Are the reductions in triacylglycerol and insulin levels after exercise related?

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ABSTRACT

Moderate exercise improves insulin sensitivity and reduces triacylglycerol (triglyceride; TG) concentrations. We hypothesized that changes in insulin sensitivity are an important determinant of exercise-induced changes in postprandial TG concentrations. Altogether, 38 men and 43 women, all of whom were normotriglyceridaemic and normoglycaemic, each underwent two oral fat tolerance tests with different pre-conditions: control (no exercise) and prior exercise (90 min of exercise at 60% of maximal O2 uptake the day before). Venous blood samples were obtained in the fasting state and for 6 h after a high-fat mixed meal. In the control trial there were significant correlations between log fasting TG concentration and log fasting insulin concentration (r = 0.42, P < 0.0005) and between log postprandial TG response (area under the curve) and log postprandial insulin response (r = 0.48, P < 0.0005). Prior exercise reduced the fasting TG concentration by 18.2 ± 2.2% (mean ± S.E.M.) (P < 0.0005), the postprandial TG response by 21.5 ± 1.9% (P < 0.0005), the fasting insulin concentration by 3.8 ± 3.1% (P < 0.01) and the postprandial insulin response by 11.9 ± 2.5% (P < 0.0005). However, there was no relationship between the exercise-induced changes in log fasting TG and log fasting insulin (r = 0.08, P = 0.50), nor between the exercise-induced changes in log postprandial TG response and log postprandial insulin response (r = 0.04, P = 0.70). These data suggest that the reductions in fasting and postprandial TG levels elicited by a session of moderate-intensity exercise are not mediated by an increase in insulin sensitivity.

INTRODUCTION

Insulin resistance, probably the defining feature of the ‘metabolic syndrome’ [1], is associated with increased triacylglycerol (triglyceride; TG) concentrations in the fasted and postprandial states [2–4]. As it is becoming increasingly clear that disturbances to lipid and insulin metabolism in the postprandial state are central to the aetiology of this syndrome [5], it is important to identify and understand interventions that lower postprandial TG concentrations and increase insulin sensitivity.

Postprandial concentrations of TG and insulin are reduced for a number of hours following an exercise session of even moderate intensity [6–14], suggesting that exercise can play a role in the management and prevention of the metabolic syndrome. However, there is considerable variation between individuals in the magnitude of these exercise-induced changes. Insulin sensitivity,
important determinant of the plasma concentration of TG [2–4] as well as that of insulin [4,15,16], is improved following a single exercise session [6,17,18]. We therefore hypothesized that changes in insulin sensitivity were an important determinant of exercise-induced changes in TG concentrations, and might therefore explain some of the variation between individuals in the magnitude of exercise-induced TG changes. To test this hypothesis, we examined the relationship between exercise-induced changes in fasting and postprandial TG and insulin concentrations in a group of 81 subjects, all of whom had undergone the same moderate-intensity exercise intervention.

**METHODS**

**Subjects**

Data obtained from 38 men (aged 21–60 years) and 43 women (aged 22–64 years) who had participated in studies investigating the effects of moderate exercise on postprandial TG metabolism [7–9,11–14] were analysed retrospectively. Some of the relevant subject characteristics are shown in Table 1. The subjects had a wide range of habitual physical activity levels, but all were apparently healthy non-smokers. They were normoglycaemic and normotriglyceridaemic, with no history of cardiovascular or metabolic disease. None was taking drugs known to affect lipid or carbohydrate metabolism. Six subjects (three men) possessed the E3/2 apolipoprotein (apo) E phenotype, 54 (27 men) possessed the E3/3 phenotype, 17 (seven men) possessed the E4/3 phenotype, and one man possessed the E4/2 phenotype.

In three women the apo E phenotype was not known. All subjects gave informed consent, and the studies were conducted in accordance with the Declaration of Helsinki and approved by the Loughborough University Ethical Advisory Committee.

