Influence of Resistance Exercise Volume on Serum Growth Hormone and Cortisol Concentrations in Women

Susan E. Mulligan, Steven J. Fleck, Scott E. Gordon, L. Perry Koziris, N. Travis Triplett-McBride, and William J. Kraemer


Reference Data


ABSTRACT

Ten eumenorrheic women (age 24.1 ± 4.3) performed 2 randomly assigned heavy-resistance exercise protocols (HREP) on separate days during the early follicular phase of the menstrual cycle. Multiple-set (MS) HREP consisted of 3 sets of 10 RM of 8 resistance exercises with a 1-min rest between exercises and sets. Single-set (SS) HREP consisted of 1 set of 10 RM of the same 8 exercises in the same order, with 1-min rest between consecutive exercises. SS total work was about one-third that of the MS. Immunoreactive serum growth hormone (GH), cortisol, and blood lactate were measured pre- and postexercise (0, 15, and 30 min). The MS produced significant (p < 0.05) increases in serum GH and cortisol above resting levels at all postexercise times. The SS significantly increased serum GH at 15 min postexercise, and cortisol at 0 and 15 min postexercise. Both protocols yielded significant increases in blood lactate above rest at all postexercise times. The MS produced the most significant hormonal and metabolic responses, indicating that exercise volume may be an important factor in hormonal and metabolic mechanisms related to resistance exercise in women.

Key Words: lactate, strength training, weight training, hypertrophy

Introduction

The stress of heavy-resistance exercise has been shown to be an effective stimulus for strength gains and muscle fiber hypertrophy (1, 9, 12-14, 16, 18, 25, 34). Initial strength gains during heavy-resistance training are attributed to neural-muscular adaptations (1, 11-15). Additional gains in strength and alterations in muscle fiber density have been credited to hormonal activity and complex interactions of physiological systems in response to exercise stress (13, 18). The exact mechanisms responsible for regulating muscular adaptations are unknown. The design of the resistance training program has been shown to have a significant impact on hormonal responses, strength improvements, and muscle hypertrophy (1, 4, 16, 18, 19, 23). Training variables such as volume of exercise, intensity, muscle recruitment, and length of recovery appear to be important determinants of magnitude of hormonal activity (4, 5, 7-9, 12, 18-20, 34, 36).

Considerable research has explored the anabolic properties of testosterone and its role in physiological adaptations to resistance training (5, 7, 12, 13, 23, 25). A lack of significant testosterone response in women, regardless of the training protocol used, has led researchers to believe that other anabolic hormones (e.g., GH and growth factor) may be the primary contributors to anabolic adaptations in female skeletal muscle tissue (14, 20, 22).

A limited body of research has specifically investigated the response of these other anabolic hormones (i.e., growth hormone, growth factor) to resistance training (17, 20, 22, 23, 31, 36). Cortisol, a catabolic hormone released in response to a wide variety of stresses, has also received much attention (13, 17, 20, 24, 25). Its antagonistic nature and concomitant circulation with the anabolic hormones make it of primary interest when investigating anabolic activities of the body.

Growth hormone (GH) is a family of peptide hormones synthesized in the anterior portion of the pituitary gland. Most research has focused on the immunoreactive GH form (i.e., peptides that react with assay antibody). GH plays a crucial role in growth and development of bone and of connective, visceral, muscle, and adipose tissue. It is believed that the anabolic properties of GH stem from its ability to promote amino acid transport into the cell and synthesize these amino acids into protein (4, 5, 7, 17). Although the exact mechanisms of its anabolic properties are unclear, it is clear that the sympathetic nervous system is involved in the secretion of GH in response to various physiological events that alter the metabolic demands of the sys-
Both endurance and heavy resistance exercise have been reported to attenuate GH activity when sufficient intensity and duration are achieved (3, 4, 8, 17, 20, 22, 31, 36). The anabolic properties of GH and its reaction to exercise stress suggest that GH is an important factor in muscle strength, local muscular endurance, and size adaptations. It has been reported that during the early follicular (3, 20, 22) and midluteal (3) phase of the menstrual cycle, women have higher baseline GH levels than men, although heavy resistance exercise protocols elicit similar responses in both genders (3, 20, 22, 31). It appears that GH is an influential factor in physiological adaptations to heavy resistance training in women, making this an important area of investigation (20, 22).

