

Moderate changes in energy balance combined with exercise do not alter insulin-like growth factor I or insulin-like growth factor binding protein 3

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Abstract

This study was designed to investigate the impact of negative (NEG) and positive (POS) energy balance (BAL) on serum concentrations of insulin-like growth factor (IGF)-I and IGF binding protein (IGFBP)-1 and relative amounts of serum IGFBP-3 during 5 days of physical activity. Eleven men (23.6 ± 0.7 years) were assigned to 1 of 3 trials in a random, crossover design. Trials consisted of varying energy intake (NEG, -2092 ; BAL, balanced; POS, $+2092$ kJ/d) but with equal proportions of carbohydrates (50%), protein (30%), and fat (20%). Each subject ran daily on a treadmill at 65% to 70% of VO_2max for approximately 30 minutes. Blood samples were obtained each morning for the measurement of serum concentrations of IGF-I, IGFBP-1, and relative amounts of serum IGFBP-3. Body weight changes were significantly different from zero during the NEG and POS trials but not for BAL (NEG, -0.5 ± 0.1 kg [$P = .03$]; POS, 0.6 ± 0.2 kg [$P = .05$]; BAL, 0.2 ± 0.2 kg). Baseline serum concentrations of IGF-I were not different among trials (NEG, 188.7 ± 8.8 ng/mL; BAL, 169.7 ± 8.8 ng/mL; POS, 175.7 ± 8.8 ng/mL) nor were they different after the diet intervention (NEG, 155.7 ± 10.0 ng/mL; BAL, 172.4 ± 8.8 ng/mL; POS, 165.4 ± 8.8 ng/mL). Relative amounts of serum IGFBP-3 at baseline were not different between treatments for the 52-kDa IGFBP-3 isoform (NEG, 0.94 ± 0.05 ; BAL, 0.88 ± 0.05 ; POS, 0.81 ± 0.05 ADU) or for the 47-kDa IGFBP-3 isoform (NEG, 0.94 ± 0.02 ; BAL, 0.83 ± 0.02 ; POS, 0.79 ± 0.02 ADU) and were not different after 5 days of exercise and diet. Alterations in energy BAL resulted in no difference in IGFBP-1 concentrations between trials IGFBP-1 (PRE—NEG, 20.3 ± 3.3 ng/mL; BAL, 23.3 ± 4.9 ng/mL; POS, 21.2 ± 2.9 ng/mL) (POST—NEG, 27.6 ± 4.8 ng/mL; BAL, 24.9 ± 3.8 ng/mL; POS, 19.72 ± 2.2 ng/mL). However, the change in IGFBP-1 was significantly different from zero during the NEG trial but not for the POS or BAL trials (NEG, 8.9 ± 3.2 ng/mL [$P = .03$]; BAL, 0.97 ± 3.0 ng/mL; POS, -1.7 ± 3.8 ng/mL). An energy deficit or surplus of 2092 kJ in conjunction with daily aerobic exercise is not sufficient to impact serum concentrations of IGF-I or IGFBP-3, but a 2092-kJ deficit may alter serum concentrations of IGFBP-1 levels in healthy, college-aged men. © 2006 Elsevier Inc. All rights reserved.

Keywords:

Human; Exercise; Energy balance; Diet; Growth factors; Nitrogen

1. Introduction

Insulin-like growth factor (IGF)-I is a protein hormone that exerts mitogenic, myogenic, and anabolic actions on tissues in both autocrine and endocrine processes [1–4].

Insulin-like growth factor-I is normally found bound to 1 of at least 6 different IGF binding proteins (IGFBPs) that differ in molecular weight, tissue distribution, and their ability to potentiate or inhibit the effects of IGF-I [5]. The effect of exercise and nutrition on the IGF-I system has received considerable attention because the IGF system influences the acquisition of bone and muscle [6–11]. A large negative

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energy balance has resulted in reductions in serum IGF-I concentrations and increased bone resorption [12], whereas elevated levels of IGF-I are associated with muscle hypertrophy, increased bone density, and lean soft-tissue mass [7,13]. Furthermore, elevated levels of IGFBP-1 have been associated with muscle protein catabolism [14].

