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Effects of exercise-training and detraining on fat cell lipolysis in men and women

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Summary. The effects of training and detraining on adipose tissue lipolysis were studied in 19 healthy subjects (7 women and 12 men) who were submitted to a 20-week aerobic training program. Thereafter, subjects refrained from exercise for a period of 50 days. Suprailiac fat biopsies were performed before training, after training, and at the end of the detraining period. Mean fat cell diameter and epinephrine stimulated lipolysis (ESL) were assessed on collagenase isolated fat cells. Body density through underwater weighing and skinfolds at seven different sites were also obtained. Training significantly increased ESL ($P < 0.05$) in men but not in women. However, ESL values in men returned to pretraining values after the exercise restriction period. No significant changes in women lipolysis were observed under any conditions. Changes in lipolysis were not correlated with changes in body fatness. However, a significant correlation was observed between the increase in ESL produced by training and the subsequent decrease caused by detraining ($r = -0.53$; $P < 0.05$). The present results suggest that lipolysis in fat cells from the female subjects seems to be insensitive to changes in energy expenditure. Moreover, the present study demonstrates that there are high and low responders in adipocytes ESL to variations in habitual energy expenditure.

Key words: adipocytes – Lipolysis – Body fatness – Training – Detraining – Sex difference

Introduction

Alteration in the lipid metabolisms is an important component of the physiological adaptation to exercise-training. Studies have shown that adipocyte lipolysis of exercise-trained rats was more sensitive to the stimulating effect of catecholamines than non-trained animals (Askew et al. 1975; Bukowiecki et al. 1980; Owens et al. 1977; Wardzala et al. 1982; Williams and Bishop 1982), with some exceptions (McGarr et al. 1976; Oscai et al. 1981). In humans, we have recently reported that the high adipocyte lipolysis of well trained marathon runners was associated with their small adipocytes size (Després et al. 1983b). However, it is not clearly established whether the alterations induced in fat metabolism by training are permanent. Parizkova and Poledne (1974) have noted a decreased adipose tissue fatty acid release in rats submitted to a program of restricted motor activity. In humans, no such information is available. Fat cell metabolism of obeses has been well documented (Gries et al. 1972; Knittle and Ginsberg-Fellner 1972), but must not be considered as reflecting only hypokinesia.

In order to investigate the effects of physical inactivity on fat cell metabolism, 19 healthy subjects were submitted to a 20-week aerobic training program followed by a period of 50 days in which they refrained from exercise. The purpose of the study was to assess the effects of endurance training and inactivity per se on the metabolism of human fat cells and to consider sex differences.

Methods

Nineteen healthy subjects (7 women and 12 men), aged 23.4 ± 3.7 (mean ± SD) years, gave their written consent to participate in this study, which was approved by the Laval University Medical Ethics Committee. Subjects were submitted to a 20-week bicycle (Monark ergometer) endurance training program which consisted of continuous cycling session, 4 times and increasing to 5 times a week, 40–45 min per session, starting at 60 and increasing to 85% of their heart rate reserve. During the 5th, 11th, 16th, and 18th weeks, two continuous sessions were replaced by intermittent cycling training, consisting of three series of 10 min

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at 80%, separated by 5 min of active recuperation. During each session, heart rate was recorded every 2 min to adjust work intensity in order to ensure that subjects were all training at the same relative intensity. Thereafter, subjects refrained from exercise for a period of 50 days. Otherwise, they were living a normal sedentary life.

All measurements performed in this experiment were done before training, after the training program and after the 50-day period of physical inactivity. Maximal aerobic power ($\dot{V}_{O_2\,max}$) was assessed using a progressive bicycle ergometer test to exhaustion, using an open circuit gas analysis system (MMC, Beckman). Percent body fat was estimated from body density measured by underwater weighing, using the Siri (1956) equation. Residual lung volume was assessed by the method of Wilmore et al. (1980). The sum of seven skinfolds (biceps, triceps, subscapular, calf, thigh, abdominal, and suprailiac) was used as an indicator of subcutaneous fat.

