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Exercise Effects on Adipose Tissue Postprandial Lipolysis and Blood Flow in Children

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Abstract

Poor suppression of lipolysis and blunted increase in blood flow following meal ingestion in obese adults may indicate resistance to the antilipolytic action of insulin. Exercise may be used to normalize lipolytic responses to food intake by increasing insulin sensitivity.

Purpose—To determine if acute bouts of aerobic exercise and/or exercise training alter lipolytic and blood flow responses to food intake in lean (LN) and obese (OB) children.

Methods—Sixty-five children (9–11 yrs) were randomized into acute exercise (EX: 16 LN and 28 OB) or control (CON: 9 LN and 12 OB) groups that exercised (EX), or rested (CON) between standardized breakfast and lunch. Microdialysis probes were inserted into the subcutaneous abdominal adipose tissue to monitor interstitial glycerol (lipolysis) and blood flow. Changes in interstitial glycerol and nutritive flow were calculated from dialysate samples before and after each meal. A subgroup (OB=15 and LN=9) from the acute exercise group underwent 16 weeks of aerobic exercise training.

Results—Poor suppression of lipolysis and a blunted increase in adipose tissue nutritive blood flow in response to breakfast was associated with BMI percentile ($r=0.3$, $p<0.05$). These responses

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were normalized at lunch in the OB in the EX ($p<0.05$), but not in OB in the CON. Sixteen weeks of exercise training did not improve meal-induced blood flow, and marginally altered the antilipolytic response to the two meals ($p=0.06$).

Conclusion—Daily bouts of acute aerobic exercise should be used to improve the antilipolytic and nutritive blood flow response to a subsequent meal in obese children.

Keywords

exercise; meal; children; lipolysis; adipose tissue blood flow

Introduction

In recent years, a dramatic increase in obesity has been noted in both adults and children (1). Obese youth are more likely to have risk factors for metabolic disorders than non-obese youth, such as insulin resistance (2, 3). Insulin resistance can manifest in reduced suppression of lipolysis in response to meals. Following the ingestion of a meal, insulin stimulates glucose uptake and also potentially inhibits lipolysis in adipocytes (4), a process that is impaired in obese compared to lean adults (5). We have previously reported using ambulatory microdialysis that suppression of lipolysis in response to meal ingestion (controlled breakfast) is reduced in obese children (6). Furthermore, an acute bout of exercise normalized the antilipolytic response to a subsequent meal (lunch) in obese children. However, the observation was based on relatively small sample size and lack of a control group. Importantly, there was no determination of the effect of chronic exercise training on the antilipolytic response to a meal. We have previously demonstrated that the reduced insulin-induced suppression of whole-body lipolysis in obese women is improved by endurance exercise training (7). Thus, the current study extends these findings to a pediatric population undergoing exercise training.

In addition to differential lipolytic responses, lean and obese individuals also differ in rates of subcutaneous adipose tissue nutritive blood flow. Adipose tissue blood flow per kilogram of tissue is lower in obese than lean adults (8). Obese adults often also have a blunted adipose tissue blood flow response to a meal (9, 10). Reduced adipose tissue blood flow responsiveness to nutrients has been linked to obesity and insulin resistance in adults (11, 12). Impaired postprandial vasodilation, a potential feature of glucose intolerance (12), could also contribute to impaired lipid metabolism in insulin-resistant subjects and predisposition to cardiovascular diseases. In addition, metabolic processes in adipose tissue require adequate substrate(s) and humoral factor delivery (11), and adipocytes communicate with other metabolically active tissues through humoral factors as well as metabolic products (13). All of these functions of adipose tissue are tightly linked to the pattern of blood supply and its regulation (14). However, it is not known if there is attenuated adipose tissue blood flow in response to nutrients in children, and whether acute exercise or exercise training will improve adipose tissue blood flow response in obese children.

