The impact of sex and exercise duration on growth hormone secretion

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Abstract:

Previous research clearly indicates a linear relationship between exercise intensity and growth hormone (GH) release and that this relationship is influenced by sex. The present study examined the GH response to increasing exercise duration in young men and women. Fifteen healthy subjects (8 men and 7 women) completed three randomly assigned exercise sessions (30, 60, and 120 min) at 70% of peak oxygen consumption. Blood samples were collected every 10 min beginning 30 min before exercise, for a total of 240 min. Total integrated GH concentration (IGHC) increased with increasing exercise duration for men and women (601, 1,394, and 2,360 µg/l·4 h; 659, 1,009 and 1,243 µg/l·4 h for 30, 60, and 120 min of exercise, respectively). Regression analysis revealed that IGHC (logarithmically transformed) was significantly influenced by exercise duration (logarithmically transformed) (120 min > 60 min > 30 min) and that a significant sex-dependent effect was present even after adjustments for fitness level and percent body fat (men > women). The slope of the regression line was greater for men than for women (1.003 vs. 0.612; $P = 0.013$), but the average height of the regression line was greater for women (7.287 vs. 6.595; $P < 0.001$). Although GH secretory pulse half-duration was greater in women ($P = 0.001$), and GH half-life was greater in men ($P = 0.001$), they were not affected by exercise duration. The total mass of GH secreted during exercise increased with exercise duration ($P < 0.001$) but was not affected by sex ($P = 0.137$). Results from the present investigation indicate that when exercise intensity is constant, exercise duration significantly increases IGHC and that this relationship is sex dependent.

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Article:

It is well established that exercise is a consistent, robust stimulator of growth hormone (GH) release (5, 11, 26, 43, 46). Although fitness level, age, and sex clearly influence exercise-induced GH secretion (17, 37, 41), exercise intensity and duration are likely to be the key factors that determine the magnitude of the exercise-induced GH response.

At rest, women exhibit a less orderly pattern of GH secretion (25) and an approximately twofold higher GH amplitude and mass of GH secreted per burst, with comparable GH half-life and pulse frequency for men and women (34). Women and men have a similar pattern of GH response to exercise (26, 44), but women have been shown to attain peak GH concentrations sooner then men (46). When exercise duration is held constant, exercise intensity induces GH release in a linear dose-dependent fashion, although women had higher concentrations of GH at any given exercise intensity (26). Increasing GH release with increasing exercise intensity has been mechanistically attributed to increased mass of GH secreted per burst, with minimal changes observed in GH half-life (26, 42).

Most studies investigating the influence of exercise duration have focused on the minimal exercise duration required to stimulate GH release. Results suggest a range of values, from <10 min to >15 min of exercise being required to elicit an initial rise in GH release (8, 11, 21, 22, 24, 29, 30, 32). The inconsistencies in the findings are probably due to differences in the exercise intensity employed in different studies. Only a few studies have investigated the effects of longer exercise durations on GH release (4, 24, 39), and only two controlled for exercise intensity throughout the exercise bout (4, 39). However, neither of these studies systematically examined the effects of exercise duration on GH release. This is particularly important given the recent guidelines from the Institute of Medicine suggesting that previous recommendations of 30 min of physical activity most days of the week may be inadequate for some individuals (3). The new guidelines suggest that 60 min of moderate-intensity exercise may be required by some individuals for weight maintenance, whereas as much as 90 min of exercise may be required for fat loss in overweight or obese individuals (3). Given the blunted GH response to 30 min of exercise in obese (20, 47) and older adults (42) and the influence of GH on postexercise fat oxidation (12, 27), understanding the GH response to increased exercise duration in young, healthy men and women is an important first step toward proper exercise prescription for individuals with altered GH release.

In the present study, we investigated the effect of exercise duration, at a constant intensity, on GH secretion in young adult men and women. We hypothesized that longer exercise durations would result in greater GH release and that young women would have greater exercise-induced GH release at any given duration compared with young men. We also hypothesized that the increase in GH secretion would largely be due to increased mass of GH secreted per pulse.

