

## EFFECTS OF THE PHYSICAL TRAINING ON THE KINETICS OF THE GH / IGF-I AXIS AND THE IMPLICATIONS ON THE GROWTH PROCESS OF CHILDREN AND ADOLESCENTS

### EFEITOS DO TREINAMENTO FÍSICO NA CINÉTICA DO EIXO GH/IGF-I E AS IMPLICAÇÕES NO PROCESSO DE CRESCIMENTO DE CRIANÇAS E ADOLESCENTES

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#### RESUMO

Os componentes do eixo GH/IGF-I são constituídos por um grupo de fatores que impactam diretamente o crescimento. No entanto, alguns estudos têm indicado que os níveis desses componentes podem ser reduzidos em resposta às sessões de treinamento. Essa redução pode estar ligada a citocinas elevadas, que podem resultar de exercícios extenuantes. O objetivo deste estudo foi investigar os efeitos do treinamento físico na cinética do eixo GH/IGF-I e as implicações no processo de crescimento de crianças e adolescentes. Uma busca em bases de dados eletrônicas foi conduzida e artigos de 1989 a 2023 foram incluídos. As concentrações de GH e IGF-I são significativamente elevadas durante a puberdade, especialmente durante o estirão de crescimento. No entanto, fatores como estado nutricional, composição corporal, concentração de hormônios e também a intensidade das sessões de treinamento físico podem influenciar a liberação de GH e IGF-I. O estudo conclui que o treinamento físico regular não afeta o crescimento de crianças e adolescentes, mas destaca a importância de compreender os papéis dos hormônios, das citocinas e do sistema muscular no exercício físico. Esse conhecimento é essencial para uma compreensão mais abrangente de como o corpo se adapta ao treinamento. As respostas hormonais podem ser valiosas para melhorar os ciclos de treinamento e monitorar a intensidade da carga, particularmente durante a puberdade.

**Palavras-chave:** Exercício. Hormônio do crescimento. Puberdade. Infância. Adolescência.

#### ABSTRACT

GH/IGF-I axis components are constituted by a group of factors that directly impact growth. However, some studies have indicated that the levels of these components can be reduced in response to training sessions. This reduction may be linked to elevated cytokines, which can result from strenuous exercise. The aim of this study was to investigate effects of the physical training on the kinetics of the GH / IGF-I axis and the implications on the growth process of children and adolescents. An electronic databases search was conducted and articles from 1989 to 2023 were included. The concentrations of GH and IGF-I are significantly elevated during puberty, especially during the growth spurt. However, factors such as nutritional status, body composition, concentration of hormones and also the intensity of physical training sessions can influence the GH and IGF-I release. The study concludes that regular physical training does not affect the growth of children and adolescents, but highlights the importance of understanding the roles of hormones, cytokines, and the muscular system in physical exercise. Such knowledge is essential for a more comprehensive understanding of how the body adapts to training. Hormonal responses can be valuable for improving training cycles and monitoring load intensity, particularly during puberty.

**Keywords:** Exercise. Growth hormone. Puberty. Childhood. Adolescence.

#### Introduction

During puberty, the release of growth hormone (GH) becomes more responsive to various stimuli, including the secretion of gonadal sex hormones. Multiple factors play a role in regulating and releasing GH, such as growth hormone-releasing hormone (GHRH), somatostatin (SRIF), brain neurotransmitters and neuropeptides. Additionally, the production of insulin-like growth factor I (IGF-I) and its binding proteins (IGFBPs), along with factors related to nutrition and physical activity, also influence GH secretion.<sup>1-3</sup>

GH/IGF-I axis components are constituted by a group of factors that directly impact growth. However, some studies have indicated that the levels of these components can be reduced in response to training sessions. A possible explanation for this situation involves the elevation of pro-inflammatory cytokines, a group of small polypeptides that play a key role in

cell-to-cell signaling, particularly in coordinating immune activity and mediating responses to both short-term and long-term inflammatory triggers.<sup>4-8</sup>