Adequate intake of calories and protein is necessary for the maintenance of normal IGF-I and IGFBP levels [15] because fasting significantly reduces IGF-I concentrations [15–17]. Clemmons et al [16] reported a 75% decline in IGF-I during 10 days of fasting in overweight men. More recently, studies in children [17] and healthy males [18] also demonstrated increases in IGFBP-1 and decreases in IGF-I and IGFBP-3 with fasting. On the other hand, overfeeding or an increase in energy intake results in an increase in IGF-I [15]. In fact, a 21% increase in serum concentrations of IGF-I was observed after 21 days of overfeeding of 5021 to 6694 kJ/d in healthy women [19]. To underscore the importance of energy intake in regulating IGF-I, it was determined that after a 5-day fast, only a diet with adequate protein and carbohydrates was sufficient in returning IGF-I to prefasting values [20].

Endurance and resistance exercise has shown varied effects on IGF-I and IGFBP-3. Manetta et al [4] reported an increase in IGF-I (~12%) and IGFBP-3 (~20%) during 4 months of training in cyclists but not in counterparts who were sedentary. Similarly, Koziris et al [21] demonstrated increased concentrations of total IGF-I by as much as 76% and IGFBP-3 from 30% to 97% in collegiate swimmers after 4 months of endurance training. In contrast to the above-mentioned studies, numerous researchers have been unable to show an increase in IGF-I and IGFBP-3 with either endurance [22–25] or resistance [21,26–29] training. These studies, however, varied in respect to the subject demographics and protocol used in each respective study. Moreover, most exercise studies relating to IGF-I do not control for energy intake, which is known to effect serum concentrations of IGF-I and IGFBPs [15].

Of the studies that have combined both exercise and nutritional interventions to determine the combined effect on IGF-I, IGFBP-1, and IGFBP-3, few use energy intake deficits or surpluses that would be typical or practical for the average person attempting to lose or gain weight. Furthermore, many of the exercise protocols are unrealistic in time and/or intensity for the average person. For instance, Nindl et al [3] investigated the IGF-I response to an energy deficit of 6694 kJ/d, sustained physical endurance type activity (~18828 kJ/d), and sleep deprivation (6.2 hours total) for 3 days and reported decreases in total IGF-I (32%) and IGFBP-3 (6%) and an increase in IGFBP-1 (~6-fold). Nemet et al [30] examined underfeeding (–8586 kJ/d) and overfeeding (+1644 kJ/d) in combination with exercise for 7 days. These researchers reported a decrease in total IGF-I in the underfed subjects (~30%) and no change in the overfed subjects [30]. The exercise prescription, however, called for 3 hours of endurance exercise per day, which was not well defined. There is a paucity of research that

examines the IGF-I response to practical dietary alterations during physical activity, controlling for energy intake.

Therefore, the purpose of this research was to determine the impact of negative and positive energy balance on serum concentrations of IGF-I, IGFBP-1, and IGFBP-3 during 5 days of strictly monitored physical activity in healthy, 20- to 25-year-old men. Moderate energy deficits (–500 kcal [–2092 kJ]) and surpluses (+500 kcal [+2092 kJ]) were used to determine how “practical” energy intake changes may alter the IGF-I, IGFBP-1, and IGFBP-3 response during 5 days of physical activity. Accordingly, the central hypotheses of this study were that positive energy balance would result in greater serum IGF-I concentrations, whereas negative energy balance would result in a decrease in serum IGF-I concentrations with associated changes in the IGFBPs.

2. Methods

2.1. Subjects

A preparticipation health history questionnaire was used to screen all individuals for inclusion in this study. Eleven healthy, male participants (19–28 years) volunteered for the study. Participants were physically active (exercised >3 days/wk for 45–60 minutes) and free from any liver, kidney, or metabolic disease. All subjects gave written consent to participate, and the protocol was approved by the Human Subjects Committee at South Dakota State University. Subject data are presented in Table 1.

2.2. Experimental protocol

Baseline testing included measurement of resting energy expenditure (REE), body composition via air displacement plethysmography, and maximal oxygen uptake (VO_2max) via indirect calorimetry. All testing was completed in the morning (6:30 to 9:30 AM) after a 10- to 12-hour fast. Forty-eight hours before the initial visit, subjects abstained from vigorous exercise, caffeine, and alcohol intake.

