

Changes in Aerobic Capacity and Visceral Fat but not Myocyte Lipid Levels Predict Increased Insulin Action After Exercise in Overweight and Obese Men

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OBJECTIVE — To examine the effect of moderate intensity physical activity on the interactions between central abdominal adiposity, myocyte lipid content, and insulin action in overweight and obese, sedentary men.

RESEARCH DESIGN AND METHODS — Myocyte lipid (biochemical triglyceride and long-chain acyl CoA [LCAC] from vastus lateralis biopsy and soleus and tibialis anterior intramyocellular lipid by ¹H-magnetic resonance spectroscopy), regional body and abdominal fat (dual-energy X-ray absorptiometry and magnetic resonance imaging), serum lipids, insulin action (hyperinsulinemic-euglycemic clamp), and substrate oxidation were measured in 18 nondiabetic, sedentary, and overweight to obese men (aged 37.4 ± 1.3 years and BMI 30.9 ± 0.7 kg/m², range 26.4–37.6) at baseline, after the first two to four bouts of aerobic exercise (55–70% of $\dot{V}O_{2max}$ for 40 min/session), and at completion of 4.1 ± 0.2 exercise sessions/week for 9.7 ± 0.5 weeks (postexercise measurements performed 24–36 h after the last exercise bout).

RESULTS — Mean whole body insulin-stimulated glucose uptake and basal fat oxidation rate increased 16 and 41%, respectively, after two to four bouts of exercise, without further increase at program end. Mean aerobic capacity increased 11%, and central abdominal fat decreased 5% at program end, but myocyte lipid levels were not significantly changed. Posttraining increases in insulin-stimulated glucose uptake were predicted by increase in aerobic capacity ($r = 0.726$, $P = 0.001$) and magnitude of reduction in visceral fat ($r = -0.544$, $P = 0.02$) and not by changes in myocyte lipid or LCAC levels.

CONCLUSIONS — These results suggest that in overweight and obese sedentary men, increase in insulin sensitivity with moderate intensity exercise is predicted by improvement in aerobic capacity and reduction in visceral fat but is independent of myocyte triglyceride or LCAC levels.

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Central adiposity and insulin resistance represent two important risk factors for type 2 diabetes and cardiovascular disease. There is a strong negative correlation between abdominal fat and insulin sensitivity (1,2), but the

mechanisms underlying the relationship remain incompletely understood. Muscle triglyceride and long-chain acyl CoA (LCAC) levels also show strong negative associations to insulin sensitivity in animal models (3–5) and in humans (1,6–13).

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Abbreviations: DXA, dual-energy X-ray absorptiometry; FFM, fat-free mass; ¹H-MRS, ¹H-magnetic resonance spectroscopic; IMCL, intramyocellular lipid; LCAC, long-chain acyl CoA; SAT, subcutaneous abdominal adipose tissue; TAT, total abdominal adipose tissue; VAT, visceral adipose tissue.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

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In one hypothesis, these relationships suggest that abdominal fat could deliver excess lipid from metabolically labile abdominal adipocytes (14) to muscle, where lipid overabundance impairs muscle insulin action (15).

Although exercise assists with weight control and improves serum lipid profile and insulin sensitivity in overweight and obese individuals, its effects on the relationship between muscle lipid metabolism and insulin action are not clear. Previous exercise training studies were often performed in lean college athletes, and there have been concerns about adipocyte contamination of muscle biopsy triglyceride measurements (16). Reports show an increase (17,18), no change (19–21), or a decrease (22) in muscle triglyceride levels with exercise training. Myocyte triglyceride content also appears paradoxically increased in insulin-sensitive endurance-trained athletes (23).

To further examine the relationships between exercise and insulin action, regional fat depots, and muscle lipids in the overweight, a moderate intensity aerobic exercise program was performed in overweight to obese, otherwise healthy, men. It was hypothesized that improved insulin action with exercise would show association to lipid availability in myocytes with a greater correlation to muscle LCAC (a metabolically active moiety of fatty acids [3]) levels than to the storage moiety of muscle triglyceride. Muscle lipid levels were measured by vastus lateralis biopsy content of both triglyceride (24) and LCAC, together with ¹H-magnetic resonance spectroscopic (¹H-MRS) quantification of intramyocellular triglyceride of soleus and tibialis anterior muscles (25,26).