Some studies have shown that some pro-inflammatory cytokines, such as, interleukin-6 (IL-6), tumor necrosis factor alpha (TNF- $\alpha$ ) and interleukin-1 beta (IL-1 $\beta$ ) may decrease circulating IGF-I levels and consequently attenuate IGF-I bioactivity by increasing inhibitory IGFBPs. Such behavior can be triggered by intense exercise sessions.<sup>5-8</sup>

Through a study involving a typical Greco-Roman wrestling training, Nemet et al.<sup>5</sup> found a significant decrease in total IGF-I, bound IGF-I and insulin levels. On the other hand, the results showed an increase in the levels of interleukin-6 (IL-6), tumor necrosis factor alpha (TNF- $\alpha$ ), interleukin-1 beta (IL-1 $\beta$ ), and insulin-like growth factor binding protein 1 (IGFBP-1), a binding protein known to inhibit the effects of IGF-I. The findings reported by Nemet et al.<sup>5</sup> support the hypothesis that an intense exercise session triggers a primarily catabolic response, as evidenced by significant alterations in growth factors and inflammatory cytokines following a standard wrestling practice.

Furthermore, some authors have investigated the behavior of the axis during longer training periods with the intention of evaluating the chronic effects of the physical training. Studies indicate that a catabolic phase may occur in the first three to five weeks of training. Possibly, this phase is followed by an anabolic phase, which may be observed around five to six weeks into a training program.<sup>9-13</sup>

According to Steinacker et al.<sup>14</sup>, comprehending the role of hormones and cytokines, along with the regulatory function of the muscular system during exercise, is essential for a better understanding of the body's complex adaptation processes to exercise and physical training. Furthermore, hormonal responses can serve as an important tool for optimizing training cycles and monitoring exercise intensity.

Since the GH/IGF-I axis plays a crucial role during puberty in children and adolescents, the aim of this review is to analyze, through studies already present in the literature, the main effects of physical training on the GH/IGF-I axis and its potential implications for the growth process in children and adolescents.

## Methods

An electronic databases search, including PubMed, Scopus, Web of Science, Scielo, Google Scholar and Springer was conducted using the search terms: children, adolescents, growth hormone (GH), insulin-like growth factor I (IGF-I), insulin-like growth factor binding protein 1 (IGFBP-1), insulin-like growth factor binding protein 3 (IGFBP-3), growth process, hormones. Articles from 1989 to 2023 were included for the preparation of this review.

## Results and analysis

### *Physiological aspects of the GH/IGF Axis*

The GH/IGF axis is composed of growth hormone (GH) and insulin-like growth factors (IGFs). These components, along with genetic inheritance directly impact growth. In this context, puberty is significantly influenced by the activation of the GH/IGF-I axis, with its interactions with gonadal steroids closely linked to the peak height velocity (PHV).<sup>15,16</sup>

According to Martinelli Jr et al.<sup>2</sup>, GH secretion occurs in pulses, mainly at night, during sleep, with a half-life of approximately 20 minutes. The amplitude of the pulses and the mass of GH secreted vary with age, increasing during puberty, the period in which the greatest secretion of this hormone occurs, and decreasing in adult life to concentrations similar to those observed in pre-pubertal individuals with a subsequent progressive decrease.

