Postexercise Insulin Action in African-American Women

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African Americans are more insulin resistant than Caucasians. A single bout of moderate-intensity exercise reduces insulin resistance in sedentary Caucasian individuals. The impact of a single bout of exercise on insulin resistance has never been studied in African Americans. The purpose of this experiment was to evaluate the impact of a single bout of exercise on insulin resistance in African-American women.

Design: Insulin resistance was assessed in 10 sedentary, overweight or obese African-American women during a sedentary and exercise condition over a two-day period. During the sedentary condition, participants fasted overnight and sat quietly in the laboratory for 75 minutes. During the exercise condition, participants completed 75 minutes of brisk walking on a treadmill. Ninety minutes following each condition, participants completed an oral glucose tolerance test (OGTT). Three-and-a-half hours later, subjects consumed a standardized meal [meal tolerance test (MIT)].

Results: The insulin response to the OGTT was 18% lower (p=0.046), and insulin sensitivity was 18% higher (p=0.042) in the exercise condition compared to the sedentary condition. There were no differences between conditions following the MIT.

Conclusions: These results indicate that overweight/obese, sedentary, insulin resistant African-American women had a significant improvement in insulin sensitivity from 75 minutes of brisk walking.

Key words: race/ethnicity ■ glucose tolerance ■ insulin resistance ■ lifestyle

INTRODUCTION

Type-2 diabetes is increasing in epidemic proportions (11 million in 2000, expected to be 29 million in 2050), especially among minority populations. Current estimates predict that a child born in the year 2000 has a 33% risk for developing type-2 diabetes in his/her lifetime. However, the incidence rates are estimated at 50% for African-American children born in 2000. On average, African Americans are twice as likely to be diagnosed with diabetes compared with Caucasians. The higher prevalence rate of type-2 diabetes among African Americans has been attributed to more severe insulin resistance.

Insulin resistance is a condition in which muscle, adipose and liver cells are less sensitive to the metabolic effects of insulin. Physiologic actions of insulin are inhibited but can be compensated for by an increased concentration of blood insulin (i.e., hyperinsulinemia). According to the 1988–1994 NHANES-III survey, impaired glucose tolerance was higher in African Americans, particularly in African-American women, compared to age- and sex-matched Caucasians. The more severe insulin resistance in African Americans might be explained by higher rates of obesity, a higher prevalence of abdominal obesity and/or less participation in physical activity. However, when compared with Caucasians matched for body mass index (BMI), body composition, age, leisure-time, self-reported physical activity, diet and socioeconomic status, African Americans’ higher rates of insulin resistance remain.

Results from the diabetes prevention program showed that lifestyle modifications, including increased physical activity, are effective in preventing or delaying type-2 diabetes in high-risk populations. Even without weight loss, exercise training has a potent effect to enhance insulin sensitivity. In the HERITAGE study, the effect of exercise training on glycemic control was assessed in 173 African-American and 423 Caucasian individuals. Although there was no ethnic difference in BMI, insulin sensitivity was 61% higher in Caucasians compared to African Americans prior to the intervention. The effect of exercise training on insulin sensitivity did not differ significantly across ethnicities, but there was a 16% improvement in African Americans as compared with an 8% improvement seen in Caucasians.

Previous research has demonstrated that it is the residual action of single exercise bouts, not adaptations to habitual training per se, that accounts for the majority of the insulin-sensitizing effects. In obese and insuli-
resistant Caucasians, Devlin et al. reported a significant improvement in insulin-stimulated glucose uptake after just one bout of high-intensity exercise. An equivalent study has not been published in African Americans.

The metabolic response to an individual bout of exercise may be different in African Americans, potentially explaining some of the ethnic difference in insulin resistance. Therefore, the purpose of this experiment was to evaluate the effect of a single bout of exercise on insulin resistance in obese, sedentary African-American women. It was hypothesized that one bout of moderate-intensity exercise would significantly reduce insulin resistance compared to a no-exercise control condition. In order to probe the persistence of the exercise effects, we assessed blood glucose and insulin responses to an oral carbohydrate challenge 90 minutes and five hours after the exercise bout.

