Additive effect of diets and training on total Insulin-like Growth Factor-1 (IGF-1) in rats

Effet additif des régimes alimentaires et de l’entraînement physique sur l’insulin-like growth factor-1 (IGF-1) chez le rat

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Résumé

Objectif. – Le but de ce travail était d’étudier l’effet additif de deux types de régimes alimentaires (hyperprotidiques et hyperglucidiques) et de l’entraînement physique pendant 30 jours sur les concentrations plasmatiques de l’IGF-1 et sur d’autres paramètres hormonaux et métaboliques.

Matériels et méthodes. – L’étude a été menée sur quatre groupes de rats mâles : un groupe de rats témoin qui est sédentaire et reçoit un régime standard (SS), un groupe entraîné qui reçoit un régime standard (SE), un groupe entraîné qui reçoit un régime hyperprotidique (PE) et un groupe entraîné qui reçoit un régime hyperglucidique (CE). Les concentrations plasmatiques d’IGF-1, de l’insuline et de la corticostérone sont mesurées.

Résultats. – L’IGF-1 plasmatique diminue avec l’entraînement physique (p<0,001) et uniquement avec le régime protidique (p<0,05). Le gain pondéral et la prise alimentaire sont significativement plus faibles chez les rats entraînés avec et sans régime (p<0,01). En revanche, la corticostéronémie augmente avec l’entraînement (p<0,05). Le régime glucidique n’apporte pas des modifications importantes sur les différents paramètres étudiés.

Conclusion. – Les taux réduits d’IGF-1 enregistrés malgré un régime hyperprotidique, connu pour son effet stimulateur sur la sécrétion d’IGF-1, et la faible variation avec le régime glucidique pourraient être attribués au bilan énergétique négatif induit par une dépense énergétique augmentée au cours de l’entraînement physique et un apport réduit en calories fournis par le régime protidique. On peut conclure que le déficit énergétique, indépendamment du type de régime utilisé, diminue la sécrétion de l’IGF-1.

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Mots clés : IGF-1 ; Régime hyperprotidique ; Régime hyperglucidique ; Entraînement ; Rats

Abstract

Objectives. – Although it is known that circulating levels of insulin-like growth factor-1 (IGF-1) are influenced by both physical exercise and dietary intake separately, there is little information regarding the additive effect of diets and training on IGF-1 regulation. To test this, we examined the combined effect of 30 days of two different diets (high-protein and high-carbohydrate) and exercise training on total IGF-1. Materials and methods. – The study was carried out with four groups of rats; the sedentary group with standard diet (SS) (control group), standard diet with exercise (SE), high-protein diet with exercise (PE) and high-carbohydrate diet with exercise (CE). Serum IGF-1, insulin, corticosterone were analyzed. Results. – IGF-1 concentrations were decreased by exercise training (p<0.001) and only with protein diet (p<0.05). Physical training, with and without diet, decreased body weight and food intake (p<0.01) and increased corticosterone levels (p<0.05). Carbohydrate diet did not cause major hormonal and metabolic alterations. Conclusion. – The main result of this study was the decreased levels of IGF-1 in spite of...
high-protein diet, which is known to enhance IGF-1 secretion, and the little changes with carbohydrate diet. This may be related to the negative energy balance as a result of the catabolic state induced by exercise training and decreased calorie intake in protein diet. Thus, it can be concluded that the caloric restriction, regardless of dietary composition, decreased IGF-1 secretion.

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Keywords: IGF-1; Protein; Carbohydrate; Diets; Training; Rats

1. Introduction

Insulin-Like Growth Factor-1 (IGF-1) plays an important role in many physiological processes, particularly in organism anabolism, for bone and muscular growth [1]. The anabolic action of IGF-1 consists of stimulating cell uptake of amino acids and glucose, with an action similar to that of insulin [2,3]. Moreover, IGF-1 plays a key role in providing fuel metabolism and cell growth during physical exercise [4].

Protein intake is a critical regulatory factor of IGF-1 secretion [5]. Actually, dietary protein has powerful regulatory influence on muscle growth and protein turnover, which may partly be mediated by IGF-1 [6]. Moreover, many studies have demonstrated the use of pre-exercise protein ingestion in preventing acute exercise-induced muscle damage, as well as the damage that may occur during prolonged periods of heavy training [7,8]. Thus, high-protein diet continues to be an extensive practice among athletes seeking to enhance their physical performance.