METHODS

Subjects. Fifteen healthy subjects (8 men and 7 women) participated in the present investigation. All subjects completed a detailed medical history and provided written informed consent for participation in this study that was approved by the Institutional Review Board at the University of North Carolina at Greensboro. Subjects were nonsmokers, were not taking medications or hormones known to alter GH release, were habitual aerobic exercisers (>30 min/day, 3–4 times/wk), and had completed at least 1 exercise session longer than 60 min within the last month. None of the women were taking oral contraceptives. Men reported training an average of 1.9 h per day, 5.5 days per week, whereas women reported an average of 1.4 h of training per day, 4.7 days per week. Women were more likely to cross-train, and all of them reported

resistance training as a part of their habitual training program. Only one man reported resistance training regularly, and four men reported that cycling was their only mode of exercise. Body weight was determined using a Detecto beam scale (Brooklyn, NY) accurate to 0.1 kg, and height was determined using a Seca stadiometer accurate to 0.1 cm. Body composition was estimated with Harpendon skinfold calipers using the standard methods outlined in the Anthropometric Standardization Reference Manual (14). All skinfold measures were taken in triplicate, and body fat percent was calculated using the Jackson-Pollock 7-site skinfold equation (1). We recognize that this is an estimate of body fat percent and not a criterion measure of body composition.

$\dot{V}o_{2\,peak}$ assessment. Subjects completed a maximal cycle ergometer graded exercise test (Lode Excalibur, Seattle, WA) to determine peak oxygen consumption ($\dot{V}o_{2\,peak}$). After a 2- to 3-min warm-up period, power output (PO) was set at 100 W for men and 50 W for women. PO increased 50 W every 2 min for men and 25 W every 2 min for women until volitional fatigue or when pedaling rate fell below 50 rpm.

Metabolic measures were collected during the $\dot{V}o_{2\,peak}$ and constant-load exercise tests using standard open-circuit spirometric techniques (Vmax 229, SensorMedics, Yorba Linda, CA). Heart rate was determined using a Polar a5 heart rate monitor (Polar Electro, Woodbury, NY), and the subject was asked to give a rating of perceived exertion (RPE) at the end of each stage. $\dot{V}o_{2\,peak}$ was chosen as the highest mean 1-min $\dot{V}o_2$ value attained during testing. All subjects attained respiratory quotient values >1.0, and maximum heart rate (HR) was achieved, expressed as a percentage of age-predicted maximum, was >90% for men (average 96.3 ± 3.6%) and women (average 92.8 ± 3.5%). Submaximal PO values were calculated at 60, 65, and 70% of $\dot{V}o_{2\,peak}$. After recovery, each subject cycled for 5 min at the PO predicted to elicit 60, 65, and 70% $\dot{V}o_{2\,peak}$. This step was completed to ensure that oxygen consumption ($\dot{V}o_2$) values would be within the proper range for the constant-load exercise session.

Constant-load exercise. The constant-load exercise sessions consisted of randomly assigned cycling sessions at 70% of $\dot{V}o_{2\,peak}$ for 30, 60, or 120 min. At least 48 h of rest were required between submaximal constant-load sessions; all sessions were completed in the morning (0600–0800 start time), after an overnight fast; and women were tested in the early follicular phase of the menstrual cycle (*days 1–8*, requiring 2–3 menstrual cycles for completion of all 3 exercise sessions). There was <30-min variation in the start time for the three exercise sessions for a given subject. After arriving at the laboratory, subjects were weighed and then rested in a supine position for ~5 min. A venous cannula was placed in an antecubital vein, and resting blood samples were taken. Blood samples were taken every 10 min throughout the 240-min session. After 30 min of rest, subjects moved to the cycle and warmed up at 50% of $\dot{V}o_{2\,peak}$ and slowly increased to 70% of $\dot{V}o_{2\,peak}$ by 5 min. Subjects then completed 30, 60, or 120 min of exercise at 70% $\dot{V}o_{2\,peak}$, followed by a 1-min cool-down at 50% $\dot{V}o_{2\,peak}$. During exercise, $\dot{V}o_2$ was measured by breath-by-breath analysis and was recorded as 1-min averages. At 15-min intervals, $\dot{V}o_2$ measures were assessed, and PO was adjusted to maintain exercise intensity at 70% $\dot{V}o_{2\,peak}$. When necessary, PO was reduced so that subjects could complete the entire exercise duration. HR was monitored continuously using a Polar HR monitor, and RPE was recorded at 15 min intervals. Average HR and RPE were calculated for each exercise session. At the completion of exercise, subjects rested quietly in the laboratory while blood sampling continued. Total work,

end-exercise $\dot{V}_{O_2}$ (over last 5 min), and total caloric expenditure were calculated for each trial. Total caloric expenditure was calculated as follows: kilocalories = total $\dot{V}_{O_2}$ (liters) × 5.