METHODS

Description of the Participants

Ten overweight/obese, African-American women between the ages of 19–45 participated in this study (Table 1). All individuals were sedentary, defined as not having participated in any structured form of aerobic exercise in the past six months. All participants had a family history of diabetes in ≥1 close family member such as a parent, grandparent or sibling. Participants were free from diagnosed cardiovascular disease, hypertension, diabetes and any other disease that could affect insulin or glucose responses. Individuals who smoked cigarettes or used pharmacologic agents (e.g., metformin, ACE inhibitors, statin drugs) or dietary supplements (e.g., chromium, ephedra) known or suspected to alter insulin action were excluded. After being provided with a full description of the study, subjects signed an informed consent document approved by the institutional review board at the University of Massachusetts, Amherst.

Pretesting Procedures

Participants completed physical activity rating questionnaires (PAR-Q) to assess overall level of physical activity for the previous six months, a score of ≤2 was classified as sedentary. Menstrual history was also recorded by having all participants recall the dates of their last menstrual cycle. They were familiarized with the exercise procedures and equipment. Dual energy x-ray absorptiometry (DEXA) (LUNAR, Madison, WI) was used to assess total body fat and obtain an estimate of abdominal fat.

Testing Procedures

All participants completed two-day-long protocols on consecutive days, which included a sedentary and exercise condition (Figure 1). The protocols were identical except for inclusion of exercise on day 2. On the night prior to day 1, subjects consumed a standardized dinner that contained 730 kilocalories (Kcal), distributed as 63% carbohydrates, 18% fat and 19% protein. After fasting overnight (10 hours), subjects arrived at the energy metabolism laboratory the following morning and sat quietly for three hours. A pedometer (Omron Healthcare Inc., Bannockburn, IL) was used to ensure that subjects were sedentary (took <300 steps) during this period. After completion of the rest period, a venous blood sample was taken from a catheter previously placed in an antecubital vein. Subjects completed a standard oral glucose tolerance test (OGTT), in which subjects drank a beverage containing 75 g of dextrose (Fisherbrand, Houston, TX). Blood samples were taken 30, 60, 90 and 120 minutes after the drink was consumed. Three-and-a-half hours after beginning the OGTT, subjects consumed a lunch meal composed of 660 kcal, distributed as 63% carbohydrates, 16% fat and 21% protein [meal tolerance test (MTT)]. Blood samples were collected immediately before and 30, 60, 90 and 120 minutes postmeal. After the final blood sample,
the catheter was removed and participants were permitted to leave. Participants were also provided with a snack and dinner to eat at home for the remainder of the test day. The standardized snack consisted of 57% carbohydrates, 24% fat and 19% protein, with total energy intake scaled to participants’ individual body weight.

The next morning, participants returned to the laboratory in the fasted state (10 hours). They walked on a motorized treadmill (Lifestyle, Schiller Park, IL) while wearing a pedometer and a heart rate monitor (Polar, Lake Success, NY). Participants walked for 15 minutes at a speed between 3.0–3.5 miles per hour, at an incline of 1.0–1.5% grade, followed by 5 minutes walking at a self-selected (recovery) pace. The protocol was repeated three more times for a total of 75 minutes of exercise. The goal was to complete 10,000 steps at a target heart rate of 130–140 beats per minute. Immediately following the exercise session, subjects rested for 90 minutes to ensure that heart rate and oxygen consumption returned to pre-exercise levels. After the rest period, participants completed the OGTT and MTT, protocols described earlier.

