



Endurance training increases the β -adrenergic lipolytic response in subcutaneous adipose tissue in obese subjects

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OBJECTIVE: The aim of this study was to assess, by longitudinal follow-up, the influence of aerobic training on the *in vivo* lipolytic activity of adipose tissue in obese male subjects.

SUBJECTS: Eleven obese non-diabetic males, aged 41.5 ± 5.77 (range 27–49 y) with body mass index (BMI) 36.5 ± 4.5 kg/m² (range 29.4–47.1 kg/m²) participated in the study.

DESIGN: Subjects took part in a 12-week aerobic training program. Before and after training, microdialysis of abdominal subcutaneous adipose tissue (SCAT) was carried out, using perfusion with graded doses of the β -adrenergic agonist isoprenaline and a single dose of the phosphodiesterase inhibitor theophylline. In addition, the response of plasma glycerol and free fatty acids (FFAs) to intravenous infusion of graded doses of isoprenaline was tested.

RESULTS: The training did not induce significant weight loss and promoted an increase in maximum aerobic capacity ($P < 0.05$). The increase of extracellular glycerol in SCAT in response to isoprenaline perfusion was enhanced after the training ($P < 0.05$), while no change in the response of interstitial glycerol to theophylline action was observed. The training did not elicit a change in the isoprenaline-induced changes of blood flow in adipose tissue. The increases of plasma FFAs and glycerol in response to intravenous isoprenaline infusion, were significantly enhanced after training.

CONCLUSION: The present study shows that aerobic training induced an increase in the response of plasma and subcutaneous adipose tissue concentration of glycerol to β -adrenergic stimulation. The effect of an agent acting at the post-receptor level (theophylline) in SCAT was not modified by training.

Keywords: lipolysis; microdialysis; training; obesity

Introduction

Regular physical activity has been accepted as an integral part of the treatment for obesity. In contrast to a hypocaloric diet, exercise training induces a modest reduction of fat mass (FM, depending on training volume) without a concomitant loss of fat free mass (FFM).¹

The hydrolysis of triglyceride stores (lipolysis) which releases free fatty acids (FFAs) and glycerol for adipose tissue, is a key step in the metabolic process leading to the decrease of FM. Lipolysis in humans is mainly stimulated through the β -adrenergic action of catecholamines and inhibited through the α 2-adrenergic pathway and by insulin.²

In healthy non-obese subjects, several studies have shown that exercise training induces an increase in catecholamine-stimulated lipolysis in isolated

adipocytes; either in cross sectional^{3–5} or longitudinal⁶ designs. An increased sensitivity of adipose tissue to the lipolytic action of catecholamines can facilitate lipid mobilization from fat stores. The results of *in vivo* studies investigating whole-body basal lipolysis at rest were unequivocal: higher⁷ as well as lower⁸ FFA release from adipose tissue, was found in trained subjects. Finally, *in situ* examination of adrenaline-stimulated lipolysis in subcutaneous adipose tissue (SCAT) using the microdialysis technique,⁹ did not find any difference between trained and untrained subjects. A recent study examined the effect of training combined with diet on *in vitro* lipolysis in obese subjects and found that the dietary-induced decline of lipolysis was blunted by training.¹⁰

To our knowledge, no study has examined whether modifications in the regulation of lipolysis in adipose tissue occur in obese subjects submitted to aerobic training without a concomitant nutritional intervention. Alterations of catecholamine-stimulated lipolysis have been reported in obese subjects^{11,12} and, therefore, it is of particular interest whether the disturbed lipolytic sensitivity can be influenced by training.

The present study was undertaken to investigate the effect of 12 weeks aerobic training on adipose tissue

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lipolysis in obese male subjects. The microdialysis method was used to assess the interstitial glycerol concentration, as an index of lipolysis, before and after the training. The microdialysis probes were perfused with agents acting at the receptor (isoprenaline, β -adrenergic agonist) and post-receptor (theophylline) level. In addition, in an attempt to evaluate the training effect quantitatively on the whole body response to isoprenaline stimulation, *in vivo* responses of plasma glycerol and FFAs to isoprenaline infusion were examined.

