Effects of prior moderate exercise on postprandial metabolism and vascular function in lean and centrally obese men

Short Running Title: Exercise and postprandial vascular function

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Structured Abstract

Objectives – We investigated whether a session of prior exercise could ameliorate postprandial endothelial dysfunction.

Background – Endothelial function is impaired following fat ingestion and this may be related to rises in triglyceride concentrations. Exercise reduces postprandial triglyceride concentrations.

Methods – Ten lean (waist <90cm) and 10 centrally obese (waist >100cm) middle-aged men each underwent two oral fat tolerance tests (blood taken fasting and for eight hours after a high-fat meal containing 80g fat and 70g carbohydrate). On the afternoon before one test, subjects performed a 90-minute treadmill walk (exercise); no exercise was performed before the control test. Endothelium-dependent and -independent microvascular function was assessed using laser Doppler imaging in the fasted state and at two hourly intervals during the eight-hour postprandial period.

Results – Exercise reduced both fasting and postprandial triglyceride concentrations by 25% in both the lean and centrally obese groups ($p<0.0005$). For all subjects taken together, exercise improved fasting endothelium-dependent function by 25% ($p<0.05$) and, although there was a significant postprandial decrease in both endothelium-dependent and -independent function in both the control and exercise trials ($p<0.01$), postprandial endothelium-dependent and -independent function were 15% and 20% higher, respectively, in the exercise trial than the control trial (both $p<0.05$).

Conclusions – A session of prior exercise improves fasting and postprandial vascular function in middle-aged men. This may be one mechanism by which exercise influences cardiovascular risk.

Keywords

Endothelial function, exercise, lipids, postprandial

Condensed Abstract

Endothelial function is impaired following fat ingestion. We investigated whether a session of prior exercise could ameliorate postprandial endothelial dysfunction in 20 middle-aged men. Subjects performed two oral fat tolerance tests: one on the day following a 90-minute treadmill walk, the other after no exercise. Exercise improved fasting endothelial function by 25% and postprandial endothelial function by 15% (both $p<0.05$). This may be one mechanism by which exercise influences cardiovascular risk.

Abbreviations list

LDL – low density lipoprotein

HDL – high density lipoprotein

VLDL – very low density lipoprotein

TG – triglyceride

NEFA – non-esterified fatty acid

IL-6 – interleukin-6

$\dot{V}O_2$ max – maximal oxygen uptake

ELISA – enzyme-linked immunoassay

ACh – acetylcholine

SNP – sodium nitroprusside

Introduction

Free living humans spend the majority of their lives in the postprandial state and the changes to metabolism seen during the hours following meal ingestion are likely to play an important role in the atherosclerotic disease process. It has been postulated that postprandial lipoproteins and their remnants directly infiltrate the arterial wall and accumulate in atheromatous plaques (1). Furthermore, high concentrations of postprandial lipoproteins facilitate the exchange of neutral lipids between triglyceride-rich and cholesterol-rich lipoproteins, promoting the atherogenic lipoprotein phenotype of small, dense LDL and low HDL (1).

More recent study has focused on non-lipid disturbances occurring in the postprandial state. It is now evident that systemic inflammation is increased (2,3) and that endothelial function is impaired (4,5) postprandially, with some studies reporting that the postprandial decrement in endothelial function is proportional to the postprandial triglyceride rise (4,5). As endothelial dysfunction and inflammation are central to atherogenic progression (6), it is likely that these transient postprandial changes, repeated on a daily basis, have implications for long-term risk of vascular disease. There is now a large body of evidence indicating that a single session of moderate exercise can reduce subsequent postprandial lipemia by ~20-25% (7). Thus, given the reported relationship between postprandial lipemia and endothelial dysfunction (4,5), we hypothesized that exercise of this nature could attenuate the postprandial decrement in endothelial function.

We chose to study centrally obese middle-aged men, a typical population at which exercise for health guidelines are targeted. We also included a comparative group of lean men. These two groups differ in insulin sensitivity (8) and exhibit marked differences in insulin-regulated postprandial glucose and lipid metabolism (9). A secondary aim of this study was to investigate whether the magnitude of exercise-

induced changes to postprandial metabolism would differ between these two subject groups with differing metabolic profiles.

Methods

Subjects

Ten lean men (waist circumference <90 cm) and 10 age-matched centrally obese (waist circumference >100 cm) men participated in this study. Their physical characteristics are shown in Table 1. All were apparently healthy normoglycemic non-smokers who displayed no symptoms of coronary artery disease during a clinical exercise stress test. None was taking any drugs thought to affect lipid or carbohydrate metabolism or vascular function. The study was conducted with the approval of North Glasgow University Hospitals NHS Trust Ethics Committee and subjects gave written informed consent prior to participation.

Study design

Subjects participated in two oral fat tolerance tests in a randomized, balanced design with an interval of 7-14 days and different pre-conditions. In one trial, subjects walked on a treadmill for 90 minutes at an intensity of ~50% of maximal oxygen uptake ($\dot{V}O_2$ max) (determined from a preliminary sub-maximal incremental treadmill test (10)) on the day prior to the oral fat tolerance test (exercise trial). In the other trial subjects performed no exercise on the day preceding the oral fat tolerance test (control trial).