Tissue biopsy and fat cell isolation

Biopsies were performed, in the fasting state, before training, 60 h after the completion of the last exercise session of the training program and at the end of the 50-day detraining period. After local skin anesthesia with xylocain 1%, 100 mg of adipose tissue were removed from the suprailiac depot using a modification of the Ritthaler et al. (1980) method. Adipocytes were collagenase isolated as previously described (Després et al. 1983a). Cell concentration and mean adipocyte diameter were measured using a Leitz microscope equipped with a graduated ocular and a hemacytometer. Five hundred isolated cells were measured per subject.

Measurement of fat cell lipolysis

Extracellular glycerol release was chosen as the indicator of fat cell lipolysis as reported previously (Després et al. 1983a). After a 15 min preincubation of the cell suspension, adipocytes were washed with fresh Krebs Ringer bicarbonate buffer and a 350 µl aliquot was incubated for 30 min in polythylene vials containing a final volume of 1.5 ml Krebs Ringer bicarbonate buffer (glucose 50 mg · 100 ml^{-1}, albumin 4%) kept at 37° C in a 95% O_2/5% CO_2 atmosphere. Maximal epinephrine stimulated lipolysis (ESL) was also assessed using an epinephrine concentration of 10^{-4} M. Incubation was stopped by transferring the vial content in polyethylene tubes maintained on ice. Floating adipocytes were aspirated and the glycerol content of the medium was assessed using a fluorometric technique (Lowry and Passonneau 1972). Determinations were made in triplicate. Fatty acid free albumin, enzymes (glycerokinase, glycerophosphate dehydrogenase) and epinephrine bitartrate were purchased from Sigma. Collagenase was obtained from Worthington Laboratories).

Statistical analysis

Differences between the three different experimental conditions were tested using the Duncan Multiple Range test (Duncan 1955). Correlation analyses were performed using the Pearson coeficient. Sex differences were evaluated using the Student's *t*-test.

Results

In the whole sample, training significantly reduced % body fat, subcutaneous fat and fat cell diameter ($P < 0.05$) and increased $\dot{V}_{O_2\,max}$ ($P < 0.01$). However, after 50 days without exercise, subjects regained their initial fatness level even though $\dot{V}_{O_2\,max}$ remained elevated. Thus no permanent training effect on body fatness was obtained. Table 1 presents changes in the characteristics of female subjects throughout the experiment. While body weight remained stable, a significant increase in $\dot{V}_{O_2\,max}$ was observed while percent body fat decreased with training. However, no significant changes in fat cell diameter and in the sum of skinfolds were noted following the training program. After detraining, all fatness indicators were comparable to pre-training levels. However, no significant decrease in $\dot{V}_{O_2\,max}$ was obtained following the 50-day detraining period.

Male subjects increased their $\dot{V}_{O_2\,max}$ following training and, as in women, no significant decrease was noted after the detraining period (Table 2). However, the body fat changes following training

Table 1. Effects of endurance training and detraining on the characteristics of female subjects ($n = 7$)

Variable	Sedentary (1)	Trained (2)	Detrained (3)	Duncan test
Body weight (kg)	55.9 (8.7)	56.7 (9.2)	55.0 (7.2)	NS
$\dot{V}_{O_2\,max}$ (l · min^{-1})	2.12 (0.54)	2.57 (0.37)	2.47 (0.32)	** 1 vs 2 ** 1 vs 3
$\dot{V}_{O_2\,max}$ (ml · kg^{-1} · min^{-1})	38.1 (8.8)	46.6 (3.5)	43.6 (3.9)	* 1 vs 2 * 1 vs 3
% Fat	23.2 (6.8)	20.6 (6.6)	24.7 (6.8)	* 1 vs 2 ** 2 vs 3
Sum of seven skinfolds (mm)	105.3 (27.4)	101.4 (30.2)	110.8 (30.7)	* 2 vs 3
Fat cell diameter (µm)	89.1 (9.3)	86.0 (9.3)	90.5 (10.2)	NS