Assays. All samples were collected in red-top vacutainers and allowed to clot at room temperature for 30 min. Samples were centrifuged at 1,500 *g* for 15 min, separated into multiple aliquots, and stored at −80°C. At the conclusion of the study, samples were shipped to the Core Laboratory facilities at the General Clinical Research Center at the University of Virginia for measurement of GH. GH concentrations in serum samples were measured using a validated ultrasensitive (0.005 µg/l threshold) chemiluminescence-based assay (Nichols, San Juan Capistrano, CA) (6, 18). The chemiluminescent assay detects predominantly the 22-kDa form of GH and has a cross-reactivity level of 34% for 20-kDa GH (methionylated). The intra-assay coefficient of variation (CV) for the GH assay was 6.0%, and the interassay CV was 9.9%. Estradiol was measured using an enzyme immunoassay from DSL (DSL-10-4300, Webster, TX), and all samples were measured in a single assay. Intra-assay CV for the estradiol assay was 7.4%.

Deconvolution analysis. A multiple-parameter deconvolution method was used to estimate pulsatile attributes of GH secretion from the measured serum GH concentrations (19). A pulse of underlying GH secretion was approximated algebraically by a Gaussian distribution (35). Basal secretion was estimated concurrently with a subject-specific two-component half-life for endogenous GH. The first component of the half-life was fixed at 3.5 min, and the second component was subject specific. Deconvolution was performed as outlined previously (45), and overdetermination of GH pulses was avoided by eliminating any successive GH pulses that were separated by less than two sampling intervals (20 min). In addition, any pulses outside the sampling window (0–240 min) by more than one sampling interval (10 min) were eliminated. Integrated GH concentration (IGHC) was calculated using trapezoidal integration. Total mass of GH secreted during exercise was calculated as the sum of GH area under all pulses during 30, 60, and 120 min of exercise, and GH production rate was calculated by multiplying the number of GH pulses by GH mass per pulse. Mean GH concentration was calculated for exercise plus the first 60 min of recovery (time used for determining the average was 90, 120, and 180 min, respectively, for the 3 sessions).

Statistical analysis. All data were analyzed by way of parametric statistical methods. Specifically, the deconvolution data and the constant-load exercise data were analyzed by way of mixed-effects repeated-measures ANOVA. Data for IGHC were also analyzed by way of random coefficient regression. The baseline data were analyzed by way of one-way ANOVA.

The model specification for the ANOVA included two categorical variables, sex and exercise duration (30, 60, and 120 min). Sex by exercise duration interaction was also modeled. Because of the repeated-measures design, the variance-covariance matrix of the ANOVA was modeled in the spatial power form, a form that is appropriate for unequally space repeated measures.

Linear contrasts of the mean response were used to test our a priori hypotheses. All of the statistical tests were two sided with the alpha level of the test set at 0.05. The multiple comparison type I error rate adjustment was based on Fisher's restricted least significant difference criterion.

The specification of the random coefficient regression model for the analysis of IGHC included one categorical variable (sex) and three continuous variables (percent body fat, exercise duration, and $\dot{V}_{O2\,peak}$). The variance-covariance matrix was model in the spatial power form. Confidence intervals for the regression coefficients were constructed based on the t-statistic multiplier. The Working-Hotelling multiplier was used to construct the simultaneous confidence bands for estimating the population mean profile for $\log e$ (IGHC) as a function of $\log e$ (exercise duration) after adjustment for percent body fat and $\dot{V}_{O2\,peak}$.

The ANOVA models for analyzing the subjects' baseline characteristics included a single categorical variable, the sex of the subject. All of the hypothesis tests from the ANOVA were two-sided with the alpha level of the test set at 0.05.

Several of the response variables were statistically analyzed on the natural logarithmic scale. This scale transformation was carried out when residual diagnostics indicated that the data were log-normally distributed. For these variables, the ANOVA estimates for the difference between the least squares means were exponentiated so that the comparison could be presented in the form of a ratio of the geometric means. The geometric mean is a location parameter similar to the arithmetic mean and median, and the ratio of geometric means is often referred to as a fold change in the response.

The PROC MIXED procedure of SAS version 9.1 (SAS Institute, Cary, NC) was used to conduct all of the statistical analyses.

RESULTS

Subject characteristics are shown in Table 1. Men were significantly taller ($P = 0.004$), were more fit ($P < 0.001$), and had less body fat ($P = 0.008$) than women, but men and women were similar in age and weight.