Before each trial, study participants consumed an isoenergetic diet (based on a dietary recall to ensure palatability) for 3 days while abstaining from any vigorous

Table 1

Characteristics for subjects participating in three 5-day exercise trials to expend 2092 kJ while consuming either a negative (–2092 kJ), balanced, or positive (+2092 kJ) energy intake

N	11
Age (y)	23.6 ± 0.7
Height (cm)	178.3 ± 1.4
% Body fat	18.1 ± 2.1
Fat mass (kg)	14.9 ± 2.1
Fat free mass (kg)	70.1 ± 2.8
Body weight (kg)	85.9 ± 2.9
VO_2max (mL/kg)	56.3 ± 1.7
Resting metabolic rate (kJ/d)	8692 ± 473

Data are means ± SD.

physical activity. After 3 days of isoenergetic nutrient intake (50% carbohydrate, 30% protein, 20% fat), subjects were randomly assigned to consume either a hypocaloric diet (negative (negative [NEG], -500 calories), isoenergetic (energy balance [BAL]), or hypercaloric diet (positive [POS], $+500$ calories) for 5 days in a crossover study design (Table 2). Subjects exercised daily on a treadmill to expend 500 calories. Blood samples were collected by antecubital venipuncture each morning from fasted subjects during the 5-day intervention and on the first posttest day (day 6). All trial periods were separated by a minimum of 5 to 7 days.

Trial 1: Energy balance. Subjects consumed enough calories to account for REE as well as daily activities and the calories expended during exercise (2092 kJ).

Trial 2: Negative energy balance by 2092 kJ. Through diet and exercise, subjects were in negative energy balance.

Trial 3: Positive energy balance by 2092 kJ. Through diet, subjects were in positive energy balance despite expending 2092 kJ/d with treadmill running.

2.3. Testing and training protocol

Resting energy expenditure was determined using indirect calorimetry (Physio-Dyne Max II, Quogue, NY) by the method of Weir [31]. Subjects were instructed to arrive at the laboratory in the morning after a 10- to 12-hour fast and with minimal previous activity. Subjects rested for 10 minutes before the beginning of this test, and then energy expenditure was measured for 20 minutes.

Estimated energy expenditure for daily activities was determined by an activity questionnaire according to the method of Ainsworth et al [32]. The appropriate energy intake needed for each subjects was determined by adding the REE, daily physical activity (based on the method of Ainsworth et al [32]), and the predetermined caloric cost of the exercise conducted in this study (2092 kJ).

Maximal oxygen consumption (VO_2max) was determined during a graded treadmill (Trackmaster, Pensacola, Fla) exercise test using a metabolic cart (Physio-Dyne Max-II) so that exercise intensity during each training day would be established as a percentage of VO_2max . The test protocol was modified for each individual by allowing them to determine a comfortable but challenging speed for the test. Once the appropriate speed was determined for the subject, it was kept constant while the grade increased 2% every 2 minutes until the subject could no longer keep pace.

Table 2

Nutritional composition of diets for subjects participating in three 5-day exercise trials to expend 2092 kJ while consuming either a negative (-2092 kJ), balanced, or positive ($+2092$ kJ) energy intake

	Negative	Balance	Positive
Energy, kJ	9891 \pm 512 ^a	12033 \pm 513 ^b	14159 \pm 557 ^c
Carbohydrates (%), g	308.2 \pm 16.8 ^a (52.2)	380.1 \pm 15.6 ^b (52.9)	442.8 \pm 18.3 ^c (52.4)
Protein (%), g	179.9 \pm 8.8 ^a (30.5)	216.7 \pm 9.7 ^b (30.2)	253.8 \pm 9.6 ^c (30)
Fat (%), g	55.7 \pm 2.3 ^a (21.2)	62.6 \pm 3.0 ^b (19.6)	74.0 \pm 3.2 ^c (19.7)

Data are means \pm SEM as determined by 2-way analysis of variance.

Treatments with different letters are significantly different ($P < .05$) from each other.

Body volume was measured via air displacement plethysmography (BodPod Life Measurement Instruments, Concord, Calif) using the procedure recommended by the manufacturer.

During the study, daily exercise consisted of exercise on a treadmill (Trackmaster) for all 3 trials. All exercises were supervised by a certified strength and conditioning specialist (CSCS, National Strength and Conditioning Association), and exercise intensity corresponded to approximately 65% to 75% of their maximal oxygen consumption. Duration of exercise varied for each individual but was approximately 30 to 40 minutes in length in order for participants to expend 2092 kJ.

All individuals were supplied with a detailed dietary plan for each day of the 3 trials during this study. All diets were analyzed with Food Processor (v. 8.1, ESHA Research, Salem, Ore). Compliance was determined through daily contact and specific questioning of the participants by the research staff.