Therefore, the purpose of the current study was to assess interstitial glycerol concentrations and adipose tissue nutritive blood flow in response to controlled breakfast and lunch meals, as well as to study the effect of acute exercise and exercise training on these responses in

preadolescent children. We hypothesized that both acute exercise and exercise training would improve postprandial suppression of lipolysis and increase subcutaneous adipose tissue nutritive flow in response to a meal in obese children, providing a basis for the reduction in metabolic and cardiovascular disease risk.

Methods

Recruitment & Inclusion Criteria

Children were recruited from Pitt County in eastern North Carolina through local pediatricians, physical education teachers, as well as through e-mail and newspaper advertisements. Participants (N=65; 32 boys and 33 girls) were children aged eight to eleven years. Children were classified as Stage I or II based on secondary sex characteristics described by Tanner, as reported by a parent using a Tanner Stage rating scale (15, 16). Participants were free from known disease and were not taking medications other than attention deficit and/or hyperactivity disorder medications. There is no known effect to our knowledge of ADHD medications on lipolysis.

Exclusions

Children performing purposeful endurance exercise training (>30 min/day, >3 day/week) prior to the study were excluded. Children with diabetes (fasting blood glucose concentration >125 mg/dL) or hypertension (>160/100 mmHg) or orthopedic problems that would prevent performance of the physical activities were excluded. The children gave assent, and their parents provided written informed consent for their child's participation, according to the Institutional Review Board at East Carolina University.

Study design

During the initial visit to the laboratory, after completion of questionnaires, body mass and height were measured for calculation of body mass index (BMI). Based on BMI, subjects were categorized as obese or lean. The obese group was defined as having a BMI $\geq 95^{\text{th}}$ percentile (17), and the lean group was defined as having a BMI < 85th percentile, where both were age- and sex-adjusted percentiles based on population data from Center of Disease Control and Prevention. Lean mass, fat mass and percent body fat were determined using dual-energy x-ray absorptiometry (DXA; GE Lunar Prodigy Advance, Madison, WI). Children were familiarized to treadmill use for one 10-minute submaximal session. Maximal treadmill tests were then conducted on separate days (at least 48 hours apart) to determine time to exhaustion: treadmill speed was held constant at 2.5 mph and the grade was increased 3% per minute until the children reached volitional fatigue. Indirect calorimetry was performed during the treadmill test using a Parvomedics metabolic cart to evaluate maximal oxygen consumption ($\text{VO}_{2\text{max}}$). The children performed at least two $\text{VO}_{2\text{max}}$ tests prior to exercise training: to increase consistency in this pre exercise training $\text{VO}_{2\text{max}}$ determination, the children performed a third test if the first two resultant maximal oxygen consumption values were not within 5% of each other.

Children reported to the laboratory on a separate day from 0700–1500 h for collection of fasting blood samples, followed by microdialysis (see Figure, Supplemental Digital Content

1, schematic of the study design showing the procedures for microdialysis visit). Breakfast was served at 0900 h and lunch started at 1300 h (see Table, Supplemental Digital Content 2, meal composition of breakfast and lunch for lean and obese children in the acute intervention group). Children were randomized into the acute exercise or control group with a 2-to-1 ratio, with the acute exercise group performing acute exercise between 1130 h and 1200 h and the control group maintaining resting conditions.

Twenty four (obese=15 and lean=9) of the children from the acute exercise group participated in a 16-week aerobic exercise training. These children returned to the laboratory for post-intervention study visits at the end of the intervention at least 48 hours after the last exercise bout.

Study visit

Collection and analysis of fasting blood samples

A venous blood sample was initially obtained after an overnight fast from an antecubital vein from each subject on the study day visit. Fasting serum glucose, insulin, total cholesterol (TC), triglycerides (TG), and high-density-lipoprotein (HDL) cholesterol were determined by commercial analysis (LabCorp, Greenville, NC), and low-density-lipoprotein (LDL) cholesterol was calculated from total and HDL using the Friedewald equation (18).

