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The effect of vigorous aerobic and standard anaerobic exercise testing on GH-IGF-1 secretion in adult females

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Introduction. Exercise-associated effects on the GH→IGF-1 axis were studied, mainly following aerobic exercise. Material and Methods. The effects of laboratory vigorous aerobic (10-min treadmill run at 85% of peak VO_2) and standard all-out anaerobic (30 s Wingate anaerobic test- WAnT) tests on the GH→IGF-1 axis were determined in 12 healthy active females (24-34 years). The tests were performed in random order. Blood samples for GH and IGF-1 were collected before and 20, 30, 40 and 60 minutes after the beginning of each exercise test. Both tests were associated with significant increases in GH. Results. Peak GH was higher following the WAnT (11.0 ± 8.3 *vs.* 7.5 ± 7.3 ng/ml, respectively) but this difference was not statistically significant. However, the GH area under the curve (AUC) was significantly greater in the anaerobic test as compared with the aerobic test. Only the WAnT was associated with a significant increase in IGF-1 levels (from 177.8 ± 47.2 to 198.8 ± 56.2, $p < 0.02$). However, no significant differences were found in peak IGF-1 and IGF-1 AUC following both tests. Vigorous aerobic and standard all-out anaerobic laboratory tests led to significant GH increases in the same female individuals. GH and IGF-1 responses were greater following the WAnT. Conclusions. GH-IGF-1 changes may be used to gauge exercise intensity, not only following aerobic but also anaerobic exercise.

KEY WORDS: laboratory testing, females, power output, endurance activity.

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What is already known on this topic?
Endurance-type exercise is known to increase growth hormone (GH) and insulin-like growth factor-1 (IGF-1) levels. Recently, an increase in components of the GH-IGF-1 axis has been reported also following anaerobic-type sprint interval trainings. However, the magnitude of the GH response to the different types of exercise (aerobic versus anaerobic) in the *same* individuals has never been studied.

Introduction

The growth hormone–insulin-like growth factor-1 (GH→IGF-1) axis is composed of hormones, growth factors, binding proteins (BP) and receptors that regulate essential growth, development, and metabolic and reparative processes. It is now well established that adaptations of the GH→IGF-1 axis also mediate many of the exercise-associated anabolic effects [1, 2]. Most previous studies on the GH→IGF-1 axis response to exercise focused on *endurance-type* exercise bouts and/or training [3, 4]. In contrast, the effect of typical *anaerobic* exercise on these mediators has not been extensively studied. Stokes et al. [5] reported an increase in GH secretion following 90 s of a supra-maximal anaerobic bout (3 consecutive Wingate anaerobic tests – WAnT). More recently, we reported that *anaerobic-type* sprint interval trainings led to significant increases in anabolic components of the GH-IGF-1 axis [6, 7].

However, the magnitude of the GH→IGF-1 response to the different types of exercise (aerobic versus anaerobic) in the *same* individuals has never been studied. This is important because the anabolic and the GH→IGF-1 effects of different types of exercise are not limited to individuals who participate in competitive sports, but may also apply to the use of different types of exercise in the diagnosis of certain diseases (e.g., short stature and GH deficiency), and for diseases that may be treated by exercise (e.g., obesity). Therefore, the aim of the present study was to investigate the effect of laboratory 10-min vigorous aerobic and standard all-out anaerobic exercises on GH and IGF-1, the two key components of the GH→IGF-1 axis, in the *same* young adult females. We chose to study young adult females, since exercise and competitive sports is very popular in this unique population, while the exercise-associated GH-IGF-1 effects are relatively understudied. We hypothesized that aerobic exercise will lead to a greater increase in both the GH and IGF-1 levels.

Materials and Methods

Participants

Twelve healthy female students of physical education (aged 24-34 years) participated in the study. The participants engaged in a weekly academic program that integrated theoretical lectures and field activity classes (such as basketball, soccer, track and field, swimming, etc.). An average of about 8 hours of activity classes was performed by the students every week, with no extra leisure time activity. Anthropometric and fitness characteristics of the participants are summarized in Table 1. Standard calibrated scales and stadiometers were used to determine body height, body mass and BMI. Skinfold measurements at four sites (triceps, biceps, sub-scapular and supra-iliac) were used to calculate percent body fat using standard equations [8]. The study was approved by the Institutional Review Board of the Meir Medical Center. Participants were informed of the experimental risks and signed an informed consent prior to the investigation.