**Study design**

The experimental protocol, which was common to all studies from which subjects were drawn, has been described previously in detail [7–9,11–14]. Briefly, subjects participated in two oral fat tolerance tests, in random order and with different pre-conditions, separated by an interval of 5–10 days. On the afternoon prior to one test, subjects walked or jogged (according to their exercise capacity) on a treadmill [7–9,11–13] or cycled on a stationary ergometer [14] for 90 min at an intensity corresponding to 61.9 ± 4.0% (mean ± S.D.) of maximal oxygen uptake ($V_{O_{2,\max}}$) (prior exercise). ($V_{O_{2,\max}}$ was determined directly for 70 subjects [7–9,12–14], but was predicted on the basis of submaximal tests in 11 postmenopausal women [11]). No exercise was performed on the afternoon preceding the other oral fat tolerance test (control).

Subjects reported to the laboratory after a 12 h fast at around 08.00 hours. A cannula was placed in an antecubital or forearm vein and, after a 10 min interval, a blood sample was obtained. Subjects then consumed a test meal comprising cream, oats, chocolate, sultanas, nuts and fruit, which provided (per kg body mass) 1.2 ± 0.1 g of fat, 1.2 ± 0.1 g of carbohydrate, 0.2 ± 0.05 g of protein and 71 ± 6 kJ of energy (means ± S.D.) (66% of energy from fat, 29% from carbohydrate and 5% from protein). Each subject consumed exactly the same meal in both tests. Further blood samples were taken 30 min after completion of the meal and then hourly for 6 h, always when subjects had been supine for at least 10 min. During the observation period subjects rested and only water was consumed; this was provided ad libitum in the first test and consumption was replicated in the second test.

Diet and exercise were carefully controlled prior to fat tolerance testing. Subjects weighed and recorded their dietary intake during the 2 days leading up to their first test, and replicated this exactly prior to their second test. No exercise was permitted for 3 days before each test (other than the controlled exercise session), only activities of daily living. Subjects abstained from alcohol consumption on the day before each test. We have shown previously that the reproducibility of the TG and insulin responses to the test meal is good when preceding diet, exercise and alcohol consumption are controlled in this way [19].

**Analytical methods**

Plasma or serum was separated from whole blood by centrifugation. Plasma was analysed for high-density lipoprotein (HDL) cholesterol (after precipitation of apo B-containing lipoproteins), total cholesterol, TG and glucose by enzymic colorimetric methods (all from

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**Table 1** Physical characteristics, fasting plasma lipoprotein lipids and fasting serum insulin for the subjects

<table>
<thead>
<tr>
<th>Parameter</th>
<th>All</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>$n$</td>
<td>81</td>
<td>38</td>
<td>43</td>
</tr>
<tr>
<td>Age (years)</td>
<td>41.2 ± 12.0</td>
<td>39.3 ± 12.4</td>
<td>42.9 ± 13.0</td>
</tr>
<tr>
<td>BMI (kg m$^{-2}$)</td>
<td>23.9 ± 2.3</td>
<td>24.7 ± 2.6</td>
<td>23.3 ± 1.8**</td>
</tr>
<tr>
<td>$V_{O_{2,\max}}$ (ml kg$^{-1}$ min$^{-1}$)</td>
<td>41.2 ± 9.9</td>
<td>45.0 ± 9.0</td>
<td>37.2 ± 8.9**</td>
</tr>
<tr>
<td>Total cholesterol (mmol l$^{-1}$)</td>
<td>4.69 ± 0.99</td>
<td>4.52 ± 0.98</td>
<td>4.85 ± 0.98</td>
</tr>
<tr>
<td>HDL cholesterol (mmol l$^{-1}$)</td>
<td>1.39 ± 0.39</td>
<td>1.16 ± 0.32</td>
<td>1.60 ± 0.33**</td>
</tr>
<tr>
<td>Fasting TG (mmol l$^{-1}$)</td>
<td>0.89 ± 0.40</td>
<td>0.98 ± 0.44</td>
<td>0.81 ± 0.36*</td>
</tr>
<tr>
<td>Fasting insulin (pmol l$^{-1}$)</td>
<td>8.3 ± 3.9</td>
<td>10.6 ± 4.2</td>
<td>6.3 ± 2.2**</td>
</tr>
</tbody>
</table>

