Growth hormone enhances effects of endurance training on oxidative muscle metabolism in elderly women

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AGING IS-associated with a loss in muscle mass and strength and an increase in body fat (9, 21). In addition, oxidative capacity and basal metabolic rate (BMR) are decreased (22). These changes have been attributed both to aging per se and to the development of a sedentary lifestyle (4). However, a causal relation to the age-related decline in growth hormone (GH) secretion has also been proposed (18). Children and young adults with GH deficiency (GHD) mimic the elderly in the sense that they also are characterized by a significant increase in body fat and a decrease in lean body mass (LBM) and BMR compared with controls. In GHD, these abnormalities are corrected by the administration of recombinant human GH (rhGH) in doses that restore serum insulin-like growth factor (IGF) I levels (13). Furthermore, administration of rhGH in supraphysiological doses to both obese women and to healthy elderly men decreases body fat and increases LBM (23, 25). These observations suggest that GH may play a role in determining body composition.

Increased muscle mass may explain the increase in LBM observed with rhGH administration. This is supported by studies showing that rhGH administration increases muscle protein synthesis (5). However, some authors have questioned whether this anabolic effect is of any significance in humans since the increase in LBM and nitrogen retention is only reflected in very small improvements in muscle strength (34). Furthermore, recent studies have not shown any additive effects of rhGH combined with strength training in humans (29, 35, 36).

So far research has focused on potential additive anabolic effects of rhGH combined with strength training. Considering the profound influence of GH on metabolism, it is somewhat surprising that no attention has been given to possible additive effects of rhGH combined with endurance training. On this background, the present study aimed at investigating whether the addition of rhGH enhances endurance training-induced adaptations. We hypothesized that rhGH combined with endurance training would increase oxidative capacity, oxidative metabolism, and fat loss more than endurance training alone.

METHODS

Subjects

Seventeen healthy women, age 75 ± 1 yr (mean ± SE), height 160 ± 1 cm, body weight 66.2 ± 2.5 kg, and body mass...
index 25.8 ± 1.0 kg/m², participated in the study. Informed consent was obtained according to the declaration of Helsinki 2, and the study protocol was approved by the Ethics Committee for Medical Research in Copenhagen (KF 02–130/97) and by the Danish Drug Agency. Before entering the study, subjects underwent a thorough medical history and physical examination, including blood tests and an exercise electrocardiogram (ECG). Exclusion criteria were metabolic and cardiac disease, anemia, previous or present cancer, and medication known to interfere with skeletal muscle and/or fat metabolism. Estrogen replacement therapy was not allowed.

**Experimental Protocol**

After inclusion, subjects were randomized in blocks of four to receive either placebo or GH, and the subjects then underwent a 12-wk closely supervised endurance-training program on cycle ergometers. Measurements were performed at baseline and after 12 wk.

**Administration of GH**

GH (Norditropin; Novo Nordisk) was administered subcutaneously in the thigh one time daily in a randomized, double-blinded, placebo-controlled design. After thorough instructions, subjects were able to perform the injections themselves at home in the evening before bedtime. Checking the syringes and reviewing the injection technique several times during the study ensured compliance. To avoid side effects, the dose was increased over 3 wk. During the first week the dose was 0.5 IU/m², during the second week 1.0 IU/m², and for the remainder of the study period 1.5 IU/m² (12 µg·kg⁻¹·day⁻¹). Side effects were controlled for by weighing, checking for edema, and questioning the subjects one time per week. If side effects occurred, the dose was cut in half until they disappeared or were tolerable to both the subject and the investigators. If a subject left the study before completion, another subject that received the same randomization number replaced her. Blinding of both investigators and subjects was maintained until data acquisition was completed for the whole study.

**Determination of Peak Oxygen Uptake**

Peak oxygen uptake (V\textsubscript{O₂ peak}) was determined on a cycle ergometer (Ergometrics ER 900 L; Ergoline). A protocol starting at 15 watts and increasing with 15 watts every 2 min until exhaustion was used. VO\textsubscript{2} and V\textsubscript{CO₂} were measured on an Oxycon system (Oxycon Champion, software version 3.12; Jaeger, Würzburg, Germany) using an external volume sensor in the open system mode, giving breath-by-breath data. The accuracy of the system was checked by combustion of 99.6% ethanol, and the flowmeter was checked by nitrogen infusion. Before each protocol, the gas analyzers were calibrated using gases of known concentration, and the flowmeter was calibrated using an external syringe of known volume. ECG and heart rate (HR) were measured continuously through chest electrodes connected to a monitor (Athena; Simonsen & Weel, Bagsvaerd, Denmark). V\textsubscript{O₂ peak} was chosen as the highest VO\textsubscript{2} attained during the test. Measurements were performed at baseline and after 12 wk.