Values are means (SD); n = number of subjects; NS = non significant
* $P < 0.05$; ** $P < 0.01$

Table 2. Effects of endurance training and detraining on the characteristics of male subjects ($n = 12$)

Variable	Sedentary (1)	Trained (2)	Detrained (3)	Duncan test
Body weight (kg)	74.6 (14.6)	73.4 (12.1)	73.6 (12.3)	NS
$\dot{V}_{O_2\,max}$ ($l \cdot min^{-1}$)	3.15 (0.36)	3.80 (0.37)	3.71 (0.33)	** 1 vs 2 ** 1 vs 3
$\dot{V}_{O_2\,max}$ ($ml \cdot kg^{-1} \cdot min^{-1}$)	43.3 (7.3)	52.7 (7.0)	51.4 (7.1)	** 1 vs 2 ** 1 vs 3
% Fat	17.4 (9.9)	15.7 (7.8)	16.7 (6.0)	NS
Sum of seven skinfolds (mm)	99.7 (54.5)	82.4 (40.9)	85.8 (42.4)	** 1 vs 2 ** 1 vs 3
Fat cell diameter (μm)	90.2 (14.4)	86.9 (14.2)	91.1 (11.6)	NS

Values are means (SD); n = number of subjects; NS = non significant
** $P < 0.01$

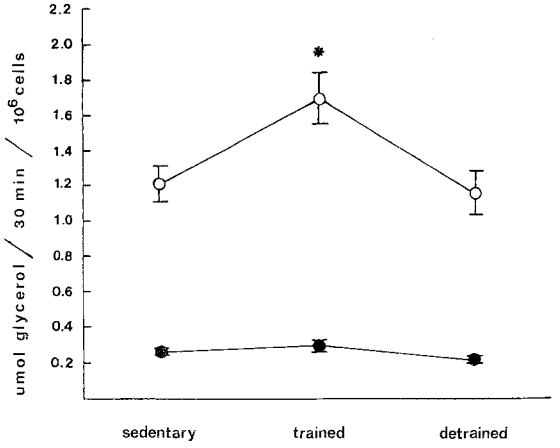

Fig. 1. Effect of training and detraining on basal *(close circles)* and maximal epinephrine stimulated lipolysis *(open circles)* of isolated fat cells (Values are means ± SEM). * Significantly different from the pre-training value, $P < 0.01$

Table 3. Correlations between changes in body fatness indicators induced by training or detraining with changes in epinephrine stimulated lipolysis (ESL)

Changes induced by training		Changes induced by detraining	
	ESL		ESL
Δ Fat mass	0.12 NS	Δ Fat mass	0.30 NS
Δ % Body fat	0.31 NS	Δ % Body fat	0.34 NS
Δ Sum of skinfolds	−0.07 NS	Δ Sum of skinfolds	0.22 NS
Δ Fat cell diameter	0.23 NS	Δ Fat cell diameter	0.03 NS

NS = non significant

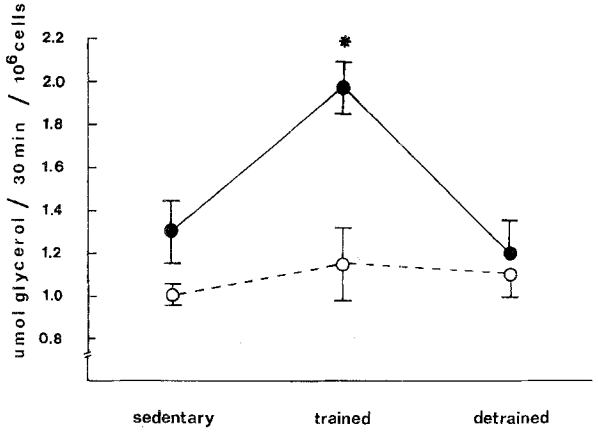

Fig. 2. Effect of training and detraining on adipocytes maximal epinephrine stimulated lipolysis of men *(closed circles)* and women *(open circles)* (Values are means ± SEM). * Significantly different in men from the women values, $P < 0.01$

were slightly different in men than in women. Although the decrease in percent body fat and fat cell diameter following training in men did not reach significance, there was a substantial decrease in the sum of skinfolds which remained lower after detraining than before training.

