Hormonal response to physical exercise
Răspunsul hormonal la efortul fizic

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Abstract
Aerobic/anaerobic physical exercise causes a series of stimuli that can induce many biochemical and hormonal changes in the whole body. Hormones are involved in physiological changes produced in the body during exercise. The duration, the intensity and the type of training modulate these hormonal fluctuations. Aging is associated with an alteration of the neuroendocrine system, which leads to a decrease in the sensitivity of endocrine glands to the action of neurohormones and to a reduction in the number, density and affinity of neurohormone receptors. Increased physical activity is accompanied by great energy loss. The imbalance between energy consumption and the much higher energy expenditure results in the activation of adaptive endocrine and neuroendocrine mechanisms of the body to high physical effort. The endocrine profile developed under various physical exercise conditions: acute, high-intensity, prolonged moderate-intensity, prolonged high-intensity exercise or during restitution is dependent on the integrity of the hypothalamic-pituitary-adrenal, hypothalamic-pituitary-gonadal, hypothalamic-pituitary-thyroid axes and on the sympathetic adrenal medullary system, to which other endogenous and environmental factors are added. The increase in the incidence of diseases, including endocrine disorders closely related to physical exercise and to the absence of physical activity, is an area of wide interest and a public health problem.

Keywords: aerobic physical exercise, anaerobic physical exercise, growth hormone, thyroid hormone, reproductive hormones, adrenal hormones

Rezumat
Efortul fizic aerob/anaerob induce numeroase modificări biochimice şi hormonale la nivelul întregului organism. Hormonii interfețează cu modificările fiziologice produse în organism în timpul efortului fizic. Durata, intensitatea, tipul de antrenament, modulează aceste fluctuații hormonale. Înaintarea în vârstă se asociază cu alterarea sistemului neuroendocrin, ceea ce conduce la scăderea sensibilității glandelor endocrine la acțiunea neurohormonilor și la reducerea numărului, densității și afinității receptorilor acestora. Creșterea activității fizice se însoțește de pierderea mare de energie. Dezechilibrul balanței dintre consum de energie și cheltuielile energeticne mult mai mari induce instalarea unor mecanisme endocrine și neuroendocrine de adaptare ale organismului la efortul fizic crescut. Profilul endocrin instalat în variante condiții de efort fizic: acut, intens, prelungit și moderat, prelungit și intens, sau în fazele de restituție, este dependent de integritatea axelor hipotalamo-hipofizoz-corticosuprarenal (AHHCSR), hipotalamo-hipofizoz-gonadic (AHHG), hipotalamo-hipofizoz-tiroidian (AHHIT) și sistemul simpatoadrenal (SSA), la care se adaugă alți factori endogeni și ambientali. Creșterea incidenței unor afecțiuni inclusiv endocrine, strâns legate de efortul fizic și de lipsa de activitate fizică, constituie un domeniu de larg interes și o problemă de sănătate publică.

Cuvinte cheie: efortul fizic aerob, efortul fizic anaerob, hormonul somatotrop, cortizolul, hormonul adrenocorticotrop, hormonul tireotrop, triiodotironina, tiroxina, prolactina, catecolaminele.

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Introduction

Physical exercise has an important impact on the whole organism, mediated by the endocrine and neuroendocrine system. Physical activity causes a series of stimuli that can induce a cascade of biochemical and hormonal changes. Over the past years, an increasing number of studies have analyzed the correlations between the endocrine system and physical exercise, as well as the consequences of exercise on the endocrine system (Soria et al., 2015).

The effect of physical exercise on hormonal profile depends on the nature, duration and intensity of exercise. Hormonal response to physical exercise is influenced by many factors that are closely related to hormone secretion: genetic, ethnic/racial, sex (female/male), age, nutrition, environmental, stress, mental factors (Staicu & Tache S, 2011).