2.4. Serum measurements

Blood samples were analyzed for serum concentrations of total IGF-I and IGFBP-1, as well as for relative amounts of IGFBP-3. All blood samples were collected in vacutainer tubes, allowed to clot at room temperature, and centrifuged. Serum was collected by centrifugation ($1500 \times g$; 30 minutes at 4°C), aliquotted, and immediately stored at -40°C until analysis. Serum concentrations of IGF-I were determined in duplicate in all samples by radioimmunoassay using acceptable published methods of Daughaday et al [33]. Recovery of [^{125}I]IGF-I added to human serum before acidified ethanol extraction was 89%. Interassay coefficient of variation (CV) was 7.1%, and intra-assay CV was 4.8%. Assay sensitivity was 5.96 pg per tube.

IGF binding protein 1 was measured by coated-tube immunoradiometric assays with the use of the DSL-10-7800 Active kit (Diagnostic System Laboratories). Assay sensitivity was 0.25 ng/mL; the interassay CV was 6.1%, whereas the intra-assay CV was 4.3%. Relative amounts of serum IGFBP-3 were analyzed by 1-dimensional SDS-PAGE [34] and Western ligand blot analysis [35]. Sera were electrophoresed through a 5% stacking gel and a 10% resolving gel. Proteins were then electrophoretically transferred to nitrocellulose membranes (Protran, 0.22 μm , BA 83; Schleicher & Schuell, Keene, NH), and IGFBP activity was detected by incubating membranes with [^{125}I]IGF-I

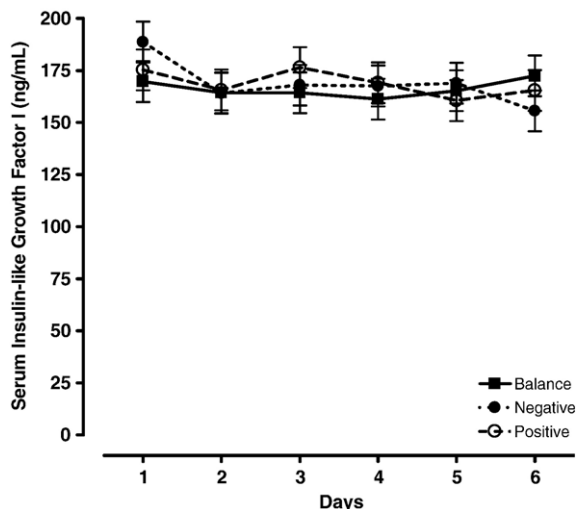


Fig. 1. Serum IGF-I concentrations (ng/mL) during negative (-2092 kJ), balanced, and positive ($+2092$ kJ) energy intake for 5 days while exercising daily to expend 2092 kJ. Data are means \pm SEM as determined by 2-way analysis of variance.

(600,000 dpm/mL Tris-buffered saline, 1%BSA[A-7030], Sigma Chemical Co; 0.1% Tween-20). Relative abundance of IGFBP-3 was determined by phosphorimagery (BioRad, Hercules, Calif). Each sample was divided by the same control to normalize each blot for comparison.

2.5. Calculations and statistics

A 2-way repeated measures analysis of variance with time and treatment as factors was used to determine the main effect of energy balance on serum concentrations of IGF-I and IGFBP-3. A 1-way repeated measures analysis of variance with treatment as a factor was used to determine if a difference between day 1 (baseline or PRE) and day 6 (POST) existed between trials. A Tukey post hoc test was used to identify significant differences when a significant F ratio was obtained. A 2-tailed t test was used to determine if the changes in variables during each of the 3 treatments were different from zero. Significance is reported at $P < .05$, and all values are reported as means \pm SEM unless otherwise stated.

3. Results

3.1. Nutritional information

Average energy intake during energy balance (12033 ± 513 kJ/d) was greater ($P = .0001$) than the negative energy balance trial (9891 ± 512 kJ/d) and less ($P = .0001$) than the positive energy balance trial (14159 ± 557 kJ/d) (Table 2).

3.2. Body weight

Change in body weight during the NEG and POS trials was different from zero (NEG, -0.5 ± 0.1 kg [$P = .03$]; POS, 0.6 ± 0.2 kg [$P = .05$]). During BAL, there was no change in body weight (BAL, 0.2 ± 0.2 kg).

