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Effect of exercise on postprandial endothelial function in adolescent boys

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Abstract

The ingestion of high-fat meals induces a state of endothelial dysfunction in adults. This dysfunction is attenuated by prior exercise. The response of young people to these nutritional and physiological stressors has not been established. Thus, the purpose of the present study was to investigate if a bout of moderate-intensity exercise influenced endothelial function (as indicated by flow-mediated dilation (FMD)) following the ingestion of a high-fat breakfast and lunch in adolescent boys (aged 12·6–14·3 years). Two, 2 d main trials (control and exercise) were completed by thirteen adolescent boys in a counter-balanced, cross-over design. Participants were inactive on day 1 of the control trial, but completed 60 min of walking at 60 % peak oxygen uptake in the exercise trial. On day 2, endothelial function was assessed via FMD prior to, and following, ingestion of a high-fat breakfast and lunch. There was no difference in fasting FMD between the control and exercise trial ($P=0·449$). In the control trial, FMD was reduced by 32 % following consumption of the high-fat breakfast and by 24 % following lunch. In the exercise trial, the corresponding reductions were 6 and 10 %, respectively (main effect trial, $P=0·002$). These results demonstrate that moderate-intensity exercise can attenuate the decline in FMD seen following the consumption of high-fat meals in adolescent boys.

Key words: CHD risk: Flow-mediated dilation: Postprandial lipaemia: TAG

In adults, the ingestion of a single high-fat meal is associated with endothelial dysfunction and elevated TAG concentrations[1–4], and such responses have been shown to be independent risk factors for CHD[5,6]. While the responses to a single high-fat meal may be transient, individuals in Western societies typically consume several meals a day and spend the majority of a day in the postprandial state[7]. Consequently, the repeated ingestion of meals high in fat, and the associated exposure to repeated endothelial dysfunction and elevated TAG concentrations, may have important implications on long-term vascular health.

The presence of fatty streaks in children confirms that CHD has its origins early in life[8]. Researchers have also noted the high prevalence and rapid progression of raised lesions in the arteries of adolescents and young adults[9]. As CHD is typically a chronic condition, which progresses and develops over decades[10], an understanding of the factors that augment and attenuate the development of the disease, even in the young, could have important clinical implications, particularly when it has been argued that the greatest benefit from a treatment occurs the earlier it is initiated[11]. Endothelial dysfunction is considered to be the first stage in atherogenesis[12] and appears to be a pre-requisite for the development of atherosclerosis[13].

In adults, many of the interventions used to combat CHD involve pharmacological therapies that, while often effective, can be costly and have numerous side effects, especially if undertaken for a prolonged period[14]. In addition, the safety and efficacy of many pharmacological treatments have not been established in young people. Exercise has been shown to attenuate the endothelial dysfunction[1,3] and rise in TAG concentrations[15] seen following the ingestion of a high-fat meal in adults. While exercise may induce similar responses in children and adolescents, this is by no means certain, because as children and adolescents grow and mature, their physiological responses to exercise may vary[16]. Recently, it has been reported that exercise can reduce postprandial TAG concentrations in adolescents[17–20], but, to our knowledge, no study has investigated the effect of exercise on postprandial endothelial function.

Therefore, the primary aim of the present study was to investigate if a bout of moderate-intensity exercise influenced

Abbreviations: FMD, flow-mediated dilation; HOMA-IR, homeostatic model assessment of insulin resistance.

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endothelial function (as indicated by flow-mediated dilation (FMD)) following the ingestion of a high-fat breakfast and lunch in adolescent boys.

Experimental methods

Participants

A total of fifteen adolescent boys (aged 12·6–14·3 years, Tanner stages 1–5 (median 4)) volunteered to participate, with thirteen boys completing the study. Non-completion of the study was due to either syncope during blood sampling or a participant's lack of time. The study was conducted according to the guidelines laid down in the Declaration of Helsinki, and all procedures were approved by the Loughborough University Ethical Advisory Committee. Before any testing took place, all participants had the procedures and risks associated with involvement in the study explained to them. Written assent from each participant and written consent from a parent were then obtained. All participants were apparently healthy and not taking any drugs known to affect lipid or carbohydrate metabolism; the physical characteristics of those who completed the study are shown in Table 1.

Study design

Participants completed preliminary tests and then undertook two, 2 d main trials that were separated by 7 d (control trial and exercise trial) in a 2 × 2 replicated (seven replicates) Latin square design.