Microdialysis

Microdialysis of subcutaneous abdominal adipose tissue was performed on the 8-h visit to monitor interstitial glycerol and adipose tissue nutritive blood flow. One LM-3 probe (Bioanalytical Systems, West Lafayette, IN) with a dialysis membrane diameter of 0.2 mm and a length of 30 mm with 20 kDa molecular cutoff was inserted percutaneously into the abdominal subcutaneous fat. The perfusate flow rate was set at 2.0 μ l/min. Dialysate samples were collected at 900, 1000 (including breakfast), 1100, 1200 (end of exercise/control), and 1300, 1400 (including lunch), and 1500 (end of study) h. The dialysate and perfusate samples were stored at -4° C until analyzed for ethanol using a previously described enzymatic fluorometric method (19), then stored at -20° C until analysis of glycerol, using a CMA 600 automated analyzer (CMA/Microdialysis, Stockholm, Sweden). The CVs of the ethanol and glycerol assays were $4.5 \pm 0.9\%$ and $6.0 \pm 1.0\%$, respectively.

Acute exercise

Children in the acute exercise group participated in a 26-min exercise session at 1130 h during the microdialysis visit. Exercise, which was performed on a treadmill, consisted of a 3-min warm-up, 20-min of exercise at 140 beats/min heart rate, and a 3-min cool-down. The length and intensity of the exercise session was designed to simulate 20–30 min recess/outdoor activity time in elementary schools. All children exercised at the same absolute exercise intensity, instead of relative exercise intensity, because there was no difference in maximal HR in these children. The average treadmill speed, exercise heart rate or rating of perceived exertion were not different between lean and obese (3.3 ± 0.2 and 3.1 ± 0.1 mph, 140 ± 2 and 137 ± 1 bpm, 4.9 ± 0.5 and 4.2 ± 0.4 for treadmill speed, heart rate and children's OMNI rating of perceived exertion using 1–10 scale (20) in lean and obese, respectively).

Meal composition

Both groups of children received standardized meals for breakfast and lunch, and were considered to approximate 25% of the individual's calculated daily energy expenditure (the calculation was based on height, age, gender and adjusted body weight from the Harris Benedict equation for basal metabolic rate and a correction factor of 1.3 to correct for daily activity level). Adjusted body weight was calculated as ideal body weight for the specific age, gender and height of the child, with an additional 25% of excess body weight added for any excess weight over ideal body weight. The weight of food given to each child was measured before and after each meal. Breakfast was served at 1000 h and lunch was served at 1400 h and was consumed within 20 minutes. Children were given the choice of a prepackaged meal (Lunchable; Oscar Mayer, Madison, WI): if the entire breakfast was not consumed, the lunch was equally reduced to match the consumed breakfast. The ranges of food components consumed across all children were 450–550 kcal, 59–71 g carbohydrate, 10–21 g protein, and 14–20 g fat (see Table, Supplemental Digital Content 2, meal composition of breakfast and lunch for lean and obese children in the acute intervention group), although each child replicated the type and caloric content of the first meal consumed at all subsequent meals.

Exercise training intervention

The 16-week exercise training intervention was conducted on the campus of East Carolina University. The goal of the program was to provide fun exercise that would result in an average heart rate of 140 beats per minute or higher for one hour to meet the physical activity recommendations provided by American College of Sports Medicine. Recreational activities such as tennis, racquetball, kickball, jump rope, and other activities were chosen by the children and led by an undergraduate student. In addition, children performed self-chosen exercise on traditional exercise equipment such as treadmills, cycle ergometers, elliptical trainers, and stairclimbing equipment for approximately 10–20 minutes per session. The average number of days/week the children attend the program was 3.1 ± 0.3 , for 181.1 ± 2.1 minutes/week (~3 hours), and the average heart rate was 153.5 ± 3.5 beats/minute during the activity sessions (not different between lean and obese group).

