Effect of an individualized physical training program on resting cortisol and growth hormone levels and fat oxidation during exercise in obese children

Effet d’un programme individualisé d’entraînement physique sur les niveaux plasmatiques de repos du cortisol et d’hormone de croissance et d’oxydation des lipides pendant l’exercice chez des enfants obèses

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Résumé

Objectifs. – Le but de l’étude était de caractériser les niveaux plasmatiques de repos du cortisol et de l’hormone de croissance (GH), et l’utilisation des substrats pendant l’exercice des enfants obèses avant et après un programme d’entraînement individualisé. Patients et méthodes. – Vingt-deux enfants obèses (13,1 ± 0,8 années) ont été inclus dans l’étude. Douze individus (six garçons et six filles ; 31,1 ± 1,1 kg/m², VO2peak = 1,92 ± 0,16 litres par minutes) ont participé à un programme d’entraînement de deux mois et dix individus (cinq garçons et cinq filles ; 30,9 ± 1,7 kg/m², VO2peak = 1,98 ± 0,12 litres par minutes) ont servi de groupe témoin. L’entraînement était individualisé au niveau du point d’oxydation maximal des lipides (Lipoxmax). L’oxydation des substrats a été évaluée par la calorimétrie indirecte. Afin de déterminer les concentrations plasmatiques du cortisol et de la GH, le sang a été prélevé au repos avant et après la période de deux mois. Résultats. – Avant le programme, aucune différence significative n’a été observée entre le groupe d’entraînement et le groupe témoin pour aucune des variables anthropométriques, métaboliques et hormonales mesurées. À la fin du programme de deux mois, le groupe entraînement a montré une augmentation de VO2peak et de l’oxydation des lipides pendant l’exercice. Après le programme, le niveaux de repos de GH et du cortisol ont été sensiblement augmentés dans le groupe entraînement (+ 0,9 ± 0,3 ng/mL et + 55,4 ± 10,3 ng/mL respectivement, p < 0,01). Après la période de deux mois il n’y avait aucun changement d’aucune variable mesurée dans le groupe témoin. Conclusion. – Le programme d’entraînement individualisé au Lipoxmax améliore l’oxydation des lipides pendant l’exercice et augmente les niveaux plasmatiques des repos de GH et du cortisol.

Mots clés : Entraînement ; Enfants obèses ; Hormone de croissance ; Cortisol ; Calorimétrie indirecte

Abstract

Objectives. – The aim of this study was to characterize the resting levels of cortisol and growth hormone (GH), and the substrate profile during exercise of obese children before and after an individualized training program. Patients and methods. – Twenty-two obese children (13.1 ± 0.8 yrs) were included in the study. Twelve individuals (six boys and six girls; 31.1 ± 1.1 kg/m², VO2peak = 1.92 ± 0.16 l/min) participated in a two-month endurance training program and 10 individuals (five boys and five girls; 30.9 ± 1.7 kg/m², VO2peak = 1.98 ± 0.12 l/min) served as controls. Training was individualized and targeting at the point were fat oxidation was maximal (Lipoxmax). Substrate oxidation was evaluated by indirect calorimetry. To determine plasma cortisol and GH concentrations, blood was collected at rest before and after the two-month period. Results. – Before the program, no significant differences were detected between the training group and the control group for any of the measured anthropometric, metabolic or

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hormonal variables. At the end of the two-month program, training group showed an increase in VO$_{2}$peak and fat oxidation during exercise. After the program, resting levels of GH and cortisol were significantly increased in the training group (+0.9 ± 0.3 ng/mL and +55.4 ± 10.3 ng/mL respectively, p < 0.01). Following the two-month period, there was no change in any variables measured in control group. Conclusion. – The present data show that an individualized endurance training program targeting Lipox$_{\text{max}}$ improves fat oxidation during exercise and increases resting levels of GH and cortisol.

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Keywords: Training; Obese children; Growth hormone; Cortisol; Indirect calorimetry

1. Introduction

Obesity is an important public health issue in the world, and children and adolescents have not eluded this emerging epidemic. Recent evidence indicates that skeletal muscle is involved in the development of obesity. More precisely, muscular abnormalities [1] disturb substrate utilization, thus facilitating fat accumulation in adipose tissue, although some studies suggest that the obese rate is associated with reduced fat oxidation and increased glucose metabolism [2].

