The Acute Effect of Exercise Intensity on Vascular Function in Adolescents

BERT BOND, SIOBHAN HIND, CRAIG A. WILLIAMS, and ALAN R. BARKER
Children’s Health and Exercise Research Centre, Sport and Health Science, College of Life and Environmental Sciences, University of Exeter, Exeter, UNITED KINGDOM

ABSTRACT

BOND, B., S. HIND, C. A. WILLIAMS, and A. R. BARKER. The Acute Effect of Exercise Intensity on Vascular Function in Adolescents. Med. Sci. Sports Exerc., Vol. 47, No. 12, pp. 2628–2635, 2015. Introduction: Impairments in vascular function are present in asymptomatic youths with risk factors for cardiovascular disease. Exercise can promote vascular health in youth, but the effects of exercise intensity and the time course in response to acute exercise are unknown. Methods: Twenty adolescents (10 male, 14.1 ± 0.3 yr) performed the following on separate days in a counterbalanced order: 1) cycling at 90% of the gas exchange threshold (moderate-intensity exercise (MIE)) and 2) 8 × 1-min cycling at 90% peak power with 75-s recovery (high-intensity interval exercise (HIIE)). The duration of MIE (25.8 ± 2.1 min) was work-matched to HIIE (23.0 min). Macro- and microvascular functions were assessed before, immediately after, and 1 and 2 h after exercise by flow-mediated dilation (FMD) and laser Doppler imaging (total reactive hyperemia). Results: FMD was attenuated immediately after HIIE (P < 0.001, effect size (ES) = 1.20) but not after MIE (P = 0.28, ES = 0.26). Compared with that before exercise, FMD was elevated 1 and 2 h after HIIE (P < 0.001, ES = 1.33; P < 0.001, ES = 1.36) but unchanged in MIE (P = 0.67, ES = 0.10; P = 0.72, ES = 0.08). Changes in FMD were unrelated to shear or baseline arterial diameter. Compared with that in preexercise, total reactive hyperemia was always greater after MIE (P < 0.02, ES > 0.60 for all) and HIIE (P < 0.001, ES > 1.18 for all). Total reactive hyperemia was greater in HIIE compared with that in MIE immediately after (P = 0.03, ES = 0.67) and 1 h after (P = 0.01, ES = 0.62) exercise, with a trend to be greater 2 h after (P = 0.06, ES = 0.45). Conclusions: Exercise intensity is positively associated with macro- and microvascular function 1 and 2 h after exercise. Performing HIIE may provide superior vascular benefits than MIE in adolescents. Key Words: CARDIOVASCULAR DISEASE, ENDOTHELIAL FUNCTION, YOUTH, TIME COURSE

Although the clinical manifestations of cardiovascular diseases (CVD) are not detectable until adulthood, it is well established that the atherosclerotic process originates in the first decade of life (32). Impaired vascular function is thought to precede structural adaptations to the vessel wall (44), and both macro- and microvascular functions have been shown to be impaired in asymptomatic adolescents with CVD risk factors (8,19). Therefore, interventions that improve vascular function in young people are warranted.

Data are available demonstrating that time spent performing vigorous-intensity, but not moderate-intensity, physical activity is related to improved macrovascular function (17) and attenuated cardiometabolic risk (7) in youth. In addition, exercise interventions have been shown to improve macrovascular function in obese adolescents (41). It has been suggested that changes in vascular function after a single exercise bout provide the foundation for these chronic adaptations (3,12). Consequently, there is value in identifying the acute vascular responses to a single bout of exercise.