3.3. Insulin-like growth factor I system response

Baseline serum concentrations of IGF-I were not different between treatments (NEG, 188.7 ± 8.8 ng/mL; BAL,

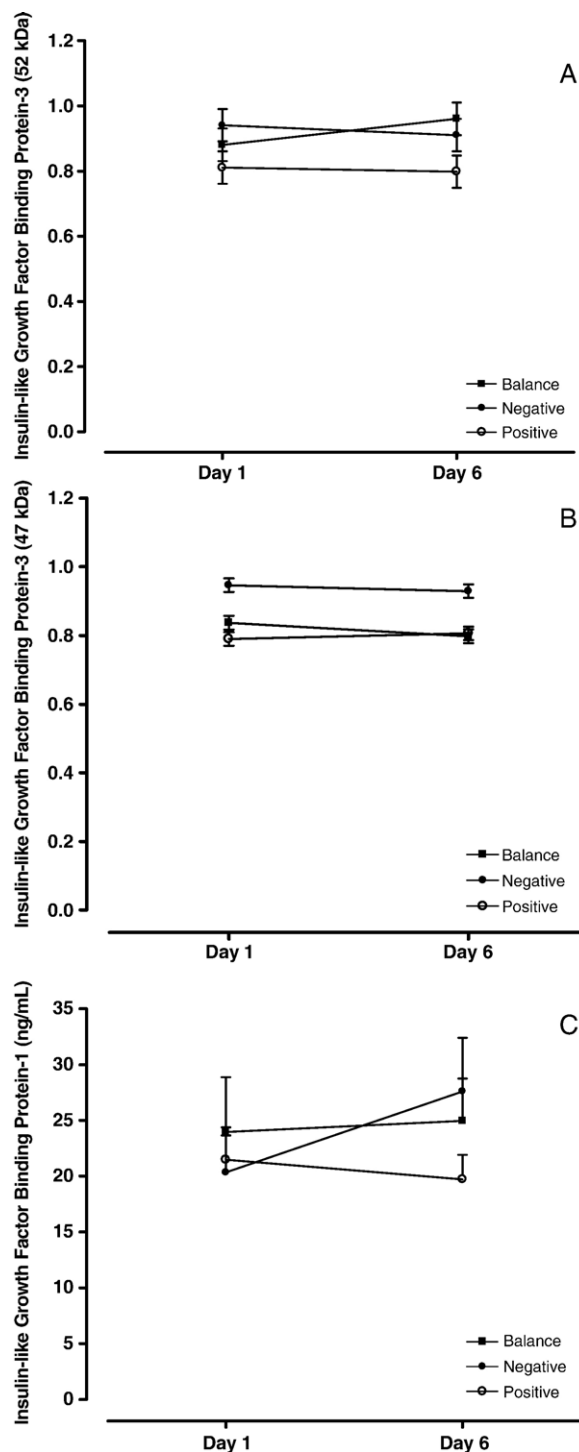


Fig. 2. Relative amounts of (A) serum IGFBP-3 (52 kDa), (B) serum IGFBP-3 (47 kDa), and (C) serum IGFBP-1 concentrations of subjects before (PRE) and after (POST) participating in three 5-day exercise trials to expend 2092 kJ while consuming either a negative (-2092 kJ), balanced, or positive ($+2092$ kJ) energy intake. Data are means \pm SEM as determined by 2-way analysis of variance.

169.7 ± 8.8 ng/mL; POS, 175.7 ± 8.8 ng/mL) (Fig. 1). Postmeasurements of serum concentrations of IGF-I were not different from baseline or between trials (NEG, 155.7 ± 10.0 ng/mL; BAL, 172.4 ± 8.8 ng/mL; POS, 165.4 ± 8.8 ng/mL) (Fig. 1).

Relative amounts of serum IGFBP-3 at baseline (PRE) were not different between treatments for the 52-kDa IGFBP-3 isoform (PRE—NEG, 0.94 ± 0.05; BAL, 0.88 ± 0.05; POS, 0.81 ± 0.05 ADU [arbitrary densitometric units]) (Fig. 2A) or for the 47-kDa IGFBP-3 isoform (PRE—NEG, 0.94 ± 0.02; BAL, 0.83 ± 0.02; POS, 0.79 ± 0.02 ADU) (Fig. 2B). After 5 days of altered energy intake, the serum IGFBP-3 concentrations were not different from baseline or between trials for the 52-kDa IGFBP-3 isoform (POST—NEG, 0.91 ± 0.05; BAL, 0.95 ± 0.05; POS, 0.79 ± 0.05 ADU) (Fig. 2A) or for the 47-kDa IGFBP-3 isoform (POST—NEG, 0.92 ± 0.02; BAL, 0.79 ± 0.02; POS, 0.80 ± 0.02 ADU) (Fig. 2B).

