Endothelial function after high-sugar-food ingestion improves with endurance exercise performed on the previous day¹–³

Edward P Weiss, Hassan Arif, Dennis T Villareal, Emanuele Marzetti, and John O Holloszy

ABSTRACT
Background: Endothelial function deteriorates after glucose ingestion. This may be attributed to hyperglycemia-induced oxidative stress. Acute endurance exercise might improve postprandial endothelial function by enhancing glucoregulation and reducing postprandial hyperglycemia.

Objective: The objective was to determine whether endurance exercise performed 17 h before high-sugar-food ingestion attenuates postprandial impairment in endothelial function.

Design: Healthy men and women (n = 13; age: 48 ± 17 y) were studied on 2 occasions: after ≥48 h with no exercise and 17 h after a 60-min bout of endurance exercise. During each trial, brachial artery flow mediated dilatation (FMD) was used to assess endothelial function before and after the ingestion of a candy bar and soft drink. Glucose, insulin, and thiobarbituric acid–reactive substances (TBARS), a marker of oxidative stress, were measured in blood obtained during each FMD measurement. The insulin sensitivity index was calculated from the glucose and insulin data.

Results: FMD decreased significantly after food ingestion in both trials. However, prior exercise shifted the entire FMD curve upward (main treatment effect: P = 0.0002), which resulted in a greater area under the curve for FMD (774 ± 122%-min) than did no exercise (607 ± 122%-min) (P = 0.01). Prior exercise shifted the glucose and insulin curves downward (main treatment effects: P = 0.05 and P = 0.0007, respectively) and resulted in a significantly greater insulin sensitivity index (10.8 ± 0.7) than did no exercise (9.2 ± 0.7) (P = 0.01). TBARS did not differ significantly between trials.

Conclusion: Postprandial endothelial function was improved by endurance exercise performed 17 h earlier. This effect was accompanied by exercise-induced improvements in insulin action and reductions in glycermia, but did not correspond with reductions in oxidative stress, as assessed by TBARS. Am J Clin Nutr 2008; 88:51–7.

INTRODUCTION
The development of impaired endothelial function is an early atherogenic event (1). Accordingly, poor brachial artery flow mediated dilation, which reflects impaired endothelial function, is an independent predictor of clinical cardiovascular events and death due to cardiovascular disease (2, 3). Whereas vascular function studies are typically performed in fasting subjects, endothelial function deteriorates acutely after glucose ingestion according to most (4–7), but not all (8, 9), studies. This effect may be attributed to hyperglycemia-induced oxidative stress (5, 7). If poor endothelial function promotes atherogenesis and endothelial function is impaired during postprandial periods, it is conceivable that the long-term development of atherosclerosis might be partly attributed to repeated exposures to impaired endothelial function after food ingestion.

Regular physical activity is independently associated with a lower risk of death due to cardiovascular disease (10, 11). Part of this effect may be attributed to exercise-induced improvements in endothelial function (12, 13). In light of evidence that postprandial hyperglycemia is reduced by exercise that was performed hours or days earlier (14) and that postprandial hyperglycemia likely contributes to postprandial impairments in endothelial function (4, 6, 15), it is conceivable that acute endurance exercise minimizes the postprandial impairment in endothelial function. If this proposition is true, it would support the notion that some of the cardioprotective benefits of exercise are attributable to improvements in postprandial endothelial function.

The purpose of the present study was to test the hypothesis that acute endurance exercise performed 17 h before high-sugar-food ingestion attenuates postprandial impairment in endothelial function. To maximize the clinical relevance of our findings, we administered a candy bar and soft drink as “high-sugar food” rather than a glucose tolerance test beverage, as has been used in other studies. Furthermore, because most meals and snacks are not immediately preceded or followed by exercise, even for individuals who perform daily exercise, we sought to determine whether acute exercise provides a vasoprotective effect that lasts for 16–19 h after exercise cessation. A secondary purpose of our study was to gain insights into the mechanisms for exercise-induced improvements in endothelial function; therefore, we also tested the hypothesis that improvements in endothelial function, if present, are accompanied by improvements in glucose regulation and reductions in oxidative stress.