Table 1. Subject characteristics for men and women

	Men ($n = 8$)	Women ($n = 7$)
Age, yr	27 (4)	27 (6)
Height, cm	179.8 (5.9)	170.1 (4.8)*
Weight, kg	71.9 (9.0)	64.8 (6.9)
Percent body fat, %	11.3 (2.9)	18.3 (5.6)*
$\dot{V}_{O2\,peak}$, l/min	4.09 (0.26)	2.33 (0.24)*
$\dot{V}_{O2\,peak}$, ml·kg^{-1}·min^{-1}	57.43 (5.33)	36.5 (5.83)*

*$P < 0.005$ Values are means (SD); n, no. of subjects. $\dot{V}_{O2\,peak}$, peak oxygen consumption

Table 2 reports total work completed, calories expended, mean end-exercise $\dot{V}_{O2}$, average HR, average RPE, and end-exercise $\dot{V}_{O2}$ expressed as a percentage of $\dot{V}_{O2\,peak}$ (%EE/$\dot{V}_{O2\,peak}$) for men and women for each exercise duration. As expected, total work and kilocalories increased significantly with exercise duration ($P = 0.005$). Average HR was similar for men and women ($P = 0.186$) and for each exercise trial ($P = 0.876$), despite differences in PO. Average RPE was similar for men and women ($P = 0.35$) and increased with longer exercise duration ($P = 0.003$).

Both sex ($P < 0.001$) and exercise duration ($P = 0.001$) significantly influenced total kilocalories and end-exercise $\dot{V}o_2$ values. As expected, men had higher absolute end-exercise $\dot{V}o_2$ values than women ($P < 0.001$). End-exercise $\dot{V}o_2$ was lower at the end of 120 min of exercise than at the end of the 30- and 60-min exercise sessions for both men and women ($P < 0.001$). All subjects required a reduction in PO to complete the 120-min exercise session. When decreases in PO were expressed as a percentage of the initial PO, the drop was $34.8 \pm 12.9\%$ for men and $36.4 \pm 4.6\%$ for women ($P = 0.77$) and when end-exercise $\dot{V}o_2$ was expressed as a percentage of $\dot{V}o_2$ peak, exercise duration affected $\%EE/\dot{V}o_2$ peak ($P = 0.001$). A significant reduction in the $\%EE/\dot{V}o_2$ peak was observed during 120 min of exercise ($P < 0.001$), with no significant sex differences in exercise time completed before the reduction in PO (34.8 ± 14.3 min for men and 27.4 ± 10.7 min for women; $P = 0.139$).

Table 2. Sex comparisons for the constant-load aerobic exercise sessions

	30 min		60 min		120 min	
	Men	Women	Men	Women	Men	Women
Total work,* kJ	368 ± 11	224 ± 7	698 ± 17	423 ± 18	1174 ± 44	726 ± 28
Total kilocalories*†	425.7 ± 11.1	241.6 ± 11.5	835.8 ± 19.9	494.6 ± 17.8	$1,497.0 \pm 77.9$	889.7 ± 35.6
Average heart rate, beats/min	164 ± 11	151 ± 13	158 ± 3	155 ± 16	160 ± 10	153 ± 14
Average RPE*	13.6 ± 1.5	14.9 ± 2.2	14.8 ± 1.7	15.1 ± 1.5	15.2 ± 2.2	16.0 ± 1.3
End-exercise						
$\dot{V}o_2$,*† ml·kg^{-1}·min^{-1}	40.33 ± 1.76	24.77 ± 1.11	39.32 ± 2.68	24.42 ± 1.44	35.46 ± 2.71	19.19 ± 1.02
End-exercise/$\dot{V}o_2$ peak,* %	70.2 ± 2.2	68.7 ± 3.1	68.2 ± 3.5	67.2 ± 2.1	61.7 ± 4.2	53.2 ± 2.7

Values are means $\pm$ SD. RPE, rating of perceived exertion; $\dot{V}o_2$, oxygen consumption. *$P < 0.005$, exercise duration effect. †$P < 0.001$, sex effect.

Figure 1 shows the mean serum GH concentrations from blood sampled at 10-min intervals over 4 h for the three exercise conditions in women (*A*) and men (*B*). The peak serum GH concentrations for women were 10 ± 1.1, 13 ± 1.5, and 14 ± 1.4 µg/l for 30, 60 and 120 min of exercise, respectively. The corresponding values in men were 13 ± 1.3, 22 ± 5.4, and 24 ± 5.3 µg/l. Peak GH attained was significantly influenced by both exercise duration (60 min and 120 min > 30 min; $P = 0.003$) and sex (men > women; $P = 0.039$). Time to reach peak GH concentration, measured from the onset of exercise, was similar for men and women for the 30-min exercise session (32.5 ± 1.6 and 32.9 ± 3.6 min, respectively). Time to reach peak GH concentration for 60 and 120 min of exercise was 37.1 ± 4.7 and 38.6 ± 4.6 min for women and 50.0 ± 4.2 and 53.8 ± 7.8 min for men, but this difference did not attain statistical significance ($P = 0.094$). Time to reach peak GH concentration was significantly influenced by exercise duration, with the times for 60 and 120 min being greater than for 30 min ($P = 0.003$).

