

Effects of a two-month rehabilitation program on substrate utilization during exercise in obese adolescents

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SUMMARY

Background: We assessed the impact of an exercise and diet program for two weeks in a specialized institute and six weeks at home on body composition and exercise metabolism in obese adolescents.

Methods: Fourteen obese adolescents took part in the two-week training course and seven continued exercise and diet at home. The substrate crossover point and the maximal fat oxidation point (Lipox max) were determined before and after the program, using indirect calorimetry. Individualized exercise training at Lipox max was programmed over the two months.

Results: At the end of the two-week program, all adolescents showed a decrease in weight ($p < 0.001$). Only the seven subjects who continued exercise training at home showed improved exercise fat use (increased crossover point of $17\% \pm 3$ ($p < 0.005$) and Lipox max of $12.5\% \pm 1.5$ ($p < 0.005$)).

Conclusion: The teenagers who had performed this targeted regular training for two months exhibit an increase in their ability to oxidize lipids at exercise. This increase is no longer found in those treated by diet alone. The efficiency of this targeted training protocol based on calorimetry for the treatment of teenager obesity will require longer studies on greater samples of subjects.

Key-words: Obesity · Adolescent · Fat Oxidation · Training · Indirect Calorimetry.

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RÉSUMÉ

Effet d'un programme de réhabilitation de deux mois sur l'utilisation des substrats énergétiques à l'exercice chez des adolescents obèses

Contexte : Le but de notre travail était de vérifier l'impact d'un programme de réhabilitation (exercice et diététique) de deux semaines dans un centre spécialisé et 6 semaines de suivi à l'extérieur, sur la composition corporelle et l'utilisation des substrats énergétiques à l'effort.

Méthodes : Sur quatorze adolescents obèses participant au stage de deux semaines, sept adolescents ont poursuivi le réentraînement à l'extérieur. Le point de croisement de l'utilisation des substrats, ainsi que le point d'utilisation maximal des lipides (Lipox max), ont été déterminés avant et après le programme, à l'aide d'une calorimétrie indirecte d'effort. Un réentraînement individualisé au Lipox max a été programmé sur deux mois.

Résultats : A l'issue de ce programme de réhabilitation, les quatorze adolescents présentaient une diminution de poids ($p < 0,001$). Seuls les sept sujets ayant poursuivi le réentraînement à l'extérieur, montraient une augmentation de l'utilisation des lipides à l'effort (augmentation du point de croisement de $17\% \pm 3$ ($p < 0,005$) et du Lipox max de $12,5\% \pm 1,5$ ($p < 0,005$)).

Conclusion : Les adolescents qui ont poursuivi pendant deux mois cet entraînement régulier ciblé présentent une augmentation de la capacité à oxyder les lipides à l'effort qui ne s'observe pas chez ceux qui ont seulement suivi un régime après leur sortie du centre. L'efficacité, dans le traitement de l'obésité de l'enfant, de ce réentraînement ciblé à partir de la calorimétrie reste à étudier à plus long terme et à plus vaste échelle.

Mots-clés : Obésité · Adolescent · Oxydation lipidique · Réentraînement · Calorimétrie indirecte.

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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. Some degree of hyperinsulinism, which is frequently found in these patients, may further contribute to this adiposity. In addition, the insulin resistance syndrome appears to be associated in muscle with not only a decrease in glucose utilization but also a defect in lipid oxidation which is strongly associated with the development of visceral obesity [2]. Presumably, this defect in lipid utilization plays a role in the worsening of insulin resistance via the so-called Randle's free fatty acid cycle [3] which appears to be largely explained by an inhibitory effect of lipids on insulin action [4]. These mechanisms have been extensively studied in adults but remain rather poorly understood in children. Childhood obesity is often accompanied by a lower ability to oxidize lipids during exercise [5]. Interestingly, it has been well demonstrated in adults that regular training improves the potential of muscle to oxidize lipids and thus compensate to some extent for the above-mentioned abnormalities [6].