¹ From the Department of Internal Medicine, Washington University School of Medicine, Saint Louis, MO (EPW, HA, DTV, and JOH); the Department of Nutrition and Dietetics, Saint Louis University, Saint Louis, MO (EPW); the Department of Aging and Geriatrics, University of Florida, Gainesville, FL (EM); and the Department of Gerontology, Geriatric and Physiatry, Catholic University of the Sacred Heart, Rome, Italy (EM).
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³ Address reprint requests and correspondence to EP Weiss, Saint Louis University, 3437 Caroline Street, Saint Louis, MO. E-mail: eweiss4@slu.edu.

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SUBJECTS AND METHODS

Subjects

Thirteen healthy men and women aged 26–75 y were recruited and gave their informed written consent to participate in the study, which was approved by the Human Research Protection Office at Washington University. Because chronic diseases may cause secondary damage to the endothelium, volunteers with self-reported diabetes or those with “provisional diabetes,” as determined by using a 75-g oral-glucose-tolerance test (16), were excluded. Volunteers were not eligible for the study if they had any major chronic diseases or conditions that would interfere with exercise, for which exercise is contraindicated, or that would interfere with interpretation of the results. Examples include self-reported or clinical evidence of coronary artery disease, significant obstructive airway disease, stroke, resting blood pressure ≥170 mm Hg (systolic) or ≥100 mm Hg (diastolic), malignancy, orthopedic or musculoskeletal problems, and current smoking. No subjects were taking medications for diabetes, metabolic disease, or cardiovascular disease or other medications or dietary supplements known to affect glucose metabolism. During the 6 mo before study enrollment, 4 of the participants were sedentary (exercise <2 d/wk) and 9 performed regular endurance exercise ≥2 d/wk. All of the participants who were screened and eligible completed the study.

Study design

The study was conducted with a crossover design, in which each subject underwent both the control and exercise treatments. The testing sequence was counterbalanced, such that half of the participants performed the control trial first and the others performed the exercise trial first. The participants reported to our laboratory 4 occasions, once for screening, body composition, and maximal oxygen uptake assessments; once for a bout of endurance exercise; and twice for postprandial endothelial function testing. The bout of endurance exercise was performed in the afternoon or evening before one of the endothelial function testing sessions (exercise trial); the other endothelial function testing session was preceded by ≥48 h of abstinence from all exercise (control trial). The control and exercise trials were separated by 10 ± 4 d.

Body composition, height, and weight

Percentage body fat was assessed by using dual-energy X-ray absorptiometry with enhanced whole-body analyses (QDR-1000/W, software version 5.73; Hologic, Waltham, MA). Height and weight were measured with a wall-mounted stadiometer and balance beam scale, respectively, and were used to calculate body mass index (kg/m²).

Maximal oxygen uptake

Maximal oxygen uptake (VO₂max) was determined by using indirect calorimetry (True Max 2400; PARvOmedics, Salt Lake City, UT) during a maximal graded treadmill exercise test as described previously (17). Heart rate was measured from electrocardiograms recorded during each stage of the test and maximal exercise.

Acute endurance exercise

For the exercise trial, a 60-min bout of endurance exercise was performed between 1500 and 1900, which was 16.8 ± 0.3 h before the commencement of endothelial function testing the next day. The exercise consisted of indoor, supervised endurance exercise on rowing and elliptical machines, a stationary cycle, and/or a treadmill. The elliptical machine and cycle both included handles for arm exercise. The heart rate associated with 70% of VO₂max was calculated for each participant by using simple linear regression analyses of the heart rate and oxygen uptake data from the VO₂max test. The participants were monitored and encouraged to maintain their heart rate within 5 beats/min of this value. The average heart rate, as measured with wristwatch-type monitors (S610, Polar Electro Oy, Kemple, Finland) during exercise was 142 ± 5 beats/min or 80 ± 1% of the measured maximal heart rate, which is equivalent to ~63% of the VO₂max based on published standards (18).

High-sugar food

The food was selected to represent a “snack” that is commonly consumed by people in the United States and consisted of a 59-g (2.07-oz) candy bar (Snickers, Mars Corporation, McLean, VA) and a 591-mL (20 fluid ounce) lemon-lime flavored soft drink (Sprite, Coca-Cola Corporation, Atlanta, GA). The candy bar contained the following ingredients: milk chocolate (sugar, cocoa butter, chocolate, lactose, skim milk, milk fat, soy lecithin, and artificial flavor), peanuts, corn syrup, sugar, skim milk, butter, milk fat, partially hydrogenated soybean oil, lactose, salt, egg whites, and artificial flavor. The soft drink contained carbonated water, high-fructose corn syrup, citric acid, natural flavors, sodium citrate, and sodium benzoate. Nutrient information for the candy bar and soft drink combined was determined by using Nutrition Data System for Research (version 5.0; Nutrition Coordination Center, University of Minnesota, Minneapolis, MN) and was as follows: energy, 534 kcal; total fat, 14 g; saturated fat, 7.4 g; trans-fat, 0 g; total carbohydrate, 101 g; glucose, 28 g; fructose, 38 g; sucrose, 27 g; starch, 2 g; and protein, 5 g.