Cortisol is the most potent glucocorticoid produced by the human adrenal cortex. It is secreted in response to stress, whether physiological or psychological, and plays a prominent role in influencing catabolic activity in skeletal muscle tissue. Cortisol acts through specific intracellular receptors and influences the physiological activity of hormones, enzymes, and nutrients (i.e., insulin for glucose regulation, proteolytic enzymes, protein degradation, conversion of amino acids to carbohydrate) (5, 9).

Studies have shown that heavy resistance exercise can elicit significant increases in cortisol (5, 13, 20, 24, 25, 32). As with the anabolic hormones, the magnitude of the response appears to be related to the volume of exercise and its intensity and duration (13, 20, 24, 25, 32). Due to the catabolic nature of cortisol in the body and its role in signaling muscle repair and restructuring, it is logical to concurrently examine this hormone's activity when investigating anabolic hormones.

Much of the recent research on resistance exercise has focused on hormonal responses to various parameters of training protocols (4, 20, 24, 31, 34). Differences in physiological responses appear to be related to distinct program variables (e.g., %1-RM, rest period length, volume of work) that ultimately comprise the exercise stress. Program variables related to percentage of maximum resistance and length of rest periods have been shown to be important factors related to the hormonal responses in both men and women (5, 7, 20, 22, 24, 31, 36).

Kraemer et al. (20) have reported marked increases in GH and cortisol concentrations in response to a moderate-resistance (10-RM) protocol with a short (1-min) rest period. Other research reports similar findings, indicating that longer rest intervals (3-min) and/or heavier loads (3- to 5-RM) produced less pronounced hormonal responses (19, 22, 24). Volume of exercise has also been shown to affect serum GH concentrations (4, 17, 22). Although significant serum GH increases have been reported in response to a protocol of low volume (28,000 J) and large muscle mass (36), and one of low volume and small muscle mass (17), more significant increases have been observed in response to protocols of higher volume exercise (49,000 and 59,000 J) (22, 23).

Resistance training is an essential part of the athlete's conditioning program. The need for greater strength, muscular endurance, and injury prevention has resulted in an increased acceptance and adoption of resistance exercise among women athletes (6, 9, 28, 33). Research has now started to investigate hormonal responsiveness, or mechanisms by which increases in muscular strength and fiber changes occur in women (3, 20, 22, 27, 33, 34).

Since volume of exercise has been implicated in hormonal sensitivity to resistance exercise, and most research to date has been conducted with men, this study was designed to address the need for more extensive data concerning the influence of resistance exercise program variables (i.e., total work performed) on hormonal responses in women. The primary purpose of this investigation was to examine the influence of different volumes of resistance exercise (1 set vs. 3 sets) on serum GH and cortisol concentrations in women.

Methods

Subjects
Ten healthy women volunteered for this study. They were informed of the risks of the investigation and signed an institutionally approved informed consent form. All had experience with resistance training but none were competitive lifters. Subjects did not use any medications during the investigation, and reported no previous history of nicotine use. Likewise, each one denied any history of anabolic drug use. All of the women were deemed eumenorrheic according to previously described methods (20). Each subject reported regular 28- to 32-day menstrual cycles throughout the previous year, and none had used oral contraceptives or intrauterine devices within the past year.

Testing Protocols
Subjects were familiarized with the experimental protocol prior to resistance exercise testing sessions. During this period, body composition and maximum oxygen consumption were determined. Body composition was determined via standard hydrostatic weighing; calculations and procedures were performed following established methodologies (20). Maximal oxygen consumption (ml · kg⁻¹ · min⁻¹) was determined using a continuous treadmill protocol as previously described by Kraemer et al. (20). Descriptive characteristics were as follows:

- Age: 24.1 ± 4.3 yrs
- Height: 161.6 ± 7.6 cm
- Body mass: 63.4 ± 11.9 kg
- Body fat: 24.3 ± 6.1%
- VO₂ max: 38.5 ± 6.6 ml · kg⁻¹ · min⁻¹

Resistant Exercise in Women 257
For comparative purposes this experiment was designed to be similar to previous investigations examining hormonal changes with resistance exercise in women (20, 22). Testing sessions were conducted on separate days during the early follicular phase of the menstrual cycle. Subjects fasted for 6 hours before testing and refrained from caffeine and alcohol for 48 hours prior to each test. No strenuous exercise was undertaken during the 72 hours prior to the experimental exercise sessions.