Regular moderate aerobic exercise is one of the main components of weight management programs because it promotes fat use by skeletal muscle and enhances muscle sensitivity to insulin [3,4]. The maximum rate of fat oxidation is called Lipox$_{\text{max}}$ and represents the exercise intensity at which fat oxidation reaches a maximum. Lipox$_{\text{max}}$ training is recommended in weight management programs for obese children [5].

Growth hormone (GH) and cortisol are key hormones involved in the pathogenesis of obesity. GH is secreted in a pulsatile manner; GH release is inhibited by somatostatin and stimulated by growth hormone releasing hormone (GHRH) (www.ihop-net.org/UniPub/iHOP/gs/88621.html). Compared to non-obese (NonOb) human, obese human have defects in pulsatile GH secretion resulting in hyposomatotropism [6,7]. Although lower 24-h integrated GH concentrations are reported in obese human, the circadian rhythmicity is still preserved. The lower concentrations are reportedly due to a marked decrease in GH secretory rates, and a somewhat shorter half-life of endogenous GH clearance [6]. In addition, the GH response to GHRH is decreased in obese human; weight loss tends to restore this response [8]. Acute aerobic exercise is a potent stimulus of GH release and several study have shown that GH secretion is related to exercise intensity in a graded fashion [9,10].

Exercise training increases spontaneous 24-h GH release in NonOb women [11], whereas short-term aerobic exercise training has no effect on exercise-stimulated GH release in obese women [12]. However, Irving et al. [13] showed that 16 weeks of supervised exercise training in adults with a metabolic syndrome increase spontaneous nocturnal GH secretion independent of exercise training intensity.

Eliaikim et al. [14] showed that in response to a metabolically matched exercise input, the GH response to exercise was reduced in obese children and adolescents. It is possible that the blunted GH and catecholamine response to exercise leads to reduced carbohydrate and fat utilization during exercise [15,16].

Although resting cortisol level in the obese may be higher compared to those in lean individuals [16], response to training is not well documented. High intensity, long-duration exercise increases cortisol concentrations; some have documented similar responses in normal and obese subjects [16,17], whereas others observed a significantly greater cortisol response in obese compared with lean subjects [18].

The aim of our study was to characterize the resting levels of GH and cortisol, and substrate utilization during exercise, before and after a two-month training program performed at Lipox$_{\text{max}}$ in obese children. To achieve this objective, we employed a submaximal cycle ergometer exercise test, with work-rates that were increased progressively (loadings corresponding to 20, 30, 40, 50 and 60% of W$_{\text{max}}$). Steady-state substrate oxidation was evaluated by indirect calorimetry [5].

Our working hypothesis was that individualized exercise training targeted at Lipox$_{\text{max}}$ would increase peak oxygen uptake and fat oxidation during exercise and resting levels of GH and cortisol in obese children.

2. Patients

Following project approval by the Research Ethics Committee at the University of Medicine of Sousse in Tunisia, 22 obese children (aged 13.1 ± 0.8 yr; body mass index [BMI] = 31.0 ± 1.4 kg/m$^2$, VO$_{2}$peak = 1.95 ± 0.14 l/min) were recruited to participate in this study. Obesity was defined as BMI > 97th percentile according to the French references [19]. All individuals were in good health as assessed by their medical history and physical examination.

The subjects did not spend more than 1 h per week in sports activities and did not take any medications known to influence the variables measured. Informed written consent was obtained from all participants and their parents. They were informed in detail of all experimental procedures and risks possibly associated with the experiments. Subjects were randomly assigned to a control group and training group targeted at the point where fat oxidation was maximal (Lipox$_{\text{max}}$) for two-month. Before the beginning of the intervention program and after two-month, body composition was measured along with aerobic capacity (VO$_{2}$peak), substrate oxidation (indirect calorimetry) and resting levels of GH and cortisol.

