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Endogenous Anabolic Hormonal and Growth Factor Responses to Heavy Resistance Exercise in Males and Females

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Abstract

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To examine endogenous anabolic hormonal responses to two different types of heavy resistance exercise protocols (HREPs), eight male and eight female subjects performed two randomly assigned protocols (i. e. P-1 and P-2) on separate days. Each protocol consisted of eight identically ordered exercises carefully designed to control for load, rest period length, and total work (J) effects. P-1 utilized a 5 RM load, 3-min rest periods and had lower total work than P-2. P-2 utilized a 10 RM load, 1-min rest periods and had a higher total work than P-1. Whole blood lactate and serum glucose, human growth hormone (hGH), testosterone (T), and somatomedin-C [SM-C] (i. e. insulin-like growth factor 1, IGF-1) were determined pre-exercise, mid-exercise (i. e. after 4 of the 8 exercises), and at 0, 5, 15, 30, and 60 min post-exercise. Males demonstrated significant ($p < 0.05$) increases above rest in serum T values, and all serum concentrations were greater than corresponding female values. Growth hormone increases in both males and females following the P-2 HREP were significantly greater at all timepoints than corresponding P-1 values. Females exhibited significantly higher pre-exercise hGH levels compared to males. The P-1 exercise protocol did not result in any hGH increases in females. SM-C demonstrated random significant increases above rest in both males and females in response to both HREPs. These data suggest that the hormonal response patterns to HREPs are variable and in females differ from those in males due to significantly higher pre-exercise and exercise-induced serum T levels in males and higher pre-exercise serum hGH concentrations in females.

Key words

Growth hormone, insulin-like growth factor 1, testosterone, anaerobic exercise, somatomedins, resistance exercise, blood lactate

Introduction

Heavy resistance exercise is a potent exercise stimulus for muscle tissue hypertrophy and strength development (22, 27). The differences observed between males and females have classically been attributed to the higher concentrations of testosterone in males (13). Still, females generally demonstrate similar relative training responses in muscular strength (2). Furthermore, the relative changes in cross-sectional area, reflecting cellular hypertrophy, are comparable (7, 27, 28). The responses in serum testosterone to resistance exercise in females have been examined, but the responses of other trophic hormones such as growth hormone and somatomedin C (insulin-like growth factor 1) have not been previously reported (11, 18, 31, 32). The purpose of this investigation was to examine the acute response patterns of several musculotrophic factors (i. e. serum testosterone, growth hormone and somatomedin-C) to heavy resistance exercise, compared between males and females. These responses were further explored by comparison of two distinctly different heavy resistance exercise protocols, one with longer rest and heavier weight (P-1), which is typically used to increase strength, muscle hypertrophy, and one with more repetitions and shorter rest periods (P-2), which is typically used to improve muscular strength, hypertrophy, and high intensity muscular endurance (19).

Methods

Eight male and eight female subjects gave written informed consent to participate in this investigation. The physical characteristics of the subjects were ($\bar{x} \pm 1$ SD): age (yrs), males, 24.7 ± 4.5, females, 23.1 ± 3.3; height (cm), males, 178.5 ± 8.2, females 161.6 ± 8.1; body mass (kg), males, 82.1 ± 12.1, females, 60.4 ± 4.46; body fat (%), males, 16.1 ± 4.5, females, 28.5 ± 6.1. All subjects had recreational experience with resistance training but none were competitive lifters. All subjects were healthy and none were using medications. Each subject denied any history of anabolic steroid use. All females were determined to be eumenorrheic according to methods previously described (8) and as defined by regular 28–32 day menstrual cycles over the previous year. None of the females had used oral contraceptives or an intrauterine device within the past year (8). A minimum of two weeks were utilized for experimental protocol familiarization, descriptive testing, and load verifications (5 RM and 10 RM) for each experimental exercise protocol. Determination of each subject's percent body fat using hydrostatic weighing (computer interfaced with a load cell) and standard body composition methodology as previously described (12, 33) was also accomplished during this time.