Dietary analysis revealed normal percentages of RDAs for caloric, vitamin, and mineral profiles. Prior to each workout a refractometer was used to measure urine specific gravity and verify hydration state. A urine specific gravity of <1.015 was recorded for all subjects prior to each workout. No significant (p ≤ 0.05) differences were observed for preexercise urine specific gravity measures between exercise test sessions. Subjects were encouraged to consume similar diets before each exercise session in order to produce similar nutrient intake reports before each test. Urine nitrogen determinations confirmed that all subjects were within normal positive nitrogen balance before each test session.

The experiment was modeled after a typical routine used by bodybuilders to induce maximal increases in muscular hypertrophy, local muscular endurance, and strength (9, 10, 20). This type of training protocol uses a 10-RM resistance and 1-min rest period between sets and exercises. The protocol employed in the present investigation consisted of 8 exercises utilizing major muscles of both the upper and lower body.

The single-set series involved 10-RM × 1 set for each exercise while the multiple-set series involved 10-RM × 3 sets for each. The exercise format and order of performance was as follows:

- Bench press
- Double-leg extension
- Military press
- Bent-leg incline sit-up
- Seated row
- Lat pulldown
- Arm curl
- Leg press

All exercises were done on Universal weight machines, except for sit-ups and arm curls which were performed with free weights. All workouts were randomized and balanced in their experimental presentation. During testing the subjects performed 3 sets of the 8-exercise protocol (multiple set [MS]) with 1 min rest between each exercise and 1 min rest between sets, or a single set of the 8-exercise protocol (single set [SS]) with 1 min rest between exercises.

The volume of work for the SS protocol was designed to be about one-third that of the MS protocol. Total work in the SS session was significantly less than in the MS session (10,526.8 ± 1,092.7 J vs. 31,580.3 ± 3,278.0 J). Lifting work was calculated as weight × the vertical distance moved per repetition × number of repetitions. Grip width used by subjects was proportional to height. Body positions (grip width and joint angles) were held constant across testing sessions. Methods and calculations are as previously described by Kraemer et al. (20, 23).

**Blood Samples**

All workouts were performed during the early follicular phase of the menstrual cycle (1 and 4 days after menses). Testing was conducted at the same time of day, 8 to 10 a.m., to minimize the effect of diurnal variations of hormonal concentrations. A 20-min equilibrium period was observed prior to drawing the pretest blood sample. Venous blood samples were obtained from the antecubital vein with the subjects slightly reclined. Significant anticipatory increases in resting hormonal concentrations were eliminated by familiarizing the subjects with the protocol prior to testing. Pilot testing had shown this to be an effective procedure. During the testing sessions, venous blood samples were obtained from a 20-gauge indwelling Teflon cannula placed in the antecubital vein. Samples were drawn, processed, and stored at −120 °C. For the purpose of this investigation, serum concentrations of GH, cortisol, and lactate for blood samples obtained preexercise, immediate postexercise (Time 0), and at 15 and 30 min postexercise were evaluated.

**Biochemical Analyses**

Blood was collected via a three-way stopcock into plastic syringes. For blood serum analysis, the blood was transferred into glass tubes, sealed, and allowed to clot at room temperature. The clotted blood was then centrifuged at 1,500 × g for 15 min at 4 °C. The resultant serum was extracted and stored in 1.5-ml Eppendorf tubes. A Beckman 5500 gamma counter and on-line data reduction system was used to determine immunoreactivity values and calculate concentrations for the radioimmunoassays.

Growth hormone and cortisol concentrations were determined in duplicate using radioimmunoassays. Growth hormone was measured with a 125I liquid-phase radioimmunoassay with double antibody technique (Cambridge Medical Diagnostics, Bellerica, MA) with a limit of detection of 0.24 μg/L. Variance were calculated to be <3.6% intraassay and <5.2% interassay. Serum cortisol concentrations were determined using a 125I solid-phase radioimmunoassay technique (Diagnostic Products, Los Angeles). Intraassay variance was calculated at <3.1% and interassay variance <7.1%. Whole blood lactate concentrations, analyzed in duplicate, were determined using a lactate analyzer (Model 640, Wolferine Medical, Grand Rapids, MI). Plasma volume changes were <10% pre- to postexercise; no corrections were made, due to the many other factors that affect hormones in circulation and the fact that the target cells interact with a given molar concentration of hormone.
Statistical evaluation was performed using a two-way ANOVA and PLSD Fisher post hoc tests when appropriate. Simple regression was used to examine selected pairwise relationships. The significance level for this investigation was set at $p \leq 0.05$.

