

Endurance training amplifies the pulsatile release of growth hormone: effects of training intensity

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WELTMAN, ARTHUR, JUDY Y. WELTMAN, ROBERT SCHURRER, WILLIAM S. EVANS, JOHANNES D. VELDHUIS, AND ALAN D. ROGOL. *Endurance training amplifies the pulsatile release of growth hormone: effects of training intensity.* J. Appl. Physiol. 72(6): 2188–2196, 1992.—The effects of intensity of run training on the pulsatile release of growth hormone (GH) were investigated in 21 eumenorrheic untrained women. The $\dot{V}O_2$ consumption ($\dot{V}O_2$) at the lactate threshold (LT); fixed blood lactate concentrations (FBLC) of 2.0, 2.5, and 4.0 mM; peak $\dot{V}O_2$; maximal $\dot{V}O_2$; body composition; and pulsatile release of GH were measured. Subjects in both the at-lactate threshold (@LT, $n = 9$) and above-lactate threshold (>LT, $n = 7$) training groups increased $\dot{V}O_2$ at LT and FBLC of 2.0, 2.5, and 4.0 mM and $\dot{V}O_{2\max}$ after 1 yr of run training. However, the increase observed in the >LT group was greater than that in the @LT group ($P < 0.05$). No change was observed for the control group ($n = 5$). No among- or within-group differences were observed for body weight, although trends for reductions in percent body fat ($P < 0.06$) and fat weight ($P < 0.15$) were observed in the >LT group, and both training groups significantly increased fat-free weight ($P < 0.05$). Significant differences ($P < 0.05$) in the pulsatile release of GH were observed within the >LT group, as a result of 1 yr of run training, for maximal peak height (7.4 $\mu\text{g/l}$ pre vs. 13.1 $\mu\text{g/l}$ post), incremental peak amplitude (6.8 $\mu\text{g/l}$ pre vs. 10.3 $\mu\text{g/l}$ post), peak area (340 $\mu\text{g}\cdot\text{l}^{-1}\cdot\text{min}^{-1}$ pre vs. 598 $\mu\text{g}\cdot\text{l}^{-1}\cdot\text{min}^{-1}$ post), nadir GH concentration (0.60 $\mu\text{g/l}$ pre vs. 2.2 $\mu\text{g/l}$ post), and integrated (24-h) concentration of GH (4,390 $\mu\text{g}\cdot\text{l}^{-1}\cdot\text{min}^{-1}$ pre vs. 7,710 $\mu\text{g}\cdot\text{l}^{-1}\cdot\text{min}^{-1}$ post). No changes were observed for these variables within the @LT or control group. Results of the present study indicate that exercise training amplifies the pulsatile release of GH. This effect occurs when some training is above the LT. Our findings may have clinical implications in conditions characterized by impoverished pulsatile secretion of GH.

exercise; lactate threshold; maximal oxygen consumption

THE GROWTH HORMONE (GH) response to acute exercise has been studied extensively (4, 5, 8, 9, 16, 25, 30, 34). The mechanism underlying this response is not well understood; however, most investigators have reported that acute bouts of exercise increase the plasma concentration of GH (4, 5, 8, 9, 16, 25, 30, 34). Several investigators have suggested that intensity and duration of acute exercise, work output during exercise, muscle mass used during exercise, and training state all influence the GH response to exercise (4, 5, 9, 30, 34). Intensity of exercise may have a key role, with a threshold of exercise inten-

sity necessary before a significant rise in GH levels is detected (5).

Less information is available, however, regarding the effects of chronic exercise training on GH levels (4, 5, 18). Many of the studies that compare training state and GH response indicate that training may blunt the GH response to acute exercise (9, 18, 30). However, most of these studies are cross-sectional and may not be controlled for differences in gender, cardiovascular fitness, and the intensity and/or duration of the evaluation protocol. Furthermore, there are no data available with regard to the effects of exercise training on the pulsatile release of GH at rest. The pulsatile mode of GH release at rest is of particular importance physiologically, because pulsatile delivery of GH is more effective than continuous administration in inducing certain specific tissue responses to GH in muscle, bone, and liver (14, 15), and the pulsatile mode of GH release is strongly modulated in conditions accompanied by accelerated growth (19–21).

In view of the reported relationships between GH availability and maintenance of lean tissue in older individuals (24, 27) and obesity (23, 35), the effects of training intensity on GH levels may have significant clinical implications. If the GH response to exercise is related to intensity of exercise, one may hypothesize that subjects who train at higher intensities would show a greater change in the pulsatile release of GH than those who either do not train or train less intensively. The present study examined this hypothesis prospectively in healthy eumenorrheic women.

METHODS

Subjects. Twenty-one healthy eumenorrheic untrained female subjects (of the 56 who entered) completed the study. Entry required that each woman have a history of clinically normal menstrual cycles (MCs; 10–12 menses/yr) and be between 18 and 40 yr of age. Exclusion criteria included fad dieting or a documented eating disorder, use of oral contraceptives within the previous 6 mo, orthopedic limitations, history of renal or hepatic disease or diabetes mellitus, and participation in a regular running program (>10 miles/wk). All subjects underwent a detailed medical history and physical examination and provided written consent in accordance with the guidelines established by the Human Investigation Committee of the University of Virginia. Baseline measures of hepatic, renal,

metabolic, hematologic, and endocrine function were normal. Ovulation was confirmed by daily blood sampling in all baseline cycles, which revealed a midcycle serum luteinizing hormone (LH) surge followed by a midluteal serum progesterone concentration >5 ng/ml.