Methods

Subjects

Eleven obese non-diabetic males, aged 41.5 ± 5.7 y (range 27–49 y) were recruited for the study. The subjects' characteristics are presented in Table 1. One patient was treated for mild hypertension with calcium channel antagonists, one patient was treated with a small dose of thyroxine (75 μ g/d) for hypothyroidism. All the subjects were sedentary prior to the study. Their weight had been stable for six months prior to the study. Their nutritional status had not changed during that period and they were instructed not to change their nutritional habits during the course of the study. The stable nutritional pattern was verified using a four-day dietary record, obtained at the beginning, at the sixth week and at the end of the study period. The experiment was approved by the Ethics Committee of the 3rd Medical Faculty of Charles University, Prague. All subjects gave their informed consent to participate in the study.

Subjects took part in the 12-week aerobic training program described below. Before and after the training program the following measurements and tests were carried out: body composition measurements, assessment of maximal oxygen uptake (VO_2 max), laboratory evaluation of blood lipids, evaluation of blood glucose and insulin response to oral glucose load, microdialysis of abdominal SCAT and a test with graded-dose intravenous isoprenaline infusion. The tests were performed at least 48 h after the last exercise session, in order to exclude its effects on the results.

Maximum aerobic capacity

VO_2 max was assessed using a graded test conducted on an electromagnetically braked bicycle ergometer (Ergometrics 800s Ergoline, Jaeger, Germany). The initial work load was 50 watts and it was increased by 0.2 Watts/kg of FFM every minute until exhaustion. VO_2 was measured using a Vmax apparatus (Sensor Medics, Yorba Linda, CA) during the test, and the highest VO_2 value was considered as VO_2 max.

Exercise training protocol

The training program consisted of exercise on a bicycle ergometer for four days each week; duration

of the session was 30–45 min, following individual prescription. The subjects cycled at a target heart rate calculated from the Karvonen equation.¹³ The heart rate corresponded to 50% of the heart rate reserve (maximal heart rate minus resting heart rate) during the first two weeks and progressed to 55–70% of the heart rate reserve during the subsequent weeks.

Anthropometric assessment

Before and after the training, body composition was determined by hydrostatic weighing using the method of Siri.¹⁴ Lung volume measurement was carried out using plethysmography (Vmax Apparatus, Sensor Medics, Yorba Linda, CA).

Oral glucose tolerance test

Oral glucose tolerance test (OGTT) was performed by oral administration of 100 g glucose. Blood glucose and plasma immunoreactive insulin were determined in the basal state, and one and two hours after glucose intake.

In vivo isoprenaline test

The subjects were examined in the supine position after an overnight fast. Two intravenous catheters were inserted into the antecubital vein, one in each arm. One catheter was used for isoprenaline infusion, the other one for blood sampling. After a 20 min rest period, the first blood sample was drawn for determination of basal values. Thereafter, the infusion of isoprenaline diluted in a saline solution was started. The isoprenaline solution was protected from light degradation by wrapping aluminium foil around the syringe and the infusion line connected to the subject. Three sequential doses of isoprenaline were used: 0.02, 0.04 and 0.06 μ g/min/kg of FFM. Each dose was infused for 10 min and blood sampling was performed during the last minute of each 10 min interval. Heart rate and blood pressure were monitored continuously. Infusion was interrupted when the subject's heart rate exceeded 130 bpm, which occurred in one subject at the highest rate of infusion.