Whether these concepts are relevant to childhood obesity remains speculative. Children today are far more sedentary than ever before [7], as sedentary activities such as watching television and playing video games – both risk factors for obesity [8] – have greatly supplanted the active physical games of the past. In fact, although it has become increasingly urgent to increase physical activity and reduce sedentary habits [7], exercise prescription for obese children has not always shown the expected results for two reasons: feasibility problems and imprecision in exercise codification. Regarding the first, certain programs simply are not compatible with the heavy academic schedules of many adolescents. Regarding the second, exercise coding in terms of intensity and duration is often imprecise [9] and not based on solid pathophysiological principles. One key point to be kept in mind, however, is that the balance of carbohydrate (CHO) and lipid use during physical activity depends on the relative intensity of exercise [10, 11].

When exercise intensity increases, CHO oxidation increases while lipid oxidation decreases. Studies in adults demonstrate that CHO becomes predominant at a lower intensity in obese patients, reflecting a decreased ability of muscle to oxidize lipids [9].

In individualized exercise programs for both children and adults, it would be useful to determine the exercise level at which lipid oxidation is maximal [12]. While it has been shown that exercise training at low intensity increases the ability to oxidize lipids [13], training at higher intensities increases the ability to oxidize CHO [14]. Individual assessment of the exact intensity at which lipid oxidation is optimal would therefore provide the best exercise prescription for training in obese children [12, 15].

This study investigated the impact of a diet and exercise program on body composition and exercise metabolism in obese adolescents. The program included a two-week period in a specialized institute with a six-week continuation at home, with exercise intensity individually prescribed from optimal lipid oxidation as defined by exercise calorimetry. We had two working hypotheses: this program would (a) positively modify anthropometric parameters (weight, body mass index (BMI)) and (b) shift the substrate balance at exercise towards a higher use of lipids.

Materials and methods

Patients

We selected 14 obese subjects (8 males, 6 females, aged 11-17 years (13.75 ± 0.7), weight = 83.6 ± 5.5), whose BMI was > 97th percentile defined by the French curves [16]. None of the adolescents had chronic disease, endocrine disorders or diabetes mellitus. None had attempted to reduce their caloric intake before the study.

Protocol

The protocol was a comparative study of anthropometric and metabolic parameters before and after a period averaging two months. More precisely, the study included a two-week training course in a rehabilitation institute and a six-week follow-up at home. All patients underwent both diet and exercise training. Parents provided informed consent for the study procedures.

Before and after the program

Initial Instructions

All subjects were asked to fast for 12 hours before the exercise testing. The conditions and requirements of the exercise testing were explained to each subject.

Information sheets filled out at the beginning of the study provided the history of each patient's obesity.

Anthropometry

Height, weight, waist and hip measurements were taken with a variability of 0.1 kg (weight) and 0.2 cm (height, waist and hip measurements).

The Z-score for BMI was calculated according to Cole [17] and Rolland-Cachera [16], with the following formula:

$$Z = [(Q/M)^L - 1]/LS$$

With: Q = BMI, M = median, L = power, S = coefficient of variation. Individual values of M, L and S were found in the tables of paper of Rolland-Cachera [16].

Exercise testing

The subjects performed an exercise testing on an electromagnetically braked cycle ergometer (800S DATALINK) connected to a MEDICAL analyzer CPX GRAPHIC CARDIO2 for cycle-by-cycle gas exchange measurement (VO_2

and VCO_2). We calculated the following theoretical values before exercise: Maximum oxygen consumption (VO_{2max} th) was calculated for each subject using the predictive equations of Wasserman [18] for obese children. These equations take into account gender and anthropometric characteristics:

Girl: $(52.8 \times \text{weight}) - 303.4$

Boy: $(28.5 \times \text{weight}) + 288.1$

The theoretical maximum power (W_{max} th) was defined using the Tanner equations:

Girl: 3 watt/fat-free mass

Boy: 3,5 watt/fat-free mass

Heart rate was monitored continuously throughout the test, which was standardized in terms of duration and step incrementation. Each test comprised a 3-min rest period during which ventilatory parameters (VO_2 , VCO_2) were recorded and then submaximal exercise that consisted of a progressive increase in workload every 6 min with 5 steady-state steps corresponding to 20, 30, 40, 50, 60% of W_{max} th. The first stage was regarded as a warm-up. The subjects were compared at similar intensities before and after the program.

