ABSTRACT

The purpose of this study was to evaluate the GH response to exercise and the effects of endurance training on this response in early middle-aged men. Seven healthy middle-aged [M; 42.0 ± 2.4 (±SD) yr old] and five young (Y; 21.2 ± 1.1 yr old) competition cyclists were investigated before and after 4 months of intensive endurance training. Subjects performed an exhaustive incremental exercise test (50 watts for 3 min) with gas exchange measurement, and blood samples for lactate, glucose, and GH determinations were drawn before exercise, at the end of the exercise, and in the recovery phase (1, 3, 5, 10, 15, 20, and 30 min). Basal insulin-like growth factor I was also investigated before and after 4 months of intensive endurance training.

The presence of an absolute or relative GH deficiency with aging has been confirmed in elderly people and in GH-deficient adults treated with recombinant GH, in whom hormone administration improved nitrogen balance and increased lean body mass (5, 6). However, the responsiveness of somatotropic cells in the elderly, tested by pharmacological substances (GHRH, insulin-induced hypoglycemia, arginine, GH-releasing peptide-6, and galanin) was not always reported to be reduced; it was either the same or lower than that in young subjects (7).

Among the physiological tests for GH secretion, exercise is considered to be a very provocative test. It has been reported that GH concentrations significantly increase during both low and high intensity aerobic exercise and during resistance exercise, remaining elevated for up to 30 min during the recovery (8, 9). The maximal GH response seems to be attained at 70% of the maximal oxygen consumption (VO2max) with no further effect at 90% VO2max (10). The effect of aging on GH response to exercise has not been investigated in depth, but researchers appear to agree that the GH response to aerobic (11) or resistance exercise (12) is reduced in the elderly.

Moreover, it has been observed that trained elderly, like young subjects, have a greater lean body mass and muscular strength than sedentary age-matched subjects (13). This suggests that training can improve muscular strength by causing changes in anabolic hormones (GH and testosterone) and growth factors (14). However, the effects of regular physical activity on baseline GH and insulin-like growth factor I (IGF-I) concentrations and on pituitary GH responsiveness are contradictory. In fact, some researchers believe that training has a positive effect on somatotropic function (15, 16), whereas others maintain that it has no effect (17, 18). All of the studies considered, however, were performed with elderly subjects (between 60–70 yr of age), although, as mentioned above, the critical period for a progressive reduction in the GH secretion rate is during early middle age, in subjects about 40 yr old (3, 4).

Therefore, the aim of our study was to ascertain whether the reduced GH response to exhaustive exercise observed in older men was also present in middle-aged men, and if exercise training could modify this response.
whether a prolonged period of intensive endurance training could influence this response.

Subjects and Methods

Subjects

Seven healthy middle-aged (mean ± sd, 42.0 ± 2.4 yr) and five young (21.2 ± 1.1 yr) competition cyclists, whose characteristics are reported in Table 1, were studied. All subjects gave their informed consent. They were investigated before and after 4 months of intensive endurance training. Subjects in the same group cycled together, following the same training program. The first test was performed in February at the beginning of the training course, and the second was performed in July during the competitive season. The training load (expressed in kilometers per week) increased progressively during the 4 months of sport activity, from 182 to 300 km/week in the middle-aged group (M) and from 350 to 600 km/week in the younger group (Y).

For the 2 days before the test, subjects were asked to eat a weight-maintaining, balanced diet, not to exercise exhaustively, to have a regular sleeping pattern, to avoid alcohol, and not to take drugs or medications known or suspected to affect hormonal secretion. On the day of the first experiment, body composition was determined by bioimpedance analysis (RJL-Akern, Florence, Italy). Subjects came to the laboratory early in the morning after an overnight fast and performed the first and the second test at the same hour between 0800–1000 h. An incremental test (50 watts every 3 min until exhaustion) was performed on an electrically braked cycle ergometer (Excalibur, Lode, Groningen, Holland) monitoring heart rate (Max 1, Marquette, Milwaukee, WI) and measuring simultaneously gases exchange (2001, MCG Graphics 2001 MGC, St. Paul, MN). Blood samples for lactate, glucose, and GH determinations were drawn from an antecubital vein kept open with saline solution before exercise, at the end of the exercise, and during the recovery phase (1, 3, 5, 10, 15, 20, and 30 min). Blood for IGF-I determination was collected at rest before the two exercise tests.