During the preliminary testing period, one repetition maximum (1 RM) testing was performed for each lift with a warm-up of 5–10 repetitions at 40–60% of the perceived maximum. After a 1-min rest and stretching, 3–5 repetitions were performed with 60–80% of the perceived maximum. Three to four subsequent attempts were then made to determine the 1 RM with 3–5 minutes rest between lifts. The test-retest reliability for each of the lifts was between 0.91 and 0.95. A complete range of motion and proper technique were required for each successful 1 RM trial. No injuries were observed in any of the testing. No 1 RM determinations were made for the sit-up exercise as only the 5 RM and 10 RM loads were determined for use in the experimental protocol.

The two distinctly different heavy resistance exercise protocols (HREPs) were performed in random order. Each experimental test was performed at the same time of day on separate days with a minimum of 72 hours rest between experimental sessions. The experimental design of each protocol is shown in Table 1. The P-1 exercise protocol was a five repetition maximum (5 RM) based workout which incorporated longer rest intervals (i. e. three minutes) and heavier weight (5 RM) lifted. The P-2 exercise protocol was a 10 RM based workout with one minute rest between sets. As heavy resistance exercise protocols, both routines produce increases in muscular strength and hypertrophy. The P-1 protocol is one typically utilized for "strength" training, while the P-2 protocol is typically used by serious resistance trainees for the development of strength, hypertrophy, and high intensity muscular endurance (19). The same order of exercise was used in both HREPs. P-2 workouts for both male and females consisted of significantly ($p < 0.05$) greater total work (J): males P-1, $49{,}980 \pm 10{,}473.9$, P-2, $60{,}427.3 \pm 13{,}428.8$; females P-1, $24{,}501.1 \pm 2{,}827.0$, P-2, $31{,}580.3 \pm 3{,}278$. Understandably, total work for the females in both P-1 and P-2 was significantly less than that of the male subjects. Still, the relative loads (% 1 RM) utilized were not significantly different between males and females in any of the lifts performed. Depending upon the exercise, the 5 RM represented a range of 80–95% of the 1 RM, and the 10 RM represented a range of 70–85% of the 1 RM.

Table 1 Experimental heavy resistance exercise protocols

Exercise order	Repetition maximum (RM) and number of sets	
	P-1	P-2
1. Bench press	5 RM × 5 sets	10 RM × 3 sets
2. Double leg extensions	5 RM × 5 sets	10 RM × 3 sets
3. Military press	5 RM × 3 sets	10 RM × 3 sets
4. Bent leg incline sit-ups	5 RM × 3 sets	10 RM × 3 sets
5. Seated rows	5 RM × 3 sets	10 RM × 3 sets
6. Lat pull down	5 RM × 4 sets	10 RM × 3 sets
7. Arm curls	5 RM × 3 sets	10 RM × 3 sets
8. Leg press	5 RM × 5 sets	10 RM × 3 sets

*P-1 used 5 RM load and 3-min rest periods, P-2 used 10 RM load and 1-min rest periods;
*Exercises 4 and 7 were performed using free weights, all other exercises were performed using a Universal weight machine.

All exercises were structured proportionally for each subject with grip widths and positions marked and kept constant for each exercise. Each workout was designed to provide the same relative exercise stress for comparative purposes. Lifting work was calculated as weight X vertical distance moved per repetition X number of repetitions. The computer program took into consideration the vertical distance moved of both the iron plates and the centers of gravity of the lifter's body segments. These distances were obtained from measurements on the subjects and equipment when they were in the starting and ending exercise positions. Anthropometric tables were used to locate body segment centers of gravity and to estimate the body segment weights from total body weight (34).

All subjects refrained from ingestion of alcohol or caffeine for 24 hrs prior to testing. Dietry analysis (Nutri-Calc, PCD System, Inc., Penn Yan, NY) for the 3 days prior to each experimental session was obtained from a food diary and demonstrated normal RDA caloric, nutrient, vitamin, and mineral intakes. Values were: (mean $\pm$ 1 SD) $62.1 \pm 4.6\%$ carbohydrate, $12.3 \pm 2.8\%$ protein, and $25.6 \pm 5.3\%$ fat. While it was not the purpose of the study to match diets on each test day, similar caloric, vitamin, mineral, and nutrient intakes were observed prior to each test. Urine nitrogen determinations verified that all subjects were within the normal range for positive nitrogen balance prior to each test session. Experimental testing of the female subjects was timed to the early follicular phase (2–4 days after the onset of menses) (8).