CHO and lipid oxidation rates were calculated from the gas exchange measurements according to the non-protein respiratory quotient technique [19]:

CHO (mg/mm) = $4.585 VCO_2 - 3.2255 VO_2$

Lipids (mg/mm) = $-1.7012 VCO_2 + 1.6946 VO_2$

VO_2 and VCO_2 were determined as the means of measurements during the fourth and sixth minutes of each step, according to Mac Rae [20].

We were thus able to determine the proportion of CHO and lipid used from the respiratory exchange ratio (RER: CO_2/O_2 in expired gases), which is a function of the balance of substrates oxidized by the body. Grossly, the RER is 1 when CHO represents 100% of the oxidized fuels, whereas it is 0.7 when 100% of energy comes from lipids.

After smoothing the curves, we calculated two parameters representative of the balance between fat and CHO utilization induced by increasing exercise intensity: the crossover point of substrate utilization and the maximal fat oxidation point [9, 10].

The "crossover concept" [10] provides a clear explanation of substrate use during exercise because it analyzes the factors responsible for the preferential use of lipids or CHO and takes into account the combined effects of training status and exercise intensity. The crossover point of substrate use is defined as the power at which energy derived from CHO becomes predominant over energy from lipids, ie, when approximately 70% of energy derives from CHO and 30% from lipids.

Maximal fat oxidation (Lipox max) is the point where the increase in lipid oxidation induced by the increasing workload reaches a maximum, which will then be followed by a decrease as CHO becomes the predominant fuel. It is calculated from the above equations, using the formula:

Lipid oxidation rate (mg/min) = $1.695 VO_2 - 1.701 VCO_2$, which can be simplified as:

Lipid oxidation rate (mg/min) = $1.7 VO_2 (1 - RER)$.

The fat oxidation rate thus appears to be the product of two different linear relationships: the decrease in $(1 - RER)$ and the linear rise in VO_2 to proportional power. Derivation of the equation gives the maximal fat oxidation rate, which is the point where the value of the derived equation is equal to zero.

Evaluation of pubertal stage (according to Tanner)

Pubertal stage was evaluated according to the Tanner classification [21] by a trained paediatrician.

The 2-month program

The 2-week institute stage included a balanced and personalized hypocaloric diet established by a dietician after an initial dietary assessment to define the total amount of calories consumed per day. The diet was set at -300 kcal/day below the actual energy requirement. It was composed of 17% proteins, 30% lipids and 53% CHO. An initial psychological assessment was made by a trained psychologist, who then followed the adolescents. Nutrition classes were held to provide theoretical and practical education and individual exercise programs were assigned, which included walking, running, water gymnastics, and collective sports (4 hours/day). Each patient worked at the heart rate corresponding to Lipox max for the endurance training and on cycloergometer for 45 minutes every day.

During the 6-week follow-up, the subjects continued an individualized exercise program (cycling 45 minutes once a week) at the heart rate corresponding to Lipox max. They also received a phone call every week to encourage them to participate in additional endurance exercise (walking or running) over the weekend.

At the beginning of the protocol, all the fourteen subjects were taken together and were submitted to the same diet and exercise combination. After the two initial weeks, they were seven children who did no longer attend the training sessions, although they still followed the diet. These subjects were considered as a "non-trained group", while the others were the "trained group". All were regularly followed by telephone calls.