Previous studies with adults report conflicting results on the effects of acute exercise on macrovascular function, with some reporting increases (16,18), decreases (3,18), and no change (3) in flow-mediated dilation (FMD). However, differences between exercise loads, modalities, the timing of the postexercise FMD measurement(s) (12), and the problems associated with reporting the ratio-scaled FMD statistic (1) currently limit our understanding of the FMD response to an acute bout of exercise. To our knowledge, only one study has assessed FMD immediately after exercise in young people (22). These authors reported that FMD immediately decreased after high-intensity, but not low-intensity, exergaming, and concluded that repeating high-intensity exergaming may provide a stimulus for favorable macrovascular adaptations. However, the exercise bouts were not work-matched in this study and FMD was only assessed immediately after exercise. Given that changes in vascular function within approximately 2 h of exercise are thought to be biphasic (12), it is important to document the time course of the change in vascular function after a single bout of exercise in youth to establish the influence of exercise intensity on the FMD response.
An impairment in microvascular reactive hyperemia has been identified in asymptomatic children with clustered CVD risk (19), and it is thought that microvascular dysfunction may play a primary role in the pathogenesis of insulin resistance (25). Microvascular function has been shown to be elevated in adolescent football players compared with that in their untrained peers (29); however, we are not aware of any study that has isolated the acute effect of exercise intensity on microvascular function in young people or adults. Furthermore, postexercise changes in microvascular reactive hyperemia have been shown to be unrelated to FMD (31). Therefore, it is inappropriate to adopt postexercise changes in FMD as a surrogate of microvascular function.

The purpose of this investigation was to test the hypothesis that macrovascular function is immediately impaired, and then subsequently improved, after high-intensity interval exercise (HIIE) but remains stable after a work-matched bout of moderate-intensity exercise (MIE) in adolescents. A secondary aim was to identify the effect of exercise intensity on the time course of the microvascular response after exercise.

**METHODS**

Twenty 12- to 15-yr-old adolescents (10 males) volunteered to take part in this study. Written 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 of any medication or substance known to influence fat metabolism or vascular function.

**Experimental overview.** This study required three visits to the laboratory and included a within-measures design. All exercise tests were completed using an electronically braked cycle ergometer (Lode Excalibur Sport, Groningen, The Netherlands).

**Visit 1: fitness assessment.** Participants were habituated to the cycle ergometer before completing a combined ramp and supramaximal test to exhaustion to establish maximal oxygen uptake (VO$_2$max) (2). Pulmonary VO$_2$ was monitored throughout (Cortex Metalyzer III B, Leipzig, Germany), and the gas exchange threshold was identified as the disproportionate increase in carbon dioxide production (VCO$_2$) relative to VO$_2$ and an increase in expired ventilation (VE) VO$_2$ with no increase in VE/VCO$_2$. All exercise was performed on an electronically braked cycle ergometer (Lode Excalibur Sport, Groningen, the Netherlands).

**Visits 2 and 3: exercise interventions.** Participants completed two experimental conditions separated by approximately 1 wk. After an approximately 12-h overnight fast, participants were transported to the laboratory at 0800 h and then consumed 30 g of commercially available Corn Flakes with 130 mL of skimmed milk. The macronutrient contribution of this breakfast is unlikely to have influenced endothelial function (40).

At 0845 h, participants rested in a darkened, temperature-controlled (24°C) room for 15 min before the simultaneous assessment of macrovascular (FMD) and microvascular (laser Doppler perfusion imaging) function (methods described in the following section).

At 0915, 1 h after breakfast, participants completed the following on separate days and in a randomized order: 1) approximately 30 min of continuous MIE at 90% of the gas exchange threshold or 2) 23 min of HIIE (4). 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 cooldown at 20 W. The duration of the MIE trial was calculated to match the total work performed during the HIIE bout. Participants provided a rating of perceived exertion (RPE) (43) in the final 10 s of exercise, before completing the 16-point Physical Activity Enjoyment Scale (23) immediately after the exercise. After their final exercise trial, each participant was asked to identify the exercise bout they preferred.

Macro- and microvascular functions were reassessed immediately after exercise cessation, with further measures 1 and 2 h after exercise to facilitate comparison between extant literature in adults (12). Participants remained seated and were inactive at all times except during the exercise bouts.