Dialysis experiment

For dialysis experiments the subjects were investigated in the supine position after an overnight fast. Two microdialysis probes (Carnegie Medecin, Stockholm, Sweden) of 20×0.5 mm and 20 000-MW cut-off were inserted percutaneously after epidermal anaesthesia (200 μ l of lidocaine 1%, Roger-Bellon, Neuilly-s-Seine, France) into the abdominal SCAT at a distance of 100 mm immediately to the right and the left of the umbilicus. The probes were connected to a microinjection pump (Harvard Apparatus, SARL, Les Ulis, France) and perfused at a flow rate of 0.5 μ l/min with sterile Ringer's solution (154 mmol/l sodium, 4 mmol/l potassium, 2.5 mmol/l calcium, 160 mmol/l chloride) supplemented with ethanol (1.7 g/l). Ethanol

was added to the perfusate in order to estimate changes in the adipose blood flow, as previously described.¹⁵ No outgoing dialysate was collected during the first 30 min after implantation. Then, the *in vivo* recovery rate was evaluated for each probe, by measuring dialysate glycerol concentrations at various perfusion rates. This calibration procedure was previously described for the estimation of the extracellular amino acid concentration in the brain,¹⁶ recently applied to interstitial glycerol concentration in muscle and adipose tissue¹⁷ and previously described by our group.¹⁵ Briefly, the probes were perfused at four successive rates (0.5 µl/min, 1.5 µl/min, 2.5 µl/min and 3.5 µl/min), separated by appropriate wash out periods, and the glycerol concentrations determined in the dialysate for each perfusion rate. Dialysate concentrations were plotted (after log-transformation) against the perfusion rates. Linear regression analysis was used to calculate the glycerol concentration at 'zero flow', corresponding to the interstitial glycerol concentration. The ratio between dialysate glycerol concentration at 2.5 µl/min and calculated interstitial glycerol concentration, represented the *in vivo* recovery rate of the probe. Then, the perfusion flow rate was maintained at 2.5 µl/min during the whole experimental period.

Four 10 min fractions of each probe were collected to evaluate basal levels and then isoprenaline was added to the perfusate with two rising concentrations (0.1 µmol/l and 1 µmol/l). Each dose was applied for 40 min (concentration-periods) and four successive fractions were collected during the different concentration-periods. Theophylline was perfused in the second probe at a constant concentration (10 mmol/l) and successive 10 min fractions were collected for 80 min.

Glycerol (lipolysis index) analysis was performed in each collected fraction. The changes in the blood flow were assessed by measuring, as previously described,^{18,19} the ethanol outflow/inflow ratio during the basal period and at each dose period.

Biochemical determination

Glycerol in dialysate (10 µl) and in plasma (20 µl) was analysed with an ultrasensitive radiometric method,²⁰

the intra-assay and interassay variabilities were 5.0% and 9.2%, respectively. Ethanol in dialysate and perfusate (5 µl) was determined with an enzymatic method,²¹ the intra-assay and interassay variabilities were 3.0% and 4.5%, respectively. Plasma glucose and FFAs were determined with a glucose-oxidase technique (Biotrol kit, Merck-Clevenor, Nogent-s-Marne, France) and an enzymatic procedure (Wako kit, Unipath, Dardilly, France), respectively. Plasma insulin concentrations were measured by radioimmunoassay (RIA) using kits from Sanofi Diagnostics Pasteur (Marnes la Coquette, France). Plasma triglycerides and cholesterol were assayed with commercial reagents.

Reagents

Isoprenaline hydrochloride (Isuprel[®]) was obtained from Winthrop (Clichy, France) and theophylline (theophylline Bruneau) from Delalande (Quétingny, France).

Statistical analysis

All the values are means ± s.e.m. Flow rate calibration data were analyzed by linear regression tested for goodness of fit. The significance of differences was assessed using Student's paired *t* test and analysis of variance (ANOVA) with Bonferroni's and Student-Newman-Keuls' tests for *post hoc* analysis. Significance values are quoted in the text and figures. *P* < 0.05 was considered statistically significant. All calculations were performed using software statistical packages (Superanova and Statview, Abacus Concepts Inc., Berkeley, CA).