Subjects were recruited as controls ($n = 5$, age = 32.3 ± 6.2 yr; wt = 67.4 ± 6.4 kg; ht = 165.6 ± 9.7 cm) or randomly assigned to one of two exercise groups: above the lactate threshold ($>LT$, $n = 7$, age = 31.6 ± 2.6 yr; wt = 65.0 ± 5.9 kg; ht = 166.8 ± 5.8 cm) or at the lactate threshold ($@LT$, $n = 9$, age = 31.4 ± 4.6 yr; wt = 67.6 ± 10.5 kg; ht = 165.4 ± 5.0 cm). For the $@LT$ and $>LT$ groups, physiological and endocrine assessments were performed during the early follicular phase of the MC (*days 1–5* after onset of menses) at baseline and every fourth MC thereafter for the remainder of the 12–14 mo of training. The control group was assessed at baseline and at 12–14 mo after baseline. Measurements of $\dot{V}O_2$ consumption ($\dot{V}O_2$) at the lactate threshold; fixed blood lactate concentrations (FBLC) of 2.0, 2.5, and 4.0 mM; and of peak $\dot{V}O_2$ ($\dot{V}O_{2\text{ peak}}$), maximal $\dot{V}O_2$ ($\dot{V}O_{2\text{ max}}$), body composition, and pulsatile release of GH were made at each assessment.

$\dot{V}O_{2\text{ max}}$. $\dot{V}O_{2\text{ max}}$ was determined using an inclined treadmill protocol. The treadmill velocity remained constant at 140 m/min, beginning at 0% grade, with an increase in grade of 2.5% every 2 min. Subjects were given verbal encouragement throughout the test, and the test was terminated when the subject would not complete a given work load. $\dot{V}O_{2\text{ max}}$ was chosen as the highest $\dot{V}O_2$ attained during the test.

$\dot{V}O_{2\text{ peak}}$. $\dot{V}O_{2\text{ peak}}$ was determined using a continuous horizontal running treadmill protocol (39). The initial treadmill velocity was 60 m/min. Each subsequent 3-min stage was increased by 10 m/min. Subjects were given verbal encouragement throughout the test, and the test was terminated when the subject would not complete a given work load. $\dot{V}O_{2\text{ peak}}$ was chosen as the highest $\dot{V}O_2$ attained during the test.

Metabolic measures. Metabolic data were collected using standard open-circuit spirometric techniques. Inspired ventilation was measured using a previously calibrated dry gas meter (Rayfield, RAM-9200) fitted with a potentiometer. Output from the potentiometer was continuously integrated into an Apple IIe computer (Rayfield, REP200). Expired ventilation was channeled from a Hans Rudolph high-velocity valve through low-resistance plastic tubing into a 7-liter mixing chamber. The concentrations of O_2 and CO_2 in the mixing chamber were continuously sampled by an Applied Electrochemistry S-3A O_2 analyzer and a Beckman LB-2 CO_2 analyzer, respectively. Output from the gas analyzers was continuously integrated by the Apple IIe computer. The gas analyzers were calibrated using commercial gases of known concentrations (micro-Scholander technique) before and after each test.

Lactate threshold and FBLCs. Blood samples were taken at rest and at the end of each stage from an indwelling venous catheter located in the back of the hand. Subjects continued to run during blood sampling while resting their hands on the rails of the treadmill. A heparinized saline solution was infused after each blood sample

to prevent clotting. Blood samples were analyzed immediately for lactate concentration with an automated lactate analyzer (Yellow Springs Instruments, model 23L).

The lactate threshold was determined by examining the blood lactate-velocity relationship observed during the $\dot{V}O_{2\text{ peak}}$ test (39). The highest velocity attained that was not associated with an elevation in blood lactate concentration above baseline was designated as the velocity associated with lactate threshold ($V-LT$). This always occurred just before the curvilinear increase in blood lactate observed with subsequent exercise intensities. A lactate elevation of ≥ 0.2 mM (the error associated with the lactate analyzer) was required for LT determination. $\dot{V}O_2$ corresponding to $V-LT$ (from individual plots of $\dot{V}O_2$ vs. velocity) was designated as the $\dot{V}O_2$ associated with the lactate threshold ($\dot{V}O_{2-LT}$). Velocities associated with FBLCs of 2.0, 2.5, and 4.0 mM were determined from the curvilinear rise in blood lactate observed from the velocity-blood lactate relationship. $\dot{V}O_2$ values associated with FBLCs were determined in a manner identical to that described for LT (39).

Body composition. Percent body fat was assessed by hydrostatic weighing (17). Each subject was weighed in air on an Accu-Weigh beam scale accurate to 0.1 kg and subsequently weighed underwater with a 9-kg Chatillon autopsy scale accurate to 10 g. Residual volume was measured using the O_2 dilution technique described by Wilmore (42). The computational procedure of Brozek et al. (3) was used to determine relative fat from body density measurements.

Blood sampling. Subjects were admitted to the General Clinical Research Center (GCRC) at the University of Virginia Health Sciences Center for blood sampling on *days 3* or *4* after the onset of menstrual bleeding. Twelve to 24 h of recovery from the subjects' last physiological evaluation were provided before blood sampling (subjects did not train on evaluation days). This duration of recovery after exercise is adequate to ensure that the acute effects of exercise do not affect the pulsatile characteristics of GH release in sedentary young women (40).