Subjects reported for the experimental session and venous blood samples were obtained in a semi-recumbant position, which was used for all samples. Testing was started in the morning (8–10 a. m.) and each subject was tested at the same time of day to reduce the effects of any diurnal variations on the hormonal concentrations. The venous blood samples were obtained from an indwelling 20 gauge teflon (3.75 cm) cannula placed in a superficial arm vein on the radial aspect of the arm. The teflon cannula was kept patent with a continuous

Table 2 The mean (±1 SD) responses of serum glucose and whole blood lactate to the heavy resistance exercise protocols

Males		Pre	Mid	0	5	15	30	60
Serum Glucose ($mmol \cdot ^{-1}$)	P-1:	5.03 (0.35)	5.09 (0.21)	5.19 (0.30)	5.24 (0.24)	5.16 (0.32)	5.09 (0.28)	4.88 (0.25)
	P-2:	5.32 (0.87)	4.77 (0.79)	4.91 (0.77)	5.21 (1.11)	5.19 (0.97)	5.17 (0.67)	4.68 (0.45)
Whole Blood Lactate ($mmol \cdot ^{-1}$)	P1:	1.33 (0.40)	3.12* (0.98)	4.39* (3.13)	2.63* (0.90)	2.15* (0.71)	1.63 (0.44)	1.27 (0.19)
	P-2:	1.15 (0.26)	7.87*[a] (2.69)	8.61*[a] (2.84)	8.52*[ab] (2.69)	6.46*[a] (2.75)	3.72*[a] (1.24)	2.44*[a] (0.93)
Females Serum Glucose ($mmol \cdot ^{-1}$)	P-1:	5.14 (0.38)	5.14 (0.38)	4.83 (0.35)	4.86 (0.23)	4.93 (0.21)	4.76 (0.36)	4.59 (0.35)
	P-2:	5.06 (0.41)	5.19 (0.94)	5.23 (0.49)	5.27 (0.75)	5.10 (0.78)	4.80 (0.55)	4.54 (0.31)
WholeBlood Lactate ($mmol \cdot ^{-1}$)	P.1:	1.40 (0.43)	3.37* (0.78)	3.14* (1.21)	2.41* (0.81)	2.31* (1.12)	1.71 (0.98)	1.48 (0.73)
	P-2:	1.36 (0.50)	7.57*[a] (1.03)	7.87*[a] (1.57)	6.20*[a] (1.79)	5.06*[a] (0.99)	3.48*[a] (0.88)	2.15 (0.85)

* = $p < 0.05$ from corresponding pre-exercise value;
[a] = $p < 0.05$ from corresponding P-1 workout;
[b] = $p < 0.05$ from corresponding female value.

flow of isotonic saline (30 $ml \cdot hr^{-1}$). Prior to obtaining a resting blood sample, a 20-min equilibration period was utilized. Subjects knew they would not immediately start to exercise after the resting blood sample was obtained. The exercise protocol started 10 min after the resting blood sample had been obtained. This procedure was shown during pilot testing to eliminate any significant anticipatory increases in hormonal responses previously thought to affect the examination of exercise responses (6). Water intake was allowed ad libitum throughout the exercise protocols and recovery. Blood samples were obtained pre-exercise, mid-exercise (i. e. after 4 exercises) and at 0 (immediately post), 5, 15, 30, and 60 min following each exercise protocol. All blood samples were processed, centrifuged for 15 minutes at 3000 × g, serum harvested, and stored at − 120 °C until analyzed.

Fresh blood samples were immediately analyzed in duplicate for whole blood lactate by an enzymatic-amperometric method (Lactate Analyzer-640, Wolverine Med Inc. Inc., Grand Rapids, MI). Serum samples were assayed for glucose concentrations by an automated glucose oxidase reaction (23-Glucose Analyzer, Yellow Springs, Inc., Yellow Springs, OH). Blood was analyzed in triplicate for hemoglobin using the cyanmethemoglobin method (Sigma Chemical Co., St. Louis, MO) and for hematocrit by microcapillary technique. Relative percent changes in plasma volume were calculated according to equations by Dill and Costill (9).