**Training Program**

The subjects trained on a cycle ergometer (model 818 E; Monark, Varberg, Sweden) three times per week for 12 wk. Each subject followed an interval program of 60 min on each training session. An interval program was chosen for psycho-logical reasons to obtain a high degree of compliance. The subjects were equipped with a wireless heart rate monitor (HRM; Polar Vantage NV; Polar Electro, Kempele, Finland) that enabled them to monitor HR and exercise duration continuously. After a 10-min warm-up period, the subjects performed seven intervals of 2-, 4-, 6-, 8-, 6-, 4-, and 2-min length, respectively, each interval being separated by 2 min from the previous interval. During the intervals, the subjects had to adjust the load so that HR, within 5 beats/min, was kept at a level corresponding to 75% of V\textsubscript{O₂ peak}. In the period between the intervals, the subjects were allowed to decrease the load to 50% of the interval load. The program was completed by a 5-min cooldown period. HR was monitored and registered continuously, and an investigator supervised each training session. During a typical training session of 60 min, HR averaged a value corresponding to an oxygen uptake of 65–70% of V\textsubscript{O₂ peak}. By using an HRM as an indicator of workload, it was ensured that the subjects trained at the same relative level of V\textsubscript{O₂ peak} during the 12 wk. The subjects were carefully instructed to continue their normal daily life without any other change than following the training program. They were especially told not to change their eating habits.

**Determination of 24-h Energy Expenditure**

In four subjects, 24-h energy expenditure (EE) was assessed by indirect calorimetry on the basis of measurements of V\textsubscript{O₂}, V\textsubscript{CO₂}, and nitrogen excretion in the urine in an open-circuit respiration chamber (1). The chamber had a floor area of 6.5 m² and a volume of 14.7 m³ and was equipped with facilities for making the stay as comfortable as possible. A standard protocol with fixed sessions of physical activity was followed throughout the 24-h stay. BMR was measured under standardized conditions between 0800 and 0900. Sleeping EE was defined as the 5-h period between 0100 and 0600. Each subject received a standardized diet, calculated to be isonenergetic from body composition measurements, providing 48% energy from carbohydrate, 37% from fat, and 15% from protein (30). HR was monitored continuously by a wireless HRM. To ensure optimal compliance to the protocol, subjects were kept under 24-h surveillance by a laboratory technician in the daytime and by a trained medical student during the night. The subject spent the night preceding the measurements in the chamber to become familiar with the environment. In addition, no training was allowed 48 h before measurements. Because of limited access to the respiration chamber, it was only possible to investigate four subjects. For the same reason, measurements were performed at baseline and after 8 instead of 12 wk of training and placebo/GH administration.

The gas exchange of the subjects was calculated from the measurements of oxygen and carbon dioxide concentrations (Ureas 3 G; Hartman and Braun analyzers, Frankfurt, Germany) at the outlet of the chamber and from measured airflow through the chamber. The room temperature was maintained constant at 24°C during the daytime and at 18°C during the night. EE was calculated using the following equation with the assumption that the contribution of methane production to EE is negligible

\[
EE (\text{cal}) = 3.87 \times \text{VO}_2(l) + 1.20 \times \text{VCO}_2(l) - 1.43 \times U_N (\text{g})
\]

where \(U_N\) is urine nitrogen.

**Dual-Energy X-Ray Absorptiometry**

The dual-energy X-ray absorptiometry (DEXA) scan was performed using a Lunar DPX-IQ scanner (software version
Muscle Biopsies

Muscle biopsies were taken from the right musculus vastus lateralis at the mid thigh level at baseline and after 5 and 12 wk of training. Sampling at 5 and 12 wk was performed 1 cm distal and 1 cm proximal to baseline sampling, respectively. The overlying skin was anesthetized with 1% lidocaine, and sampling was done through an incision using a 5-mm Bergström needle (2). A suction device in conjunction with the biopsy needle was used to create a negative pressure while sampling, which allowed for a larger sample specimen. Samples were immediately frozen in liquid N₂, transferred to a vial, and stored at −80°C until analysis.