Results

Physical characteristics

The training program resulted in an increase of total VO₂ max by 6.3%, but the increase was not significant when VO₂ max was related to FFM (Table 1). Maximum work output on the bicycle ergometer increased by 8.9%. The training did not produce any significant

Table 1 Characteristics of obese subjects submitted to 12 weeks of aerobic training

	Before training	After training	
Anthropometric parameters			
Weight (kg)	111.3 ± 5.0	109.1 ± 5.5	NS
Body mass index (kg/m ²)	36.5 ± 1.4	35.8 ± 1.5	NS
Fat mass (%)	37.8 ± 2.1	36.6 ± 2.3	<i>P</i> < 0.05
Fat free mass (kg)	68.6 ± 2.3	68.5 ± 2.6	NS
Waist circumference (cm)	116.7 ± 3.3	113.8 ± 4.0	<i>P</i> < 0.05
Physical fitness			
VO ₂ max (l/min)	3.0 ± 0.2	3.2 ± 0.1	<i>P</i> < 0.05
VO ₂ max/fat free mass (ml/kg/min)	45.6 ± 1.8	48.8 ± 1.8	NS
Maximal work output (watts)	223.2 ± 13.6	243.6 ± 11.0	<i>P</i> < 0.05
Maximal heart rate (bpm)	171.5 ± 4.0	168.3 ± 3.4	NS

Values are mean ± s.e.m.

NS = not statistically significant; VO₂ max = maximal oxygen uptake.

change in body weight, the percentage of FM decreased significantly, but there was no change in FFM. There was a significant decrease in the waist circumference.

Blood results

FFA concentrations were slightly higher after, than before, training, the difference not being significant and no significant change was observed in plasma glycerol concentrations (Table 2). Total cholesterol concentrations in plasma decreased after training (5.32 ± 0.20 mmol/l vs 6.16 ± 0.34 mmol/l, $P < 0.01$), while no change was observed in plasma high density lipoprotein (HDL) cholesterol (1.21 ± 0.05 mmol/l vs 1.20 ± 0.07 mmol/l) or triglyceride (2.31 ± 0.30 mmol/l vs 2.93 ± 0.51 mmol/l) concentrations.

OGTT

The basal plasma concentrations of glucose and insulin, were not changed by training (5.01 ± 0.32 vs 5.54 ± 0.51 mmol/l and 21.2 ± 3.1 vs 24.3 ± 2.7 μ U/ml, respectively). OGTT was performed before and after training. The calculated area-under-the-curve (AUC) for plasma glucose, was significantly lower after, than before, training (18.4 ± 2.5 vs 23.7 ± 2.7 mmol/120 min; $P < 0.003$). The calculated AUC for plasma insulin was lower after training, however the decrease was not significant, due to large interindividual variations (174.3 ± 31.9 vs 238.9 ± 49.8 μ U/ml/120 min).

In vivo isoprenaline test

The isoprenaline-induced increase in plasma glycerol and FFA concentrations was significantly more pronounced after training than before (Table 2). Isoprenaline induced a weak increase in plasma glucose concentration after training but not before, the corresponding calculated AUCs for isoprenaline-induced changes in plasma glucose, were 1.8 ± 0.3 and -0.4 ± 0.3 mmol/30 min ($P < 0.03$). The isoprenaline-induced increase in plasma insulin concentration tended to be greater after training, but the difference was not significant, due to large interindividual

variations (AUCs were 78.2 ± 15.5 vs 57.0 ± 6.6 μ U/ml/30 min; $P < 0.17$). Training did not modify resting heart rate (60.8 ± 1.8 vs 63.5 ± 2.3 bpm; $P = 0.14$). However, the isoprenaline-induced increase in heart rate was higher after training; the increases were 24.3 ± 1.8 , 45.4 ± 3.2 , 58.8 ± 2.5 vs 17.9 ± 3.5 , 38.3 ± 3.6 , 47.5 ± 4.4 bpm, for 0.02, 0.04 and 0.06 μ g/min/kg FFM of isoprenaline infusion, respectively (ANOVA with repeated measures, $P < 0.01$).

Effect of training on lipolytic activity in subcutaneous adipose tissue

In order to evaluate the modifications of lipolysis and sensitivity of the β -adrenergic pathway, the microdialysis examination of abdominal SCAT was carried out. No training-induced difference in the baseline extracellular glycerol levels was detected (320.0 ± 20.1 μ mol/l after vs 295.6 ± 6.8 μ mol/l before training).