**Measures of vascular function.** FMD was measured using high-resolution ultrasonography in duplex mode (Sequoia 512, Acuson; Siemens Corp., Aspen, CO) using a 12- to 14-MHz linear array transducer in accordance with recent guidelines (33) and our earlier work (4). Baseline and postocclusion brachial artery diameter was assessed during end-diastole using validated ECG-gating software (Medical Imaging Applications LLC, Coralville, IA) (10.21). 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 induced by rapid forearm pneumatic cuff inflation (Hokanson, Bellevue, WA) to 220 mm Hg (33). The between-trial coefficient of variation for FMD was 9.7%.

During the FMD protocol, microvascular function was simultaneously assessed using a laser Doppler perfusion imager (Periscan PIM II; Perimed, Järfalla, Sweden) at a reproducible point on the distal third of the forearm (11). 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. Peak reactive hyperemia (PRH) was defined as the highest point after occlusion. The total hyperemic response was calculated by determining the area under the postocclusion reactive hyperemic curve minus the baseline (preocclusion) blood flow (expressed as a percentage of PRH) multiplied by the time taken for reactive hyperemia to return to baseline (42). When calculated in this manner, the postocclusion hyperemic response is known to be nitric oxide independent (42) and accounts for differences in baseline skin perfusion. The between-trial coefficients of variation for PRH and the total hyperemic response were 13.3% and 21.7%, respectively.

**Standardization of diet and physical activity.** 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 were subsequently assessed for total energy and macronutrient intake (CompEat Pro; Nutrition Systems, United Kingdom). Participants were instructed to avoid strenuous exercise and wear a triaxial accelerometer on their wrist (GENEActiv; ActivInsights Ltd, Cambridge, United Kingdom) during the 48 h before each visit. Time spent performing moderate-to-vigorous activity was determined using established cut points for pediatric groups (13).

**Statistical analyses.** The primary outcome for macrovascular function was the difference between log-transformed peak and baseline arterial diameter, adjusted allometrically for baseline diameter (1). Data were analyzed using a linear mixed model with a random intercept (accounting for repeated measures within participants) plus fixed effects for condition (MIE, HIIE), time (before, after, 1 h, 2 h), and their interaction. As appropriate for a crossover trial, we also adjusted for any period effect. Differences on the log-scale were back-transformed to provide percent (ratio) effects. Point estimates are presented together with 95% confidence intervals.

Data were analyzed using a linear mixed model ANOVA, and baseline arterial diameter, adjusted allometrically for baseline stature, was included as a covariate. The physiological and perceptual responses of the boys and girls during HIIE and MIE were analyzed using independent-samples t-tests. Differences in the physiological and perceptual responses of boys and girls were analyzed using paired-samples t-tests. Parameters of macro- and microvascular functions were analyzed using a mixed-model ANOVA, with trial (MIE, HIIE) and sex (male, female) as the main effects. The inclusion of sex into the ANOVA model did not reveal a significant interaction effect for parameters of macro- and microvascular functions. Data were subsequently pooled for these outcomes. Pairwise comparisons between means were interpreted using the P value, 95% CI, and standardized effect sizes (ES) to document the magnitude of the effect using the thresholds, as follows: small (0.2), moderate (0.5), and large (0.8) (9). Relations between changes in vascular outcomes and mechanistically important variables were explored using Pearson correlations.

### RESULTS

Baseline participant characteristics are presented in Table 1. The maturation status for boys and girls was as follows: Tanner stage 2, n = 1 and n = 6; stage 3, n = 3 and n = 10; stage 4, n = 5 and n = 7; and stage 5, n = 1 and n = 3. 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 > 0.50, ES < 0.20) (Table 2).

The physiological and perceptual data from the exercise trials are presented in Table 3. All participants completed both exercise trials. The highest $\dot{V}O_2$ achieved during the HIIE condition equated to 96% ± 5%. The average length of the MIE trial was 25.8 ± 2.1 min. Nine boys and eight girls indicated that they preferred the HIIE exercise bout.