Subjects weighed and recorded their dietary intake and abstained from alcohol for the two days prior to the first oral fat tolerance test and replicated this prior to the second fat tolerance test. In addition, subjects were instructed to perform no exercise, other than the treadmill walk in the exercise trial, during the three days preceding each oral fat tolerance test.

Treadmill walk

The walk in the exercise trial was performed on the afternoon prior to the oral fat tolerance test and completed ~16-18 hours prior to ingestion of the test meal. Oxygen uptake and carbon dioxide production were measured using an online gas analysis system (CPX/D BreezeEx v3.0, MedGraphics Cardiorespiratory Diagnostic Systems, St Paul, Minnesota, USA), heart rate was measured by short range telemetry (Polar Electroky, Kempele, Finland) and ratings of perceived exertion (11) were obtained at 15-minute intervals during the walk.

Oral fat tolerance tests

On the morning of the oral fat tolerance tests subjects reported to the laboratory after a 12-h fast. Forearm microvascular function was assessed using laser Doppler imaging with iontophoresis (see below for description). A venous cannula was then inserted and, after an interval of 10 minutes, a baseline blood sample was withdrawn. Subjects then consumed a high-fat test meal comprising whipping cream, fruit, cereal, nuts and chocolate which provided 80g fat, 70g carbohydrate, 12g protein and 4.3 MJ energy. Further blood samples were obtained 20, 40, 60, 90, 120, 240, 360 and 480 minutes postprandially. Microvascular function was assessed again following the 120, 240, 360 and 480-minute blood samples. Subjects rested throughout this day and consumed only water. This was provided *ad libitum* during the first fat tolerance test and the volume and pattern of water intake was replicated during the second test.

Assessment of microvascular function

Peripheral microvascular function was assessed using a validated technique to quantify vasodilator responses to iontophoresis of 1% acetylcholine (ACh, endothelium dependent) and 1% sodium nitroprusside (SNP, endothelium independent), which has been described in detail elsewhere (12,13). Subjects lay in a semi-recumbent position in

a temperature-controlled room, with their non-cannulated forearm supported by an armrest. Iontophoresis chambers were attached to the volar aspect of the forearm with ACh and SNP introduced into the anodal and cathodal chambers, respectively. Drug iontophoresis was by a constant-current controller (MIC-1ev; Moor Instruments Ltd.), incremented from 5 μA to 20 μA (8mC total charge). Non-invasive measurement of skin perfusion was by a laser Doppler imager (Moor Instruments Ltd). Twenty repetitive scans were performed, including a control scan (no current). For each scan, median flux values within each chamber were determined, corrected for variation in skin resistance (12) and the area under the corrected flux *vs* time curve defined the overall microvascular response. The within-day and between-day coefficients of variation for this method are both <10% (12).

Analytical procedures

Blood samples were collected into potassium EDTA tubes and lithium heparin tubes and placed on ice. Plasma was separated within 15 minutes of collection. Plasma for lipoprotein analyses was stored at 4°C, the remainder was divided into aliquots and stored at -70°C. In the fasted state and 8 hours postprandially, a small sample of whole blood was retained for the determination of white blood cell count.

Plasma VLDL cholesterol, LDL cholesterol and HDL cholesterol concentrations were determined in the fasted state according to the Lipid Research Clinics Program Manual of Laboratory Operations (14). TG, glucose and non-esterified fatty acid (NEFA) concentrations were determined by enzymatic colorimetric methods using commercially available kits (Roche Diagnostics GmbH, Mannheim, Germany and Wako Chemicals USA, Inc., VA, USA). Insulin was determined using a commercially available enzyme-linked immunoassay (ELISA) with <0.01% cross-reactivity with pro-insulin (Mercodia AB, Uppsala, Sweden). Interleukin-6 (IL-6) concentrations were determined using a commercially available high-sensitivity ELISA (R&D Systems Inc.,

Oxon, UK). White blood cell count was measured in a Coulter counter in the routine hospital hematology laboratory. Other than lipoprotein analyses and white blood cell count, which were performed on fresh samples, all samples for each subject were analyzed in the same run. Coefficients of variation were <5% for all non-ELISA assays and <10% all for ELISA assays.

Calculations and statistics

Energy expenditure during the 90-minute treadmill walk was calculated using indirect calorimetry assuming no protein oxidation (15).

Where appropriate, the time-averaged postprandial concentration – defined as the trapezium rule-derived area under the plasma concentration *vs* time curve, divided by the duration of postprandial observation period (8 h) – was used as a summary measure of the postprandial responses. The postprandial rise in concentration was defined as the time-averaged postprandial concentration minus the fasting concentration (i.e. the incremental area under the concentration *vs* time curve, divided by eight hours).

Statistical analyses were performed using Statistica (version 6.0, StatSoft Inc, Tulsa) and Minitab (version 13.1, Minitab Inc, State College). Data sets were tested for normality using Anderson-Darling normality tests and, where necessary, data were logarithmically transformed prior to statistical analysis. Comparisons of fasting values and summary postprandial responses were made using two-way ANOVA (group x trial) with repeated measures on the trial (exercise or control) factor. Where it was necessary to determine changes over the postprandial period three-way ANOVA (group x trial x time) were performed with repeated measures on the trial and time factors. *Post-hoc* Fisher LSD tests were used to identify exactly where any differences lay. *A priori* power calculations, based on our data for intra-subject reproducibility of ACh vasodilator responses (within-day and between-day coefficients of variation both <10% (12)) and postprandial TG responses (between-day coefficient of variation 10.1%,

unpublished data), indicated that 10 subjects per group would enable detection of exercise-induced changes of ~10% in either response. Significance was accepted at the $P < 0.05$ level and data are presented as mean ± SEM unless otherwise stated.