3. Methods

3.1. Anthropometric measures

Body mass was assessed to the nearest 0.1 kg with a digital scale (OHAUS, Florhman Park, NJ) and waist and hip circumferences to the nearest 0.2 cm with a soft tape. Height was measured
with a standing stadiometer and recorded with a precision of 0.1 cm. BMI (kg/m²) was calculated as body mass divided by height squared.

The Z-score for BMI was calculated according to Rolland-Cachera [20], using the following formula: \( Z = \frac{|(Q/M) - L|}{S} \).

With: \( Q = \text{BMI}, M = \text{median}, L = \text{power}, S = \text{coefficient of variation}. \)

Skinfold thicknesses were determined in triplicate at two sites (triceps and sub-scapular), using a standard, recently calibrated Harpenden calliper (Holtain, Cross-well, UK) by the same trained anthropometrist to the nearest 0.1 mm. Three measurements were taken at each site and the closest two measurements were averaged for use in the analysis.

The percentage of body fat (%BF) was calculated using the equation of Slaughter et al. [21] for children with triceps and subscapular skinfolds < 35 mm:

Boys : %BF = 1.21 (sum of 2 skinfolds) - 0.008 (sum of 2 skinfolds)² - 1.7

Girls : %BF = 1.33 (sum of 2 skinfolds) - 0.013 (sum of 2 skinfolds)² - 2.5

and for children with triceps and subscapular skinfolds greater than 35 mm:

Boys : %BF = 0.783 (sum of 2 skinfolds) - 1.7

Girls : %BF = 0.546 (sum of 2 skinfolds) + 9.7

The test-retest data were then used to calculate the accuracy of all body composition measurements. Each anthropometric measurement was performed by the same technician for all participants before and after the two-month intervention.

The pubertal stage was evaluated according to the Tanner classification [22] by a trained paediatrician, before and after the two-month intervention (Table 1). Prepubertal children included those subjects who were at Tanner stage I, pubertal children at Tanner stage II–III and postpubertal children at Tanner stage IV–V. Table 1 provides the subjects’ characteristics.

### 3.2. Dietary energy intake

To determine dietary energy intake and macronutrient content, subjects recorded meal times and the quantities of all food eaten for a week before and after the two-month program. Verbal and written instructions on accurate record keeping were provided. Total energy intake and percentages of energy intake derived from CHO, fat, and protein were analyzed using a Bilnut 4 software package (SCDA Nutrisoft, Cerelles, France), a computerized database that calculates the food intake and composition from the National Institute of Statistics in Tunis 1978.

### 3.3. Physical training program

All subjects completed a questionnaire on their physical activity habits. Before the program, all subjects practiced 1 h per week only of guided physical activity in their school. The control group was instructed to maintain current level of physical activity. Children in the training group received a two-page summary of information about exercises prepared by an exercise physiologist. It included a list of the general health benefits of regular exercise as well as various recommendations and precautions about exercise.

Exercise training program was supervised, occurred four times per week (90 min/day) for a two-month period, and consisted of warming-up, running, jumping and playing with a balloon. The exercise intensity was fixed at a participant’s heart rate (HR) corresponding to the Lipox max value assessed at the first visit. The intensity of the exercise was controlled by monitoring the HR with a Sport-tester device (Vantage NV; Polar Electro, Kempele, Finland). The training schedule was composed of 10-min warm up, 30-min training at Lipox max, 5-min...
active recovery, 30-min training fixed at Lipoxmax and 10-min of relaxation.

3.4. Exercise testing

Two progressive cycle-ergometer tests were carried out, before and after the two-month period. All tests were performed in the laboratory between 8:00 and 10:00 am after an ~12-h overnight fast. The laboratory temperature was held between 22–24 °C at a relative humidity of 76% during the test period. Subjects exercised on an electromagnetically-braked cycle-ergometer (Ergoline, Bitz, Germany) according to the protocol as previously described [5]. Peak oxygen uptake (VO2peak) testing and gas exchange (VO2 and VCO2) were determined via breath by breath analysis of expired gases during testing using a metabolic cart (ZAN 600; ZAN Meßgeräte, Oberthulba, Germany). HR was monitored continuously throughout the test (ZAN ECG 800; ZAN Meßgeräte).