* Statistical analyses were performed on logarithmically transformed data.
Boehringer Mannheim G.m.b.H., Lewes, E. Sussex, U.K.) using a centrifugal analyser (Cobas Bio or Cobas-Mira; Roche, Basle, Switzerland). Serum was analysed for insulin by RIA (COAT-A-COUNT Insulin; Diagnostic Products Corp., Los Angeles, CA, U.S.A.). All samples for one subject were analysed in the same run where possible. Quality control sera (from Roche, Boehringer Mannheim, Sigma and Sero AS, Billingstad, Norway) were used to ensure accuracy and precision. Within-batch coefficients of variation were ≤ 1.3% for TG, ≤ 1.2% for glucose and ≤ 4.5% for insulin. Apo E phenotypes were determined by isoelectric focusing using Western blot techniques [20].

**Calculations and statistics**

The postprandial TG, glucose and insulin responses to the test meal were defined as the 6 h areas under the postprandial TG, insulin and glucose concentration against time curves respectively, calculated using the trapezium rule. The incremental TG response was quantified as the area under the TG concentration against time curve after subtraction of the fasting TG concentration from each TG value. The homeostasis model assessment (HOMA) was used as a validated index of insulin sensitivity [21]. Differences in responses between the control and prior exercise tests were assessed using paired \( t \)-tests, those between men and women using unpaired \( t \)-tests, and those between groups with different apo E phenotypes using ANOVA. Relationships between variables were evaluated using Pearson product-moment correlation coefficients. Fasting TG and insulin concentrations and their postprandial responses were not normally distributed, and were therefore transformed prior to statistical analysis. Significance was adopted at the 5% level. Data are presented as means ± S.E.M. unless otherwise stated. Statistical analyses were performed using Minitab 13 (Minitab Ltd, Coventry, U.K.).

**RESULTS**

**Plasma and serum concentrations in the control trial**

Fasting and postprandial TG, insulin and glucose concentrations are shown in Figure 1. Fasting and postprandial TG levels were significantly related to fasting and postprandial insulin levels and to HOMA (see Table 2 for values). It is, however, interesting to note that the insulin indices were poorer predictors of the incremental TG response than of either fasting TG concentrations or total postprandial TG responses.

Log fasting TG concentration was a strong predictor of log postprandial TG response \( (r = 0.88, P < 0.0005) \), but was correlated to a lesser extent with log incremental TG response \( (r = 0.41, P < 0.0005) \). Log fasting insulin concentration was correlated strongly with HOMA \( (r = 0.92, P < 0.0005) \) and with log postprandial insulin response \( (r = 0.78, P < 0.0005) \). HOMA was also strongly correlated with log postprandial insulin response \( (r = 0.85, P < 0.0005) \).
There were significant inter-relationships between indices of fatness [body mass index (BMI), waist circumference, sum of skinfolds], age and fasting on the one hand, and postprandial TG and insulin responses on the other. There was no significant correlation between $V_{O_2,\text{max}}$ and TG or insulin concentrations or responses. These relationships are summarized in Table 3.

### Effects of exercise on TG and HDL cholesterol

Exercise reduced fasting TG concentration by a mean of $18.2 \pm 2.2\%$ (control, $0.89 \pm 0.04$ mmol·l$^{-1}$; prior exercise, $0.71 \pm 0.04$ mmol·l$^{-1}$; $P < 0.00001$), the postprandial TG response (6 h area under the curve) by $21.5 \pm 1.9\%$ (control, $9.29 \pm 0.44$ mmol·l$^{-1}$·h; prior exercise, $7.21 \pm 0.38$ mmol·l$^{-1}$·h; $P < 0.00001$) and the incremental TG response by $21.9 \pm 3.1\%$ (control, $3.95 \pm 0.24$ mmol·l$^{-1}$·h; prior exercise, $2.95 \pm 0.20$ mmol·l$^{-1}$·h; $P < 0.00001$) (see Figure 1). There was no effect of exercise on the fasting HDL cholesterol concentration (control, $1.39 \pm 0.04$ mmol·l$^{-1}$; prior exercise, $1.40 \pm 0.04$ mmol·l$^{-1}$; $P = 0.66$). There was a strong correlation between exercise-induced changes in log fasting TG concentration and log postprandial TG response ($r = 0.82, P < 0.0005$). By contrast, the exercise-induced change in log fasting TG concentration was not significantly related to the change in log incremental TG response ($r = 0.16, P = 0.16$).