Both before and after training, locally administered isoprenaline induced a concentration-dependent increase in extracellular glycerol concentrations (Figure 1A). The increase above the baseline level (fractions, 10–40 min) was already significant ($P < 0.05$) at the concentration of 0.1 μ mol/l, before as well as after training. At a concentration of 1.0 μ mol/l, the glycerol levels rose significantly ($P < 0.05$) above that of the previous concentration in both periods. The two curves representing the concentration-dependent increase of glycerol before vs after training were different (ANOVA with repeated measures, $P < 0.05$). The blood flow in SCAT was evaluated using the ethanol inflow/outflow ratio. No change due to training was found in basal values. The inflow/outflow ratio decreased ($P < 0.05$) during isoprenaline perfusion in a concentration-dependent manner in both periods, indicating the vasodilating effect of isoprenaline (Figure 1B). The curves representing the concentration-dependent response of the inflow/outflow ratio to isoprenaline before and after training were not different (ANOVA with repeated measures), which indicated no training-induced change in the vasodilating effect of isoprenaline in adipose tissue.

Table 2 Effect of isoprenaline infusion on plasma free fatty acids (FFAs) and glycerol concentrations in obese subjects submitted to 12 weeks of aerobic training

Isoprenaline (μ g/min/kg)	Free fatty acids (μ mol/l)		Glycerol (μ mol/l)	
	Before training	After training	Before training	After training
0	567 \pm 67	783 \pm 71	78 \pm 7	85 \pm 5
0.02	722 \pm 85	1345 \pm 174	113 \pm 12	128 \pm 11
0.04	977 \pm 85	1568 \pm 116	135 \pm 11	164 \pm 12
0.06	1186 \pm 88	1699 \pm 100	154 \pm 13	196 \pm 16
AUC	954 \pm 128	1823 \pm 315 $P < 0.04$	129 \pm 18	177 \pm 25 $P < 0.05$

Values are mean \pm s.e.m.

After basal measurement, isoprenaline was infused at rates of 0.02, 0.04 and 0.06 μ g/min/kg fat free mass (FFM), for 10 min at each rate. Areas-under-the-curve (AUCs; μ mol/l/30 min) were calculated using the absolute increments of plasma FFAs and glycerol concentrations.