Serum concentrations of IGFBP-1 were not different at baseline between treatments (PRE—NEG, 20.3 ± 3.3 ng/mL; BAL, 23.3 ± 4.9 ng/mL; POS, 21.2 ± 2.9 ng/mL) (Fig. 2C). Alterations in energy balance resulted in no difference in IGFBP-1 concentrations between trials (POST—NEG, 27.6 ± 4.8 ng/mL; BAL, 24.9 ± 3.8 ng/mL; POS, 19.72 ± 2.2 ng/mL) (time × treatment; $P = .17$). However, the change in IGFBP-1 was significantly different from zero during the NEG trial but not for the POS or BAL trials (NEG, 8.9 ± 3.2 ng/mL; BAL, 0.97 ± 3.0 ng/mL; POS, -1.7 ± 3.8 ng/mL). A 1-way analysis of variance with treatment as a factor was performed on the change in IGFBP-1 from baseline to POST with differences between trials approaching significance ($P = .09$).

4. Discussion

Although energy balance and exercise are known to impact the IGF-I system, the response of IGF-I, IGFBP-1, and IGFBP-3 to practical energy balance manipulation and exercise has not been determined. To our knowledge, this study is the first to demonstrate that moderate energy changes (-2092 kJ/d, balanced, or +2092 kJ/d) combined with daily exercise in 18- to 25-year-old men result in no changes to IGF-I or IGFBP-3; but slight changes in IGFBP-1 occurred. Therefore, the present study did not support our original hypotheses that the main effect of positive energy balance would result in elevated serum concentrations of IGF-I, and negative energy balance would result in lower serum concentrations of IGF-I during 5 days of exercise.

In support of our results, Loucks et al [12,36] report that an energy intake above 126 kJ/kg lean body mass (LBM) per day when exercising results in the maintenance of IGF-I, IGFBP-1, and IGFBP-3 in regularly menstruating women. Decrements in the IGF system were, however, observed with both 20 and 10 kcal/kg LBM per day. In the present study, 30 kcal/kg LBM per day is equivalent to an energy intake of approximately 8786 kJ/d. This is below the

total number of kilojoules consumed even in our NEG treatment group.

Furthermore, Nemet et al [30] reported that a energy deficit of approximately 2000 kcal/d induced by diet and approximately 3 hours of exercise per day resulted in a decline in serum total and free IGF-I levels (39%). Similarly, Smith et al [37] reported a 46% reduction in IGF-I when a energy deficit of approximately 5021 to 6694 kJ/d was induced with exercise or diet manipulation. It is possible that the decline observed in these studies was because of the magnitude of energy deficit versus the present study, which only induced a energy deficit of 2092 kJ/d. Therefore, it appears there may be a threshold in energy balance needed to observe changes in serum concentrations of IGF-I (less than 126 kJ/kg LBM per day) that we did not cross [3,12,36-38].

Similarly, there may be an upper energy threshold (ie, greater than the 2092 kJ/d as used in the present study) needed to induce an increase in serum IGF-I. Kraemer et al [38] examined the hormonal response of 9 resistance trained men to 3 days of heavy-resistance training and 7 days of a high-caloric supplementation and found that baseline IGF-I increased approximately 18.5% by day 3 of exercise when consuming an additional 6590 to 10355 kJ/d. In addition, Forbes et al [19] observed a 14% and 21% increase in serum concentrations of IGF-I after 14 and 21 days, respectively, of overfeeding (5021-6694 kJ/d) in healthy, normal weight women (18-41 years old). In the current study, additional 2092 kJ during a running program did not effect serum concentrations of IGF-I.

