Leptin concentrations experience a delayed reduction after resistance exercise in men

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ABSTRACT

Leptin concentrations experience a delayed reduction after resistance exercise in men. Med. Sci. Sports Exerc., Vol. 34, No. 4, pp. 608–613, 2002. Purpose: Leptin is an important metabolic hormone providing the brain with information concerning energy balance. Most studies have reported that circulating leptin concentrations are unaffected by acute, moderate exercise. We hypothesized that these studies have been limited by short sampling schemes (<4 h) postexercise and may have missed a time-delayed reduction in circulating leptin concentrations. Methods: Ten men (age = 21 ± 1 yr, height = 177 ± 2 cm, body mass = 79 ± 3 kg, body fat = 11 ± 1%BF, VO_{max}= 51 ± 1 mL·kg\(^{-1}\)·min\(^{-1}\)) completed an acute heavy-resistance exercise protocol (AHREP) (50 total sets comprised of the squat, bench press, leg press, and lat pull-down) from 1500 to 1700 h. Blood was sampled hourly postexercise until 0600 h the next morning and also during a time-matched control period. Leptin concentrations were measured by an immunoradiometric assay. Resting energy expenditure (REE) was measured via indirect calorimetry using a ventilated hood beginning ~0600 h after both nighttime conditions. Results: The estimated caloric expenditure from the AHREP was 856 ± 114 kcal. No significant differences (P > 0.05) between the control and exercise conditions were observed for serum leptin concentrations until 9 h postexercise. Significant interaction effects (P < 0.05) indicated lower serum leptin concentrations postexercise at hours 9 (2.9 vs 2.2 ng·mL\(^{-1}\)), 10 (2.7 vs 2.0 ng·mL\(^{-1}\)), 12 (2.5 vs 1.8 ng·mL\(^{-1}\)), and 13 (2.6 vs 1.6 ng·mL\(^{-1}\)). This delayed reduction was accompanied by a 12% elevation (P < 0.05) in morning-after REE (0.25 ± 0.02 vs 0.28 ± 0.02 L·min\(^{-1}\)). Conclusion: Leptin concentrations experience a delayed (~9 h) reduction in the systemic circulation after acute resistance exercise. This decline is likely associated with the disruption in metabolic homeostasis created by the high-intensity, long-duration, energy expenditure and subsequent excess post oxygen consumption from the AHREP and is not due to losses in fat mass. Key Words: HORMONE RESPONSES, ENERGY EXPENDITURE, RESTING ENERGY EXPENDITURE, WEIGHT LIFTING, STRENGTH TRAINING, ADIPOSE TISSUE

The adipocyte-derived hormone leptin has been the subject of several recent investigations. This circulating hormone acts as a peripheral feedback signal informing the hypothalamus about available energy stores and may serve a key role in the eventual understanding of the etiology of obesity (10,17,21,23). It has also been postulated that leptin plays a pivotal role in reproductive health and fuel homeostasis by modulating pituitary secretion of luteinizing hormone and growth hormone (1,5,14,16,17,20). Leptin concentrations are directly proportional to adipose tissue mass, and changes in fat mass resulting from weight loss are known to be associated with a corresponding decline in systemic leptin (9,18,21). The neuroendocrine mechanisms by which leptin serves to regulate feeding behavior and metabolism have yet to be fully elucidated. Also poorly understood is the relative influence of acute exercise resulting in weight reduction corresponds to a decline in leptin concentrations. It is accepted that chronic exercise resulting in weight reduction corresponds to a decline in leptin concentrations (18,21,24). There is more controversy surrounding the effects of acute exercise bouts and the corresponding changes, or lack thereof, in leptin concentrations (2,3,13,22,25).

Weltman et al. (25) recently reported that regardless of exercise intensity, leptin concentrations were unchanged during a 3.5-h recovery period after 30 min of aerobic exercise. Weltman’s data are corroborated by similar negative findings after other acute exercise bouts reported by

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other researchers (7,11,12,18,19). Conversely, Tuominen et al. (23) found a 34% decline in plasma leptin 44 h after a 2-h treadmill run. Essig et al. (3) subsequently confirmed this finding by reporting a 30% decline 48 h after aerobic exercise performed at 70% VO2max. The longest observation period postexercise for the studies showing no change in leptin was 3.5 h. We hypothesized that if leptin undergoes a “delayed” reduction after exercise, it would have been missed by the short sampling period of the previously described studies. We sought to test this hypothesis by extending the sampling period (13 h) to more fully describe the leptin response pattern than has been done previously. Moreover, as all previous studies have used an aerobic mode of exercise, we elected to study an acute heavy-resistance exercise bout in young, fit men to provide further information on the endocrine responses to resistance exercise.