An indwelling heparin lock cannula was inserted in a forearm vein at 0700 h. Serial blood sampling (2.5 ml/sample) was initiated at 0800 h and continued at 10-min intervals for 24 h. A heparinized saline solution (0.2 ml) was infused after each blood sample to prevent blood clotting. Subjects were allowed restricted activity, and meals (the content of the meals was not controlled, but similar menu choices were provided at each assessment) were served at 0900, 1200, and 1700 h. Serum GH concentrations were assayed in duplicate by immunoradiometric assay using the standards provided by the procedure of Nichols Institute Diagnostics (San Juan Capistrano, CA). The inter- and intra-assay coefficients of variation for this assay are $<10\%$ for concentrations >1.5 $\mu\text{g/l}$. Assay sensitivity is 0.5 $\mu\text{g/l}$.

Analysis of pulsatile release of GH. Mean and integrated serum concentrations of GH were calculated by the Cluster analysis program (32, 36). To enumerate GH peak frequency and amplitude, the algorithm was adjusted to require a threshold increase corresponding to a t statistic of 2.6 for the peak upstroke and 2.6 for the downstroke with nadir and peak test cluster sizes of 2 points. These

parameters constrain the rate of false positive peak detections while preserving a minimal false negative rate on both in vivo biological data and computer simulations (32, 33).

Pulse parameters compared include number of detected peaks, interpeak interval (min), maximal peak height ($\mu\text{g/l}$), incremental peak amplitude (algebraic difference between the maximal peak height and pre-peak nadir value, $\mu\text{g/l}$), peak area ($\mu\text{g} \cdot \text{l}^{-1} \cdot \text{min}^{-1}$), number of valleys, and nadir hormone concentration ($\mu\text{g/l}$). Integrated (24-h) serum concentrations of GH ($\mu\text{g} \cdot \text{l}^{-1} \cdot \text{min}^{-1}$) were also compared.

Training protocol. Both training groups completed similar weekly training mileage at differing training intensities. The distance covered during the 1st wk of training was 5 miles; the weekly mileage gradually increased to 24 miles/wk by week 20 and continued at 24 miles/wk until week 40. After week 40 the weekly mileage increased by 1.25 miles/wk for 3 wk out of 4. Subjects in the training groups were running 35–40 miles/wk by week 52.

Intensity of training was dependent on the group to which the subject was assigned. The >LT group trained three times per week at the velocity corresponding to their individual LT. The >LT group also trained three times per week above their LT velocity, at the velocity corresponding to the midpoint between the velocity at LT and maximal velocity (as determined from the LT/peak test). Up to one-half of the weekly mileage, not to exceed 5 miles/session (15 miles/wk), was covered at this pace. Training above the LT was performed continuously. The @LT group trained six times per week at a pace that corresponded to the velocity at LT. Subjects were supervised on an outdoor track three times per week (the >LT subjects were always supervised on their >LT training days). During these supervised sessions, the training pace was monitored on a lap-by-lap basis; subjects were provided feedback about their training pace and corrections were made as required. Subjects were permitted to train within ± 10 m/min of their assigned training pace. Training logs were completed and evaluated on a weekly basis to ensure that appropriate training velocity was maintained on the unsupervised training days. Training paces were adjusted after each physiological evaluation (i.e., every 4th MC) to reflect training changes that may have occurred. The control group did not engage in any run training.

Nutritional analysis. Total energy intake and its distribution among protein, carbohydrate, and fat were determined from 7-day food records. These data have been presented in detail elsewhere (26).

Statistical analysis. Data were analyzed using a two-way analysis of variance (ANOVA) with repeated measures (groups \times time with repeated measures over time). An alpha level of $P = 0.05$ was chosen a priori. When mean differences were observed, post hoc comparisons were made with the 1985 General Linear Models Procedure using the least squares means (SAS 5.18, Cary, NC).

RESULTS

To examine adequately the effects of intensity of training on the pulsatile release of GH adequately, it is important to document that a differential training re-

sponse occurred. Table 1 presents the changes in $\dot{V}\text{O}_2$ at LT; FBLC of 2.0, 2.5, and 4.0 mM; and $\dot{V}\text{O}_{2\text{max}}$ (the highest value attained from either the $\dot{V}\text{O}_{2\text{max}}$ or $\dot{V}\text{O}_{2\text{peak}}$ protocols) after 1 yr of run training. Subjects in both the @LT and >LT groups increased $\dot{V}\text{O}_2$ at LT; FBLC of 2.0, 2.5, and 4.0 mM; and $\dot{V}\text{O}_{2\text{max}}$ after 1 yr of run training. However, the increase observed was greater in the >LT group than in the @LT group ($P < 0.05$). No change in $\dot{V}\text{O}_2$ was observed for the control group. Therefore a differential training response occurred.

Table 1 also presents the body composition changes as a result of 1 yr of run training. No among- or within-group differences were observed for body weight, percent body fat, or fat weight, although trends for reductions in percent body fat ($P < 0.06$) and fat weight ($P < 0.15$) were observed in the >LT group. Both the @LT and >LT groups significantly increased fat-free weight as a result of 1 yr of run training ($P < 0.05$).