Cruzat et al.<sup>3</sup> state that GH secretion in the adenohypophysis is modulated by both stimulatory and inhibitory influences, involving the interaction between somatostatin, which inhibits GH, and growth hormone-releasing hormone. The synthesis of growth hormone-releasing hormone and somatostatin is influenced by neurotransmitters such as serotonin, dopamine, acetylcholine, and norepinephrine, as well as peripheral hormones like insulin and glucocorticoids. Other factors, such as nutritional status, sleep, body fat, stress, and physical activity, also affect GH secretion. GH exerts anabolic actions (stimulating tissue growth) and metabolic actions (modifying nutrient metabolism) through the specific GHR receptor, which belongs to the cytokine receptor family.<sup>2,3</sup>

These actions can be divided into direct, mediated by the intracellular signaling cascade after GH binding to its receptor, and indirect, mainly through the regulation of insulin-like growth factors (IGFs) and their binding proteins (IGFBPs). IGFBPs increase the half-life of IGFs and modulate their actions, enhancing or inhibiting their autocrine, paracrine and endocrine functions. Furthermore, IGFBPs are produced in various organs and have their own functions, including the regulation of apoptosis and cell growth.<sup>2</sup>

In relation to lipolytic and glycolytic metabolism, the direct actions of GH are antagonistic to the effects caused by insulin, that is, GH increases the concentration of circulating glucose and, consequently, stimulates the release of more insulin to maintain adequate glycemia.<sup>17</sup> In this case, GH reduces the oxidation and uptake of glucose in tissues, increases lipolysis and oxidation of fatty acids in adipose tissue and muscles, in addition to stimulating hepatic glucose production via glycogenolysis.<sup>3,17</sup> The most important indirect effect of GH is the modulation of IGF-I synthesis, the main mediator of its anabolic effects, especially on height growth.

IGF-I is produced mainly in the liver, but also in several other tissues, where it exerts autocrine and paracrine actions. Its synthesis is influenced by factors such as GH concentration, nutritional status, body composition and hormones and metabolites.<sup>2,3,17,18</sup>

Summarily, GH/IGF axis, involving GH and IGFs, is vital for growth and development, especially during puberty when GH levels peak. GH is released in pulses, mainly during sleep, and is regulated by hormones, neurotransmitters, and lifestyle factors. It acts directly through receptors and indirectly by stimulating IGFs and their binding proteins, which enhance IGF function. IGF-I, mainly produced in the liver, mediates GH's anabolic effects on growth. Additionally, GH influences metabolism by increasing fat breakdown and blood glucose levels, counteracting insulin's effects.

### *GH/IGF-I axis and puberty*

The term *puberty* refers to the physical changes that occur during the growth of girls and boys during the transitional period between childhood and adulthood. The main physical manifestations involve acceleration of the growth process, development of primary and secondary sexual characteristics, changes in body composition, and alterations in the circulatory and respiratory systems.<sup>19</sup>

The growth spurt during adolescence is primarily characterized by a significant increase in growth velocity and elevation in the secretion of three hormones: sex steroids, GH, and IGF-I. Studies show that GH concentrations secreted during this phase can be up to twice as high with each pulse, significantly increasing the average serum concentration of GH over a 24-hour period, where the peak of GH coincides with the peak of growth velocity.<sup>1,2,15</sup>

In females, the increase in estradiol secretion is associated with the acceleration of growth velocity; on the other hand, in males, the increase in testosterone secretion appears to stimulate the rise in GH and IGF-I, subsequently accelerating growth.<sup>20-21</sup>

Rose et al.<sup>22</sup> assessed GH levels in 132 children and adolescents, collecting samples every 20 minutes for 24 hours. GH levels increased during puberty in both sexes, with the

nocturnal rise occurring earlier in girls due to the greater amplitude of the pulses, not the frequency. In girls, the amplitude increased before puberty, being greater between the ages of 12 and 14 than in girls aged 8 or younger. In boys, the pubertal increase in GH was later, with lower average GH levels over the 24-hour period and at night. However, the amplitude of the GH pulse was higher in boys aged 11 to 13 years.

In a long-term study, Viru et al.<sup>23</sup> evaluated the hormonal responses to exercise in 34 girls across the 5 stages of puberty. Annually, for 3 years, the participants cycled for 20 minutes at 60% of their maximal oxygen uptake. Blood samples were collected in two different moments, before and after exercise, in order to measure cortisol, insulin, GH, estradiol, progesterone, and testosterone. There was an increase in cortisol, GH, and estradiol levels, and a decrease in insulin, across all stages of puberty. Pre-exercise GH levels were higher than cortisol levels, and the highest levels of estradiol and testosterone occurred at the end of puberty, near menarche. After menarche, the late follicular phase also showed an increase in GH levels. Thus, the greatest hormonal responses to exercise are associated with the pubertal years.