Of the 81 subjects, 68 (32 men) had a lower fasting TG concentration after exercise and 73 (35 men) had a lower postprandial TG response after exercise, but there was wide individual variation in the magnitude of the exercise-induced changes (Figure 2). There were no differences between men and women in the exercise-induced decreases in either fasting TG (men, $18.6 \pm 3.3\%$; women, $17.8 \pm 3.0\%; P = 0.85$) or the postprandial TG response (men, $23.5 \pm 2.7\%$; women, $19.8 \pm 2.7\%; P = 0.34$). Similarly, there were no differences between subjects possessing the E3/2, E3/3 and E4/3 apo E phenotypes in the magnitude of the exercise-induced decreases in fasting TG (apo E3/2, $19.9 \pm 3.5\%$; apo E3/3, $18.5 \pm 2.7\%$; apo E4/3, $16.9 \pm 5.5\%; P = 0.94$) and the postprandial TG response (apo E3/2, $22.6 \pm 3.0\%$; apo E3/3, $21.9 \pm 2.4\%$; apo E4/3, $20.6 \pm 4.8\%; P = 0.96$). The man possessing the apo E4/2 phenotype had a 37.1% reduction in fasting TG and a 34.4% reduction in the postprandial TG response after exercise.

There were no significant correlations between age, BMI, waist circumference or sum of four skinfolds on the one hand and exercise-induced changes in log fasting TG, log postprandial TG response or log incremental TG response on the other. There were also no significant correlations between control trial values of log fasting insulin concentration, HOMA or log postprandial insulin response and exercise-induced changes in any of the TG indices. Control trial values for log postprandial TG response and log incremental TG response were not significantly related to the exercise-induced changes in any of the TG indices, although log fasting TG concentration in the control trial was a significant predictor of the exercise-induced decrease in log fasting TG concentration ($r = 0.32, P = 0.004$), but not of the decreases in either the postprandial or incremental TG responses. There were significant correlations between $V_{O_2,\text{max}}$ and the exercise-induced changes in log post-

### Table 2 Correlations between TG, insulin and HOMA in the control trial

All data except for HOMA scores were logarithmically transformed for statistical analysis. Postprandial responses were defined as the area under the postprandial concentration against time curve. The incremental TG response was defined as the area under the postprandial concentration against time curve above the fasting concentration. *Correlation significant at the $P < 0.05$ level.

<table>
<thead>
<tr>
<th></th>
<th>Fasting TG</th>
<th>Postprandial insulin response</th>
<th>Incremental TG response</th>
<th>Fasting insulin</th>
<th>Postprandial insulin response</th>
<th>HOMA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting TG</td>
<td>0.42*</td>
<td>0.48*</td>
<td>0.46*</td>
<td>0.19</td>
<td>0.24*</td>
<td>0.29*</td>
</tr>
<tr>
<td>Postprandial TG response</td>
<td>0.40*</td>
<td>0.48*</td>
<td>0.44*</td>
<td>0.08</td>
<td>0.05</td>
<td>0.34*</td>
</tr>
<tr>
<td>Incremental TG response</td>
<td>0.28*</td>
<td>0.33*</td>
<td>0.29*</td>
<td>-0.09</td>
<td>-0.16</td>
<td>-0.08</td>
</tr>
</tbody>
</table>

### Table 3 Correlations between physical characteristics and TG and insulin data in the control trial

All TG and insulin data except for HOMA scores were logarithmically transformed for statistical analysis. Skinfold sites were biceps, triceps, suprascapular and suprailiac. Data are for $n = 81$, except $n = 60$. *Correlation significant at the $P < 0.05$ level.