RESEARCH DESIGN AND METHODS

Subject recruitment

Subjects were recruited by advertisement in local newspapers. In view of known

differences in body composition and abdominal fat between sexes, which may have increased complexity in subsequent analyses and correlations, a single-sex study was performed with men. Selection criteria included a sedentary lifestyle (<1 h moderate exercise/week) and BMI >25 kg/m² with stable weight in the preceding 6 months. Exclusion criteria included a glucose tolerance test diagnostic of diabetes (plasma glucose fasting \geq 7.0 mmol/l or 2 h \geq 11.1 mmol/l [27]); any history of cardiovascular disease; or use of tobacco, hypolipidemic, antihypertensive medications, or systemic steroids. The study protocol was approved by the Human Research Ethics Committee at St. Vincent's Hospital, Sydney.

Study design

Habitual physical activity was assessed by a Framingham Physical Activity Index–modified questionnaire (28) and aerobic capacity assessed at the first visit (week –1). Measurements of insulin action, substrate oxidation, body composition and abdominal fat, and muscle and serum lipids were performed a week later (week 0) and repeated (apart from body composition and abdominal fat) after performing two to four bouts of exercise in the following week (week +1). On completion of at least 6 weeks of aerobic exercise training, the investigations performed at week 0 were repeated at program end (week E), with aerobic capacity assessed after continued exercise a week later (week E+1). Postexercise measurements were performed 24–36 h after the last bout of exercise, with similar intervals on each visit. Muscle biopsy and ¹H-MRS were performed before insulin clamps on study days. Subjects were instructed not to make dietary changes during the study.

Exercise program

Subjects were instructed to perform aerobic exercise (brisk walking mixed with light jogging) 4–5 days per week for 40 min/session for a minimum of 6 consecutive weeks. Exercise intensity was targeted at 55–70% $\dot{V}O_{2max}$, judged with heart rate monitoring (Polar Electro Oy, Kempele, Finland). Subjects recorded exercise details in a diary and had regular monitoring contact.

Anthropometry

Measures were weight (nearest 0.1 kg), stadiometer height (barefoot, nearest

0.01 m), and waist circumference (nearest 0.5 cm) at the narrowest region between the lower edge of ribs and iliac crest. BMI was calculated as weight in kilograms divided by height in meters squared.

Aerobic capacity

A cycle ergometer (Monark Model 818E; Monark Exercise, Varberg, Sweden) and the modified YMCA protocol was used (29), performed under identical environmental conditions. This submaximal protocol allowed safe quantification of change in estimated $\dot{V}O_{2max}$ ($\dot{V}O_{2maxest}$) with training. Pre- and postexercise $\dot{V}O_{2maxest}$ were corrected for fat-free mass (FFM) as determined by dual-energy X-ray absorptiometry (DXA) instead of body weight to minimize bias from loss of fat with exercise.

Insulin action and substrate oxidation

Subjects fasted for 8 h overnight before each assessment. Intravenous cannulae were placed in each forearm, one for glucose and insulin infusions, the other retrogradely in a forearm warmed under a heating blanket for collection of arterialized plasma glucose measurements (YSI 2300; StatPlus, Yellow Springs Instruments, Yellow Springs, OH). After a 20-min rest, indirect calorimetry was performed with a ventilated hood system (Deltatrac; Datex, Helsinki, Finland) for 25 min and repeated during the last 25 min of the clamp. Measurements of oxygen consumption and carbon dioxide production allowed calculation of respiratory quotient and fat oxidation rate (30). After basal calorimetry, insulin was infused at 50 mU · m⁻² · min⁻¹ for 150 min. Plasma glucose measurements were obtained every 10 min and the glucose infusion rate adjusted to maintain plasma glucose close to 5.0 mmol/l. The steady-state glucose infusion rate, measuring whole body insulin-stimulated glucose uptake, was calculated over the last 40 min of the clamp and corrected for FFM.

Body composition

Subjects were assessed with DXA (software version 1.35y; Lunar DPX–Lunar Radiation, Madison, WI). Measurements included FFM, total body fat, and limb fat (the sum of arm and leg fat). Central abdominal fat was fat mass in a window 9.8 cm in vertical dimension with lower bor-

der at the level of the superior iliac crests; lateral dimensions of the window were adjusted to match lateral borders of the inferior costal margin (2).

