Hormonal responses to consecutive days of heavy-resistance exercise with or without nutritional supplementation

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Kraemer, William J., Jeff S. Volek, Jill A. Bush, Margot Putukian, and Wayne J. Sebastianelli. Hormonal responses to consecutive days of heavy-resistance exercise with or without nutritional supplementation. *J. Appl. Physiol.* 85(4): 1544–1555, 1998.—Nine resistance-trained men consumed either a protein-carbohydrate supplement or placebo for 1 wk in a crossover design separated by 7 days. The last 3 days of each treatment, subjects performed resistance exercise. The supplement was consumed 2 h before and immediately after the workout, and blood was obtained before and after exercise (0, 15, 30, 45, and 60 min postexercise). Lactate, growth hormone, and testosterone were significantly ($P \leq 0.05$) elevated immediately postexercise. The lactate response was significantly lower during supplementation on *days 2* and *3*. Growth hormone and prolactin responses on *day 1* were significantly higher during supplementation. After exercise, testosterone declined below resting values during supplementation. Cortisol decreased immediately postexercise on *day 1*; the response was diminished on *days 2* and *3*. Glucose and insulin were significantly elevated by 30 min during supplementation and remained stable during placebo. Insulin-like growth factor-I was higher during supplementatiom on *days 2* and *3*. These data indicate that protein-carbohydrate supplementation before and after training can alter the metabolic and hormonal responses to consecutive days of heavy-resistance exercise.

testosterone; growth hormone; insulin; insulin-like growth factor-I; protein; carbohydrate; anabolic; weight training

TO ENHANCE THE DEVELOPMENT of muscular strength and size with heavy-resistance training, optimal conditions for recovery from the individual exercise training sessions are necessary. Recovery involves the coordinated functioning of several physiological processes that are heavily influenced by the availability and actions of specific hormones and nutrients. Qualitative and quantitative changes in skeletal muscle contractile proteins are all supported and signaled by a host of systematic trophic influences from hormones to nutrient availability (47, 49, 50, 52). Clearly, heavy-resistance exercise disrupts or damages certain muscle fibers that later must undergo a remodeling repair process. Dietary nutrients, hormones, and growth factors interact to regulate this remodeling of skeletal muscle proteins (16).

Although a considerable amount of information exists regarding the acute hormonal responses to a single resistance exercise protocol (29–35), no data are available concerning the acute hormonal responses to consecutive days of heavy-resistance exercise training sessions. In addition, there is virtually no information concerning the influence of nutrition and dietary supplementation on consecutive days of heavy-resistance training. To our knowledge, only two studies have examined the effects of ingesting a dietary supplement composed of protein and carbohydrate on the hormonal responses to heavy-resistance exercise. Chandler et al. (8) demonstrated that insulin and growth hormone concentrations during recovery from a single heavy-resistance training session were significantly higher and testosterone concentrations were lower when subjects consumed a protein-carbohydrate supplement immediately before and 2 h after the workout. Fahey et al. (14) reported that insulin concentrations were higher at the end of exercise when subjects consumed a protein-carbohydrate supplement 30 min before and intermittently during a 2-h weight-training session. These studies indicate that dietary nutrients consumed before, during, and after resistance exercise alter the typical hormonal response patterns.

Independent of exercise, dietary energy and nutrients may influence hormonal concentrations and thus help to mediate physiological mechanisms related to recovery from heavy-resistance exercise. An increase in caloric intake above energy requirements enhances growth hormone, testosterone, and insulin-like growth factor-I (IGF-I) concentrations (17). Branched-chain amino acids (BCAAs) have been shown to alter concentrations of growth hormone (6), insulin (15), testosterone (7), and cortisol (37). In addition, BCAAs have been shown to attenuate protein degradation (5, 9, 40), enhance lean body mass (36, 45), and prevent fatigue (11). The quantity and composition of dietary fat may also impact resting (52) and exercise-induced (42) testosterone concentrations in healthy men. Further evidence supporting the importance of nutrition in regulating circulating hormone concentrations is the well-known negative effects of energy and/or protein restriction on serum IGF-I concentrations (50).

Regulation of hormones by nutrients may be hypothesized to become increasingly important during consecutive days of intense heavy-resistance exercise in which anabolic/catabolic turnover (e.g., glycogen synthesis/breakdown, protein synthesis/degradation, and intramuscular triglyceride repletion/depletion) are acceler-

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ated. For example, inadequate carbohydrate intake during recovery may compromise glycogen resynthesis and impair performance (4). Protein intake at the level of the recommended daily allowance (RDA) in weight lifters may result in a negative nitrogen balance (37, 49) and thus potentially compromise gains in muscular size and strength. Thus optimizing nutrition during the recovery period between exercise training sessions may lead to a more favorable nitrogen balance and glycogen levels between training sessions.

Dietary nutrients have the ability to alter circulating hormones and thus influence the effectiveness of the exercise stimulus to elicit training adaptations. However, our understanding of these complex interactions is incomplete, especially related to heavy-resistance exercise in which several other aspects of program design (e.g., intensity and duration, rest periods, muscle mass involvement) and individual characteristics (e.g., age, gender, training status) also contribute to the exercise-induced hormonal responses (29). The intent of this investigation was to characterize the acute hormonal responses to heavy-resistance exercise and to examine how dietary alterations impact the anabolic milieu in the circulation. We hypothesized that ingesting a protein-carbohydrate supplement before and after resistance exercise would enhance anabolic hormonal responses (insulin, growth hormone, and IGF-I) and possibly reduce the acute catabolic response to intense resistance exercise. Thus the primary purpose of this investigation was to examine the influence of a high-calorie liquid carbohydrate-protein supplement rich in BCAAs on the acute hormonal responses to heavy-resistance exercise. In addition, a secondary purpose was to examine these hormonal response patterns over multiple days.

METHODS

Subjects. Nine healthy resistance-trained men volunteered to participate in this investigation. The physical characteristics of the subjects were the following: age, 21.3 ± 1.2 (SD); height, 181.6 ± 2.7 cm; body mass, 85.3 ± 12.9 kg; and body fat, 14.2 ± 4.9%. All subjects were informed as to the possible risks of the investigation before giving their written informed consent in accordance with the Pennsylvania State University Institutional Review Board for use of human subjects. All subjects were currently resistance training and were considered moderately to highly trained with 6.4 ± 2.8 yr of resistance training experience. Subjects were training four to six times per week. Training programs were periodized for intensity and volume of training by using multiple sets, heavy resistance [6–12 repetitions maximum (RM)], and varied rest periods (1–4 min). An important point to note was that none of the subjects were performing any high-intensity aerobic endurance training or other strenuous activities outside of their resistance training workouts (35). Thus the subjects in this study were homogenous with regard to their "training status." Subjects were not taking any nutritional supplements, nor did any of the subjects report the use of anabolic drugs. Medical screening indicated that none of the subjects had any orthopedic, endocrine, or other medical problems that would confound their participation in the study.