**Results**

For the MS protocol, a significant increase in serum GH and cortisol above resting levels was reported for all postexercise time points: immediate postexercise and at 15 min and 30 min postexercise. Similarly, a significant lactate response was reported for all 3 postexercise time points. Only one significant random correlation was observed between postexercise GH and lactate values. None were observed between postexercise lactate values and cortisol concentrations.

For the SS protocol, the only significant serum GH response was observed at 15 min postexercise. No significant increase above resting levels of serum GH or cortisol was observed at any other postexercise time point. Serum cortisol increases were observed at 0 and 15 min postexercise. A significant increase in lactate in response to the resistance exercise session was reported immediately postexercise and at 15 and 30 min postexercise. No significant correlation between postexercise lactate values and serum GH or cortisol concentrations was observed.

No significant difference between any resting values of blood concentrations was observed between the testing protocols. Significant differences in serum GH concentrations between the two testing sessions were observed immediately following exercise (0) and at 15 min postexercise. Figure 1 shows the serum growth hormone responses between the two protocols.

A significant increase in cortisol concentrations was seen immediately postexercise and at 15 min postexercise for both test protocols. The MS protocol demonstrated higher cortisol concentrations at 0 and 15 min postexercise. Figure 2 shows the serum cortisol concentrations for the testing protocols.

A significant lactate increase above resting levels was reported for all postexercise time periods in both protocols. No significant difference between the two immediate postexercise lactate responses was observed. However, the MS protocol resulted in a significantly greater increase in lactate at 15 min and 30 min postexercise. Figure 3 shows the blood lactate responses for both exercise protocols.

**Discussion**

The primary finding in this investigation was that volume of resistance exercise significantly influences peripheral circulating blood concentrations of growth hormone, cortisol, and lactate in women.

Current research on resistance training has investigated the role of various training program factors in stimulating adaptational responses. Acute elevations in serum GH and cortisol have been reported in response to a variety of weight-training protocols (4, 20, 21, 31, 36). The design of the resistance training program will ultimately affect the extent of hormonal activity, strength improvements, and muscle hypertrophy. This study extends work by Kraemer et al. (20) and other investigators demonstrating how single variables such as intensity, amount of muscle mass used, and length of rest period will affect the magnitude of hormone and lactate secretion (4, 8, 18, 21-23, 36).

Volume of exercise appears to be another important determinant in hormonal responses (4, 12, 18, 22).
Figure 2. Response of serum cortisol to SS (top) and MS (bottom) exercise protocols. *p < 0.05 from corresponding preexercise value; #p < 0.05 from corresponding SS time point value.

Our observations support what has previously been reported with regard to the role of specific exercise variables: heavy-resistance exercise protocols using high volume (3 sets), moderate to heavy loads (8- to 10-RM at 70 to 85% of 1-RM resistance), and short rest periods (<1 min) augment the magnitude of the GH response in both men and women (4, 20, 22). A less significant and/or no GH response has been reported with exercise configurations of lower volume, lower intensity, and/or longer rest periods (20, 22–24, 31, 34, 36). The degree of variance in physiological activity between the exercise protocols may be attributed to such factors as duration of training session, acid-base shifts, anaerobic work performance, circulation of associated sympathetic hormones, age, or muscle mass used; all of these have been reported to affect serum hormone and lactate values (4, 5, 9, 18, 20, 31).

Since growth hormone is highly responsive to its environment, the greater hormonal concentrations seen during the high volume protocol (MS) may be related to the acid/base shift incurred due to its higher anaerobic component and longer stimulus exposure time in completing 3 sets of the resistance exercise protocol. The greater anaerobic intensity of the MS workout is also
reflected in the more pronounced increase and sustained elevation of blood lactate. The delayed GH response in the SS protocol may be due to the shorter training session and time required for growth hormone to respond to physiological changes.