Table 1. Anthropometric and fitness characteristics of participants

Age	(years)	27.3 ± 1.1
Body mass	(kg)	56.2 ± 2.0
Body height	(m)	164.1 ± 2.2
BMI	(kg/m^2)	20.8 ± 0.6
Body fat	(%)	24.2 ± 1.5
Peak VO_2	(ml/kg/min)	39.9 ± 4.5
Peak anaerobic power	(watts/kg)	9.4 ± 0.9
Mean anaerobic power	(watts/kg)	6.8 ± 0.9
Fatigue index	(%)	27.8 ± 6.9

Design and Methodology

Exercise testing: Each participant performed two separate laboratory exercise tests in random order.

Aerobic test: Aerobic exercise consisted of a 10-min treadmill run (motor-driven treadmill; Woodway, PPS Med, Weil am Rhein, Germany), in constant ambient conditions. To ensure similar exercise intensities, the work rate was calculated for each subject to be equivalent to 85% of peak VO_2 (determined from previous peak VO_2 testing). This protocol was chosen because it had been previously shown that during aerobic-type exercise, circulating GH levels increased only in response to exercise intensity above but not below the lactic anaerobic threshold (LAT) [10, 11]. Moreover, the duration of aerobic exercise for the stimulation of GH secretion should be at least 10 minutes [12], since exercise of shorter duration (e.g. 5 min at or above LAT [10]) was not accompanied by increases in circulating GH levels. Therefore, the current endurance laboratory test protocol was defined as "vigorous aerobic exercise" that was performed above each subject's anaerobic threshold level.

Anaerobic testing: Anaerobic testing consisted of the WAnT using the Monark 834k cycle ergometer (Monark, Stockholm). Seat height was adjusted to each participant's satisfaction and clips with straps were used to prevent the feet from slipping off the pedals. Each participant cycled for 30 s against constant resistance. Resistance was set at 0.05 kg per the participant's kg body weight. Participants were instructed to pedal as fast as possible throughout the 30 s of the test period, and were verbally encouraged throughout the test.

In each test maximal power output, mean power output, minimal power output and fatigue index were measured. All power output measurements were based on 5-sec averages calculated with the WAnT computer software, and were reported in watts/kg. Maximal power output (peak power) was calculated from the highest five-sec work output. Mean power output, reflecting anaerobic capacity, was calculated as the mean power output

throughout the 30 s of the test. Minimal power output was calculated as the lowest five-sec work output. Fatigue index was calculated as the percentage of power output drop throughout the test from maximal power output [9].

Blood sampling and analysis: Hormonal measurements included GH and IGF-1, i.e. the two key anabolic elements of the GH→IGF-1 axis. In addition, we measured serum lactate levels, a commonly used marker for the assessment of aerobic and anaerobic training intensity. The tests were performed in the morning, following an overnight fast. An indwelling venous catheter was inserted 30 min prior to the first blood draw, after allowing subjects to rest and sit quietly. Since the peak exercise-induced GH level occurs 25-30 min after the start of exercise, irrespective of exercise duration [13], blood samples were collected before and 20, 30, 40 and 60 min after the beginning of each exercise testing. Blood samples were immediately spun at 3000 rpm and at 4ºC for 20 min. The serum was separated and stored at –80ºC. All serum specimens from both exercise sessions from each individual were analyzed in the same batch by an experienced technician, who was blinded to the type of exercise testing and to the order of the samples. Exercise tests were performed during the follicular phase of the menstrual cycle (first 5 days of the cycle).

Growth hormone. GH serum concentrations were determined by ELISA with the use of the DSL-10-1900 Active kit (Diagnostic System Laboratories, Webster, Texas). Intra-assay CV was 3.3-4.5%, inter-assay CV was 5.5-12.9% and the sensitivity was 0.03 ng/ml.

Insulin-like Growth Factor-1: Serum IGF-1 was measured with immune-chemi-luminescent assay (ICMA) using the Immulite 2000 Siemens Analyzer with analytical sensitivity of 25 μg/L, and intra- and inter-assay coefficient of variation < 8%.

Lactate. Blood lactate concentration was measured by finger-prick using a portable lactate analyzer (Accusport, Boehringer Mannehein, Germany) at the end of each exercise test.