Experimental design and exercise testing. Subjects acted as their own controls. All subjects were exposed to a supplement treatment condition and a placebo treatment condition in a balanced, double-blind, crossover design. The duration of each treatment was 1 wk. Initially, subjects were randomly assigned to receive either the supplement or placebo and then were assigned to the remaining treatment condition after a 1-wk washout period after the completion of the first condition. A 1-wk washout period was chosen to allow adequate recovery between experimental training sessions and to provide sufficient time for equilibration of metabolic and hormonal responses to baseline conditions. Again, the subjects served as their own controls, thus enhancing the internal validity of the study. All subjects completed 3 consecutive days of heavy-resistance exercise on the last 3 days of each 7-day dietary treatment condition. During the 1-wk washout period, subjects performed two resistance exercise workouts (on their own) and one workout during the initial 2 days of each 7-day condition. Thus subjects refrained from training for a minimum of 48 h before the first workout of each 7-day condition. The experimental time line is illustrated in Fig. 1.

All subjects were completely familiarized with all of the experimental procedures, had anthropometric measurements made, and had their 10 RM determined for each of the four exercises used in the resistance exercise protocol (i.e., squat, bent over row, bench press, and military press), as previously described (30, 34). The resistance exercise protocol involved four sets each of four exercises (16 sets total) performed in the following order: squat, bent over row, bench press, and seated military press with exactly 2 min recovery between all sets and exercises. The resistance was adjusted appropriately on each set so that 10 repetitions (i.e., 10 RM) could be performed for all sets (30). Subjects reported back to the laboratory on the following day at the same time and completed the same resistance exercise protocol. The time of day was

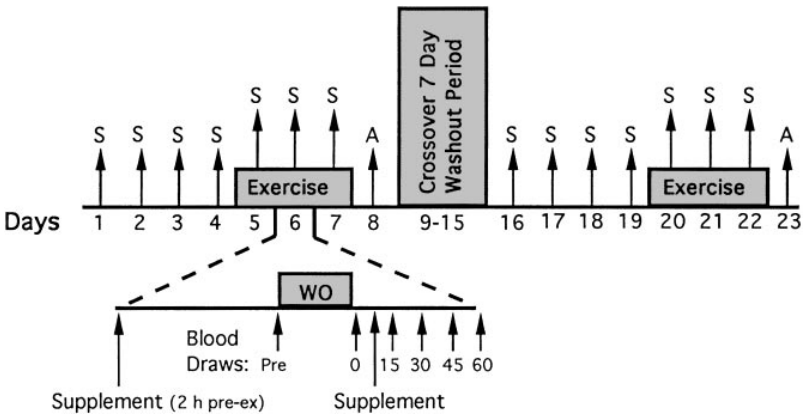

Fig. 1. Experimental time line. Subjects consumed either a high-calorie protein-carbohydrate supplement or placebo for 1 wk (*days 1–7*). After a 1-wk washout period (*days 9–15*), subjects were assigned the opposite condition for another week (*days 16–22*). A heavy-resistance exercise workout (WO) was performed the last 3 days of each 1-wk supplement period. Internal time line for 1 experimental day is shown for *day 6*. Subjects consumed the supplement 120 min before (2 h pre-ex) and immediately after exercise. Blood samples were obtained preexercise (Pre) and at 0, 15, 30, 45, and 60 min postexercise. A, anthropometric measurements; S, supplementation days.

standardized to minimize potential diurnal variations in exercise performance and hormones (43, 51). This was repeated again the following day for a total of 3 consecutive days of heavy-resistance training workouts. The acute program variables (e.g., exercise selection, number of sets and repetitions, rest periods, and relative load) over the three workouts were not altered to minimize confounding variables and facilitate comparison of the hormonal responses over the 3 days. All exercise sessions were performed on a Plyometric Power System (Lismore, New South Wales, Australia) interfaced to an online computer system as previously described (53). Briefly, resistance is provided by a barbell that can only move up and down in the vertical direction, similar to a Smith machine setup with linear bearings attached to both ends of the bar which allow it to slide up two steel shafts with minimal friction. An adjustable bench was placed underneath the bar for performance of the bench press and seated military press exercises.

Nutritional protocol. During each 7-day treatment condition, subjects consumed a high-calorie liquid supplement (MassFuel, Twin Laboratories, Ronkonoma, NY) or an equivalent amount of placebo containing xylitol, microcrystalline cellulose, cocoa powder, dried cream extract, guar gum, aspartame, and natural chocolate flavor. The placebo was specifically designed to look and taste identical to the supplement while providing minimal carbohydrate, protein, and calories. The supplement was composed of 33% protein (predigested casein and albumin) and 67% carbohydrate (glucose polymers, glucose, crystalline fructose, and xylitol). One serving of the supplement also contained between 50 and 1,000% of the US RDA for all essential vitamins and minerals (Table 1). Subjects were provided with individual packets of either the placebo or supplement in powder form with written instructions to mix the contents of each packet in 16 ounces of water. Subjects consumed three packets throughout the day (morning, afternoon, evening) in addition to their normal dietary intake. On exercise days, subjects drank one-half of a serving 2 h before their workout and one-half of a serving after the immediate postexercise blood draw. The remaining two servings were consumed later in the evening. Written documentation and verbal verification after the study indicated compliance with the supplement protocol was 100%. Each full serving of the supplement was calculated and individually measured to provide each subject daily with 7.9 kcal/kg, 1.3 g carbohydrate/kg, and 0.7 g protein/kg. Thus the one-half servings consumed 2 h pre- and immediately postexercise provided ~4.0 kcal/kg, 0.7 g/kg, and 0.4 g protein/kg. On the basis of body mass differences between subjects, the supplement provided between 525 and 825 kcal per serving.

Table 1. *Nutritional information per serving of the protein-carbohydrate supplement used in the experimental condition*

Energy, kcal	600	PABA, mg	5
Protein, g	50	Choline, mg	250
Carbohydrate, g	100	Inositol, mg	250
Fat, g	0	Calcium, mg	1,000
β-Carotene, IU	5,000	Magnesium, mg	250
Vitamin D, IU	200	Potassium, mg	2,000
Vitamin C, mg	60	Zinc, mg	30
Vitamin E, IU	30	Manganese, mg	10
Vitamin B_1, mg	5	Copper, mg	1
Vitamin B_2, mg	5	Iron, mg	5
Vitamin B_6, mg	5	Phosphorus, mg	350
Vitamin B_{12}, μg	18	Iodine, μg	75
Niacin, mg	50	Selenium, μg	200
Panothenic acid, mg	100	Chromium, μg	300
Folic acid, μg	400	Molybdenum, μg	150
Biotin, μg	300	Boron, mg	3

Values are based on assumption of a 75-kg subject. PABA, *p*-aminobenzoic acid.