Preparation for endothelial function tests

The participants were advised to refrain from taking nutritional supplements, medications, and alcohol during the day before endothelial function assessments and fasted for 12–14 h before testing. Furthermore, for 1 d before the first study trial (ie, control or exercise trial), the participants kept a diary of all foods consumed and were asked to replicate this diet during the second study trial. On arrival for testing, the participants were questioned to confirm that they complied with all preparation instructions. If any of the instructions were not followed, the testing was rescheduled.

Endothelial function

Participants arrived at the laboratory at 1030 and rested quietly in the supine position for ≥20 min before any assessments began. Blood pressure was measured in the left arm with an automated oscillometric noninvasive monitor (Dinamap 1846SX; Critikon Inc, Tampa, FL). Brachial artery flow mediated dilation (FMD) was measured twice before and every 30 min for 2.5 h after the consumption of the high-sugar food. The participant’s right arm was immobilized in a custom-made device with the shoulder abducted at 70–90° and the elbow fully extended. Ultrasound images were acquired using an ultrasound system (SONOS 5500; Agilent, Andover, MA) equipped with an 11-3L linear array transducer. After the image was optimized, the probe was
secured with a stereotactic clamp (MG Holder MG61003; Noga Engineering, Ltd, Shlomi, Israel) to maintain constant positioning over the artery. The images were fed to a separate computer for real-time (30 ± 2 samples/s) quantification of the arterial diastolic diameter with Vascular Imaging Analysis software (VIA, version 9.60) (19, 20). Baseline diameter was recorded for 2 min after which a pneumatic cuff (Hokanson E20 Rapid Cuff Inflator and AG101 Cuff Inflator Air Source; PMS Instruments, Ltd, Maidenhead, United Kingdom) on the right forearm was inflated to 200 mm Hg to occlude blood flow. After 5 min of occlusion, the cuff was deflated and arterial diameter was recorded continuously for 5 min. FMD was calculated as the percentage increase in diameter from baseline to peak diameter, where baseline diameter was the average diastolic diameter over the 2-min baseline, and peak diameter was recorded as the 10-s average of the highest diastolic diameter after cuff deflation. During some FMD assessments, a shift in baseline diameter was evident by comparing the preocclusion diameter with the diameter measured after the dilatory response had ended and the blood vessel was again constricted. In these cases, the end-of-test diameter was used as “baseline diameter,” provided that the diameter had decreased from peak and was stable.

Data from the 2 FMD measures performed before food ingestion were averaged to reflect fasting FMD. Area under the curve (AUC) was calculated with the fasting and all postprandial FMD data by using the trapezoidal rule (21).

Glucoregulation

Venous blood was drawn from an indwelling catheter in the participant’s left arm during each FMD assessment. Plasma was isolated and stored at −20 °C for later analysis. Glucose was analyzed by using the glucose oxidase method (Micro-Stat GM7; Analox Instruments Inc, Lunenberg, MA) and insulin by using a double-antibody radioimmunoassay (22). The samples were analyzed in duplicate, and all samples for each subject were batch analyzed to eliminate interassay variability.

For both insulin and glucose, the 2 measures obtained before food ingestion were averaged to reflect fasting values, and the AUCs were calculated from the fasting values and all postprandial values by using the trapezoidal rule (21). Furthermore, the insulin sensitivity index (ISI) was calculated as follows:

\[
\text{ISI} = 10000 \left[ \frac{(\text{FPG} \times \text{FPI})}{\text{MPI} \times \text{MPI}} \right]^{0.5} \]

where FPG is fasting plasma glucose (mg/dL), FPI is fasting plasma insulin (μU/mL), MPG is mean plasma glucose (mg/dL) from all time points (ie, 0–150 min), and MPI is mean plasma insulin (μU/mL) from all time points. This method is based on that of Matsuda and DeFronzo (23). However, the original ISI method was developed for use with a 2-h 75-g oral-glucose-tolerance test (23), whereas our test was longer (2.5 h) and used a candy bar and soft drink. The homeostasis model assessment of insulin resistance (HOMA-IR) was calculated as follows (24, 25):

\[
\text{HOMA} = \frac{\text{fasting glucose}(\text{mmol/L}) \times \text{fasting insulin}(\mu \text{U/mL})}{22.5} \]