Blood Sampling

Blood for determination of GH, insulin-like growth factor (IGF)-I, IGF-II, IGF-binding protein 3 (IGFBP-3), and acid-labile subunit (ALS) was sampled from a radial artery in the morning after an overnight fast. Samples were allowed to clot for 10 min at room temperature and were centrifuged at 4°C for 15 min to obtain serum. Serum was stored at −80°C until analysis. Sampling was performed at baseline and after 12 wk.

Analytical Methods

Serum. GH. GH was determined by time-resolved immunofluorescence assay (Delfia; Wallac, Turku, Finland). The detection limit was 0.03 ± 0.02 mU/L. Inter- and intra-assay coefficients of variation were 5.9% (at 16.54 mU/L) and 2.2% (at 14.1 mU/L), respectively.

Total IGF-I. Total IGF-I was determined by RIA as described previously (14). Briefly, serum was extracted by acid-ethanol and was cryoprecipitated before analysis to remove interfering IGFBP. Inter- and intra-assay coefficients of variation were <9 and 6%, respectively.

IGF-II. IGF-II was determined by an immunoradiometric assay (Diagnostic Systems Laboratories, Webster, TX). Briefly, this assay is a noncompetitive assay in which the analyte is sandwiched between two antibodies. Samples were pretreated (1:1,000) with acid-ethanol extraction to separate IGF-II from its binding proteins before measurement. Inter- and intra-assay coefficients of variation were 6.3–10.4% and 4.2–7.2%, respectively (37).

IGFBP-3. IGFBP-3 was determined by RIA as described previously (3). Reagents for the assay were obtained from Medigast (Tübingen, Germany). Sensitivity was 0.29 μg/L (defined as 3 SD from the mean of the zero standard). Inter- and intra-assay coefficients of variation were 10.7 and 2.4% (at bound-to-free ratios of 0.4–0.5), respectively.

ALS. ALS was determined by a newly developed commercially available enzyme-linked immunoabsorbent assay (Diagnostic Systems Laboratories). Standards ranged from 1.09 to 70 mg/L. In our hands, interassay coefficients of variation (n = 22) were 20.4 (at 2.8 mg/ml) and 12.1% (at 17.6 mg/L). Intra-assay coefficients of variation (n = 20) were 8.6% (at 30.1 mg/L) and 7.4% (at 8.4 mg/ml; see Ref. 15).

Muscle biopsies. Approximately 10 mg of each muscle sample were used for the preparation of muscle homogenate. Briefly, the samples were freeze-dried for 48 h at −40°C and were dissected free of blood, fat, and connective tissue at −20°C and 30% relative humidity using a stereomicroscope. Samples were then transferred to homogenization tubes containing phosphate buffer with BSA and were placed on ice [400 μl buffer/mg muscle; preparation of buffer: 20 ml 0.3 M phosphate buffer (pH = 7.7) + 100 μl BSA]. After homogenization, the homogenate was spun for 2 min at 11,000 rpm, and the supernatant was transferred to an Eppendorf vial and stored at −80°C until further analysis. The maximal enzymatic activities (expressed as μmol metabolized substrate·g muscle mass⁻¹·min⁻¹ at 25°C) of citrate synthase (CS), 1,3-hydroxyacyl-CoA dehydrogenase (HAD), phosphofructokinase (PFK), and lactate dehydrogenase (LDH) were determined on a Cobas analyzer (Cobas Fará II; Hoffmann-La Roche, Diagnostics Division) using NAD⁺-NADH enzymatic fluorometric assays.

Statistics

All data are presented as means ± SE. A nonparametric ranking sum test was used to detect significant differences between unpaired (Mann-Whitney) and paired (Wilcoxon) data before and after the training period. P < 0.05 (2-tailed testing) was considered significant.

RESULTS

Subjects

Sixteen out of seventeen recruited subjects completed the study. One subject left the study after 3 wk because she felt the training program was too demanding. Demographic data for the sixteen remaining subjects, divided into a placebo group (n = 8) and a GH group (n = 8), are presented in Table 1. Body weight was significantly greater in the GH group compared with the placebo group (P < 0.05). The groups were similar with respect to all other subject characteristics.

