Exercise intensity and the protection from postprandial vascular dysfunction in adolescents

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Bond B, Gates PE, Jackman SR, Corless LM, Williams CA, Barker AR. Exercise intensity and the protection from postprandial vascular dysfunction in adolescents. Am J Physiol Heart Circ Physiol 308: H1443–H1450, 2015. First published March 27, 2015; doi:10.1152/ajpheart.00074.2015.—Acute exercise transiently improves endothelial function and protects the vasculature from the deleterious effects of a high-fat meal (HFM). We sought to identify whether this response is dependent on exercise intensity in adolescents. Twenty adolescents (10 male, 14.3 ± 0.3 yr) completed three 1-day trials: 1) rest (CON); 2) 8 × 1 min cycling at 90% peak power with 75 s recovery [high-intensity interval exercise (HIIE)]; and 3) cycling at 90% of the gas exchange threshold [moderate-intensity exercise (MIE)] 1 h before consuming a HFM (1.50 kg/kg fat). Macrovascular and microvascular endothelial function was assessed before and immediately after exercise and 3 h after the HFM by flow-mediated dilation (FMD) and laser Doppler imaging [peak reactive hyperemia (PRH)]. FMD and PRH increased 1 h after HIIE (P < 0.001, effect size (ES) = 1.20 and P = 0.048, ES = 0.56) but were unchanged after MIE. FMD and PRH were attenuated 3 h after the HFM in CON (P < 0.001, ES = 1.78 and P = 0.02, ES = 0.59), and in MIE compared with CON (P < 0.001, ES = 1.47) and CON (P < 0.001, ES = 2.54), and in MIE compared with CON (P < 0.001, ES = 1.40). Compared with CON, PRH was greater 3 h after the HFM in HIIE (P = 0.02, ES = 0.71) and MIE (P = 0.02, ES = 0.84), with no differences between HIIE and MIE (P = 0.71, ES = 0.16). Plasma triacylglycerol concentration and total antioxidant status concentration were not different between trials. We conclude that exercise intensity plays an important role in protecting the vasculature from the deleterious effects of a HFM. Performing HIIE may provide superior vascular benefits than MIE in adolescent groups.

cardiovascular disease; endothelial function; postprandial lipemia; young people

IT IS WELL ESTABLISHED THAT the atherosclerotic process originates in childhood (58) and that cardiovascular disease (CVD) risk factors in youth are associated with the progression of atherosclerosis during adulthood (40). Endothelial dysfunction is a sentinel event in the progression of atherosclerosis, precede the development of fatty streaks, and holds prognostic value in predicting CVD end points and patient mortality (59). Conduit artery endothelial function has been shown to be impaired in asymptomatic adolescents with CVD risk factors (16), whereas microvascular function is also impaired in children with clustered CVD risk (36). The ingestion of a high-fat meal (HFM) causes a transient period of macro- and microvascular dysfunction (5, 54, 70), and, given the central role endothelial dysfunction plays in the atherosclerotic process (12), it is likely that repeat exposure of the vasculature to this environment has long-term implications for vascular health.

In adults, acute moderate- and high-intensity exercise has transient benefits on macrovascular endothelial function in the fasted and postprandial state (30, 70), with the benefits more pronounced following high-intensity exercise possibly due to favorable changes in total antioxidant status (70). Prior exercise has also been shown to protect the microvasculature from the deleterious effects of a HFM in adults (26). In children, cross-sectional evidence suggests that high-intensity exercise may have a positive effect on fasting vascular function (32). Additionally, a single bout of moderate-intensity exercise (MIE) (54) and sprint interval exercise (53) has been shown to preserve postprandial macrovascular function following the first day in adolescent boys. However, the total exercise stimulus in these two studies was not equivalent, and the authors did not include a measure of microvascular function. Therefore, it is currently unknown whether exercise intensity modulates the postprandial macro- and microvascular dysfunction observed after a HFM in adolescents, which may have important public health implications, since much of the day may be spent in the postprandial state. Furthermore, it has recently been shown that performing even small amounts (~4 min) of high-intensity exercise is superior than MIE at modifying cardiometabolic risk factors in youth (15). Considering that few adolescents meet the current recommended minimum of 60 min of moderate-intensity physical activity/day (50), and that habitual physical activity likely declines during adolescence (37, 69), it is pertinent to identify how small volumes of exercise can be optimized for vascular health in this group.