Figure 1 shows three examples of 24-h pulsatile serum GH concentration patterns from baseline to 1 yr. For the control (C) subject represented in this figure, 24-h integrated GH concentration was 3,648 $\mu\text{g/l}$ at baseline compared with 4,341 $\mu\text{g/l}$ at 1 yr. For the @LT subject, 24-h integrated GH concentration was 3,920 $\mu\text{g/l}$ at baseline compared with 2,921 $\mu\text{g/l}$ at 1 yr. For the >LT subject, 24-h integrated GH concentration was 3,750 $\mu\text{g/l}$ at baseline compared with 9,387 $\mu\text{g/l}$ at 1 yr.

Data regarding the pulsatile release of GH before and after 1 yr of run training are presented in Figs. 2–4. No differences were observed for the number of detected GH peaks, GH interpeak interval, or number of valleys either among or within groups or before or after 1 yr of run training (Fig. 2). The mean number of GH peaks for all groups was 8.0 peaks/24 h pretraining compared with 8.4 peaks/24 h posttraining ($P = 0.73$). The GH interpeak interval was 186 min at baseline compared with 173 min at 1 yr ($P = 0.50$). Valleys (8.0 and 8.2) were detected pre- and posttraining, respectively ($P = 0.84$).

Significant differences ($P < 0.05$) were observed within the >LT group as a result of 1 yr of run training for maximal GH peak height (7.4 $\mu\text{g/l}$ pre vs. 13.1 $\mu\text{g/l}$ post), incremental GH peak amplitude (6.8 $\mu\text{g/l}$ pre vs. 10.3 $\mu\text{g/l}$ post), GH peak area (340 $\mu\text{g} \cdot \text{l}^{-1} \cdot \text{min}^{-1}$ pre vs. 598 $\mu\text{g} \cdot \text{l}^{-1} \cdot \text{min}^{-1}$ post), nadir GH hormone concentration (0.60 $\mu\text{g/l}$ pre vs. 2.2 $\mu\text{g/l}$ post; Fig. 3), and integrated (24-h) concentration of GH (4,390 $\mu\text{g/l}$ pre vs. 7,710 $\mu\text{g/l}$ post; Fig. 4). No statistically significant changes were observed for these variables within the @LT or control groups.

No among-group differences were observed for these GH variables at baseline. After training, no differences were observed between the control and @LT groups; the >LT group had significantly higher values than the control group for maximal GH peak height, incremental GH peak amplitude, GH peak area, nadir GH hormone concentration (Fig. 3), and integrated (24-h) concentration of GH (Fig. 3; $P < 0.05$); the >LT group had significantly higher values than the @LT group for nadir GH hormone concentration (Fig. 3) and integrated (24-h) concentration of GH (Fig. 4; $P < 0.05$). A significant interaction was observed for nadir (Fig. 3) and integrated (24-h) GH

TABLE 1. $\dot{V}O_2$ -LT; $\dot{V}O_2$ at FBLC of 2.0, 2.5, and 4.0 mM; $\dot{V}O_{2max}$; and body composition parameters before and after 1 yr of run training in eumenorrheic women

Variable	Control		@LT		>LT	
	Pre	Post	Pre	Post	Pre	Post
$\dot{V}O_2$						
LT	24.2±6.4	24.5±6.5	23.3±4.3	29.7±6.9	26.2±6.9	36.6±3.4
FBLC						
2.0 mM	31.2±6.1	30.0±6.1	30.7±5.1	36.0±5.9	32.6±6.3	41.8±4.1
2.5 mM	33.4±6.7	31.9±6.6	32.8±5.4	37.9±5.8	34.7±6.4	43.3±4.2
4.0 mM	37.0±7.9	35.8±7.4	38.0±5.6	42.0±5.8	39.1±6.4	46.9±2.1
$\dot{V}O_{2max}$	40.9±9.3	40.6±8.4	42.7±6.2	47.4±8.0	44.2±5.5	50.1±4.6
%Body fat	27.9±5.6	30.3±7.3	29.2±3.3	28.7±3.3	27.4±6.6	25.9±4.5
Fat wt, kg	21.4±7.9	20.6±6.6	20.0±5.2	19.7±5.0	18.1±5.6	16.7±3.8
Lean wt, kg	46.0±3.2	46.3±2.7	47.6±5.8	48.4±6.1	46.9±3.1	47.5±3.3

Values are means \pm SD. $\dot{V}O_2$ -LT, O_2 consumption associated with lactate threshold; FBLC, fixed blood lactate concentration; $\dot{V}O_{2max}$, maximal $\dot{V}O_2$. For $\dot{V}O_2$ 1) both @LT and >LT increased $\dot{V}O_2$ at LT; FBLC of 2.0, 2.5, and 4.0 mM; and $\dot{V}O_{2max}$ after training ($P < 0.05$); 2) increase observed in >LT group was greater than observed in @LT group ($P < 0.05$); 3) no changes were observed in C group. For body composition 1) both @LT and >LT increased fat-free weight after training ($P < 0.05$); 2) a trend toward a decrease in %body fat ($P < 0.06$) and fat weight ($P < 0.15$) was observed in >LT group after training.

concentration (Fig. 4), with the increase observed in the >LT group greater than in either the @LT or C groups.