Statistical Analysis

Repeated measure ANOVA with Bonferroni corrections was used to assess the effect of aerobic and anaerobic testing on lactate, GH and IGF-1 levels. In addition we compared, using a paired t-test, the GH and IGF-1 area under the curve, for both exercise tests. Data were presented as means ± SEM. The level of statistical significance was set at $p < 0.05$.

Results

There were no significant differences in the end exercise heart rate between the anaerobic and the aerobic exercise tests (187.7 ± 2.9 versus 185.1 ± 5.1 beats/min in the anaerobic and aerobic exercise tests, respectively; $p = 0.4$). The lactate levels were higher following the anaerobic exercise compared to the aerobic exercise; however, this difference was not statistically significant (10.4 ± 1.3 versus 6.8 ± 1.0 mmol/L in the anaerobic and aerobic exercise tests, respectively; $p = 0.1$).

The effect of aerobic and anaerobic exercise on GH and IGF-1 is summarized in Figures 1 and 2. Both types of exercise sessions were associated with a significant increase in GH levels. Levels returned towards baseline

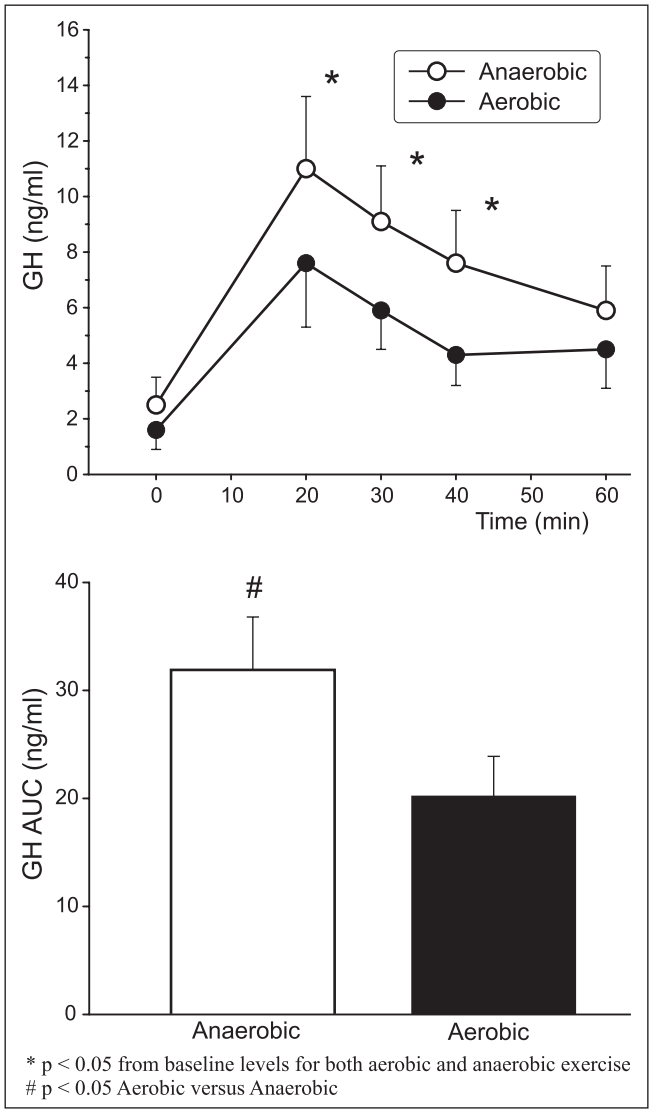

Figure 1. The effect of aerobic and anaerobic exercise on GH levels (Upper panel), and GH AUC (Lower panel)