<table>
<thead>
<tr>
<th></th>
<th>Fasting TG</th>
<th>Postprandial TG response</th>
<th>Incremental TG response</th>
<th>Fasting insulin</th>
<th>Postprandial insulin response</th>
<th>HOMA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.22*</td>
<td>0.31*</td>
<td>0.33*</td>
<td>0.19</td>
<td>0.24*</td>
<td>0.29*</td>
</tr>
<tr>
<td>BMI</td>
<td>0.35*</td>
<td>0.36*</td>
<td>0.23*</td>
<td>0.37*</td>
<td>0.49*</td>
<td>0.34*</td>
</tr>
<tr>
<td>Waist circumference†</td>
<td>0.49*</td>
<td>0.54*</td>
<td>0.46*</td>
<td>0.70*</td>
<td>0.73*</td>
<td>0.71*</td>
</tr>
<tr>
<td>Sum of four skinfolds†</td>
<td>0.40*</td>
<td>0.47*</td>
<td>0.42*</td>
<td>0.54*</td>
<td>0.59*</td>
<td>0.59*</td>
</tr>
<tr>
<td>$V_{O_2,\text{max}}$</td>
<td>-0.09</td>
<td>-0.16</td>
<td>-0.20</td>
<td>-0.02</td>
<td>-0.18</td>
<td>-0.08</td>
</tr>
</tbody>
</table>

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prandial TG response \( (r = 0.33, P = 0.003) \) and log incremental TG response \( (r = 0.32, P = 0.003) \), but not the change in log fasting TG \( (r = 0.19, P = 0.095) \). This, however, may reflect differences in the energy expended during exercise, rather than differences in \( V_{\text{O}_2\text{max}} \) per se, as the correlation between exercise energy expenditure (per kg body mass) and \( V_{\text{O}_2\text{max}} \) was high \( (r = 0.96, P < 0.0005) \). Exercise energy expenditure (per kg body mass) was significantly correlated with the exercise-induced changes in log postprandial TG response \( (r = 0.35, P = 0.002) \) and log incremental TG response \( (r = 0.35, P = 0.002) \).

**Effects of exercise on insulin, glucose and HOMA**

The insulin responses to the test meal are shown in Figure 1. Exercise induced a small \((6.6 \pm 2.9\%)\), but statistically significant, reduction in fasting insulin concentration in men (control, \(10.6 \pm 0.7 \mu\text{units} \cdot \text{ml}^{-1} \); prior exercise, \(9.6 \pm 0.6 \mu\text{units} \cdot \text{ml}^{-1}; P = 0.003\)), but not in women (control, \(6.3 \pm 0.3 \mu\text{units} \cdot \text{ml}^{-1} \); prior exercise, \(6.0 \pm 0.4 \mu\text{units} \cdot \text{ml}^{-1}; P = 0.31\)). Similarly, exercise induced a reduction in the HOMA score in men (control, \(2.47 \pm 0.20\); prior exercise, \(2.19 \pm 0.16; P = 0.002\)), but not in women (control, \(1.24 \pm 0.07\); prior exercise, \(1.16 \pm 0.08; P = 0.25\)). However, exercise reduced the postprandial insulin response in both men (control, \(179 \pm 18 \mu\text{units} \cdot \text{ml}^{-1} \cdot \text{h} \); prior exercise, \(156 \pm 14 \mu\text{units} \cdot \text{ml}^{-1} \cdot \text{h}; P < 0.0007\)) and women (control, \(93 \pm 4 \mu\text{units} \cdot \text{ml}^{-1} \cdot \text{h}; \) prior exercise, \(77 \pm 4 \mu\text{units} \cdot \text{ml}^{-1} \cdot \text{h}; P < 0.0001\)), with no significant difference between the sexes in the magnitude of the exercise-induced decrease (men, \(8.4 \pm 3.9\%\); women, \(15.0 \pm 3.2\%\); \(P = 0.19\)). The exercise-induced changes in log fasting insulin concentration and log postprandial insulin response were not significantly related \( (r = 0.19, P = 0.09) \). Of the 81 subjects, 52 (24 men) had a lower fasting insulin concentration after exercise, whereas 64 (28 men) had a lower postprandial insulin response after exercise (Figure 2). There were no significant correlations between age, BMI, waist circumference, sum of four skinfolds or \( V_{\text{O}_2\text{max}} \) on the one hand and exercise-induced changes in log fasting insulin, HOMA or log postprandial insulin response on the other. There were, however, significant correlations between log fasting insulin concentration and HOMA in the control trial and the exercise-induced changes in these indices \( (r = 0.29, P = 0.008 \text{ and } r = 0.55, P < 0.0005 \) respectively). No significant relationship existed between log postprandial insulin response and the exercise-induced change in this parameter \( (r = 0.15, P = 0.179) \).
Exercise induced a small, but statistically significant, decrease in the fasting glucose concentration (control, $4.72 \pm 0.07 \text{ mmol} \cdot \text{l}^{-1}$; exercise, $4.64 \pm 0.07 \text{ mmol} \cdot \text{l}^{-1}$; $P = 0.04$), but conversely induced a small increase in the postprandial glucose response (control, $29.0 \pm 0.4 \text{ mmol} \cdot \text{l}^{-1} \cdot \text{h}^{-1}$; exercise, $29.4 \pm 0.4 \text{ mmol} \cdot \text{l}^{-1} \cdot \text{h}^{-1}$; $P = 0.03$) (Figure 1).

