillometric blood pressure analyzer (model HEM-705C, Omron, Tokyo, Japan). Plasma glucose was measured using the glucose oxidase method (GM7 Analyser, Analox Instruments, Hammersmith, London, UK). Serum-free insulin concentrations were measured using a double-antibody radioimmunoassay (Pharmacia Insulin RIA kit, Pharmacia, Uppsala, Sweden) after precipitation with polyethylene glycol. Lactate was measured by enzymatic analysis (16).

Statistics. Group comparisons were performed with ANOVA followed by Tukey’s Studentized range test. Pearson’s correlations were calculated where appropriate. The statistical computation was performed with the SAS statistical program package (SAS Institute, Cary, NC). The results are expressed as means ± SE.

RESULTS

Characteristics of the study groups. Body weight was greater in the weight lifters than the endurance athletes and the sedentary subjects (Table 1). The percent body fat was lower in both groups of athletes than in the sedentary group (Table 1). VO₂max (ml·kg⁻¹·min⁻¹) was markedly increased in the endurance athletes (71 ± 2) but was similar in the weight lifters (42 ± 2, P < 0.001) and sedentary subjects (42 ± 2, P < 0.001).

The absolute left ventricular mass was similarly increased in the endurance athletes (290 ± 15 g) and the weight lifters (264 ± 19 g) compared with the sedentary men (186 ± 16 g, P < 0.01) (Fig. 1). These differences persisted after adjustment for body surface area (Table 2). Left ventricular systolic and diastolic diameters were slightly but not significantly higher in the athletes than in the sedentary men, but the differences did not reach statistical significance (Table 2). The posterior wall of the left ventricle and the interventricular septum were thicker in the endurance athletes and the weight lifters than in the sedentary men (P < 0.01). Resting blood pressure, heart rate, and the rate-pressure product were comparable among the groups (Table 2).

Whole body and skeletal muscle glucose uptake. Plasma glucose (5.0 ± 0.1, 4.8 ± 0.1, and 5.0 ± 0.2 mmol/l in endurance athletes, weight lifters, and sedentary men) and serum-free insulin concentrations (72 ± 12, 56 ± 4, and 64 ± 6 mU/l, respectively) were comparable during hyperinsulinemia. The weight lifters and the sedentary men had comparable rates of insulin-stimulated rates of whole body (38 ± 4 vs. 34 ± 2 μmol·kg⁻¹·min⁻¹, weight lifters vs. sedentary men) and femoral muscle (59 ± 12 vs. 63 ± 7 μmol·kg muscle⁻¹·min⁻¹, respectively) glucose uptake. In con-
Muscle VO$_2$\textsubscript{max} and skeletal muscle glucose uptake were positively correlated ($r = 0.58$, $P < 0.02$) and positively correlated with each other ($r = 0.67$, $P < 0.01$). Examples of PET images of insulin-stimulated glucose uptake in skeletal muscle is shown in Fig. 3.

Contrast, the endurance athletes had enhanced insulin-stimulated rates of glucose uptake at the level of the whole body ($65 \pm 3 \mu\text{mol} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$, $P < 0.01$) and in skeletal muscle ($125 \pm 16 \mu\text{mol} \cdot \text{kg muscle}^{-1} \cdot \text{min}^{-1}$, $P < 0.01$) compared with the two other groups (Fig. 2). VO$_2$\textsubscript{max} and skeletal muscle glucose uptake were positively correlated ($r = 0.67$, $P < 0.001$), and skeletal muscle and whole body glucose uptake values were correlated with each other ($r = 0.84$, $P < 0.001$). An example of PET images of insulin-stimulated glucose uptake in skeletal muscle is shown in Fig. 3.