Before the beginning of the study, each subject met with a registered dietitian and was provided with specific verbal and written instructions and procedures for reporting detailed dietary intake, including how to record portions by using household measures, combination foods, preparation technique, and nutrient content descriptors (e.g., light, fat free, lean, reduced, etc.). Subjects were instructed to consume their normal diet during the first experimental period in addition to the supplement and to duplicate these conditions during the second 7-day experimental condition. Individual food records were returned to subjects to facilitate replication of their diet during the second phase of the study. Dietary information, including supplements, recorded from each 7-day period were analyzed for dietary energy and macronutrient composition by using Nutritionist IV, Version 4, nutrient analysis software (N-Squared Computing, First Databank Division, Hearst, San Bruno, CA). This software contains a currently updated database of over 13,000 foods, including many brand name manufacturers' items and products from national fast-food chains. The nutrient data are based primarily on all available US Department of Agriculture data and scientific journal and industry sources. If a nutrient value was missing, information from other food tables or information provided by food manufacturers was obtained.

Anthropometric measurements. Body mass was measured on a Toledo electronic scale (Reliance Electronic, Worthington, OH) to the nearest 100 g at each exercise session. Circumferences and skinfold measurements were obtained during experimental familiarization and the day after each 7-day supplementation period by using standard methods (38). Skinfold measurements from seven sites (triceps, subscapular, midaxillary, chest, suprailiac, abdomen, and thigh) and circumference measurements from four sites (arm, thigh, waist, and hips) were obtained on the right side in serial fashion by the same investigator. Skinfold thickness and circumference measurements were based on the average of two trials that differed by <1.0 and 5 mm, respectively.

Blood collection and analyses. On experimental days, subjects reported to the laboratory and sat down quietly for 15 min. A 20-gauge 1.25-in. Teflon cannula was inserted into an antecubital forearm vein from which blood samples were obtained by using a stopcock and syringe set up at the following time points: preexercise (resting) and 0, 15, 30, 45, and 60 min postexercise. The cannula was kept patent with periodic injections of isotonic saline. The blood was processed and centrifuged, and the resultant serum was stored at −84°C until analyzed. Serum lactate was determined in duplicate via a lactate analyzer (YSI model 1500 Sport Lactate Analyzer, Yellow Springs Instruments, Yellow Springs, OH). Serum glucose and creatine kinase (CK) activity were determined in duplicate via spectrophotometry (Novaspec II, Pharmacia LKB Biochrom, Cambridge, UK) and commercial assay kits (Sigma Diagnostics, St. Louis, MO). Hemoglobin was analyzed in triplicate by using the cyanmethemoglobin method (Sigma Diagnostics), and hematocrit was analyzed in triplicate from whole blood via microcentrifugation and microcapillary technique. Percent changes in plasma volume were calculated by using hemoglobin and hematocrit values (12). Serum total testosterone, cortisol, prolactin, growth hormone, sex hormone-binding globulin (SHBG), insulin, and IGF-I were determined in duplicate by using standard RIA procedures. Serum total testosterone, cortisol, prolactin, and insulin were assayed by using a solid-phase ^{125}I RIA (Diagnos-

Table 2. *Daily dietary intake and anthropometric data*

Variable	Supplement	Placebo
Dietary intake		
Energy, kcal	3,831 ± 365*	2,463 ± 680
Protein, g	234 ± 32*	104 ± 21
Protein, %	24 ± 3*	17 ± 3
Carbohydrate, g	570 ± 59*	350 ± 134
Carbohydrate, %	60 ± 4	56 ± 8
Fat, g	58 ± 14	64 ± 23
Fat, %	14 ± 3*	24 ± 8
Alcohol, %	2 ± 2	3 ± 2
Body mass, kg		
Workout *day 1*	82.4 ± 10.1*	81.6 ± 10.2
Workout *day 2*	83.1 ± 10.3*	81.5 ± 10.2
Workout *day 3*	83.3 ± 10.3*	82.0 ± 10.1
Day 4	83.0 ± 10.2*	82.0 ± 9.9
Σ7 Skinfolds, mm	92.8 ± 29.7	89.2 ± 28.2
Circumferences, cm		
Arm	32.6 ± 2.8	33.0 ± 3.1
Thigh	57.9 ± 4.7	56.5 ± 3.9
Waist	83.6 ± 9.0	83.4 ± 9.3
Hips	102.1 ± 7.0	100.0 ± 5.5

Values are means ± SD. For 1 wk, subjects consumed a protein-carbohydrate supplement or placebo. Workout days were performed the last 3 days of each week (i.e., *days 1*, *2*, and *3*). Skinfold thickness and circumference measurements were determined the day after the last workout (i.e., *day 4*). *$P \leq 0.05$ compared with corresponding value for placebo.

tic Products, Los Angeles, CA) with detection limits of 0.14 nmol/l, 5.5 nmol/l, 3.7 μg/l, and 8.6 pmol/l, respectively. Human growth hormone was measured with a double-antibody ^{125}I liquid-phase RIA (Nichols Institute Diagnostics, San Juan Capistrano, CA) with a detection limit of 0.02 μg/l. SHBG was determined via an immunoradiometric assay (Diagnostic Systems Laboratories, Webster, TX) with a sensitivity of 3.0 nmol/l. IGF-I was assayed by using an ^{125}I double-antibody disequilibrium technique, including an extraction that used ODS-silica columns (INCSTAR, Stillwater, MN). The minimum detectable amount of IGF-I for this assay is <2.0 nmol/l. Intra- and interassay variances for all assays were <5%.

Statistical analysis. Statistical evaluation of the data was accomplished by using a two-way analysis of variance with repeated-measures design. The two factors were supplement condition (protein-carbohydrate vs. placebo) and repeated measures (pre- and postexercise blood samples over time). When a significant *F* value was achieved, a Fisher's least significant difference post hoc test was used to locate the pairwise differences between means. Statistical power calculations ranged from 0.78 to 0.80. The level of significance for this investigation was set at $P \leq 0.05$.

RESULTS

Repetitions performed per set for workout *days 1*, *2*, and *3* were 9.5 ± 0.3, 9.6 ± 0.2, and 9.8 ± 0.2 during placebo and were 9.5 ± 0.4, 9.6 ± 0.2, and 9.6 ± 0.4 during supplement, respectively. There were no significant differences in the total volume of weight lifted (weight × repetitions) or the average weight lifted (total volume/total repetitions) from *day 1*, *day 2*, and *day 3* between treatment conditions. Dietary intake and anthropometric data are shown in Table 2. Dietary energy was 1,368 kcal/day higher during the week of supplementation. Protein and carbohydrate intakes were also higher during supplementation. Expressed as a percentage of total dietary energy, protein was higher and fat was lower during supplementation. Body mass was significantly higher during supplementation at each of the three exercise sessions compared with placebo. There were no significant differences in skinfold thickness or circumference measurements between treatment conditions.