GH Administration

Of the eight subjects receiving GH, five experienced side effects that necessitated a dose reduction. With no side effects, a typical end dose was 2.5–3.0 IU/day (12

Table 1. Anthropometric data for subjects completing the study

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>GH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>74.8 ± 1.7 (70.8–82)</td>
<td>75.0 ± 1.1 (71.7–79)</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>23.9 ± 1.0 (19.5–27.0)</td>
<td>27.6 ± 1.4 (21.9–32.7)</td>
</tr>
<tr>
<td>Height, cm</td>
<td>160.0 ± 2.4 (148–170)</td>
<td>160.9 ± 1.5 (156–167)</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>61.2 ± 2.7 (49.4–72.5)</td>
<td>71.3 ± 3.6* (59.4–89.0)</td>
</tr>
<tr>
<td>Body fat, kg</td>
<td>23.1 ± 2.0 (14.7–30.9)</td>
<td>30.0 ± 2.7 (18.1–40.8)</td>
</tr>
<tr>
<td>Body fat, %body wt</td>
<td>37.4 ± 2.3 (28.4–47.5)</td>
<td>41.6 ± 2.1 (29.7–49.0)</td>
</tr>
</tbody>
</table>

Values are means ± SE with ranges in parentheses; n = 8 subjects in each group. GH, growth hormone; BMI, body mass index.

*Significant difference between groups (P < 0.05).
In subjects experiencing side effects, a typical end dose was 1.5–2.0 IU/day (7 μg·kg⁻¹·day⁻¹). Side effects appeared from 4 to 10 wk after GH start and were mainly ankle edema (n = 5), swollen fingers (n = 2), carpal tunnel syndrome (n = 2), and headache during the night and early morning (n = 1). Eventually, all side effects disappeared after stopping GH administration. Some side effects persisted until 3 wk after stopping GH administration (ankle edema and carpal tunnel syndrome).

\[ \text{\( \dot{V}O_2 \text{peak} \)} \]

Results are presented in Table 2. There were no differences in \( \dot{V}O_2 \text{peak} \) either at baseline or after 12 wk of training between the two groups expressed in absolute terms, relative to body weight, or relative to LBM. \( \dot{V}O_2 \text{peak} \) (expressed as ml·min⁻¹·kg⁻¹) increased by 19 ± 5% in the placebo group and by 17 ± 2% in the GH group (P < 0.02 and P < 0.02, respectively) in response to training. In absolute terms (i.e., as l/min), \( \dot{V}O_2 \text{peak} \) increased by 16 ± 5% in the placebo group and by 17 ± 2% in the GH group (P < 0.02 and P < 0.02, respectively), and when expressed relative to LBM (ml·min⁻¹·kg LBM⁻¹), \( \dot{V}O_2 \text{peak} \) increased by 16 ± 4% in the placebo group and by 9 ± 3% in the GH group (both P < 0.02).

**Serum GH, IGF-I, IGF-II, IGFBP-3, and ALS**

Markers for the GH-IGF axis are presented in Fig. 1. At baseline, there were no differences in serum GH, IGF-I, IGF-II, IGFBP-3, or ALS between the two groups, whereas all markers, except for IGF-II, were significantly greater in the GH group after 12 wk of training. IGF-II tended to increase from 738 ± 4% in the placebo group (P = 0.02), arm LBM (22%, P < 0.01), and leg LBM (17%, P < 0.02) than in the placebo group. There were no changes in body weight or total or regional body composition in the placebo group as a result of training, although leg LBM tended to increase by 16 ± 4% and 6 ± 6% in the placebo group and by 9 ± 3% in the GH group (both P < 0.02).

**Muscle Enzyme Activities**

At baseline, there were no differences in muscle CS, HAD, LDH, or PFK activities between groups. After 12 wk, CS activity was increased by 35 ± 12% in the placebo group (P < 0.02) and by 52 ± 7% in the GH group (P < 0.02). The increase in the GH group was significantly larger compared with the placebo group (P < 0.05; Fig. 4). No change in HAD activity was observed in the placebo group, whereas an increase of 24 ± 6% was seen in the GH group (P < 0.02). There were no changes in LDH or PFK activities, although there was a tendency for LDH to increase by 21 ± 10% in the GH group (P < 0.07).