Given the above, this investigation sought to test the hypothesis that a single bout of high-intensity interval exercise (HIIE) provides superior protection of macrovascular function following a HFM compared with a work-matched bout of MIE in adolescents. We also assessed whether postprandial differences in macrovascular function were present at the microvascular level, and if differences in vascular function between trials were related to plasma triacylglycerol concentration (triglyceride) or total antioxidant status.

METHODS

Twenty 12- to 15-yr-old adolescents (10 males) volunteered to take part in this study. Participant assent and parental consent were obtained before participation in the project, which was approved by the institutional ethics committee. Exclusion criteria included the use

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of any medication or substance known to influence fat metabolism or vascular function.

Body mass, seated height, and stature were measured to the nearest 0.1 kg and 0.1 cm. Percentage body fat was estimated using triceps and subscapular skinfold thickness according to Slaughter et al. (57), and pubertal status was determined by a self-assessment of secondary sexual characteristics using adapted drawing of the five Tanner stages of pubic hair development (43).

Visit 1: Fitness assessment. The first visit included a validated combined ramp and supramaximal test to exhaustion to establish maximal oxygen uptake (VO₂ max) (6). Pulmonary VO₂ was monitored throughout (Cortex Metalyzer III B, Leipzig, Germany), and the gas exchange threshold was identified as the disproportionate increase in carbon dioxide production relative to VO₂. All exercise was performed on an electronically braked cycle ergometer (Lode Excalibur Sport, Groningen, The Netherlands).

Visits 2–4: Exercise and postprandial measures. Participants completed three experimental conditions, separated by ~1 wk (Fig. 1). Following an ~2-h overnight fast, participants were transported to the laboratory at 07:45 and rested for 15 min before providing a fasting fingertip capillary blood sample for plasma [triacylglycerol]; Participants then consumed 30 g of commercially available Corn Flakes with 130 ml of skimmed milk, which is unlikely to have influenced endothelial function (71).

At 08:45, participants rested in a darkened, temperature-controlled (24°C) room for 10 min before the simultaneous assessment of macrovascular [flow-mediated dilation (FMD)] and microvascular (laser Doppler perfusion imaging) function. Immediately afterward, capillary blood samples were obtained for plasma [triacylglycerol], 3-hydroxybutyrate concentration ([3-hydroxybutyrate]), and total antioxidant status. These measurements were repeated 1 h after exercise (but before the HFM) and 3 h after the HFM to coincide with peak plasma [triacylglycerol] (67).

At 09:45, 1 h after breakfast, participants either: 1) remained seated in the laboratory (CON); 2) performed ~30 min of continuous MIE at 90% of the gas exchange threshold; or 3) completed 23 min of HIIE. These trials were completed on separate days and in a randomized order. The HIIE bout consisted of a 3-min warm up at 20 W, followed by 8 × 1 min intervals at 90% of the peak power determined from the ramp test to exhaustion, interspersed with 75 s of recovery at 20 W, before a 2-min cool down at 20 W. The duration of the MIE trial was calculated to match the total work performed during the HIIE bout for each participant. Participants provided a rating of perceived exertion (73) in the final 10 s of exercise. Participants also completed the 16-point Physical Activity Enjoyment Scale (44) immediately after exercise cessation. After their final exercise trial, each participant was asked to identify which exercise bout they preferred. Plasma [triacylglycerol] and total antioxidant status were assessed 1 h after the exercise/rest condition. Plasma [3-hydroxybutyrate] was also assessed as a marker of hepatic fatty acid oxidation and very low-density lipoprotein (VLDL) secretion (27). Participants then consumed a milkshake of three parts Cornish ice cream and one part double cream between 10:45 and 11:00, which provided ~1.50 g/kg (80 kJ/kg) of fat in accordance with other postprandial investigations in this group (54, 67, 68) and our earlier work (11). Plasma [triacylglycerol] was assessed at hourly intervals during the 3-h postprandial period. Participants remained seated in the laboratory throughout the postprandial period.

