A Single Session of Low-Intensity Exercise Is Sufficient to Enhance Insulin Sensitivity Into the Next Day in Obese Adults

Sean A. Newsom, phd
Allison C. Everett, bs
Alexander Hinko, phd
Jeffrey F. Horowitz, phd

OBJECTIVE—The purpose of this study was to determine the effect of a relatively modest session of exercise on insulin sensitivity and fatty acid uptake the next day in obese adults.

RESEARCH DESIGN AND METHODS—Eleven sedentary obese adults (male/female: 3/8; BMI 37 ± 1 kg/m^2; peak oxygen uptake [VO_2peak] 20 ± 1 mL/kg/min) completed three experimental trials. On two of these occasions, subjects exercised to expend 350 kcal in the afternoon. These two exercise trials were identical except for the exercise intensity (50% VO_2peak [EX50] and 65% VO_2peak [EX65]) and the duration of exercise necessary to expend 350 kcal (EX50 = ~70 min; EX65 = ~55 min). Subjects also completed a control trial (CON), without exercise. The next morning, we measured insulin sensitivity (hyperinsulinemic-euglycemic clamp) and whole-body fatty acid uptake (palmitate rate of disappearance from plasma [R_d]).

RESULTS—Exercise increased insulin sensitivity the next day, but whereas the 35% improvement after EX50 compared with CON was statistically significant ($P = 0.01$), the 20% improvement after EX65 was not ($P = 0.17$). Despite nearly identical values between CON and EX65 ($P = 0.88$), systemic fatty acid uptake was lower after EX50 compared with EX65 ($P = 0.02$), but not quite significant compared with CON ($P = 0.07$). Importantly, the change in fatty acid uptake after exercise compared with CON was negatively correlated with the change in insulin sensitivity for all trials ($r = -0.60$, $P = 0.003$).

CONCLUSIONS—A relatively modest single session of exercise in obese adults improved insulin sensitivity the next day, and a reduction in systemic fatty acid uptake in the several hours after exercise may be important for this effect.

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Exercise is a cornerstone treatment for obesity-related metabolic complications, including insulin resistance (1), which is a primary cause of type 2 diabetes and many other chronic diseases. Contrary to popular belief, much of the insulin-sensitizing effect of exercise can be attributed to the most recent session(s) of exercise rather than to an accumulated effect of training and/or "fitness" (2,3). Even a single session of exercise can greatly enhance insulin sensitivity in insulin-resistant obese individuals (4); however, this beneficial effect is typically short-lived (i.e., 24–48 h) (2,3,5). For these reasons, we contend that exercise prescriptions aimed at improving insulin sensitivity in obesity should be tailored to maximize the beneficial effects that occur in the several hours after each session of exercise.

Surprisingly, the minimal "dose" of exercise required to significantly enhance insulin sensitivity is not known. Devlin and Horton (4) were the first to demonstrate that a single session of vigorous exercise (e.g., high-intensity interval exercise until fatigue) could significantly improve insulin sensitivity measured the next day in insulin-resistant obese adults. Clearly this level of strenuous exercise does not translate into a viable exercise prescription for most obese people, yet little is understood about the effects of a lower exercise stimulus (e.g., lower intensity and duration) on insulin sensitivity in obesity. The very few studies that have attempted to examine the metabolic benefit of less intense and/or shorter exercise sessions in obese subjects have yielded inconsistent results (6,7). The use of indirect assessments of insulin sensitivity (e.g., 24-h glycemia, homeostasis model assessment of insulin resistance) and variations in the control of the energy expended during the exercise sessions likely contributed to these equivocal findings. The primary aim of our study was to examine the insulin-sensitizing effects of an exercise session performed at either a rather mild intensity (50% peak oxygen uptake [VO_2peak]) or a slightly more intense exercise session (65% VO_2peak) in obese adults who are at risk for developing type 2 diabetes. Importantly, the energy expended during exercise was identical between our two exercise treatments (350 kcal), and these exercise sessions were far less rigorous than those previously used to demonstrate improved insulin sensitivity in obesity (4,8,9).

RESEARCH DESIGN AND METHODS

Subjects

A total of 11 obese women and men (female/male: 8/3; BMI 30–45 kg/m^2; age 18–45 years; fasting blood glucose concentration <125 mg/dL) were recruited to participate in this study (Table 1). Subjects were not taking any medications (consistent use of oral contraceptives was permitted), and all subjects underwent a comprehensive medical examination. All subjects were nonsmokers, weight stable (i.e., ±2 kg for ≥6 months), and sedentary

From the Substrate Metabolism Laboratory, School of Kinesiology, University of Michigan, Ann Arbor, Michigan.
Corresponding author: Jeffrey F. Horowitz, jeffhoro@umich.edu.
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Table 1—*Participant characteristics*

Age (years)	28 ± 2
BMI (kg/m^2)	37 ± 1
Body mass (kg)	102 ± 3
Body fat (%)	48 ± 2
Fat mass (kg)	50 ± 3
Fat-free mass (kg)	53 ± 2
VO_2peak (mL/kg/min)	20 ± 1

Values are mean ± SEM.