Total IGHC over 4 h increased in an exercise duration-dependent manner (601 ± 65.4, $1,394 \pm 312.3$ and $2,360 \pm 480.0$ µg/l·4 h in men and 659 ± 89.0, $1,009 \pm 139.1$ and $1,243 \pm 139.1$ µg/l·4 h in women for exercise durations of 30, 60, and 120 min, respectively). IGHC was significantly influenced by exercise duration (120 min > 60 min > 30 min) ($P < 0.001$), but it was not influenced by sex ($P = 0.21$). However, there was a trend for a sex × exercise duration interaction on IGHC ($P = 0.059$). A similar response pattern was observed for mean GH concentration calculated for exercise plus the first 60 min of recovery (Table 3). Mean GH concentration was significantly influenced by exercise duration (120 min > 60 min > 30 min) ($P < 0.001$) but not by sex ($P = 0.10$). As observed with IGHC, there was a trend for a sex by exercise duration interaction with mean GH concentration ($P = 0.068$).
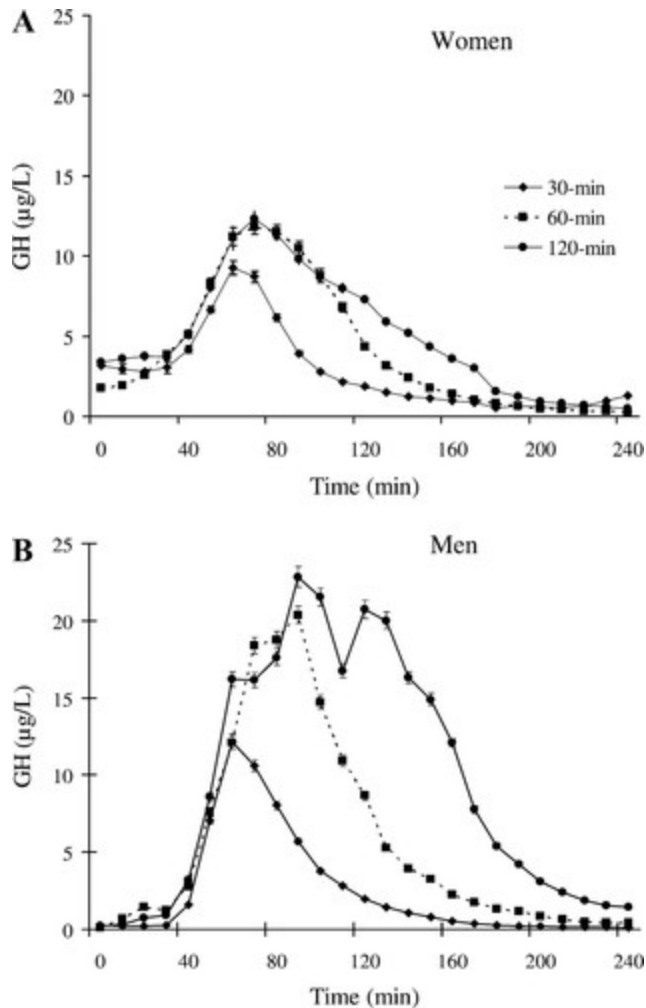
Fig. 1. Serum growth hormone response profiles for women (*A*) and men (*B*) for 30, 60, and 120 min of exercise. Values are means ± SD.

Table 3. Effects of increasing exercise duration on measures of GH secretion during 4 h of blood sampling in young men and women as determined by deconvolution analysis