Results

Treadmill walk

For the 90-minute treadmill walk, the lean men walked at a speed of 6.0 ± 0.2 $km.h^{-1}$, up a 4.3 ± 0.6% gradient and the centrally obese men walked at 5.8 ± 0.1 $km.h^{-1}$, up a 3.6 ± 0.5% gradient. Mean $\dot{V}O_2$ and heart rate was 22.1 ± 0.9 $ml.kg^{-1}.min^{-1}$ (50.6 ± 0.9% $\dot{V}O_2max$) and 119 ± 3 $beat.min^{-1}$ for the lean men and 20.5 ± 0.7 $ml.kg^{-1}.min^{-1}$ (51.1 ± 1.1% $\dot{V}O_2max$) and 126 ± 3 $beat.min^{-1}$ for the centrally obese men. The lean and centrally obese subjects rated the intensity of the walk as 11.8 ± 0.5 (between 'fairly light' and 'somewhat hard') and 12.9 ± 0.5 ('somewhat hard'), respectively, on the Borg scale of 6-20 (11). There were no significant differences between the lean and centrally obese men in any of the above factors. However, as a consequence of their greater body mass, the overall gross energy expenditure of the walk was higher in the centrally obese men (3.7 ± 0.1 MJ) than the lean men (2.9 ± 0.2 MJ) ($p = 0.003$).

Plasma concentrations in the fasted state

Plasma concentrations in the fasted state are shown in Table 2. Concentrations of TG, glucose, insulin and IL-6 were all significantly higher and the concentration of HDL cholesterol was significantly lower in the centrally obese than the lean men (all $p < 0.05$). Exercise reduced fasting TG concentrations to the same degree in the lean and centrally obese men (25% reduction for both, $p = 0.001$). Concentrations of NEFA were significantly higher in the exercise trial than the control trial.

Metabolic responses to the test meal

Figure 1 shows the metabolic responses to the test meal with summary measures of these responses shown in Table 3. As expected, the centrally obese men exhibited greater postprandial metabolic perturbations than the lean men with significantly higher postprandial plasma TG, insulin, glucose and NEFA responses. Exercise significantly reduced postprandial TG concentrations (and postprandial rises in TG concentration) by ~25% in both the lean and centrally obese groups ($p < 0.0005$ for both). ANOVA main effects indicated that the postprandial insulin response was significantly reduced by exercise ($p = 0.037$), but *post hoc* analysis revealed that this was only evident in the centrally obese group (11% reduction, $p = 0.015$), with no significant reduction occurring in the lean subjects (3% reduction, $p = 0.63$). Postprandial NEFA ($p = 0.006$) concentrations were both significantly higher the exercise trial than the control trial, but postprandial glucose concentrations did not differ significantly between the two trials.

Microvascular responses to ACh and SNP in the fasted and postprandial states

Microvascular responses to ACh and SNP did not differ significantly between the lean and centrally obese groups. Data from the two groups were therefore combined for further statistical analyses. These combined responses are shown in Figure 2. The fasting ACh response was 25% higher in the exercise trial than the control trial ($p = 0.02$). In both trials, the ACh responses at 2, 4, 6 and 8 hours postprandially were significantly lower than the responses in the fasted state ($p < 0.01$) but the average ACh response over the postprandial observation period (mean of 2, 4, 6 and 8 hour responses) was 15% higher in the exercise trial than the control trial (10745 ± 986 flux units *vs* 9349 ± 857 flux units, $p = 0.048$). In contrast to the ACh responses, SNP responses did not differ significantly between the control and exercise trials in the fasted state ($p = 0.98$). In the control trial, SNP responses at 2, 4, 6 and 8 hours postprandially were significantly lower than the responses in the fasted state ($p < 0.01$) and in the exercise SNP responses 4, 6 and 8 hours postprandially were significantly lower than

fasting values ($p < 0.05$). However, the average SNP response over the postprandial observation period was 20% higher in the exercise trial than the control trial (11111 ± 847 flux units *vs* 9230 ± 790 flux units, $p = 0.036$).

Inflammatory responses to the test meal

The inflammatory responses to the test meal are shown in Figure 3. In all trials IL-6 concentrations rose significantly following ingestion of the test meal and were significantly higher than concentrations in the fasted state at the late postprandial time points. The time-averaged postprandial IL-6 concentration did not differ significantly between control and exercise trials or between the lean and centrally obese groups and there was no significant group x trial interaction. White blood cell counts were significantly higher at 8 hours postprandially than in the fasted state in both the control and exercise trials for both the lean and centrally obese subject groups (all $p < 0.01$). There were no significant differences between the control and exercise trials or between the lean and centrally obese subjects, nor were there any significant interactions.