Serum testosterone (T), human growth hormone (hGH), and somatomedin-C (SM-C) (i. e. insulin-like growth factor, IGF-1) concentrations were determined in duplicate blinded analyses by radioimmunoassay (RIA). Male and female RIAs for T were performed in different assays to allow for appropriate sensitivity adjustments of the standard curves. Determinations of different serum immunoreactivity values were accomplished with the use of a Beckman 5500 gamma counter and on-line data reduction system. Serum samples were analyzed in duplicate for T using an ^{125}I solid phase radioimmunoassay (Diagnostic Products Corp., Los Angeles, CA), which was sensitive to a detection limit of 0.38 $nmol \cdot l^{-1}$. Intra- and inter-assay variances were calculated to be less than 3.6% and 4.7%, respectively, with a 3.3% crossreactivity with dihydrotestosterone. Serum samples were analyzed in duplicate for human growth hormone utilizing an ^{125}I liquid phase RIA with a double antibody technique (Cambridge Medical Diagnostics, Bellerica, MA). The assay was sensitive to a detection limit of 0.24 $\mu g \cdot l^{-1}$. Intra- and inter-assay variances were calculated to be less than 4.2% and 4.8% respectively. Serum samples were analyzed in duplicate for SM-C (IGF-1) using an ^{125}I double antibody disequilibrium RIA with a preliminary ODS-silica extraction procedure (Inc-Star Corp., Stillwater, MN). Total serum SM-C (IGF-1) was determined in this assay. The assay was sensitive to a detection limit of < 2.0 $nmol \cdot l^{-1}$ and had < 0.01% crossreactivity with IGF-2. Intra- and inter-assay variances were less than 4.5% and 4.9%, respectively.

Statistical analyses of the data were accomplished utilizing a multivariate two-way analysis of variance with repeated measures. Tukey post-hoc tests were calculated to determine pairwise differences. Significance in this investigation was chosen at $p < 0.05$.