Measures of vascular function. FMD was measured using high-resolution ultrasonography (Sequoia 512, Acuson; Siemens) with a 13-MHz linear array transducer and in accordance with recent guidelines (19, 61) and our earlier work (25). All FMD analyses were performed by a primary investigator who was blinded to the condition. Baseline and postocclusion brachial artery diameter was assessed during end diastole using validated ECG-gating software (Medical Imaging Applications) (41, 61). Baseline arterial diameter was measured for 1.5 min. Endothelium-dependent vasodilation was calculated as the percentage increase in arterial diameter after a 5-min ischemic stimulus (45) induced by rapid forearm pummel cuff inflation (Hokanson) (8) to 220 mmHg. The area under the curve for estimated shear rate was calculated from the last 30 s of occlusion until the time of peak dilation (SR_max) (61). To address concerns about the ratio-scaled FMD statistic (4), FMD was also allometrically scaled according to published guidelines (3). The between-day coefficient of variation for FMD was 10.5%.

During the FMD protocol, microvascular function was simultaneously assessed using a laser Doppler perfusion imager (Periscan PIM II; Perimed, Järfälla, Sweden) at a reproducible point on the distal third of the forearm (20). High-resolution data were collected at 4.33 Hz, and then interpolated to 1-s averages before being smoothed using a 5-s moving average. Resting flux was measured over 2 min before cuff inflation. Peak reactive hyperemia (PRH) was defined as the highest point after occlusion, and the between-day coefficient of variation was 16.2% for this variable.

Blood analyses. For each blood sample, ~600 μl of capillary blood was collected and centrifuged immediately at 13,000 g for 15 min at 4°C. Plasma was then removed and stored at ~8°C for no more than 1 mo. Plasma [triacylglycerol], [3-hydroxybutyrate], and total antioxidant status were quantified in duplicate by enzymatic, colorimetric methods using an assay kit according to the manufacturer’s guidelines (Cayman Chemical). The within-batch coefficients of variation for plasma [triacylglycerol], [3-hydroxybutyrate], and total antioxidant were 2.9, 3.8, and 4.2%, respectively. The total (TAUC) and incremental (IAUC) area under the curve analyses were performed using the time point immediately before the HFM for plasma [triacylglycerol] and the time point immediately before exercise for plasma [3-hydroxybutyrate] and total antioxidant status.

Control of diet and exercise. With parental supervision, participants were asked to replicate their evening meal before each laboratory visit. Participants also completed a food diary during the 48-h period immediately preceding each visit, which was subsequently assessed for total energy and macronutrient intake (ComEat Pro; Nutrition Systems). Participants were instructed to avoid strenuous exercise and wear a triaxial accelerometer on their wrist (GENEActiv; Activinsights, Cambridge, UK) during the 48 h before each visit. Time spent performing moderate to vigorous activity was determined using established cut points for pediatric groups (48).

Statistical analyses. Descriptive statistics were calculated using SPSS (version 19.0) and presented as means ± SD. Mean differences in descriptive statistics between boys and girls were analyzed using independent-samples t-tests. The mean differences in the physiological and perceptual responses of the boys and girls during HIIE and MIE were analyzed using paired-samples t-tests. Analysis of plasma [triacylglycerol], [3-hydroxybutyrate], and total antioxidant status and parameters of macro- and microvascular function were performed using a mixed-model ANOVA with trial (CON, MIE, HIIE) and sex (male, female) as the main effects. For clarity, the main effects for

![Fig. 1. Protocol schematic. CON, rest; MIE, moderate-intensity exercise; HIIE, high-intensity interval exercise; HFM, high-fat meal. Arrows represent the assessment of macro- and microvascular function and capillary blood samples for plasma 3-hydroxybutyrate concentration ([3-hydroxybutyrate]) and total antioxidant status.](http://ajpheart.physiology.org/)

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Table 1. Participant characteristics