Calculations

Insulin resistance index (HOMA-IR) was calculated according to the formula: fasting insulin concentration (microU/L) $\times$ fasting glucose concentration (nmol/L)/22.5. The ethanol outflow/inflow ratio (O:I ratio) was calculated using the concentration of ethanol in the perfusate fluid and the concentration of ethanol in each dialysate sample (ethanol concentration in the dialysate/ethanol concentration in the perfusate fluid). Dialysate glycerol data were converted to interstitial glycerol based on the measured relative *in vitro* recoveries of ethanol and glycerol, the measured relative *in vivo* recovery of ethanol, and the calculated *in vivo* glycerol recovery. This calculated *in vivo* glycerol recovery is based on the assumption that the relationship between the relative recoveries of two compounds remains similar *in vitro* as compared to *in vivo* (21).

Statistical analysis

Data are presented as mean $\pm$ standard error. Fasting values of plasma variables, ethanol O:I ratios, interstitial glycerol and macronutrient content of the meals were compared between obese and lean groups using nonpaired *t* tests. Two-way (time by obesity status) repeated measures analyses of variance (ANOVA) were separately performed in acute exercise and control groups when analyzing interstitial glycerol, and O:I ratios over 8-h in lean and obese children. To assess the response to meal, changes in interstitial glycerol concentrations or ethanol O:I were calculated from one-hour dialysate samples collected before and after ingestion of each meal (the difference between 900 h and 1100 h for the response to breakfast and the difference between 1300 h and 1500 h for the response to lunch) and were compared between obese and lean groups using nonpaired *t* tests. Pearson product-moment *r* correlation was conducted to assess the relationship between the lipolytic response to breakfast and obesity status (BMI percentile). Percent changes in interstitial glycerol concentrations or ethanol O:I ratio were also calculated and two-way (meal time by obesity status) ANOVAs were separately performed in acute exercise and control groups.

To examine the effect of training intervention on fasting basal interstitial glycerol and nutritive blood flow, two-way (intervention by time) repeated measures ANOVA were performed. To examine the effect of exercise training on interstitial glycerol, and ethanol O:I ratios over 8-h, three-way (intervention by time by obesity status) repeated measures ANOVA were performed in the training group in lean and obese children before and after aerobic training intervention. Significant interactions were followed by *t*-tests with Bonferroni adjustment. Statistical analyses were completed using SPSS 16.0 (SPSS Inc., Chicago, IL) and the significance level was $p < 0.05$.

Results

Subject characteristics

Descriptive characteristics of the lean and obese groups are shown in Table 1. BMI percentile was different between the lean and obese by definition. Consistent with obesity status, obese had significantly higher body mass, fat mass, lean mass, plasma insulin, total cholesterol, triglyceride, HOMA-IR, and lower HDL cholesterol compared to lean. Obese children also had greater absolute $\text{VO}_{2\text{max}}$ and lower time to exhaustion during the maximal treadmill test compared to lean children. There were no differences in descriptive characteristics between obese and lean subjects in either acute exercise or control groups (data not shown), suggesting our randomization was successful.

Meal composition

There was no difference in meal composition within or between lean and obese groups for breakfast and lunch (see Table, Supplemental Digital Content 2, meal composition of breakfast and lunch for lean and obese children in the acute intervention group). In the subgroup of subjects who completed exercise training, there was no difference in meal composition before and after training (see Table, Supplemental Digital Content 3, meal composition of breakfast and lunch for lean and obese children in subgroups before and after training).