The biological hormonal effect is achieved following a cellular response, which depends on hormone concentration, the number and affinity of cell receptors and the genetic characteristics of each cell. At cellular level, hormone actions induce important biochemical changes, membrane transport and protein synthesis changes, and facilitate the activation of messengers (via protein G): cyclic AMP, Ca²⁺, inositol triphosphate and diacylglycerol (Hackney & Smith-Ryan, 2013).

Hormonal fluctuations secondary to sports activity depend on the type of exercise (aerobic/anaerobic), the intensity, the duration, the frequency of the training sessions, and the degree of physical training (O’Connor, 2007; Lencu, 2015).

The intensity of physical exercise has a particular impact on hormone secretion. Thus, intense exercise is associated with the production of lactic acid, which modulates hormonal profile during effort. High-intensity short-duration physical training is accompanied by an increase in the production of hormones (except for insulin), while moderate-intensity long-duration training causes a decline and an alteration of hormone homeostasis (Borresen & Lambert, 2009). The duration of rest between the sets of exercises of a prolonged (resistance) training session influences hormonal profile after the cessation of training (Meuusen et al., 2013).

Previous studies have demonstrated a direct connection between the aerobic/anaerobic type of exercise and hormone balance.

Aerobic exercise uses oxygen from outside the body, without consuming the body’s oxygen reserves. It lasts for a longer time (several hours), the amount of lactic acid produced does not significantly change, and there is no marked fatigue. Benefits include peripheral cell oxygenation and an improvement of the cardiovascular system (the cardiovascular system functions within normal limits, cardiac rhythm changes are almost imperceptible). The most common examples of aerobic exercise are: spinning, treadmill running and swimming.

Anaerobic exercise consumes the body’s oxygen reserves. It lasts for a relatively short time, it is performed at a high intensity, and the amount of lactic acid produced is high. Heart rate significantly changes, but returns to normal after the cessation of exercise. Examples of anaerobic exercise: bodybuilding, sprinting.

The increase of physical activity is accompanied by a greater energy loss. The imbalance between energy consumption and the much higher energy expenditure leads to the activation of adaptive endocrine and neuroendocrine mechanisms of the body to increased physical exercise (Madhusmita, 2014). The activation of these mechanisms has consequences on the body and bone composition and on weight.

Changes in the somatotropic hormone (STH/GH) – somatomedin C (insulin-like growth factor 1/IGF-1) axis during exercise

Somatotropic hormone is a polypeptide hormone consisting of 191 amino acids, which is secreted by the anterior pituitary lobe. Its secretion is regulated by neurogenic, metabolic and hormonal factors (Thorner, 1998). STH has many actions, of which the most significant are metabolic and linear growth effects. Insulin-like growth factors (IGF-1, IGF-2) are protein substances similar in structure to insulin. The major form is IGF-1, primarily produced by the liver, in response to stimulation exerted by the somatotropic hormone. Among the actions of growth factors, the stimulation of bone and cartilage growth is of great importance (Orasan, 2001).

Young women subjected to intense physical exercise had significant changes of the hormones involved in bone metabolism and the maintenance of calcium balance. Physical exercise has beneficial effects on bone mineral density through a mechanism that is incompletely understood. The exercise response of receptors in the bone system is modulated by hormones. Postmenopausal women with osteopenia had a significant increase of somatotropic hormone during exercise. Subsequently, at the cessation of exercise, its levels decreased to an even lower level than the initial baseline value. The same study did not demonstrate a significant IGF-1 fluctuation during exercise (Kemmler et al., 2003).

Other research evidenced a more marked response of the growth hormone during exercise in postmenopausal women under hormone replacement therapy; this can be explained by the implication of estrogen in the modulation of GH secretion during sports activity (Kemmler et al., 2003). Moderate aerobic training is accompanied by a progressive increase in the plasma concentration of most hormones (including GH/STH). Anaerobic training is associated with an abrupt GH response (Peake et al., 2014). Other study demonstrated in athletes running at a progressively increasing speed a 6-fold elevation of somatotropic hormone levels in the warm-up period, with a 20-fold higher value at the end of the race compared to the initial value; 24 hours after exercise, the values were comparable to baseline. So, progressive physical exercise associated with a considerable anaerobic energy production is associated with an increase of GH, which is significant at the end of exercise; values remain high for another hour after cessation of effort, after which they return to normal (Peake et al., 2014).