Oxidative stress

Serum was isolated from venous blood samples drawn during each FMD assessment and stored at −20 °C for later batch analyses for thiobarbituric acid–reactive substance (TBARS) concentrations—a marker of lipid peroxidation and oxidative stress. TBARS were measured in duplicate with a colorimetric assay (Cayman Chemical, Ann Arbor, MI). This assay is based on the formation of a malondialdehyde-thiobarbituric acid adduct in acidic conditions at 100 °C. The concentration of the adduct was determined at 540 nm with a Synergy HT Multi-Detection microplate reader (BioTek, Winosook, VT). The 2 fasting TBARS values were averaged, and the AUC was calculated from the fasting values and all postprandial values by using the trapezoidal rule (21).

Statistical analyses

Because we hypothesized that prior exercise attenuates or prevents postprandial reductions in endothelial function and postprandial increases in glucose, insulin, and TBARS, we analyzed these outcomes by using 2-factor (treatment and time) ANOVAs with repeated measures. The treatment-by-time interaction from these analyses was interpreted to determine whether the time-dependent changes in these outcomes were different between the control and exercise conditions. When the interaction term was not significant, main effects of treatment and test time were evaluated. A main effect of treatment was interpreted to mean that differences existed between the control and exercise conditions at baseline and that the difference remained throughout the postprandial period. A main effect of time was interpreted to mean that differences existed between time points (eg, a difference between the fasting and 30-min values) and that this occurred regardless of the treatment condition. As secondary analyses, several outcomes that are represented by one data point (ie, fasting values, AUCs, ISI, and HOMA-IR) for each trial were analyzed by using one-factor ANOVAs with repeated measures to compare the exercise and control trial data. These tests were performed because fasting values, AUCs, and indexes of insulin action are commonly presented in this type of study but were also performed to help interpret the results from the 2-factor ANOVAs. The methods used for the calculation of fasting values, AUCs, ISI, and HOMA-IR are described above along with information about data acquisition. Residuals were examined for normality and homogeneity of variance. When necessary, data were transformed as follows to achieve normality before final data analyses were performed: FMD data were square root transformed, baseline brachial artery diameter data were rank transformed, and insulin, HOMA-IR, and TBARS data were log transformed. For clarity, the nontransformed means and error terms are presented; however, the P values are based on the analyses of transformed data where transformations were used. Statistical significance was accepted at P ≤ 0.05. Data are presented as means ± SEMs unless noted otherwise. Analyses were conducted with SAS for Windows XP Pro (version 9.1, SAS Institute, Cary, NC).

RESULTS

Subjects

Characteristics of the participants are presented in Table 1. On average, the participants were middle-aged with a mean body
participants had high V̇O2 max values and others had low values. On the basis of fasting and 120-min plasma glucose concentrations from a standard 75-g oral-glucose-tolerance test (16), 2 participants had prediabetes and all others had normal glucose tolerance. Averages for systolic and diastolic blood pressures were within normal ranges and were not different between the control and exercise trials (Table 2).

Glucoregulatory function

Plasma glucose and insulin concentrations increased after high-sugar-food ingestion (Figure 1) and returned to baseline by the end of the trial. For both glucose and insulin, the interaction between treatment (control or exercise) and test time was not significant, but the main effect of treatment was significant. These results indicate that the shape of the glucose and insulin curves did not differ between the exercise and control trials; however, the glucose and insulin curves were shifted downward in the exercise trial (Figure 1). As a secondary analysis to help in interpreting the glucose and insulin results, we also compared fasting glucose and insulin values and AUCs between the control and exercise trials. Although the fasting values for the plasma glucose and insulin concentrations and their AUCs were not significantly different between study trials (Table 2), there were weak tendencies for lower values in the exercise trial (Table 2).