Preliminary tests

Height and sitting height were measured to the nearest 0·1 cm using a wall-mounted stadiometer (Seca) and body mass was measured to the nearest 0·01 kg using a beam balance scale (Avery). Skinfold thicknesses were measured to the nearest 0·2 mm at four sites (biceps, triceps, subscapular and suprailiac) using callipers (Harpenden; Baty International), and waist and hip circumferences were measured to the nearest 0·1 cm. Each participant was asked to make a self-assessment of maturity based on secondary sexual characteristics[21], and age from peak height velocity was also estimated[22]. Finally, peak oxygen uptake (VO_2 peak) was measured and the relationship between oxygen uptake and treadmill incline was established[17].

Table 1. Physical characteristics of participants
(Mean values and standard deviations, *n* 13)

	Mean	SD
Age (years)	13·6	0·6
Height (m)	1·57	0·12
Body mass (kg)	56·2	17·1
BMI (kg/m^2)	22·3	4·2
Sum of four skinfolds (mm)*	44·4	20
Waist circumference (cm)	71·6	9·2
Hip circumference (cm)	89·5	11·2
Waist:hip ratio	0·80	0·02
SBP (mmHg)	116	9
DBP (mmHg)	67	7
Age from PHV (years)	−0·7	1·0
VO_2 peak (ml/kg per min)	48·1	7·5

SBP, systolic blood pressure; DBP, diastolic blood pressure; PHV, peak height velocity; VO_2 peak, peak oxygen uptake.
* Four skinfold sites were biceps, triceps, subscapular and suprailiac.

Main trials

Participants were instructed to refrain from physical activity for 2 d and not to consume alcohol or supplements in the 7 d before the main trials. Participants also completed a food diary for 2 d before the first main trial and were asked to replicate this diet for the subsequent trial.

On day 1 of the control trial, the participants were physically inactive, whereas in the exercise trial, they reported to the laboratory at 16.00 hours and walked on a treadmill at 60 % VO_2 peak for 60 min. The walking was divided into four 15 min blocks interspersed with 3 min rest periods. Heart rate, ratings of perceived exertion and expired air samples were collected in the last minute of each block. Energy expenditure was estimated using indirect calorimetry[23].

On day 2 of each main trial, participants reported to the laboratory at 08.00 hours, following an overnight fast, and FMD was assessed and a capillary blood sample collected. Participants then ate breakfast and a clock was started on the commencement of the meal. After breakfast, the participants rested for 6·5 h. Lunch was provided at 3·5 h. FMD was assessed again at 3 and 6·5 h, and additional blood samples collected at 0·5, 1, 3, 4, 4·5 and 6·5 h.

Meals

Breakfast consisted of croissant, chocolate spread and a chocolate milkshake (chocolate power, whole-fat milk and double cream), providing 1·5 g fat (60 %), 1·8 g carbohydrate (33 %), 0·4 g protein (7 %) and 92·9 kJ/kg body mass. Participants were given 15 min to consume breakfast. Lunch consisted of a cheese sandwich (white bread, butter and cheese), ready salted potato chips and a chocolate milkshake (chocolate powder and whole-fat milk), providing 1·1 g fat (50 %), 1·9 g carbohydrate (37 %), 0·6 g protein (13 %) and 84·6 kJ/kg of body mass. Participants were given 20 min to consume lunch. Participants consumed water *ad libitum* during the first trial and any intake was replicated in the subsequent trial.

Endothelial function assessment by flow-mediated dilation

FMD measurements were made using previously published guidelines and recommendations[24–26]. Briefly, for each FMD measurement a pneumatic blood pressure cuff (Hokanson) was placed on the participant's right arm immediately distal to the elbow. Participants then rested in a supine position for 20 min, with their right arm extended at approximately 90° from their torso. The brachial artery was imaged longitudinally in the distal third of the upper arm

using ultrasound (11 MHz linear array transducer, attached to a high-resolution ultrasound machine Power Vision 6000; Toshiba). A baseline scan of the artery was conducted over twenty consecutive cardiac cycles. Then, the blood pressure cuff was inflated to 200 mmHg for 5 min. Further images were captured continuously following cuff release for 3 min. Images were captured on the r-wave of each cardiac cycle (Vascular Imager, version 4.1.3; Medical Imaging Applications LLC).