Abdominal fat

A total of 16 axial T1-weighted magnetic resonance abdominal scans (5 mm thickness, 5-mm intervals) were obtained between levels of T12/L1 and L4/5 intervertebral discs using a 1.5 Tesla medical magnetic resonance scanner (General Electric, Milwaukee, WI). Fat was visually outlined on each slice using National Institutes of Health Image (Version 1.62, National Institutes of Health, Bethesda, MD) to allow measurement of visceral adipose tissue (VAT) (within the abdominal wall muscles) and subcutaneous abdominal adipose tissue (SAT) (between the skin and abdominal wall muscles) areas. Volumes of VAT and SAT were estimated by interpolation between scanned slices. Total abdominal adipose tissue (TAT) was the sum of VAT and SAT.

Soleus and tibialis anterior intramyocellular lipid

The right lower leg of each subject was scanned within an extremity coil (1.5 Tesla scanner; General Electric, Milwaukee, WI). Voxels were positioned in soleus (2×2×2 cm voxel size) and tibialis anterior (1.5×1.5×1.5 cm voxel size) muscles, visible interfascial fat avoided, and voxel sites matched in position at each appointment. Spectra were acquired by PRESS sequence (echo time 135 ms and repetition time 1,500 ms). Peak areas of proton resonances were estimated with time-domain fitting (AMARES; MRUI version 99.2, Eur. Union) with constraints to improve reliability of fitting. Gaussian lineshapes were assigned apart from a lorentzian lineshape for the water peak. Ratios for intramyocellular (IM) CH₂:CH₃ and extramyocellular (EM) CH₂:CH₃ peaks were 0.60 for soleus spectra and 0.70 for tibialis anterior spectra; the ratios were determined from analysis of well-deconvoluted spectra, similar to recent methods (31). Peak areas were corrected for T1 and T2 times. Intramyocellular lipid (IMCL) content was quantitated as the ratio between the proton resonance areas of IMCH₂ and creatine.

Vastus lateralis muscle biopsy

Local anesthetic (1% lignocaine) was infused subcutaneously ~20 cm above the

patella over the vastus lateralis muscle, usually of the right leg. Muscle biopsy was performed with a 6-mm diameter university college hospital needle with suction assistance. Specimens were immediately blotted for blood, frozen in liquid nitrogen, and stored at -80°C .

Muscle triglyceride assay

Before assay, 50 mg muscle was freeze-dried for 20 h and, using a dissecting microscope ($6.3\times$), the tissue was dissected free of extramyocellular fat and connective tissue, yielding ~ 10 mg dry muscle. This technique minimizes adipocyte contamination (24). Lipid extraction and colorimetric assay to quantitate muscle triglyceride were performed (32) and expressed as micromoles per gram of dry weight muscle.

Muscle LCAC assay

This assay was performed as previously described (3). LCAC extracted from 100–150 mg muscle was injected into a C18 column (Waters Nova-Pak) for high-performance liquid chromatographic identification of individual acyl CoA peaks (Waters 996 photodiode array). Quantification was by comparison of sample peak areas with the areas of acyl CoA standards. Total LCAC content was calculated as the sum of palmitoyl, palmitoleoyl, oleoyl, linoleoyl, and linolenoyl moieties, expressed as nanomoles per gram of wet weight muscle.

Serum chemistry

Radioimmunoassay was performed for serum insulin (Linco Research, St. Charles, MO). Fasting (~ 8 h) serum was assayed for total and HDL cholesterol, triglycerides (all by enzymatic colorimetry; Roche), free fatty acids (enzymatic colorimetry; Wako, Osaka, Japan), and apolipoprotein-B (immuno-turbidometric method; Roche).

Statistics

Data were analyzed using Statview 5 (SAS Institute, Cary, NC). Results are presented as the mean \pm SE unless otherwise stated. Repeated-measures ANOVA was used for within-subject comparisons of more than two measurements. Significance of change between pairs of measurements was assessed by paired *t* tests. Data were also analyzed for predictors of change in insulin action and abdominal fat, and the simple regression coefficient

(*r*) was used to express the magnitude of correlation. An α level of 0.05 was used.