**Macrovascular function.** Baseline arterial diameter, $SR_{AUC}$, and FMD are illustrated in Figure 1. A time–trial interaction was present for FMD (P < 0.001). No differences in mean FMD at baseline were apparent between trials (P = 0.62; 95% CI, −1.2 to 0.7; ES = 0.12). Compared with that in baseline, FMD was attenuated immediately after HIIE (P < 0.001; 95% CI, −4.4 to −2.3; ES = 1.20) but was unchanged immediately after MIE (P = 0.28; 95% CI, −1.5 to 0.4; ES = 0.26). Consequently, FMD was lower in HIIE compared with that in MIE immediately after exercise (P < 0.001; 95% CI, −3.4 to −1.6; ES = 1.57). FMD was not different from baseline 1 h (P = 0.67; 95% CI, −0.8 to 1.2; ES = 0.10) and 2 h (P = 0.72; 95% CI, −0.8 to 1.1; ES = 0.08) after MIE; however, FMD was greater than baseline after HIIE at these time points (P < 0.001; 95% CI, 1.7–3.7; ES = 1.33; and P < 0.001; 95% CI, 1.8–3.7; ES = 1.36, respectively). Consequently, FMD was greater in HIIE compared with that in MIE immediately after exercise (P < 0.001; 95% CI, −3.4 to −1.6; ES = 1.57). FMD was not different from baseline 1 h (P = 0.67; 95% CI, −0.8 to 1.2; ES = 0.10) and 2 h (P = 0.72; 95% CI, −0.8 to 1.1; ES = 0.08) after MIE; however, FMD was greater than baseline after HIIE at these time points (P < 0.001; 95% CI, 1.7–3.7; ES = 1.33; and P < 0.001; 95% CI, 1.8–3.7; ES = 1.36, respectively). Consequently, FMD was greater in HIIE compared with that in MIE 1 h (P < 0.001; 95% CI, 1.8–3.8; ES = 1.31) and 2 h (P < 0.001; 95% CI, 1.8–3.8; ES = 1.33) after exercise.

### Table 1. Participant characteristics.

<table>
<thead>
<tr>
<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>14.1 ± 0.3</td>
<td>14.1 ± 0.3</td>
<td>0.72</td>
</tr>
<tr>
<td>Body mass (kg)</td>
<td>61.6 ± 15.9</td>
<td>54.9 ± 46</td>
<td>0.23</td>
</tr>
<tr>
<td>Stature (m)</td>
<td>1.66 ± 0.10</td>
<td>1.65 ± 0.08</td>
<td>0.82</td>
</tr>
<tr>
<td>$VO_{2max}$ (L min$^{-1}$)</td>
<td>2.77 ± 0.80</td>
<td>2.04 ± 0.36</td>
<td>0.02</td>
</tr>
<tr>
<td>$VO_{2max}$ (mL min$^{-1}$ kg$^{-1}$)</td>
<td>44.8 ± 6.4</td>
<td>37.1 ± 5.3</td>
<td>0.01</td>
</tr>
<tr>
<td>GET (L min$^{-1}$)</td>
<td>1.36 ± 0.35</td>
<td>1.08 ± 0.17</td>
<td>0.04</td>
</tr>
<tr>
<td>GET (% $VO_{2max}$)</td>
<td>49 ± 4</td>
<td>53 ± 6</td>
<td>0.11</td>
</tr>
</tbody>
</table>

Data are presented as mean ± SD. GET, gas exchange threshold.

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

<table>
<thead>
<tr>
<th>MIE</th>
<th>HIIE</th>
<th>P Value</th>
<th>ES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate-to-vigorous activity (min d$^{-1}$)</td>
<td>36 ± 12</td>
<td>36 ± 15</td>
<td>0.50</td>
</tr>
<tr>
<td>Total energy intake (kcal d$^{-1}$)</td>
<td>1945 ± 301 1887 ± 341</td>
<td>0.59</td>
<td>0.18</td>
</tr>
<tr>
<td>Energy from CHO (%)</td>
<td>47 ± 5</td>
<td>47 ± 5</td>
<td>0.84</td>
</tr>
<tr>
<td>Energy from fat (%)</td>
<td>38 ± 4</td>
<td>38 ± 6</td>
<td>0.96</td>
</tr>
<tr>
<td>Energy from protein (%)</td>
<td>15 ± 4</td>
<td>15 ± 3</td>
<td>0.73</td>
</tr>
</tbody>
</table>

95% CI, confidence limits for the true difference.