**DISCUSSION**

A major finding in the present study is the larger increase in muscle oxidative enzyme activity when rhGH administration is combined with physical endurance training compared with the effect of training alone (Fig. 4). From the present study, mechanisms behind this effect of GH can only be hypothesized. In this respect, it is interesting that the myogenic tran-
scription factor myogenin not only has been shown to be involved in muscle differentiation (8, 10, 17) but also may play a role in shifts from glycolytic to typically oxidative metabolism without concomitant changes in myosin heavy chain composition (11). Thus GH, by increasing IGF-I, may enhance transcriptional activity through myogenin, and this may enhance the exercise effect on muscle oxidative enzymes.

The combination of rhGH and physical endurance training or the effect of rhGH per se on muscle oxidative enzyme activity has, to our knowledge, not been studied in humans. Only a few animal studies exist, but they are difficult to compare, and the results are diverging (6, 7, 16, 32). Thus no clear picture emerges from the literature. However, from the present study, it is unclear whether GH per se stimulates oxidative enzyme activity in skeletal muscle. Previous studies in elderly men have not been able to demonstrate any additive effects of GH on strength training in terms of increased strength, hypertrophy, or increased muscle protein synthesis rate (28, 29, 36). Endurance training represents an entirely different stimulus to the muscle than resistance training, and muscle adaptation to endurance training may be regulated differently from strength training.

Both VO\textsubscript{2}\text{peak} and oxidative muscle enzymes (but not the glycolytic enzymes) increased in response to endurance training by 19 and 35\%, respectively. This is in agreement with adaptations that potentially can be achieved with training in this age group (19) and underscores the high compliance among subjects toward

### Table 3. 24-h Oxygen uptake, energy expenditure, and oxidized fat in 4 individuals

<table>
<thead>
<tr>
<th>Group</th>
<th>Subject</th>
<th>Time Point</th>
<th>24 h VO\textsubscript{2}, ml·min\textsuperscript{-1}·kg\textsuperscript{-1}</th>
<th>24 h EE, kj/kg</th>
<th>Oxidized Fat, g/24 h</th>
</tr>
</thead>
<tbody>
<tr>
<td>GH</td>
<td>A</td>
<td>Baseline</td>
<td>4.00</td>
<td>117</td>
<td>77</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>Baseline</td>
<td>3.64</td>
<td>107</td>
<td>70</td>
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<tr>
<td></td>
<td></td>
<td>8 wk</td>
<td>4.74</td>
<td>137</td>
<td>122</td>
</tr>
<tr>
<td></td>
<td></td>
<td>8 wk</td>
<td>4.60</td>
<td>133</td>
<td>134</td>
</tr>
<tr>
<td>Placebo</td>
<td>C</td>
<td>Baseline</td>
<td>3.82</td>
<td>112</td>
<td>61</td>
</tr>
<tr>
<td></td>
<td></td>
<td>8 wk</td>
<td>3.64</td>
<td>106</td>
<td>65</td>
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<tr>
<td>Placebo</td>
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<td>Baseline</td>
<td>4.30</td>
<td>125</td>
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<tr>
<td></td>
<td></td>
<td>8 wk</td>
<td>3.99</td>
<td>117</td>
<td>73</td>
</tr>
</tbody>
</table>

Measurements performed in the respiration chamber at baseline and after 8 wk of training per placebo/growth hormone; n = 2 subjects in each group. EE, energy expenditure. Individual values are presented. Subject A lost 0.7 kg body weight and 3.7 kg body fat. Subject B lost 4.0 kg body weight and 4.3 kg body fat. Subject C gained 1.3 kg body weight and 0.4 kg body fat. Subject D lost 0.8 kg body weight and 0.7 kg body fat.

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Fig. 1. Resting arterial serum concentrations of selected parameters representing the growth hormone (GH)-insulin-like growth factor (IGF) axis at baseline and after 12 wk of training per placebo/GH. IGFBP-3, IGF-binding protein 3; ALS, acid-labile subunit. Bars and error bars represent mean values and SE, respectively; n = 8 subjects in both groups. *Significant change within a group; #significant difference between groups (both \( P < 0.05 \)).
the training program. When rhGH was combined with endurance training, \( V\dot{O}_2 \text{peak} \) did not improve further, whereas oxidative enzyme activity in the contracting skeletal muscle improved by an additional 17%. This illustrates a specific peripheral effect on muscle rather than any effect on the central circulatory system or improved peripheral tissue oxygen extraction.