Ultrasound settings (gain, focus zone and depth) were set to optimise longitudinal B-mode images of the lumen–arterial wall interface. Pulsed-wave Doppler was used, simultaneously with B-mode imaging, to assess blood flow velocity; data were collected at an insonation angle $\leq 70°$, with the sample volume minimised and positioned in the centre of the artery. Ultrasound settings were standardised for each participant for every subsequent measurement. Measurement location was also standardised for each participant based on anatomical landmarks, snapshot images and an ink marker placed on the skin that was maintained between trials.

Recorded images were later digitised using specialised edge-detection and wall-tracking software (Brachial analyzer, version 4.1.3; Medical Imaging Applications LLC). Peak diameter following occlusion was determined using a three-frame moving average. FMD was calculated as the percentage change from basal diameter to peak diameter, and was also normalised for the post-occlusion shear rate[25].

CV made on measurements made 7 d apart for fasting basal diameter and FMD in our laboratory were 0·6 and 9·7 % and in the postprandial state were 0·8 and 10·0 %, respectively.

Blood sampling and biochemical analysis

From a warmed left hand, capillary blood was collected into 500 µl potassium-EDTA-coated microvettes (Sarstedt) and immediately centrifuged at 1500 ***g*** for 10 min at 4°C. The resulting plasma was then stored at −20°C for later analysis. Plasma TAG and glucose concentrations were determined by enzymatic and colorimetric methods (HORIBA ABX Diagnostics). Plasma insulin concentration was determined by ELISA (Mercodia). Within-batch CV were as follows: TAG 1·2 %, glucose 0·5 % and insulin 8·8 %.

Statistical analysis

Data were analysed using the PASW statistics software version 18.0 for Windows (SPSS, Inc.). The total and incremental (after correcting for fasting concentrations) area under the plasma concentration *v.* time curves for TAG, glucose and insulin were calculated using the trapezium rule. Insulin resistance was evaluated according to the homeostatic model assessment of insulin resistance (HOMA-IR)[27]. Residual errors were tested for normality using the Shapiro–Wilk test and, where necessary, data were logarithmically transformed prior to statistical analysis. Fasting basal diameter, peak diameter, FMD, normalised FMD and plasma TAG, glucose and insulin concentration, area under the plasma concentration *v.* time curves and HOMA-IR were compared between trials using paired Student's *t* test. A mixed-effects general linear model with two fixed factors (trial and time) and one random factor (participant) was used to compare differences between trials over time, and any possible interactions between trial and time, for basal diameter, peak diameter, FMD, normalised FMD and plasma TAG and glucose and insulin concentrations. For further information on this design and analysis, see Winer[28]. Where there was a violation of compound symmetry, based on Mauchly's test, the df were adjusted using the Huynh–Feldt epsilon. The least significant difference was used to identify exactly where any main effects of time lay. When a significant trial × time interaction was revealed, targeted pairwise comparisons were used, specifically comparisons within trials with respect to the fasting measure and between trials at the same time point. Pearson's correlation coefficient was calculated in the control and in the exercise trial for fasting plasma TAG concentration and fasting FMD; for the change in FMD and the total area under the plasma TAG concentration *v.* time curve from 0 to 3 h; and for the change in FMD and the total area under the plasma TAG concentration *v.* time curves from 0 to 6·5 h (six correlations in total). Statistical significance was accepted at the $P<0·05$ level. All participant characteristics are presented as population marginal mean and standard deviation, and all experimental data are presented as population marginal mean and standard error.

Results

Responses to treadmill exercise

Mean oxygen uptake during the bouts of walking was 28·8 (SEM 1·3) ml/kg per min, which represented 59·9 (SEM 0·4) % of the participants' VO_2 peak. Mean heart rate, ratings of perceived exertion and gross energy expenditure were 156 (SEM 2) beats/min, 12 (SEM 1) and 1·92 (SEM 0.41) MJ or 34·9 (SEM 1·5) kJ/kg body mass, respectively.

Measures in the fasted state

No differences were observed between trials for fasting basal diameter (Table 2, $P=0·471$), peak diameter (Table 2, $P=0·707$), FMD (Fig. 1(a), $P=0·449$), normalised FMD (Fig. 1(b), $P=0·379$), plasma glucose concentration (Fig. 2(b), $P=0·190$) and plasma insulin concentration (Fig. 2(c), $P=0·343$). No differences were observed between trials for fasting HOMA-IR (control *v.* exercise; 3·0 (SEM 0·5) *v.* 2·8 (SEM 0·8), $P=0·971$). The fasting plasma TAG concentration was 0·17 mmol/l lower in the exercise trial (Fig. 2(a); $P=0·001$).