Control of Diet and Activity

Because energy imbalance has an independent effect on insulin sensitivity, measures were taken to minimize the possibility that subjects were in energy surplus or deficit. To estimate resting energy requirements, resting metabolic rate (RMR) was calculated using the Harris-Benedict equation specific to women: 655 + 9.5 (weight in kg) + 1.9 (height in cm) – 4.7 (age).16 To estimate total daily energy expenditure (TDEE) the RMR was multiplied by 1.4, the activity factor appropriate for sedentary individuals.16 The TDEE was used to design meals containing the appropriate energy content for each subject. These meals were provided to all participants throughout the duration of the study. The energy content of the pretesting dinner and lunch meal were the same for each subject. The energy content of the snack was varied so that total daily energy intake was matched to estimate total daily energy expenditure for each individual subject.

Control of Menstrual Cycle

All women participating in this study were instructed to record the onset and cessation of menses because insulin sensitivity may change as concentrations of estrogen and progesterone vary during the menstrual cycle.20,21 To avoid a systematic bias due to menstrual cycle phase, five participants completed pre- and posttesting of insulin sensitivity during the follicular phase, and five subjects were tested during the luteal phase.

Biochemical Assays

Samples of venous blood were collected in heparinized syringes and transferred to vacutainers containing a glycolytic inhibitor (sodium fluoride) for analysis of glucose and an anticoagulant (K3 EDTA) for analysis of insulin. All samples were immediately centrifuged and plasma transferred to cryogenic vials and frozen at -70°C until analysis. Glucose concentrations were determined by the glucose oxidase method using a glucose analyzer (Analog Instruments, Lunenburg, MA). Insulin concentrations were determined by competitive binding using a human-specific radioimmunoassay (Linco Research Inc., St. Charles, MO).

Calculations

To determine abdominal fat mass, a quadrilateral box was manually drawn around the L1–L4 abdomen region from the DEXA scan. Bony landmarks located on the bottom of the ribcage (last floating rib) and pelvis (top of the superior iliac crest) were used to identify this abdominal region.22,23 The DEXA L1–L4 region compared to a computed tomography (CT) scan has been shown to be both accurate (r=0.967) and reliable (R=0.97) in estimating abdominal obesity.

The glucose and insulin responses to the OGTT were entered into mathematical models designed to assess insulin sensitivity. The composite insulin sensitivity index (C-ISI) = (10,000 / √(FPG x FPI) x (MPG x MPI)) where FPG = fasting plasma glucose, FPI = fasting plasma insulin, MPG = mean postprandial glucose concentrations during the OGTT and MPI = mean insulin concentrations during the OGTT.24 According to the C-ISI calculation, whole-body insulin sensitivity ranges from 0–12 (0 = maximally

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**Figure 1. Experimental protocol**

<table>
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<tr>
<th>Sedentary Condition (Day 1)</th>
<th>Exercise Condition (Day 2)</th>
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<tr>
<td>Resting OGTT MTT</td>
<td>Exercise Resting OGTT MTT</td>
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VOL. 98, NO. 11, NOVEMBER 2006
insulin resistant, 12 = maximally insulin sensitive). Fasting plasma insulin and glucose concentrations were also used to estimate insulin resistance using homeostasis model assessment (HOMA). The HOMA = [(FPI x FPG)/22.5] on a scale of 1–8 (1 = insulin sensitive, 8 = insulin resistant).

**Statistical Analysis**

All statistical analyses were performed with SAS software. Descriptive statistics located in the tables, including age, height, weight, body mass index and insulin action, are expressed as mean and standard deviation. Graphical data located in the figures, including area under the curve (AUC), are expressed as mean and standard error. A paired t test was used to compare pre- and postexercise differences in fasting glucose and insulin concentrations, glucose AUC, insulin AUC and estimated insulin sensitivity during both the OGTT and MTT. Differences between conditions were considered statistically significant when the 95% confidence intervals (95% CI) around the mean difference did not include 0.

**RESULTS**

**Exercise Condition**

All participants were able to complete 75 minutes of brisk walking on the treadmill, during which they completed ≥8,500 steps (compared to 665 on the sedentary day). All participants reached a target heart rate >130 beats per minute, and expended ≥350 kcal during exercise (Table 2).