RESULTS

Subject characteristics and exercise details

The 18 subjects were aged 37.4 ± 1.3 years (range 29–47), overweight to obese (BMI 30.9 ± 0.7 kg/m², range 26.4–37.6), with sedentary lifestyles (physical activity score 205 ± 3 , range 189–248) and low aerobic fitness ($\text{VO}_{2\text{maxest}}$ 47.8 ± 1.3 ml O₂ · min⁻¹ · kg FFM⁻¹, range 32.1–55.1, or 31.4 ± 0.9 ml O₂ · min⁻¹ · kg body wt⁻¹, range 21.2–37.3). All subjects were Caucasian. Plasma glucose was 5.4 ± 0.1 mmol/l fasting (range 4.6–6.1) and 7.0 ± 0.4 mmol/l 120 min post-75-g oral glucose (range 3.6–10.2). Impaired glucose tolerance was present in five subjects with one also having impaired fasting glucose (27). Five subjects had one first-degree relative with type 2 diabetes. Exclusion of subjects with impaired glucose tolerance or family history of type 2 diabetes did not alter the results, and these subjects were therefore included in analyses. Subjects completed 9.7 ± 0.5 weeks (range 6–15) of aerobic exercise with a frequency of 4.1 ± 0.2 sessions/week (range 2.8–5.6). Exercise was interrupted in some subjects because of unforeseen health, occupational, or personal reasons; the range in duration includes these interruptions with one 6-week period of uninterrupted exercise.

Aerobic capacity, whole body insulin sensitivity, and substrate oxidation rate

There was a significant increase of $\sim 11\%$ in aerobic capacity after the exercise program ($P = 0.001$; Fig. 1A). Insulin levels attained during hyperinsulinemic-euglycemic clamp did not differ between study days (week 0/baseline 111.9 ± 4.3 ; week +1/after two to four bouts 105.1 ± 4.6 ; week E/program end 111.6 ± 5.0 mU/l; $P = 0.45$). Insulin-stimulated glucose disposal increased significantly ($\sim 16\%$) after two to four bouts of exercise in the first week and remained significantly increased but did not increase further after several weeks exercise ($P = 0.006$ by repeated-measures ANOVA; paired *t* tests in Fig. 1B). Basal fat oxidation rates increased $\sim 41\%$ after two to four bouts of exercise in the first week and similarly did not increase further at pro-

gram end ($P = 0.006$ by repeated-measures ANOVA; paired *t* tests in Fig. 1C).

Body composition and abdominal fat

Weight and waist measurements did not change between baseline and after two to four bouts of exercise, although a significant reduction in waist circumference was detected at program end ($P = 0.0006$ vs. baseline) (Table 1). Compared with baseline, subjects showed a significant but small ($\sim 2\%$) increase in limb FFM at program end ($P = 0.02$) and an approximate 5% decrease in central abdominal fat mass ($P = 0.01$). This was consistent with an approximate 5% decrease in TAT ($P = 0.01$) by magnetic resonance imaging, with VAT being $\sim 5.5\%$ lower ($P = 0.06$) and SAT $\sim 4.5\%$ lower ($P = 0.007$). There were no significant changes in the ratios of central abdominal fat to limb fat, VAT to SAT, or VAT to limb fat after the exercise program.

Serum lipids

Serum cholesterol was lower ($\sim 10\%$, $P = 0.005$) after the exercise program compared with baseline, as were serum triglycerides ($\sim 36\%$ lower, $P = 0.01$), with triglycerides reduced $\sim 31\%$, even after two to four bouts of exercise ($P = 0.04$) (Table 1). There were no significant changes in HDL cholesterol, free fatty acids, or apolipoprotein B levels.

Muscle lipids

No significant change in IMCL content of soleus or tibialis anterior muscles was detected after two to four bouts of exercise or at program end (soleus $P = 0.50$, tibialis anterior $P = 0.66$ by repeated measures ANOVA) (Table 1). Vastus lateralis biopsy also showed no significant change in muscle triglyceride and LCAC after two to four bouts of exercise and at program end compared with baseline (triglyceride $P = 0.15$, LCAC $P = 0.25$ by repeated-measures ANOVA).