It is clear that the growth of children during puberty is largely regulated through the actions of the GH/IGF-I axis. However, a variety of factors, such as nutritional status, physical activity, training level, body composition, and others, can alter the concentrations of the components of this axis.

#### *Acute effects of training on the GH/IGF-I axis*

The GH/IGF-I axis is a network of growth mediators, receptors, and binding proteins that regulate somatic and tissue growth across various species. Although exercise programs may influence this anabolic process through the action of this axis, some research indicates that the circulation of these components may be decreased following training sessions.<sup>4-6</sup>

Martinelli Jr et al.<sup>2</sup> and Cruzat et al.<sup>3</sup> state that GH exerts its anabolic action by stimulating tissue growth, as well as its metabolic action, where it alters the flow, oxidation, and metabolism of virtually all nutrients in circulation, through the specific receptor (GHR).

Eliakim et al.<sup>24</sup> investigated the effects of a 5-weeks intensive training program on IGF-I concentrations in 44 adolescent girls (aged 15 to 17). Authors found a 14% decrease in serum IGF-I levels in the trained group compared to the control group over the training program. The authors suggested that short-term training may have resulted in a catabolic hormonal response in this group of girls.

The elevation of cytokines induced by intense exercise sets may be one of the possible explanations for such a situation.<sup>4-8,25-28</sup> Cytokines, such as interleukin-6, interleukin-1 receptor antagonist (IL-1ra), and tumor necrosis factor alpha, are known to directly suppress the anabolic activity of the GH/IGF-I axis.<sup>5,29</sup>

Through a study involving a typical Greco-Roman wrestling training, Nemet et al.<sup>5</sup> found a significant decrease in total IGF-I ( $-11.2 \pm 2.3\%$ ), bound IGF-I ( $-11.2 \pm 2.4\%$ ), and insulin ( $-42 \pm 10\%$ ) levels. On the other hand, the results found by Nemet et al.<sup>5</sup> showed an increase in the levels of the interleukin-6 ( $795 \pm 156\%$ ), tumor necrosis factor alpha ( $30 \pm 12\%$ ), interleukin-1 beta ( $286 \pm 129\%$ ) and IGFBP-1, a binding protein known to inhibit the effects of IGF-I. The authors concluded that intense exercise in young athletes led to a catabolic response, with reductions of the anabolic mediators and increases of the cytokine's levels.

Similarly, Nemet et al.<sup>8</sup> evaluated the effects of a water polo training session on female adolescents' GH/IGF-I axis, cytokines and immune function. The results indicated a reduction in insulin levels and a significantly increase in circulating interleukin-6 ( $396 \pm 162\%$ ), interleukin-1 receptor antagonist ( $71 \pm 20\%$ ) and IGFBP-1 ( $1344 \pm 344\%$ ), suggesting a catabolic response to an intense water polo session. But, specifically in this study, although the pattern of changes in IGF-I values observed in female water polo players was quantitatively

similar to that observed in boys practicing Greco-Roman wrestling, Nemet et al.<sup>8</sup> were not able to detect statistical significance regarding to IGF-I levels.

Scheett et al.<sup>6</sup> investigated the hypothesis that reductions in IGF-I levels in children and adolescents would be supported by increasing cytokines due to exercise. The study involved prepubertal children, divided into two different groups: control group (n=14) and an experimental group (n=12). The experimental group participated in a 90-minute aerobic exercise program, five times per week, for five weeks. The activities included games, running, and various sports, with variations in intensity and duration. The results showed a significant increase in interleukin-1 beta, tumor necrosis factor alpha and IGFBP2, and a decrease in IGF-I and IGFBP3, suggesting a catabolic state. Despite these findings, the boys showed an improvement in physical fitness, along with a significant increase in peak oxygen uptake.