**Fasting Glucose, Insulin and HOMA**

There was no significant difference in fasting plasma glucose concentrations between the exercise and sedentary conditions before the OGTT (95% CI -0.08–0.27; p=0.25) or MTT (95% CI -1.39–0.68; p=0.46) (Table 3). Exercise had no significant effect on fasting plasma insulin concentrations before the OGTT (95% CI -14.04–13.09; p=0.94) or MTT (95% CI -222.11–11.49; p=0.07), although it tended to be higher during the MTT. After exercise, there was also no significant difference in HOMA scores before the OGTT (95% CI -0.52–0.53; p=0.98) or the MTT (95% CI -10.87–0.98; p=0.09).

**Effects of Exercise on Glucose Tolerance (Table 4)**

The plasma glucose responses during the OGTT and MTT are shown in Figure 2a and Figure 2b, respectively. Exercise had no significant impact on plasma glucose AUC during the OGTT (95% CI -93.81–4.6; p=0.07), although it tended to be lower after exercise. There were no significant differences during the MTT (95% CI -6.78–45.38; p=0.13).

**Effects of Exercise on Insulin Action**

There was no effect of menstrual cycle phase on insulin response (p=0.39). The plasma insulin responses to the OGTT and MTT are shown in Figure 3A and 3B, respectively. The plasma insulin AUC during the OGTT

<table>
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<th>Table 3. Fasting glucose and insulin concentrations; C-ISI and HOMA scores</th>
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<tr>
<td><strong>SED–OGTT</strong></td>
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<td>FPG (mM)</td>
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<td>FPI (pM)</td>
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<td>C-ISI score</td>
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<td>HOMA</td>
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| **SED–MTT** | **Mean ± (SD)** | **EX–MTT** | **Mean ± (SD)** | **p Value** |
|---|
| FPG (mM) | 4.1 ± 0.6 | FPG (mM) | 4.4 ± 1.2 | 0.46 |
| FPI (pM) | 118.4 ± 113.5 | FPI (pM) | 223.7 ± 244.2 | 0.07 |
| C-ISI score | 5.4 ± 3.6 | C-ISI score | 4.4 ± 3.5 | 0.30 |
| HOMA | 3.8 ± 4.1 | HOMA | 7.3 ± 2.1 | 0.09 |

Values are mean ± SD. SED: sedentary condition; EX: exercise condition; OGTT: oral glucose tolerance test; MTT: meal tolerance test; FPG: fasting plasma glucose; FPI: fasting plasma insulin; C-ISI: composite insulin sensitivity index; HOMA: homeostasis mathematical assessment. Significance set at alpha level of 0.05.

<table>
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<th>Table 4. Glucose and insulin area under the curve</th>
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<td><strong>Area under the Curve</strong></td>
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<td>Glucose (mM*time)</td>
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<td>Insulin (pM*time)</td>
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Values are mean ± SD. SED: sedentary condition; EX: exercise condition; OGTT: oral glucose tolerance test; MTT: meal tolerance test. Significance level at alpha <0.05.
was significantly lower in the exercise condition (95% CI -4511– -52; p=0.046) compared to the sedentary condition. During the MTT, however, there was no significant difference between conditions in plasma insulin AUC measured during the MTT (95% CI -204–2,721; p=0.08).

**Effects of Exercise on Estimated Insulin Sensitivity**

During the OGTT, insulin sensitivity calculated by the C- ISI was significantly higher during the exercise condition compared to the sedentary condition (95% CI 0.03–1.12; p=0.042). There was no effect of exercise on insulin sensitivity during the MTT (95% CI -2.95–1.02; p=0.30) (Table 4).

**DISCUSSION**

The major finding of this study was that a single bout of exercise at a moderate intensity improved estimated insulin sensitivity in African-American women during an OGTT administered 90 minutes postexercise. The enhanced sensitivity after exercise was not evident during a mixed meal that followed the OGTT.