Discussion

The major novel finding in this study is that a single session of moderate exercise significantly improved small vessel vasodilator function in both the fasted and postprandial states in a group of middle-aged men. Prior exercise increased the ACh response in the fasted state by 25%, with no change in the SNP response, indicating that this improvement in vascular function was endothelium dependent. This is likely to be clinically important as endothelial function measures predict future cardiovascular events and do so independent of conventional risk factors (6). Moreover, although it has been demonstrated that endothelial function can be improved following a number of weeks of exercise training (16), we believe that this is the first study to demonstrate an improvement in endothelial function sustained until the day following a single exercise

session. Thus, in common with changes in TG metabolism (7) and insulin sensitivity (17), exercise training-induced improvements to endothelial function may, at least in part, be a consequence of relatively short-term changes in response to recent exercise.

We assessed microvascular function using the relatively novel method of laser Doppler imaging with iontophoresis. This non-invasive *in vivo* method, which assesses the cutaneous microcirculation, provides a robust surrogate marker of vascular function in other vascular beds. Reduced cutaneous responsiveness to iontophoresis of ACh has been observed in hypercholesterolaemia (18) and diabetes (19), and in these conditions there is a parallel reduction of the ACh response in the forearm circulation (predominantly a skeletal muscle vascular bed) assessed by venous occlusion plethysmography (20-22). The iontophoresis method has also revealed an inverse relationship between blood pressure and the ACh response (23), and ACh-induced vasodilatation of both forearm skin and muscle is reduced in essential hypertension (24). Moreover, attenuated cutaneous responses to ACh iontophoresis of heart transplant patients (25) are paralleled by reduced responsiveness of coronary blood vessels to ACh in this group (26). Thus, many conditions affecting the cardiovascular system appear to result in global endothelial dysfunction, affecting cutaneous vessels as well as vascular beds more directly involved in the pathogenesis of vascular disease.

We found no significant correlations between the exercise-induced change in fasting TG, insulin, glucose, NEFA, IL-6 or white blood cell count, and the exercise-induced change in the fasting ACh response (data not shown). This is in accord with a recent report which found that changes to endothelial function elicited by longer-term exercise programs were not significantly related to the exercise-induced changes in a number of cardiovascular risk factors (16), suggesting that exercise may improve endothelial function via other mechanisms. The improvement in the fasting ACh response following exercise may be due to increased blood flow augmenting shear stress on the endothelium, thereby stimulating nitric oxide (NO) release. Indeed recent

evidence suggests that this is evident in vascular beds which are not actively exercising as well as in the exercising tissues (27). Furthermore, the effects of moderate exercise on blood flow persist for a number of hours following exercise cessation; it has been reported that leg blood flow is almost 40% higher during the day following a 2-hour moderate intensity exercise session than following a day with no exercise (28) and that subcutaneous adipose tissue blood flow is elevated for a number of hours post-exercise (29). This prolonged increase in blood flow during recovery from exercise may enable augmented endothelial function to persist for a number of hours post-exercise, in line with the present findings.

In both the control and the exercise trials, the ACh response declined significantly postprandially, in agreement with other reports (4,5). However, postprandial ACh responses were significantly higher in the exercise trial than the control trial, indicating that prior exercise acted to oppose the postprandial decrement. Interestingly, there was a postprandial decline in the SNP response which tracked the decrease in the ACh response, indicating that the postprandial decrement in microvascular function cannot be attributed with certainty to endothelial as opposed to smooth muscle vascular structures. However, as postprandial SNP responses were higher in the exercise than the control trial, it seems likely that prior exercise also ameliorated any postprandial decline in vascular smooth muscle vasoactivity. These findings mirror the effects of fenofibrate on vasodilator function in hypertriglyceridaemic patients (30) in which fibrate treatment reduced TG concentrations and improved resistance vessel vasodilator responses to both ACh and SNP to a similar degree. Thus, it is possible that the TG-mediated impairment of resistance vascular function may, to some extent, be mediated by endothelium-independent mechanisms and this may differ somewhat from the effects of TG on conduit vessel vascular function, where it appears that that the postprandial decrement in vasodilator response is mediated by endothelium dependent mechanisms (4,5).

Certainly, i*n vitro* studies have demonstrated that remnants and fatty acids derived from the hydrolysis of TG-rich lipoproteins are cytotoxic to vascular smooth muscle cells (31,32). Moreover cardiovascular risk factors such as hypercholesterolaemia (33), hypertension (34) and type 2 diabetes (20) have been linked to the perturbance of both endothelium dependent and independent vasodilation (however measured) and their treatments often improve both responses (22,33).