Factors predicting change in insulin sensitivity

Change in insulin sensitivity between baseline and program end correlated to change in aerobic capacity ($r = 0.73$, $P = 0.001$; Fig. 2A) and VAT ($r = -0.54$, $P = 0.02$; Fig. 2B) such that a greater increase in aerobic capacity or a greater decrease in VAT predicted a greater increase in insu-

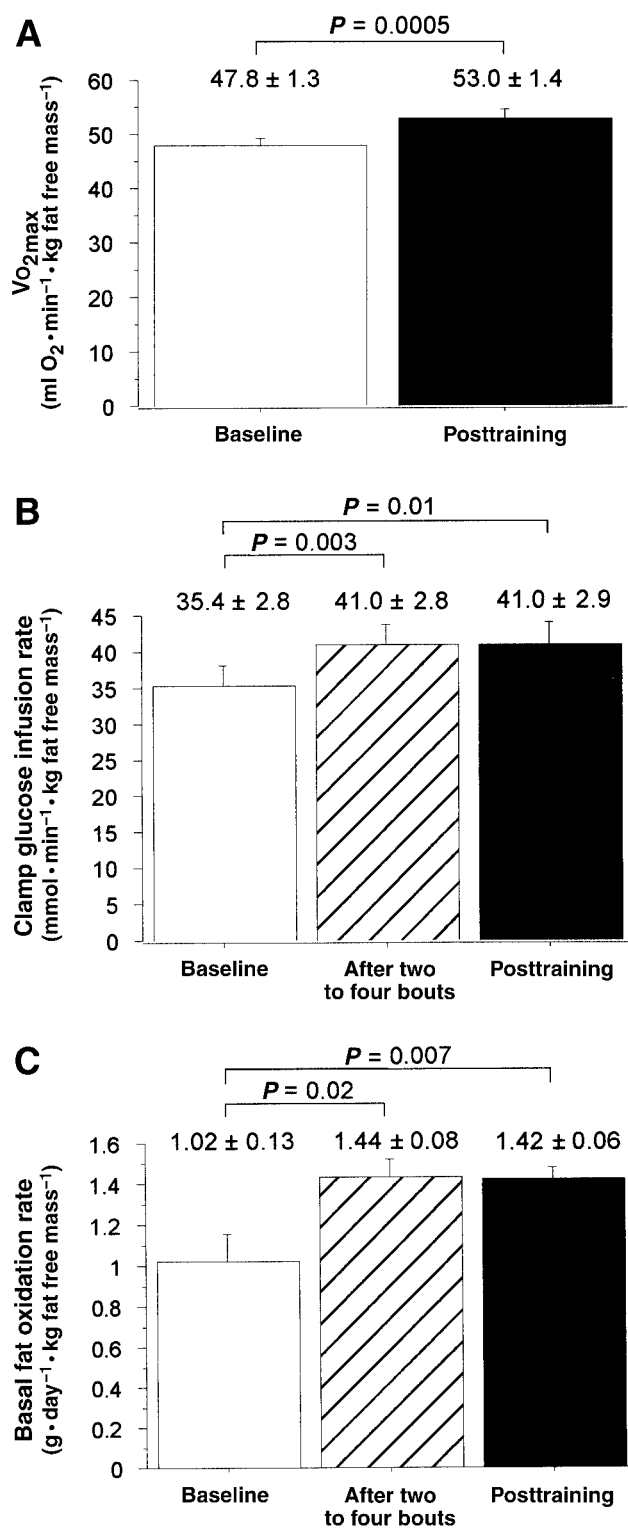


Figure 1—Measurements of estimated Vo_{2max} (A), clamp glucose infusion rates (B), and basal fat oxidation rates (C) taken at baseline, after two to four bouts of exercise (for B and C only), and at program end. Values shown are means \pm SE. P values stated are for the paired t tests between pairs of values indicated.

lin sensitivity. VAT change also correlated negatively with change in aerobic capacity ($r = -0.67$, $P = 0.003$; Fig. 2C).