Fasting serum FFA concentrations were slightly but not significantly lower in the endurance athletes ($390 \pm 45 \mu\text{mol/l}$) than in the weight lifters ($629 \pm 98 \mu\text{mol/l}$) or the sedentary subjects ($560 \pm 39 \mu\text{mol/l}$). During hyperinsulinemia, serum FFA concentrations were similarly suppressed in the endurance athletes ($103 \pm 12 \mu\text{mol/l}$), the weight lifters ($140 \pm 9 \mu\text{mol/l}$), and the sedentary subjects ($111 \pm 15 \mu\text{mol/l}$). Plasma lactate concentrations were significantly higher in the endurance athletes ($1.4 \pm 0.1 \text{mmol/l}$, $P < 0.05$) than in the weight lifters ($1.1 \pm 0.1 \text{mmol/l}$) and sedentary subjects ($1.0 \pm 0.1 \text{mmol/l}$) during hyperinsulinemia. Rates of whole body ($r = 0.66$, $P < 0.005$) and skeletal muscle ($r = 0.58$, $P < 0.02$) glucose uptake were significantly correlated with the plasma lactate concentration during hyperinsulinemia.

Heart glucose uptake. The rate of insulin-stimulated myocardial glucose uptake per gram of myocardium was 48% lower in the endurance athletes ($544 \pm 50 \mu\text{mol} \cdot \text{kg muscle}^{-1} \cdot \text{min}^{-1}$, $P < 0.01$) and 37% lower in the weight lifters ($651 \pm 45 \mu\text{mol} \cdot \text{kg muscle}^{-1} \cdot \text{min}^{-1}$, $P < 0.01$) than in the sedentary men ($1,041 \pm 78 \mu\text{mol} \cdot \text{kg muscle}^{-1} \cdot \text{min}^{-1}$). Rates of myocardial glucose uptake per unit mass of myocardium were comparable in the weight lifters and endurance athletes (Fig. 1). Left ventricular glucose uptake (per gram of myocardium) was also significantly inversely correlated with left ventricular mass ($r = -0.67$, $P < 0.001$). Examples of PET images of insulin-stimulated glucose uptake in heart muscle in the three groups are shown in Fig. 3. In contrast to skeletal muscle, plasma lactate levels did not correlate with heart glucose uptake, suggesting that the lower rate of glucose uptake in the weight lifters than the sedentary men was not due to increased lactate uptake via lactate mass action.

Table 2. Cardiac dimensions and hemodynamic parameters in weight lifters, endurance athletes, and sedentary men

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Endurance Athletics</th>
<th>Weight Lifters</th>
<th>Sedentary Men</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left ventricular mass index, g/m(^2)</td>
<td>$146 \pm 6^*$</td>
<td>$128 \pm 7^*$</td>
<td>$93 \pm 7$</td>
</tr>
<tr>
<td>Left ventricular diameter, mm</td>
<td>systole $36 \pm 1$</td>
<td>$35 \pm 1$</td>
<td>$34 \pm 1$</td>
</tr>
<tr>
<td></td>
<td>diastole $56 \pm 1$</td>
<td>$55 \pm 1$</td>
<td>$52 \pm 2$</td>
</tr>
<tr>
<td>Posterior wall, mm</td>
<td>systole $15.5 \pm 0.6^*$</td>
<td>$16.4 \pm 0.5^*$</td>
<td>$13.0 \pm 0.7$</td>
</tr>
<tr>
<td></td>
<td>diastole $10.5 \pm 0.5^*$</td>
<td>$9.8 \pm 0.4^*$</td>
<td>$8.3 \pm 0.2$</td>
</tr>
<tr>
<td>Septum, mm</td>
<td>systole $14.6 \pm 0.2^*$</td>
<td>$15.5 \pm 0.6^*$</td>
<td>$11.4 \pm 0.6$</td>
</tr>
<tr>
<td></td>
<td>diastole $11.0 \pm 0.5^*$</td>
<td>$10.7 \pm 0.6^*$</td>
<td>$8.6 \pm 0.4$</td>
</tr>
<tr>
<td>Blood pressure, mmHg</td>
<td>systolic $126 \pm 3$</td>
<td>$113 \pm 4$</td>
<td>$121 \pm 4$</td>
</tr>
<tr>
<td></td>
<td>diastolic $72 \pm 5$</td>
<td>$73 \pm 4$</td>
<td>$80 \pm 3$</td>
</tr>
<tr>
<td>Heart rate, beats/min</td>
<td>$61 \pm 3$</td>
<td>$60 \pm 4$</td>
<td>$66 \pm 5$</td>
</tr>
<tr>
<td>Rate-pressure product, mmHg:</td>
<td>$7,690 \pm 405$</td>
<td>$6,830 \pm 615$</td>
<td>$8,040 \pm 776$</td>
</tr>
<tr>
<td>beats · min(^{-1})</td>
<td>$102 \pm 3$</td>
<td>$98 \pm 6$</td>
<td>$83 \pm 7$</td>
</tr>
<tr>
<td>Stroke volume, ml</td>
<td>$6.6 \pm 0.3$</td>
<td>$6.1 \pm 0.6$</td>
<td>$5.7 \pm 0.5$</td>
</tr>
<tr>
<td>Cardiac output, l/min</td>
<td>$615 \pm 48$</td>
<td>$583 \pm 41$</td>
<td>$661 \pm 48$</td>
</tr>
</tbody>
</table>