Figure 1 illustrates the values of basal and epinephrine stimulated lipolysis for all subjects combined in the three conditions, i.e., sedentary, trained and detrained. No modification of basal lipolysis was noted throughout the program. A significant effect of training was obtained for adipocyte ESL. However, after the exercise restriction period, a decrease in epinephrine stimulated lipolysis to pre-training values was observed.

Significant sex differences in the reaction to the different experimental conditions were found (Fig.

2). While an increase in ESL was observed in men following training, no change was obtained in women. Moreover, the exercise restriction period had no effect on adipocyte ESL in women, while a significant decrease was observed in men.

As shown in Table 3, no correlation was observed between changes in ESL and changes in body fat indicators induced by training or detraining. However, even though results are not shown, a significant correlation ($r = -0.53$; $P < 0.05$) was observed between the increase in ESL and the subsequent decrease caused by detraining.

Discussion

The exercise program caused a decrease in % body fat, subcutaneous fat and fat cell diameter over the whole sample, with no change in body weight, suggesting an increase in fat free mass. These observations, indicate that there was a decrease of fat mass with a preservation of lean body mass which is a well known advantage of exercise-training as a mean to decrease body fatness (Oscai and Holloszy 1969). However, sex differences in the adaptation to the experimental program were noted. The observation that women decreased their level of body fat is not in agreement with a previous report from our laboratory (Després et al. 1984b) showing that, for a training comparable in intensity and duration to the present one, men lost fat while there was no significant change in women. However, an explanation can be provided for this discrepancy. First, in the previous study, despite the fact that women had not on the average lowered their fatness level, there were large inter-individual variations in the response to the training program. Some women lost a substantial amount of fat while some even increased their fat stores. This could explain the lack of significant change following training in this previous study. In the present sample, which was smaller ($n = 7$) than in the first study ($n = 11$), women fatness changes were more homogeneous. Moreover, although we have not monitored the caloric intake during the program and made no attempt to modify the eating habits of the subjects, a posteriori interviews revealed that, in the present study, women adhered to the program to lose weight and were concerned about their diet during the training program. In men, although the decrease in percent body fat did not reach significance ($P > 0.05$), the substantial decrease in skinfold thicknesses ($P < 0.01$) indicates that a lost of subcutaneous fat was achieved. The discrepancy between skinfold and percent body fat changes following training in men and in women is an additional indication that the relationship between subcutaneous fat and total fat is not constant and can be altered by numerous factors such as sex, training status, and others as well (Lohman 1981).