Assays

Blood glucose and lactate were measured by enzymatic methods using commercial kits (Boehringer Mannheim, Indianapolis, IN).

Plasma GH was determined by immunoenzymetric assay (Medgenics Diagnostics SA, Fleurus, Belgium). The intraassay coefficients of variation were 3.6% and 2.1% at serum concentrations of 1.94 and 13.1 µIU/mL, respectively. The interassay coefficients of variation were 6.8% and 7.1% at serum concentrations of 4.1 and 15.5 µIU/mL. Plasma IGF-I was determined by immunoradiometric assay (Diagnostic Systems Laboratories, Inc., Webster, TX).

Statistical analysis

Data are expressed as the mean ± se. The statistical differences between groups were assessed by ANOVA. Differences within each group were evaluated by Student’s test for paired data. Linear regression was used to evaluate correlations between GH peaks or areas under the curve (AUCs) and body mass index (BMI) and fat mass (FM). The significance level for all tests was set at P < 0.05.

### TABLE 1. General, cardiorespiratory, and metabolic parameters

<table>
<thead>
<tr>
<th></th>
<th>Middle-aged pretraining (n = 7)</th>
<th>Middle-aged posttraining (n = 7)</th>
<th>Young pretraining (n = 5)</th>
<th>Young posttraining (n = 5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wt (kg)</td>
<td>74.7 ± 0.6</td>
<td>73.7 ± 1.0</td>
<td>78.1 ± 3.8</td>
<td>76.9 ± 3.2</td>
</tr>
<tr>
<td>Body mass index (kg/m^2)</td>
<td>24.8 ± 0.2</td>
<td>24.5 ± 0.2</td>
<td>23.5 ± 1.1</td>
<td>22.5 ± 1.1^a</td>
</tr>
<tr>
<td>Fat mass (%)</td>
<td>19.8 ± 1.5</td>
<td>18.3 ± 0.7</td>
<td>23.5 ± 1.1</td>
<td>22.5 ± 1.1^a</td>
</tr>
<tr>
<td>VO2max (L/min)</td>
<td>3448 ± 104</td>
<td>3905 ± 147^b</td>
<td>4756 ± 145^a</td>
<td>5397 ± 199^b,a</td>
</tr>
<tr>
<td>VO2max (mL/kg · min)</td>
<td>46.0 ± 1.5</td>
<td>53.0 ± 2.2^b</td>
<td>61.6 ± 2.7^b</td>
<td>72.3 ± 2.9^b</td>
</tr>
<tr>
<td>HR max (beats/min)</td>
<td>172 ± 4.3</td>
<td>171 ± 3.4</td>
<td>189.2 ± 4.4^a</td>
<td>186.6 ± 4.7^a</td>
</tr>
<tr>
<td>Blood glucose peak (mg/dL)</td>
<td>106.8 ± 7.0</td>
<td>109.6 ± 2.5</td>
<td>117.0 ± 5.7</td>
<td></td>
</tr>
<tr>
<td>Blood lactate peak (mmol/L)</td>
<td>10.5 ± 1.3</td>
<td>8.7 ± 0.7</td>
<td>10.8 ± 0.9</td>
<td>11.7 ± 1.0^c</td>
</tr>
</tbody>
</table>

Values are the mean ± se. VO2max, Maximal oxygen consumption; HRmax, maximal heart rate.

^a P < 0.05, comparing differences between groups.

^b P < 0.05, comparing differences within each group before and after training.

Results

The overall anthropometric, cardiorespiratory, and metabolic findings for M and Y are listed in Table 1. Before the first examination, mean BMI and FM were similar in the two groups; after training, BMI showed a slight, but not significant, reduction in both groups. The training, in absolute values, was higher in the younger subjects, but the percent increase was about the same in both groups (64.8% in M vs. 71.4% in Y).

As expected by the different ages and pre- and post-training VO2max values, maximal power and the absolute maximal heart rate (HRmax) were significantly higher in Y (Table 1). However, the VO2max percent increase was similar in both groups (M, +15.2%; Y, +17.5%), showing that the efficiency of training was comparable. Moreover, there were no differences in the relative HRmax of the two groups (calculated from the formula 220 – age in years), confirming that the intensities of the exercise tests were similar.