<table>
<thead>
<tr>
<th></th>
<th>Boys (n = 10)</th>
<th>Girls (n = 10)</th>
<th>P Value</th>
<th>ES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>14.8 ± 0.2</td>
<td>14.1 ± 0.9</td>
<td>0.06</td>
<td>1.07</td>
</tr>
<tr>
<td>Body mass, kg</td>
<td>61.1 ± 11.9</td>
<td>54.5 ± 9.3</td>
<td>0.19</td>
<td>0.62</td>
</tr>
<tr>
<td>Stature, m</td>
<td>1.69 ± 0.07</td>
<td>1.61 ± 0.09</td>
<td>0.04</td>
<td>0.99</td>
</tr>
<tr>
<td>Body fat, %</td>
<td>10 ± 4</td>
<td>20 ± 4</td>
<td>&lt;0.001</td>
<td>2.50</td>
</tr>
<tr>
<td>( \text{VO}_2\text{max}, \text{l/min} )</td>
<td>2.76 ± 0.54</td>
<td>2.03 ± 0.27</td>
<td>0.001</td>
<td>1.71</td>
</tr>
<tr>
<td>( \text{VO}_2\text{max}, \text{ml/min} \cdot \text{kg}^{-1} )</td>
<td>45.5 ± 6.4</td>
<td>37.8 ± 4.5</td>
<td>0.01</td>
<td>1.39</td>
</tr>
<tr>
<td>GET, ‰</td>
<td>1.40 ± 0.25</td>
<td>1.09 ± 0.20</td>
<td>0.001</td>
<td>1.37</td>
</tr>
<tr>
<td>GET, % ( \text{VO}_2\text{max} )</td>
<td>51 ± 6</td>
<td>54 ± 7</td>
<td>0.39</td>
<td>0.46</td>
</tr>
</tbody>
</table>

Data are presented as means ± SD; n, no. of subjects. \( \text{VO}_2\text{max}, \) maximal oxygen uptake; GET, gas exchange threshold; ES, effect size.

time and condition are not discussed if the ANOVA output revealed a significant interaction effect. The inclusion of sex into the ANOVA model did not reveal a significant interaction effect for plasma [3-hydroxybutyrate] and total antioxidant status or parameters of macro- and microvascular function. Data were subsequently pooled for these outcomes. Pairwise comparisons between means were interpreted using the P value and standardized effect sizes (ES) to document the magnitude of the effect using the following thresholds: small (0.2), moderate (0.5), and large (0.8) (18). Relationships between changes in vascular outcomes and mechanistically important variables were explored using Pearson’s correlations.

RESULTS

Baseline participant characteristics are presented in Table 1. The maturation status for boys and girls was as follows: Tanner stage 3, \( n = 4 \) and 1; stage 4, \( n = 4 \) and 8; and stage 5, \( n = 2 \) and 1. No differences in energy intake, individual macronutrient contributions, or time spent performing moderate to vigorous physical activity were apparent for boys or girls during the 48 h preceding each laboratory visit (\( P > 0.14, \) ES < 0.20; Table 2).

Table 3 presents the physiological and perceptual data from the exercise trials. The highest \( \text{VO}_2 \) achieved during the HIIE condition equated to 93 ± 5 and 96 ± 5% \( \text{VO}_2 \text{max} \) for boys and girls, respectively. Average length of the MIE trial was 24.9 ± 2.3 min. Nine boys and nine girls indicated that they preferred the HIIE exercise bout.

Blood analyses. Mean differences in plasma [triacylglycerol] during the postprandial period are shown in Fig. 2A. Mean fasted plasma [triacylglycerol] was lower across all trials in girls (\( P = 0.03, \) ES = 0.96). There was no trial-by-sex interaction (\( P = 0.44 \)) for TAUC-triacylglycerol, but there was a trend for TAUC-triacylglycerol to be lower in girls across all trials (\( P = 0.05 \)). There was no trial-by-sex interaction (\( P = 0.58 \)) for IAU-triacylglycerol.