Relationship between change in TG and change in insulin with exercise

There were no significant relationships between exercise-induced changes in log fasting insulin, log postprandial insulin response or HOMA and changes in log fasting TG, log postprandial TG response or log incremental TG response when all subjects were considered together (Table 4). There were also no significant relationships between any of these indices when the data from men and women were analysed separately.

DISCUSSION

A session of dynamic, aerobic exercise of moderate intensity reduced fasting and postprandial TG concentration and postprandial insulin concentration in both men and women, and also lowered fasting insulin concentrations and the HOMA score in men. Thus exercise of this nature influences aspects of the metabolic syndrome for both sexes and over a wide range of ages.

Insulin sensitivity was not measured directly in the present study, but can be inferred from surrogate insulin concentration indices. HOMA is a validated index of insulin sensitivity which correlates strongly with insulin sensitivity, as assessed using the euglycaemic hyperinsulinaemic clamp ($r = 0.6–0.8$ in non-diabetic individuals) [15, 21]. However, in non-diabetic individuals such as the present subjects, the insulin response to dynamic metabolic stress is likely to provide the best indirect measure of insulin sensitivity. The insulin response to an oral glucose load correlates more strongly with clamp-assessed insulin sensitivity than HOMA [15], and the day-long insulin response to a test meal (containing both fat and carbohydrate) is highly correlated with insulin resistance determined from steady-state plasma glucose using a modified insulin suppression test ($r = 0.82$) [4]. Indeed, the insulin response following a mixed meal and steady-state plasma glucose were found to be equally predictive of lipid and lipoprotein variables in multivariate analysis [4]. Thus the insulin indices used in the present study, particularly the postprandial insulin response, provide valid surrogate measures of insulin sensitivity.

In agreement with previous studies, the present data demonstrate correlations between indices of insulin sensitivity and TG metabolism [2–4] in the unexercised state. In addition, the previously reported relationships between TG and insulin concentrations on the one hand and age and indices of body fatness on the other [22–24] are evident in the present data set. Interestingly, waist circumference was the best physical predictor of fasting and postprandial TG and insulin concentrations, probably due to its close association with visceral adiposity [25] – a key determinant of insulin resistance [26]. Additionally, our data demonstrate that physical fitness per se – as measured by $V_{O_{\text{max}}}$ – was not a predictor of TG or insulin concentrations in this group with a wide range of physical fitness levels. This is in accordance with the concept of a dissociation between ‘physical fitness’ and ‘metabolic fitness’ [27]. However, despite their clear associations with TG and insulin concentrations in the control trial, the exercise-induced changes in fasting and postprandial TG and insulin concentrations were unrelated to age or indices of body fatness. There was, however, a significant correlation between $V_{O_{\text{max}}}$ and the exercise-induced changes in the postprandial TG response and the incremental TG response. This, however, may not reflect differences in fitness per se, as subjects all performed 90 min of exercise at 60% of their own $V_{O_{\text{max}}}$, so fitter individuals performed exercise at a higher absolute intensity. The high correlation between $V_{O_{\text{max}}}$ and energy expended during exercise (per kg body mass) ($r = 0.96$) implies that these two variables were highly related. Our previous work suggests that the exercise-induced reduction in postprandial lipaemia is related to the energy expended during exercise [7, 8], and in the present study significant correlations existed between