Endothelial function

Baseline arterial diameter from the FMD tests did not change from fasting to the postprandial state in either the exercise or control trial and did not differ between trials (Figure 2). FMD decreased after ingestion of the high-sugar food, as indicated by a significant main effect of treatment (Table 2). There was no difference in the time course for the postprandial decrease in FMD, as indicated by the nonsignificant treatment-by-time interaction. However, as indicated by the significant main effect of treatment, the entire FMD curve was shifted upward in the exercise trial. Secondary analyses were used to compare fasting and postprandial FMD to help interpret the FMD results. Fasting FMD did not differ between treatments. However, the FMD AUC was significantly greater in the exercise trial (Table 2).

Oxidative stress

Serum TBARS concentrations decreased steadily after ingestion of the high-sugar food, as reflected by a significant test time effect (Figure 3). The time course for this decrease was not different between conditions, as indicated by the nonsignificant treatment-by-time interaction. Furthermore, acute exercise did not shift the curve upward or downward, as indicated by the nonsignificant main effect of treatment.

**DISCUSSION**

Results from the present study suggest that a single bout of endurance exercise performed ≈17 h before high-sugar-food consumption enhances postprandial endothelial function. This was evidenced by an upward shift in the entire FMD curve, such that the lowest postprandial FMD in the exercise condition was approximately equal to the greatest FMD value that occurred in the control condition. Furthermore, the AUC for FMD was ≈28% greater in the exercise trial.

The results from the 2-factor ANOVAs of FMD, glucose, and insulin suggest that fasting values started out different in the control and exercise trials (Table 2).

### TABLE 1

<table>
<thead>
<tr>
<th>Characteristics of the study participants</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (n)</td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>5</td>
</tr>
<tr>
<td>Women</td>
<td>8</td>
</tr>
<tr>
<td>Age (y)</td>
<td>48 ± 17</td>
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<tr>
<td>Weight (kg)</td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>81.8 ± 9.0</td>
</tr>
<tr>
<td>Women</td>
<td>66.5 ± 7.0</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>24.0 ± 2.2</td>
</tr>
<tr>
<td>Body fat (%)</td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>16.8 ± 4.2</td>
</tr>
<tr>
<td>Women</td>
<td>29.2 ± 11.4</td>
</tr>
<tr>
<td>VO₂max (L/min)</td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>3.90 ± 0.86</td>
</tr>
<tr>
<td>Women</td>
<td>2.37 ± 0.79</td>
</tr>
<tr>
<td>VO₂max (mL · kg⁻¹ · min⁻¹)</td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>47.6 ± 8.8</td>
</tr>
<tr>
<td>Women</td>
<td>36.4 ± 13.8</td>
</tr>
<tr>
<td>Fasting glucose (mg/dL)²</td>
<td>91 ± 7</td>
</tr>
<tr>
<td>120-min glucose (mg/dL)²</td>
<td>96 ± 29</td>
</tr>
</tbody>
</table>

1 All values are x ± SD, except for sex, VO₂max, maximal oxygen uptake.
2 Fasting and 120-min glucose concentration data were collected by using a 75-g oral-glucose-tolerance test for diabetes screening (16).

### TABLE 2

<table>
<thead>
<tr>
<th>Control trial</th>
<th>Exercise trial</th>
<th>P²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting systolic BP (mm Hg)</td>
<td>114 ± 4</td>
<td>115 ± 4</td>
</tr>
<tr>
<td>Fasting diastolic BP (mm Hg)</td>
<td>66 ± 2</td>
<td>66 ± 2</td>
</tr>
<tr>
<td>Fasting glucose (mg/dL)</td>
<td>87 ± 2</td>
<td>84 ± 2</td>
</tr>
<tr>
<td>Glucose AUC (mg/dL · min)</td>
<td>16 828 ± 689</td>
<td>15 858 ± 689</td>
</tr>
<tr>
<td>Fasting insulin (μU/mL)</td>
<td>3.0 ± 0.3</td>
<td>2.6 ± 0.3</td>
</tr>
<tr>
<td>Insulin AUC (μU/mL · min)</td>
<td>3898 ± 518</td>
<td>3158 ± 518</td>
</tr>
<tr>
<td>Insulin sensitivity index</td>
<td>9.2 ± 0.7</td>
<td>10.8 ± 0.7</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>0.64 ± 0.06</td>
<td>0.54 ± 0.06</td>
</tr>
<tr>
<td>Fasting FMD (%)</td>
<td>4.7 ± 1.0</td>
<td>5.5 ± 1.0</td>
</tr>
<tr>
<td>FMD AUC (% · min)</td>
<td>607 ± 122</td>
<td>774 ± 122</td>
</tr>
<tr>
<td>Fasting TBARS (μmol/L)</td>
<td>13.0 ± 3.2</td>
<td>16.4 ± 3.2</td>
</tr>
<tr>
<td>TBARS AUC (μmol/L · min)</td>
<td>1735 ± 218</td>
<td>1733 ± 218</td>
</tr>
</tbody>
</table>