Mean differences in plasma [3-hydroxybutyrate] are shown in Fig. 2B. A time-by-trial interaction (\( P = 0.04 \)) was apparent for plasma [3-hydroxybutyrate], which was elevated 3 h after the HFM in HIIE compared with CON (\( P = 0.01, \) ES = 0.59), with no differences between MIE and CON (\( P = 0.16, \) ES = 0.26) or HIIE and MIE (\( P = 0.13, \) ES = 0.29). An increase in TAUC plasma [3-hydroxybutyrate] in HIIE was associated with lower TAUC-triacylglycerol (\( P = 0.01, \) \( r = 0.61 \)) but not for MIE (\( P = 0.22, \) \( r = 0.30 \)).

Mean differences in total antioxidant status are provided in Fig. 2C. There was no time-by-trial interaction (\( P = 0.53 \)) or effect of trial (\( P = 0.88 \)), but there was a main effect of time for total antioxidant status (\( P = 0.04 \)). Mean total antioxidant status across conditions was lower after the HFM compared with baseline (\( P = 0.02, \) ES = 0.39). Changes in total antioxidant status were not related to parameters of vascular function (\( P > 0.05 \) and \( r < 0.2 \)).

Macrovascular function. Differences in FMD between trials are presented in Fig. 3A. There was a time-by-trial interaction (\( P < 0.001 \)) for FMD. FMD was greater 1 h after HIIE compared with before (\( P = 0.001, \) ES = 1.20), but unchanged after MIE (\( P = 0.22, \) ES = 0.09) and CON (\( P = 0.99, \) ES < 0.01) compared with before exercise. Consequently, FMD was greater after HIIE compared with MIE (\( P = 0.002, \) ES = 1.14) and CON (\( P = 0.002, \) ES = 1.15), with no difference between MIE and CON (\( P = 0.59, \) ES = 0.15) 1 h after exercise.

Table 2. Accelerometer and food diary data during the 48 h preceding each trial

<table>
<thead>
<tr>
<th></th>
<th>CON</th>
<th>MIE</th>
<th>HIIE</th>
<th>MIE vs. CON (95% CI)</th>
<th>HIIE vs. CON (95% CI)</th>
<th>HIIE vs. MIE (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate-vigorous activity, min/day</td>
<td>75 ± 30</td>
<td>73 ± 36</td>
<td>75 ± 27</td>
<td>−35 to 19</td>
<td>−37 to 23</td>
<td>−18 to 24</td>
</tr>
<tr>
<td>Total energy intake, kcal/day</td>
<td>1,862 ± 427</td>
<td>1,980 ± 388</td>
<td>2,027 ± 551</td>
<td>−122 to 245</td>
<td>−134 to 455</td>
<td>−171 to 369</td>
</tr>
<tr>
<td>Energy from carbohydrates, %</td>
<td>46 ± 7</td>
<td>47 ± 5</td>
<td>45 ± 5</td>
<td>−1 to 5</td>
<td>−3 to 3</td>
<td>−5 to 2</td>
</tr>
<tr>
<td>Energy from fat, %</td>
<td>37 ± 6</td>
<td>36 ± 4</td>
<td>37 ± 6</td>
<td>−5 to 2</td>
<td>−5 to 2</td>
<td>−4 to 4</td>
</tr>
<tr>
<td>Energy from protein, %</td>
<td>17 ± 4</td>
<td>17 ± 3</td>
<td>18 ± 3</td>
<td>−4 to 2</td>
<td>−1 to 3</td>
<td>0 to 4</td>
</tr>
</tbody>
</table>

Data are presented as means ± SD. Data have been pooled since ANOVA revealed no main effect for sex, CON, control trial; MIE, moderate-intensity exercise trial; HIIE, high-intensity interval exercise trial; 95% CI, 95% confidence limits for the true difference.