Data analysis

The population has a normal distribution as assessed by the Kolmogorov-Smirnov test. All the values were expressed as mean (\pm SEM). Paired Student's *t*-test was used for comparison within the same group and unpaired Student's *t*-test was used for group comparisons. Repeated-measure ANOVAs were used to compare the responses of different groups, at different times of the test, before and after the program. The Tukey post-hoc test was used to compare means. For all statistical analyses, significance was accepted at $p < 0.05$.

Table I

Anthropometric characteristics in the 14 subjects.

	Before the program	After the program	Delta	p
Weight (kg)	83.6	79.88	-3.72	0.0001
±	5.52	5.66	0.14	
BMI	31.77	30.15	-1.62	0.0001
±	1.45	1.58	0.13	
Z-scores	3.91	3.57	-0.34	0.002
±	0.19	0.03	0.16	
Height (cm)	161.2	161.85	0.65	0.0009
±	3.07	3	-0.07	
Waist (cm)	91.32	87.59	-3.73	0.0004
±	2.82	3.05	0.23	
Hips (cm)	108.71	103.57	-5.14	0.0001
±	3.49	3.74	0.25	

FM: fat mass. FFM: fat-free mass. Delta: difference between after and before program.

Results

General results

Pubertal stages were as follows: two pre-pubertal, four at the beginning of puberty, three peri-pubertal and five at the end of the puberty. *Table I* summarizes the anthropometric characteristics of the group at the beginning and end of the program. The anthropometric parameters that measure adiposity all showed significant reduction, with a satisfactory loss of weight over two months (-4.5%).

Regarding the exercise metabolic parameters, the crossover point, Lipox max and RER during exercise did not significantly change after 2 months, when the whole group was considered.

Comparison of the two groups before and after the program

Comparisons of the two groups showed that they were matched for anthropometric parameters, age (*Tab II*), and pubertal stage. In the trained group (3 girls and 4 boys), one was pre-pubertal (stage I), two were at the beginning of puberty (stage II), two were peri-pubertal (stage III) and two at the end of the puberty (stage IV). In the non-trained group (3 girls and 4 boys), one was in stage I, two in stage II, one in stage III, three in stage IV.

There is no significant difference between the two groups before and after the program for anthropometric parameters. There was a non significant tendency towards a reduction in weight of -4.2 kg in the trained, and -3.2 kg in the non-trained group ($p = 0.06$).

With regard to exercise metabolic parameters, the ANOVA of RER showed a time effect in both groups ($F =$

Table II

Anthropometric characteristics: G1: trained group, G2: untrained group, in pre-program.

	G1 Trained group	G2 Non-trained group	p
Age	13.7	13.8	NS
±	0.7	0.7	
Sex (Girls/Boys)	3/4	3/4	NS
Weight (kg)	82.57	84.62	NS
±	6.47	9.48	
Height (cm)	162.68	159.72	NS
±	3.91	4.99	
BMI (kg/m ²)	30.9	32.6	NS
±	1.43	2.62	
Z-score	3.77	4.04	NS
±	0.15	0.35	
Waist (cm)	92.14	90.5	NS
±	3.06	4.99	
Hips (cm)	107.42	110	NS
±	3.98	6.03	

83.28, $p < 0.00001$). An interaction effect was also found between the two groups (trained or untrained) and the program (before and after): $F = 9.06$, $p < 0.01$, only in the trained group. The Tukey post-hoc test locates a time effect (evolution of stage during the exercise test) and an effect of interaction before and after the program in the trained group. In the untrained group we locate an effect of time.

The curves below (*Fig 1*) show that the trained group had a lower RER at the time of the second exercise test (better lipid use). The comparison of metabolic parameters between the two groups is presented in *figures 2a* and *2b*.

The trained group followed the program correctly (45 minutes of bicycling + an endurance activity on the week-end) and shift their crossover point (+ 17% (± 3.03) of W_{max} th), and their Lipox max (+ 12.5% (± 1.2) of W_{max} th). The untrained group, who did not continue with the exercise program beyond the two weeks, had a crossover point decrease of -1.7% (± 1). However, they shifted their Lipox max towards a lower absolute power by 1.7% (± 0.2).