Theoretical maximal oxygen intake (VO2maxth) and theoretical maximal aerobic workload (Wmaxth) were calculated for each subject before each exercise testing using the predictive equations of Wasserman et al. [23] for obese children. These equations take into account sex and anthropometric characteristics:

For girls: \[ \text{VO2maxth} = (52.8 \times \text{body mass (kg)}) - 303.4 \]

For boys: \[ \text{VO2maxth} = (28.5 \times \text{body mass (kg)}) + 288.1 \]

and the following equation was used to calculate Wmaxth [23]:

\[ \text{Wmaxth} = \left[ \text{VO2maxth} - 10 \times \text{body mass (kg)} \right] / 10.3. \]

One day before the exercise test all children were familiarized with the cycle ergometer. A 3-min rest period was followed by a five-stage progressive submaximal exercise test (20, 30, 40, 50 and 60% of Wmaxth), with 6-min of exercise at each work rate. The exercise test ended with a 4-min active recovery period at 20% of Wmaxth.

After the two-month program, the subjects underwent the same exercise test than before program at the same percentage of their Wmaxth. Individual incremental workload determined by Wmaxth was the same before and after the program. Ventilatory parameters (VO2 and VCO2) were recorded during the last 3-min of each workload, according to MacRae et al. [24], for calculations of the substrate oxidation flow rates. Whole body substrate oxidation was calculated from the measurement of the respiratory exchange ratio (RER = VCO2/VO2 in expired gases).

The percentage of CHO and fat oxidation were calculated using the following equations [25]:

\[ \% \text{CHO} = \left( \frac{\text{RER} - 0.71}{0.29} \right) \times 100 \]

\[ \% \text{Lipid} = \left( \frac{1 - \text{RER}}{0.29} \right) \times 100 \]

Fat and CHO oxidation rates were calculated from the gas exchange measurements according to the non-protein respiratory quotient technique [26], as protein breakdown contributes little to energy metabolism during exercise [27]:
GH and cortisol and peak oxygen uptake (liters per minute). There were no group differences in average daily energy intake. The training group consumed 3262 ± 257 kcal/day, and the control group consumed 3241 ± 227 kcal/day. The percentages of calories derived from protein, CHO, and fat were also similar. The mean W_{max} calculated before the intervention and used to set intensity of exercise testing before the program was 236.9 ± 59.6 watts. The HR corresponding to the Lipox_{max} point used to set the intensity of the training program was 133.2 ± 3.2 beats/min corresponding to 75.2 ± 4.7 Watts. On a 60-min training period targeted at Lipox_{max}, the children carried out 49 ± 4 min at the HR corresponding to Lipox_{max}.

Two-month of training program targeted at Lipox_{max} decreased body mass and BMI in the training group. There were no changes in anthropometric parameters in the control group after the two-month period (Table 1).

Fig. 2B displays the change in fat oxidation rates at each workload for the two groups. Before the program, fat oxidation at 0% and 50% of W_{max} was significantly higher in training group compared to control. After the program, fat oxidation at 0, 20, 30, 40, 50 and 60% of W_{max} increased significantly in the training group (Fig. 1A) and the Lipox_{max} point was increased by 90.1 ± 16.8 mg/min; p < 0.01. Any change was observed in control group for these parameters (Fig. 1B).

Table 1 shows that the training group had a lower RER_{peak} at the time of the second exercise test (better lipid use).

After the program, resting levels of GH and cortisol were significantly increased (Fig. 2A and B) in the training group (+0.9 ± 0.3 ng/mL and +55.4 ± 10.3 ng/mL, respectively). No change was observed in the control group for the resting levels of GH (Fig. 2A) and cortisol (Fig. 2B). At the end of the program, the VO_{2peak} was increased (1.92 ± 0.16 vs. 2.36 ± 0.18) in the training group (Table 1).