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FMD was greater 3 h after the HFM in HIIE compared with MIE (P/H11021 0.001, ES/H11005 1.47) and CON (P/H11021 0.001, ES/H11005 2.54), and in MIE compared with CON (P/H11021 0.001, ES/H11005 1.40). FMD was attenuated after the HFM in CON (P/H11021 0.001, ES/H11005 1.78) compared with before the meal. FMD remained elevated after the HFM compared with baseline in HIIE (P/H11021 0.001, ES/H11005 1.56). Differences in SRAUC between trials are provided in Fig. 3B. Changes in FMD were not related to SRAUC in any trial. Consequently, FMD was not normalized for SRAUC. There was no time-by-trial interaction for SRAUC (P/H11005 0.25), resting arterial diameter (P/H11005 0.11, Fig. 3C), or time taken to reach peak dilation (P/H11005 0.37).

Microvascular function. Differences in PRH between trials are presented in Fig. 3D. There was a time-by-trial interaction (P/H11005 0.002) for PRH. PRH was greater 1 h after HIIE (P = 0.004, ES = 0.82) but unchanged after MIE (P = 0.22, ES = 0.26) and CON (P = 0.27, ES = 0.26). Compared with CON, PRH was greater 3 h after the HFM in HIIE (P = 0.02, ES = 0.71) and MIE (P = 0.02, ES = 0.84), with no difference between HIIE and MIE (P = 0.72, ES = 0.16). PRH was attenuated 3 h after the HFM in CON (P = 0.02, ES = 0.59). There was no effect of trial (P = 0.15), time (P = 0.40), or a trial-by-time interaction (P = 0.27) for time taken to achieve PRH.

DISCUSSION

The novel findings from this study are: 1) macro- and microvascular function was enhanced 1 h after HIIE compared

FMD was greater 3 h after the HFM in HIIE compared with MIE (P < 0.001, ES = 1.47) and CON (P < 0.001, ES = 2.54), and in MIE compared with CON (P < 0.001, ES = 1.40). FMD was attenuated after the HFM in CON (P < 0.001, ES = 1.78) compared with before the meal. FMD remained elevated after the HFM compared with baseline in HIIE (P < 0.001, ES = 1.56). Differences in SRAUC between trials are provided in Fig. 3B. Changes in FMD were not related to SRAUC in any trial. Consequently, FMD was not normalized for SRAUC. There was no time-by-trial interaction for SRAUC (P = 0.25), resting arterial diameter (P = 0.11, Fig. 3C), or time taken to reach peak dilation (P = 0.37).

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The novel findings from this study are: 1) macro- and microvascular function was enhanced 1 h after HIIE compared
with CON and MIE, and remained elevated 3 h after a HFM; 2) a single bout of MIE did not alter macro- or microvascular function 1 h after exercise, but prevented the decline in function observed 3 h after a HFM; and 3) the interactions between exercise intensity and vascular function were independent of changes in plasma [triacylglycerol] or total antioxidant status. These data show for the first time that the effect of exercise on postprandial vascular function is dependent on exercise intensity. Specifically, macrovascular function after a HFM is preserved by MIE, and augmented by HIIE. These findings may have a clinically important public health message, since a significant proportion of time is spent in the postprandial state, and endothelial function predicts cardiovascular events independently of conventional CVD risk factors (12).

The HFM reduced FMD by 21% in CON, which is consistent with other adolescent (54) and adult (5, 70, 71) data. For the first time in adolescents, we provide evidence that a single bout of MIE performed 1 h before a HFM may preserve endothelial function, and that an equivalent bout of HIIE not only prevents this attenuation but improves endothelial function despite no reduction in plasma [triacylglycerol]. Whereas the benefits of prior moderate-intensity (54) and sprint interval (55) exercise on postprandial macrovascular function have been shown to be unrelated to changes in plasma [triacylglycerol] in adolescents, we are the first to identify an independent effect of exercise intensity. Our findings concur with those reported by Tyldum et al. (70); however, these authors identified that this protective effect of exercise performed the day before a HFM was related to an exercise-induced increase in antioxidant capacity, which we did not observe in this study. It is known that postprandial lipemia impairs vascular function via oxidative stress (5), which may reduce nitric oxide bioavailability (72). FMD is considered to be largely nitric oxide dependent (28), but we did not observe an effect of exercise on total antioxidant status, or a relationship between FMD and total antioxidant status. However, Johnson et al. (35) also reported no relationship between postexercise FMD and oxidative stress, and this may be related to the limitation of a single measurement of oxidative stress rather than rate of antioxidant depletion (22). Furthermore, the exercise bouts in this study were performed 1 h, compared with 16–18 h (70), before the ingestion of the HFM, and thus the process(es) underlying the response in pro/antioxidant state are likely to be mechanistically different. Indeed a recent investigation failed to observe any changes in postprandial antioxidant status after MIE and HIE when exercise was performed 1 h after a HFM (14). Additionally, we cannot account for the influence of training status on the changes in pro/antioxidant status following the exercise bouts (10). However, based upon recommended $\bar{V}_{O_2\text{max}}$ cutoff values for cardiometabolic health (1), five of the boys and two of the girls included in this study could be identified as “at risk,” and the $\bar{V}_{O_2\text{max}}$ values observed in the present study were typically lower than those reported in trained groups (2).