Measures in the postprandial state: basal diameter, peak diameter, flow-mediated dilation and normalised flow-mediated dilation

Basal diameter and peak diameter increased following the ingestion of the high-fat test meals, but did not differ between trials (Table 2; basal diameter: main effect trial ($P=0·239$),

Table 2. Basal diameter and peak diameter* of the brachial artery during the measurement of flow-mediated dilation in the control and exercise trials (Mean values with their standard errors, *n* 13)

	Control						Exercise					
	0 h		3 h		6·5 h		0 h		3 h		6·5 h	
	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM	Mean	SEM
Basal diameter (mm)†‡	3·54	0·15	3·64	0·15	3·70	0·15	3·51	0·15	3·60	0·14	3·61	0·15
Peak diameter (mm)‡	3·83	0·16	3·84	0·14	3·93	0·15	3·81	0·16	3·89	0·14	3·89	0·15

*Data were analysed using a mixed-effects general linear model with two fixed factors (trial and time) and one random factor (participant) for both basal and peak diameter: main effect trial, $P>0·05$; main effect trial, $P<0·05$; and interaction effect trial × time, $P>0·05$. Least significant differences were used to identify where significant main effects lay.
†Main effect − time: difference between 0 and 3·5 h ($P<0·05$).
‡Main effect − time: difference between 0 and 6·5 h ($P<0·05$).

main effect time ($P<0·001$) and interaction effect trial × time ($P=0·253$); peak diameter: main effect trial ($P=0·961$), main effect time ($P=0·030$) and interaction effect trial × time ($P=0·190$)).

Postprandial FMD was lower in the control compared with the exercise trial, both before (Fig. 1(a); main effect trial ($P=0·002$); main effect time ($P=0·023$); and interaction effect trial × time ($P=0·088$)) and after (Fig. 1(b); main effect trial ($P=0·003$); main effect time ($P=0·002$); and interaction effect trial × time ($P=0·036$)) normalisation for the post-occlusion shear rate. Pairwise comparisons identified that normalised FMD was significantly lower compared with the fasting measure at both 3 h ($P=0·005$) and 6·5 h ($P=0·013$) only in the control trial, and that normalised FMD was significantly higher in the exercise trial, compared with the control trial, at 3 h ($P=0·003$) and 6·5 h ($P=0·011$).

Measures in the postprandial state: TAG, glucose and insulin concentrations

Postprandial plasma TAG concentration was lower in the exercise compared with the control trial (Fig. 2(a); main effect trial ($P=0·009$); main effect time ($P<0·001$); and interaction effect trial × time ($P=0·276$)). The total area under the plasma TAG concentration *v.* time curve was 22 % lower in the exercise compared with the control trial (control *v.* exercise; 12·68 (SEM 1·37) *v.* 9·84 (SEM 0·75) mmol/l × 6·5 h, $P=0·018$). The incremental area under the plasma TAG concentration *v.* time curve was 24 % lower in the exercise compared with the control trial; however, this did not reach statistical significance (control *v.* exercise; 7·16 (SEM 1·22) *v.* 5·45 (SEM 0·62) mmol/l × 6·5 h, $P=0·169$).

Postprandial plasma glucose concentrations did not differ between trials (Fig. 2(b); main effect trial ($P=0·877$); main effect time ($P<0·001$); and interaction effect trial × time ($P=0·367$)). No differences were observed between the exercise and control trials for the total or incremental area under the plasma glucose concentration *v.* time curve (control *v.* exercise; 42·91 (SEM 0·66) *v.* 42·62 (SEM 0·83) mmol/l × 6·5 h, $P=0·429$ and 6·77 (SEM 0·97) *v.* 7·02 (SEM 0·73) mmol/l × 6·5 h, $P=0·490$, respectively).

Postprandial plasma insulin concentrations did not differ between trials (Fig. 2(c); main effect trial ($P=0·078$); main effect time ($P<0·001$) and interaction effect trial × time ($P=0·558$)). However, the total area under the plasma insulin concentration *v.* time curves was lower in the exercise compared with the control trial, but the incremental area under the plasma insulin concentration *v.* time curves was not (control *v.* exercise; 1854·0 (SEM 283·8) *v.* 1713·6 (SEM 276·0) pmol/l × 6·5 h ($P=0·047$) and 1397·4 (SEM 286·8) *v.* 1298·4 (SEM 189·0) pmol/l × 6·5 h ($P=0·935$) respectively).