After the training program, the change in Lipox_{max} was significantly positively correlated with VO_{2peak} (r = 0.31; p < 0.05), GH (r = 0.42; p < 0.01) and cortisol (r = 0.48; p < 0.01) and negatively correlated with body mass (r = −0.21; p < 0.05), waist/hip ratio (r = −0.231; p < 0.05), RER_{peak} (r = −0.35; p < 0.01) and HR_{peak} (r = −0.27; p < 0.05) in obese children. No significant correlations between Lipox_{max} and other parameters were observed in the control group.

5. Discussion

The aim of the present study was to analyse the resting levels of GH and cortisol and substrate profile during exercise before and after a two-month individualized training program targeted at Lipox_{max} in comparably obese children consuming a diet providing adequate energy and a similar macronutrient composition. Our study shows a greater absolute increase in peak oxygen uptake, resting levels of GH and cortisol concentrations and fat oxidation, which was reflected by the shift in the power at which fat oxidation was maximal (Lipox_{max}) at the end of the two-month training program in obese children.
The intensities of effort were set using Wasserman’s equations [23]; these approximate values of VO2max and Wmax could be over- or under-estimated in some subjects, and this would modify the crossover points as reported in our survey. However, this methodological problem is minimized because values for the two observation periods are compared within a given subject.

A shift towards a higher ability to oxidize lipids during exercise was more pronounced in the training group who exercised for the two-month period than for the control group. This improvement in lipid oxidation was indicated by RER values and by an increase in the absolute fat oxidation rates at various intensities between 0 and 60% of Wmax in obese children who had performed an exercise training program.

Zachwieja et al. [28] showed that the dependence with respect to the lipids as a source of energy during submaximal exercise is higher after endurance training because lipids are the greatest energy reserve and lipid utilization spares glycogen stores. Training-induced increases in fat oxidation are due primarily to increased oxidation of non- plasma-derived fatty acids, perhaps from intramuscular triacylglycerol stores [29].

GH is an anabolic polypeptide secreted by the anterior pituitary gland in a pulsatile fashion [30]. Both aging and obesity are associated with a reduction in GH secretion [31,6]. GH secretion increases gradually during childhood, peaks during puberty, and then declines during adult life [31]. This progressive fall in GH secretion is associated with somatic changes that occur as part of the aging process [32]. These include a loss of lean body mass, decreased muscle strength, and increased fat mass. Apart from the aging process [32], these changes are associated with a reduction in GH secretion [31,6]. GH increases within a few minutes of onset of both aerobic and resistance exercise and remains elevated for up to 30 min during recovery [31,35].

A maximal GH response is achieved at 70% of the maximal oxygen uptake (VO2max) [36]. The magnitude of this rise is dependent on a number of variables, including hypoxia, change in body temperature, and availability of energy substrates [37,38]. Acute aerobic exercise is also a provocative stimulus of GH release in NonOb individuals. The magnitude of response is influenced by the mode of exercise, intensity, duration, aerobic vs. anaerobic exercise, and intense chronic training [39,40,9]. Few studies have investigated the effect of exercise on GH secretion in obese individuals, and these studies yielded variable results, probably due to insufficient exercise stimuli and insensitive GH assays [17,41]. Eliakim et al. [42] demonstrates that in healthy prepubertal girls, cardiorespiratory and anatomic indices of fitness are associated with an activated, more anabolic GH→IGF-I axis. In contrast, a brief endurance-type exercise training program seemed to have resulted in catabolic rather than anabolic responses of the GH→IGF-I system of mediators despite the fact that training led to increased muscle volume and improved cardiorespiratory responses to exercise (such as peakVO2).

Several studies have shown that higher levels of physical activity are associated with increased GH pulsatility, and, eventually, with increased circulating IGF-I in children [42,43]. Indeed, physical activity can influence growth and development through its influence on anabolic and catabolic mediators [44]. Relative adiposity and VO2 peak have been shown to have significant inverse relationships with 24-h integrated GH concentrations [40]. In the present study, aerobic fitness, defined as VO2peak (ml/min), was higher in the training group (+22.9%; p < 0.01) compared with the control group (+1.5%; p = 0.7) after the two-month period.