1 All values are x ± SEM; n = 13 subjects who underwent both the control and exercise treatments. AUC, area under the curve; BP, blood pressure; FMD, flow mediated dilation of the brachial artery; HOMA-IR, homeostasis model assessment of insulin resistance; TBARS, thiobarbituric acid–reactive substances.
2 P values reflect the significance of differences between the control and exercise conditions, which were performed by using one-factor (treatment) ANOVAs with repeated measures.
3 Insulin sensitivity index is unitless and was determined according to Matsuda and DeFronzo (23) using all data from the 150-min test.
4 HOMA-IR is a unitless index and was calculated according to Matthews et al (24).
control and exercise trials and that the values remained different throughout the postprandial period (based on nonsignificant interactions paired with significant main treatment effects). However, the one-factor ANOVAs of fasting values (Table 2) indicated no treatment effect on fasting values. We suspect that 2 factors contributed to this apparent discrepancy for fasting values: 1) the treatment effect on fasting values was weaker than it is for postprandial values and that this difference between effects on fasting and postprandial values cannot be detected with a 2-factor ANOVA (interaction term) because it is very small, and 2) the treatment effects on fasting glucose and insulin values are nonsignificant because of a statistical power limitation for these analyses and that with more statistical power, as may be present in the 2-factor ANOVA, the treatment effect would be significant. Our a priori decision was to interpret the results of the 2-factor ANOVAs for our main conclusions and the paired comparisons were performed as secondary analyses. However, in light of the discrepant results from these analytic approaches, we refrained from making strong comments and conclusions about treatment effects on fasting FMD, glucose, and insulin.

Only one other study assessed the effects of acute exercise on postprandial endothelial function (27). Zhu et al showed that 45 min of treadmill exercise commenced immediately after ingestion of a 75-g glucose beverage resulted in greater postprandial FMD values compared with a control trial on the same subjects. Our study supports these findings and advances them in several respects. First, in our study, exercise was performed in the afternoon or evening before the postprandial vascular function tests rather than during the postprandial period. The results showed that exercise is vasoprotective after a meal or snack consumed many hours after exercise cessation. This difference is clinically relevant because most people do not exercise immediately after consuming every meal. Second, our test meal consisted of a candy bar and a soft drink, which represents a commonly consumed snack in the United States, rather than a glucose-tolerance test beverage. Although there is no strong reason to believe that the glucoregulatory and vascular effect of these meals differ,
pure glucose is rarely consumed in real world settings. High-sugar foods, such as those used in the present study, typically contain fructose, sucrose, and other sugars as well as fat, protein, preservatives, and other ingredients, which could conceivably alter postprandial physiology. Finally, whereas Zhu et al exclusively studied 19–26-y-old men, our sample included men and women with a range of age, body weight, and exercise habits, making the results more applicable to the general population.

We hypothesized that acute endurance exercise enhances endothelial function because hyperglycemia impairs endothelial function (4, 6, 15) and because acute endurance exercise enhances glucose regulation and reduces postprandial glycemia (14). Our findings support this hypothesis because the exercise-induced improvement in postprandial endothelial function was accompanied by significant reductions in plasma glucose and insulin concentrations (significant treatment effects from 2-factor ANOVAs), increases in the ISI (calculated from fasting and postprandial glucose and insulin concentrations), and reductions in the HOMA-IR (calculated from fasting glucose and insulin concentrations).

It has been suggested that hyperglycemia impairs endothelial function by increasing oxidative stress because coadministration of antioxidant vitamins with glucose prevents the postprandial decline in FMD (5, 7). Furthermore, oxidative stress has been shown to increase after ingestion of a 75-g glucose beverage, as evidenced by postprandial increases in neutrophil superoxide anion formation (5) and plasma TBARS concentrations (6). However, another study reported no change in plasma malondialdehyde or erythrocyte glutathione, glutathione peroxidase, or superoxide dismutase (7). In our study, serum TBARS concentrations did not increase in the postprandial period, but rather decreased. This unexpected result suggests that the postprandial impairment in endothelial function is not necessarily caused by oxidative stress. Although an explanation for the postprandial decrease in oxidative stress in our study was not clear, 2 ingredients in the soft drink that we used, citric acid and sodium citrate, may have increased the antioxidant capacity of blood. Although these compounds are not recognized as biologically important antioxidants, they have antioxidant properties for which they are used as preservatives in soft drinks (28).