Correlations between flow-mediated dilation and TAG concentrations

The correlations between fasting FMD and plasma TAG concentrations were as follows: control, r −0·106, $P=0·730$; exercise, r 0·104, $P=0·736$. The correlations between the change in FMD and the total area under the plasma TAG concentration *v.* time curve from 0 to 3 h were as follows: control, r −0·138, $P=0·653$; exercise, r 0·214, $P=0·482$. The correlations between the change in FMD and the total area under the plasma TAG concentration *v.* time curve from 0 to 6·5 h were as follows: control, r 0·190, $P=0·534$; exercise, r 0·223, $P=0·465$.

Discussion

The key finding of the present study was that, for the first time in adolescent boys, a bout of moderate-intensity exercise was shown to attenuate the decline in FMD observed in a control trial following the ingestion of high-fat meals. In fact, once FMD had been normalised for the post-occlusion shear rate, prior exercise prevented the postprandial decline in FMD entirely. No relationships were found between postprandial FMD and plasma TAG concentrations.

The present study is the first to investigate endothelial function following the ingestion of high-fat meals in adolescent boys. The ingestion of breakfast and lunch containing substantial quantities of fat (60 and 50 % by energy content, respectively) reduced FMD by 32 % after breakfast and 24 % after lunch compared with fasting. This observed endothelial dysfunction (as indicated by a decline in FMD) following the consumption of high-fat meals has been demonstrated repeatedly in adults. While this decline in FMD in asymptomatic adults can range between 17[29] and 70 %[2], the majority of studies report changes between 30 and 50 %[3,4,30–32]. Importantly,

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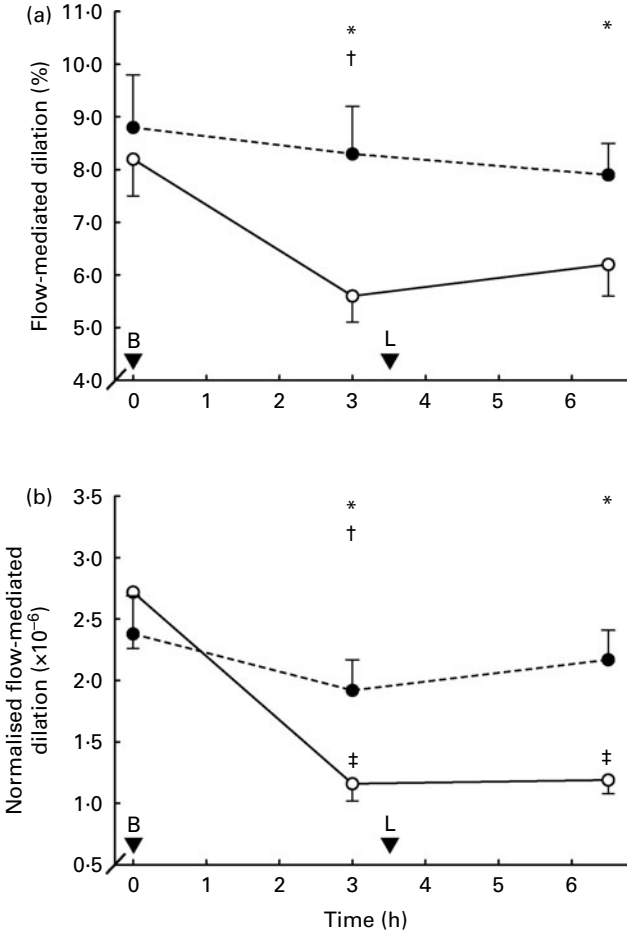


Fig. 1. (a) Flow-mediated dilation and (b) normalised flow-mediated dilation. B, breakfast; L, lunch. Values are means, with their standard errors represented by vertical bars (n 13). Data were analysed using a mixed-effects general linear model with two fixed factors (trial and time) and one random factor (participant). Least significant differences *post hoc* analysis was used to identify where significant main effects lay and when a significant time × trial interaction was identified, pre-specified planned comparisons were used, specifically comparisons within trial with respect to the fasting measure and between trials at the same time point. (a) Flow-mediated dilation: main effect trial ($P=0{\cdot}002$); main effect time ($P=0{\cdot}023$); and interaction effect trial × time ($P=0{\cdot}088$). (b) Normalised flow-mediated dilation: main effect trial ($P=0{\cdot}004$); main effect time ($P=0{\cdot}004$); and interaction effect trial × time ($P=0{\cdot}040$). * Difference from 0 h ($P<0{\cdot}05$). † Difference from previous time point ($P<0{\cdot}05$). ‡ Difference from 0 h in the same trial and difference from exercise trial at the same time point ($P<0{\cdot}05$). -○-, Control; -●-, exercise.

the adolescent boys in the present study had none of the factors associated with CHD risk. Yet, the consumption of high-fat meals induced endothelial dysfunction to a similar extent to that previously observed in adults. Therefore, the present study supports the assertion that ingestion of meals containing high quantities of fat place strain on the endothelium and clearly demonstrates that this is the case even in healthy adolescents.