Previous studies with healthy adults report that FMD either increases (35, 70), decreases (22, 35) or remains unaltered (23, 52) after a single bout of exercise; however, these data are difficult to interpret due to inconsistencies in the intensity, duration, and modality of exercise and the timing of the FMD measurement(s) (22). The present study is the first to incorporate a work-matched exercise protocol to isolate the influence of exercise intensity on vascular function in adolescents, and our data show that FMD is increased 1 h after HIIE but remains unaltered after MIE. In contrast, an exercise intensity-dependent decrease in FMD has been shown immediately after cycling in adults (9), and exergaming in children (42). It is likely that this disparity is due to the timing of our FMD measure (1 h vs. immediately after exercise), since the FMD response postexercise is biphasic in nature (23). Indeed, it is thought that the temporary blunting of FMD observed after high-intensity, but not MIE (9, 35, 42), is the stimulus for subsequent improvements in FMD (47); however, no study has yet identified the time course of the FMD response following work-matched exercise in adolescents.

Changes in FMD after exercise have been attributed to differences in baseline arterial diameter and shear rate (22). However, these remained unaltered between trials in the present study, and there was no relationship between the magnitude of the FMD response and $\text{SR}_{\text{AUC}}$, which is consistent with existing data in children (62) and following exercise in adults (38). However, we did not quantify shear stress during the exercise bouts. Given that the exercise conditions were work matched, it is likely that the disparate responses in FMD observed postexercise are related to the positive association between brachial artery shear and the intensity of cycling exercise (29, 63). This has been shown to play a leading role in modulating the postexercise FMD response (64, 65), probably due to an upregulation in endothelial nitric oxide synthase and subsequent increase in the bioavailability of nitric oxide (34). We are unable to partition out the influence of the HFM on the postprandial FMD response following MIE and HIIE. For example, it is possible that postprandial FMD could have been higher still following HIIE. However, considering that FMD has been demonstrated to return to baseline 2 h post-high-intensity exercise (35), and the lack of change in total antioxidant status in the present study, it would appear that the inclusion of a HFM 1 h after exercise did not modulate the postexercise nitric oxide bioavailability. Further study is needed to confirm this.

A novel feature of this investigation was the simultaneous assessment of microvascular function during the FMD protocol. Whereas the endothelium only plays a part of the PRH effect (20), impaired microvascular reactive hyperemia is associated with elevated blood pressure (56), obesity (24), and insulin resistance (33) and has been identified in healthy children with clustered CVD risk factors (36). Therefore, it follows that the assessment of PRH as a surrogate of microvascular function in the current study may provide useful information regarding vascular health in asymptomatic individuals. We observed a significant impairment in postprandial microvascular function in CON, suggesting that a fatty meal presents a global challenge to the vasculature. This dysfunction was prevented in both exercise trials, but not in an intensity-dependent manner. To our knowledge, no other study has identified the effect of exercise intensity on subsequent postprandial microvascular function; however, Gill et al. observed a similar protective effect of MIE performed the evening before a HFM in adults, and this was endothelium dependent (26).