	30 min		60 min		120 min	
	Men	Women	Men	Women	Men	Women
IGHC,[c] μg/l·4 h	601±65.4	659±89.0	1,394±312.3	1,009±139.1	2,359±480.0	1,243±139.1
Mean GH,[a,c] μg/l	5.39±0.57	4.76±0.55	7.73±0.76	6.79±0.92	12.14±2.48	6.29±0.59
Half-duration,[b,f] min	16.7±1.1	22.4±1.8	15.3±2.6	24.0±3.0	17.2±1.3	21.3±1.9
Half-life,[c,f] min	17.9±0.8	13.5±1.4	21.5±1.7	14.1±1.9	20.8±2.0	17.7±1.6
No. of GH pulses[g]	1.8±0.3	3.3±0.6	4.0±0.4	3.6±0.5	4.8±0.5	4.1±0.5
GH mass/burst, μg/l	27.0±3.7	23.7±5.0	31.5±12.8	30.0±7.7	24.3±3.7	16.1±1.7
Production rate,[e] μg/l·4 h	30.7±3.5	38.0±5.5	82.1±34.0	67.4±15.2	92.7±12.2	30.7±3.5
Peak GH,[e,f] μg/L	13.3±1.3	9.9±1.1	22.4±5.3	13.1±1.5	24.3±5.3	13.5±1.4
Time to peak GH,[d,e] min	32.5±1.6	32.9±3.6	50.0±4.2	37.1±4.7	53.8±7.8	38.6±4.6

Values are means ± SD. GH, growth hormone; IGHC, integrated GH concentration, [a]Mean GH secreted during exercise and first 60 minutes of recovery. [b]Half-duration is calculated as SD · 2.354. [c]Second-component half-life (First-component half-life held constant at 3.5 min). [d]Time measured from the onset of exercise. [e]$P < 0.05$, exercise duration effect. [f]$P < 0.05$, sex effect. [g]$P < 0.005$, sex difference during 30-min trial.

Figure 2 depicts the regression of log (IGHC) and log (exercise duration) for men and women. Because there were significant sex differences in fitness level and percent body fat and because these markers have been shown to alter GH production, we included the factors in the random

coefficient regression model. When log (exercise duration) was used as the primary variable of interest, the P values for the tests of interaction of sex with fitness level and sex with percent body fat were not significant ($P = 0.428$ and $P = 0.579$, respectively). Thus, although fitness level and percent body fat influence GH production, the influence was approximately equal in men and women and these factors were given equal weighting in the regression equations, regardless of sex. However, even after these adjustments, the regression of log (IGHC) and log (exercise duration) was significantly influenced by sex ($P = 0.013$). The slope of the regression line was greater for the men than for the women {1.003 [95% confidence interval (CI) (0.794, 1.212)] vs. 0.612 [95% CI (0.356, 0.868)]; $P = 0.013$}, but the average height of the regression line was greater for women than for men {7.287 [95% CI (6.950, 7.624)] vs. 6.595 [95% CI (6.291, 6.899)]; $P < 0.001$}.
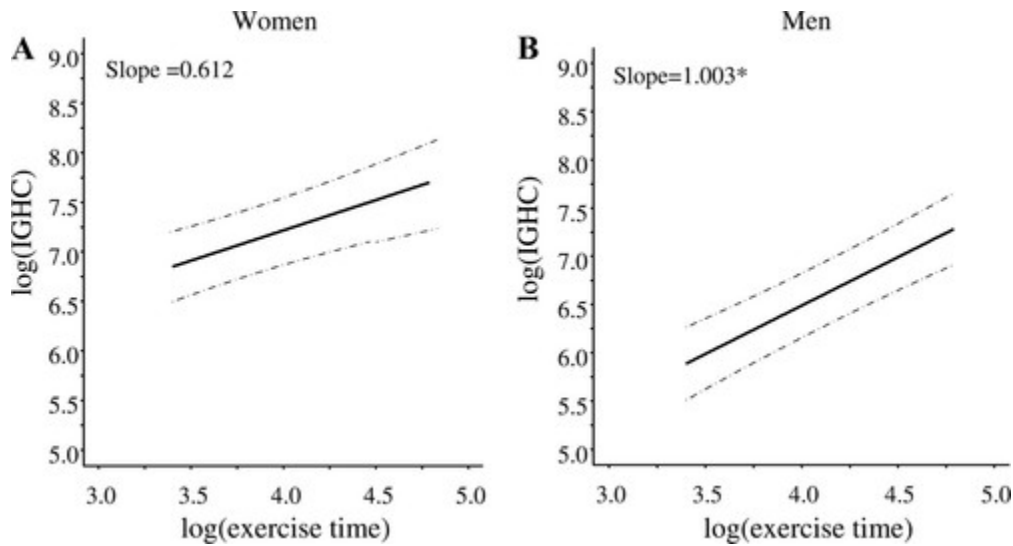
Fig. 2. Regression for log [(IGHC)] with log (exercise time) for women (*A*) and men (*B*). Slope and 95% confidence intervals (dotted lines) are given as log values. Equation for the relationship in women is log e (integrated GH concentration) = log $e^{4.086}$(time)$^{\cdot 0.612}$(peak oxygen consumption)$^{\cdot 0.731}$(%fat)$^{-0.722}$ and for men is log e (integrated GH concentration) = log $e^{1.796}$(time)$^{\cdot 1.003}$(peak oxygen consumption)$^{\cdot 0.731}$(%fat)$^{-0.722}$.