Since ingestion of high-fat meals blunts vasodilator function (4,5), but ingestion of a low-fat meal does not (4), it seems likely that the postprandial decrement in vascular function is a consequence of fat ingestion *per se*. However, as yet, the mechanisms responsible have not been fully elucidated. Some studies have reported that the postprandial decrement in vasodilator function correlates with the postprandial rise in TG (4,5), but this is not a universal finding (35) and in the present study we found no significant relationships between postprandial TG concentrations or rises in concentration and postprandial ACh responses in either the control or exercise trial (data not shown). We similarly found no significant relationships between exercise-induced changes in postprandial TG concentrations or rises in concentration and exercise-induced changes in postprandial ACh responses (data not shown), suggesting that differences in TG may not explain the changes in ACh response observed in the present study. Alternatively postprandial increases in systemic inflammation may contribute to endothelial dysfunction (3); in the present study there was clear evidence of a postprandial increase in inflammation with rises in IL-6 concentrations and white blood cell counts. However, we observed similar postprandial inflammatory responses in the control and exercise trials suggesting that either differences in these inflammatory markers were not a major mediator in the exercise-induced improvements to postprandial vasodilator responses or that the study had insufficient power to detect a clear effect of exercise on these inflammatory responses. A further possibility is that prior exercise influenced endothelial function through effects on postprandial oxidative

stress or anti-oxidant mechanisms. It has been reported that co-ingestion of anti-oxidant vitamins with fat abolishes the postprandial decrement in endothelial function (36) and moderate exercise may act though a similar mechanism as it has been demonstrated that moderate exercise training increases plasma antioxidant defenses (37). Whether this occurs in response to a single exercise session warrants further investigation. Alternatively, it is possible that the higher postprandial ACh responses seen after exercise were a direct consequence of the higher ACh baseline response, rather than a specific effect of exercise on postprandial metabolism.

We did not observe significant differences in microvascular function between the lean and the centrally obese subjects in this study, however, ACh responses were, overall, ~10% lower in the centrally obese than the lean subjects. This difference between groups was substantially smaller than that observed for the postprandial TG response (control trial response 79% higher in the centrally obese subjects, $p < 0.01$, see Table 2) or the postprandial insulin response (106% higher, $p < 0.01$) and suggests that the effects of obesity on microvascular function may be more subtle than its effects on TG metabolism and insulin sensitivity. The present study, with 10 subjects in each group, had insufficient power to determine whether this small difference in microvascular function between the groups was real and further investigation in a larger study is warranted to address this issue.

The results from this study demonstrate that a session of prior moderate exercise effectively reduces postprandial TG concentrations in both lean and centrally obese middle-aged men. The percentage reductions in TG were remarkably similar in the two groups – ~25% for each – but the centrally obese subjects, by virtue of their higher TG concentrations experienced a greater absolute TG fall. The percentage TG reductions observed are comparable with those found in other reports (7). However, these earlier reports have generally studied subjects with lower TG concentrations than those of the centrally obese subjects in the present study and thus our findings extend the evidence

base demonstrating the efficacy of moderate exercise in reducing postprandial lipemia in a range of study populations. Importantly, despite many of the men being unused to walking long distances, all managed to complete the 90-minute treadmill walk without difficulty and none complained of undue tiredness or muscle soreness, indicating that, while this goes beyond the current '30 minutes per day' exercise recommendation (38), walks of this intensity and duration are not beyond the capability of inactive centrally obese middle-aged men.

In conclusion, this study has demonstrated that a single session of moderate intensity exercise, which was well tolerated by the study participants, improved fasting and postprandial resistance vessel vasodilator function in a group of middle-aged men. Furthermore, prior exercise reduced postprandial lipemia to the same degree in lean and centrally obese men and reduced postprandial insulin concentrations in the centrally obese men. These findings indicate that moderate exercise is effective in attenuating many of the adverse metabolic and vascular changes occurring during the hours after ingestion of dietary fat and thus contribute to our understanding of the mechanisms by which exercise can reduce cardiovascular risk.

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Figure 1

Postprandial plasma TG concentrations (top panels), insulin (2nd top panels), glucose (2nd bottom panels) and NEFA (bottom panels) concentrations in the lean (n =10, left panels) and centrally obese (n = 10, right panels) in the control and exercise trials. Summary statistics for these responses are shown in Table 3.

Figure 2

Microvascular responses to ACh (top panel) and SNP (bottom panel) in the fasted and postprandial states for the lean and centrally obese subjects combined in the control and exercise trials (n = 20). Statistics performed on logarithmically transformed data. *different from fasting value in the same trial, $p < 0.05$ (** $p < 0.01$), †difference between control and exercise trials at the same time point, $p < 0.05$.

Figure 3

Postprandial plasma IL-6 (top panels) and white blood cell counts (bottom panels) in the lean (n =10, left panels) and centrally obese (n = 10, right panels) in the control and exercise trials. different from fasting value in the same trial, $p < 0.05$ (** $p < 0.01$), †difference between control and exercise trials at the same time point, $p < 0.05$.

Table 1. Subject characteristics.

	Lean men (n = 10)	Centrally obese men (n = 10)
Age (years)	47.9 ± 8.4	46.5 ± 10.5
Waist (cm)	82.3 ± 5.4	107.1 ± 8.0*
Body mass index ($kg.m^{-2}$)	23.0 ± 1.9	31.7 ± 4.7*
Sum of 4 skinfolds[†]	39.8 ± 8.4	88.3 ± 43.1*
Systolic blood pressure (mm Hg)	112 ± 5	118 ± 12
Diastolic blood pressure (mm Hg)	70 ± 7	74 ± 7
Maximal oxygen uptake[‡] ($ml.kg.^{-1}min^{-1}$)	43.9 ± 6.2	40.6 ± 6.6

Data are mean ± SD. *significantly different from lean group, $p < 0.01$

[†]Skinfolds are biceps, triceps, subscapular and suprailiac.

[‡]Estimated from a 4-stage submaximal incremental treadmill test (10).