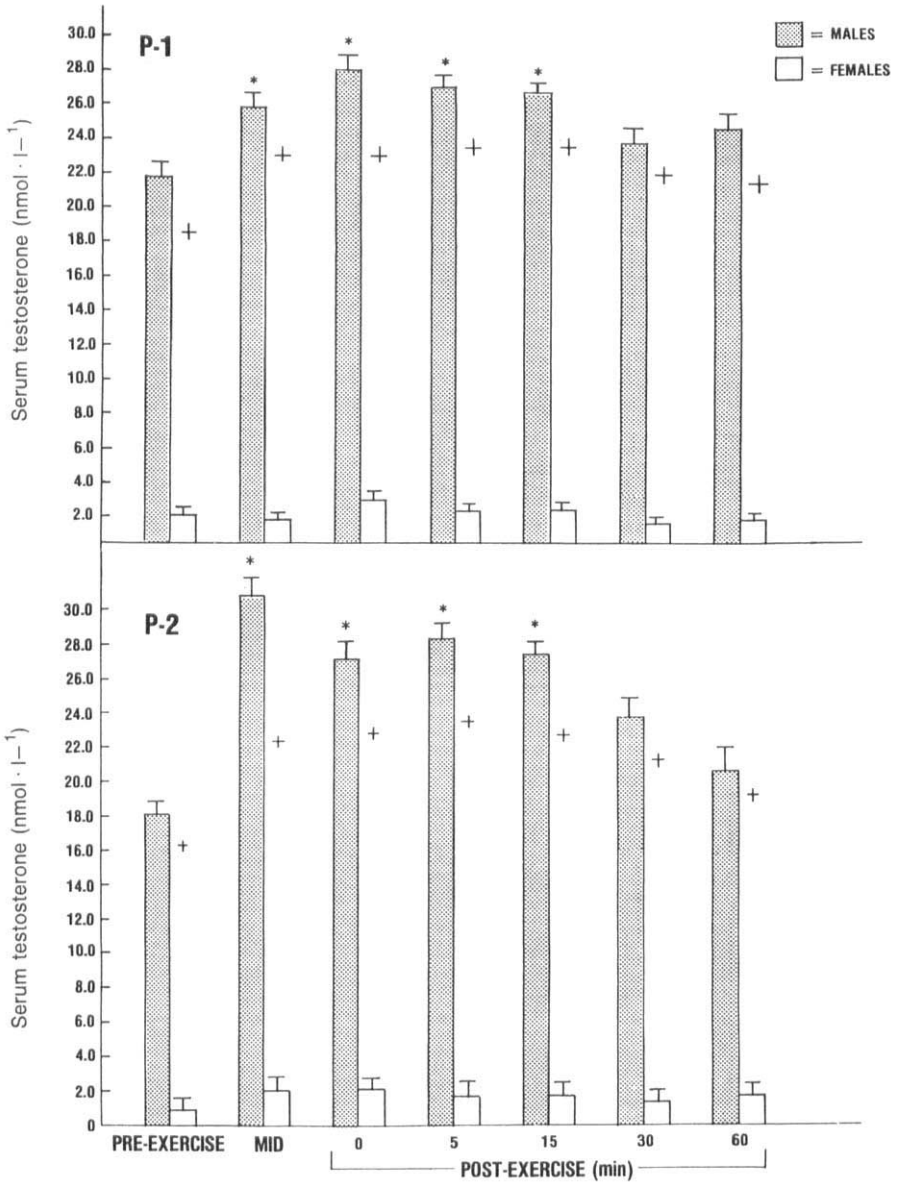

Fig. 1 Mean (+ SE) serum testosterone concentrations for males and females to P-1 and P-2 HREPs are presented. * = $p < 0.05$ from corresponding pre-exercise values and + = $p < 0.05$ from corresponding female values

Results

The effects of the two resistance exercise protocols on whole blood lactate and serum glucose values for males and females are shown in Table 2. No changes or differences were observed in serum glucose concentrations. Whole blood lactate concentrations were significantly elevated by both protocols in both males and females, and concentrations were increased more in the P-2 exercise protocols than in the P-1 workout for both males and females. There was only a transiently higher concentration in the male P-2 exercise protocol compared to the females (at 5-min recovery period interval).

Serum testosterone responses are shown in Fig. 1. Concentrations were increased in males by both exercise protocols and for up to 15 min into the recovery periods. Mid-exercise values in males were significantly greater in P-2 than in P-1. All male values were significantly higher than corresponding female values at every timepoint measured. Additionally, the 60-min values for P-1 were significantly greater than corresponding P-2 serum T concentrations for males.

Growth hormone responses are shown in Fig. 2. Markedly different response patterns were observed between the two HREPs for both males and females, with a significantly greater increase in hGH concentrations in P-2; mid-exercise values in the males were significantly greater than in P-1. In P-1, significant increases in serum levels above pre-exercise values were observed for the males at mid-exercise and at 30 min following the exercise protocol. No significant hGH increases above pre-exercise values were observed in P-1 for female subjects. Furthermore, in both P-1 and P-2 HREPs, females exhibited significantly higher pre-exercise serum hGH values than males. In P-2, females demonstrated significant increases in serum hGH at mid-exercise and at 0, 5, and 15 min following exercise, and males increased hGH at all time points. For both males and females, P-2 values, other than pre-