Pires et al.<sup>27</sup> examined the kinetics of the interleukin-6, interleukin-10 (IL-10), and tumor necrosis factor alpha in adolescent swimmers throughout a training season, focusing on their connection to serum levels of IGF-I and IGFBP-3. The study showed a significant inverse relationship between interleukin-6 and IGF-I serum levels during the most intense phase of training, which occurred in the preparatory period. Additionally, an increase in serum concentrations of IGF-I and interleukin-10 was observed during the tapering phase.

On the other hand, in a study conducted by Tourinho et al.<sup>30</sup>, 9 Brazilian Jiu-Jitsu athletes were evaluated acutely during a standard training session, but the authors observed no significant changes in IGF-I and IGFBP-3 concentrations, which could be attributed to the athletes' advanced training level.

Some studies indicate a strong correlation between cytokine levels, particularly interleukin-6, and the intensity and duration of exercise—longer and more intense exercise tends to result in higher circulating cytokine levels.<sup>31</sup> In this sense, Pedersen<sup>25</sup> highlights that newer studies reveal that interleukin-6 is also released during both eccentric and concentric movements even without muscle damage, since interleukin-6 is produced in large quantities by skeletal muscles during physical activity. For example, interleukin-6 levels in marathon runners have shown an increasing up to 100 times following a race. But, in this scenario, it is believed that interleukin-6 is the most responsive cytokine to exercise and plays a positive role in supporting metabolic changes due to its role as a growth factor.<sup>25</sup>

According to Bruunsgaard et al.<sup>32</sup>, the largest increases in cytokine levels occur during the eccentric phase of the movement. The authors also found a strong correlation ( $r = 0.725$ ) between interleukin-6 levels and plasma creatine kinase (CK) enzyme levels. However, the increase in circulating cytokine levels is not solely linked to muscle damage or repair processes—adaptive microtrauma.<sup>14,25</sup>

As reported by Steinacker et al.<sup>14</sup>, muscle glycogen content affects interleukin-6 release during exercise. When glycogen stores are nearly depleted, glycogenolysis and glucose transporters need to be reduced in muscles and the liver, as well as the production of IGF-I, due to its insulin-like effect on blood glucose levels. This leads to the development of transient insulin resistance. Steinacker et al.<sup>14</sup> suggest that glycogen depletion is linked to increased local cytokine expression (interleukin-6 in muscles), a reduction in glucose transporters, elevated cortisol, decreased insulin secretion and activation of  $\beta$ -adrenergic stimulation. Cytokines serve as signals to the hypothalamus, leading to a reduction in IGF-I levels through the GH/IGF-I axis.

Pilz-Burstein et al.<sup>7</sup> examined the impact of a Taekwondo fight simulation (three 6-minute fights with 30-minute intervals) on anabolic hormones (IGF-I, luteinizing hormone, follicle-stimulating hormone, estradiol, testosterone) and the catabolic hormone (cortisol) in adolescent fighters (aged 12-17). The findings revealed a significant reduction in IGF-I, luteinizing hormone, follicle-stimulating hormone and testosterone levels, alongside a significant increase in cortisol levels in both genders. The authors concluded that the

Taekwondo fight simulation induced a catabolic hormonal response, which may affect systems such as the muscular, immune, and cardiorespiratory systems. They suggested that these responses could be useful optimizing training cycles and monitoring training load in combat sports.

Steinacker et al.<sup>14</sup> go beyond the conclusions made by Pilz-Burstein et al., stating that comprehending the role of hormones and cytokines, along with the regulatory function of the muscular system during exercise, is essential for a better understanding of the body's complex adaptation processes to exercise and physical training.

