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The Effect of a Brief Sprint Interval Exercise on Growth Factors and Inflammatory Mediators

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ABSTRACT

Meckel, Y, Eliakim, A, Seraev, M, Zaldivar, F, Cooper, DM, Sagiv, M, and Nemet, D. The effect of a brief sprint interval exercise on growth factors and inflammatory mediators. *J Strength Cond Res* 23(1): 225–230, 2009—Exercise training efficiency depends on the intensity, volume, duration, and frequency of training, as well as on the athlete's ability to tolerate it. Recent efforts to quantify the effects of aerobic exercise training on hormonal response have suggested that exercise leads to simultaneous changes of antagonistic mediators. The effects of anaerobic exercise on these mediators are not known. Therefore, the aim of the present study was to evaluate the effects of a brief sprint interval session on the balance between anabolic (growth hormone [GH]→ insulin-like growth factor [IGF]-I axis) and catabolic hormones (cortisol), and circulating inflammatory cytokines such as interleukin (IL)-6. Twelve healthy elite junior handball players (17–20 years) participated in the study. Exercise consisted of a 4×250-m run on a treadmill, at a constant intensity of 80% of the personal maximal speed. Each run was separated by 3 minutes of rest. Blood samples were collected before, immediately after each 250-m run, and 1 hour after the last run. Exercise led to significant increases in GH (0.3 ± 0.2 to 5.1 ± 2.2 ng·ml^{-1}, $p < 0.05$), IGF binding protein (IGFBP)-3 (4191 ± 2.48 to 4875 ± 301 ng·ml^{-1}, $p < 0.05$), IL-6 (1.3 ± 0.2 to 2.1 ± 0.3 pg·ml^{-1}, $p < 0.002$), testosterone, and testosterone/cortisol ratio, and to a significant decrease in IGFBP-1 levels. Levels of IL-6 remained elevated 1 hour after the end of exercise. Exercise had no significant effects on IGF-I and cortisol levels. Changes in the GH–IGF-I axis and testosterone/cortisol ratio after the brief sprint interval exercise suggested exercise-related anabolic adaptations. The increase in IL-6 may indicate its important role in muscle tissue repair after anaerobic exercise. Changes in the anabolic-catabolic hormonal balance and in inflammatory mediators can be used as an objective tool to gauge the training intensity of different types of anaerobic exercises and training periods.

KEY WORDS growth hormone, insulin-like growth factor-I, cytokines, anaerobic exercise

INTRODUCTION

The efficiency of exercise training depends on the intensity, volume, duration, and frequency of training, and on the athlete's ability to tolerate it. Thus, many efforts are made to objectively quantify the balance between training load and the athlete's tolerance. One of the major beneficial effects of exercise training is muscle growth. However, the mechanisms that mediate exercise-induced muscle hypertrophy are not completely understood. Recent reports suggest, rather surprisingly, that exercise leads to a simultaneous increase in antagonistic mediators. On the one hand, exercise stimulates anabolic components of the growth hormone (GH) → insulin-like growth factor (IGF)-I axis (1,16), and, on the other hand, exercise elevates catabolic proinflammatory cytokines such as interleukin (IL)-6, IL-1, and tumor necrosis factor-α (11,13). Therefore, it was suggested that assessment of the changes in these circulating mediators after different types of exercise training may assist in quantifying training loads.

Previous studies have mainly focused on the effects of endurance-type and resistance exercise bouts and/or training on the GH–IGF-I axis and on inflammatory cytokines (11–13). Stokes et al. (18) recently have reported an increase in GH secretion after 30 seconds of supramaximal anaerobic exercise (Wingate anaerobic test). The effect of typical anaerobic/interval exercise on other components of

the GH→IGF-I axis and inflammatory mediators was never studied.

Therefore, the aim of the present study was to evaluate the effects of a brief sprint interval exercise session (4 repetitions of a 250-m run at 80% of the maximal speed) on the balance between anabolic and catabolic hormones, and circulating cytokines.