Changes in VAT-to-SAT and VAT-to-limb fat ratios also correlated negatively to change in aerobic capacity (VAT-to-SAT

ratio $r = -0.56$, $P = 0.02$; VAT-to-limb fat ratio $r = -0.66$, $P = 0.004$) and insulin sensitivity (VAT-to-SAT ratio $r = -0.51$, $P = 0.03$; VAT-to-limb fat ratio $r = -0.54$, $P = 0.02$). Changes in other regional fat measures, muscle lipids, serum lipids, or fat oxidation rate did not show a significant relationship to changes in insulin sensitivity or aerobic capacity with the exercise program.

Subgroup analysis according to upper and lower 50th percentiles of BMI were limited in statistical power ($n = 9$ in each group), but in general, results were not different between the two groups (data not shown).

CONCLUSIONS— These results confirm that in overweight and obese men, there were increases in insulin action ($\sim 16\%$) and fat oxidation rate ($\sim 41\%$) 24–36 h after two to four bouts of moderate intensity exercise. These group improvements were not increased further after at least 6 weeks of moderate aerobic exercise, which increased mean aerobic capacity by $\sim 11\%$. As there was heterogeneity in response to the exercise program, however, correlative analyses showed that subjects with greater improvement in aerobic capacity did show greater increases in insulin sensitivity and reduction in VAT but did not show a relationship to changes in myocyte triglyceride or LCAC content.

Previous reports have shown that insulin sensitivity after exercise training matches pretraining levels when studied 4 days after the last bout of exercise (33). Exercise-trained athletes also show no difference in insulin sensitivity compared with sedentary control subjects when studied 4–10 days after the last bout of exercise (34–37), suggesting that there is no additional effect of exercise training on insulin sensitivity beyond the last bout of exercise. The measurements taken at the shorter postexercise interval in this study (24–36 h) demonstrate, however, that there appears to be a detectable greater improvement in insulin action seen in subjects who achieved greater improvement in aerobic capacity compared with those with lesser improvement. This suggests that exercise training may still impart greater improvements in insulin sensitivity, if only for the brief period postexercise before insulin action declines to preexercise levels. The number of subjects who achieved greater increases

Table 1—Changes in body composition, regional fat, muscle lipid, and serum lipids during the exercise program

| | Baseline | Two to four bouts | Program end |
|--|---------------|-------------------|---------------|
| Anthropometry | | | |
| Weight (kg) | 94.1 ± 2.0 | 94.1 ± 2.0 | 92.8 ± 2.0 |
| BMI (kg/m ²) | 30.9 ± 0.7 | 30.8 ± 0.7 | 30.4 ± 0.8 |
| Waist (cm) | 105.0 ± 1.5 | 105.0 ± 1.5 | 103.0 ± 2.0*† |
| DXA | | | |
| FFM (kg) | | | |
| Total | 62.0 ± 1.3 | — | 62.6 ± 1.3 |
| Limb | 29.5 ± 0.7 | — | 30.1 ± 0.8* |
| Fat (kg) | | | |
| Total | 32.3 ± 1.5 | — | 30.9 ± 1.5* |
| Central abdominal | 2.37 ± 0.10 | — | 2.25 ± 0.10* |
| Limb | 13.2 ± 0.7 | — | 12.8 ± 0.7 |
| Central abdominal-to-limb fat ratio | 0.184 ± 0.008 | — | 0.181 ± 0.008 |
| Abdominal MRI | | | |
| TAT (l) | 6.11 ± 0.32 | — | 5.81 ± 0.34* |
| SAT (l) | 3.88 ± 0.31 | — | 3.70 ± 0.31* |
| VAT (l) | 2.23 ± 0.12 | — | 2.11 ± 0.12 |
| VAT-to-SAT ratio | 0.63 ± 0.05 | — | 0.62 ± 0.05 |
| VAT-to-limb fat ratio (ml/g) | 0.178 ± 0.014 | — | 0.173 ± 0.013 |
| Serum lipids | | | |
| Total cholesterol (mmol/l) | 4.84 ± 0.22 | 4.63 ± 0.21 | 4.35 ± 0.21*† |
| HDL cholesterol (mmol/l) | 0.77 ± 0.04 | 0.78 ± 0.04 | 0.81 ± 0.05 |
| Triglycerides (mmol/l)‡ | 2.35 ± 0.59 | 1.60 ± 0.22§ | 1.50 ± 0.15 |
| Free fatty acids (mmol/l) | 0.42 ± 0.03 | 0.42 ± 0.02 | 0.45 ± 0.03 |
| Apolipoprotein B (g/l) | 1.07 ± 0.05 | NA | 1.03 ± 0.05 |
| ¹H-MRS | | | |
| Intramyocellular lipid (IMCH2-to-creatinine ratio) | | | |
| Soleus | 11.1 ± 0.8 | 11.7 ± 0.8 | 11.6 ± 0.8 |
| Tibialis anterior | 6.1 ± 0.8 | 5.7 ± 0.8 | 5.5 ± 0.7 |
| Vastus lateralis biopsy | | | |
| Muscle triglyceride (μmol/g dry wt) | 36.6 ± 4.9 | 27.5 ± 3.3 | 28.9 ± 3.8 |
| Muscle LCAC (nmol/g wet wt) | 3.77 ± 0.29 | 3.44 ± 0.27 | 3.26 ± 0.33 |