In summary, it can be stated through the studies analyzed that the acute effects of exercise on the GH/IGF-I axis represent a predominantly catabolic response due to the increase in pro-inflammatory cytokine concentrations.

#### *Chronic effects of physical training on the GH/IGF-I axis*

Few studies have investigated the duration of the reduction in IGF-I levels or the GH/IGF-I axis following a series of intense exercises<sup>33</sup> and even fewer have examined anabolic and catabolic behavior of the mediators throughout a training season.<sup>10,11,34</sup>

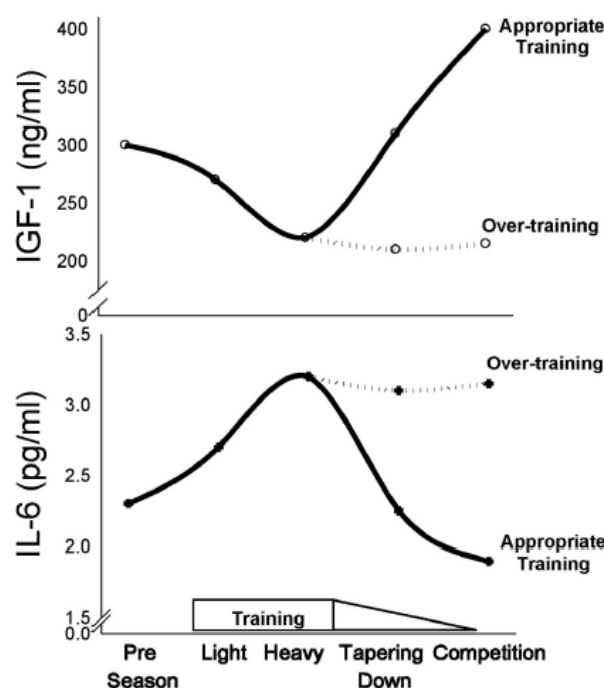
To explore the kinetics of the GH/IGF-I axis during extended training periods, some researchers have proposed the existence of a catabolic phase in response to physical exercise, which may occur in the first three to five weeks of training, followed by an anabolic phase that could occur five to six weeks into a training program.<sup>9-12</sup>

Koziris et al.<sup>35</sup> investigated the effects of a five-month training program in experienced swimmers (18–22 years) on total IGF-I, free IGF-I, IGFBP-1 and IGFBP-3 serum levels. Blood samples were collected at different times throughout the season. The results showed that training increased IGF-I levels, but a significant peak was only reached after a relatively long period of training. Furthermore, elevated IGF-I levels persisted even with a reduction in training volume during the tapering phase. The authors concluded that intense training can increase and maintain free and total IGF-I levels, as well as IGFBP-3, even during a decrease in training volume.

The increases in IGF-I levels observed after a longer training period (4 to 9 weeks) align with findings from animal studies, which showed increased IGF-I gene expression in skeletal muscle tissue and higher circulating IGF-I levels.<sup>36</sup> However, it remains unclear whether the hypothesis suggesting that the GH/IGF-I axis undergoes both catabolic and anabolic phases during a prolonged training program also applies to humans.<sup>12</sup>

Mejri et al.<sup>37</sup> investigated the impact of a soccer training program on GH and IGF-I levels in 13 players (19 ± 1 year old) through submaximal tests performed at the beginning, middle and end of the season. Blood samples were collected at rest, post-exercise and during recovery (30 and 60 minutes). The results showed that GH levels increased during exercise, but were significantly higher at the beginning of the season, with lower responses at the middle and end, suggesting an adaptation to training. IGF-I levels remained consistent throughout the season, suggesting that their concentration post-exercise may not be directly linked to GH production. The study did not support the hypothesis that the GH/IGF-I axis undergoes catabolic and anabolic phases during a training season.