Data have been pooled, as ANOVA analysis revealed no main effect for sex.

### Table 3. Physiological and perceptual responses to MIE and HIIE.

<table>
<thead>
<tr>
<th>MIE</th>
<th>HIIE</th>
<th>P Value</th>
<th>ES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean HR (bpm)$^a$</td>
<td>129 ± 14</td>
<td>150 ± 14</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean HR (% HR$_{max}$)$^a$</td>
<td>66 ± 6</td>
<td>77 ± 6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean $VO_2$ (L min$^{-1}$)</td>
<td>1.19 ± 0.26</td>
<td>1.49 ± 0.37</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean $VO_2$ (% $VO_{2max}$)</td>
<td>51 ± 8</td>
<td>63 ± 7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>RER</td>
<td>0.91 ± 0.05</td>
<td>1.03 ± 0.06</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>RPE</td>
<td>4 ± 2</td>
<td>7 ± 7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Physical Activity Enjoyment Scale</td>
<td>57 ± 9</td>
<td>65 ± 7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Work performed (kJ)</td>
<td>117 ± 18</td>
<td>117 ± 18</td>
<td>—</td>
</tr>
<tr>
<td>Energy Expenditure (kJ)</td>
<td>770 ± 182</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

Data are presented as mean ± SD and pooled for sex.

n = 20 unless otherwise indicated.

$^a$n = 18 due to loss of telemetry.

Copyright © 2015 by the American College of Sports Medicine. Unauthorized reproduction of this article is prohibited.
Changes in FMD after exercise were not related to age, maturity (Tanner stage), or aerobic fitness in either MIE or HIIE (r \(= 0.43\) and \(P = 0.10\) for all).

There was a main effect of time (\(P < 0.001\), but not trial (\(P = 0.68\)), or time–trial interaction (\(P = 0.09\)) for baseline arterial diameter. Baseline arterial diameter was greater immediately after exercise compared with preexercise values in MIE (\(P = 0.03\); 95% CI, 0.01–0.22; ES = 0.32) and HIIE (\(P = 0.01\); 95 CI, 0.05–0.35; ES = 0.51). Baseline diameter was not different from preexercise values at any other point in either trial (\(P > 0.21\), ES < 0.20 for all).

**Microvascular function.** Differences in parameters of microvascular function are presented in Figure 2. There was a main effect of trial (\(P = 0.002\)) and time (\(P < 0.001\)) for PRH but no time–trial interaction (\(P = 0.14\)). There were no differences between trials in mean PRH at baseline (\(P = 0.51\); 95% CI, 0.18 to 0.09; ES = 0.12). Compared with that at baseline, PRH increased immediately after MIE (\(P = 0.048\); 95% CI, 0.02–0.46; ES = 0.72) and HIIE (\(P < 0.001\); 95% CI, 0.26–0.61; ES = 1.16). PRH was greater in HIIE compared with that in MIE immediately after (\(P = 0.02\); CI, −10 to 358; ES = 0.55) and HIIE (\(P = 0.08\); 95% CI, −27 to 394; ES = 0.64) compared with that in baseline. $\text{SR}_{\text{AUC}}$ was not different from baseline 2 h after exercise for either trial (\(P > 0.14\), ES < 0.36 for both).

There was a main effect of time (\(P < 0.001\), but not trial (\(P = 0.68\)), or time–trial interaction (\(P = 0.09\)) for baseline arterial diameter. Baseline arterial diameter was greater immediately after exercise compared with baseline in MIE (\(P = 0.03\); 95% CI, 0.01–0.22; ES = 0.32) and HIIE (\(P = 0.01\); 95 CI, 0.05–0.35; ES = 0.51). Baseline diameter was not different from preexercise values at any other point in either trial (\(P > 0.21\), ES < 0.20 for all).