Although Figs. 2–4 present changes between baseline and 1 yr (because the C group was assessed only at baseline and 1 yr), the MC was used to time experiments in the exercising groups, with data collection every four MC. A 2×4 ANOVA was run on the two exercise groups (@LT vs. >LT; baseline vs. MC 4, MC 8, and MC 12) to determine how soon after the start of training changes in GH parameters occurred. Within the @LT group no significant differences were observed for any GH parameter at any time frame. Within the >LT group the following

changes were observed over time. 1) For maximal GH peak height, no changes were observed from baseline to MC 4. At MC 8 and MC 12, maximal GH peak height was significantly increased above baseline ($P < 0.05$). No differences were observed between MC 8 and MC 12 for maximal GH peak height. 2) For incremental GH peak amplitude, no changes were observed from baseline through MC 8. At MC 12, incremental GH peak amplitude was significantly greater than baseline ($P < 0.05$). 3) For GH peak area, no differences were observed from baseline to MC 4. The increase in GH peak area approached the level of statistical significance at MC 8 ($P =$

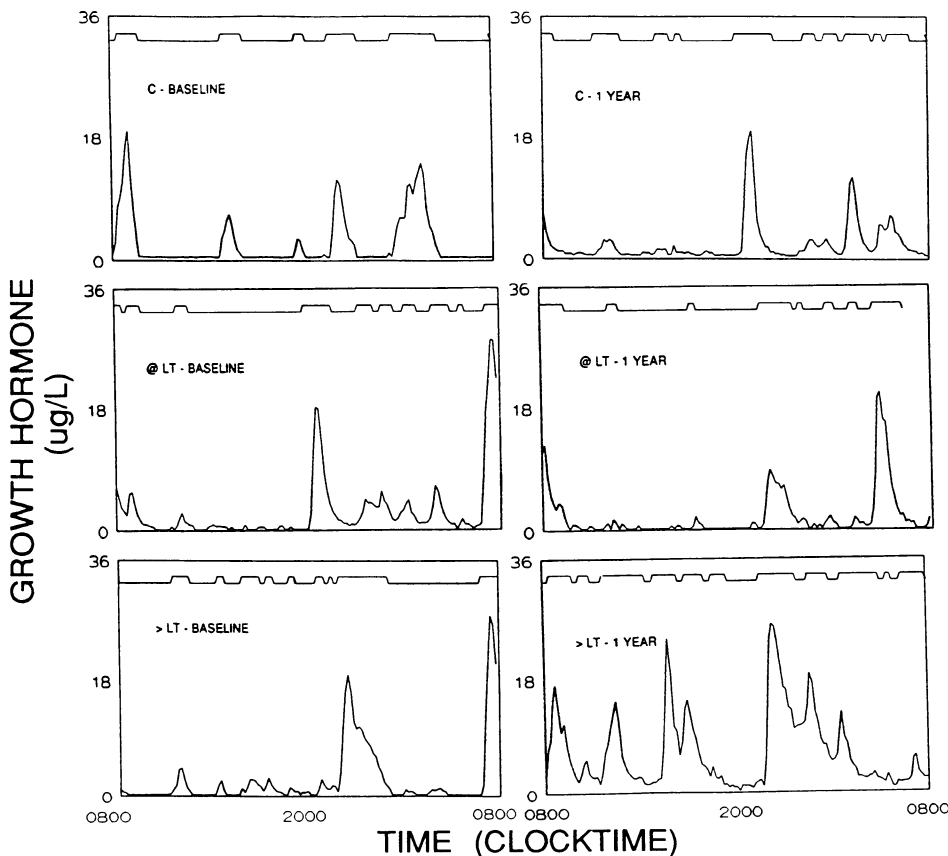


FIG. 1. Twenty-four-hour serum growth hormone (GH) concentrations in 3 subjects at baseline and after 1 yr of training. C, control; @LT, at lactate threshold; >LT, above lactate threshold.

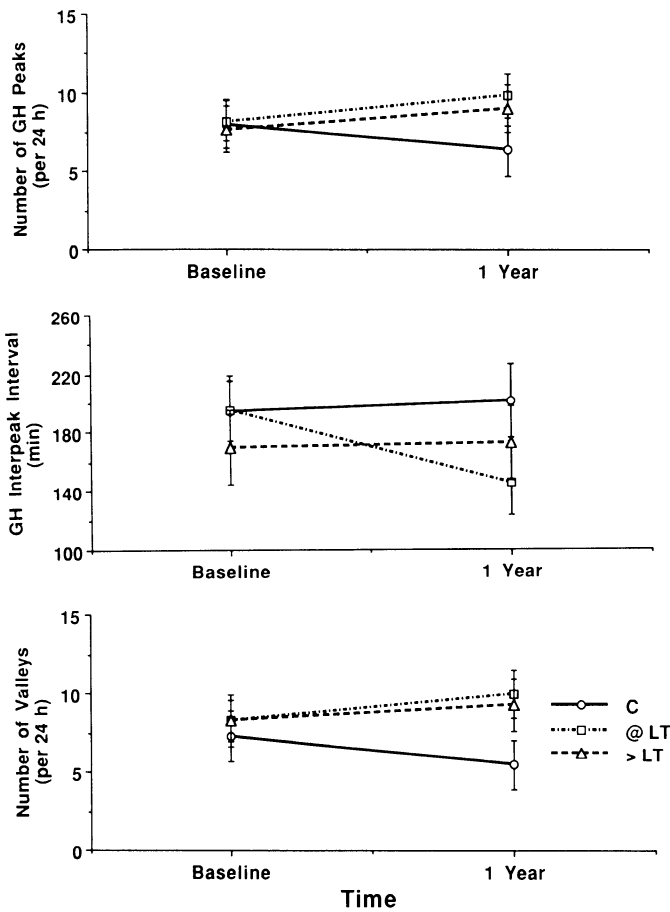


FIG. 2. Effects of 1 yr of run training on number of serum GH concentration peaks, GH interpeak interval, and number of interpeak valleys.