The trained group improved the crossover (from 35.1% to 52.14%) and Lipox max (from 32.1% to 44.5%) after the two month program. There was no significant change for the untrained group.

Figure 3 shows the lipid oxidation rates at different exercise intensity levels before and after the two months protocol. In the non-trained group (*Fig 3b*) there is no significant change in this metabolic process, while there is a significant increase in the trained group (*Fig 3a*). Thus, when training is added to the diet, there is both a right-shift of lipid oxidation and an increase in its flow rate values.

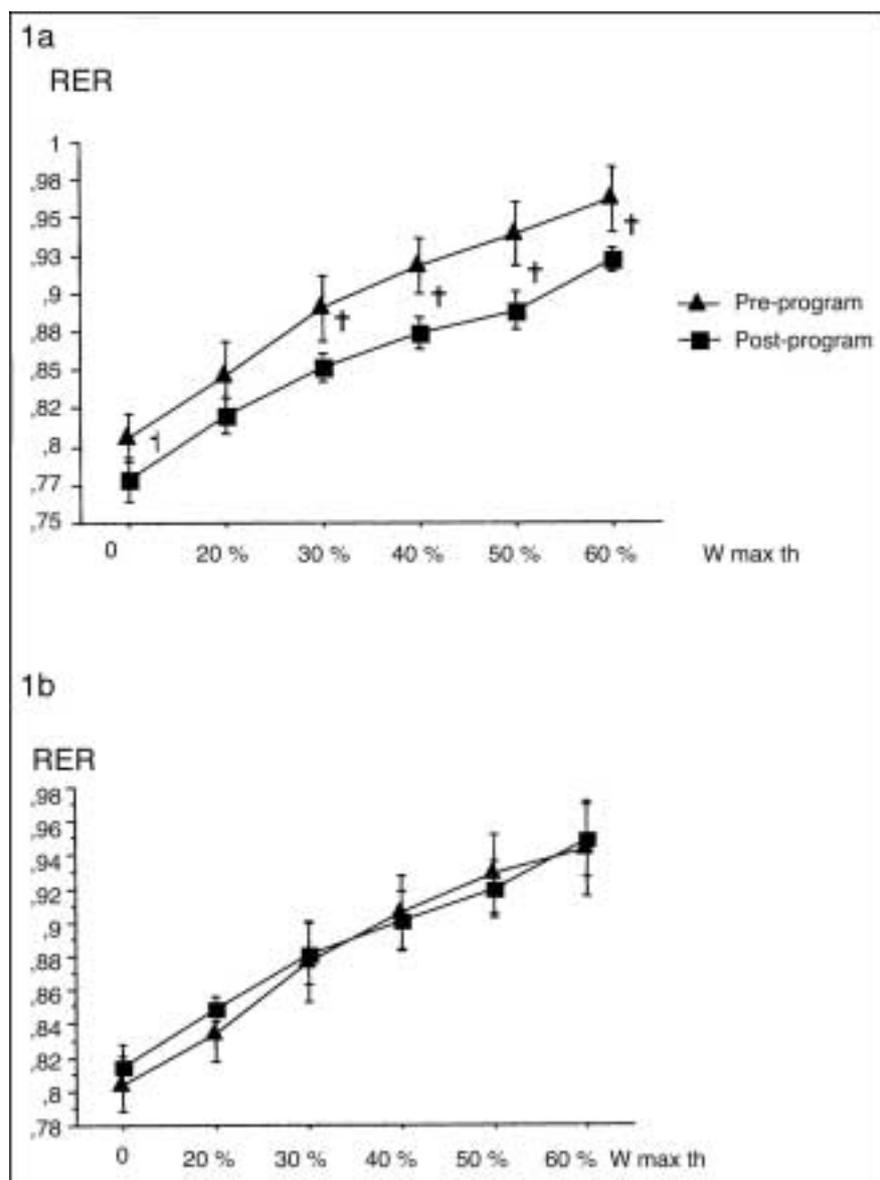


Figure 1
RER (respiratory exchange ratio) evolution in the trained group (a) and in the non-trained group (b) before and after the program. * $p < 0.05$, significantly different between after and before the program.