**Microvascular function.** Differences in parameters of microvascular function are presented in Figure 2. There was a main effect of trial (\(P = 0.002\)) and time (\(P < 0.001\)) for PRH but no time–trial interaction (\(P = 0.14\)). There were no differences between trials in mean PRH at baseline (\(P = 0.51\); 95% CI, 0.18 to 0.09; ES = 0.12). Compared with that at baseline, PRH increased immediately after MIE (\(P = 0.048\); 95% CI, 0.02–0.46; ES = 0.72) and HIIE (\(P < 0.001\); 95% CI, 0.26–0.61; ES = 1.16). PRH was greater in HIIE compared with that in MIE immediately after (\(P = 0.02\); CI, −10 to 358; ES = 0.55) and HIIE (\(P = 0.08\); 95% CI, −27 to 394; ES = 0.64) compared with that in baseline. $\text{SR}_{\text{AUC}}$ was not different from baseline 2 h after exercise for either trial (\(P > 0.14\), ES < 0.36 for both).

There was a main effect of time (\(P < 0.001\), but not trial (\(P = 0.68\)), or time–trial interaction (\(P = 0.09\)) for baseline arterial diameter. Baseline arterial diameter was greater immediately after exercise compared with preexercise values in MIE (\(P = 0.03\); 95% CI, 0.01–0.22; ES = 0.32) and HIIE (\(P = 0.01\); 95 CI, 0.05–0.35; ES = 0.51). Baseline diameter was not different from preexercise values at any other point in either trial (\(P > 0.21\), ES < 0.20 for all).

**Microvascular function.** Differences in parameters of microvascular function are presented in Figure 2. There was a main effect of trial (\(P = 0.002\)) and time (\(P < 0.001\)) for PRH but no time–trial interaction (\(P = 0.14\)). There were no differences between trials in mean PRH at baseline (\(P = 0.51\); 95% CI, 0.18 to 0.09; ES = 0.12). Compared with that at baseline, PRH increased immediately after MIE (\(P = 0.048\); 95% CI, 0.02–0.46; ES = 0.72) and HIIE (\(P < 0.001\); 95% CI, 0.26–0.61; ES = 1.16). PRH was greater in HIIE compared with that in MIE immediately after (\(P = 0.02\); CI, −10 to 358; ES = 0.55) and HIIE (\(P = 0.08\); 95% CI, −27 to 394; ES = 0.64) compared with that in baseline. $\text{SR}_{\text{AUC}}$ was not different from baseline 2 h after exercise for either trial (\(P > 0.14\), ES < 0.36 for both).
95% CI, 0.05–0.44; ES = 0.73) and 1 h after exercise (P = 0.002; 95% CI, 0.13–0.48; ES = 0.67). There was also a trend for PRH to be greater in HIIE 2 h after exercise (P = 0.08; 95% CI, −0.03 to 0.42; ES = 0.43). There was a main effect of trial (P = 0.01) and time (P < 0.001) for the total hyperemic response but no time–trend interaction (P = 0.17). There were no differences in total hyperemic response between trials at baseline (P = 0.65; 95% CI, −28 to 18; ES = 0.12). Compared with that at baseline, the total hyperemic response was greater at all times after MIE (P < 0.02 and ES > 0.60 for all) and HIIE (P < 0.001 and ES > 1.18 for all). The total hyperemic response was greater in HIIE compared with that in MIE immediately after (P = 0.03; 95% CI, 3–57; ES = 0.67) and 1 h after exercise (P = 0.01; 95% CI, 12–72; ES = 0.62), with a strong trend for a statistical difference 2 h after exercise (P = 0.06; 95% CI, −1 to 56; ES = 0.45).

**DISCUSSION**

The purposes of this investigation were to establish the effect of exercise intensity on macro- and microvascular functions in adolescents and to document the time course of the response. The novel findings from this study are as follows: compared with baseline, 1) FMD was attenuated immediately after a single bout of HIIE but not after MIE, 2) FMD was elevated 1 and 2 h after HIIE but was unchanged in MIE, 3) PRH and total hyperemic response are both increased during the 2 h immediately after MIE and HIIE and the magnitude of this increase is greater after HIIE than that after MIE. This is the first study to isolate the effect of exercise intensity and include serial measures of vascular function in adolescents after a single bout of exercise. The findings indicate that exercise intensity has an independent effect on macro- and microvascular functions in young people, which likely have important implications for vascular health.