Besides, it is well known that carbohydrates are the main sources of energy at rest and during physical activity [9]. It has been demonstrated that carbohydrate intake delays the onset of fatigue during exercise and aids in protein synthesis and restoration of muscle glycogen stores in post-exercise [10]. However, there are conflicting opinions about the IGF-1 response to carbohydrate diet with either increased [11] or decreased levels [12].

Indeed, it is known that circulating levels of IGF-1 fluctuate in response to changes in nutritional status [12]. Many studies have shown that circulating IGF-1 concentrations decrease in animals fed low-protein diets [5,13,14] or during caloric restriction with fat or carbohydrate regimen [12] and increase with high-protein diets [15]. Referring to these observations, one might expect that prolonged intake of protein diet would lead to an increase in IGF-1 concentrations. However, only a few studies have focused on testing the interaction of high-protein diet and physical training on IGF-1 regulation [16,17,18], with some discrepancy in the results with either increased [16] or unchanged levels [17,18]. Some studies have attributed this discordance to the different energy balance [12,18,19]. Accordingly, the main purpose of this study was to examine the effect of prolonged intake of high-protein diet during exercise training on IGF-1 regulation and to inspect the combined effect of two different diets and exercise training on hormonal and metabolic changes.

2. Methods and materials

2.1. Animals and diets

Male albino Wistar rats weighing 110–150 g obtained from SIPHAT (Tunis, Tunisia) were used in this study. Before any experiment, all animals were kept for one week in the same laboratory conditions of temperature (22 ± 2°C), relative humidity (70 ± 4%), and a 12 h light/dark cycle. They received a nutritionally standard diet (SICO, Sfax, Tunisia) and tap water. All experiments were carried out with the approval of the local animal use committee.

Animals were randomly divided into four groups of 12 rats: the standard diet sedentary group (SS) (control group) (62% carbohydrate, 17% protein, 4% fat; 352 Kcal), standard diet with exercise (SE), high-protein diet with exercise (PE) (42% carbohydrate, 23% protein, 3% fat; 287 Kcal) and high-carbohydrate diet with exercise (CE) (71% carbohydrate, 15% protein, 3% fat; 371 Kcal).

2.2. Experimental protocol

Food intake and animal weight were measured every day. Animals in the trained groups were subjected to swimming exercise in groups of six rats in a 50 cm deep swimming tank measuring 100×50 cm and filled with tap water. The water temperature was kept at 32 ± 2°C. The trained groups swam 1 h/day five times weekly for four weeks. During 10 days before the experiment, the animals were acclimated to the water and exercise with a gradual increase in swimming period. All animals were sacrificed by decapitation after 24 h of the last bout of exercise. Blood was collected into dry tubes and centrifuged at 3000 g for 15 min at 25°C to separate serum. After blood collection, whole muscles and liver were dissected out and immediately immersed in 0.9% NaCl solution. Glucose concentration was immediately measured. All samples were stored frozen at -30°C until analysis.

2.3. Determination of hormonal and biochemical parameters

IGF-1, corticosterone and insulin concentrations were determined using specific radioimmunoassay kits for the determination of hormone levels in rat serum (DSL-Texas-USA). Plasma glucose, triglyceride and proteins were measured by colorimetric methods using commercial kits obtained from BIOMAGHREB (Tunis, Tunisia). Liver and muscle glycogen was determined immediately after the sacrifice using the method of Good et al. [20]. Tissue lipids were measured using the Folch et al. method [21], and tissue proteins by the method of Bradford [22].

2.4. Statistical analysis

Results are expressed as mean ± SE. Statistical comparisons between groups were done by Student t test. Significance was accepted at the level of p < 0.05.
3. Results

At the end of the study, all trained animals reached a lower weight gain than did sedentary rats with different diets (SE, PE, CE vs. SS; p < 0.001), particularly with the protein diet (PE vs. SE; p < 0.01) (Table 1). Food intake was significantly decreased with training (SE vs. SS; p < 0.001) and in rats consuming protein (PE vs. SS; p < 0.01) and carbohydrate diet (CE vs. SS; p < 0.001) (Table 1). These results were statistically similar to those of energy intake in groups SE and PE (Table 1), whereas, energy intake in group CE was significantly higher in comparison with the other trained groups (SE and PE vs. CE; p < 0.05) (Table 1).