Table 4 Correlations between exercise-induced changes in TG, insulin and HOMA

<table>
<thead>
<tr>
<th></th>
<th>Change in fasting insulin</th>
<th>Change in postprandial insulin response</th>
<th>Change in HOMA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change in fasting TG</td>
<td>0.08</td>
<td>0.05</td>
<td>0.05</td>
</tr>
<tr>
<td>Change in postprandial TG response</td>
<td>0.17</td>
<td>0.04</td>
<td>0.13</td>
</tr>
<tr>
<td>Change in incremental TG response</td>
<td>0.19</td>
<td>–0.05</td>
<td>0.17</td>
</tr>
</tbody>
</table>
energy expended during exercise (per kg body mass) and the exercise-induced changes in the postprandial TG response and the incremental TG response. Thus differences in energy expenditure, rather than differences in fitness, may be the underlying cause of the relationship between the exercise-induced decreases in TG and $\dot{V}_{\text{O}_2,\text{max}}$.

While a moderate-intensity exercise session influenced both TG and insulin concentrations, its effect on TG was greater and more consistent than its effect on insulin, suggesting that changes in insulin were not the primary determinant of the reduction in TG elicited by prior moderate exercise. Indeed, the fact that no relationships existed between the exercise-induced changes in any of the TG and insulin indices suggests that the mechanisms underlying the TG and insulin effects may be different. One point to note, however, is that exercise-induced decreases in both TG and insulin were greater in the postprandial state than when subjects were fasted, suggesting that measurements made on subjects in the postprandial state enable changes in metabolism to be detected with a greater degree of sensitivity than those made in the fasted state.

Exercise did not significantly reduce the fasting insulin concentration or the HOMA score in women (although it reduced their postprandial insulin response to the same extent as in men). This may be because the women in this subject group generally had low fasting insulin concentrations and HOMA scores, as significant correlations were observed between control trial fasting insulin concentrations and HOMA scores and the exercise-induced changes in these indices. It is unclear why this relationship between initial value and exercise-induced change should exist for fasting insulin and HOMA, but not for the postprandial insulin response, but this finding raises the possibility that exercise may reduce insulin concentrations to a greater extent in hyperinsulinaemic individuals. Control trial values of the insulin indices were not, however, significantly related to exercise-induced changes in any TG index, implying that exercise-induced changes in TG metabolism might not be influenced by an individual’s initial degree of insulin sensitivity.

The present study used a retrospective design to examine the relationship between exercise-induced changes in TG and insulin. This approach has potential limitations, particularly with respect to the standardization of experimental and environmental variables. However, addressing this research question requires the study of a large number of subjects, and the time-consuming and invasive nature of the investigations means that a retrospective study is the only feasible approach. All the experimental investigations were performed in the same laboratory, and the standardization of diet, alcohol consumption and physical activity on the days preceding the oral fat tolerance tests was identical for all subjects. All subjects performed 90 min of exercise at the same relative exercise intensity (~ 60% of $\dot{V}_{\text{O}_2,\text{max}}$). Each subject consumed exactly the same meal before the control and exercise trials. The meals for all subjects had the same macronutrient composition, with only a slight variation in energy provided by the test meal (per kg body mass) between studies (S.D. = 8%). Thus, although the present study pooled data from research performed over a 5-year period, the data drawn from the different studies are comparable.

It is well established that insulin sensitivity is improved following a single exercise session, and that these changes are evident 15–24 h after exercise [6,17,18], which corresponds with the observation period in the present study. Furthermore, recent evidence shows that glucose clearance across the leg after a mixed high-fat meal is increased on the day following a session of moderate exercise [28]. It is therefore reasonable to suggest that the changes in HOMA and the postprandial insulin response seen after exercise were the consequence of improved insulin sensitivity. However, as these indices provide a whole-body index of insulin sensitivity, it is not possible, from the present data, to determine which tissues elicited this effect. A number of studies have demonstrated that exercise improves insulin sensitivity in skeletal muscle, and these changes appear to be restricted predominantly to the exercised muscle [29,30]. Until recently it was believed that changes in skeletal muscle were solely responsible for the post-exercise increase in whole-body glucose uptake [30,31], whereas net hepatic glucose uptake was unchanged [32] or reduced [31] following exercise, implying that exercise-induced changes in insulin sensitivity were confined to (exercised) skeletal muscle. However, it has recently been suggested that net hepatic glucose uptake is increased by prior exercise [33], although this increase is quantitatively much smaller than the increase observed in skeletal muscle. Thus the weight of available evidence suggests that the changes in whole-body insulin sensitivity that are evident after exercise are mediated predominantly by changes in skeletal muscle. As a consequence, exercise-induced improvements in insulin sensitivity might only be expected to influence exercise-induced changes in TG metabolism if these also are predominantly a consequence of changes in exercised muscle.