During anaerobic physical exercise GH levels doubled, while during aerobic training values were even 14 times higher. After the cessation of both types of training, no significant changes in hormone secretion were found (Weltman et al., 2008).
Overweight, although affecting hormonal response to physical activity, does not alter somatotropic hormone secretion. Obesity induces a negative IGF-1 response to physical exercise (Rubin et al., 2015). Insulin-like growth factor 1 is a polypeptide with a role in growth and development processes; at the same time, it is an indicator of fatigue, physical exhaustion and negative energy balance (Nemet et al., 2004; Elloumi et al., 2005; Nindl et al., 2007). Under the conditions of an energy imbalance in the body caused by caloric restriction, physical overtraining or both, IGF-1 bioavailability decreases (Nemet et al., 2004; Gomez-Merino et al., 2004). Short-duration exercise is accompanied by an increase of IGF-1 (Copeland & Heggie, 2008; Nindl et al., 2009; Eliakim & Nemet, 2013), while prolonged training causes a reduction in polypeptide levels (Nemet et al., 2004; Gomez-Merino et al., 2004). Thus, studies performed in postmenopausal vs. premenopausal women subjected to prolonged sports activity demonstrated a diminution of IGF-1 concentration in both studied groups; these values remained low after the cessation of training (Copeland & Vergosa, 2014). Although the implication of female steroid hormones in the modulation of IGF-1 secretion is known (Waters et al., 2003), no differences were found between premenopausal and postmenopausal women (Copeland & Vergosa, 2014).

IGF-1 secretion is modulated through the somatotropic hormone and the energy balance of the body, but it is independent of menstrual status (Waters et al., 2001). In young women performing prolonged physical activity (gymnasts, athletes, dancers, ballerinas), which induces an energy imbalance in the body, low somatomedin C (IGF-1) values were found (Maimoun et al., 2013).

Under the conditions of an imbalance between energy production and consumption, adaptive neuroendocrine mechanisms are activated in the body, which are accompanied by an increase of STH secretion, concomitantly with a decrease of IGF-1 (Mathusmita, 2014).

**Changes in the lactotropic hormone (PRL - prolactin) axis during exercise**

Prolactin is a polypeptide hormone composed of 199 amino acids, which is secreted by the lactotroph cells of the anterior pituitary gland; it is characterized by a structural homology (amino acid sequences) to the somatotropic hormone (STH) and the placental lactogenic hormone (hPL), which might explain common aspects of the physiology of these hormones.

Prolactin acts through prolactin receptors; these are situated in the mammary gland, liver, gonads (ovary/testis), prostate. The main action of prolactin is the induction and maintenance of lactation (Thorner et al., 1998).

Prolactin increases during physical exercise, proportionally to the intensity of training. The increase of prolactinemia is explained by a reduction in the levels of dopamine (a prolactin inhibitor) and by the intervention of stress factors (psychological, thermal, physical).

**The response of the hypothalamic-pituitary-thyroid axis to physical exercise**

Thyroid-stimulating hormone (TSH) belongs to the category of glycoprotein hormones, along with follicle-stimulating hormone (FSH), luteinizing hormone (LH) and human chorionic gonadotropin. TSH has a trophic effect on the thyroid gland and stimulates the synthesis/secretion of thyroid hormones. TSH secretion is regulated through hypothalamic thyroliberin and through feedback mechanisms by thyroid hormones. Thyroid hormones regulate the growth, differentiation and development processes of tissues and organs; they play a role in basal metabolism, in carbohydrate, lipid, protein and vitamin metabolism. Thyroid dysfunctions induce changes in the body which cause an alteration of exercise tolerance; on the other hand, exercise can affect thyroid function, through the activation of neuroendocrine mechanisms, which lead to changes in the thyrotropic axis, with the alteration of hormone homeostasis (Klubo-Gwiezdzinska et al., 2013).