Table 3 presents the deconvolution results for men and women for each of the exercise bouts. GH secretory pulse half-duration and GH half-life were significantly influenced by sex ($P = 0.001$ and $P = 0.001$, respectively), but they were not changed by exercise duration. GH secretory pulse half-duration was greater in women than in men ($P = 0.001$), whereas GH half-life was consistently greater for men than women ($P = 0.001$). The total mass of GH secreted and GH production rate were influenced by exercise duration ($P < 0.001$ for both), but they were not influenced by sex ($P = 0.238$ and $P = 0.63$). Production rate of GH during 60 and 120 min of exercise was similar, but it was greater than the GH production during 30 min of exercise. A similar pattern was observed for total mass of GH secreted. Men had more GH pulses than women during 60 and 120 min of exercise, but men had significantly fewer GH pulses during the shortest exercise trial (30 min; $P = 0.004$). The GH mass secreted per burst was not influenced by sex ($P = 0.36$) or exercise duration ($P = 0.40$).

Estrodiol (E_2) levels were measured in each woman at baseline for each exercise session and did not significantly differ across trials ($P = 0.45$) (average E_2 was 93.0 ± 11.0, 105.2 ± 14.8, and 82.7 ± 9.3 pg/ml for the 30-, 60-, and 120-min exercise sessions, respectively).

DISCUSSION

The major findings of the present investigation indicate that in young men and women when exercise intensity is controlled, the relationship between IGHC and exercise duration (logarithmically transformed) is linear (up to 120 min of exercise) and sex dependent even after controlling for fitness and percent body fat.

To our knowledge, this is the first study to systematically compare the influence of exercise duration on GH secretion in young men and women. Previous studies observed a continual increase in GH concentration until ~60 min of exercise (4, 24, 39), but only one study completed an exercise session longer than 60 min. Viru et al. (39) reported a nonsignificant drop in GH concentrations from 60 to 120 min, but no information about the pattern of GH release was available, because GH samples were taken only at 60 and 120 min of exercise. Frequent sampling during exercise in the present study confirms steady increases in GH concentration until 60 min of exercise was completed (90 min into the protocol); continued exercise resulted in a plateau or slight decline in GH in both men and women. This corroborates previous research indicating that the pattern of exercise-induced GH secretion is independent of sex (4, 5, 26, 42, 43, 46), despite well-documented sex-dependent differences in GH secretion at rest (9, 13, 15, 25, 31, 33, 46) and large interindividual variability in GH (10, 11, 43).

Our regression analysis revealed that when log transformed, the slope of the regression line for IGHC and exercise duration was greater for men compared with women. This is antipodal to our original hypothesis that women would have greater GH release at any given exercise duration. Because the women in the present study were less fit and had greater percent body fat than the men and previous research has shown that body fat and fitness level alter GH release (7, 37, 41), we investigated whether or not body fat and fitness level were the primary cause of the sex-dependent differences in the slope of the regression line. Further analysis revealed that even after adjustments for fitness and body fat, there was a sex-specific influence on the regression of log (IGHC) and log (exercise duration) ($P = 0.013$), with men having a greater slope than women. These analyses clearly show that other sex-dependent factors are important for determining the exercise-induced GH response when exercise duration is increased in a systematic fashion.

Previous research indicates that submaximal aerobic exercise-induced GH release may not adhere to the normal autofeedback pattern and may partially "break through" GH autofeedback (21, 38). Veldhuis et al. (38) reported that despite significant negative feedback during exercise, marked stimulation of GH secretion still occurred with exercise in both women and men, indicating that feedback resistance with exercise is partial, not complete. Only two studies have directly compared the sensitivity of the GH autofeedback system in men and women (36, 38). When pharmacological concentrations of GH (>100 ng/ml) were used, women had markedly greater fractional feedback inhibition of pulsatile GH secretion at rest. Although suppression of exercise-induced GH secretion was significant and equivalent in both men and women, it was only partial (38). When physiological concentrations of GH were used at rest, the extent of