**Macrovacular function.** Our data demonstrate that an immediate postexercise nadir in FMD is present after HIIE but not after MIE, which is consistent with work-matched data in adults (3,18) and the only available data in young people (22). Mills et al. (22) hypothesized that this attenuation in FMD after high-intensity exercise might precede an increase in FMD and therefore be considered to be beneficial. However, these authors did not include serial measures of FMD in their investigation, and evidence of this response in endothelial function after exercise is scarce (18). Furthermore, the “high-intensity” exergaming trial included by Mills et al. (22) elicited a peak VO2 of 3.6 ± 2.5 METs, which the authors correctly classified as moderate intensity (24). Therefore, the present study extends the work by Mills et al. (22) and, to our knowledge, is the first to confirm that the initial impairment in FMD after high-intensity exercise precedes an increase in macrovascular function and that this improvement is present at least 2 h later. Thus, exercise that elicits a greater acute challenge on the vasculature may be associated with larger increases in FMD in adolescents, and the evidence of a biphasic response in FMD after high-intensity exercise is compelling.

Our failure to observe any changes in FMD immediately after MIE is consistent with the data provided by Mills et al. (22) after “low-intensity” exergaming (22); however, we extended their findings and report that endothelial function remained unchanged during the 2 h that followed. Interestingly, the lack of change in FMD in the hours after MIE is consistent with some (3,18), but not all (16,39), data in healthy adults. However, in addition to differences in exercise stimulus, the timing of the FMD measurement and interpretation of the ratio-scaled FMD statistic (1,12), an independent effect of training status (16), has been observed on the acute FMD response. Furthermore, evidence suggests that age might modulate vascular reactivity to the FMD protocol (34). Although we were unable to confirm a potential confounding effect of age, maturity ( Tanner stage), or aerobic fitness on the change in FMD after MIE and HIIE, it seems that a direct comparison between our findings with apparently healthy adolescents and the available adult literature may be problematic.

Shear (when expressed as SR_AUC) is thought to be the main stimulus underlying the FMD response in healthy adults at rest (26). However, the relation between SR_AUC and FMD is not as robust after exercise (20). Indeed, we report here that FMD remained elevated in the hours after HIIE despite a steady decline in SR_AUC. The relation between SR_AUC and FMD has been shown to be weak in young people even at rest (34), a finding also observed in this study. It is therefore not surprising that differences in the FMD response 1 and 2 h after exercise were independent of changes in SR_AUC. Considering that baseline arterial diameter remained unchanged 1 and 2 h after MIE and HIIE and that we followed recent statistical guidelines designed to partition out the influence of vessel caliber (1), our findings are also not explained by this factor. We are therefore unable to identify the mechanism(s) underlying the disparity in FMD response presented here. It has been speculated elsewhere that the initial impairment in FMD immediately after exercise relates to an increase in oxidative stress (12,18), which may reduce the bioavailability of nitric oxide (6). Although we did not measure this outcome, an increase in oxidative stress after high-intensity exercise is not consistent with the augmented FMD response observed 1 and 2 h after HIIE. Conversely, an exercise-intensity dependent increase in total antioxidant status has been reported during the hours after work-matched HIIE but not MIE (39), which would prevent the reduction in nitric oxide bioavailability associated with an increase in exercise-induced oxidative stress. However, this is not a consistent finding (16,18), and we have previously reported that changes in FMD 1 h after identical HIIE in adolescents were not related to total antioxidant status (4). Alternatively, given that the exercise bouts were work-matched in the present study, our data may be explained by a positive association between the intensity of exercise and subsequent activity of endothelial nitric oxide synthase. Indeed, data in adults demonstrate that brachial artery shear increases with the intensity of cycling exercise (35), and this has been demonstrated to play a leading role in the postexercise FMD response (36). We did not quantify brachial artery shear during...
the exercise bouts because this is technically challenging during HIIE. However, we have previously observed a reduction in postprandial systolic blood pressure in the 5 h after HIIE, but not MIE, in adolescents (5), which would be consistent with an upregulation in endothelial nitric oxide synthase activity.