Serum lactate, CK activity, and glucose responses are shown in Table 3. Serum lactate concentrations in-

Table 3. *Serum lactate, creatine kinase activity, and glucose responses to 3 consecutive days of heavy-resistance exercise*

	Lactate, mmol/l		Creatine Kinase, U/l		Glucose, mmol/l	
	Supplement	Placebo	Supplement	Placebo	Supplement	Placebo
Day 1						
Preexercise	2.01 ± 0.47	1.89 ± 0.52	158.2 ± 116.6	129.2 ± 94.1	5.58 ± 0.88	6.15 ± 1.56
0	15.30 ± 1.76*	15.47 ± 1.53*	186.4 ± 120.6	196.7 ± 145.9*	5.59 ± 1.10	5.56 ± 1.42
15	9.28 ± 2.48*	10.59 ± 1.83*	195.9 ± 99.2	202.6 ± 172.8*	5.94 ± 0.86	5.59 ± 0.89
30	5.94 ± 2.17*	6.81 ± 1.72*	183.5 ± 113.0	182.6 ± 154.1*	6.79 ± 1.97*	5.65 ± 1.44
45	3.79 ± 1.09*	4.79 ± 1.21*	186.9 ± 97.7	194.4 ± 127.5*	7.12 ± 1.81*	5.56 ± 1.05
60	2.91 ± 0.66	3.20 ± 0.68*	221.9 ± 117.1	191.1 ± 157.2*	5.56 ± 1.90	5.24 ± 1.25
Day 2						
Preexercise	1.75 ± 0.64	1.74 ± 0.43	332.4 ± 236.1§	314.6 ± 391.2§	5.54 ± 0.69	5.34 ± 0.77
0	13.40 ± 2.46*§	14.82 ± 1.71*	357.1 ± 244.4§	360.9 ± 420.4*	5.57 ± 0.59	6.41 ± 1.94
15	8.35 ± 2.00*†	9.87 ± 1.81*	364.4 ± 209.3§	358.5 ± 392.2*	6.22 ± 1.09	5.86 ± 1.30
30	4.93 ± 1.72*†§	6.60 ± 1.37*	315.4 ± 236.3	346.8 ± 375.1	7.15 ± 1.75*†	5.51 ± 1.33
45	3.74 ± 0.97*†	4.42 ± 1.09*	316.3 ± 196.1§	332.6 ± 369.4	6.56 ± 1.69*†	5.48 ± 1.45
60	2.92 ± 0.75*†	3.37 ± 0.80*	313.9 ± 197.5	315.7 ± 331.6	5.55 ± 1.51	5.30 ± 1.28
Day 3						
Preexercise	1.81 ± 0.43	1.67 ± 0.56	251.6 ± 142.6	278.7 ± 266.7	4.66 ± 0.34†§	5.52 ± 1.02
0	12.81 ± 2.16*†§	13.77 ± 1.60*	269.5 ± 172.7	313.9 ± 329.1	4.98 ± 0.64	5.52 ± 1.07
15	7.65 ± 2.36*†§	9.33 ± 1.76*§	279.7 ± 198.4	249.2 ± 244.2	6.00 ± 1.40	5.36 ± 1.06
30	4.32 ± 1.36*†§	5.99 ± 1.18*§	288.2 ± 164.6	236.7 ± 209.0	6.32 ± 1.55	5.35 ± 0.98
45	3.30 ± 0.91*†	4.25 ± 0.96*	261.9 ± 176.6	262.1 ± 274.9	5.42 ± 1.17§	5.21 ± 0.91
60	2.70 ± 0.57	3.26 ± 0.81*	256.6 ± 163.4	263.8 ± 271.6	4.24 ± 0.60§	4.84 ± 0.86

Values are means ± SD. *$P \leq 0.05$ from corresponding preexercise value. †$P \leq 0.05$ from corresponding value for placebo. §$P \leq 0.05$ from corresponding time point on *day 1*.

creased immediately postexercise and stayed elevated above baseline through 60 min postexercise. Compared with placebo, lactate concentrations were significantly lower during supplementation at several time points on *days 2* and *3*. Immediately postexercise on *days 1* and *2* during placebo, there was a significant increase in CK activity which remained above preexercise values the entire 60 min on *day 1* and 15 min postexercise on *day 2*. There were no significant differences between treatment conditions in CK activity. Serum glucose concentrations were significantly elevated above preexercise concentrations at 30 and 45 min postexercise on *days 1* and *2* and 15 and 30 min postexercise on *day 3* during supplementation, whereas glucose remained stable during placebo. Compared with placebo, supplementation resulted in significantly higher glucose concentrations at 30 and 45 min postexercise on *day 2* and a significantly lower preexercise value on *day 3*.

Serum total testosterone and SHBG responses are shown in Fig. 2. Testosterone significantly increased immediately postexercise for both treatment conditions on all 3 days. After the immediate postexercise increase, total testosterone concentrations declined to below resting values on *day 3* during placebo and on *days 2* and *3* during supplementation. Testosterone concentrations were significantly higher during placebo at rest and 45 min postexercise on *day 2* and at 30 min postexercise on *day 3*. There were no significant differences for any time points on *days 2* and *3* compared with corresponding time points on *day 1*. Serum SHBG concentrations tended to increase with exercise and then decline below resting values. Compared with *day 1*, immediate postexercise values during supplementation were lower on *days 2* and *3*. Similar to total testosterone, SHBG values during placebo were significantly higher at several time points compared with those during supplementation. There were no significant differences in the free-androgen index (total testosterone/SHBG) between treatment conditions at any time point on any day (Table 4).

Serum growth hormone concentrations significantly increased immediately postexercise and returned to resting concentrations by 60 min of recovery (Fig. 3). On *day 1*, growth hormone concentrations at 0, 15, and