Eliakim e Nemet<sup>13</sup> suggest that pro-inflammatory cytokines increase, leading to a reduction in IGF-I levels. However, if training adaptation is successful, pro-inflammatory cytokines decrease, which in turn reduces the suppression of IGF-I. Possibly, this may result in an anabolic rebound of the axis, where IGF-I levels surpass those seen before training. (Figure 1).



**Figure 1-** Effects of a training season on circulating levels of IGF-I and interleukin-6 (IL-6) suggested by Eliakim and Nemet.<sup>13</sup>

**Source:** The authors.

To determine the concentrations of IGF-I and its binding proteins, Chicharro et al.<sup>38</sup> evaluated seven professional cyclists during a competition, one week after, and three weeks after. Blood samples were collected, and significant differences were found in total IGF-I and its binding protein IGFBP-1. However, due to training adaptation, these concentrations remained stable after three weeks.

Similarly, eight young CrossFit athletes were evaluated at three different times over a 3-month period.<sup>39</sup> Despite the training session being rated by the participants as moderate/intense, the findings related to the IGF-I and IGFBP-3 levels were not significant. Alipio et al.<sup>39</sup> believe that these findings can be explained by the athletes' adaptation to intense training, which is a strong characteristic of this specific sport.

The hypothesis of a biphasic pattern in the GH/IGF system during a long-term training program was also not supported by Pisa et al.<sup>40</sup> No significant differences were found in the hormonal concentrations of volleyball players throughout the season, which could also indicate chronic adaptation to training.

Tourinho et al.<sup>41</sup> evaluated nine male swimmers aged 16 to 19 to assess the concentrations of IGF-I, IGFBP-3, and ALS throughout a training season. The results revealed that IGF-I and IGFBP-3 levels were responsive to both the acute and chronic effects of training. Furthermore, they observed for the first time a biphasic pattern in the GH/IGF-I axis, with a catabolic phase occurring in the middle of the season when training intensity was high, followed by an anabolic phase, marked by a significant increase in IGF-I levels during the final phase of the season.

Similarly, Fornel et al.<sup>42</sup> assessed GH, IGF-I, IGFBP-3, creatine kinase, and lactate dehydrogenase levels in young male soccer players over a 7-month period. Blood samples were taken before and after standard training sessions at three different points during the season. IGF-I levels were notably higher during the middle phase of the season compared to the final phase, suggesting that IGF-I is a sensitive biomarker for both the acute and chronic effects of

training, exhibiting a biphasic pattern in the axis. These findings are consistent with the study of Kohama et al.<sup>43</sup>, who evaluated 11 young male soccer players in the under-15 category throughout a training season. They found variations in both IGF-I and IGFBP-3 during the competition phases, indicating these markers were responsive to both acute and chronic effects of competition. Kohama et al.<sup>43</sup> propose that components of the GH/IGF-I axis, like IGF-I and IGFBP-3, may be valuable indicators of an athlete's training status.

Based on the studies analyzed, it is possible to observe that the GH/IGF-I axis, when examined over longer periods, exhibits effects that characterize a catabolic phase (the first weeks of training), where GH and IGF-I levels are suppressed, and as the training volume decreases in the following weeks, these effects are followed by an anabolic phase, where GH and IGF-I levels are elevated again. However, there is still controversy regarding this pattern in the axis observed during a training season, as this behavior can vary when evaluated across different sports modalities and also due to athletes' adaptation to training.

#### *Possible repercussions on growth in childhood and adolescence*

It is possible to find authors in the literature who state that regular physical activity can be important in the growth process of children and adolescents, since physical activity improves bone mineral content and acts directly on different tissues. Some authors also state that regular physical activity does not alter the growth processes and final height of children and adolescents.<sup>44,45</sup>

In order to determine the effect of diet and exercise on plasma IGF-I levels in children, Denison and Ben-Ezra<sup>46</sup> recruited 37 children aged 8-10 years (18 swimmers and 19 controls). All children kept a 3-day food record for 2 weeks before fasting blood samples were collected. Both groups had normal caloric intake, with twice the recommended protein intake for their age group. Plasma IGF-I levels were significantly higher ( $p < 0.007$ ) in swimmers compared with controls, but still within the normal range for their age. The authors concluded that children aged 8 to 10 years who engage in regular physical activity and maintain an adequate diet have IGF-I levels within the expected range for their age.