0.07) and was statistically significant at MC 12 ($P < 0.05$). 4) A significant increase was observed in nadir GH concentration from baseline to MC 4 ($P < 0.05$). This increase in nadir GH concentration remained consistent through MC 12. 5) For integrated (24-h) GH concentration, no changes were observed from baseline to MC 4. At MC 8 and MC 12, integrated GH concentration was significantly increased above baseline ($P < 0.05$). No differences were observed between MC 8 and MC 12 for integrated GH concentration.

The effects of the present training program on the reproductive axis have been presented in detail elsewhere (26). Briefly, no significant differences were observed within either exercise group for MC length (26–29 days) or length of the follicular phase (13–16 days). No change in the length of the luteal phase was observed within the @LT group (13 days), whereas a 1.4-day decrease in the length of the luteal phase was observed within the >LT group (14.4 days at baseline vs. 13.0 days at 1 yr, $P < 0.05$). No changes were observed in any parameter of LH pulsatility (with the exception of a slight but statistically significant increase in LH peak concentration in the >LT group).

No changes were observed either between or within groups for the total energy intake and distribution (absolute and percentage) of energy among protein, carbohydrate, and fat (26).

DISCUSSION

Although marked increases in the plasma concentration of GH during and after acute exercise have been well documented (4, 5, 8, 9, 16, 25, 30, 34), we are not aware of any studies that have examined the effects of prospective exercise training on the release of GH at rest. Because resting levels of GH can affect a number of physiological processes, the effects of training on the resting levels of GH may have physiological relevance. The pulsatile mode of GH release is important, because it conveys relevant biological signaling information to target tissues (14, 15). Moreover, patterns of episodic GH release are susceptible to physiological regulation and specific pathophysiological alterations (1, 12, 19–21, 23, 35). For example, gonadal steroid hormones, age, gender, pubertal state, nutritional status including feeding and short-term fasting, and obesity all modulate the pulsatile mode of GH release (1, 12, 19–21, 23, 35). Short-term caloric deprivation and insulin-dependent diabetes mellitus in humans are associated with profound increases in the frequency and amplitude of intermittent GH release (1, 12), whereas obese subjects have fewer secretory bursts of GH and a shorter half-life of endogenous GH than normal-weight individuals (35). The present data extend these concepts to prolonged endurance training and indicate that the pulsatile mode of GH release is amplified in young women who train by running, provided that the intensity of some training is above the LT.

The present data indicate that, in addition to $\dot{V}O_2$ (Table 1), the pulsatile release of GH may be affected by training intensity. That is, neither the C nor the @LT group showed within-group increases in any parameter of pulsatile GH release (Figs. 2–4). In contrast, the >LT group had significantly increased maximal GH peak height, incremental GH peak amplitude, GH peak area, nadir GH concentration, and 24-h integrated serum GH concentration as a result of 1 yr of run training (Figs. 3 and 4). These are the most reliable parameters of GH release in women (41). However, it should be noted that maximal GH peak height, GH peak area, and incremental GH peak amplitude all increased (although not significantly; $P = 0.13, 0.31, \text{ and } 0.12$, respectively) from baseline to 1 yr in the @LT group (Fig. 3). Therefore a dose-response effect of training (rather than a threshold) cannot be excluded.

The mechanism for the amplification in the pulsatile mode of GH release, in those women who trained >LT, cannot be determined from the present data. However, our findings appear to support the animal model suggested by Borer (2), who discovered that voluntary running accelerates linear and skeletal growth in mature golden hamsters and has used this model to determine whether submaximal endurance physical activities alter the neuroendocrine controls of skeletal and somatic growth. Borer's data suggest that exercise facilitates GH secretion and that both endogenous opiates as well as catecholamines may stimulate GH secretion by inhibiting somatostatin release (2). Recent data in humans suggest that both β -endorphin and catecholamine levels are related to intensity of exercise as well as to blood lactate levels (6, 10, 22, 28). Goldfarb et al. (10) compared the