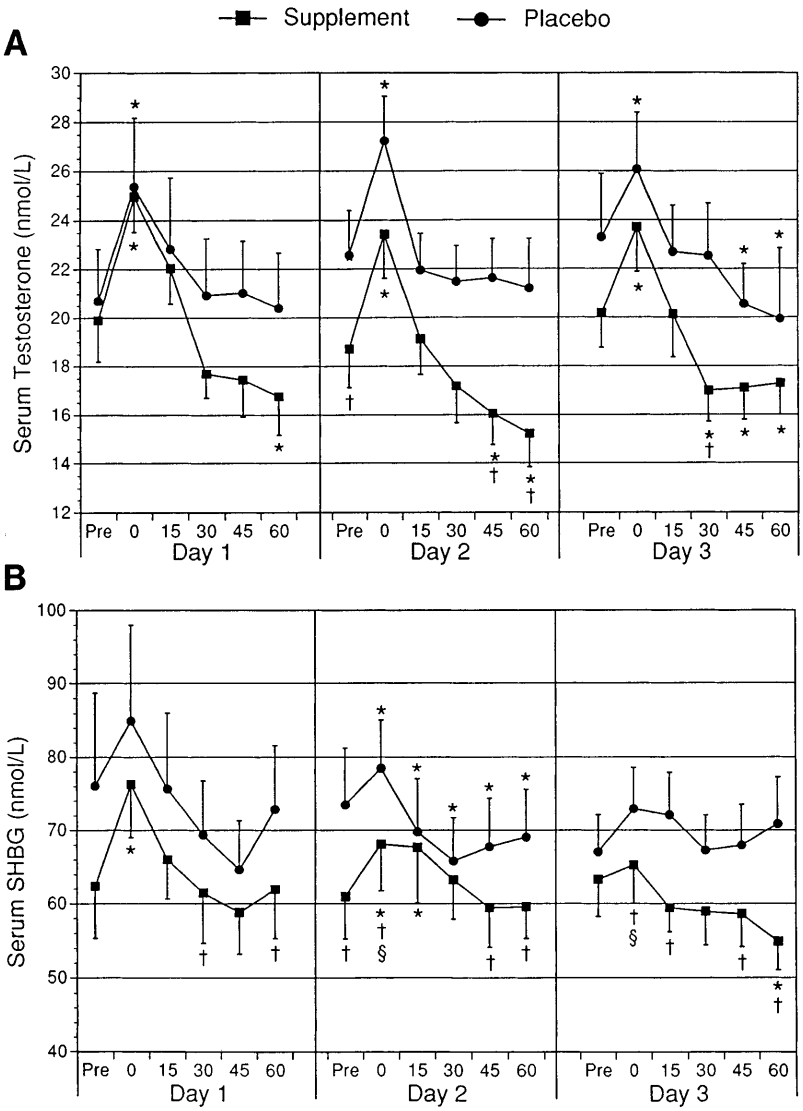

Fig. 2. Serum total testosterone (*A*) and sex hormone-binding globulin (SHBG; *B*) responses to 3 consecutive days of heavy-resistance exercise. During the supplement condition, subjects consumed a protein-carbohydrate drink 2 h before and immediately after workouts, and during placebo condition subjects consumed a placebo drink at the same time points. Values are means ± SE. 0, 15, 30, 45, and 60, postexercise time points (min). *$P \leq 0.05$ from corresponding preexercise value. †$P \leq 0.05$ from corresponding value for Placebo. §$P \leq 0.05$ from corresponding time point on *day 1*.

Table 4. *Free-androgen index (total testosterone/SHBG) response to 3 consecutive days of heavy-resistance exercise*

	Supplement	Placebo
Day 1		
Preexercise	0.35 ± 0.16	0.30 ± 0.16
0	0.35 ± 0.11	0.32 ± 0.11
15	0.35 ± 0.11	0.32 ± 0.10
30	0.32 ± 0.12	0.32 ± 0.10
45	0.30 ± 0.06	0.35 ± 0.15
60	0.28 ± 0.06	0.31 ± 0.14
Day 2		
Preexercise	0.33 ± 0.11	0.32 ± 0.08
0	0.37 ± 0.13	0.35 ± 0.06
15	0.31 ± 0.10	0.33 ± 0.07
30	0.29 ± 0.09	0.34 ± 0.06
45	0.29 ± 0.11	0.33 ± 0.07
60	0.27 ± 0.09*	0.31 ± 0.08
Day 3		
Preexercise	0.33 ± 0.08	0.36 ± 0.12
0	0.38 ± 0.11*	0.37 ± 0.10
15	0.34 ± 0.09	0.33 ± 0.07
30	0.30 ± 0.08	0.35 ± 0.12
45	0.30 ± 0.08	0.31 ± 0.07
60	0.32 ± 0.07	0.29 ± 0.07*

Values are means ± SD. SHBG, sex hormone-binding globulin. *$P \leq 0.05$ from corresponding preexercise value.

30 min postexercise were significantly higher than placebo. The growth hormone response to exercise during supplementation on *day 1* was significantly higher at all time points compared with the corresponding time points on *days 2* and *3*. Serum prolactin concentrations significantly increased immediately postexercise on *day 1* during supplementation and *days 1* and *2* during placebo (Table 5). By 60 min postexercise, prolactin concentrations had returned to preexercise values. Serum cortisol concentrations significantly increased immediately after exercise on *day 1* during supplementation and on *days 1* and *2* during placebo (Fig. 3). The cortisol response to exercise during supplementation was significantly higher at all time points compared with the corresponding time points on *days 2* and *3*.

Serum insulin and IGF-I responses are shown in Fig. 4. Insulin concentrations were not different at any time point during placebo. However, insulin was significantly greater than preexercise concentrations at 30, 45, and 60 min postexercise on all 3 days during supplementation. Furthermore, the 15- and 30-min postexercise time points were significantly greater on *day 3* compared with *day 1* during supplementation. Serum IGF-I concentrations were not significantly elevated after exercise in either treatment condition. The values were higher at all time points during supplementation; however, only the preexercise values on *days 2* and *3* were significantly greater than placebo.

Changes in plasma volume shifts during recovery were not significantly different between experimental treatment conditions. On all 3 days, plasma volume tended to decrease immediately postexercise (less than −10% decrease), increased above resting values by 15 min postexercise (−3% to +17%), and peak ~30–45 min postexercise intake (+13 to +22% increases) because of fluid supplement intake. Because no significant differences were observed between treatment conditions, we report the absolute blood values that were not corrected for plasma volume shifts per our previous experimental study rationale (30, 31, 33).

DISCUSSION

The primary findings of this study were that dietary intakes of protein and carbohydrate significantly affect the hormonal response patterns to a heavy-resistance exercise protocol. In addition, it was remarkable how similar the hormonal response patterns to resistance exercise were in the placebo conditions despite consecutive days of training. This study was specifically designed to examine the effects of ingesting a liquid supplement containing carbohydrate and protein on the acute metabolic and hormonal responses to 3 consecutive days of heavy-resistance exercise. Subjects served as their own controls, and the relative intensities of the workouts were designed to be similar in the respect that each set was performed with a resistance that allowed performance of 10 repetitions (i.e., each set was a 10-RM resistance). There were no significant differences between treatment conditions in the total volume of weight lifted and the average weight lifted per set on corresponding workout days. The goal of supplementing the diet was to increase dietary energy, protein, and carbohydrate intake to induce metabolic and hormonal responses that would enhance anabolic processes (e.g., glycogen resynthesis and protein synthesis) during recovery, especially during the immediate postexercise period. Indeed, calculated dietary intake over the 1-wk supplementation periods showed that this was the case. Thus any differences in the concentrations of blood variables are most likely due to these differences in the quantity and/or composition of dietary nutrients ingested. Whether the chronic effects of supplementation (i.e., 7 days in this study) were responsible for the altered hormonal responses cannot be assessed with confidence because of the acute (i.e., immediately postexercise) ingestion of the supplement.