A British study followed elite young athletes from different sports (gymnastics, tennis, soccer, and swimming) for three years, with training of different volumes and intensities. Baxter-Jones and Helms<sup>47</sup> reported that, for the most part, the participants maintained the same height and weight percentile during the period. There was no evidence to suggest that physical training had an impact on the athletes' growth or sexual development. The authors concluded that the positive social, psychological, and health benefits of engaging in sports outweighed any potential negative effects of intense training.

On the other hand, some studies indicate that high-intensity exercise can affect the growth of young athletes.<sup>6,48,49</sup> Intense physical exercise when associated with caloric restriction not only affects growth, but also pubertal development, reproductive function and bone mineralization.<sup>48,49</sup>

Theintz et al.<sup>48</sup> conducted a two-and-a-half-year longitudinal study to evaluate the impact of intense physical activity on the growth of adolescent female athletes. The study included 22 gymnasts and 21 swimmers, with an average age of 12 years, measuring height, weight, body fat, and pubertal stage. The gymnasts' growth rate was significantly slower, especially in leg length, which may affect their adult height. The authors suggest that this change in growth may be caused by inhibition of the hypothalamic-pituitary-gonadal axis, possibly combined with restrictive diets.

Based on the studies analyzed, it is possible to conclude that intense physical training does not interfere with the growth of children and adolescents, as long as it is practiced correctly and regularly, accompanied by adequate caloric intake and assisted by a qualified professional.



## Final Considerations

Based on the studies analyzed for the preparation of this literature review, the important role of the GH/IGF-I axis during the growth of children and adolescents is clear. The behavior of the axis during growth can be explained by the concentrations of GH and IGF-I that are significantly elevated during puberty, especially during the growth spurt, a period in which increases in the secretion of these hormones are directly related to the increase in growth rate.

However, there are some factors such as nutritional status, body composition, concentration of hormones and metabolites and also the intensity of physical training sessions, which can directly influence the GH and IGF-I releasing.

Regarding the acute effects of exercise on the GH/IGF-I axis, it can be concluded that high-intensity exercise, in most cases, causes a suppression of the axis, which characterizes a predominantly catabolic behavior. Apparently, this behavior occurs due to the increase in pro-inflammatory cytokines such as interleukin-6 and IGFBP-1, a binding protein known to inhibit the effects of IGF-I.

Unfortunately, there is still a lack of longitudinal studies in the literature evaluating the chronic effects of exercise on the GH/IGF-I axis. Apparently, over a long period of training, it is possible to observe a catabolic action, which occurs in the first weeks, and then an anabolic action, which occurs when the athletes are already adapted to training, and where there are changes in the intensity and volume of training. However, more studies are still needed to test this hypothesis that there is a catabolic action followed by an anabolic action during long periods of physical training in young athletes of different modalities.

Although there are few studies investigating the effects of exercise on the growth of young athletes, it is possible to state that regular physical training does not affect the growth of children and adolescents. Furthermore, it is essential to emphasize that physical exercise is only beneficial for growth when practiced correctly, along with an adequate caloric intake. Otherwise, inadequate practice can cause injuries and consequently alter the growth of children and adolescents.

Therefore, it is necessary to develop more longitudinal studies, so that we can have a concrete position on the effects of physical training on the GH/IGF-I axis and, as a result, monitor its impact on the growth and development processes of children and adolescents.

Comprehending hormonal and cytokine functions, along with the regulatory function of the muscular system during exercise is extremely important for a more complex understanding of the body's adaptation mechanisms to physical training. It is believed that hormonal responses may be served as an important tool for optimizing training cycles and monitoring exercise loads.

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