As has been observed with GH, blood cortisol levels also respond according to the protocol performed (19, 20, 24, 25, 30, 35). Certain exercise variables (i.e., exercise intensity, duration, rest interval, volume) that affect circulating concentrations of GH likewise have been found to affect serum cortisol concentrations (19, 20, 24, 25, 30, 35). Muscle tissue growth and associated strength gains depend on the balance between the activity of the anabolic and catabolic hormones. Furthermore, an individual's training status may alter the response of cortisol to the exercise stimulus. It has been reported that well-trained athletes had a less pronounced cortisol elevation during exercise than unconditioned individuals (5). The effect of training status on GH response to resistance exercise remains unclear (3, 5, 17, 21, 32, 36).

Volume of exercise is an important variable in training periodization. One strategy behind periodization is to manipulate the training intervals to expose the athlete to high volume, high intensity workouts designed to initiate optimal physiological responses and adaptations to excess stress (1, 9, 26). The magnitude of cumulative effects of training depends on the volume of work completed, duration of training phase, and psychological responses to the training protocol (1, 9, 26, 29). It appears that the hypertrophy phase that utilizes loads of about 10-RM may best enhance the intended anabolic environment with the use of multiple sets and short rest periods. This would increase the anabolic response and enhance local muscular endurance as well.

While most data indicate that heavy resistance exercise may bring about acute elevations in GH concentrations, this is the first study to demonstrate the impact of subtle volume effects in women. Although elevated resting plasma cortisol levels have been reported in response to overtraining, it is the resting concentrations that determine the carryover day to day on physiological status. Our data demonstrate that the exercise-induced elevations needed for acute metabolic homeostasis during recovery differ between the two protocols.

These findings seem particularly relevant when designing training programs, since a primary goal of training is to manipulate work and recovery factors to provide optimal physiological adaptations and progressively improve athletic performance. Due to growth hormone's proposed role in anabolic activity in female musculature, providing sufficient stimulus to optimize its activity is of interest.

Similar training responses, in terms of muscular strength (2, 9, 28, 37) and cellular hypertrophy (14, 22, 27, 37), have been reported in both women and men. Although it is unlikely the same absolute strength gains will be realized, when expressed as a percentage of improvement or in relation to lean body mass, strength gains in women have been shown to be similar (2, 6, 9, 15, 27, 37). However, research indicates that women have less ability to develop equivalent absolute increases in muscle mass (2, 6, 9, 15, 37).

Differences in muscle hypertrophy are thought to be primarily due to the anabolic effects of testosterone on male musculature, the larger cross-sectional area of muscle found in men, and fiber type variances between men and women (2, 5–7, 9, 10, 13, 28, 37). Most of the research reports that there do not appear to be significant differences in GH response to training between men and women (3, 20, 22, 31).

We found that during the early follicular phase of the menstrual cycle, women had significantly higher resting GH values than men (20, 22). Other investigators have reported similar findings during the midfollicular and midluteal phases of the menstrual cycle (3). Baseline differences in serum GH concentrations may be related to estrogen sensitization of GH (3, 20, 22). The exact contribution of exercise-induced alterations of GH to muscle tissue growth and physiological adaptation to exercise stress in women, and the importance of heavy resistance exercise as a modality to elicit these changes, needs further investigation.

From the results of this research and that conducted in the past, it appears the appropriate program variables (volume, intensity, duration, short rest interval) must be in place in the training program in order to elicit desired hormonal responses that may be needed to stimulate optimal physiological adaptations (e.g., bone and muscle) with training.

**Practical Applications**

The results of this study indicate that volume of exercise is a significant factor in the acute hormonal and lactate responses to resistance exercise in women. When designing a resistance exercise protocol, the number of sets that dictate the amount of work must be considered an important factor in the subsequent hormonal environment related to the recovery process from heavy resistance exercise. Growth hormone has been shown to be involved in a variety of biological actions related to maintaining the body's normal structure and metabolic function, and it has been implicated as an important component in physiological adaptations to training in women. Thus, optimizing the natural anabolic environment can be accomplished by program design.

**References**

3. Bunt, J., R. Boileau, J. Bahr, and R. Nelson. Sex and training dif-

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Current affiliations: N. Travis Triplett-McBride, Center for Exercise Science and Sport Management, Southern Cross University, Lismore, NSW 2480, Australia; S.J. Fleck, Fleck’s Rx, Inc., 30 Villegge St., Colorado Springs, CO 80906; L.P. Koziris, Dept. of Kinesiology, University of Illinois–Chicago Circle, Chicago, IL 60680.