Discussion

This study is the first to our knowledge that investigates the combined effects of diet and exercise in adolescents by monitoring exercise intensity with exercise calorimetry. Our results show that the program resulted in a mean reduction of 3.7 kg in weight and increased the ability to oxidize fat during exercise, which was reflected by the shift in the cross-over point and the power at which fat oxidation was maximal (Lipox max).

Some methodological aspects of the study should be mentioned: the age of patients (between 11 and 17 years) may imply some degree of heterogeneity with regard to puberty, a point that is not without importance since Bar-Or [22] reported modified substrate utilization at exercise with advancing age (children burn relatively more fat and less CHO

than adults). The increased function of the growth hormone-IGF axis over the course of puberty is one of the physiologic changes likely to increase both lipolysis and fat oxidation [23]. In fact, because of the study design, this pubertal heterogeneity was not likely to introduce a strong bias in our results, since the subjects served as their own controls. Statistical analysis was performed with tests for comparison of paired values and these tests evidenced highly significant differences. In addition, as shown on Table II, the two subgroups were well matched so that they could be expected to behave similarly if submitted to the same treatment.

The validity of indirect calorimetry for intensities higher than the lactate threshold should also be discussed. Metabolic acidosis involves an increase in the mobilization of bicarbonate ions (HCO_3^-) in order to plug the H^+ ions. This