METHODS

Subjects. Ten young, healthy, fit men (age = 21 ± 1 yr, height = 177 ± 2 cm, body mass = 79 ± 3 kg, body fat = 11 ± 1%BF, VO2max = 51 ± 1 mL·kg−1·min−1) participated in this investigation, which was approved by The Pennsylvania State University’s Human Use Institutional Review Board and the University Park General Clinical Research Center (GCRC) Scientific Review Committees. Written informed consent was obtained from each subject after they were familiarized with the study procedures. A medical evaluation was subsequently performed by a physician before subject’s inclusion into the study. All subjects were familiar with resistance exercise and reported having performed resistance exercise training ≥ 2 d·wk−1 for the previous 6 months. Percent body fat was assessed by hydrostatic weighing, and maximal volume of oxygen consumption was measured by a treadmill protocol.

Strength assessment. One-repetition maximums (1 RM)s were tested for the following exercises: squat, bench press, leg press, and lat pull-down using Universal (Universal Equipment, Omaha, NE) and York Barbell equipment (York Barbell, York, PA). The 1 RM’s were subsequently used to calculate the relative loads for the acute heavy-resistance exercise protocol.

Dietary control. All subjects completed 3-d dietary intake diaries before each overnight trial. Subjects were asked to consume the same diet for the 3 d preceding each overnight trial. Dietary analyses (Nutritionist IV, First DataBank, Inc., San Bruno, CA) of these records verified that the caloric content and composition was similar for the 3 d before each overnight stay (see Table 1). On the day of their overnight trials, the entire day’s meals were provided for the subjects. These meals were prepared by registered dietitians at the GCRC and had the following macronutrient distribution: 55% carbohydrate, 15% protein, and 30% fat. Calories were based on the Harris Benedict standard formula, plus an activity factor of 1.6 based on our subjects’ age, gender, and physical activity levels. Meal times were breakfast: 0630 h; lunch: 1130 h; and dinner: 1900 h. Lunch and dinner times were scheduled around the 1500–1700 h afternoon workout to ensure all subjects exercised in the postabsorptive state. Subjects were allowed to consume water ad libitum.

Acute heavy-resistance exercise protocol (AHREP). Table 2 lists the AHREP which was designed to be a high-volume workout (i.e., high total work) that recruited and activated a large amount of muscle tissue. This was accomplished by performing multi-joint exercises that required the use of major muscle groups in both the lower and upper body (e.g., the squat, leg press, bench press, and lat pull-down). The relative loads for each exercise alternated between 10- and 5-RM loads. The 10- and 5-RM loads were calculated as 70% and 85% of the exercise 1 RM, respectively. Subjects completed a total of 50 sets (squats: 15 sets; bench press: 15 sets; leg press: 10 sets; lat pull-down: 10 sets). Sets of exercises alternated between the lower and upper body. A 90-s rest period was given after each exercise. All subjects completed the entire workout. The mean ± SE time for completion of the AHREP was 125.3 ± 3.4 min. Total work in kJ performed during the AHREP was estimated from the number of repetitions times the product of weight in newtons and vertical distance in meters moved per repetition for the free or stack weight and each body segment. The work for the entire session was the sum of the work done in all of the exercise sets performed. Additionally, energy expenditure during the AHREP was estimated according to the following formula (15):

\[\text{kcal} = 0.086 \times (\text{body mass in kg}) \times (\text{duration of exercise in minutes})\]

Overnight trials. Subjects underwent two randomized, counterbalanced overnight trials at the GCRC. One of these overnights served as the control trial: when the subject reported to the GCRC at 1430 h and rested quietly until 1700 h, whereupon a catheter was inserted into the antecubital vein and serial blood was drawn at a rate of 1 draw every 10 min from 1700 h to 1800 h and 1 draw every hour thereafter until 0600 h the following morning. During each overnight trial, subjects were allowed to move freely on the floor, watch TV, receive phone calls, study quietly, etc. Bedroom lights were turned off at 2200 h and the TV turned off at 2300 h. Subjects were allowed to sleep, and self-reports indicated no differences in sleep quality between the two experimental trials. Venous blood sampling followed the same procedures during the exercise condition, which was performed from 1500 to 1700 h. Blood was obtained as soon as possible after the completion of the last set. Serial blood draws were performed throughout the night every hour. Blood was collected in glass Vacutainers, allowed to

| TABLE 1. Nutritional analysis (caloric and macronutrient breakdown) for experimental subjects; there were no significant differences between the main effects for control vs exercise conditions; significant main effects were observed for the 3-d dietary intake vs the 1-d values for the GCRC provided diet in total calories and protein calories; the means for these main effect are provided. (*P < .05). |
|-----------------|-----------------|-----------------|-----------------|
| 3-Day Dietary Intake | GCRC diet |
|-----------------|-----------------|-----------------|
| Total calories  | 2714            | 3030*           |
| Carbohydrate calories (% of total calories) | 1380 (51%) | 1528 (50%) |
| Fat calories (% of total calories) | 867 (32%) | 895 (30%) |
| Protein calories (% of total calories) | 467 (17%) | 607* (20%) |