Table 2. Plasma concentrations in the fasted state

	Lean men (n = 10)		Centrally obese men (n = 10)		P for group	P for trial
	Control	Exercise	Control	Exercise		
TG* ($mmol.l^{-1}$)	0.85 ± 0.08	0.64 ± 0.05	1.74 ± 0.20	1.31 ± 0.20	<0.0005	0.001
Total cholesterol ($mmol.l^{-1}$)	4.96 ± 0.24	5.01 ± 0.23	5.00 ± 0.28	4.82 ± 0.23	0.82	0.38
HDL cholesterol ($mmol.l^{-1}$)	1.32 ± 0.09	1.37 ± 0.09	0.97 ± 0.07	1.00 ± 0.06	0.005	0.11
LDL cholesterol ($mmol.l^{-1}$)	3.24 ± 0.15	3.33 ± 0.16	3.36 ± 0.24	3.27 ± 0.22	0.92	0.99
Glucose ($mmol.l^{-1}$)	5.04 ± 0.12	5.00 ± 0.10	5.60 ± 0.21	5.56 ± 0.16	0.017	0.45
Insulin ($\mu U.ml^{-1}$)	4.03 ± 0.65	3.97 ± 0.35	7.95 ± 1.23	7.63 ± 1.54	0.017	0.63
NEFA ($mmol.l^{-1}$)	0.35 ± 0.03	0.44 ± 0.03	0.44 ± 0.03	0.46 ± 0.03	0.17	0.017
IL-6* ($pg.ml^{-1}$)	0.95 ± 0.14	0.78 ± 0.10	1.93 ± 0.28	1.61 ± 0.22	0.002	0.13

Data are mean ± SEM.

*Statistics performed on logarithmically transformed data

P for group – ANOVA main effect for lean vs centrally obese

P for trial – ANOVA main effect for control vs exercise

No significant group by trial interactions

Table 3. Metabolic responses to the test meal

	Lean men (n = 10)		Centrally obese men (n = 10)		P for group	P for trial
	Control	Exercise	Control	Exercise		
Postprandial TG concentration* ($mmol.l^{-1}$)	1.40 ± 0.12	1.05 ± 0.07	2.51 ± 0.32	1.91 ± 0.33	0.002	<0.0005
Postprandial TG rise in concentration* ($mmol.l^{-1}$)	0.55 ± 0.06	0.41 ± 0.04	0.77 ± 0.15	0.60 ± 0.14	0.282	<0.0005
Postprandial insulin concentration* ($\mu U.ml^{-1}$)	8.61 ± 0.79	8.36 ± 0.76	17.75 ± 2.62	15.86 ± 2.96	0.003	0.037
Postprandial glucose concentration ($mmol.l^{-1}$)	5.15 ± 0.11	5.18 ± 0.09	5.77 ± 0.14	5.73 ± 0.15	0.003	0.80
Postprandial NEFA concentration ($mmol.l^{-1}$)	0.35 ± 0.01	0.38 ± 0.02	0.41 ± 0.02	0.45 ± 0.02	0.009	0.006

Postprandial concentrations and postprandial rises in concentration calculated as the area under the total or incremental concentration *vs* time curve divided by the duration of the postprandial observation period (8 h).

Data are mean ± SEM.