Prior MIE (67) and HIIE (60) can attenuate postprandial lipemia in adolescents; however, we were unable to replicate these findings in this study, possibly due to our use of a 1-day
EXERCISE INTENSITY AND ADOLESCENT VASCULAR HEALTH

protocol (74) and a short (3-h) postprandial observation period. It has been hypothesized that exercise-induced changes in hepatic very low density lipoprotein (VLDL) output may explain some of the reduction in postprandial lipemia after a HFM (39), particularly when the time between exercise cessation and consumption of the test meal is short due to the delay in the upregulation of lipoprotein lipase (55). Our data would appear to be consistent with this theory, since [3-hydroxybutyrate] was elevated 3 h after the HFM in HIIE compared with CON and significantly correlated with the reduction in TAUC-triacylglycerol, suggesting a shift toward hepatic fatty acid oxidation rather than reesterification and VLDL synthesis during the HIIE condition (27).

Repeated sprint cycling the day before a HFM has previously been demonstrated to preserve postprandial macrovascular function in adolescents (53). However, these authors reported that one-third of the participants failed to complete the exercise protocol. In contrast, all participants in the present study completed the HIIE bout. Furthermore, our data indicate that HIIE was perceived to be more enjoyable than MIE for both boys and girls, despite a greater physiological stress. This is encouraging considering that adolescents rarely sustain exercise for longer than 10 min (50); therefore, low-volume, high-intensity exercise may be a suitable method of optimizing this pattern of activity provided that the exercise is not an “all-out” effort. Further work is needed to identify the long-term adherence to a HIIE training intervention in this group; however, preliminary evidence is promising (13). Indeed, our data add to a growing body of evidence that indicates that HIIE is a feasible and attractive alternative to MIE in adolescents (11, 21, 49).

This is the first study to isolate the influence of exercise intensity on postprandial vascular function in adolescents. A further novelty of this study is the simultaneous assessment of microvascular function during the FMD protocol. However, our findings should be interpreted in light of a number of methodological considerations. First, whereas postocclusive reactive hyperemia has been used as a marker of microvascular function in adolescents (51), the mechanisms underlying the PRH response to 5 min of ischemia following exercise and a HFM are yet to be fully determined, but likely involve other pathways in addition to changes in endothelial function (20). However, postprandial microvascular function has been shown to be improved following exercise elsewhere, and this was endothelium dependent (26). Therefore, it is likely that some of the improvements observed in macrovascular endothelial function via FMD in the present study are present at the microvascular level. Second, we were unable to control for the menstrual cycle, which has been shown to influence FMD in women (31). The median stage of maturity (Tanner 4) suggests that some girls would be pre- or postmenarche (7), and, although there was no significant interaction effect of sex on macro- or microvascular function in the present study, further work is necessary to explicitly establish whether sex influences this outcome in adolescents and in children. Third, the HFM used in this study has limited ecological validity but provided a metabolic challenge in accordance with other postprandial investigations with adolescents (11, 54, 66, 68). This meal also provided an average of 35 g of sugar, which could plausibly have contributed to the postprandial responses (17), although this is equivocal (46). Future work is needed to identify how prior exercise can alter macro- and microvascular function following more habitual fat loads and feeding regimes. Finally, we were unable to determine endothelial-independent function via a sublingual spray of nitroglycerin (19), and this remains an area of future research.

In conclusion, macro- and microvascular dysfunction occurs in concert after a HFM in adolescents. We have shown that postprandial vascular function can be preserved after MIE, or improved after HIIE, and these changes were not related to plasma [triacylglycerol] or total antioxidant status. Whereas these findings cannot be extrapolated beyond healthy adolescents, they may have clinical importance, since repeat impairment in endothelial function likely plays a key role in the development of CVD, which is known to have its origins in childhood (58). Future work is needed to assess the efficacy of different exercise intensities on postprandial endothelial function in adolescents with risk factors for CVD (e.g., obesity, type I diabetes). Finally, we also report here that HIIE was perceived to be more enjoyable than MIE, despite the greater physiological stress. Taken together, low-volume HIIE may be a feasible and attractive strategy to reduce CVD risk from an early age.

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

AUTHOR CONTRIBUTIONS


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EXERCISE INTENSITY AND ADOLESCENT VASCULAR HEALTH