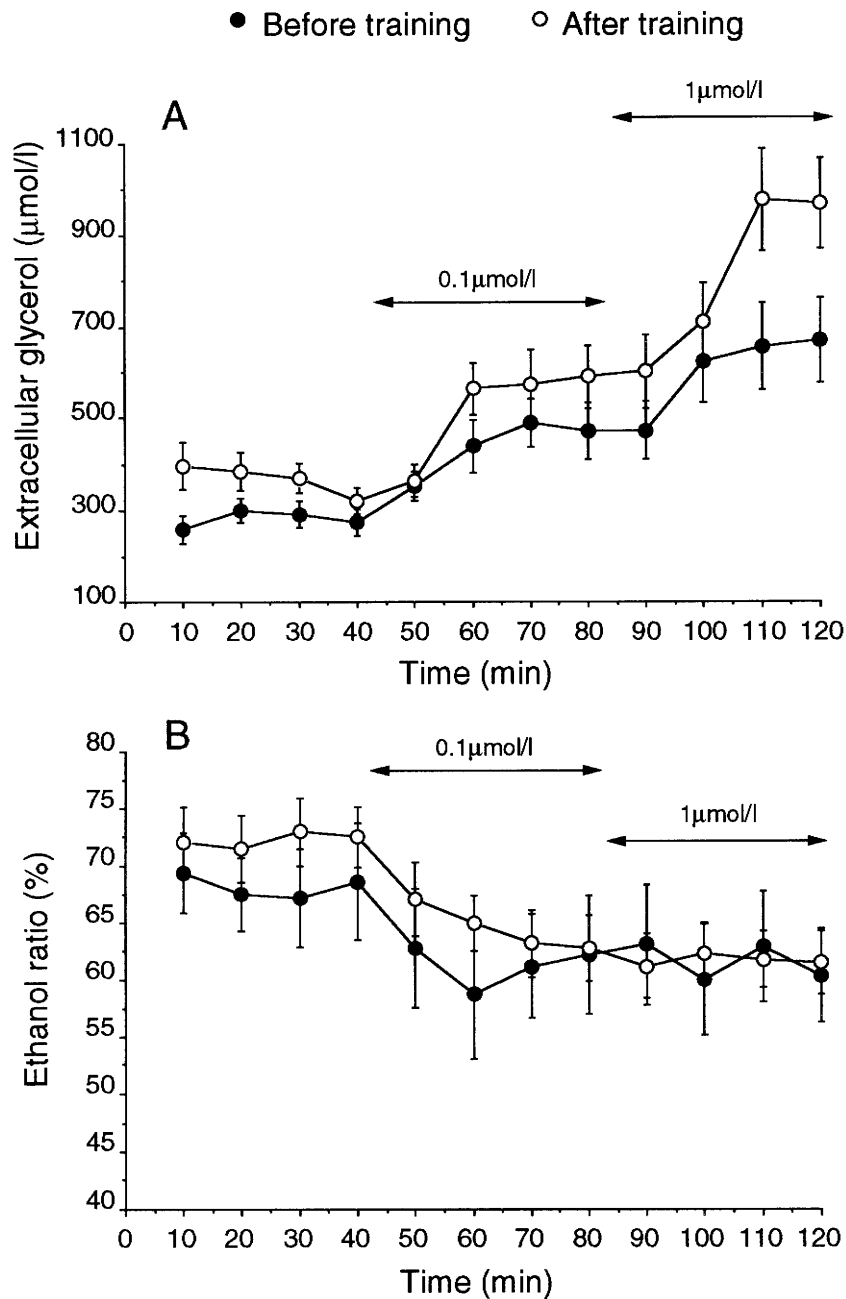


Figure 1 A. Effect of the non-selective β -adrenoceptor agonist isoprenaline on the interstitial glycerol levels in subcutaneous adipose tissue (SCAT) from obese subjects ($n=11$) before and after 12 weeks of aerobic training. After 40 min (basal period), increasing concentrations of isoprenaline were added to the perfusate, indicated by arrows. Values are means \pm s.e.m. Statistical comparison of the curves was performed using ANOVA for repeated measures, with training period (after vs before) and time as factors in this analysis. The two curves were different ($F=3.56$; $P<0.05$). B. Effect of the non-selective β -adrenoceptor agonist isoprenaline on the ethanol ratio (ethanol dialysate level/ethanol perfusate level) in SCAT from obese subjects ($n=11$) before and after 12 weeks of aerobic training. Values are means \pm s.e.m. Statistical comparison of the curves was performed using ANOVA for repeated measures, with training period (after vs before) and time as factors in the analysis. The two curves were not different.

In order to evaluate the putative role of post- β -adrenergic receptor mechanisms in the increase of isoprenaline-induced extracellular glycerol concentration observed after training, theophylline was perfused in the second probe at a constant concentration (10 mmol/l). As for the first probe, no training-induced differences in the extracellular glycerol concentrations in the basal fractions were detected ($271.6 \pm 16.5 \mu\text{mol/l}$ after vs $309.6 \pm 14.2 \mu\text{mol/l}$ before training). Theophylline induced a significant

increase of extracellular glycerol concentrations above the basal values (fractions 10–40 min) in both periods (Figure 2A) ($P<0.05$). The two curves depicting the overall responses to theophylline before and after training were not statistically different (ANOVA with repeated measures). The basal blood flow measured in this second probe was not different before and after training (Figure 2B). In both periods theophylline decreased the ethanol outflow/inflow ratio compared to basal values ($P<0.05$), indicating

a vasodilating effect. The curves of the ethanol out-flow/inflow ratio depicting the overall response to theophylline were not statistically different.