METHODS

Experimental Approach to the Problem

The effects of a single exercise and/or exercise training on the GH–IGF-I axis and on inflammatory cytokines were studied mainly after endurance-type and resistance training; the effects of anaerobic exercise on these systems are unknown. Therefore, the aim of the present study was to evaluate the effects of a typical single anaerobic sprint interval session on anabolic and catabolic hormones and on inflammatory mediators in elite young handball players. We chose a typical sprint interval session of a 4×250-m run on a treadmill, at a constant intensity of 80% of the personal maximal speed. Each run was separated by 3 minutes of rest. Blood samples were collected via intravenous catheter before, immediately after each 250-m run to assess a cumulative effect of each sprint, and 1 hour after the last run to evaluate the recovery effect. Hormonal measurements included circulating levels of the anabolic hormones GH, IGF-I, IGF binding protein (IGFBP)-3, and testosterone, and the catabolic hormones cortisol and IGFBP-1. Measurements of inflammatory mediators included the proinflammatory markers IL-6 and IL-1β and the antiinflammatory markers IL-1 receptor antagonist (IL-1ra) and IL-10. In addition, we measured serum lactate levels, a commonly used marker for the assessment of anaerobic training intensity.

Subjects

Twelve healthy elite Israeli junior elite handball players (age range, 17–20 years) participated in the study. The study was approved by the institutional review board of the Meir General Hospital, and informed consent was obtained from all the participants. All participants played in the Israeli premier handball league, and some of the players belonged to the Israeli national junior handball team.

The study was performed during the final stages of the regular handball season, when the players are in the best shape. Training involved mainly tactical and technical drills emphasizing handball skills and team strategies, speed drills with and without the ball and longer interval sessions (e.g., several repetitions of 20–40 seconds running at 80% of the maximal speed). No resistance training was done at the time of the study. Anthropometric characteristics of the participants are summarized in Table 1. Standard calibrated scales and stadiometers were used to determine height, body mass, and body mass index. Skinfold measurement at 4 sites (triceps, biceps, subscapular, and suprailiac) was used to calculate percent body fat using standard equations (10).

TABLE 1. Anthropometric characteristics of the study participants.

|	
Age (y)	20.3 ± 1.0
Body weight (kg)	74.5 ± 2.3
Body height (m)	1.79 ± 0.02
Body mass index (kg·m^{-2})	23.1 ± 0.8
Body fat (%)	13.7 ± 0.6

Procedure

Exercise Protocol. Each participant performed a maximal outdoor 100-m run 2 times. The best result was used to calculate the speed of the interval exercise session. Exercise consisted of 4 250-m runs on a treadmill (motor-driven treadmill; Woodway, PPS Med, Weil am Rhein, Germany) at a constant intensity of 80% of the maximal speed (calculated from the speed of the 100m run), with 3 minutes of rest between each of the 250-m runs.

Blood Sampling and Analysis. Tests were performed in the morning, after an overnight fast. An indwelling venous catheter was inserted 30 minutes before the first blood draw. Pre, immediately after every 250-m run (within 2 minutes from the end of each run), and 60 minutes post the last 250-m run (recovery), blood samples were drawn from the catheter (Figure 1). Blood samples were immediately spun at 3000 rpm, at 4°C for 20 minutes. The serum was separated and stored at −80°C. All pre- and postexercise specimens from each individual were analyzed in the same batch by an experienced technician who was blinded to the order of samples.

Growth Hormone. Growth hormone serum concentrations were determined by ELISA with the use of the DSL-10-1900 Active kit (Diagnostic System Laboratories, Webster, Tex). Intraassay coefficient of variation (CV) was 3.3–4.5%, interassay CV was 5.5–12.9%, and the sensitivity was 0.03 ng·ml^{-1}.

Insulin-Like Growth Factor-I. Insulin-like growth factor-I was extracted from IGFBPs by using the acid-ethanol extraction
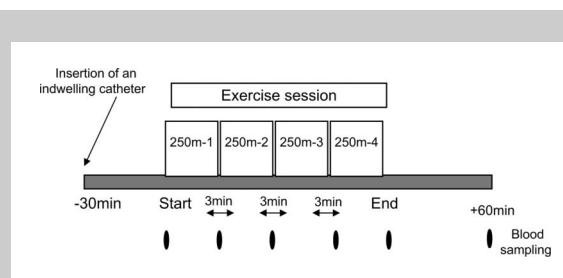
Figure 1. Exercise protocol and blood sampling procedure.

method. Serum IGF-I concentrations were determined by a 2-site immunoradiometric assay by using the DSL-5600 Active kit (Diagnostic System Laboratories, Webster, Tex). The intraassay CV for IGF-I was 1.5–3.4%, and the interassay CV was 3.7–8.2%. Assay sensitivity was 0.8 ng·ml^{-1}.