Data are mean ± SE. *P < 0.05 for program end vs. baseline; †P < 0.05 for program end vs. two to four bouts; ‡serum triglycerides were log-transformed for statistical tests; §P < 0.05 for two to four bouts vs. baseline.

in aerobic capacity in the present study were, however, not large, and this observation would need further confirmation.

An alternative explanation, perhaps less likely, is that subjects with greater improvement in aerobic capacity in this study performed a more intense final bout of exercise immediately preceding the program end measurements compared with subjects with lesser improvement in aerobic capacity. Although we are not aware of any data in the literature to estimate whether such an effect is likely to arise from our study design, this possibility could have resulted in different increases in insulin sensitivity (38,39), leading to interpretation as an apparent training effect. Regardless of the reasons

underlying this finding, the study data are in general consistent with previous studies indicating that maintenance of regular exercise in overweight men is important in sustaining enhanced insulin sensitivity and fat oxidation rate.

The observation that change in VAT was the only fat depot to correlate with the change in aerobic capacity and insulin sensitivity is of interest. There is a tendency for greater loss of VAT compared with other fat depots after calorie restriction (40–43), but a similar effect has not been shown with negative energy balance from increased exercise (44–46). In the present study, heterogeneity in exercise response prevented the demonstration of

significant group changes in mean VAT-to-SAT or VAT-to-limb fat ratios between baseline and program end. Correlative analyses, however, demonstrated significant negative relationships between both VAT-to-SAT or VAT-to-limb fat ratios to the changes in both aerobic capacity and insulin sensitivity. Thus, these results suggest a tendency for relatively greater visceral abdominal fat loss in subjects with greater increases in aerobic capacity and insulin sensitivity from exercise, although confirmation is required with larger studies. On one hand, this result is consistent with and emphasizes the view that visceral fat has a closer relationship to insulin sensitivity than other fat depots (47). It is not possible from our data, however, to determine whether the improvement in insulin sensitivity seen was related mainly to mechanisms resulting from an increased aerobic capacity, a reduction in visceral fat, or a combination of effects.

Although cross-sectional studies have shown a negative correlation between myocyte lipid and insulin action (1,6–13), there are a number of possible explanations for the lack of association between changes in both myocyte triglyceride and LCAC levels and the improvement in insulin sensitivity with exercise in this study. Increased extramyocellular adipocytes in muscles of overweight and obese men could have reduced accuracy of measurement of intramyocyte triglyceride levels. The finding of no overall change in myocyte LCAC content (which is minimally present in adipocytes) would, however, support the possibility that there was indeed little relationship between change in these myocyte lipid moieties and insulin action. It is possible that other lipid moieties, such as diacylglycerol and ceramide, could show a greater relationship to insulin action with exercise (15), but these possibilities remain to be studied.