Values are expressed as means ± SE. *$P < 0.05$ vs. sedentary group.

![Fig. 1. Left ventricular (LV) masses (top) and heart glucose uptake rates (middle, bottom) in endurance athletes (EA), weight lifters (WL), and sedentary men (S). Heart glucose uptake rate (middle) is shown per unit mass of myocardium. **$P < 0.01$ vs. S.](image1)

![Fig. 2. Rate of glucose uptake in skeletal muscle of EA, WL, and S as measured with positron emission tomography (PET) and 2-deoxy-2-[F\(^18\)]fluoro-D-glucose (\[^{18}\text{F}\]FDG). **$P < 0.01$ vs. EA.](image2)
Total left ventricular glucose uptake was calculated by multiplying myocardial glucose uptake by left ventricular mass, and it was comparable in endurance athletes (161 ± 13 µmol/min), weight lifters (172 ± 18 µmol/min), and sedentary men (190 ± 18 µmol/min) (Fig. 1). Rates of left ventricular glucose uptake were also comparable if expressed per body surface area (81 ± 7, 83 ± 7, and 95 ± 8 µmol·m⁻²·min⁻¹ for endurance athletes, weight lifters, and sedentary men). Whole left ventricular glucose uptake (µmol/min) correlated with cardiac work as determined from the rate-pressure product in endurance athletes (r = 0.85, P < 0.05), weight lifters (r = 0.71, P = 0.05), and sedentary men (r = 0.63, P = 0.09).

**DISCUSSION**

The present study is the first to relate cardiac structural changes to myocardial metabolism in resistance- and aerobically trained subjects. We found the heart to be enlarged in both groups and to utilize less glucose per unit mass than that of sedentary subjects. The rate of glucose uptake was similarly proportional to the degree of left ventricular hypertrophy in both weight lifters and endurance athletes. These similarities in cardiac adaptation were contrasted by a marked difference in the response of skeletal muscle to insulin between the two groups of athletes. In the weight lifters, the rate of insulin-stimulated skeletal muscle glucose uptake was similar to that in the sedentary men, whereas it was markedly enhanced in the endurance-trained athletes.