The ingestion of high-fat meals is not uncommon in adolescents, with 60 % of teenagers in the USA reported to eat 'fast food' (which is typically high in fat content) at least once a week[33] and 30 % reported to eat such foods every day[34]. Therefore, a substantial number of adolescents may be exposed, on a regular basis, to the risks associated with the consumption of meals high in fat. While the observation period in the present study was very short and the endothelial dysfunction following ingestion of a high-fat meal has been shown to be transient, certainly in adults[2,4], if the responses observed in the present study were to be repeated on a regular basis over many years, then the strain on the vasculature could be substantial and have a lasting deleterious effect. Interventions that might reduce or prevent this strain on the vasculature could have important clinical implications. Research with adults suggests that moderate-intensity exercise undertaken before the ingestion of a high-fat meal reduces the subsequent postprandial endothelial dysfunction[1,3]. Interestingly, if the exercise is of a high-intensity (85–95 % of maximum heart rate) the dysfunction is prevented[3]. In the present study, we observed that after a bout of moderate-intensity exercise (performed 14 h prior to the ingestion of the high-fat breakfast and lunch) the decline in FMD was attenuated. In fact, once FMD had been normalised for the post-occlusion shear rate, prior exercise prevented the postprandial decline in FMD entirely, indicating that prior exercise negated the deleterious effects of high-fat meals on the endothelium.

It has been argued that postprandial decreases in FMD do not signify endothelial dysfunction, but are purely a consequence of an increase in basal diameter[31,35]. Arteries with large diameters have been shown to exhibit lower FMD than arteries with small diameters[36–39], as the post-occlusion shear stress stimulus (the stimulus for post-occlusion dilation) is inversely related to vessel diameter[36,37]. As an increase in mean basal diameter from 0 to 3 h was observed in both the control and the exercise trial in the present study, which could influence the FMD responses, an attempt was made to account for this increase in basal diameter by normalising FMD to the area under the shear rate v. time curves. Normalised FMD is not associated with basal diameter[37,39]. As postprandial FMD was lower in the control compared with the exercise trial, both before and after normalisation for the post-occlusion shear rate, despite the similar changes in basal diameter in the control and exercise trials, it is likely that the lower FMD observed in the control trial is not solely a consequence of an increase in basal diameter.

In the present study, as well as observing lower postprandial TAG concentrations following exercise, we also noted a reduction in fasting TAG concentration. The reduction in fasting TAG concentration, seen as a result of exercise in the present study, has also been observed frequently in previous studies[17,40,41]. Given that the correlations between fasting TAG concentration and FMD in the control and exercise trials in the present study were low and not statistically significant, it is unlikely that the differences in fasting TAG concentration in the control and exercise trials would have confounded the main results of the study.

In previous research, a relationship between TAG concentrations and FMD has been demonstrated postprandially, but no relationship between these variables was evident in the fasted state[4,42,43]. In previous studies, where a relationship has been found between postprandial TAG concentrations and change in endothelial function, Pearson correlations have ranged from $-0{\cdot}31$[30] to $-0{\cdot}70$[2]. This has led to the