In this study, glucose and insulin responses to oral glucose were used to estimate whole-body insulin sensitivity. The most direct measure of peripheral insulin sensitivity is the glucose rate of infusion during a hyperinsulinemic-euglycemic clamp. Yeni-Komshian et al. demonstrated that approximately two-thirds of the variability in clamp-measured insulin sensitivity are explained by the total insulin AUC during an OGTT. The C- ISI is also strongly correlated with clamp-measured insulin sensitivity in subjects with normoglycemia, impaired glucose tolerance and diabetes. Therefore, the 18% changes in insulin AUC and C-ISI observed after exercise are likely to reflect real changes in whole-body insulin sensitivity.

Although statistically significant, an 18% change after one bout of exercise is generally less than what other researchers have observed. Heath et al. reported a 33 % decrease in insulin AUC during an OGTT after a single bout of high-intensity exercise in lean men and women. Young et al. observed a 30% decrease in insulin AUC one day after low-to-moderate-intensity exercise in trained and untrained men. Direct comparisons with these other studies is problematic because differences in gender, ethnicity, exercise intensity, duration and total energy expenditure all affect the magnitude of the response.

For example, the intensity of exercise plays an important role in enhancing insulin sensitivity. Hayashi et al. reported no change in glucose uptake and insulin sensitivity during a frequently sampled intravenous tolerance test after a single bout of exercise at 50% maximum oxygen uptake (VO2max), but improvements were seen after higher-intensity exercise at 70% VO2max. Young et al. reported a trend toward a larger change (-43%) in the plasma insulin AUC after a single bout of exercise at 80% VO2max compared with the change (-28%) after lower-intensity exercise at 40% VO2max. These data suggest that higher-intensity exercise enhances muscle insulin sensitivity more than lower-intensity exercise. The moderate-intensity, long-duration protocol used in the current study may have been an insufficient stimulus to elicit a large improvement in insulin sensitivity.

The enhanced sensitivity observed after a single bout of exercise in this study appeared to be short lived. Greater insulin sensitivity during the OGTT (90 minutes postexercise) did not persist during the MTT (five hours...
postexercise). This short time course may seem inconsistent with several studies that have shown the enhanced sensitivity can last up to 72 hours.\textsuperscript{29-33} Before attributing this discrepancy to an ethnic difference, however, alternative explanations are possible. Enhanced glucose uptake in the postexercise period is related to the depletion/repletion of muscle glycogen.\textsuperscript{31} The enhanced glucose uptake erodes as glycogen stores are replenished by food (particularly carbohydrate) intake. In the present study, an average of 425 kcal were expended during exercise. Assuming that 50% of energy came from muscle glycogen (this is likely a generous assumption), exercise required about 50–55 g of muscle glycogen. The OGTT provided 75 g of rapidly absorbed carbohydrates. It is likely that the carbohydrate content of the OGTT and the timing within the two-hour "critical window," known to result in high rates of muscle glycogen synthesis, fully replenished muscle glycogen and blunted glucose uptake during the subsequent MTT. In fact, insulin AUC tended to be higher during the MTT in the exercise condition, suggesting that the high carbohydrate "load" consumed during the OGTT had a negative impact on whole-body insulin sensitivity. This finding is consistent with that of Larsen et al.,\textsuperscript{34} who examined the effects of exercise on postprandial glucose responses in patients with type-2 diabetes. After 45 minutes of cycling at 45% maximum oxygen uptake, plasma insulin levels decreased in response to a breakfast MTT, but this effect did not persist during the following lunch meal.

Although the differences were not significant, the plasma insulin concentrations before the MTT tended to be higher after the exercise condition. Because the sample size was modest, the possibility of a type-2 error has to be considered. Individual data show that the trend was entirely attributable to three subjects, who were markedly hyperinsulinemic at the onset of the MTT. Whether this response was related to exercise-insulin changes in insulin clearance, or some other factor cannot be determined from the available data. Despite the variability in pre-MTT insulin concentrations, insulin sensitivity estimated from the glucose and insulin responses was clearly not different between conditions. Additionally, the HOMA scores for these subjects was 7.3.