The response of thyroid hormones to exercise is controversial.

Some studies demonstrated in male athletes subjected to intense physical exercise for 1 week an alteration of the thyroid function, with the reduction of the hormones triiodothyronine (T₃), tetraiodothyronine (T₄) and TSH, proportionally to the degree of training (Hackney et al., 2012). Subsequently, other research evidenced in militaries exposed to stress caused by physical overtraining, food and sleep deprivation, an alteration of the hypothalamic-pituitary-thyroid system and implicitly, a reduction of T₃, T₄, TSH hormones; similar results were obtained in young female athletes following very high intensity training (Baylor & Hackney, 2003).

Recent research carried out in male athletes demonstrated during anaerobic treatment an increase of free T₄, T₃, TSH, proportional to the intensity of exercise; at the same time, a reduction of T₃, free T₄ explained by a decrease of the T₃ to T₄ conversion rate was shown (Ciloglu et al., 2005). In trained men, the suppression of T₃ to T₄ conversion during high difficulty sports activity was demonstrated.

**The response of the hypothalamic-pituitary-adrenal axis to physical exercise**

Adrenocorticotropic hormone (ACTH) is a polypeptide hormone consisting of 39 amino acids. Its main biological action is aimed at the adrenocortical gland, where it stimulates the biosynthesis and secretion of adrenocortical hormones. ACTH secretion is regulated through hypothalamic corticoliberin and through negative feedback by cortisol, produced by the adrenocortical gland. Cortisol is a hormone that is indispensable to life, secreted from the fascicular and reticular zones of the adrenocortical gland. Stress, hypoglycemia, hemorrhage and ACTH stimulate cortisol secretion. The biological actions of cortisol include its role in carbohydrate, lipid and protein metabolism, the anti-inflammatory, immunosuppressive, stimulating effect on gastric acid secretion, the tonic effect on the central nervous system. In excess, it diminishes bone mineralization, disturbs bone protein matrix synthesis and inhibits the development of growth cartilage.

Cortisol is a gluconeogenetic hormone, whose levels increase during physical exercise, proportionally to the degree of training (St Pierre & Richard, 2013). The increase of cortisol represents an adaptive mechanism of the body to stress caused by an energy imbalance (Madhusmita, 2014).
Studies performed on groups of young athletes subjected to aerobic and anaerobic physical exercise evidenced an elevation of cortisol levels during effort, more significant in the case of aerobic exercise; after aerobic exercise, cortisol values remained unchanged; the cessation of anaerobic exercise was followed by an increase of cortisolemia (Balsalobre-Fernandez et al., 2014). In contradiction to the previous study, Kemmler demonstrated in postmenopausal women with osteopenia a decrease of cortisol during effort; the values remained low two hours after the completion of training (Kemmler et al., 2003).

Anterior research showed a moderate activation of the hypothalamic-pituitary-adrenal system and mild hypercortisolism in persons with a high degree of physical training; the values were almost similar to those evidenced in patients with depression or nervous anorexia. These changes represent an adaptive mechanism to stress induced by exhausting physical exercise, which may cause an energy imbalance or important psychological changes.

Elite gymnasts have high basal cortisol values and no circadian cortisol fluctuations; this reflects an adaptation of the body to stress induced by intense and prolonged exercise, concomitantly with a negative energy balance (Maimoun et al., 2013). Regarding ACTH secretion, no significant changes during exercise were found (Madhusmita, 2014).