We hypothesized that acute exercise enhances postprandial endothelial function by decreasing postprandial glycemia and thereby reducing postprandial oxidative stress. Whereas exercise reduced postprandial glycemia, TBARS concentrations were unaffected, which suggested that reduced oxidative stress is not the mechanism for the observed improvements in postprandial endothelial function. An alternative mechanistic explanation is that exercise transiently induces endothelial nitric oxide synthase (eNOS), thereby leading to greater flow-mediated nitric oxide production, increased nitric oxide bioavailability, and greater dilation. While this explanation is speculative, it is noteworthy that acute endurance exercise transiently increases eNOS mRNA (29, 30) and total NOS activity (31) in skeletal muscle. Furthermore, when cultured endothelial cells are exposed to acute shear stress of a magnitude similar to that which occurs during exercise, eNOS mRNA and eNOS protein concentrations increase (32, 33). However, to our knowledge, it is not known whether acute exercise increases eNOS mRNA or protein concentrations in the endothelium of the intact vasculature.

Chronic endurance exercise training has been shown to improve fasting FMD in the blood vessels of exercised limbs but not in nonexercised limbs (34). We cannot determine from our study whether the beneficial effects of exercise on endothelial function are localized to the exercised limbs because we measured FMD in the brachial artery and our participants performed exercises that included upper body exercise. However, it is important to recognize that brachial artery FMD is clinically important because it correlates with coronary artery dilatory function (35). Because the heart is exercised during all types of endurance exercise, it would be expected that the coronary arteries benefit from acute endurance exercise, as did the brachial artery in our study.

We intentionally studied a heterogeneous sample that included men and women with a wide range of ages and physical activity levels so that the results would be applicable to the general population. However, a drawback to using such a heterogeneous sample is that it introduces the possibility that the significant findings are largely driven by a subset of the participants (eg, younger participants may have benefited from exercise, whereas older participants may not have). Although our sample size is too small to perform valid subgroup analyses or covariate analyses, it is noteworthy that exercise improved the AUC for FMD and ISI in almost all subjects (11 of 13). Therefore, it appears that acute exercise has beneficial effects on vascular function in a fairly heterogeneous population.

In exercise-related research, it is often argued that, from a biological perspective, the exercised state is “normal” and the sedentary state is “abnormal” because during nearly all of the evolutionary past for humans/primates, large amounts of physical activity were required for survival. Therefore, an alternative interpretation of our findings was that abstinence from exercise for ≥48 h results in “abnormal” or poor endothelial function. This perspective may be especially relevant in light of the fact that 69% of our subjects exercise at least twice weekly.

The results from this study have several implications. First, as was previously shown in response to glucose beverage ingestion (4–7), a commonly consumed snack consisting of a candy bar and soft drink impaired vascular endothelial function for ≈2 h. This adverse effect occurred regardless of the presence or absence of prior exercise, although endothelial function during the entire fasting-to-postprandial period was better when preceded by acute endurance exercise. Although speculative, it is possible that routine exposure to this adverse effect may have long-term health consequences that are related to endothelial dysfunction, such as the development of atherosclerosis (1). This research also demonstrated 2 important benefits of endurance exercise. First, a single bout of exercise protects against the adverse effects of high-sugar-food ingestion on endothelial function, and this effect is evident ≈17 h after exercise. Furthermore, as has been shown by others (14), acute endurance exercise enhances glucose regulatory function.

Conclusions

Endothelial function after high-sugar-food ingestion was improved by a single bout of endurance exercise performed ≈17 h earlier. This improvement was associated with exercise-induced improvements in glucose regulation, but was not accompanied by reductions in oxidative stress.

The authors’ responsibilities were as follows—EPW: designed the study, analyzed and interpreted the data, and drafted the manuscript; HA and JOH:
participated in designing the study and revising the manuscript for intellectual content and approved the final manuscript; DTV: assisted in the interpretation of the data, provided critical intellectual feedback for the manuscript, and approved the manuscript; EM: assisted in the interpretation of the data, provided critical intellectual feedback for the manuscript, and approved the manuscript. None of the authors had a conflict of interest related to any part of this study or manuscript.

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