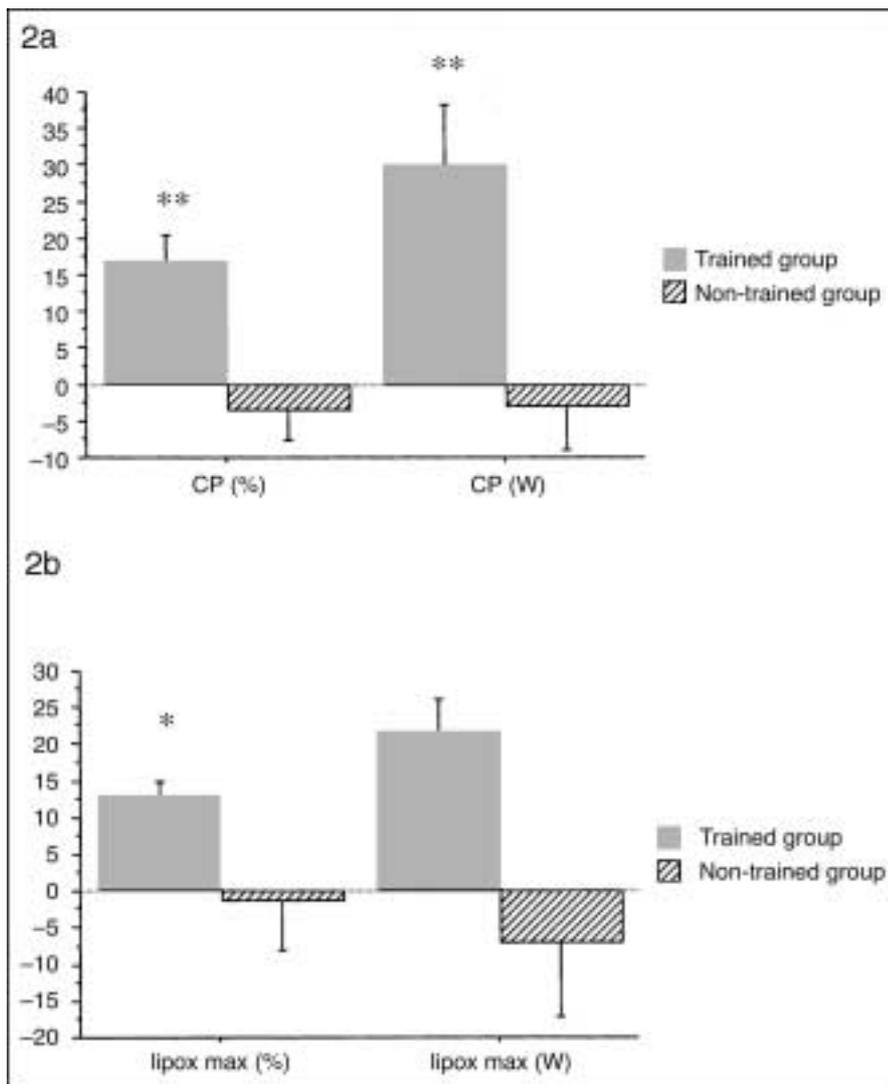


Figure 2

Delta comparison (difference before and after the program), for (a) the crossover point (CP) (percentage (%), absolute power output (Watt), heart rate(HR)) and for (b) the Lipox max (percentage (%), absolute power output (Watt), heart rate (HR)). ** $p < 0.005$. * $p < 0.05$.

mechanism increases CO_2 production, which might have raised the RER (VCO_2/VO_2), thereby distorting the results. However, the share of CO_2 coming from HCO_3^- ions is negligible (increases ~ 1%) compared with the total CO_2 production explained by the balance of substrates itself [24]. Therefore, exercise calorimetry appears to be valid for measurement of substrate oxidation during submaximal steady-state exercise bouts.

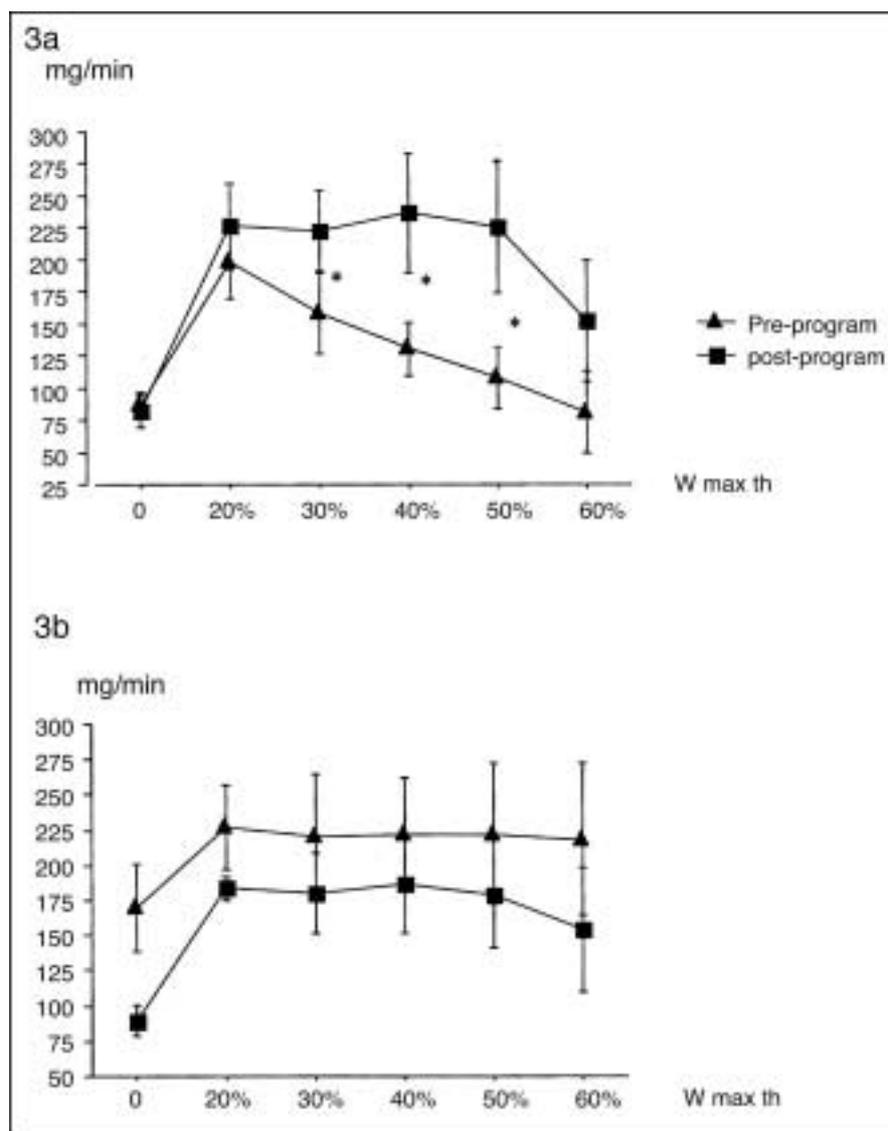
The sub maximal exercise test was carried out on the basis of theoretical values of VO_2max and Wmax . Determinations by graded maximal exercise were not made because we could include only two exercise tests (before and after the program) in the program for ethical reasons. Moreover, to avoid overestimating Wmax in obese adolescents in connection with an excess of fat mass, we used the Tanner formulas, taking into account the fat-free mass percentage.