Although there was a significant improvement in the C-1SI (measured in response to the glucose challenge), the mean HOMA score of 2.6 (measured in the fasting state) was unaffected by exercise. This result is not surprising given that insulin resistance is primarily manifested in the postprandial state. A single bout of exercise does not usually alter fasting glucose and insulin concentrations in either trained or untrained subjects.\textsuperscript{16,26,30,32}

A limitation of this study is that the order of the sedentary and exercise conditions was not balanced across subjects. The sedentary condition was always performed the day before the exercise condition. We accepted this limitation for several reasons. Because we assumed that the residual effects of exercise would last up to 72 hours, at least 4–5 days following the exercise condition would have been required as a washout period. Waiting >4 days between conditions would likely have placed the female subjects at different points in the menstrual cycle. Women are usually more insulin resistant in the luteal phase of the menstrual cycle when concentrations of estrogen and progesterone are high.\textsuperscript{39,41} We considered it important to impose each condition at the same point in their menstrual cycle. Therefore, a balanced design would have required a month between testing dates, making it likely that dietary intake and habitual physical activity would have changed. Therefore, despite the possibility of intro-

![Figure 3. Insulin areas under the curve](attachment:image)

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<th>Figure 3. Insulin areas under the curve</th>
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<td>A: During the oral glucose tolerance test</td>
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<tr>
<td>OGTT</td>
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<tr>
<td>Insulin Concentrations (pm)</td>
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<td>Time (min)</td>
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<td>p=0.046</td>
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<th>B: During the meal tolerance test</th>
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<tr>
<td>MTT</td>
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<td>Insulin Concentrations (pm)</td>
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Values are mean ± SE. SED: sedentary condition; EX: exercise condition
ducing an “order effect” as a confounding variable, we chose to complete the sedentary condition on the first day of the study, immediately followed by the exercise condition. Because it is unlikely that the sedentary condition, a typical day for these inactive subjects, would have any confounding effects on their “normal” insulin sensitivity, confounding effects of not balancing the study protocol were expected to be minimal compared to a balanced design with a 28-day washout period.

The surgeon general’s report on physical activity and health recommends that, in order to prevent or delay onset of disease, individuals should accumulate 30 minutes of moderate physical activity (such as brisk walking) on all or most days of the week.35 Tudor-Locke et al. reported that >10,000 steps/day as measured by a pedometer corresponds with the current recommendations for physical activity.36 The current study is unique in demonstrating that overweight, sedentary, insulin-resistant women can gain a significant benefit from one bout of exercise that consists of brisk walking following the “10,000 steps per day” guidelines.37 Although 10,000 steps enhanced insulin sensitivity at least up through the next meal (but maybe not longer), it is relatively modest in magnitude. It is important to note that the single bout of exercise attenuated but did not eliminate insulin resistance in this study group. Although they were 18% more insulin sensitive, all participants were still classified as insulin resistant after the exercise. Larger benefits likely require either completing a larger portion of those 10,000 steps at a higher intensity, walking >10,000 steps a day, or accumulating multiple 10,000-step “days” on a regular basis. From a clinical standpoint, it is important to know that walking, which can be safely performed and easily incorporated into daily living, can be an effective means of improving insulin sensitivity and potentially reducing risk of diabetes in African-American women.

There was no direct comparison with Caucasian women in this study; hence, these data provide few clues about ethnic differences in the metabolic response to exercise. Future research focused on directly comparing effects of prior exercise on insulin action in Caucasian and African-American women matched for age, BMI, level of physical activity and family history of disease will address the potential for ethnic differences in response to exercise.

ACKNOWLEDGEMENTS

The authors would like to thank the research participants for their enthusiasm and commitment of time and effort. We also acknowledge helpful assistance from Priscilla Clarkson, PhD; Stuart Chipkin, MD; David Pober, MS; Carrie Sharoff, MS; Todd Hagobian, MS; and Kaila Holtz, BS.

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