After the training program, an increase in adipocyte epinephrine maximal stimulated lipolysis was noted. This adaptation of adipose tissue of trained subjects in favor of an increased lipid mobilization capacity has been previously reported in animals (Askew et al. 1975; Bukowiecki et al. 1980; Owens et al. 1977; Shepherd et al. 1981; Wardzala et al. 1982; Williams and Bishop 1982) and in humans (Després et al. 1984a, b). Moreover, after 50 days of physical inactivity, ESL returned to the pretraining level, indicating that hypokinesia reversed the effect of aerobic training on adipocyte stimulated lipolysis. Poledne and Parizkova (1975) have shown that turnover of FFA in hypokinetic animals was only one half that of controls suggesting a diminished lipid mobilization in inactive animals. The present experiment would generally support this finding. Furthermore, in the present study, the alteration in lipid metabolism following training in the direction of an increased mobilization of fat by catecholamines was different from that obtained when fat is lost through fasting (Burns et al. 1979), hypocaloric diet (Berlan et al. 1981) or jejuno-ileal bypass (Smith et al. 1979). Indeed, these conditions are reported to decrease catecholamine stimulated lipolysis of fat cells. Therefore, one could speculate that the increased epinephrine stimulated lipolysis induced by physical training could be associated with a greater fat loss for a given caloric deficit, caused by a better mobilization of fat stored in the adipose tissue. However, the fact that we have investigated only fat cells from the suprailiac depot could perhaps explain the difference noted between the effects of training in comparison with those of diets and fasting on adipose tissue lipolysis since regional differences in the metabolism of adipose tissue in humans have been documented (Lafontan et al. 1979; Östman et al. 1979; Smith et al. 1979). The effect of training on fat cell lipolysis will have to be investigated in many fat depots before a general conclusion can be drawn.

Given the above observation, it was felt appropriate to test whether subjects with the largest increase in epinephrine stimulated lipolysis had the greatest fat loss following training and the converse with detraining. However, in the two experimental conditions (training, detraining), changes in ESL were not significantly related to changes in body fat. This finding adds evidence to the fact that alterations in fat cell lipolysis are not always dependent of adipocyte size. Exercise-training and hypokinesia per se have an effect on fat cell lipolysis. The fact that alterations in body fatness were small could also explain the lack of statistical relationship. Following a

training program, Bukowiecki et al. (1983) have observed larger fat cell size in rats fed sucrose than in sedentary chow fed rats. They also found higher catecholamine stimulated lypolysis in the former group than in the latter, thus reinforcing the concept that the relationship between body fatness, fat cell size and catecholamine stimulated lipolysis is not a simple one.

A sex difference in the adaptation of epinephrine maximal stimulated lipolysis to the different conditions was observed. Male adipose tissue metabolism was altered by training and inactivity, while no significant changes were noticeable in women. In a previous training study, we have reported a lower but significant increase in adipocyte epinephrine stimulated lipolysis in women than in men (Després et al. 1984b).

However, in the present study it must be recognized that there was considerable variation in the ESL response of women to training. Some women had increases in maximal stimulated lipolysis while others displayed no change. This situation resulted in an increase in the coefficient of variation of ESL, i.e., from 14% in the sedentary state to 39% in the trained condition (from Fig. 2). Since the sample was small ($n = 7$ subjects), no significant increase in stimulated lipolysis was obtained in women with training in the present experiment. Moreover, neither caloric intake nor menstrual cycle were controlled during this study. These two factors should, however, be considered in trying to account for the sex difference observed. Studies have suggested that gonadal steroids could be involved in the control of fat cell metabolism (Hamosh and Hamosh 1975; Hansen et al. 1980; Kim and Kalkhoff 1975).

High responders to training for epinephrine stimulated lipolysis tended also to be high responders to detraining, i.e., the higher the increase in ESL induced by training, the larger the reduction in ESL associated with physical inactivity. This could indicate that some subjects were sensitive to variation in energy expenditure, while others were resistant. It was recently reported that variation in epinephrine stimulated lipolysis and the response to training of fat cell lipolysis could be genetically determined (Després et al. 1984a). On the basis of these previous results from our laboratory it could be speculated that the low responders of the present study have possibly a genetically determined alteration in the fat cell lipolytic mechanism that makes them less sensitive to variations in environmental conditions such as exercise-training or detraining.

In summary, the present study demonstrates that endurance training increases epinephrine maximal stimulated lipolysis of isolated fat cells in men and that this effect is reversed by 50 days of physical inactivity. The alteration in fat cell lipolysis induced by hypokinesia seems to be dissociated from the variation in body fatness. In addition, the present study suggests that fat cell lipolysis from the suprailiac region is less sensitive to variations in patterns of exercise habits in female subjects than in males.

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