Insulin-Like Growth Factor Binding Proteins. Insulin-like growth factor binding protein-1 was measured by a coated-tube immunoradiometric assay with the use of the DSL-10-7800 Active kit (Diagnostic System Laboratories). Intraassay CV was 2–4%, and interassay CV was 1.7–6.7%. Assay sensitivity was 0.33 ng·ml^{-1}. Concentrations of IGFBP-3 serum were determined by ELISA with the use of the DSL 10-6600 Active kit (Diagnostic System Laboratories). Intraassay CV was 7.3–9.6%, interassay CV was 8.2–11.4%, and the sensitivity was 0.04 ng·ml^{-1}.

Lactate. Serum lactate was measured spectrophotometrically (YSI 1500, Yellow Springs, Ohio). Intraassay CV was 2.8%, interassay CV was 3.5%, and the sensitivity was 0.2 mg·dl^{-1}.

Cortisol. Serum cortisol levels were determined by a commercial RIA (Diagnostic Products Corporation, Los Angeles, Calif). The intra- and interassay CV for this assay were 3.2 and 6.8%, respectively.

Testosterone. Testosterone serum concentrations were determined by ELISA with the use of the DSL commercial kit (Diagnostic System Laboratories, Webster, Tex). Intraassay CV was 4.8–5.3%, interassay CV was 2.8–4.9%, and the sensitivity was 0.04 ng·ml^{-1}.

Inflammatory Mediators. Inflammatory mediators were analyzed by ELISA, using the R&D system Quantikine High Sensitivity commercial kits (R&D system; Minneapolis, Minn). For IL-6, intraassay CV was 3.8–11.1%, interassay CV was 7.1–29.5%, and the sensitivity was 0.0094 pg·ml^{-1}. For IL-1β, intraassay CV was 1.6–4.0%, interassay CV was 5.3–9.0%, and the sensitivity was 0.059 pg·ml^{-1}. For IL-1ra,

intraassay CV was 3.1–6.2%, interassay CV was 4.4–6.7%, and the sensitivity was 22 pg·ml^{-1}. And, for IL-10, intraassay CV was 8.1–15.6%, interassay CV was 6.6–8.2%, and the sensitivity was 0.5 pg·ml^{-1}.

Statistical Analyses

Repeated-measures analysis of variance was used to assess the effects of exercise on circulating components of the GH–IGF-I axis and inflammatory mediators, with time serving as the within-group factor. Data are presented as mean ± *SEM*. Significance was taken at $p \leq 0.05$.

RESULTS

Blood lactate increased significantly during the interval exercise, reaching a level of 11.63 ± 1.1 mmol·L^{-1}. The effects of the sprint interval exercise on the anabolic and catabolic hormones are summarized in Table 2 and Figure 2. Exercise was associated with a significant increase in GH, IGFBP-3, and testosterone levels. Exercise was associated with a significant decrease in IGFBP-1 levels. These levels returned to baseline values during recovery. There were no significant effects of exercise on IGF-I and cortisol levels. In addition, exercise led to a significant increase in the testosterone/cortisol ratio (Figure 3).

The effects of the interval exercise on inflammatory mediators are summarized in Table 2 and Figure 4. Exercise was associated with a significant increase in IL-6 levels. The level of IL-6 remained elevated 1 hour after the end of exercise. There were no significant effects of exercise on IL-ß, IL-1ra, and IL-10 levels.

DISCUSSION

Sprint interval training is one of the most commonly used training methods in anaerobic-type sports (9). Usually, athletes and coaches use measurements of serum lactate levels during the exercise task to assess the training intensity (5). However, although this measure can determine the

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TABLE 2. The effect of the sprint interval exercise on blood lactate, circulating anabolic and catabolic hormones, and inflammatory mediators.