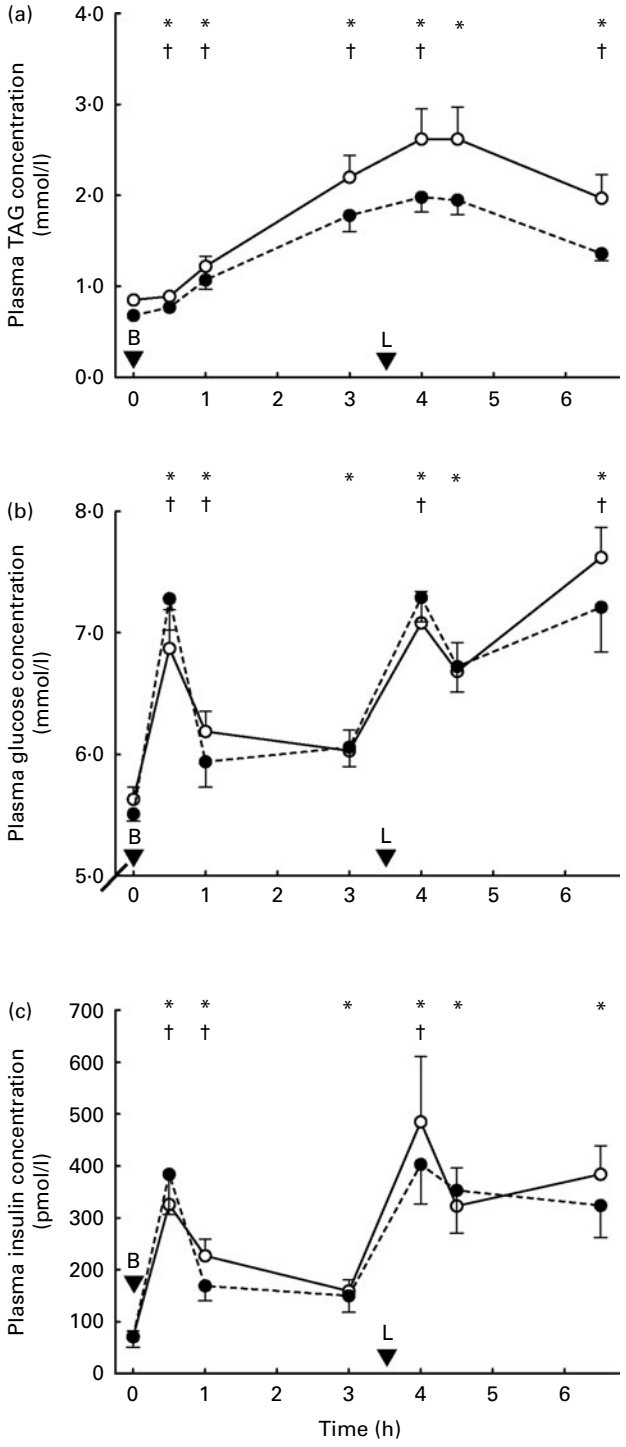


Fig. 2. Plasma (a) TAG, (b) glucose and (c) insulin concentrations. B, breakfast; L, lunch. Values are means with their standard errors represented by vertical bars (n 13). Data were analysed using a mixed-effects general linear model with two fixed factors (trial and time) and one random factor (participant). Least significant differences *post hoc* analysis was used to identify where significant main effects lay; TAG and insulin data were Ln transformed prior to the analysis. (a) TAG: main effect trial (P=0·009); main effect time (P<0·001); and interaction effect trial × time (P=0·276). (b) Glucose: main effect trial (P=0·877); main effect time (P<0·001); and interaction effect trial × time (P=0·361). (c) Insulin: main effect trial (P=0·078); main effect time (P<0·001); and interaction effect trial × time (P=0·558). * Difference from 0 h (P<0·05) and † Difference from previous time point (P<0·05). -○-, Control; -●-, exercise.

hypothesis that prior exercise can prevent the postprandial endothelial dysfunction by reducing postprandial TAG concentrations[1]. However, not all studies have observed this association (for a review, see Wallace *et al.*[44]). In the present study, postprandial TAG concentrations were lower and FMD higher in the exercise compared with the control trial, but we found no evidence of a direct association between these variables. A lack of association between the exercise-induced changes in TAG concentration and endothelial function has also been noted by Tyldum *et al.*[3], who found that exercise reduced postprandial endothelial dysfunction but did not affect postprandial TAG concentration. Gill *et al.*[45] also observed that postprandial endothelial function was similar before and after a period of detraining, despite the postprandial TAG concentration being higher following detraining. There are a number of possible factors that may contribute to the inconsistent associations observed across studies between postprandial TAG and endothelial function, including differences in the methods used to quantify variables, variability in the timing of measurements and in the timing of postprandial events *in vivo* and differences in the lipid load and in the number of study participants[44,46].

The lack of association between TAG concentration and endothelial function in the present study may suggest that while postprandial changes in TAG concentrations and FMD may coincide, they are not dependent on each other; however, due to the small sample size, such conclusions need to be drawn cautiously. Nonetheless, elevated postprandial TAG concentrations are an independent risk factor for CHD[6] and, consistent with other reports from the literature that have used a single meal[17–20], the results of the present study demonstrate that exercise reduces postprandial plasma TAG concentrations following the ingestion of two high-fat meals in adolescent boys.