The high-intensity nature of the resistance exercise protocol used was reflected by the high serum lactate concentrations. These lactate responses are comparable to previously reported data in our laboratory during similar heavy-resistance exercise workouts (31, 33, 35). The lactate responses were diminished on *days 2* and *3* during supplementation and on *day 3* during placebo despite a similar total volume and intensity of the workouts. These lower lactate responses may be due to a relative increase in the proportion of lipid as a fuel source over carbohydrate, or, alternatively, there may have been a greater conversion of lactate into glycogen during the rest periods between sets during exercise and/or the immediate postexercise period. Although we know of no information on the effects of carbohydrate ingestion after resistance exercise on lactate during recovery, it has been estimated that between 50 and 90% of the lactate formed during endurance exercise is resynthesized back to glycogen in the muscle (2, 26, 28). Other possibilities include

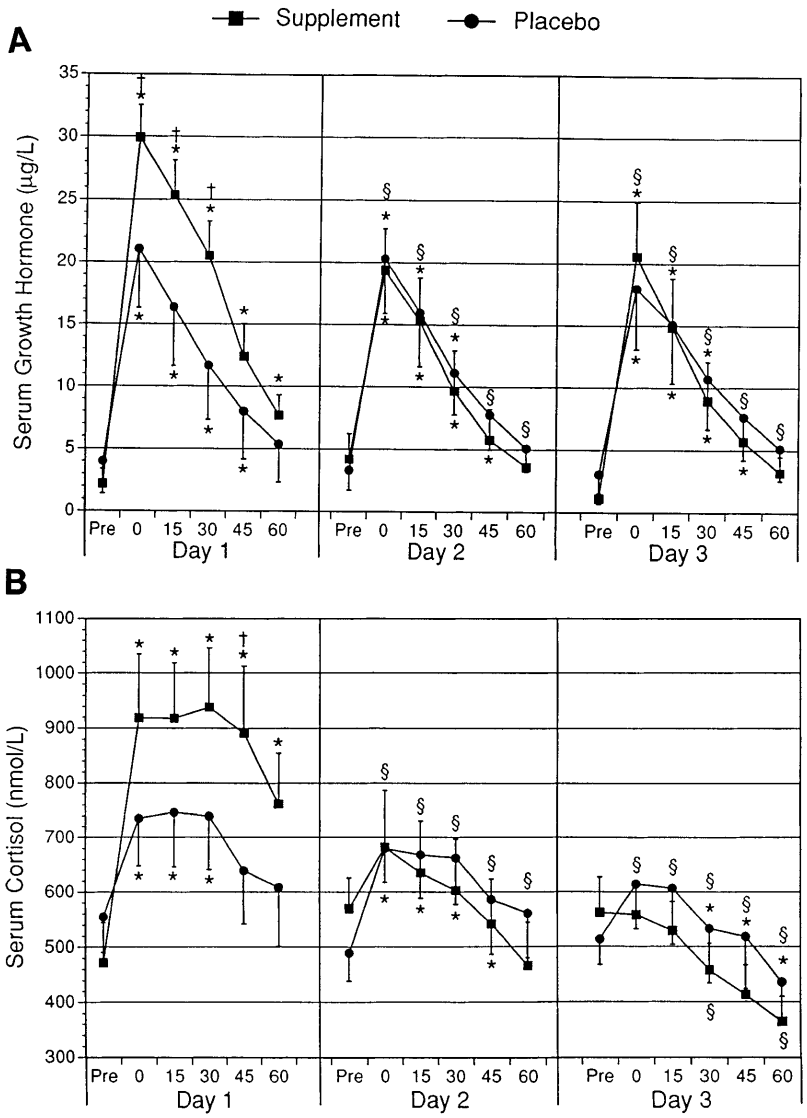

Fig. 3. Serum growth hormone (*A*) and cortisol (*B*) responses. During supplement condition, subjects consumed a protein-carbohydrate drink 2 h before and immediately after the workouts, and during placebo condition subjects consumed a placebo drink at same time points. Values are means ± SE. *$P \leq 0.05$ from corresponding preexercise value. †$P \leq 0.05$ from corresponding value for placebo. §$P \leq 0.05$ from corresponding time point on *day 1*.

increased clearance of lactate via gluconeogenesis in the liver or oxidation by skeletal muscle.

Testosterone concentrations increased immediately postexercise and then returned toward resting levels over the next 60 min of recovery for placebo. In contrast, testosterone fell to below resting values during supplementation. Chandler et al. (8) observed a similar phenomenon in men who consumed a liquid supplement containing both protein and carbohydrate compared with a noncaloric placebo. These data indicate that calories, in the form of carbohydrate and/or protein, have an acute attenuating effect on circulating testosterone concentrations. Although there is a general lack of information on the impact of dietary substances on testosterone, we propose two potential dietary-related factors that may explain our findings. First, percent dietary fat during supplementation was significantly lower than during the placebo condition (14 vs. 24% of total energy). In healthy active men, a diet with a low percentage of dietary fat is associated with lower testosterone concentrations (53). Second, the protein-to-carbohydrate ratio during supplementation was significantly higher than during placebo treatment condition (0.4 vs 0.3). A high protein-to-carbohydrate ratio is also associated with lower testosterone concentrations in healthy active men (52). Furthermore, switching from a high-protein diet to a low-protein diet (i.e., decreasing the protein-to-carbohydrate ratio) has been shown to significantly increase total testosterone and SHBG (1). In support of this theory, both testosterone and SHBG concentrations were lower during the supplement condition in which the protein-to-carbohydrate ratio was higher compared with placebo. The exact mechanism(s) by which the quantity and composition of dietary nutrients regulate testosterone and its binding proteins remain to be fully elucidated.