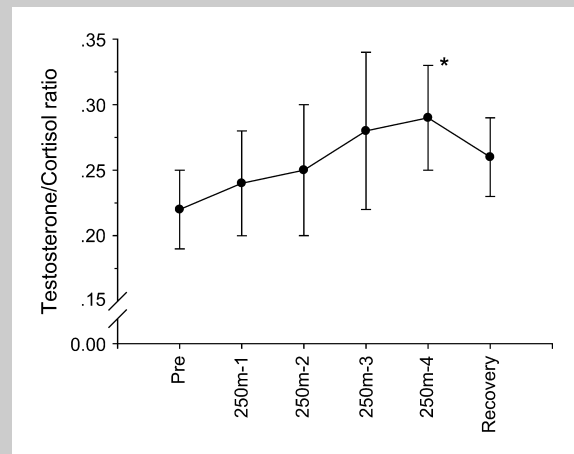|	Pre	250 m: first run	250 m: second run	250 m: third run	250 m: fourth run
Lactate (mmol·L^{-1})	1.5 ± 0.9	7.5 ± 1.0*	8.75 ± 0.8*	10.45 ± 1.1*	11.63 ± 1.1*
IGF-I (ng·ml^{-1})	324.1 ± 44.0	354.7 ± 47.5	363.9 ± 51.8	365.7 ± 43.6	384.8 ± 38.7
Testosterone (nmol·L^{-1})	0.15 ± 0.03	0.16 ± 0.04	0.16 ± 0.11	0.17 ± 0.03*	0.17 ± 0.04*
Testosterone (ng·ml^{-1})	4.3 ± 1.0	4.7 ± 1.2	4.7 ± 3.3	4.9 ± 1.0*	4.9 ± 1.1*
Cortisol (nmol·L^{-1})	562.8 ± 77.2	571.1 ± 88.2	571.1 ± 88.2	543.5 ± 80.0	529.7 ± 74.5
IL-1ß (pg·ml^{-1})	1.3 ± 0.4	1.9 ± 0.9	1.7 ± 0.8	1.3 ± 0.5	1.4 ± 0.5
IL-1ra (pg·ml^{-1})	433.9 ± 79.7	375.7 ± 61.2	439.7 ± 94.7	409.8 ± 79.0	430.6 ± 83.6
IL-10 (pg·ml^{-1})	0.6 ± 0.5	0.7 ± 0.4	0.9 ± 0.6	0.7 ± 0.5	0.6 ± 0.3

IGF = insulin-like growth factor; IL = interleukin.
*Significant exercise-related increase from baseline levels ($p < 0.05$).
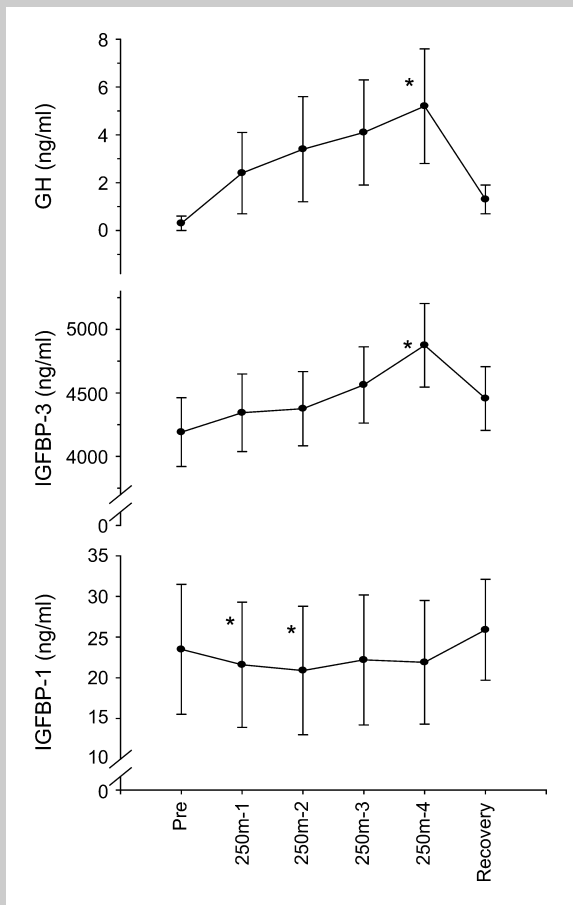
Figure 2. The effect of the sprint interval exercise on circulating growth hormone (GH), insulin-like growth factor binding protein (IGFBP)-3, and IGFBP-1 levels. Exercise was associated with a significant increase of GH and IGFBP-3 and with a significant decrease in IGFBP-1 ($*p < 0.05$). Values returned to baseline levels during recovery.