In the exercise trial, despite no change in HOMA-IR, the total area under the plasma insulin concentration *v.* time curve was lower than in the control trial, while glucose concentrations were not different, suggesting that the insulin sensitivity of the participants was improved after exercise. The only other study that has measured both postprandial glucose and insulin concentrations in adolescents following high-fat mixed meals found no effect of exercise[18]. When HOMA-IR values were compared between the present study and the study by MacEneaney *et al.*[18], the participants in the present study were found to be more insulin resistant; this may explain the difference in findings between the two studies. It is well-established that during puberty a transient state of insulin resistance is experienced, with the greatest insulin resistance occurring mid-puberty (Tanner stage 3)[47,48]. MacEneaney *et al.*[18] did not state the pubertal status of the boys in their study; however, the boys were older than those in the present study (15·9 (SD 0·4) *v.* 13·6 (SD 0·6) years, respectively) and therefore would be expected to be more mature and therefore less insulin resistant. Previous studies have identified greater insulin sensitivity in adolescents who are more physically active[49–51] or have undergone a period of exercise training[52,53]. The present study suggests that an acute bout of exercise also has the ability to

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improve insulin sensitivity. Clearly, this finding warrants further investigation.

The present study did not directly investigate the mechanisms by which exercise attenuates endothelial dysfunction, but a number of possibilities have been proposed. Measures of endothelial function, including FMD, are essentially markers of NO bioavailability[26], and a decrease in NO production and/or an increase in NO inactivation can result in a decline in FMD. It has been suggested that prior exercise may reduce the postprandial rise in oxidative stress by increasing the body's antioxidant capacity, consequently reducing the inactivation of NO and so attenuating the decline in FMD[3]. Exercise may also increase endothelial NO synthase mRNA expression and induce phosphorylation of endothelial NO synthase[54], both of which will increase the production of NO, which would attenuate the decline in FMD. Therefore, there are several mechanisms that may explain why exercise reduces the strain experienced by the endothelium following ingestion of high-fat meals.

Due to the study design, it was not possible to determine the mechanisms for the observed exercise-induced reduction in TAG concentration, but, based on other research literature, it appears that exercise reduces TAG concentration through two complementary pathways: an increased clearance of TAG-rich lipoproteins and/or a reduced hepatic secretion of VLDL TAG[15]. Recent data from kinetic studies suggest that the predominant cause of exercise-induced reductions in TAG concentration is the increased clearance of TAG-rich lipoproteins, with the increased clearance being mediated by the secretion of fewer but more TAG-rich VLDL particles by the liver following exercise[43,55,56]. These TAG-rich VLDL particles are hydrolysed faster by lipoprotein lipase and removed faster from the circulation[57,58]. In addition, TAG clearance may be enhanced by increases in skeletal muscle lipoprotein lipase activity after exercise[59,60].

While CVD is typically a chronic problem in which the potentially terminal manifestations, such as myocardial infarction and stroke, usually occur later in the life cycle, the experimental evidence from the present study emphasises that exercise might offer an acceptable, non-pharmacological means of influencing CHD risk when individuals are young. It also implies that interventions that begin early in an individual's life (such as encouraging regular physical activity or exercise) are likely to be beneficial.

A possible limitation of the present study was that smooth muscle function was not assessed. Typically, this is assessed as the dilation of a blood vessel following administration of a single, high dose of nitroglycerin[24]. However, given the participant group, the authors elected not to administer nitroglycerin for ethical reasons. Also, it has been argued that repeated administration of nitroglycerin could influence subsequent FMD measurements[61]. Furthermore, the dilation following a dose of nitroglycerin has been shown previously to be similar before and after the ingestion of high-fat meals[3,4,31]. A further limitation is that only adolescent boys were included in the present study. Future research should be conducted to investigate if similar responses are observed in girls.

In conclusion, 60 min of moderate-intensity exercise, performed 14 h before the ingestion of a high-fat breakfast and lunch, attenuated the postprandial endothelial dysfunction that was observed in a control trial where no exercise was performed. These results demonstrate for the first time that meals high in fat place a strain on the endothelium of healthy adolescent boys, but also that exercise has prophylactic properties that negate at least some of the deleterious effects associated with the consumption of these meals.

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