At rest, blood glucose concentrations were within the normal range both before and after training (M: pretraining, 76.3 ± 3.1; posttraining, 86.4 ± 2.5 mg/dL; Y: pretraining, 66.6 ± 1.5; posttraining, 68.2 ± 2.9 mg/dL). After exercise, blood glucose slightly increased, showing a similar peak in both groups (Table 1). On the other hand, blood lactate showed a small decrease in peak values in M and a small increase in Y when comparing pre- and posttraining values (Table 1).

On the contrary, a marked difference in the GH response to exercise was seen between the groups (Fig. 1). In Y, GH concentrations increased to about 7-fold the resting values, showing a mean peak between the end of the exercise and the 10th minute of the recovery period. In M, the maximal GH response to exercise was delayed (between the 15th and 30th minute) and much lower than that in Y both before (8.1 ± 1.3 vs. 57.1 ± 15.5 µg/L; P < 0.01) and after (6.7 ± 1.0 vs. 61.0 ± 12.9 µg/L; P < 0.01) training. Moreover, the mean of each subject’s GH peak (12.6 ± 3.4 in M vs. 55.9 ± 14.3 in Y, and 7.9 ± 1.0 vs. 67 ± 14.9 µg/L before and after training, respectively), was similar to the GH values averaged over each time point of the curve (Fig. 2). Similarly, the integrated responses of GH response, expressed as the AUC, were significantly lower in M than in Y (201.1 ± 74.8 vs. 1438.3 ± 337 µg/L; P < 0.005) and were not modified by training (209.4 ± 68 vs. 1568.7 ± 290.3 µg/L; P < 0.002; Fig. 2). No correlation
was found comparing GH peaks and AUC with BMI or FM in the two groups both before and after training.

As expected, IGF-I levels were lower in M than in Y, but values were in the normal range for age. After training, IGF-I concentrations decreased slightly, but not significantly, in the two groups (from 149.5 ± 14.1 to 123.4 ± 16 ng/mL in M and from 274.4 ± 78 to 227 ± 23.2 ng/mL in Y).

Discussion

We investigated the GH response to maximal exercise in young and early middle-aged subjects before and after 4 months of endurance intensive training. Our most interesting finding was that middle-aged subjects had a markedly lower GH response to exercise compared with the younger subjects and that 4 months of training did not change this response.

It is well known that GH secretion declines with aging. Studies of 24-h GH secretion have shown that from the third decade of life, there is a progressive reduction in the number and amplitude of spontaneous GH pulses (3, 4). Conversely, the GH secretory response to pharmacological provocative tests was not always found to be reduced in the elderly; sometimes it was reported to be similar to that in young subjects (7, 9).

Exercise represents a powerful physiological stimulus for GH secretion (8, 9). Until now, the GH response to exercise was tested in young and elderly subjects. There is a general agreement that elderly people show a reduced GH response to aerobic and resistance exercise (11, 12, 17). Our results demonstrate that the GH response is also impaired in early middle-aged subjects when tested with a graded exhaustive exercise. Data from deconvolution analysis of 24-h GH secretion revealed that starting from the third decade of life, the GH production rate and the GH half-life decrease by, respectively, 14% and 6% with each advancing decade (19). Therefore, a slight reduction in the GH peak response (~30%) could be expected in our middle-aged subjects, but the extent of the response that we found was much lower (~7-fold lower) than that of young subjects. This finding was fully confirmed by the mean of each subject’s GH peak and by the integrated GH response (AUC).

The blunted GH response in our middle-aged subjects could have been determined by differences in the intensity of the exercises, in the maximal blood lactate and glucose levels, or in body composition.

It is known that a threshold of exercise intensity must be exceeded before a significant rise in serum GH concentrations occurs (20), but exercise intensities above 75% VO$_{2\text{max}}$ did not further increase GH concentrations (10). Our exercise test greatly exceeded the 75% VO$_{2\text{max}}$, as shown by the high levels of blood lactate at exhaustion. Although the maximal power and the absolute HRmax were higher in the younger group, the relative intensity of the effort was not different in the two groups, as shown by the similar percentage of maximal heart rates and by the comparable maximal lactate concentrations. Thus, we rule out that those differences in exercise intensity affected the GH response.
Lactate has been suggested to be an independent adjunctive stimulating factor in the exercise-induced GH response (10). However, even if a significant difference between groups has been found after a training period, the maximal blood lactate concentration did not appear to influence the GH response. In fact, despite blood lactate variations, GH peaks were similar in the two groups before and after training.