The response of catecholamine secretion to physical exercise

Catecholamines (adrenaline, noradrenaline) are synthesized by pheochromocytes of the adrenal medulla; adrenaline is produced exclusively by the adrenal medulla; noradrenaline is released by pheochromocytes of the adrenal medulla, as well as by nerve endings. The secretion of adrenal medullary hormones is regulated by sympathetic stimuli. The biological actions of catecholamines are exerted on the heart, metabolism, muscles and the endocrine system. Aerobic/anaerobic physical exercise induces an increase of catecholamine secretion; the response is more marked for noradrenaline during anaerobic training. The alteration of the sympathetic nervous system, with the diminution of catecholamine response, inhibits alpha- and beta-adrenoreceptors in the adipose tissue, reduces lipolysis and favors fat storage and obesity. On the other hand, a low-calorie diet favors the positive effect of catecholamines on lipolysis in obese persons. Consequently, it is recommended to combine a hypocaloric diet with physical training to stimulate the mobilization and use of lipids and implicitly, weight loss (Zouhal et al., 2013).

Changes in the hormones of the endocrine pancreas during physical exercise

The main hormones of the endocrine pancreas are insulin, glucagon and somatostatin. Of these, only insulin undergoes obvious changes in relation to physical exercise. For the other hormones, no significant variations during exercise were found. The alteration of insulin levels during exercise is influenced by glycemia and catecholamines. During aerobic physical exercise, glucose levels are unchanged, and noradrenaline and adrenaline depress insulin secretion. During anaerobic exercise, hyperglycemia inhibits the suppressive effect of catecholamines on insulin (Staicu & Tache, 2011).

The response of the hypothalamic-pituitary-gonadal axis to physical exercise

The female gonad secretes estrogens, progesterones and androgens. Their secretion is regulated by the hypothalamic-pituitary system through the follicle-stimulating hormone (FSH) and the luteinizing hormone (LH). The biological effects of the follicle-stimulating hormone in women are follicular development and estrogen hormone secretion; the luteinizing hormone plays a role in the triggering of ovulation, the initiation and maintenance of corpus luteum activity and not least, in the stimulation of androgen hormone synthesis in thecal and luteal cells.

Estrogen hormones have many effects, the most important of which are the stimulating and proliferative effects on the female reproductive system (along with progesterone), and the metabolic, tonic and excitatory effects on the central nervous system.

The predominant hormone of the male is testosterone, its secretion being regulated by gonadotrophic hormones (FSH, LH). Among the significant biological effects of gonadotropic hormones, we mention the stimulation of spermatogenesis (through FSH) and the stimulation of testosterone secretion by the testicular Leydig cells (through LH). Testosterone has mainly a direct action on the male genital tract, a metabolic and growth-stimulating action on muscle and bone tissue. Estrogen and testosterone levels increase during both aerobic and anaerobic exercise, without a significant difference between the two types of training (Wojtys et al., 2015; Orvoll, 2016).

Regarding gonadotropic hormones in young female athletes subjected to physical exercise at an increased intensity, an alteration of luteinizing hormone (LH) pulsations, without an obvious change of the follicle-stimulating hormone (FSH), was demonstrated (Mathusmita, 2014).

The increase in the incidence of diseases, including endocrine disorders closely related to physical exercise or more precisely, to the absence of physical activity, is an area of wide interest and a public health problem.

Conclusions

1. Many fundamental studies currently detail the hormonal profile during physical exercise in relation to the degree, the duration of exercise and rest periods in healthy subjects of different age, sex or physiological status, as well as in patients with metabolic syndrome in particular (obesity, diabetes mellitus, dyslipidemia, arterial hypertension).

   2. Physical exercise induces common changes as well as individual differences conditioned by psycho-emotional and environmental factors in all endocrine axes – sympathetic-adrenal, HPA, HPG, HPT, STH, parathormone, pancreas, renin-angiotensin-aldosterone or various peptides with a neurotransmitter or neuromodulator role.

3. Clinical studies have identified pathological endocrine aspects induced by different types of physical exercise: amenorrhea and a predisposition to osteoporosis in female athletes under estrogen deficiency conditions, an alteration of the muscle mass through an excess of STH and anabolic steroids.
Conflicts of interest
Nothing to declare.

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