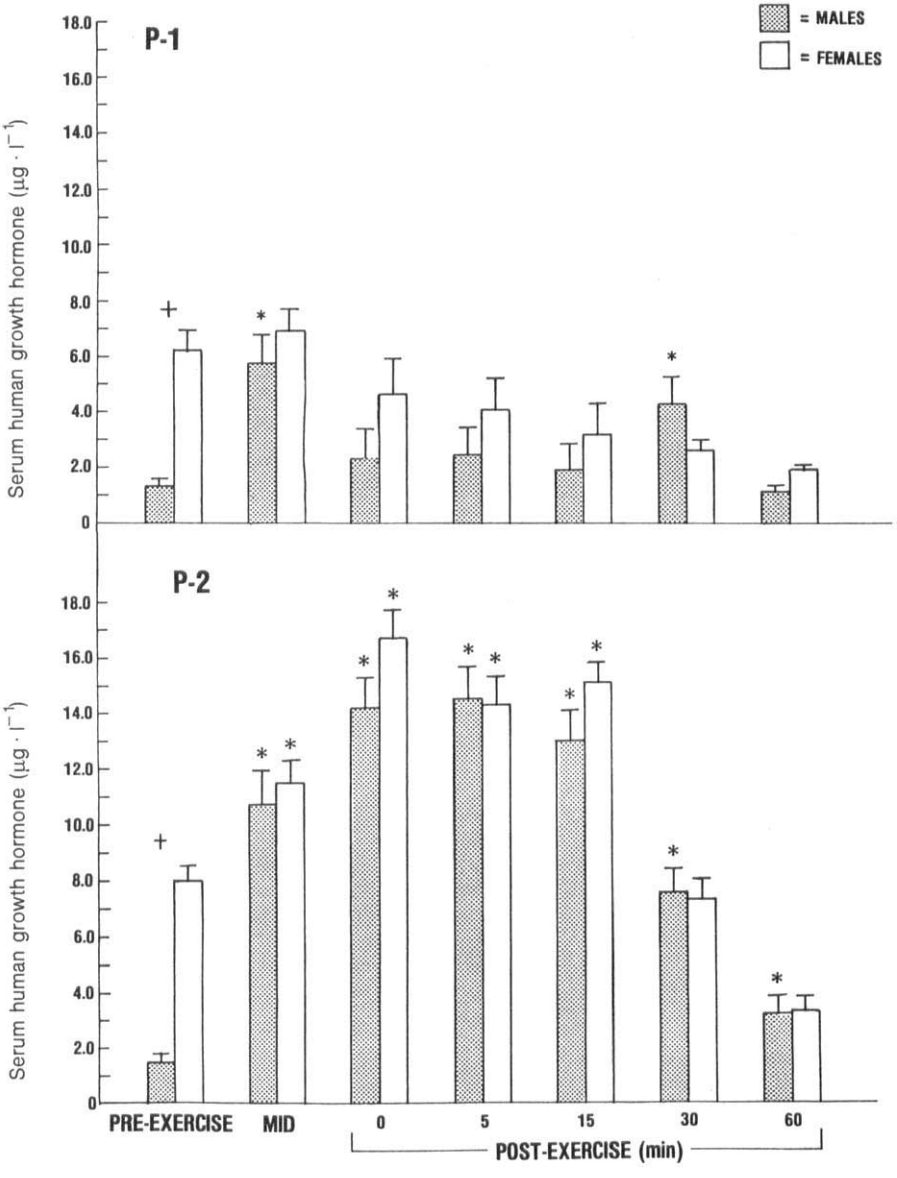

Fig. 2 Mean (+ SE) serum human growth hormone concentrations for males and females to P-1 and P-2 HREPs are presented. * = $p < 0.05$ from corresponding pre-exercise values and + = $p < 0.05$ from corresponding female values

exercise, were all significantly greater than corresponding P-1 serum hGH concentrations.

Fig. 3 shows the responses of serum somatomedic-C (insulin-like growth factor 1) to P-1 and P-2 resistance exercise protocols. In P-1, males demonstrated significant increases in serum values immediately following exercise, and females significantly increased serum SM-C 60 min following exercise. For the females, P-1 values at 60 min post-exercise were significantly greater than corresponding P-2 values. In P-2, SM-C significantly increased above resting levels at mid-exercise, 0 and 5 min for the males and at mid-exercise and immediately following exercise for the females. For the females, P-2 values at mid-exercise were significantly greater than corresponding P-1 values.

Changes in plasma volume shifts during recovery were negligible. The greates % change in plasma volume were observed pre- to immediately post-exercise and were as follows ($\bar{x} \pm 1$ SD): males P-1 = $-4.1 \pm 8.4\%$, P-2 = $-4.1 \pm 8.8\%$; females, P-1 = $-0.5 \pm 7.7\%$, P-2 = $-6.0 \pm 7.2\%$.