suppression of GH secretory-burst mass was less in young women than in men, but this study did not include an exercise stimulus (36). Studies employing recombinant human GH infusions to investigate GH autofeedback have consistently reported decreases in GH secretion within 120 min of infusion (2, 28, 36, 38). This could suggest that during prolonged exercise, the declining GH secretion may be partially related to autofeedback. As suggested by Veldhuis et al., this feedback inhibition is only partial, because GH pulses continued to be observed throughout the entire 120 min of exercise in both men and women, indicating continued stimulation of GH secretion despite significantly elevated circulating GH. Compared with women, men had greater peak GH concentrations, greater mean GH concentrations (calculated for exercise plus the first 60 min of recovery), and greater IGHC with the longer exercise durations (60 and 120 min), with minimal sex differences observed during 30 min of exercise. It is possible that during longer durations of exercise, women may be more sensitive to fractional feedback inhibition from GH secretion than men, regardless of the GH concentration attained.

Increasing exercise intensity results in a sex-dependent, positive linear increase in GH release, with young women exhibiting greater GH release compared with young men at all exercise intensities and increased GH secretion mechanistically attributable to increased mass of GH secreted per burst (26, 42). In contrast, systematic increases in exercise duration resulted in significantly greater GH secretion in young men compared with young women (slope = 1.003 vs. 0.612, for men and women). Mechanistically, the increase in GH secretion appears to be largely related to an increased number of GH pulses with increasing exercise duration in men. This contradicts our original hypothesis that increases in GH secretion would be mechanistically due to increased mass of GH per burst. In women, a combination of changes occurred that resulted in increased GH secretion with increasing exercise intensity, but pulse number did not increase as significantly as it did for men. This corroborates our suggestion that during longer durations of exercise, women may experience greater fractional feedback inhibition of GH secretion then men.

During exercise, peripheral markers of heightened adrenergic outflow (epinephrine and norepinephrine) have been shown to be correlated to exercise-intensity-dependent GH release and thus implicated as a possible moderator of exercise-induced GH release (40). Horton et al. (16) reported that during 120 min of exercise at 40% of maximal $\dot{V}o_2$, epinephrine and norepinephrine were significantly greater in men than women. Stimulation of α_2-adrenoreceptors with an agonist such as clonidine results in GH release by decreasing somatostatin release and increasing GH-releasing hormone release, and this α_2-adrenoreceptor mediated GH release is significantly higher in young men than young women (23). Although we did not measure peripheral catecholamine concentrations in the present study, it is possible that higher exercise-induced GH concentrations observed in men with increasing duration of exercise may be partially due to sex-dependent differences in exercise-induced catecholamine release.

Because of the slow component of $\dot{V}o_2$ (e.g., oxygen drift) associated with higher exercise intensities, reductions in PO were necessary for all subjects to maintain exercise intensity at 70% $\dot{V}o_{2\ peak}$ throughout exercise. Average HR was similar for all the exercise sessions, which suggests that even when $\dot{V}o_2$ was slightly below the intended intensity, the stress on the cardiovascular system was similar. Average RPE data also suggest that despite drops in PO, subjects perceived the work to be hardest in the 120-min exercise session. Although total work

completed and %EE/$\dot{V}o_{2\,peak}$ were not influenced by sex ($P = 0.094$ and $P = 0.272$, respectively), men did maintain a slightly higher intensity at the end of the 120-min bout of exercise. Therefore, given the influence of exercise intensity in determining GH secretion (26, 42), we cannot completely negate this nonsignificant difference as a partial mediator of GH secretion in the present study. Also, it is possible that because women were more likely to cross-train then men and were less likely to cycle exclusively as their mode of exercise, we did not obtain a true $\dot{V}o_{2\,peak}$ for the women in the study. When we investigated this possibility we found that women were just as likely to meet the criteria for achieving $\dot{V}o_{2\,peak}$ as men. Thus, although we acknowledge that we may not have achieved a true $\dot{V}o_{2\,peak}$ for all subjects, the issue does not appear to be sex specific.

In summary, it appears that both intensity and duration of exercise are important modulators for determining the magnitude of the exercise-induced GH response, but the overall importance of either factor may be influenced by the sex of the individual performing the exercise. These results have implications for exercise prescription because intensity of exercise appears to be more influential in determining the magnitude of the exercise-induced GH response in young women, whereas exercise duration appears more influential in young men. If current physical activity recommendations for weight loss favor longer durations of exercise (60–90 min), then consideration must be given to how this influences the hormonal and metabolic responses. This is particularly important because previous research indicates that the postexercise fat oxidation rate is directly related to GH release (12, 27). Thus the optimal combination of exercise intensity and duration that will increase the GH response to exercise may be particularly critical for older and obese adults in whom the GH response to exercise is impaired (20, 42).

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