There is also accumulating evidence of contraction-related cellular signaling and biochemical mechanisms, such as AMP kinase activation, which increase glucose uptake and metabolism as well as lipid oxidation without necessarily involving changes in proximal insulin signaling pathways (48–52). This raises the possibility that increased insulin sensitiv-

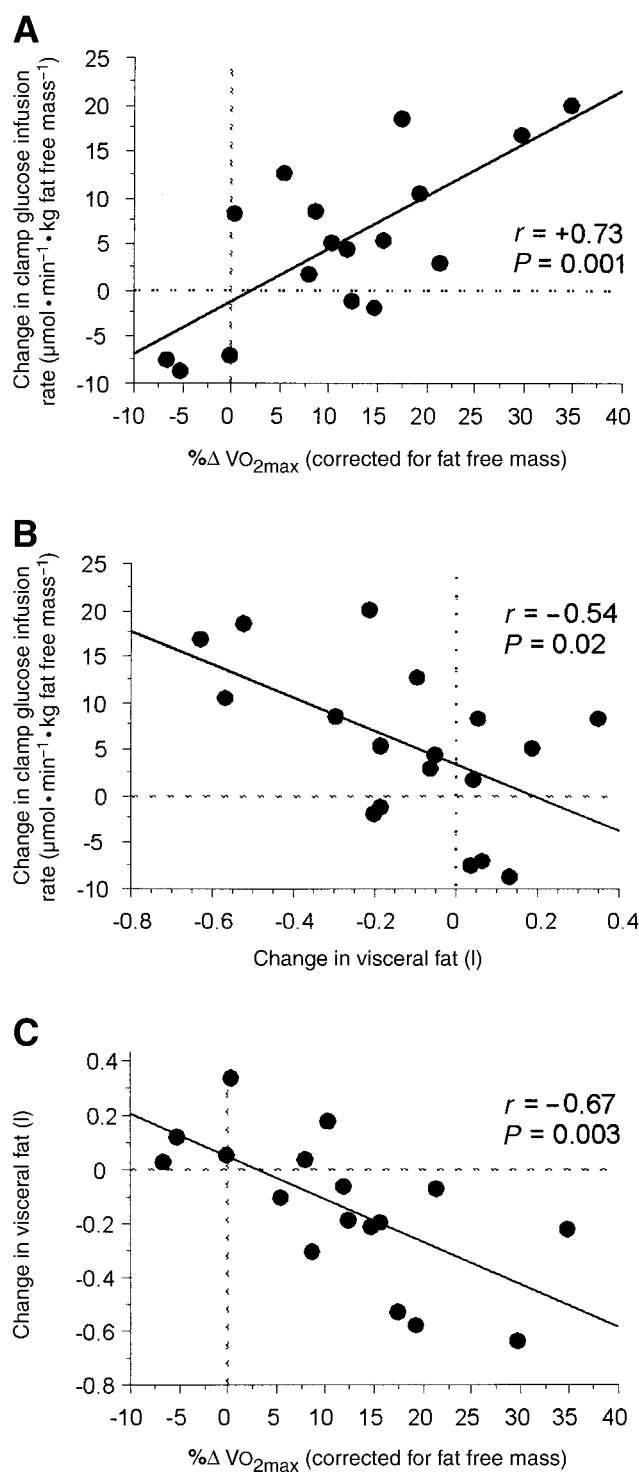


Figure 2—Correlations shown for the change between baseline and posttraining in clamp glucose infusion rate versus percentage change in estimated $\text{VO}_{2\text{max}}$ (A) and change in visceral abdominal fat volume (B). The correlation for the change in estimated $\text{VO}_{2\text{max}}$ versus the change in visceral abdominal fat volume is also shown (C). The simple regression coefficients (r) for each correlation and their respective P values are indicated.

ity after exercise may not necessarily show a simple relationship to measures of myocyte lipid availability per se.

The intensity of exercise and duration of exercise training performed in the present study may also have been signifi-

cant factors. Studies of acute exercise indicate that myocyte triglyceride may decrease during (53) and/or after (32,53–55) an exhaustive bout of exercise in lean trained subjects, although no change was recently reported after submaximal running (31). This supports a view that muscle triglyceride lipolysis occurs mainly with high-intensity, but not lower-intensity, exercise (38). The moderate-intensity exercise performed in this study, therefore, may have also contributed to the lack of change in myocyte triglyceride seen.

Thus, improvement of insulin sensitivity with moderate-intensity exercise in overweight to obese men is predicted by improvement in aerobic capacity, and VAT does not appear to relate to change in myocyte triglyceride and LCAC levels. Mechanisms unrelated to myocyte triglyceride and LCAC levels appear primarily responsible for increased insulin sensitivity with exercise in overweight and obese men.

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