Discussion

The main finding of this study is that, in obese male subjects, aerobic training (corresponding to the training volume used in routine clinical practice for the obese), promotes an increase in β -adrenergic-stimulated lipolytic activity *in situ* in SCAT. In this study, the training produced a minor (although significant)

change in the physical fitness of subjects (evaluated by maximum aerobic capacity). It did not produce a significant change in body weight while there was a slight decrease in the FM and no change in FFM. The modest effects of this kind of training are in agreement with other reports on the effects of moderate aerobic training on obese subjects.^{22–24} In spite of the mild effects on physical fitness and body composition, the training resulted in a decrease of plasma total cholesterol and in a significant improvement of glucose tolerance estimated with OGTT.

The basal rate of lipolysis did not appear to be changed by training: as judged by the lack of significant change in basal plasma concentrations of glycerol and FFAs. In response to isoprenaline infusion, the plasma concentrations of both metabolites increased in a dose-dependent manner and the increase was more pronounced in the post- vs pre-training state (Table 2). This finding suggests an enhancement of the lipolytic response to catecholamines: the plasma insulin response to isoprenaline infusion, which could influence the response of glycerol and FFAs, was not modified by training. A similar training-induced enhancement of the response of plasma FFAs and glycerol to adrenaline infusion, has been observed in non-obese subjects.²⁵ Obese subjects have been shown to have a lower isoprenaline-induced FFA and glycerol release.²⁶ From the present study, it appears that this impairment could be changed by training. However, the training-induced increase of plasma glycerol and FFA responses to isoprenaline may reflect more than the changes of *in vivo* adipose tissue lipolytic rates, because the metabolite plasma concentrations are determined by both lipolysis and utilization rates. In addition to the isoprenaline-infusion-induced effect on lipid metabolites, we found a training-induced increase of the response of heart rate to isoprenaline stimulation, suggesting an increased sensitivity of cardiac chronotropic function to β -adrenergic action. This corresponds to previous findings in obese subjects during training.²⁷

In the microdialysis examination, the baseline values of interstitial glycerol in adipose tissue (calculated from the glycerol concentrations in dialysate) were not changed after training (Figure 1A). The values of interstitial glycerol found in the obese subjects of the present study are in agreement with those observed previously by others²⁸ and ourselves.²⁹ In both the pre- and post-training states, isoprenaline induced an increase in interstitial glycerol concentration in SCAT. The pre-training isoprenaline-induced increase in interstitial glycerol concentration was close in magnitude to that found in our previous microdialysis study of obese subjects.²⁹ The response of interstitial glycerol to isoprenaline stimulation was higher after 12 weeks of training. A similar enhancement of isoprenaline-induced interstitial glycerol concentration *in situ* was found during the very-low-calorie diet (VLCD) in our previous study of obese subjects.²⁹