IGF-1 concentrations decreased in response to exercise training (p < 0.01) and only with protein diet (PE vs. SE; p < 0.05) (Fig. 1). Physical training increased corticosterone levels (SE vs. SS; p < 0.05, Fig. 2), whereas, insulin concentration was not affected by neither diet composition nor exercise training (Fig. 3).

No significant difference was observed between groups in plasma glucose and muscle glycogen, whereas, liver glycogen content was significantly lower in the trained rats with protein diet (PE vs. SS; p < 0.05) (Table 2).

Plasma triglycerides were significantly affected by both training and diet composition. Physical training significantly decreased triglycerides concentration (SE vs. SS; p < 0.005) (Table 2). Trained rats consuming protein diet had the lowest levels of plasma triglycerides (PE vs. SS; p < 0.001, PE vs. SE; p < 0.01) (Table 2). There was no significant effect of training and diet on muscle and liver lipids (Table 2).

Plasma protein concentration was decreased by both training (SE vs. SS; p < 0.05) and diet composition (PE vs. SS; p < 0.01 and CE vs. SS; p < 0.001) (Table 2). Liver protein content was higher in the trained rats with protein diet (PE vs. SE; p < 0.01) (Table 2), but no significant effect of training and diet was found on muscle protein content (Table 2).

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Table 1

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<thead>
<tr>
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<th>SS</th>
<th>SE</th>
<th>PE</th>
<th>CE</th>
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<td>Weight gain/30d (g)</td>
<td>89.96 ± 3.3</td>
<td>67.86 ± 3.4</td>
<td>50.66 ± 5.3</td>
<td>59.37 ± 7.6</td>
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<td>Food intake (g/day)</td>
<td>15.82 ± 0.29</td>
<td>13.83 ± 0.27</td>
<td>13.64 ± 0.74</td>
<td>13.48 ± 0.53</td>
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<td>Energy intake (Kcal/day)</td>
<td>55.68 ± 1.05</td>
<td>48.69 ± 0.94</td>
<td>46.81 ± 2.53</td>
<td>54.93 ± 2.89</td>
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Data are mean ± SE; (n = 12). SS: the standard diet sedentary group (control group); SE: standard diet with exercise, PE: high-protein diet with exercise; CE: high-carbohydrate diet with exercise.

* Significantly different from group SS.

** Significantly different from group SE.

*** Significantly different from group PE.

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Fig. 1. Effect of exercise training (exercise [E], sedentary [S]) and the different diets (standard [S], protein [P] and carbohydrate [C]) on IGF-1 concentrations of serum rats. Values are mean ± SE of measurements from 12 rats.

* p < 0.05 vs. SS, **p < 0.01 vs. SS, ***p < 0.001 vs. SS, α p < 0.05 PE vs. CE. 

Effet de l’entraînement physique (entraîné [E], sédentaire [S]) et de différents types de régimes (standard [S], hyperprotidique [P] et hyperglucidique [C]) sur les concentrations plasmatiques de l’IGF-1 total. Moyenne ± ES; (n = 12).

* p < 0.05 vs. SS, **p < 0.01 vs. SS, ***p < 0.001 vs. SS, α p < 0.05 PE vs. CE.

Fig. 2. Effect of exercise training (exercise [E], sedentary [S]) and the different diets (standard [S], protein [P] and carbohydrate [C]) on corticosterone concentrations of serum rats. Values are mean ± SE of measurements from 12 rats.

* p < 0.05 vs. SS, **p < 0.01 vs. SS, α p < 0.05 PE vs. CE.

Effet de l’entraînement physique (entraîné [E], sédentaire [S]) et de différents types de régimes (standard [S], hyperprotidique [P] et hyperglucidique [C]) sur les concentrations plasmatiques de la corticostérone. Moyenne ± ES; (n = 12).

* p < 0.05 vs. SS, **p < 0.01 vs. SS, α p < 0.05 PE vs. CE.

Fig. 3. Effect of exercise training (exercise [E], sedentary [S]) and the different diets (standard [S], protein [P] and carbohydrate [C]) on insulin concentrations of serum rats. Values are mean ± SE of measurements from 12 rats.

* p < 0.05 CE vs. PE.