*P < 0.05.
subjects reclined in a semi-darkened, thermoneutral (22°C) environment under a flow-thru Plexiglas hood (Brooks Instruments, Hatfield, PA) for 30 min. Air was pulled through the hood at a rate of 50 L.min⁻¹ to maintain a slight negative pressure, allowing fresh air movement through the hood at all times. A continuous open-circuit expired gas collection was analyzed by Hartman-Braun (Frankfurt, Germany) differential paramagnetic O₂ (Magnos G.4, Hartman and Braun) and nondispersive infrared CO₂ (Uras, Hartman and Braun) analyzers. The analyzers were calibrated before collection with known gas concentrations.

**Resting energy expenditure (REE).** After subjects were awoken at 0600 h, they were transported by wheelchair to an adjacent room for measurement of their REE. The subjects reclined in a semi-darkened, thermoneutral (22 ± 1°C) environment under a flow-thru Plexiglas hood (Brooks Instruments, Hatfield, PA) for 30 min. Air was pulled through the hood at a rate of 50 L.min⁻¹ to maintain a slight negative pressure, allowing fresh air movement through the hood at all times. A continuous open-circuit expired gas collection was analyzed by Hartman-Braun (Frankfurt, Germany) differential paramagnetic O₂ (Magnos G.4, Hartman and Braun) and nondispersive infrared CO₂ (Uras, Hartman and Braun) analyzers. The analyzers were calibrated before collection with known gas concentrations.

**Leptin assay.** Serum leptin was measured using a two-site immunoradiometric (IRMA) assay (Diagnostic Systems Laboratories, Webster, TX). In this assay, the IRMA was a noncompetitive assay in which the analyte to be measured was sandwiched between two antibodies. The first antibody was immobilized to the inside walls of the tubes. The other antibody was radiolabeled for detection. The analyte present in the unknowns, standards, and controls was bound by both the antibodies to form a sandwich complex. Decanting and washing the tubes removed unbound reagents. Radioactivity was measured on a Cobra gamma counter (Packard Instruments, Downers Grove, IL). To eliminate interassay variance, all samples were measured in one assay. Intra-assay variance was < 5%, and the sensitivity was 0.10 ng·mL⁻¹.

**Statistical analyses.** All data are reported as mean ± SE. An analysis of variance with repeated measures was used for statistical evaluation. The main effects were condition (control vs exercise) and time (hours postexercise). Baseline measures were included for the analysis. Differences in REE were determined with a Student’s t-test. An alpha level of P < 0.05 was used for all statistical analyses.

**RESULTS**

The mean ± SD for each of the IRM lifts was squats (135 ± 12 kg), bench press (110 ± 8 kg), leg press (196 ± 11 kg), and lat pull-down (84 ± 5 kg). The estimated total work performed and energy expenditure during the AHRP was 314 ± 48 kcal and 856 ± 114 kcal, respectively. Table 3 shows these estimates for all 10 subjects. To more clearly delineate the effect of the postexercise treatment (Fig. 1) versus the exercise treatment (Fig. 2), the leptin response patterns are shown for the first hour and for the entire 13-h period.
FIGURE 2—Overnight leptin concentrations sampled every hour for 13 h; * denotes significance at P < 0.05.

DISCUSSION

This study evaluated overnight leptin concentrations sampled every hour for 13 h and morning-after REE following acute heavy-resistance exercise performed in young, lean, fit men. Leptin concentrations exhibited a delayed reduction in the systemic circulation after the resistance-exercise protocol. Leptin concentrations were decreased at the singular time points of 9 (−26%), 10 (−28%), 12 (−30%), and 13 (−33%) h postexercise. Concomitant with the decline in circulating leptin concentrations was a 12% higher resting REE the morning after exercise. This study is distinctive in that 1) it is the first to evaluate circulating leptin concentrations after a bout of resistance exercise, and 2) rigorous blood sampling (i.e., every hour for 13 h) was used to more precisely assess the time course for the leptin response pattern than has been done previously. The fact that REE was elevated for up to 13 h after the exercise session suggests that the observed leptin response pattern was a direct result of the intensity, duration, high energy expenditure (estimated to be 856 ± 114 kcal), and subsequent excess post oxygen consumption (EPOC) of the acute resistance exercise protocol. The findings from our study support the prevailing consensus that leptin suppression is not due to exercise per se but rather the energy deficit induced by the EPOC after acute, heavy-resistance exercise (3,8).