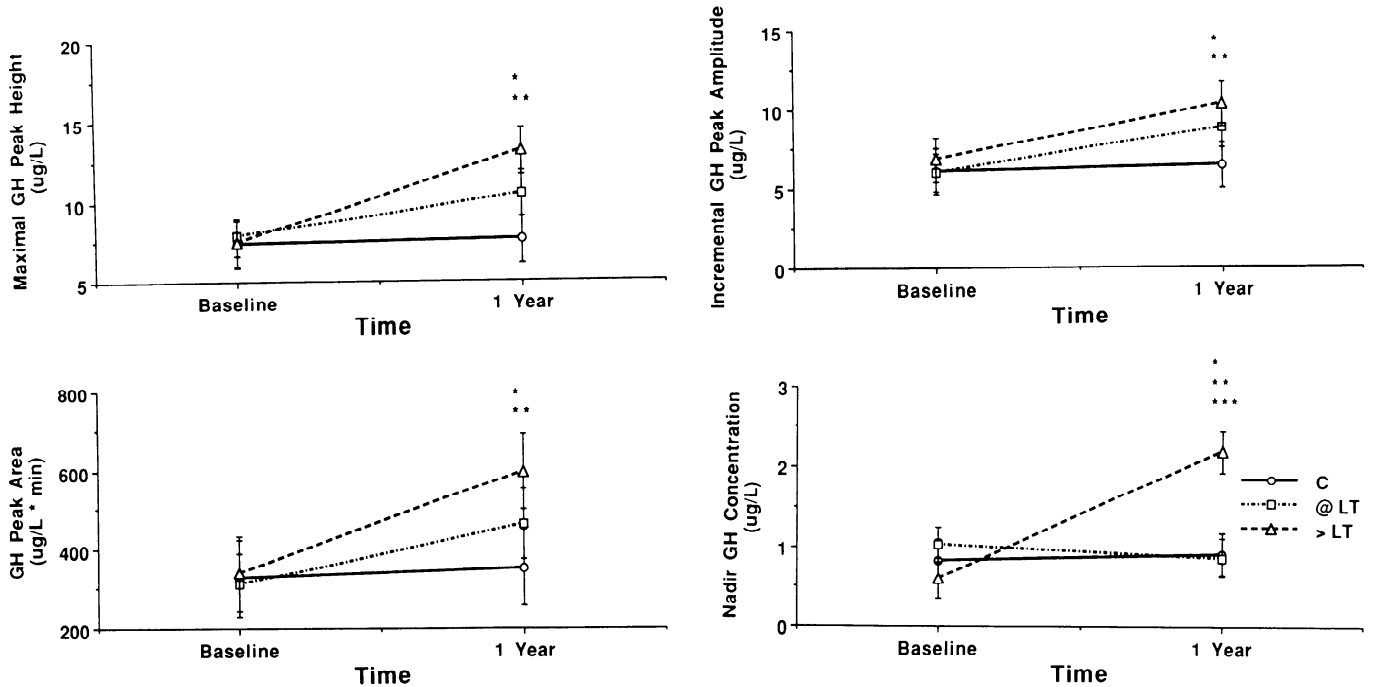


FIG. 3. Effects of 1 yr of run training on maximal serum GH concentration peak height, incremental GH peak amplitude, GH peak area, and nadir GH concentration. *1 yr > baseline in >LT group ($P < 0.05$); **at 1 yr >LT group > C group ($P < 0.05$); ***at 1 yr >LT group > @LT group ($P < 0.05$).

β -endorphin responses to 30 min of exercise at 60, 70, and 80% of $\dot{V}O_{2\max}$. They found that exercise at 60% of $\dot{V}O_{2\max}$ had no effect on circulating levels of β -endorphin, but exercise at 70 and 80% of $\dot{V}O_{2\max}$ significantly increased circulating levels of β -endorphin. Furthermore, the higher the exercise intensity, the more rapid the onset and the greater the circulating levels of β -endorphin. In addition, these authors reported a significant correlation between blood lactate and β -endorphin ($r = 0.78$). Similarly, Coplan et al. (6) reported that 20 min of exercise at an intensity 25 W greater than the LT resulted in a significantly greater elevation of catecholamines than did 20 min of exercise at 25 W below the LT ($2,270 \pm 190$ vs. 900 ± 230 pg/ml norepinephrine, $P < 0.001$; 509 ± 69 vs. 150 ± 18 pg/ml epinephrine, $P < 0.001$). Mazzeo and Marshall (22) have suggested that a strong relationship (perhaps causal) exists between the inflection in plasma epinephrine and the LT during a graded exercise test. Finally, Schwarz and Kindermann (28) recently reported

that circulating levels of β -endorphin increased disproportionately when the individual anaerobic threshold was reached during a graded exercise test and that the extent of the increase in β -endorphin was correlated with the level of blood lactate concentration. These authors also reported that the epinephrine response to supra-maximal exercise was similar to the β -endorphin response. Thus it is possible that women in the present study who trained >LT were habitually (i.e., 3 times per week) exposed to increased circulating levels of both β -endorphin and epinephrine. This, in turn, may have resulted in a reduction of somatostatin tone and an increase in GH secretion. This is consistent with the animal model of Borer (2) and could explain why the women who trained >LT had a greater GH response to training than the women who trained @LT. However, it should be realized that circulating levels of β -endorphin and catecholamines may not necessarily reflect dynamic changes within regions of the hypothalamus that are not directly accessible to circulating regulators in the plasma.

The increase in maximal GH peak height, GH peak area, and nadir GH concentration in the >LT group are all consistent with an increased mass of GH secreted per burst, as suggested by recent mathematical modeling of episodic endocrine gland signaling (37). An alternative explanation is prolonged GH half-life. For example, if high-intensity exercise training induced an increase in the circulating GH binding protein, a prolonged GH half-time might result. The increase in incremental GH peak amplitude observed in the >LT group (independent of an increase in the mass of GH secreted per burst or an increase in GH half time) may be important to target tissues (14, 15), inasmuch as this pattern is seen in healthy children during their pubertal growth spurt (19–21), presumably secondary to the stimulatory actions of andro-