Both aerobic and resistance training are associated with an increase in left ventricular mass (6, 17, 30). This was also observed in the present study (Fig. 1, Table 2). In keeping with the data of Longhurst and Stebbins (14) and reviews of the literature (5, 9, 14), the absolute left ventricular mass and the left ventricular mass divided by surface area were slightly, albeit not significantly, lower in the weight lifters than in the endurance athletes (Fig. 1, Table 2). Regarding cardiac dimensions, we found, consistent with previous data (5, 9), increases in both posterior and septal wall thicknesses in the endurance athletes and weight lifters compared with the sedentary men. In the metanalysis of Fagard (6), increases in left ventricular end-diastolic diameter, wall thickness, and left ventricular mass were for endurance athletes 10, 18, and 48%, and for resistance-trained athletes 2.5, 15, and 25%. In our study, respective values were for endurance athletes 8, 27, and 56% and for weight lifters 6, 22, and 42%. Thus, in the present study, the left ventricular end-diastolic diameter in the weight lifters was slightly greater than that predicted from Fagard's metanalysis. On the other hand, in the study of Spirito et al. (30), in which morphology of the athlete's heart was assessed by echocardiography in two groups of elite athletes, long-distance runners and weight lifters, these athletes had similar left ventricular internal diameters (53.3 vs. 53.3 mm) and wall thicknesses (10.5 mm vs. 10.3 mm) (30). In addition, in a recent study of Fisman et al. (8), 29 endurance athletes and 16 weight lifters were found to have similar increases in both left ventricular mass and in septal and posterior wall thicknesses compared with 20 sedentary subjects. One might argue that these inconsistencies are attributable to confounding effects of dynamic components in resistance-training programs. This was unlikely the case for the weight lifters participating in the present study, because rate of maximal oxygen consumption, an accurate estimate of exposure to dynamic exercise compo-
Lactate uptake is unlikely to explain the decrease in myocardial glucose uptake, at least not via lactate mass action, in the weight lifters, because plasma lactate concentrations were comparable between weight lifters and sedentary subjects.

Endurance training is associated with increases in insulin sensitivity of glucose uptake in skeletal muscle, in direct proportion to maximal aerobic power (18, 25, 36). The present study confirms, by direct measurement of glucose uptake in skeletal muscle, that resistance training does not increase insulin-stimulated glucose uptake per unit mass of skeletal muscle (36). The failure of resistance training to enhance muscle insulin sensitivity could be due to the inability of resistance training to increase muscle capillary density (11) or to change muscle fiber types toward an insulin-sensitive direction (27, 31). Of note, the lack of favorable effects of resistance training on insulin sensitivity is also the likely explanation for why serum lipids and lipoproteins (12, 37) do not appear to change in an antiatherogenic direction by this type of training.

The present data demonstrate that the heart of a resistance-trained athlete closely resembles that of an endurance-trained athlete and is characterized by diminished rather than increased glucose uptake per unit heart mass. Under hyperinsulinemic conditions such as those prevailing in the present study, serum FFA concentrations are almost completely suppressed. Because FFAs are utilized in a concentration-dependent manner in the human heart (20, 22), and because FFA concentrations were similarly suppressed in all of the three groups, it is unlikely that myocardial rates of FFA utilization differed among the groups. Because FFAs and glucose represent the two most important fuels for the human myocardium under resting aerobic conditions (20, 22), it is unlikely that the lower rates of glucose uptake in the trained groups were due to increased utilization of fuels other than glucose. Consistent with this, direct measurement of rates of myocardial FFA utilization under fasting conditions have not revealed differences between endurance athletes and sedentary subjects (32). Regarding plasma lactate concentrations, the athletes exhibited higher levels during hyperinsulinemia than the two other groups. We have previously demonstrated that plasma lactate concentrations were comparable between weight lifters and sedentary subjects.

In conclusion, the present data demonstrate that the heart of a resistance-trained athlete closely resembles that of an endurance-trained athlete with respect to the rate of glucose uptake during hyperinsulinemia. In both groups of athletes, the rate of glucose uptake per unit mass of myocardium was decreased compared with sedentary men. When the rate of glucose uptake per unit mass was multiplied by heart size, glucose uptake was similar in all groups.

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REFERENCES

3. Devereux, R. B., and N. Reichek. Echocardiographic determina-
6. Fagard, R. H. Athlete’s heart: a meta-analysis of the echocardiog-
8. Fisman, E. Z., P. Embon, A. Pines, A. Tenenbaum, Y. Drory, I. Shapiro, and M. Motro. Comparison of left ventricular function using isometric exercise Doppler echocardiography in competitive runners and weightlifters versus sedentary individu-
specific synthesis of no-carrier-added 2-[18F]fluor-3-deoxy-
D-glucose using aminopolyether supported nucleophilic substitu-
16. Marbach, E. P., and M. H. Weil. Rapid enzymatic measure-
alainen, M. Teräs, M. Haaparanta, O. Solin, and H. Yki-