Our results confirm our initial hypothesis, since the program reduces weight and fat mass, and improves the use of

the lipids during exercise. These findings should probably not be interpreted as the sole effect of training. Diet, psychological management, and other factors were important in the weight loss and metabolic improvements. Indeed, it is clear that obesity management requires a combination of all these approaches to achieve good results [25] and thus is likely to be seen more important in the case of children. Therefore, a holistic approach to obesity management that includes exercise training was investigated here, rather than the effects of training alone.

In the study, the fact that a closer follow-up after the initial two weeks stage, resulted in an improvement of fuel metabolism at exercise which was not observed after the stage alone, demonstrates that the combination for a longer time of exercise and diet has a stronger effect on fuel metabolism.

In the whole sample of subjects, significant weight loss was achieved. There was only a non significant tendency

**Figure 3**

Lipid oxidation rate during exercise in the trained group (a) and in the non-trained group (b) before and after the program. * $p < 0.05$, significantly different between after and before the program.

towards a reduction in weight in the trained and non-trained group. By contrast, a clear difference appeared between the two groups for the balance of substrate oxidation at exercise. While this balance was unchanged in the subgroup of children who stopped exercise after the initial two-week period, a shift towards a higher ability to oxidize lipids at exercise was clearly evidenced in the subjects who exercised for the full eight weeks. Saltin and Astrand [27] and Zachwieja [26] 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. Our RER results indicate that the adolescents became able to oxidize more lipids after training.

This improvement in lipid oxidation was indicated by two changes: the first was a shift of the transitional zone between lipids and CHO towards higher power intensities;

the second was an increase in the absolute lipid oxidation rates at various intensities between 30 and 60% of $W_{max\ th}$.

Although in this study, we cannot demonstrate that the amount of fat loss is significantly higher in the trained group, it seems logic to assume that this increase in the ability to oxidize lipids at exercise may be beneficial for the management of obesity, as already postulated by several authors [11].

By contrast, we observe that this improvement in fat oxidation is no longer found in the group of children that have stopped training after the initial two weeks session. These findings indicate that the metabolic benefits of training are quite rapidly lost when the subjects stop exercising, as already shown by others [28]. Therefore, a short duration training has probably a very limited interest if it is not followed by a regular physical exercise program.

Conclusion

This study shows that two months training at an exercise level targeted after exercise calorimetry is able to increase the ability to oxidize lipids at exercise in teenagers submitted to a moderately hypocaloric diet. However, this effect appears to be of short duration, so that prolonged training protocols are required. Whether such a targeted approach of training improves the efficiency of the treatment of obesity will require further studies.

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