Figure 3. The effect of the sprint interval exercise on testosterone/cortisol ratio. Exercise was associated with a significant increase in this ratio ($*p < 0.05$).

threshold) to stimulate GH secretion, and that the exercise duration should be at least 10 minutes (4). Interestingly we found that the brief anaerobic interval exercise training led to a significant increase in GH levels. Moreover, previous studies have indicated that the exercise-induced GH peak occurs 25–35 minutes after the start of exercise irrespective of the exercise duration (2,16,18,22). Therefore, when the exercise task is brief, GH peak may occur after its cessation, but when the exercise is long (e.g., 45 minutes), a peak may be reached while the individual is still exercising. Blood sampling, however, should be timed to the exercise-induced GH peak. Because an increase in GH was not anticipated,
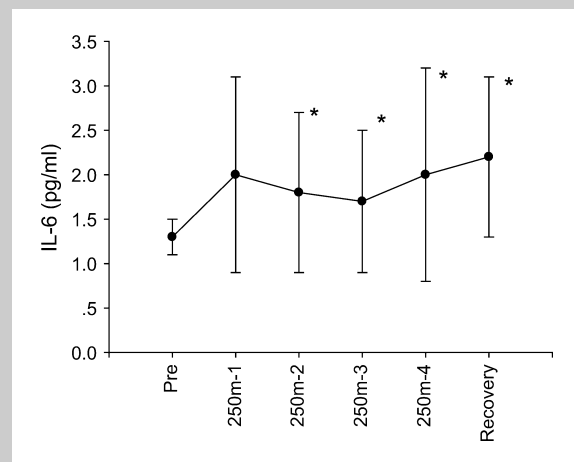
exercise intensity, its ability to evaluate the anabolic and/or catabolic effect of training is limited. In the present study, we determined the effects of a brief sprint interval exercise (the total duration of the exercise session including the rest intervals was less than 12 minutes) on anabolic and catabolic hormones and circulating pro- and antiinflammatory mediators. Exercise was associated with significant increases in GH, IGFBP-3, testosterone, and the testosterone/cortical ratio, and it was associated with a decrease in IGFBP-1. These results indicate that the exercise led to an anabolic-type hormonal response. In addition, exercise led to a significant increase in the proinflammatory cytokine IL-6. Levels of IL-6 remained significantly elevated during the recovery period.

Previous studies have examined the effects of endurance-type exercise on the GH–IGF-I axis. These studies have suggested that the exercise input should be sufficient to cause a sizeable metabolic effect (e.g., above the lactic anaerobic

Figure 4. The effect of the sprint interval exercise on circulating interleukin-6 (IL-6) levels. Exercise was associated with a significant increase in IL-6. Levels remained significantly elevated 1 hour after the exercise ($*p < 0.05$).

228

blood samples were not collected 25–30 minutes after exercise. Therefore, it is possible that the sprint interval exercise–related GH peak might have been higher.

The exercise had no effect on circulating IGF-I levels. Insulin-like growth factor-I plays a central role in exercise-induced muscle adaptation (1). Previous reports have suggested that very short supramaximal exercise efforts (e.g., 90 seconds) (8) lead to increases in IGF-I levels, and that IGF-I peaks after 10 minutes of endurance-type exercise (3,16). Therefore, it is possible that the present exercise was not intense enough to increase IGF-I levels.

We also measured the effects of exercise on IGF-I binding proteins-1 and -3. The bulk of IGF-I is bound to binding proteins; the most important among them is BP-3, because it binds more than 95% of circulating IGF-I (15). Interestingly, some of these IGFBPs, such as IGFBP-3, stimulate IGF-I bioactivity, whereas others, such as IGFBP-1, inhibit its anabolic effects. Therefore, our findings of increased exercise-associated IGFBP-3 and decreased IGFBP-1 suggest an anabolic effect of exercise. Moreover, the results support the notion that the exercise-related effects on IGF-I are not mediated only through alteration in IGF-I levels per se but, rather, by the effect on its binding proteins. The mechanism for the increase in IGFBP-3 is not clear. Although IGFBP-3 synthesis is GH dependent, both GH and IGFBP-3 peaked at the same time (immediately after the fourth 250-m run), indicating that a GH-mediated increase of IGFBP-3 is unlikely (Figure 2). We speculate that the increase in IGFBP-3 resulted from a release from more available vascular marginal pools, or from an increase in the proteolytic activity of IGFBPs (11,16).