An alternative explanation for the lack of change in IGF-I is that protein intake may contribute to the effect on serum IGF-I. Isley et al [20] fasted subjects for 5 days on 3 occasions and then refed them a normal diet, an isoenergetic/low-protein diet, or a hypoenergetic/low-protein diet for 5 days. These authors reported that a normal diet, adequate in energy and protein, returned IGF-I to approximately 70% of prefast values, whereas an isoenergetic/low-protein diet only returned IGF-I concentrations to 50% of prefast values [20]. Musey et al [39] also support the conclusion that protein has a significant impact on IGF-I. These researchers administered a hypoenergetic diet enriched with protein, fat, or carbohydrate for 2 weeks and reported a decrease in serum IGF-I in all groups except for individuals who received the high protein [39]. In the present study, protein intake was based on what subjects were normally consuming as determined by a 3-day diet record obtained during the screening process. The protein consumption was approximately 2 g kg⁻¹ d⁻¹ (most likely a positive nitrogen balance) during all treatment and may have been enough of a stimulus for IGF-I not to decrease during the negative energy balance trial [40,41]. In fact, a positive nitrogen balance has been shown to maintain serum concentrations of IGF-I despite a 75% reduction in energy intake [42].

Relative amounts of serum IGFBP-3 did not change in response to negative or positive energy balance combined

with exercise in the present study. Although, Nindl et al [3] has shown a 6% decrease in IGFBP-3 after 3 days of exercise and severe energy deprivation, Chen et al [43] reported no change in IGFBP-3 during 3 days of fasting. Similarly, Smith et al [44] detected no change in IGFBP-3 with a reduced energy intake. Similar to the present study, Nemet et al [30] reported no change in IGFBP-3 in response to exercise and either an energy deficit (~8368 kJ/d) or energy surplus (~1674 kJ/d). The ~1674 kJ/d energy surplus used by Nemet et al [30] was less than what was used in the present study; therefore, it is not a surprise that these authors did not report an increase in IGFBP-3. In addition, Nemet et al [30] did not report a decrease in IGFBP-3 with an energy deficit of approximately 8368 kJ/d; however, their exercise prescription was not clearly described and was a limitation to their study. Moreover, subjects in the studies of Nemet et al [30] and Smith et al [44] were ingesting more than 1 g/kg of protein per day, indicating that protein intake may have negated any effect the energy intake may have had on IGFBP-3.

IGF binding protein 1 concentrations may respond rapidly to large metabolic perturbations [3,30,39,45] but not to practical changes in energy balance as was observed in the present study. A decrease in insulin, as seen during fasting, has been associated with an increase in IGFBP-1, which may serve to limit the insulin-like activity of IGF-I [45]. However, during exercise, factors other than insulin may be responsible for changes in IGFBP-1 concentrations [45–48]. Hopkins et al [48] reported that the ingestion of a glucose polymer during more than 2 hours of cycle exercise did not prevent the increase in IGFBP-1 despite insulin levels remaining constant. Changes in IGFBP-1 were correlated with changes in glucose but not insulin [48]. Koistinen et al [49] also reported no changes in plasma insulin during a marathon run; yet, IGFBP-1 increased 10-fold. To explain this discrepancy, Lavoie et al [45] has provided evidence that during exercise, the increase in IGFBP-1 concentrations is linked to changes in liver glycogen and not insulin. The 30 to 40 minutes of exercise needed to expend 2092 kJ in the present study was probably not enough to deplete liver glycogen stores even during the NEG trial. In the present study, the carbohydrate content (52% of energy intake, 300–440 g/d) appears to have been enough to maintain liver glycogen stores and thus minimize large changes in serum IGFBP-1.

Some possible limitations must be considered. First, dietary compliance by participants may not have allowed for proper energy intake. We attempted to minimize this by providing detailed food diaries and by addressing compliance issues daily by personal contact. We also had our research staff present at every exercise training session to ensure compliance. In addition, we demonstrated weight loss with negative energy balance and weight gain with positive energy balance, indicating that subjects were following the research protocol.

In conclusion, the data from this study indicate that a practical energy deficit or surplus of 2092 kJ in conjunction with daily aerobic exercise is not enough of a stimulus to impact serum IGF-I or IGFBP-3 concentrations in apparently healthy, college-aged men. Thus, there may be a threshold effect for the amount of energy needed to attenuate or augment the serum IGF-I system response during exercise. In addition, protein intake, when high enough, may offset any change in IGF-I or IGFBP-3 because of energy balance alone. Reductions in serum concentrations of IGF-I have negative consequences on bone formation [12] and may limit the adaptive response of muscle to physical activity [7]. Thus, the implications from this study and others [7,12,14,36] would indicate that individuals in a weight control program consisting of a practical energy restriction through diet and physical activity would be able to maintain the IGF system without possible negative implications on bone health and muscle adaptations.

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