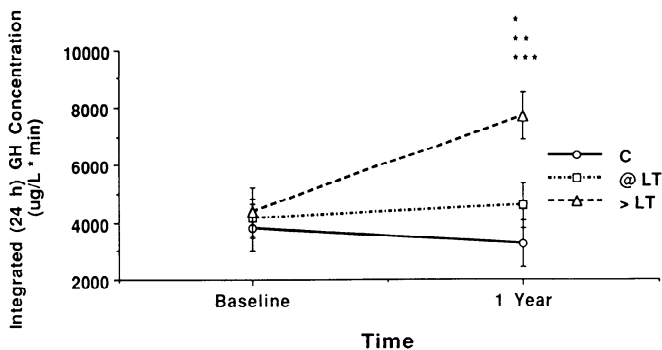


FIG. 4. Effects of 1 yr of run training on 24-h integrated serum GH concentrations. *1 yr > baseline in >LT group ($P < 0.05$); **at 1 yr >LT group > C group ($P < 0.05$); ***at 1 yr >LT group > @LT group ($P < 0.05$).

gen and/or estrogen on the somatotrophic axis (21, 31). Increased interpeak GH concentration may also be a physiological adaptation that would result in increased tissue responses to GH. For example, in the human, high nadir GH concentrations correlate very well with plasma insulin-like growth factor-1 (IGF-1), an index of tissue response to GH (11). Finally, the increase in 24-h integrated serum GH concentration, independent of changes in parameters of pulsatile GH release, may be important physiologically because of the high degree of biological variability associated with some of the parameters of the pulsatile release of GH. In contrast, mean 24-h integrated serum GH concentrations are maintained with high fidelity (41).

Although the long-term physiological implications of the adaptation in the pulsatile mode of GH release to endurance training cannot be determined from the present data, there are several conditions in which similar increases in GH have been reported. For example, normal puberty (19), hyperthyroidism (13), and exogenous administration of testosterone or estradiol (21, 31) have been shown to increase GH release to a degree similar to that observed in the present study. In contrast, there are a number of conditions associated with decreased exercise (such as healthy aging and obesity) in which the pulsatile release of GH is reduced (24, 27, 35). This suggests that some clinical conditions may be influenced by exercise. The latter is commonly used as a lifestyle intervention, although not necessarily to try to alter GH release.

For example, the reduction in lean body mass associated with aging is accompanied by reduced GH availability in older adults (24, 27), although the relationship is not necessarily causal. Poehlman and Copeland (24) have reported that lower levels of IGF-1, a product of GH action, in aging men are related at least in part to diminished physical activity. Rudman et al. (27) recently observed that 6 mo of administration of biosynthetic GH in men over the age of 60 who had plasma IGF-1 concentrations of <350 U/l resulted in a significant increase in lean body mass (8.8%) and a significant decrease in fat mass (14.4%). However, long-term GH administration could result in adverse reactions resulting from one or more consequences of hypersomatotropism (27). Whether training above the LT in older individuals will result in an increase in GH pulsatility remains to be explored. However, because GH is a potent anabolic agent that facilitates the transport of amino acids into cells, it can be hypothesized that, if endurance training above the LT increases the pulsatile mode of GH release in older populations, this should be accompanied by a concomitant increase in lean body mass.

Obesity is another condition in which training intensity may have an impact on the somatotrophic axis. Obese individuals have fewer GH secretory bursts, significantly prolonged intersecretory burst intervals, a daily GH production rate reduced to one-fourth that of normal, and shorter half-life of endogenous GH than do normal-weight men (35). Whether the normal dynamics of spontaneous pulsatile GH secretion and/or normal GH metabolic clearance can be restored by exercise, caloric, and/or nutritional manipulations in obese subjects has not been resolved. This issue is important because GH treat-

ment (exogenous) in obese individuals helps promote lipid mobilization and limit protein breakdown during periods of restricted nutrient intake (35). Furthermore, independent of age, GH is one of the major lipolytic hormones. This suggests that, if endurance training can alter the pulsatile mode of GH release, a favorable adaptation in body composition should occur. The present data support this notion in that the >LT group increased fat-free mass and demonstrated a trend for reduced percent body fat and fat weight as a result of 1 yr of run training (Table 1). This suggests that the role of exercise intensity in the alteration of GH secretion and/or clearance in obese subjects merits further investigation.

It should be realized that training above the lactate threshold in an older or obese population will result in a distinctly different exercise prescription than the one applied in the present study. That is, it is probably unrealistic to expect that a sedentary older and/or obese population will run 35–40 miles/wk. However, it is realistic to expect that older and obese subjects can exercise 30 min/day, 3 days/wk, at an intensity that is above their individually determined LT (although the absolute exercise intensity may be lower than reported in the present study, it will be the same relative intensity when based on the LT).

The issue of intensity of exercise training may also have relevance to the study of growth in children. GH has profound effects on longitudinal bone growth. If training in a growing population alters the pulsatile mode of GH release, this may be associated with increased growth. For example, physical training in adolescent boys may result in an accelerated growth velocity for age (7). Similar findings have been reported in prepubertal boys who were involved in a 12-wk strength training program (38). Although an adequate exercise stimulus seems to be required to induce an acute elevation in serum GH concentrations in children (29), whether intensity of long-term exercise training modulates the pulsatile release of GH and growth patterns in children has not yet been defined.

In summary, the present data indicate that exercise training amplifies the pulsatile release of GH by amplitude enhancement. This facilitative effect occurs when training intensity is above the LT. Our observations may have implications for exercise intervention strategies in clinical conditions characterized by impoverished pulsatile secretion of GH.

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