An interesting finding of the present study is that the magnitude of the increase in FMD observed 1 h after HIIE was also present after 2 h. Further study is needed to identify the precise decay in this favorable response after high-intensity exercise, although this benefit has been reported the following day in adults (39). In addition, we have previously observed that a similar increase in FMD is present 4 h after exercise despite the consumption of a meal, which impaired FMD in a nonexercise control trial (4), whereas Sedgwick et al. reported an increase in postprandial FMD the day after repeated sprint cycling in adolescent boys (30). Therefore, a single bout of HIIE seems to provide a potent stimulus for macrovascular health and may provide superior health benefits compared with MIE if repeated on a regular basis. Indeed, high-intensity interval training has been demonstrated to be more effectual in improving HIIE if repeated on a regular basis. However, we have previously observed a reduction in the magnitude of the increase in FMD observed 1 h after HIIE. However, we are the first to show that a single bout of MIE or HIIE can improve microvascular function in the hours after exercise and that HIIE may provide a superior benefit. Although we were unable to identify the time course of the decay in these favorable responses after exercise, Gill et al. reported that endothelium-dependent microvascular function remained elevated 16–18 h after 90 min of walking at 50% VO_{2max} in adults (14). Therefore, repeating a single bout of exercise may have some utility in promoting microvascular function the following day, although this needs to be confirmed in adolescents. Conversely, there is evidence suggesting that the intensity of habitual physical activity may not influence microvascular endothelial function in adolescents (27). However, this study determined microvascular function by means that are considered to be NO dependent, which is mechanistically disparate from our assessment (42). Currently, no study has identified the efficacy of HIIE training on microvascular health in asymptomatic adolescents. Further study is therefore needed to identify whether the acute benefits in microvascular function observed in the present study translate into meaningful benefits in this group with time.

**Considerations.** This is the first study to isolate the effect of exercise intensity on vascular function in adolescents. The strengths of this investigation include a work-matched design, control of previous physical activity and dietary factors, serial measures of macro- and microvascular function, and allometric scaling of the FMD statistic. However, apart from reporting SRAUC and baseline arterial diameter, we are not able to provide any mechanistic data that could potentially explain the changes in vascular function after MIE and HIIE. Further limitation is that we were unable to measure the time course of these changes beyond 2 h after exercise. Thus, the rate of decay in microvascular function after MIE and HIIE and macrovascular function after HIIE remains unknown. We also cannot rule out that an increase in skin temperature after exercise influenced our measure of microvascular function. However, this unavoidable confounding effect is likely limited to the time point immediately after exercise, as participants were acclimatized to the temperature-controlled (24°C) room for all other vascular measures. Furthermore, our analysis of the postocclusive reactive hyperemic response accommodates differences in baseline perfusion (42). Finally, we are unable to comment on the interaction between exercise intensity and diurnal variation in FMD. Data in adults suggest that FMD could decline by approximately 1% from baseline values over the course of our measurement period (28). However, the magnitude of this effect is far lower, and in the opposite direction, than the change observed after HIIE in the present study.

**CONCLUSIONS**

Our data indicate that the intensity of exercise has an independent effect on macro- and microvascular functions in adolescents. Specifically, macrovascular function was improved in the hours after HIIE but not after MIE. In addition, both exercise bouts promoted microvascular function, although
the magnitude of this increase was greater after HIIE. Therefore, it is likely that repeating high-intensity exercises may provide superior health benefits and lower CVD risk compared with moderate-intensity activities. Given that HIIE was deemed to be more enjoyable than MIE, HIIE may provide an attractive alternative to traditional MIE.

REFERENCES

9. Cohen J. 2015 by the American College of Sports Medicine. Unauthorized reproduction of this article is prohibited.