GH release is suppressed by hyperglycemia (21). Our subjects were healthy, and their resting blood glucose concentrations were within the normal range; the glucose response to exercise showed a moderate, similar increase in both groups, ruling out possible effects of hyperglycemia on the GH response in our middle-aged group.

A negative correlation among BMI, adiposity, waist/hip ratio, and GH secretion has been reported (7, 19, 22). We found a negative, but not significant, correlation when comparing BMI and FM (measured only at the beginning of the study) with the GH response. Similarly, no significant correlation was observed between FM and/or BMI and GH peaks or AUC, suggesting that body composition did not affect GH secretion in our subjects.

We found that training did not modify basal IGF-I levels or the GH response to exercise in both middle-aged and young subjects. In the latter group, our results agree with those of previous cross-sectional studies (23–25), in which no differences between the GH response to acute aerobic exercise were found comparing trained and sedentary young adults. In older people, reports are contradictory. In sedentary older subjects, Hagberg et al. (11) found that 12 weeks of aerobic exercise training improved the GH response to acute exercise, although this response was lower than that of trained or sedentary younger subjects. In the same study, however, IGF-I levels did not change in older subjects. Moreover, it has been shown that 12 weeks of resistance strength training failed to increase the postexercise GH concentration (12).

In a more recent cross-sectional study, Ambrosio et al. (15) showed an increased GH responsiveness to GHRH in active older subjects compared with that in paired sedentary controls, suggesting that chronic participation in physical activity can attenuate the age-associated deficit in GH/IGF-I levels. However, it must be observed that in this study, the waist/hip ratio was higher in sedentary than in trained subjects; thus, differences in body composition could have influenced the results.

Differences in methods and in recruitment of subjects can explain different results for the effect of training on the GH response to exercise. Our subjects were early middle-aged, younger than those in Hagberg’s study (11), and were not sedentary, but normally engaged in regular physical activity. The first test was performed during their lowest level of physical fitness, and the second was performed after a 4-month period of vigorous training. Moreover, even if the level of physical activity and the absolute training volume were greater in the young group, the improvement in fitness was similar in the two groups, as demonstrated by the similar and significant increases in the VO₂max and maximal work capacity. We cannot estimate the exact functional impact of these two factors on the GH responsiveness to our exercise test, but in our opinion, the blunted GH response to exercise is probably more dependent upon an aging effect than upon a different level of physical activity. The unchanged IGF-I levels also sustain this hypothesis.

There is evidence that the age-related decline in GH release may reflect either an increase in the hypothalamic somatostatin content or a progressive decrease in the secretion or action of GHRH (7, 15, 26) and that the exercise-induced GH release depends on an increase in endogenous GHRH, probably mediated by an increase in the central adrenergic tone (27). Our data do not explain how the GH response to exercise is blunted in early middle-aged subjects. Further investigations should clarify this.

In conclusion, early middle-aged subjects, compared with young people, show a blunted GH response to graded exhaustive exercise that is not changed by 16 weeks of intensive training. This physiological test gives evidence of the low secretary GH response in early middle age, as previously suggested by some studies with pharmacological stimuli. Thus, the known age-related decline in GH release is also substantial in early middle age.

References


Second International Symposium on Vertebrate Sex Determination
Honolulu, Hawaii
April 10–14, 2000

The second symposium on the biology of sex determination in the vertebrates will be held at the Hawaii Prince Hotel, Honolulu, from April 10th to April 14th, 2000. The symposium will cover the process of sex determination in vertebrate animals from fish to humans. For an idea of the range of topics covered please consult the proceedings of the first symposium held in 1997, which are published in J. Exptl. Zool. 281(5):357–530, 1998. Contributed papers on any topic in sex determination are welcome. Presentations may be oral or poster. Attendance at the second symposium will be limited to 200.

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