*Statistics performed on logarithmically transformed data

P for group – ANOVA main effect for lean vs centrally obese

P for trial – ANOVA main effect for control vs exercise

No significant group by trial interactions

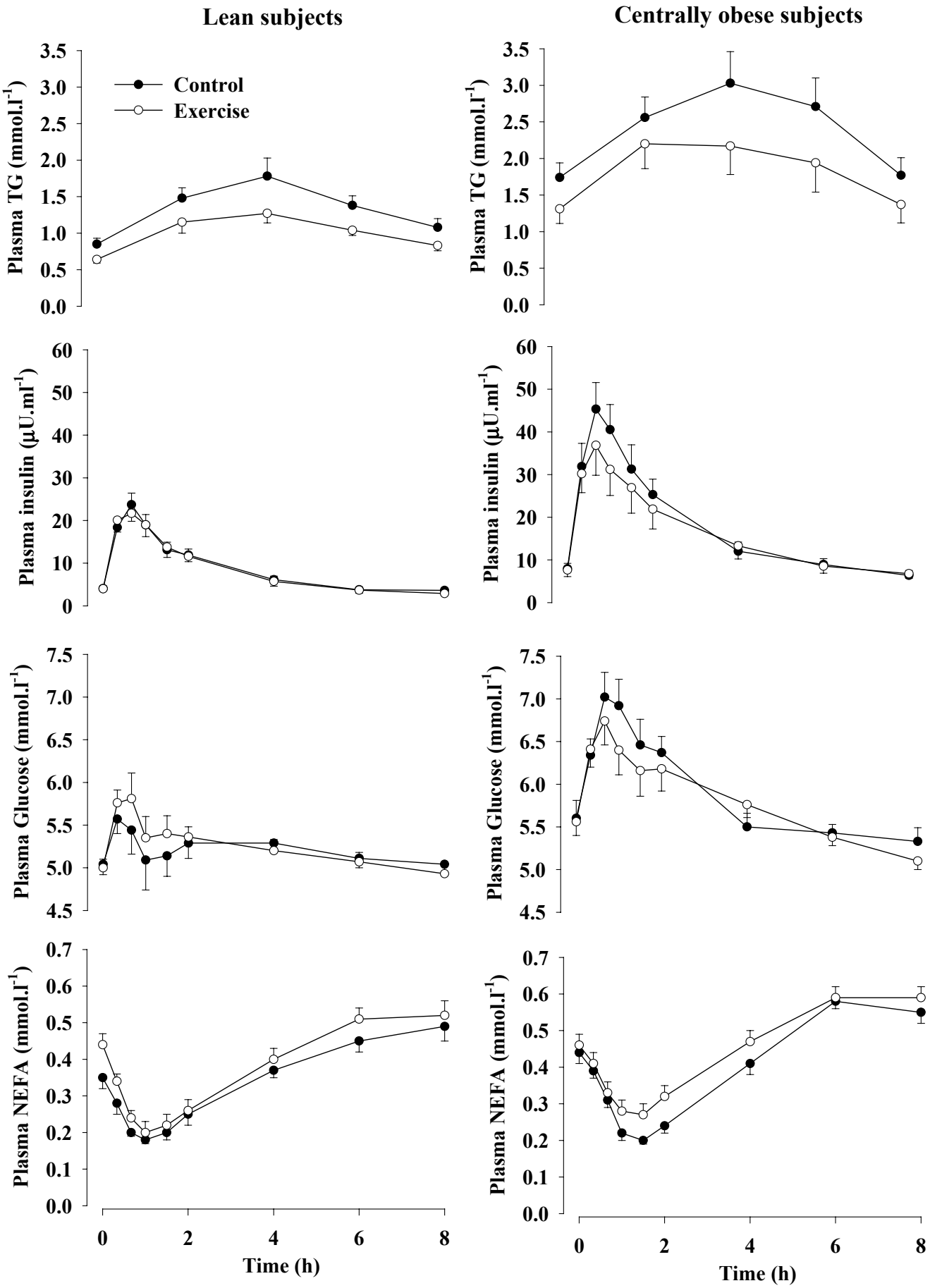
Lean subjects
Centrally obese subjects
Control
Exercise
Plasma TG (mmol.l-1)
Plasma insulin (µU.ml-1)
Plasma Glucose (mmol.l-1)
Plasma NEFA (mmol.l-1)
Time (h)

Figure 1

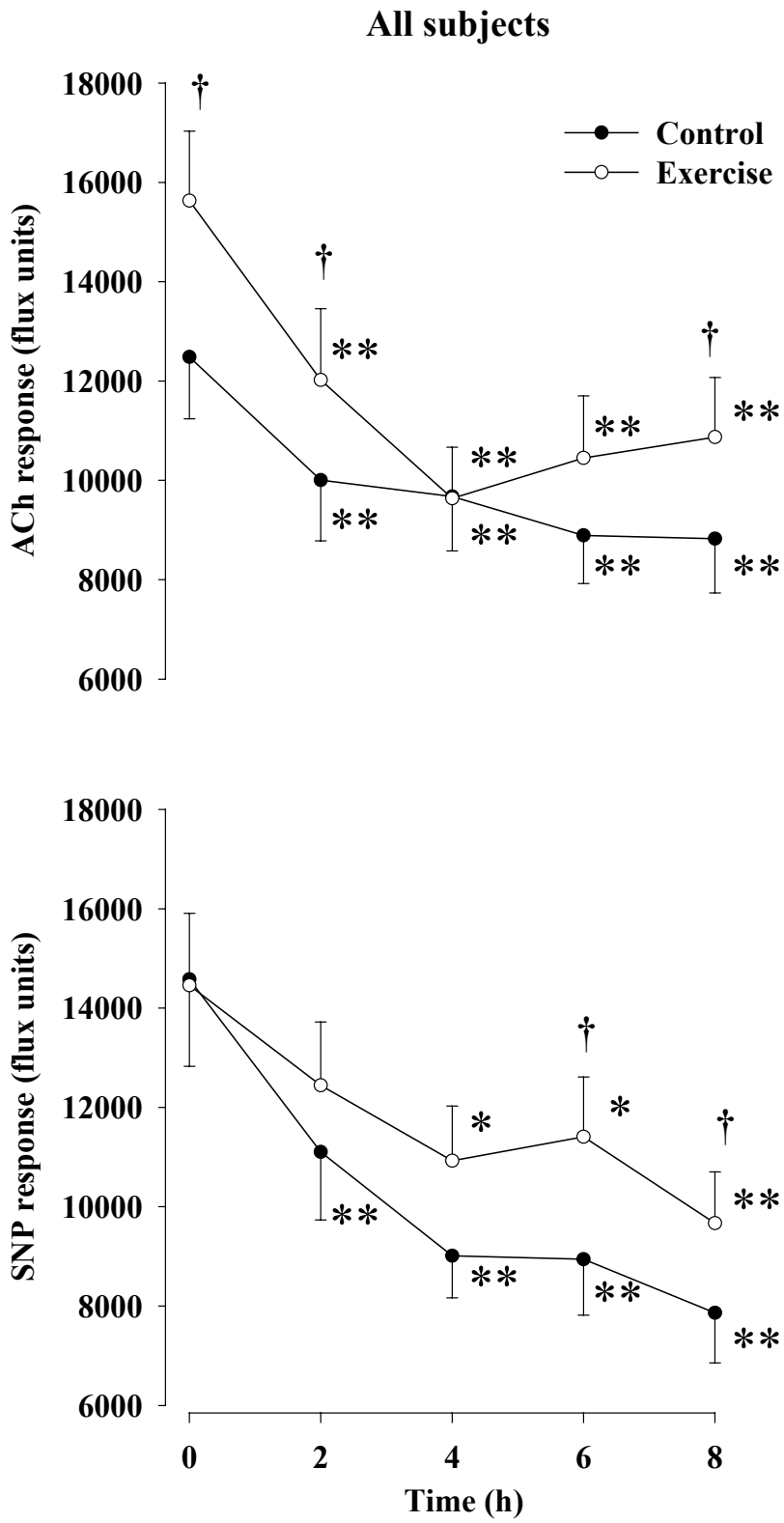
All subjects
ACh response (flux units)
SNP response (flux units)
18000
16000
14000
12000
10000
8000
6000
Control
Exercise
†
**
*
0
2
4
6
8
Time (h)