The lower testosterone values in the study by Chandler et al. (8) occurred at the same time insulin concentrations were elevated, suggesting an interaction between these two anabolic hormones. Interestingly, the same inverse pattern of response between testosterone and insulin was also observed in this study. That is, when insulin concentrations were highest, testosterone concen-

Table 5. *Serum prolactin response to 3 consecutive days of heavy-resistance exercise*

	Supplement	Placebo
Day 1		
Preexercise	10.0 ± 5.2	9.9 ± 4.8
0	19.8 ± 12.2*	14.8 ± 13.2*
15	17.8 ± 9.9*	14.3 ± 12.1*
30	14.7 ± 6.5	13.9 ± 9.5
45	11.9 ± 4.4	11.6 ± 6.4
60	10.3 ± 2.8	9.9 ± 4.4
Day 2		
Preexercise	10.1 ± 3.4	9.2 ± 3.9
0	13.2 ± 6.8	13.8 ± 7.1*
15	10.9 ± 4.4†	13.4 ± 10.6*
30	11.0 ± 3.7†	11.4 ± 7.3
45	9.9 ± 3.3†	9.7 ± 4.4
60	9.4 ± 2.1	8.2 ± 3.7
Day 3		
Preexercise	9.8 ± 3.7	10.1 ± 4.9
0	10.6 ± 5.1	11.9 ± 6.8
15	9.5 ± 4.7†	11.9 ± 6.9
30	9.9 ± 3.6†	11.2 ± 8.6
45	9.1 ± 3.1†	8.9 ± 5.4†
60	8.7 ± 3.1	8.0 ± 4.3

Values are means ± SD in μg/l. *$P \leq 0.05$ from corresponding preexercise value. †$P \leq 0.05$ from corresponding time point on *day 1*.

trations were lowest, and when insulin concentrations were lowest, testosterone concentrations peaked. In support of our data and those of others (8), it has been shown that in adult men insulin is negatively correlated with both testosterone and SHGB (41, 46). Additionally, there may have been an increase in biologically active or free testosterone despite a lower total testosterone during supplementation. An indirect measure of the biologically active testosterone, the free-androgen index (total testosterone/SHGB), was not significantly different between supplement and placebo conditions. Thus, although total testosterone was lower at some time points during the supplement condition, it is very likely that the biologically active free testosterone was not different. Finally, it is possible that there was a greater clearance of circulating testosterone or a reduction in secretion after exercise and supplementation. The relative contributions of these mechanisms to circulating testosterone during intense exercise and dietary supplementation require further investigation.

There were no differences between conditions in resting serum growth hormone concentrations; however, the postexercise growth hormone response was higher on *day 1* during supplementation. The control of growth hormone synthesis and release is predominantly thought to reside at the level of the hypothalamus via regulation by growth hormone-releasing hormone and somatostatin. However, the amplitude and frequency of growth hormone-secretory pulses may be regulated by several other factors, including nutrition and exercise, as well as circulating substrates, hormones, and growth factors (24). For example, lactate and H^+ have been shown to play a role in exercise-induced stimulation of growth hormone (22, 39). Thus the higher lactate response on *day 1* may explain the enhanced growth hormone response on *day 1* during supplementation. Fry et al. (18) demonstrated a reduction in postexercise concentrations of lactate and growth hormone after 1 wk of high-volume weight-lifting training that was similar to our data showing a diminished response of lactate and growth hormone after 3 days of intense exercise. Furthermore, the slightly lower preexercise glucose concentration during supplementation may have contributed to the greater increase in growth hormone on *day 1*, because high levels of glucose inhibit the exercise-induced increase in growth hormone (20). Finally, several amino acids have been shown to increase serum growth hormone concentrations, including the BCAA leucine (6). If the leucine-enriched protein-carbohydrate supplement contributed to the enhanced growth hormone response on *day 1*, then the growth hormone response on *days 2* and *3* should have been elevated to a similar magnitude. Because this was not the case, the elevated growth hormone response on *day 1* was most likely not related to the leucine content of the supplement.

As in a previous study in our laboratory (34), no significant increases in IGF-I were observed after the resistance exercise. Growth hormone has been shown to stimulate the release of IGF-I from the liver, with peak values of IGF-I occurring ~16–28 h after growth hormone stimulation (10). This delay in growth hormone-stimulated release of IGF-I corresponds nicely with the significantly greater postexercise increase in growth hormone on *day 1* and the significantly greater resting IGF-I concentrations ~23 h later on *day 2* during supplementation. However, a growth hormone-induced increase in IGF-I does not explain the greater IGF-I concentrations on *day 3*, which occurred despite no significant differences in the resting and postexercise responses of growth hormone on *day 2* during supplementation. Thus another mechanism was acting in concert with growth hormone-stimulated release of IGF-I to account for the higher concentrations observed during supplementation in this study. Decreases in total energy and protein content of the diet decrease (50) and overfeeding increases (17) serum IGF-I concentrations. The higher intake of essential amino acids (primarily BCAAs) may also have contributed to the higher IGF-I during supplementation, because essential amino acids have been shown to impact serum IGF-I and nitrogen balance to a greater extent than do nonessential amino acids (50). Thus the higher caloric and protein intake combined with the stimulus of resistance exercise may have stimulated an increase in IGF-I.

As might be expected, prolactin followed a pattern of response similar to that of growth hormone. An exercise-induced increase in prolactin has been observed in previous studies (23, 27) and appears to be related to the intensity of exercise (39). Hickson et al. (27) used a similar resistance exercise protocol to that used in this investigation and observed a similar increase in prolactin. The prolactin response on *day 1* during supplementation was greater than on *days 2* and *3*. Similar to growth hormone, prolactin has also been shown to be