Classic studies have demonstrated that prolonged, vigorous exercise can increase lipoprotein lipase (LPL) activity, principally in skeletal muscle [34–36], and therefore increase TG clearance [37–39]. However, more recent studies have shown that other mechanisms may be involved, at least when prior exercise is of moderate intensity. Specifically, the reduction in fasting and postprandial TG concentrations following a session of moderate-intensity exercise cannot be explained by increases in whole-body TG clearance [12], TG uptake into skeletal muscle [28] or skeletal muscle LPL activity.
Collectively, these findings suggest that changes in tissues other than skeletal muscle probably contribute to the decrease in plasma TG after exercise, and offer a possible explanation for the lack of a relationship between the exercise-induced changes in TG and insulin in the present study. While the effects of exercise on adipose tissue metabolism have not been extensively studied, it is unlikely that changes in this tissue are a major mediator of the exercise-induced decrease in TG concentration. Changes in adipose tissue LPL activity following vigorous exercise are an order of magnitude smaller than the changes in skeletal muscle [40], and adipose tissue blood flow in the postprandial state is not increased following moderate exercise [28]. This, taken together with the fact that TG clearance at a whole-body level is not increased following moderate exercise [12], suggests that increased TG uptake into adipose tissue would not have been a large determinant of the exercise-induced decrease in TG. Thus the mechanisms via which a session of moderate-intensity exercise reduce fasting and postprandial TG concentrations are not clear, but studies showing that these changes are characterized by large decreases in TG from very-low-density lipoprotein-sized particles imply that changes in hepatic TG metabolism (i.e. reduced hepatic TG secretion) may play an important role [13,28]. This possibility warrants further investigation.

An alternative explanation for our findings could be that the exercise-induced changes in TG concentration and insulin sensitivity were related, but that changes in HOMA and the postprandial insulin response do not accurately reflect changes in insulin sensitivity. It is possible that increased peripheral blood flow, secondary to increased insulin sensitivity but not reflected in circulating insulin concentrations, contributed to the exercise-induced decrease in TG concentration. Such an effect would have increased substrate availability to LPL and thereby facilitated TG clearance. However, because it seems likely that mechanisms other than increased TG clearance were largely responsible for the exercise-induced decrease in TG (for reasons described above), it is unlikely that increased blood flow – insulin-mediated or otherwise – was a major mediator of the exercise-induced decrease in TG. While it is also conceivable that changes in hepatic insulin sensitivity that were not reflected in our whole-body insulin indices influenced hepatic TG secretion, the extent to which this might have occurred is very difficult to quantify. Given the fact that the weight of evidence suggests that exercise-induced changes in insulin sensitivity occur largely in skeletal muscle [29–31], it is likely that the magnitude of this phenomenon (i.e. changes in hepatic insulin sensitivity not accounted for by changes in global insulin indices) would be relatively small, but this warrants further investigation. However, such studies would be difficult to undertake, as conventional tools to measure insulin sensitivity (e.g. glucose clamps) only assess whole-body insulin sensitivity, and direct assessment of hepatic insulin sensitivity requires extremely invasive experimental methods and are generally not performed using human subjects.

In conclusion, a session of moderate-intensity exercise reduces fasting and postprandial concentrations of TG and insulin in a majority of normotriglyceridaemic individuals, having beneficial effects on (at least) two features of the metabolic syndrome. However, the exercise-induced changes in TG and insulin appear to be unrelated, suggesting that the mechanisms responsible may be different. Our study highlights the fact that, although insulin resistance and TG concentration have been shown to be related in the present study and others [2–4], interventions that influence TG concentration might not necessarily affect insulin resistance.

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