Glycerol and nutritive flow basal comparisons and response to breakfast

Fasting basal interstitial glycerol was not statistically different between obese and lean (347.2 ± 39.5 and 336.0 ± 29.4 μM for lean and obese, respectively). The obese group had a significantly higher ethanol O:I ratio (inversely related to nutritive blood flow) than the lean group during fasting (0.63 ± 0.03 and 0.72 ± 0.02 for lean and obese, respectively, $p < 0.05$), indicating lower rates of adipose tissue nutritive blood flow in obese and therefore lower rates of fasting glycerol release in obese considering the lack of difference in basal interstitial glycerol between obese and lean. The decrease in interstitial glycerol following breakfast was significantly greater in lean compared to obese (-194.7 ± 39.2 and -70.4 ± 32.3 μM in lean and obese, respectively, $p < 0.05$), regardless of acute intervention group. In addition, the magnitude of the decrease in glycerol following breakfast (lipolytic suppression) was inversely correlated with BMI percentile ($r = -0.30$, $p < 0.05$). Similarly, the change in ethanol O:I ratio following breakfast was significantly different between lean and obese (-0.05 ± 0.03 and 0.03 ± 0.01 in lean and obese, regardless of acute intervention group, $p < 0.05$). Furthermore, the change in ethanol O:I ratio following breakfast was also positively correlated with increasing BMI percentile ($r = 0.26$, $p < 0.05$).

Acute exercise intervention

There was a main effect of time for interstitial glycerol in both the acute exercise condition (Figure 1A) and the control condition (Figure 1B). However, there was a higher overall interstitial glycerol in the obese compared to lean group ($p < 0.05$ for a main effect of obesity) in the control condition but not in the acute exercise condition, suggesting an effect of acute exercise in mitigating the differences between obese and lean.

A meal by adiposity interaction was detected in the acute exercise group (Figure 2A) because the antilipolytic response of breakfast was greater in lean than obese ($p < 0.05$) but the response to lunch was not different between these groups. Furthermore, there was a decreased antilipolytic response to lunch compared to breakfast in the lean group ($p < 0.05$). In the control condition there was also a decreased antilipolytic response to lunch compared to breakfast ($p < 0.05$ for a main effect of meal, Figure 2B).

Overall ethanol O:I ratio was significantly greater in obese than lean in the acute exercise condition ($p < 0.05$ for a main effect of obesity, Figure 3A) and there was a main effect of time in the control condition ($p < 0.05$, Figure 3B). The blood flow response to lunch was significantly improved compared to that of breakfast in obese ($p < 0.05$, Figure 4A). In the control group, there were no interaction or main effects (Figure 4B).

Effect of exercise training

Cardiorespiratory fitness was significantly improved with exercise training in both lean (absolute VO_2max from 1.49 ± 0.1 to 1.62 ± 0.1 L/min and time to exhaustion from 433 ± 27 to 464 ± 28 s, $p < 0.05$) and obese subjects (absolute VO_2max from 1.76 ± 0.08 to 1.90 ± 0.08 L/min and time to exhaustion from 332 ± 20 to 411 ± 21 s, $p < 0.05$), but there was no effect of exercise training on fasting blood variables (glucose, insulin, cholesterol, etc.) or body composition (data not shown). There were no effects of exercise training on fasting basal interstitial glycerol in either the lean or the obese group or two groups combined

(325.8 ± 30.5 and 307.7 ± 40.9 μM for pre and post training for two groups combined, respectively) or nutritive blood flow (0.69 ± 0.03 and 0.68 ± 0.03 for pre and post training for two groups combined, respectively).

In the subjects who completed exercise training, obese had higher overall interstitial glycerol values than lean ($p < 0.05$, main effect of obesity, Figure 5A&B) and overall interstitial glycerol was decreased over the 8-hour microdialysis sampling time both before and after training ($p < 0.05$, main effect of time). The effect of exercise training on reducing overall interstitial glycerol concentrations approached statistical significance ($p = 0.06$ for main effect of training).

There was no effect of training on subcutaneous adipose tissue blood flow in lean or obese. In the training intervention group, obese had an overall higher ethanol O:I (lower blood flow) compared to lean ($p < 0.05$, main effect of obesity, Figure 5C&D).