Discussion

The most remarkable finding of this investigation was the difference in hGH stimulation by the two resistance exercise protocols for both men and women. The more anaerobic P-2 HREP produced a clear and sustained elevation of hGH, while the P-1 exercise protocol had virtually no effect on hGH concentrations in the female subjects. Furthermore, a substantially lower hGH response in the P-1 compared to the P-2 protocol was observed in the males. While the relative contributions of various physiological mechanisms to the observed response patterns remain unclear, changes in hGH have been shown to be influenced by hypoxia, acid base shifts, and breath holding (10, 26, 29). Differential response patterns of hGH using heavy and light leg press exercise protocols have been shown previously for men in a study by Van Helder et al. (30). The data from this investigation demon-

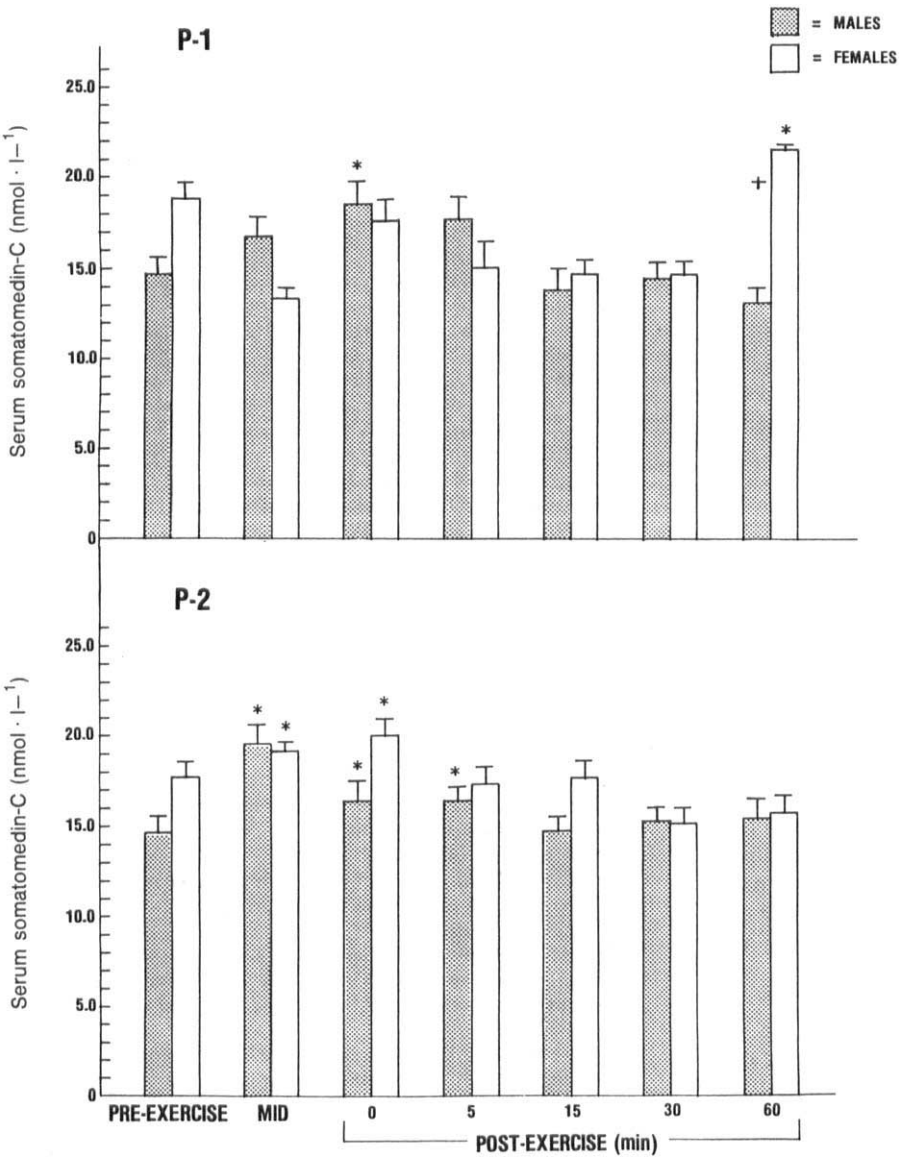

Fig. 3 Mean (+ SE) serum somatomedin-C (IGF-1) concentrations for males and females to P-1 and P-2 HREPs are presented. * = $p < 0.05$ from corresponding pre-exercise and + = $p < 0.05$ from corresponding female values