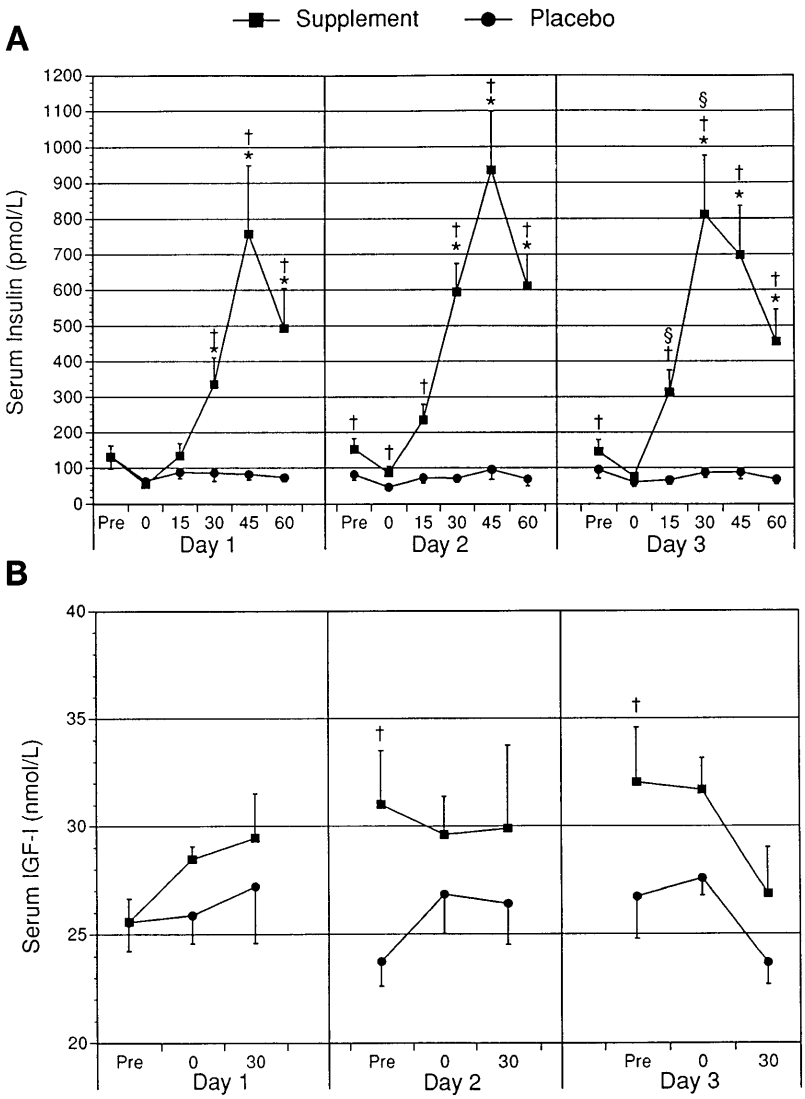

Fig. 4. Serum insulin (*A*) and insulin-like growth factor-I (IGF-I; *B*) responses. During supplement condition, subjects consumed a protein-carbohydrate drink 2 h before and immediately after workouts, and during placebo condition subjects consumed a placebo drink at same time points. Values are means ± SE. *$P \leq 0.05$ from corresponding preexercise value. †$P \leq 0.05$ from corresponding value for placebo. §$P \leq 0.05$ from corresponding time point on *day 1*.

influenced by lactate (40). Thus the increased prolactin response on *day 1* during supplementation when lactate was also higher adds further support to the theory that increases in lactate and H^+ contribute to growth hormone and prolactin secretion during exercise. The physiological significance of prolactin in men is unclear. Prolactin and growth hormone share similar sequence homology and immune system activities (19) and therefore may be important factors involved in the recovery from exercise-induced muscle disruption.

The cortisol response to exercise was diminished by *day 3* compared with *day 1* for both treatment conditions. A similar decrease in the exercise-induced cortisol response was reported by Fry et al. (18) in elite junior weight lifters exposed to 1 wk of high-volume resistance training. This response has been attributed to altered hypothalamic and/or pituitary function on the basis of the fact that subjects exhibited depressed β-endorphin concentrations (18). Both β-endorphin and ACTH are cleaved from the same precursor, propiomelanocortin polypeptide, and therefore less ACTH was available to interact with the adrenal cortex, resulting in a reduced stimulus for cortisol secretion and biosynthesis. Because we did not measure either β-endorphin or ACTH, the significance of these factors in contributing to the lower cortisol response in the present investigation is only speculative. Yet, in a study by Kraemer et al. (32), it was shown that β-endorphin, ACTH, and cortisol response patterns are linked in magnitude in response to a given heavy-resistance exercise protocol.

Blood CK is a well-accepted marker of skeletal muscle tissue disruption, and resistance exercise has been shown to elevate this enzyme (31). The response time between increases in CK and muscle damage probably vary with the mode and intensity of exericse. In this study, CK values were lowest before exercise on *day 1*, highest during recovery on *day 2*, and midway between these values on *day 3*. Kraemer et al. (31) observed a significant correlation between peak cortisol concentrations immediately after an intense resistance exercise protocol and peak CK values 24 h later. Similarly, the cortisol response to exercise was significantly higher on *day 1*, which corresponds with the significantly higher CK values observed on *day 2* in this

study. This delayed response of CK is probably attributable to the fact that cortisol has catabolic effects on muscle tissue that induce the breakdown of cellular proteins, thus liberating this specific enzyme. In this study, supplementation did not attenuate the magnitude of sarcolemma disruption, as measured by serum CK.

Serum glucose responses were variable; however, values began to rise after the immediate postexercise ingestion of the supplement, whereas glucose was more stable during placebo. The slightly lower preexercise glucose during supplementation may be an artifact of a prior surge in insulin resulting from ingestion of the supplement 2 h before exercise (i.e., "rebound hypoglycemia").

Serum insulin concentrations were lowest immediately postexercise, peaked near 45 min postexercise, and declined toward resting values at 60 min postexercise during supplementation. Remarkably, peak serum insulin concentrations at 45 min postexercise were ~500% above rest during supplementation, well above normal peaks due to pulsatility (13) and peaks due to carbohydrate ingestion alone (8). The differences in both blood glucose and insulin concentrations during recovery are primarily attributed to ingestion of the supplement immediately postexercise. The inclusion of protein and extra BCAAs with the carbohydrate in the supplement probably accounted for the large peaks in insulin as protein acts in a synergistic fashion with carbohydrate to enhance the response of insulin in the blood (8, 55). The insulin values observed in this study were similar to those reported by Chandler et al. (8) in subjects supplemented with a liquid protein-carbohydrate supplement immediately after resistance exercise. Furthermore, these large insulin responses were not attenuated over the three resistance exercise workout sessions; in fact, the insulin response was significantly greater on *day 3* compared with *day 1*. Insulin has a positive effect on glycogen resynthesis and protein synthesis (25). Thus a peak in insulin concentration 45 min postexercise may support important events involved in the recovery process. Furthermore, because subjects consumed ~60 g carbohydrate and 30 g protein 2 h before and immediately after each workout, the availability of nutrients for glycogen resynthesis and protein synthesis would most likely not be a limiting factor. This is important because insulin has been shown to be involved in the stimulation of amino acid uptake and incorporation of proteins after exercise (3, 21).

Although muscular performance was not a primary focus of this study, it is interesting to note that there were no significant differences between treatment conditions in the total volume of weight lifted and the average weight lifted per set on corresponding workout days. Thus the extra protein and carbohydrate provided by the supplement did not enhance acute muscular performance. One of the hypothesized benefits of ingesting the supplement was to help maintain elevated muscle glycogen concentrations over consecutive days of heavy exercise. However, there are data demonstrating that lower than normal preexercise glycogen levels do not influence the rate of glycogenolysis (44) or short-term high-intensity exercise performance (48, 54) and that higher than normal glycogen levels do not offer any addtional benefits during short-term, high-intensity exercise (55). Perhaps the duration of the resistance exercise protocol used in this investigation was not long enough to deplete glycogen concentrations to a level that would impair exercise performance. Whether ingestion of the supplement over longer periods of time would provide for enhanced recovery and improved performance is unknown.

In summary, these data indicate that consuming a nutritional supplement before and immediately after heavy-resistance training workouts performed over 3 consecutive days results in different exercise-induced patterns of metabolic and hormonal variables. Specifically, consuming a protein-carbohydrate supplement before and after a resistance training session increases the concentrations of glucose, insulin, growth hormone, and IGF-I while decreasing lactate accumulation. Such responses would be predicted to enhance glycogen and protein synthesis during recovery; however, this was not determined in this investigation. These responses were observed in a group of moderately resistance-trained men and may not apply to other populations (i.e., untrained individuals, women, etc.). These data demonstrate that protein-carbohydrate supplementation before and after training may alter the metabolic and hormonal responses to consecutive days of heavy-resistance exercise.

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