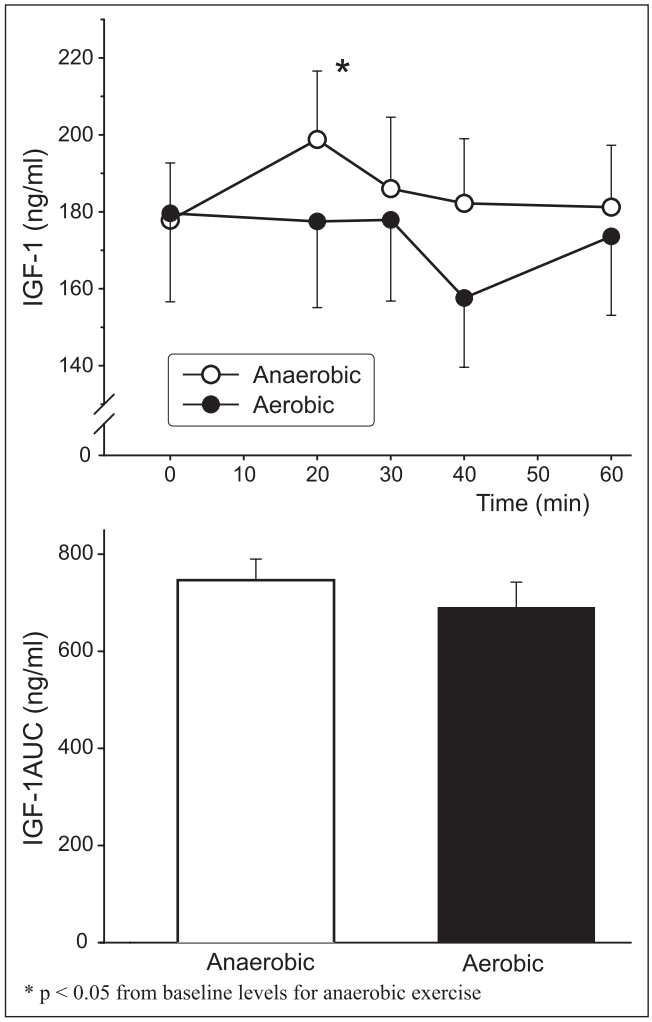

Figure 2. The effect of aerobic and anaerobic exercise on IGF-1 levels (Upper panel) and IGF-1 AUC (Lower panel)

values 60 min after the exercise. GH levels were higher following the anaerobic exercise; however this difference was not statistically significant. The GH area under the curve was significantly greater following the anaerobic exercise test.

Only the anaerobic exercise was associated with a significant increase in IGF-1 levels; however, no significant difference was found in the IGF-1 response to both exercise tests. There was no significant difference in the IGF-1 area under the curve following both exercise tests.

Discussion

The present study determined the effect of vigorous aerobic and standard anaerobic laboratory tests on anabolic components of the GH→IGF-1 axis in the same individuals. Both the vigorous aerobic (10 min at 85% of VO_2max) and the standard anaerobic (WAnT) exercise tests were associated with a significant increase in GH levels. Moreover, the GH area under the curve response to the anaerobic exercise was significantly greater. The results suggest that an anabolic-type hormonal response also occurs following anaerobic exercise.

The majority of previous studies examined the effects of endurance-type exercise on the GH→IGF-1 axis. These studies suggested that in order to stimulate GH secretion, the exercise input should be sufficient to cause a sizeable metabolic effect (e.g. above the lactic anaerobic threshold), and that the exercise duration should be at least 10 min [for review see 3 and 13]. Similarly, an increase of other hormones that may mediate the GH response, e.g. catecholamines, cortisol and inflammatory cytokines, also occurs only or mainly during exercise above the LAT [3]. Consistent with that lactate levels at the end of the vigorous aerobic exercise test were 6.8 ± 1.0 mmol/L, which greatly exceeded the lactic anaerobic threshold load. Therefore, one could argue that such an exercise protocol can be performed only by well-trained individuals and that such an exercise does not rely solely on aerobic metabolic resources, but on anaerobic metabolism as well. It is possible that the higher GH response to the anaerobic exercise may be explained by the higher lactate increase following the WAnT (10.4 ± 1.3 as compared with 6.8 ± 1.0 mmol/L, although statistically non-significant).

It was shown that the exercise-induced GH peak occurs 25-30 min after the start of aerobic exercise, irrespective of exercise duration [13]. It also occurs a few minutes earlier in females [14]. Therefore, it is not surprising that peak GH levels occurred 20 minutes after the beginning of the aerobic exercise in the female participants in the present study. Interestingly, GH peaked at 20 min following the brief WAnT as well suggesting similar exercise-induced GH peak timing and indicating that in order to determine exercise-induced GH peak in both exercise types, blood sampling should be properly timed.