Discussion

The main novel finding of the study was that there was less suppression of lipolysis and a blunted increase in nutritive blood flow in subcutaneous abdominal adipose tissue in obese compared to lean children in response to breakfast that was improved at lunch, likely due to an intervening acute bout of aerobic exercise. Furthermore, exercise training did not provide alterations in meal-induced suppression of lipolysis or increases in blood flow in response to breakfast and lunch.

Interstitial glycerol following food intake

Following the ingestion of a meal, insulin stimulates the uptake of nutrients such as glucose into specialized tissues and also potentially inhibits lipolysis in adipocytes (4). Conditions such as obesity and Type 2 diabetes are characterized by a pathophysiological state in which these tissues become unresponsive to insulin, which contribute to the adverse long-term sequelae of related metabolic diseases (22). Fatty acid plasma concentrations, and rate of appearance from adipose tissue, are reduced by insulin less rapidly in obese adults than in those of normal body weight (9).

Earlier work from our lab has shown that lean children exhibited robust suppression of lipolysis in response to breakfast while obese children have minimal lipolytic suppression in response to breakfast (6). Furthermore, an acute bout of exercise normalized (made similar to lean) the antilipolytic response to lunch in obese children. However, the observation was based on a study that lacked a non-exercise control group. We now extend those findings by demonstrating the effect of acute exercise in increasing the postprandial suppression of lipolysis in subcutaneous adipose tissue in obese, but not lean children. In addition, the current study also demonstrates that in the control condition, where there was no intervening exercise between breakfast and lunch, the suppression of lipolysis following lunch was similar between obese and lean children.

It should be noted that there was diminished suppression of lipolysis in response to lunch compared to breakfast in the control group. Although the mechanism underlying this

diminished response following a second identical meal is not clear, it may be similar to the second-meal phenomenon previously reported in both lean and obese adults, which is the effect of a prior meal in decreasing the rise in blood glucose concentration following a subsequent meal (23, 24). Interestingly, postprandial glycaemia following the second meal was reported to be higher in the immediate post-exercise period compared to following rest (25), suggesting metabolic response is diminished with a second meal unless the second meal is preceded by an acute bout of exercise.

The potential mechanism for increased suppression in lipolysis after exercise in the obese children may be related to the antilipolytic effect of insulin. The obese children in our study were more insulin resistant than the lean (as reflected in higher HOMA scores), and acute exercise is known to increase insulin sensitivity. Acute exercise may therefore be used to improve insulin sensitivity, thereby normalizing lipolytic responses to food intake. An alternative hypothesis relates to the previous observation in that an acute bout of aerobic exercise activates antilipolytic α -2 adrenergic receptors in obese more than lean non-trained adults, despite comparable epinephrine and norepinephrine concentrations (26). It is possible that the increased α -2 adrenergic receptor sensitivity may contribute to the improved suppression of lipolysis in response to a subsequent meal in obese children following the acute exercise bout in our study.

Adipose tissue nutritive blood flow

Consistent with our previous study (6), we observed lower subcutaneous adipose tissue nutritive blood flow in obese children compared to lean children throughout the day, as indicated by a higher adipose tissue ethanol O:I ratio. Due to relatively small sample size (total $n=9$) in our previous study, we were unable to detect an effect of obesity on meal-induced changes in adipose nutritive flow (6). We have extended this previous work by now showing greater increases in subcutaneous adipose nutritive blood flow in lean compared to obese children following breakfast, with a negative correlation between increases in nutritive blood flow and BMI percentile in children. This is consistent with the previous report that glucose ingestion or mixed meal ingestion increases adipose tissue blood flow in lean, but not in the obese adults (10, 27). The mechanism of the post-prandial adipose tissue blood flow increase appears to be via stimulation of vascular beta-adrenoceptors in the subcutaneous adipose tissue, as continuous intravenous propranolol infusion abolishes the rise in post-prandial adipose tissue blood flow but does not affect the overall metabolic and hormonal response to the meal (28). Therefore, the post-prandial rise in adipose tissue blood flow is diminished in obese children, likely due to either a blunting of the beta-adrenergic mediated vasodilator response after a meal or due to a greater alpha adrenergic mediated vasoconstriction in the obese children. There was heterogeneity in the adipose tissue blood flow response to breakfast between subjects in the obese group in the intervention and control group. This may be due to the limitation with randomization of acute intervention. Although the responsiveness of adipose tissue blood flow to nutrient ingestion may be related to obesity, obesity only explains part of the variability in postprandial regulation of adipose tissue blood flow observed between subjects. Karpe et al. has shown that in adults, insulin sensitivity, not BMI, is significantly correlated with the responsiveness of adipose