Figure 2

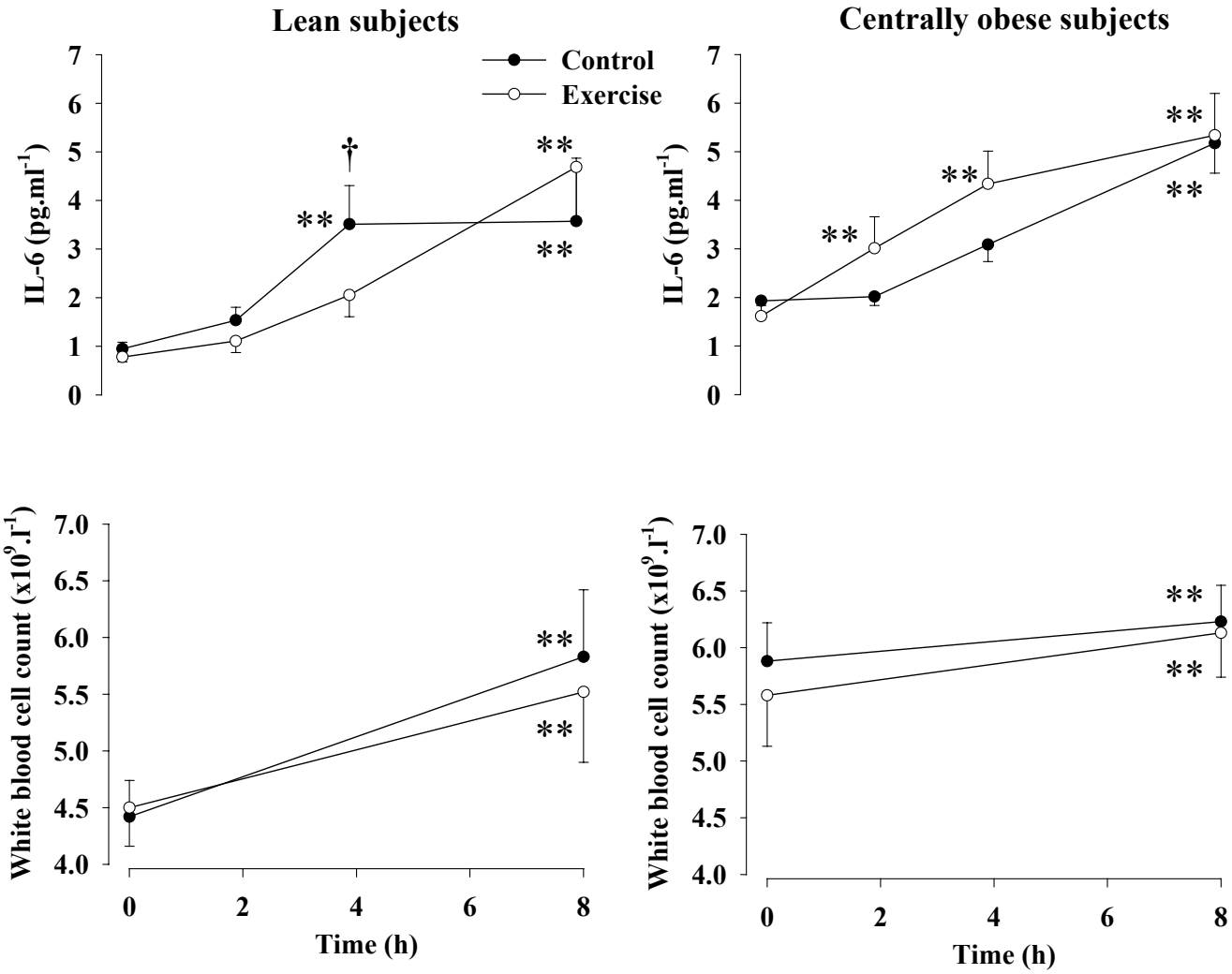
Lean subjects
Centrally obese subjects
Control
Exercise
IL-6 (pg.ml-1)
White blood cell count (x10^9.l-1)
Time (h)
**
†

Figure 3