Our results show that the improvement of GH level was associated with the decrease in body mass (~3.5 kg) at the end of the training program. Abdominal obesity, specifically increased amounts of abdominal visceral fat, is associated with lower serum IGF-I concentrations, decline in GH production and 24-h GH release [40,45]. In contrast to these studies, Holt et al., [46] only found a relationship between biochemical and physical indicators of fat mass and GH secretion in the older age groups. There was no association between fat mass and GH secretion in the young groups in that study, implying that age is more important than fat mass in determining the exercise-induced generation of GH in young men. In our study, the amount of abdominal fat, estimated from the waist/hip ratio, was significantly lower in obese children after the training program targeted at Lipoxmax. There was a relationship between the abdominal fat and the training-induced GH response in our study.

GH exerts a lipolytic effect predominantly in the visceral adipose tissue, and to a lesser extent in the sub-cutaneous adipose tissue, resulting in increased free fatty acid (FFA) flux from the adipose tissue. The specific effect of GH in adipose tissue could be explained by the fact that GH increases lipolysis by increasing adipose tissue hormone-sensitive lipase (HSL) activity [47]. GH stimulates triglycerides (TG) uptake in the skeletal muscle primarily by increasing lipoprotein lipase expression; thereby promoting lipid utilization [48]. The lipids taken up by the skeletal muscle can be either stored as intramyocellular TG (IMTG) or broken down to release energy via either lipolysis or lipid oxidation [48]. A favourable effect on adipocytokines could also be involved [49]. After exercise of sufficient intensity, FFA utilization increases, perhaps due to the dominant lipolytic effects of GH. Pritzlaff et al. [50] reported that the positive relationship between exercise intensity and energy expenditure from fat during the recovery period is due to GH release. In our study, two-month of training targeted at Lipoxmax increased the ability to oxidize lipids during exercise. Hence, this increase was positively correlated (p < 0.01) with the improvement of resting level of GH.

Cortisol is the main glucocorticoid in humans; it is secreted by the zona fasciculata of the adrenal gland. Cortisol secretion is controlled by the hypophysial adrenocorticotropic hormone (ACTH), which is released in response to the hypothalamic corticotrophin releasing hormone (CRH); this cascade is known as the hypothalamic-pituitary-adrenal axis (HPA axis). In response to physical exercise, cortisol changes is related to the intensity and duration of the exercise; cortisol level increase in relation to the percentage of VO2max [51]. However, it is admitted that the increase of cortisol level occurs when VO2max reaches 60% of VO2max [52]. Cortisol level may also change with physical training; in individuals following an intensive training, cortisol level are generally increased [52]. It has been traditionally thought that cortisol aids in the release and mobilization of fatty acids
from muscle and adipose tissue, indicating that this hormone may increase lipolysis. Samra et al., [53] demonstrated that cortisol may actually suppress, rather than stimulate, lipolysis in fat cells. Our study shows that training of sufficient intensity and duration (targeted at Lipomax) leads to a marked shift toward fat oxidation and increases the post-training resting level of cortisol in obese children.

Clearly, adipose tissue is actively involved in energy production during exercise, providing both FFA and glycerol for energy production. The sympathetic nervous system (SNS) and the catecholamines appear to provide the underlying stimulus for lipid metabolism. The SNS and the catecholamines also act on insulin to lower its anti-lipidaemic effect and act to increase hypothalamic CRH and GHRH, resulting in increases in cortisol and GH.

These latter two hormones work synergistically to enhance lipolysis to a greater extent than either one would independently [54]. Any feedback between cortisol and inhibition of GH appears to be suppressed [55], potentially by the catecholamines [56]; thus GH increases. Also, cortisol appears to have only a small influence on lipid metabolism, but a major effect on gluconeogenesis [57]. The acute neuroendocrine responses to exercise regulating lipolysis appear to be related to catecholamines, insulin, GH and cortisol.

6. Conclusion

Our results demonstrated that a two-month individualized exercise training program increases lipid utilisation during exercise and resting levels of GH and cortisol in obese children while controlling for variables known to confound these responses (i.e. diet prior to measurements, training volume/history, and pubertal stage).

Conflict of interest

No such conflict exists.

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