The leading finding of this study was the delayed attenuation in circulating leptin concentrations after acute high-volume heavy-resistance exercise. The divergence in leptin concentrations between the control and exercise conditions did not appear until 9 h after the cessation of resistance exercise. Unfortunately, the only other acute postexercise leptin studies that are available for comparison are for aerobic exercise. Although the majority of these previous studies have failed to observe any effect of exercise on leptin (7,11,12,18,19,25), our data support and extend the recent findings of Essig et al. (3), who also reported a delayed effect of exercise on leptin concentrations after treadmill running at 70% VO2max and those of Elias et al. (2), who reported a decrease after a treadmill run to exhaustion. Essig et al. (3) found a decrease in plasma leptin only at 48 h after exercise, but not at 0 or 24 h. Moreover, Törjman et al. (22) failed to find any effect on leptin concentrations for 4 h after either maximal or prolonged treadmill running at 50% max VO2, whereas Leal-Cerro et al. (13) reported decreased concentrations in men immediately after a marathon. Collectively, the current data on leptin responses after acute exercise suggest that decrements may be observed immediately after extreme or prolonged exercise, whereas responses to more moderate-intensity exercise exhibit a delayed effect. The lack of a leptin response in previous studies may be due to the low energy demands of the exercise session, or to an inadequate blood-sampling duration during recovery. Of the studies providing energy cost estimates for their exercise protocols, Weltman et al. (25) reported no changes in leptin concentrations after 3.5 h of aerobic exercise ranging from 150 ± 11 to 529 ± 45 kcal, whereas Essig et al. (3) reported leptin declines 48 h after energy expenditures of 800 and 1500 kcal, respectively, and Leal-Cerro et al. (13) found a decline immediately after a marathon estimated to expend 2800 kcal. From these data, it would appear that the threshold for exercise-induced energy expenditure that is required to disrupt homeostatic fuel regulation resulting in lowered leptin concentrations lies in the proximity of −530−800 kcal. The estimated energy expenditure from the acute heavy-resistance exercise protocol in this study was 856 ± 114 kcal and, hence, above this hypothesized threshold.

The delayed decline in systemic leptin concentrations is a notable finding in that this differs from the typical hormonal stress response pattern in which an immediate increase postexercise is followed by a restoration back to baseline values during the recovery period. This underscores the importance of observing leptin responses after exercise perturbations during an extended follow-up period. Extended sampling can provide worthwhile information on how long-lasting exercise influences leptin concentrations. Although those engaging in resistance training may be most interested
in targeting and building muscle and lean tissue mass (4,6), this study has demonstrated that blunted leptin secretion from the adipocyte is also one of the many physiological effects of a resistance exercise session. Fat cells should now be considered a hormone-releasing tissue that is affected by resistance exercise. We believe that the delayed decrease in leptin was not from effects inherent to repetitive muscular contractions but from peripheral feedback signals to the central nervous system modulating energy requirements. The caloric expenditure and subsequent lingering EPOC from the high intensity and prolonged duration of the resistance exercise bout in this study likely combined to induce a disruption in energy homeostasis with a resulting delayed reduction in leptin concentrations.

Several limitations of the present study should be mentioned. Unfortunately, the measurement of mediators (i.e., free fatty acids, glucose, insulin) of the leptin decrement were outside the scope of this study. Some have suggested that the effects of exercise on leptin concentrations may be mediated through an acute increase in insulin sensitivity induced by the exercise bout. For example, Essig et al. (3) reported that after exercise, insulin was suppressed and that the decline preceded any observable decline in leptin. As elevated insulin concentrations are known to stimulate leptin concentrations, it may be possible that a reduction in insulin during and after exercise may mediate a down regulation in synthesis/release in leptin. However, inasmuch as Houmard et al. (9) reported that the improvement in insulin action with exercise was not associated with a decrease in leptin concentrations, the association between insulin and leptin warrants further study. Some authors have reported that leptin is secreted in an episodic manner (8,25). We did not sample frequently enough to characterize the pulsatile parameters; thus, we are limited in our interpretations to hourly values. Additionally, we did not directly measure the actual energy cost of the exercise and are thus left with approximate estimates of the caloric cost of the exercise bout. Finally, we have used a group of young, lean, and fit men in the current study. Although Essig et al. (3) had postulated that it might be easier to detect leptin decline in subjects with high leptin levels, we have shown that leptin decreases after exercise is observable in subjects approaching the lower extremes of leptin concentrations. However, our results are not necessarily generalizable to other populations differing in age or fitness level from those in the current study.

In conclusion, this study has provided further insight in the leptin dynamics by demonstrating that a delayed reduction in circulating leptin concentrations occurred approximately 9 h postexercise. Our data illustrate that acute exercise can suppress systemic leptin concentrations and that this decline occurs without an appreciable change in fat mass. Future studies are needed that will clarify the physiological mechanisms and consequences of this exercise-induced delayed reduction in circulating leptin concentrations.

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