(i.e., they did not regularly participate in any purposeful exercise activities for at least 6 months before enrolling in the project). Any history of metabolic or cardiovascular disease resulted in exclusion from participation. Written, informed consent was obtained from all subjects before initiating participation. All procedures of this study were approved by the University of Michigan institutional review board.

Preliminary testing

At least 1 week before the experimental protocol, subjects performed an incremental VO_2peak test on a stationary cycle ergometer (Examiner; Lode B.V., Groningen, the Netherlands) to assess aerobic fitness using a metabolic cart (MaxII; Physio-Dyne Instrument Corp., Quogue, NY). In addition, dual-energy X-ray absorptiometry (Lunar Prodigy Advance; GE Healthcare, Buckinghamshire, U.K.) was used to assess body composition.

Experimental protocol

All subjects participated in three separate experimental trials (i.e., two exercise trials and one no-exercise "control" trial) (Fig. 1), performed in a randomized order and separated by ≥7 days. The evening before each trial, subjects ingested a standardized meal at 1900 h (55% carbohydrate, 30% fat, and 15% protein; one-third of total daily energy requirements estimated from fat-free mass as previously described) (10). The next morning (day 1), after an overnight fast, subjects were admitted to the Michigan Clinical Research Unit at 0830 h. Subjects were provided a standardized breakfast at 0930 h and lunch at 1230 h (see STUDY DIETS). Because the duration of exercise varied between the two exercise trials, subjects began exercise at different times so that the exercise session in both trials was completed at 1600 h. Subjects exercised at either 50 or 65% of their predetermined VO_2peak for the duration required to expend 350 kcal. Energy expended during exercise was divided equally between treadmill walking/jogging and cycle ergometry exercise, with no rest provided between these modes of exercise. We measured VO_2 and VCO_2 using a metabolic cart (Physio-Dyne Instrument Corp.) at the beginning of exercise and approximately every 20 min thereafter. During the no-exercise trials, subjects remained seated quietly. Exactly 1 h after exercise (1700 h), a meal tolerance test was conducted by providing a standardized meal (~20% of total daily energy requirements; 55% carbohydrate, 30% fat, and 15% protein), with blood samples collected every 15 min for 2 h to measure plasma glucose and insulin concentrations. Another meal was provided at 2000 h, and an evening snack was eaten at 2200 h. Subjects remained sedentary in the hospital until completion of the trial the next day.

Beginning at 0450 h the next morning, three blood samples were taken in 5-min intervals (i.e., 0450 h, 0455 h, and 0500 h) from an intravenous catheter in a heated hand vein to obtain arterialized blood samples (11), for determination of background enrichment of [6,6 d_2]glucose and [1-^{13}C]-palmitate. At 0500 h, we began a primed, constant rate infusion of [6,6 d_2]glucose (35 μmol/kg priming dose; 0.41 μmol/kg/min continuous infusion; Isotec, Miamisburg, OH). We next measured resting energy expenditure (and fat oxidation) using ventilated hood indirect calorimetry for 30 min starting at 0700 h (Vmax Encore; CareFusion, San Diego, CA). At 0730 h, we obtained a skeletal muscle sample (~100 mg) from the vastus lateralis. Muscle biopsy samples were dissected free of adipose and connective tissue, rinsed in saline, blotted dry, and then frozen in liquid nitrogen. At 0800 h, we began a constant-rate infusion of [1-^{13}C]-palmitate (0.04 μmol/kg/min continuous infusion; Cambridge Isotopes, Andover, MA). After 45 min of the [1-^{13}C]-palmitate isotope infusion, three arterialized blood samples were obtained from the heated hand vein in 5-min intervals for determination of fatty acid rate of appearance (R_a) and disappearance (R_d) to/from the circulation (fatty acid mobilization and uptake, respectively), as well as determination of basal hepatic glucose production via isotope dilution of the constant rate infusion of [6,6 d_2]glucose. These blood samples were also analyzed for plasma concentrations of triacylglycerol, fatty acids, glucose, and insulin. At 0900 h, we began a hyperinsulinemic-euglycemic clamp to assess insulin sensitivity, as described previously (12). In brief, the clamp was performed using a constant 2-h insulin infusion at a rate of 100 mU/m^2/min. We used this relatively high insulin dose during the clamp to largely suppress hepatic glucose production, which allows our findings to highlight the effects of prior exercise on peripheral glucose uptake. Plasma glucose concentration was monitored every 5 min during the clamp using a glucose autoanalyzer (Yellow Springs Instruments; Yellow Springs, OH), while glucose (D20 dextrose solution) was infused at a variable rate to maintain euglycemia. Importantly, this glucose infusion solution was enriched with [6,6 d_2]glucose (2.5% enriched) to limit changes in glucose tracer enrichment in plasma during the clamp procedure (13). In addition to the small blood samples collected every ~5 min to assess plasma glucose concentration, additional plasma samples were collected in 5-min intervals during the final 20 min of the 2-h clamp for assessment of insulin and plasma enrichment of [6,6 d_2]glucose. Subjects also received an intravenous infusion of potassium (KCl) during the clamp to prevent hypokalemia.