The WAnT resulted in a significant increase of circulating IGF-1 levels. IGF-1 plays a central role in exercise-induced muscle adaptation [15]. Stokes et al. previously reported [5] that supra-maximal exercise (e.g., three consecutive WAnT– 90 s) led to an increase in IGF-1 levels. The results of the present study indicate that even a shorter maximal anaerobic exercise (i.e., 30 s) leads to an increase in the IGF-1 level. IGF-1 was

also higher following increasing (i.e., 100 – 200 – 300 – 400 m) and decreasing distance (i.e., 400 – 300 – 200 – 100 m) interval training [7]. In contrast, significant increases of IGF-1 were not noted following brief, constant-distance interval training (4 × 250 m) [6]. Therefore, it is suggested that IGF-1 may also play an important role in muscle adaptation to anaerobic interval training and that the IGF-1 response depends on the specific type, length and intensity of anaerobic training. Interestingly, like GH, peak IGF-1 levels also occurred 20 min after exercise. This suggests that similarly to aerobic exercise, the anaerobic exercise-induced IGF-1 increase is also GH independent, and that the source of the post-exercise IGF-1 rise is probably more readily available in the marginal pools [2].

The importance of the anaerobic exercise-induced increase in GH is not limited to competitive athletes, but may also be applied to the use of exercise in the diagnosis of GH deficiency. GH is secreted from the pituitary gland in a pulsatile manner. The majority of pulses occur during the night, and during most of the day GH levels are very low or even undetectable. Therefore, a single random blood sample for circulating GH levels can not differentiate between healthy and GH-deficient patients. To overcome this, a number of pharmacological provocation tests to stimulate pituitary GH release have been developed [16]. The interpretation of a normal GH response to *pharmacological* stimuli is questionable because it does not necessarily apply to *physiological* GH secretion. These confounding factors have led a number of investigators to emphasize the role of *physiological* stimulation tests, such as exercise, in the diagnosis of GH-deficiency [17]. It was further suggested that the major diagnostic role of physiological GH stimulation tests such as exercise is in patients with suspected partial GH deficiency. In these children, the response to a pharmacological provocation might be partial, but the response to a physiological stimulation will be blunted. So far, only aerobic exercise protocols, such as the one used in the present study, have been standardized for this purpose [13]. However, the complexity of the testing (the need for at least two laboratory visits, one to determine peak aerobic power and one for the actual testing at an intensity of about 85% of peak VO_2) has limited the practical use of exercise provocation test for GH secretion. Moreover, one can argue that children's participation in continuous, longer than 10 minutes, aerobic exercise at intensities above the LAT is both rare, and non-physiological. The significant increase in GH levels following the WAnT – a 30 s of supra-maximal cycle exercise bout against resistance that is calculated relative to each individual's body mass – is very promising since this type of exercise stimulation test for GH secretion requires only a single laboratory visit. In addition, this type of exercise represents better the explosive activity patterns of children, in whom GH testing for the assessment of short stature is needed more often. Therefore, while this study was performed in young adult females who already completed growth, it highlights the need to further investigate the use of supra-maximal anaerobic testing for the evaluation of GH secretion in children with short stature.

In addition, a significantly reduced aerobic exercise-associated GH response in otherwise healthy obese children [18] and adults [19] was previously demonstrated. Several investigators [e.g., 20] have speculated that the beneficial effects of exercise on weight reduction and changes in body composition in obese subjects might be limited, due to the suppressed exercise-associated GH response. The finding that GH increases following anaerobic exercise in normal weight females should lead to an evaluation of the GH response to anaerobic exercise in obese individuals. If successful, this may change the optimal exercise selection for obese individuals.

In summary, both vigorous (10 min treadmill run at 85% of peak VO_2) aerobic and standard all-out anaerobic laboratory exercise tests were associated with a significant increase in GH levels in the same female individuals. The GH area under the curve was significantly greater following the anaerobic exercise. The WAnT also led to a significant increase in IGF-1 levels. The study suggests that changes in GH and IGF-1 may be used to gauge training intensity, not only following aerobic exercise, but also following anaerobic-type exercise. This may aid athletes and their assisting teams in designing an optimal training regimen. The GH→IGF-1 response to the different types of exercise may also apply to other fields, and improve disease diagnosis and treatment.

What this study adds?

This is the first study to examine the effect of vigorous aerobic and standard anaerobic laboratory exercise tests in the *same* female individuals (an under-investigated population in the field of exercise science despite increased popularity of participation

in habitual and competitive sports). Both vigorous aerobic and standard anaerobic tests were associated with a significant GH increase. GH area under the curve was significantly greater following the anaerobic exercise. The WAnT also led to a significant increase in IGF-1. The results suggests that GH and IGF-1 changes may be used to gauge training intensity following anaerobic exercise as well. This may assist athletes and coaches in designing an optimal training regimen. The role of anaerobic testing for GH secretion in the pediatric population should be further investigated.

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