Effet de l’entraînement physique (entraîné [E], sédentaire [S]) et de différents types de régimes (standard [S], hyperprotidique [P] et hyperglucidique [C]) sur les concentrations plasmatiques de l’insuline. Moyenne ± ES; (n = 12).

* p < 0.05 CE vs. PE.
4. Discussion

As a main result of this study we showed that changes in serum IGF-1 concentrations during physical training were not dependent on protein supplements but on the energy balance. In fact, we found decreased levels of IGF-1 in spite of high-protein diet, which is known to enhance IGF-1 secretion [15,16,23]. On the other hand, we observed a small change with carbohydrate diet, which is known to reduce IGF-1 levels [12,16].

It has been shown that IGF-1 concentrations are sensitive to food intake [24,25] with a specific role of protein diet [26,27]. Several studies have been conducted to investigate the effect of high-protein diet on plasma IGF-1. Most of them have demonstrated increased levels with protein supplementation [15,16,23]. For example, Norat et al. have demonstrated that IGF-1 levels were positively related to protein intake [15], and Hoppe et al. noticed that high intake of proteins increased concentrations of IGF-1 [23]. In addition, Ballard et al. have demonstrated that a protein supplement consumed during a strength and conditioning program led to an increase in plasma concentrations of IGF-1 in comparison with persons who also trained but consumed a calorically equivalent carbohydrate supplement [16].

Besides, many studies have explored the use of pre-exercise protein ingestion in preventing acute exercise-induced muscle damage, as well as the damage that may occur during prolonged periods of regular resistance training [7,8]. The authors found that protein supplementation significantly increased strength and lean mass when compared to placebo. Also, individuals consuming the protein supplement experienced greater increases in body mass, strength, serum levels of IGF-1, and intramuscular levels of IGF-1 mRNA [28].

Regarding post-exercise timing, ingestion of amino-acids after resistance exercise has been shown at many different time points to stimulate increases in muscle protein synthesis, cause minimal changes in protein breakdown and increase overall protein balance [29,30].

In the present study, we found decreased levels of serum IGF-1 in spite of high-protein diet. These seemingly contradictory findings might be explained by the substantial role that overall energy balance plays in the regulation of circulating IGF-1. Negative energy balance, whether caused by increasing exercise energy expenditure with an exercise training program or by reducing energy intake without increasing exercise, causes reduction in circulating IGF-1 within several days [31]. Conversely, IGF-1 increases with overfeeding, even without a change in physical activity [32].

Our results are in agreement with some previous reports with [16,18,19] or without exercise training in their protocols [12,14]. Research with physical training has attributed the small effect of high-protein diet on serum IGF-1 to the negative energy balance [17,18]. Actually, energy balance results from the equilibrium between energy expenditure during exercise training and energy intake (over or underfeeding independently of the protein content in diets). Nemet et al. have demonstrated that energy balance during periods of exercise training influences circulating IGF-1 [19]; they demonstrated that training plus an energy intake deficit causes a reduction in IGF-1. Moreover, Alemany et al. noticed that energy restriction coupled with high energy expenditure from arduous work results in negative energy balance and decreased IGF-1 concentrations [18].

Therefore, decreased levels of serum IGF-1 in the present study can be attributed on the one hand, to the high energy expenditure caused by the strenuous and continuous exercise training (60 min/day, 5 days/wk during 30 days), and on the other hand, to the significant low energy intake in the case of protein diet (Table 1). The small changes with carbohydrate diet can be explained by the significant higher energy intake in comparison with protein diet (Table 1). Moreover, negative energy balance can be explained, also, by the significant decrease in weight gain and feed intake observed in trained groups. This last result was in agreement with the study of Ebal et al. who have demonstrated that exercise training leads to decreases in food intake and weight gain [33].
We found decreased IGF-1 concentrations in response to training. However, regular physical exercise generally amplifies serum concentrations of IGF-1 [34]. Conversely, it has been observed that high intensity training or prolonged endurance activities, as in the case of the present study, provoke a long-term decrease in IGF-1 levels [35]. Our results are in agreement with the study of Izquierdo et al. [36] who have shown a significant reduction in resting IGF-1 after prolonged strength training, whereas Gomes et al. [37] did not observe an alteration in circulating IGF-1 in rats trained for six weeks. The divergence in the results found in the literature can be explained by the influence of duration and intensity of the different types of exercise applied.