tissue blood flow to nutrient ingestion, although BMI was significantly correlated with the indexes of insulin sensitivity (12).

The current study is also the first demonstration of improved postprandial nutritive blood flow after acute exercise in obese children. Acute exercise may have normalized the blood flow response to lunch through increased vasodilator response to beta-adrenergic stimulation and/or increased nitric oxide production. The exact mechanisms remains unclear and warrants further investigations, as this hold significance for increased cardiovascular disease risk in obese children.

Effect of exercise training

In isolated fat cells from both obese and nonobese adults, fasting and weight reduction cause a significant enhancement of sensitivity to the antilipolytic effects of insulin (29, 30). However, we observed a marginal lowering of lipolytic response to the meals, and no additional improvement in meal-induced increases in blood flow, with aerobic exercise training in children. This is consistent with previous studies on the effect of endurance exercise training on lipolysis and blood flow in adults. Ten days of endurance exercise training did not improve insulin-induced increases in adipose tissue nutritive blood flow in obese women (7). Lange et al. (31) have shown that endurance training did not affect subcutaneous abdominal adipose tissue lipolysis either at rest or during exercise, as reflected by similar levels of interstitial adipose tissue glycerol, subcutaneous abdominal nutritive flow, and plasma nonesterified fatty acids before and after completion of the training program in elderly women. Whole body lipolysis during exercise was not significantly impacted by exercise training in young normal weight women (32), obese women (33), or young men (34). In the current study, the effect of exercise training in lowering overall lipolysis approached statistical significance ($p=0.06$) in the training group, while no change was found in the control group. The reduced overall lipolysis may be considered an improvement in response (suppression) to the combined effect of two meals, and would be consistent with an improved antilipolytic response to insulin previously demonstrated in obese premenopausal women (7).

Limitations

Two limitations of this study should be considered. First, we did not employ a counterbalanced design for the acute exercise/control intervention to reduce the subjects' time commitment. However, there was a relatively large sample size with sufficient statistical power for this study. Second, we did not obtain blood samples during the microdialysis study visit in response to meals and exercise. While additional blood samples might provide further mechanistic insight at the whole-body level regarding the hormonal (e.g. insulin) effects, this would not be indicative of local hormonal concentrations in the studied adipose tissue depot, and would increase discomfort of children.

In summary, microdialysis gives novel information of adipose tissue lipolysis and nutritive blood flow in ambulatory lean and obese children throughout the day. The present data indicate there was a poor suppression of lipolysis and blunted increase in nutritive blood flow in subcutaneous abdominal adipose tissue in obese children compared to lean children

in response to breakfast that was improved at lunch. These improved responses were likely due to an intervening acute bout of aerobic exercise, as the responses were not seen in a no acute-exercise control group. Our data extend our understanding of the lipolytic profile in lean and obese children over the course of the morning to mid-afternoon in a controlled setting. While a 16-week aerobic exercise training program had a marginal benefit of lowering overall lipolysis over the course of the day, exercise training did not appear to improve meal-induced increases in blood flow. These studies underscore the important physiological role of acute exercise in improving postprandial lipid metabolism and blood flow in obese children, providing a basis for treatment of childhood obesity and concomitant cardiovascular disease. These beneficial effects were from acute bouts of exercise without further improvement with chronic exercise training, indicating that obese children should perform daily bouts of exercise or vigorous physical activity.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Figure 1.