In this study, rhGH enhanced both the CS and HAD activity in muscle biopsy tissue. This finding is interesting in view of the data obtained from the respiration chamber. Although only four of the subjects were studied this way, the data clearly indicate that rhGH administration causes a substantial increase in 24-h EE and a shift in substrate oxidation. GH administration has been shown previously to increase the BMR in normal (33) and in GH-deficient subjects (12). However, in these studies, the EE was only measured in a short period postprandially. From the present preliminary data, it is not possible to identify by which mech-

Fig. 2. Change in fat mass and lean body mass as a result of 12 wk of endurance training + placebo/GH, measured by dual-energy X-ray absorptiometry. Values from total body scans divided into total and regional (arm, trunk, and leg) compartments. Changes calculated as % of fat mass and % of lean body mass. Bars and error bars represent mean values and SE, respectively; \( n = 8 \) subjects in both groups. *Significant change within a group; #significant difference between groups (\( P < 0.05 \)).

Fig. 3. Change in fat mass (kg) over 12 wk related to fat mass at baseline (kg). Individual values for the 16 subjects are presented.

Fig. 4. Maximal enzyme activities in muscle homogenates obtained from vastus lateralis muscle at baseline and after 5 and 12 wk of endurance training + placebo/GH. Activity measured as \( \mu \text{mol metabolized substrate} \cdot \text{g muscle mass}^{-1} \cdot \text{min}^{-1} \) at 25°C. CS, citrate synthase; HAD, 1,3-hydroxyacyl-CoA dehydrogenase. Bars and error bars represent mean values and SE, respectively; \( n = 8 \) subjects in both groups. *Significant change within a group; #significant difference between groups.
organisms GH increases the EE and changes the oxidative metabolism. However, it can easily be calculated that neither the increase in HR (33) nor the shift in substrate oxidation observed with GH administration is able to account for >5–10% of the increase in EE. It is tempting to speculate that mechanisms stimulating uncoupling proteins (24, 26, 27), and hence futile cycling, quantitatively may contribute to the EE-enhancing effect of GH, but further studies are needed to elucidate this.

Body composition was estimated by the use of DEXA scanning, which evidently limits the amount of detailed information that can be extracted (Fig. 2). However, it can be stated that total FM did only decrease significantly with training if this was accompanied by the administration of GH (Fig. 2). Also, this decrease occurred in all body regions. Our study design does not allow us to determine whether the effects are due to GH per se or the combination of GH and training. The observed increase in LBM with GH administration should be interpreted with some caution. It may represent an increase in muscle mass but is probably almost exclusively explained by the fluid retention induced by GH (20). In support of the latter, recent results from our laboratory have shown that LBM declines within days after stopping GH administration.

In the present study, elderly women received exogenous GH, aiming at a dose of 1.5 IU/m². However, almost all individuals developed side effects at this dose, resulting in an almost halving of the dose in most individuals for the remainder of the training period. Despite this very moderate dose, all individuals receiving GH more than doubled their IGF-I serum levels (Fig. 1). This increased level is comparable to, and even above, levels seen in young, healthy individuals in their second decade (14). In addition to this, serum GH, IGF-II, IGFBP-3, and ALS were also increased in the GH group. Somewhat surprising, a trend (P < 0.08) toward an increase in serum IGF-II was observed in the placebo group. In animals, it has been shown that GH administration is able to induce skeletal muscle hypertrophy (31). In that study, the increase in skeletal muscle mass was associated with a marked upregulation of both IGF-I and IGF-II mRNA locally in the muscle. The present study suggests that even physical training aiming at increasing endurance and oxidative capacity rather than muscle hypertrophy and strength stimulates the release of IGF-II from human skeletal muscle. The role of IGF-II in the present study is unknown. Possibly IGF-II could play a role, together with IGF-I, in stimulating myogenic factors and thus could account for the larger response in enzyme activity observed in the training group receiving GH.

In conclusion, the present study confirms our hypothesis that, in healthy elderly women, rhGH combined with endurance training increases skeletal muscle oxidative enzyme activity more than endurance training alone. In addition, we suggest that the marked loss of body fat seen with rhGH administration is due to increased 24-h EE with increased relative and absolute fat combustion over a 12-wk period.

REFERENCES