Besides, our results showed increased levels of plasma corticosterone in response to exercise training. Generally, periods of substantially increased volume or intensity training have been shown to increase cortisol secretion [36] thereby indicating this hormone can be a useful marker of chronic strength training stress [38]. The increased levels of corticosterone observed in this study confirm that the type of training applied to the rats represented a high intensity exercise.

In addition, there is a persistent belief in the literature that endurance training implies hypercortisolism [33,39], and it was reported that stress related cortisol secretion is associated with low IGF-1 secretion [40,41]. Rosmond et al. [40] showed negative relationships between IGF-1 and cortisol secretion in adult men. Thus, decreased levels of IGF-1 in the present study can be attributed, in part, to the increased levels of corticosterone.

Moreover, there are many beneficial actions that glucocorticoids exert in exercising subjects, such as increasing the availability of metabolic substrates to supply muscles with energy needs, maintaining normal vascular integrity, and protecting the organism from an overreaction of the immune system [39].

Besides, our results showed a significant increase in liver corticosterone in response to exercise training. Generally, periods of substantially increased volume or intensity training have been shown to increase cortisol secretion [36] thereby indicating this hormone can be a useful marker of chronic strength training stress [38]. The increased levels of corticosterone observed in this study confirm that the type of training applied to the rats represented a high intensity exercise.

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Moreover, there are many beneficial actions that glucocorticoids exert in exercising subjects, such as increasing the availability of metabolic substrates to supply muscles with energy needs, maintaining normal vascular integrity, and protecting the organism from an overreaction of the immune system [39].

However, it was demonstrated, as well, that hypercortisolism, particularly when is prolonged, can result in deleterious effects, such as muscle catabolism [39]. However, in our study, we didn’t find any significant change in muscle and liver proteins, whereas we observed significant decreased levels on plasma proteins in trained groups. Given the minimal effect of hypercortisolism on protein tissues, this may be explained by the hypothesis proposed by Duclos et al. [39] who demonstrated that endurance-trained subjects might develop adaptive mechanisms to protect muscle and other glucocorticoid-sensitive tissues against the deleterious effect of cortisol secretion.

Besides, our results showed a significant increase in liver protein levels only in the group of rats consuming protein diet. This may be explained by the type of diet, particularly enriched in proteins.

It was demonstrated that regular endurance training leads to a multitude of metabolic adaptations in skeletal muscle that result in a decreased use of carbohydrates and a concomitant increase in fat oxidation and lipid use as energetic substrate during exercise [42], which may provoke small changes in carbohydrate metabolism. In the present study, muscle and liver glycogen levels did not differ between trained and sedentary rats. These data were similar to those reported by Gomes et al. [37] who did not observe differences in muscle and liver glycogen accumulation between trained and sedentary rats after chronic endurance training. Hokama et al. [43] didn’t observe, as well, any change in muscle glycogen between sedentary and trained rats. Moreover, plasma levels of glucose and insulin were not affected by training. This was consistent with the study of Donovan et al. [44] who reported that treadmill training in rats had no effect on resting glucose levels.

Furthermore, in comparison with the other groups, our data showed a small, non significant, decrease on plasma glucose in rats consuming a carbohydrate diet. This result can be explained on the one hand, by the effect of carbohydrate intake during training period that aids in restoration of muscle and liver glycogen stores [10], and on the other hand, by the type of glucose used in carbohydrate diet. Effectively, we used cornstarch, which has a very low glycemic index and does not enhance glycemia and insulin secretion [45].

Besides, the decreased levels of liver glycogen observed in rats with protein diet can be explained by the lower energy intake in this group.

Moreover, in spite of the small changes noted in liver lipids, our results showed decreased levels of plasma triglycerides in response to endurance training. This result proves the previous argument concerning the increased use of lipids as energetic substrates during endurance training. We noted, as well, increased levels of muscle lipids, which showed a real adaptation to endurance training.

5. Conclusion

In summary, high-protein diet during 30 days of endurance and strenuous training resulted in decreased serum IGF-1, whereas, high-carbohydrate diet produced less changes. This was related to the negative energy balance resulting from the high energy expenditure caused by exercise training and the low energy intake in the protein diet. We can conclude that the IGF-1 response to exercise training depends on the overall energy balance and not on the dietary composition.

Conflict of interest

None.

References