Interstitial glycerol in the subcutaneous abdominal adipose tissue of LN and OB children in the acute exercise group (1A) and control group (1B) over the course of an 8-h period from the morning to midafternoon. Two-way (time by obesity status) repeated measures ANOVA were separately performed in acute EX and acute CON. § $p < 0.05$ for main effect of time; ‡ $p < 0.05$ for main effect of obesity

EX - acute exercise group; CON – control group.

Figure 2.

Percent change in interstitial glycerol in response to breakfast and lunch in LN and OB children in the acute exercise group (2A) and control group (2B). Two-way (time by obesity status) repeated measures ANOVA were separately performed in acute EX and acute CON.* $p < 0.05$ for meal by obesity interaction; § $p < 0.05$ for main effect of time. EX - acute exercise group; CON - control group.

Figure 3.

Ethanol O:I ratio (inversely related to nutritive blood flow) of LN and OB children in the acute exercise group (3A) and control group (3B) over the course of an 8-h period from the morning to midafternoon. Dialysate samples were collected from the subcutaneous abdominal adipose tissue and analyzed for ethanol concentration. Data are presented as the ethanol O:I ratio, which is inversely related to nutritive blood flow. ‡ $p < 0.05$ for main effect of obesity; § $p < 0.05$ for main effect of time.

EX - acute exercise group; CON - control group.

Figure 4.

Percent change in ethanol O:I ratio in response to breakfast and lunch in LN and OB children in the acute exercise group (4A) and control group (4B). Two-way (time by obesity status) repeated measures ANOVA were separately performed in acute EX and acute CON. * $P < 0.05$ meal by obesity interaction.

EX - acute exercise group; CON – control group.

Figure 5.

Interstitial glycerol in the subcutaneous abdominal adipose tissue of LN and OB children before exercise training (5A) and after 16-week aerobic exercise training (5B), and ethanol O:I ratio (inversely related to nutritive blood flow) of LN and OB children before exercise training (5C) and after 16-week aerobic exercise training (5D) over the course of an 8-h period from the morning to midafternoon. Three-way (intervention by time by obesity status) repeated measures ANOVA were performed in the training group in lean and obese children before and after aerobic training intervention. § $p < 0.05$ for main effect of time; ‡ $p < 0.05$ for main effect of obesity.

Pre-train – before exercise training; Post-train – after exercise training.

Table 1**Subject Characteristics**

	Lean (n=25)	Obese (n=40)
Age (y)	9.8±0.2	9.5±0.2
Tanner stage	1.2±0.1	1.2±0.1
Body mass (kg)	34.8±1.3	59.2±1.9 †
Height (cm)	144.9±1.8	147.8±1.1
BMI percentile (%)	41.2±3.9	97.4±0.3 †
Fat mass (kg)	6.5±0.6	25.2±1.3 †
Lean mass (kg)	26.5±1.1	31.7±0.8 †
Percent body fat (%)	17.6±1.8	42.2±1.0 †
Absolute VO _{2max} (L/min)	1.45±0.07	1.79±0.06 †
Time to exhaustion (s)	388±27	328±13 †
Glucose (mg/dl)	82.4±4.9	81.5±4.4
Insulin (microU/L)	6.4±0.6	11.6±1.2 †
Total cholesterol (mg/dl)	154.5±4.4	168.4±4.2 †
HDL cholesterol (mg/dl)	57.6±2.0	47.9±1.5 †
LDL cholesterol (mg/dl)	78.8±5.8	91.8±5.6
Triglyceride (mg/dl)	49.7±2.6	86.7±10.6 †
HOMA_IR	1.3±0.2	2.6±0.3 †

Values are means ± SE. Blood data are fasting.

HDL - high density lipoprotein; LDL - low density lipoprotein; VO_{2max} - maximal oxygen consumption; Time to exhaustion - time to exhaustion during the treadmill test

† P < 0.05 between lean and obese.