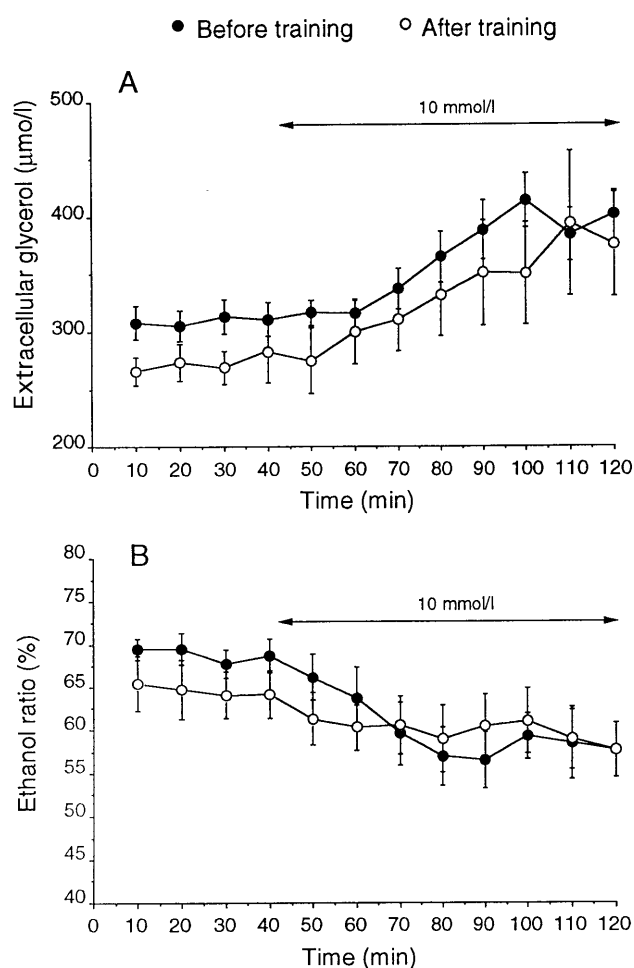


Figure 2 A. Effect of the phosphodiesterase inhibitor theophylline on the interstitial glycerol concentrations in subcutaneous adipose tissue (SCAT) from obese subjects ($n=11$) before and after 12 weeks of aerobic training. After 40 min (basal period), theophylline was added to the perfusate, indicated by arrows. Values are means \pm s.e.m. Statistical comparison of the curves was performed using ANOVA for repeated measures, with training period (after vs before) and time as factors in the analysis. The two curves were not different. B. Effect of the phosphodiesterase inhibitor theophylline on the ethanol ratio (ethanol dialysate level/ethanol perfusate level) in SCAT from obese subjects ($n=11$) before and after 12 weeks of aerobic training. Values are means \pm s.e.m. Statistical comparison of the curves was performed using ANOVA for repeated measures with training period (after vs before) and time as factors in the analysis. The two curves were not different.

The isoprenaline perfusion of the dialysis probe induced a concentration-dependent increase of blood flow, as evaluated by the ethanol wash-out technique. The relative change of the adipose tissue blood flow in response to isoprenaline was not different before and after training. This suggests that the vasodilator effect of isoprenaline was not modified by training and thus, the increase of interstitial glycerol in response to isoprenaline was influenced in the same manner before and after training. Consequently, the higher isoprenaline-induced increase in interstitial glycerol concentration after training, suggests that training induced an enhancement of β -adrenergically mediated lipolysis in fat cells.

The results of the microdialysis measurement in this study are in agreement with one of the rare longitudinal studies in which the training-induced increase of adrenaline-stimulated lipolysis of adipocytes *in vitro* was observed after 20 weeks training in non-obese subjects.⁶ The only microdialysis study which examined changes in lipolysis in SCAT related to training was that of Stallknecht *et al.*⁹ They found, in a cross-sectional design, no differences in adrenaline-stimulated lipolysis between trained and untrained subjects. The results of our study are hardly comparable with those of Stallknecht *et al.*⁹ because of the different design: 1) the latter study compared two groups of individuals with highly different training status and body fatness and 2) a different way was used for catecholamine administration (intravenous).

In order to try to further elucidate the level of the lipolytic cascade at which the training-induced changes in β -adrenergic lipolytic action occurs, the response to a post-receptor agent (a phosphodiesterase inhibitor, theophylline) perfused in the probes was evaluated. A significant increase in the response of interstitial glycerol concentration to this agent was observed before as well as after the training and a significant vasodilating effect of the substance was found. The theophylline-induced responses did not differ in the pre- vs post-training state. This suggests that the training-induced enhancement of β -adrenergic lipolytic action is produced at a level proximal to cyclic AMP formation. However, an effect of training to blunt the normal effect of isoprenaline to stimulate phosphodiesterase cannot be ruled out.

It has been shown that the *in situ* lipolytic response of adipose tissue to an acute exercise bout is specific with respect to fat deposit location and gender.³⁰ The gender-specific and the location-specific effects of training were also found in *in vitro* studies.^{4,5,31} Therefore, it is important to note that the training-induced modifications in the present study are specific for male subjects and for subcutaneous abdominal deposits.

Conclusion

The present study reports that, in obese males, 12 weeks of aerobic training promotes an increase in the response of plasma and subcutaneous adipose tissue concentration of glycerol during β -adrenergic stimulation. This suggests an increase in β -adrenergically mediated lipolysis. The effect of an agent acting at the post-receptor level (theophylline) in SCAT was not modified by training. The results suggest that the lowered β -adrenergic responsiveness reported in obese subjects may be improved by exercise training.

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