The sprint interval exercise was associated with increases in testosterone levels and the testosterone/cortisol ratio. The testosterone/cortisol ratio is used frequently as an indicator of the anabolic-catabolic balance to determine the physiological strain of training (7,20). Therefore, its increase after the brief sprint interval exercise may indicate anabolic adaptations. Interestingly, the exercise-related testosterone and testosterone/ cortisol ratio peaks paralleled the peaks of the anabolic GH–IGF-I axis factors (i.e., GH and IGFBP-3), suggesting a possible mechanistic link for the exercise-associated stimulation, secretion, or release of these hormones.

The increase in the testosterone/cortisol ratio resulted from the increase in testosterone levels, because cortisol levels did not change during the exercise task. It is known that the exercise-induced cortisol increase depends on the duration and intensity of the physical activity. A significant increase in cortisol levels requires a duration of exercise of at least 20 minutes and an intensity of at least 60% of the maximal oxygen consumption (21). Therefore, it is possible that the exercise duration in the present study was not long enough to cause an increase in cortisol level. Another possible explanation is that the diurnal circadian rhythm of cortisol, which leads to decreased cortisol levels during the day, masked more subtle exercise-induced changes.

Exercise was associated with an increase in IL-6 levels, and levels of IL-6 remained elevated during the recovery period. There was no significant change in IL-1β, IL-1ra, or IL-10 levels after the sprint interval exercise task. Previous studies have found increases in IL-6, IL-1β, and IL-1ra after intense, prolonged, endurance-type exercise sessions (11–13,17). Therefore, our finding of an increase only in IL-6 after anaerobic-type exercise suggests that IL-6 is probably the most sensitive inflammatory cytokine to exercise, or that anaerobic exercise may lead to a different hormonal catabolic environment.

The major source for the exercise-related IL-6 increase is the skeletal muscle (5). Interleukin-6 increases during exercise both with and without evidence of muscle damage. However, IL-6 is believed to play an important mediatory role in the inflammatory response needed for the exercise-associated muscle damage repair (14,17). This may explain why, in the present study, levels of IL-6 remained elevated during the recovery period from the anaerobic-type exercise as well.

It has been demonstrated previously that IL-6 may alter IGF-I activity through a variety of mechanisms including direct inhibition of IGF-I production (6). It is possible that the prolonged exercise-related increase in IL-6 prevented the increase in IGF-I after the sprint interval exercise.

Finally, the present study examined the hormonal and inflammatory responses to a single typical sprint interval session. Different anaerobic training protocols may lead to different anabolic/catabolic and inflammatory responses. Moreover, we studied the immediate effects of exercise and the short recovery effect (1 hour postexercise). It is possible that later hormonal, receptoral, and postreceptoral signaling molecule interactions may occur during the recovery period from acute exercise and from longer training periods, and these may contribute to the overall response to exercise training.

PRACTICAL APPLICATIONS

The present study has examined the hormonal and inflammatory responses to a single typical anaerobic training. The changes observed in the GH→IGF-I axis and testosterone/ cortisol ratio suggest mainly exercise-related anabolic adaptations, and increases of IL-6 may indicate its important role in muscle tissue repair after anaerobic exercise. The results indicate that changes in the anabolic-catabolic hormonal balance and in circulating inflammatory cytokines can be used to gauge the training intensity of anaerobic-type exercise. It is clear that different training protocols with longer and/or more intense exercise, shorter rest periods, and/or different fitness status of the athlete may lead to different responses. However, the response of these hormones to different types of training sessions or longer training periods can be learned by the athlete, coach, and his or her supporting stuff and may be used as an objective tool to monitor the training load and to better plan training cycles throughout the training season and competition period.

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