strate that hGH responses in men are sensitive to both HREPs, but the high volume, 10 RM load, using short rest periods appears to augment the magnitude of the hGH response in both males and females. The adaptational importance of an augmented response of serum hGH to such a high volume, 10 RM load, and short rest protocol HREP, (i. e. P-2) for exercise prescription of resistance training for women during various phases of the menstrual cycle remains to be investigated. At present, the combined effects of a higher volume, shorter rest, and moderate intensity resistance workout produce a dramatic stimulus to serum hGH responses. Studies are needed to partition out the individual effects of single variables.

The baseline differences in serum hGH concentrations between males and females are almost certainly related to the estrogen sensitization of somatotrophs which gives a well-established increased responsiveness to a wide variety of stimuli in women (26). It is unclear why female responses to the HREPs were not greater than those observed for the males. It is possible that despite the same relative exercise stress, the lower absolute total work for each of the HREPs might account for the lack of a greater exercise responsitivity. The relative stress (% 1 RM) for each HREP was comparable for men and women. Still, the contribution of absolute total work, irrespective of other exercise variables (e. g. load, rest periods, etc.), remains to be examined.

The absence of a consistent response pattern of serum SM-C (IGF-1) may be due to a variety of mechanisms involved with determining peripherial blood levels. A direct response of SM-C to the increased hGH stimulation observed in this study might not have been expected over the 1-hr recovery time period observed, since hGH stimulated mRNA synthesis (which results in an increased SM-C production) does not peak until 3 to 9 hrs later (1, 3, 14, 23). Due to the complex interactions of SM-C secretion with transporter protein attachment and release, receptor equilibrium, and receptor binding actions, the serum response patterns may reflect a more integrated response of such physiological mechanisms. Alternatively, the significant increases which were observed

could represent a non-hGH mediated release or transient increases in serum transporter protein release due to receptor binding turnover. Further study is needed to clarify such mechanisms.

In contrast to the hGH hormonal response, T was acutely stimulated by both HREPs in males. Previous studies in male subjects have demonstrated that serum T responses are a function of the amount of muscle mass utilized in the exercise protocol and the total work performed (11, 15, 18, 25, 31). Conversely, in this study, serum T concentrations in females remained unaffected by either HREP. This suggests that the serum increases observed in males is mediated through the pituitary-testicular axis, either by increased secretion rates or by alterations in testicular blood flow, instead of through systematic fluid shifts or reduced hepatic clearance rates (4, 24).

Although levels of androstenedione are 10-fold higher than T in females and responsive to resistance exercise, T and dihydrotestosterone are still the more potent musculotrophic androgens (1, 13, 16, 17, 20, 31), with important target receptors and effects in the upper body musculature. The lower levels of these androgens normally encountered in females and the absence of any stimulation by these two different HREPs suggest reasons why females typically do not achieve levels of upper body muscularity and strength achieved by males (2). While one study has demonstrated that small increases in serum T may be possible in females (6), our study supports previous investigations which have not found any acute effects on serum T concentrations (11, 18, 31, 32). Thus in females, it appears that other endogenous anabolic hormonal mechanisms may play a more prominent role in physiological adaptations to heavy resistance training.

In summary, heavy resistance exercise stimulates acute endogenous anabolic responses. These responses may differ depending upon the type of exercise protocol utilized. Growth hormone appears to be the most sensitive to change in program design. Female hormonal responses in this study appear to differ due to higher resting levels of growth hormone during the early follicular stage of menstrual cycle and a general lack of testosterone responsiveness to either heavy resistance exercise protocol. The adaptational effects of such differential hormonal responses to heavy resistance exercise on cellular adaptations in muscle, connective tissue, and bone remain to be demonstrated.

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Human Research

Human subjects participated in these studies after giving their free and informed voluntary consent. Investigators adhered to AR 70–25 and USAMRDC Regulation 70–25 on Use of Volunteers in Research.

The views, opinions, and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy, or decision, unless so designated by other official documentation.

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