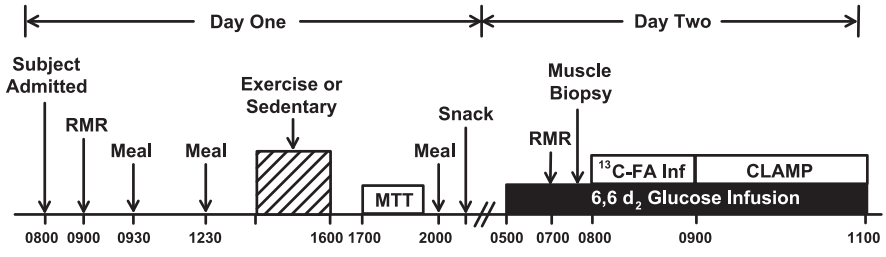

Figure 1—*Timeline of experimental events. Subjects participated in three separate 2-day trials. On two occasions, subjects expended 350 kcal during an exercise session in the afternoon of the first day. These two exercise trials were identical except for the intensity of exercise performed (50% VO_2peak [EX50] and 65% VO_2peak [EX65]). Subjects also completed a control trial in which they remained sedentary. CLAMP, hyperinsulinemic-euglycemic clamp; ^{13}C-FA Inf, [1-^{13}C]-palmitate isotope infusion; MTT, meal tolerance test; RMR, resting metabolic rate.*

Study diets

During the first day of each trial (day 1), the total energy content of diet matched estimated daily energy expended (10) (see CALCULATIONS below). Breakfast (0930 h), lunch (1300 h), and the postexercise meal (1700 h) each contained ~20% of the daily energy intake. At dinner, ~30% of the total daily energy requirement was provided (2000 h), and ~10% of daily energy requirement was provided in the evening snack (2200 h). Subjects ingested the exact same meal during the meal tolerance test (1700 h) and consumed an identical snack at 2200 h in all trials (i.e., identical in both absolute energy content and macronutrient composition). After the snack, subjects did not eat anything until completion of the clamp procedure the next day. The relative macronutrient content of the diets was 55% carbohydrate, 30% fat, and 15% protein (expressed as percent of total energy intake).

Analytical procedures

Plasma substrate and hormone concentrations. Plasma concentrations of glucose, fatty acid, triacylglycerol, and insulin were assessed using commercially available kits as previously described (14). The calculated coefficients of variation (CVs) of these assays were ~3, 2, 1, and 10%, respectively, which are in agreement with the manufacturer-reported CVs.

Plasma fatty acid and glucose kinetics. The tracer-to-tracee ratio (TTR) for plasma palmitate and glucose was determined by gas chromatography–mass spectrometry (Agilent 5973 Networks, Mass Selective Detector; Agilent Technologies, Palo Alto, CA) with capillary column, as previously reported by our laboratory (14).

Muscle glycogen concentration. Muscle biopsy samples were lyophilized at –60°C for 48 h, and aliquots were weighed to the nearest 0.1 mg. Muscle glycogen was determined from the measurement of glucose after acid hydrolysis as previously described (15). In our laboratory, repeated analysis of glycogen concentration using this acid hydrolysis assay yielded a CV of ~6%, which is similar to the CV reported by others using this same assay (16,17).

Muscle lipid concentrations. Muscle triacylglycerols and diacylglycerols were measured from generated fatty acid methyl esters (FAMEs), by gas chromatography with capillary column (Agilent Technologies). FAMEs were detected by electron-impact mass spectrometry with selective ion monitoring and quantified using FAME standards. Analysis of skeletal muscle ceramide concentration was performed after lipid extraction via liquid chromatography-triple quadrupole mass spectrometry (Agilent Technologies 6410 Triple Quadrupole Mass Spectrometer). Further details concerning these methods can be found in the Supplementary Data.

Calculations

Energy expenditure and fat oxidation. Energy expenditure during rest and exercise was calculated from VO_2 and VCO_2 measurements using the Weir equation (18). Because the duration of exercise was different between trials, daily energy expenditure for each trial was estimated as follows: ([((VO_2 during exercise in L/min × 3.941) + (VCO_2 during exercise in L/min × 1.11)) × (duration of exercise in min)] + [(1.5 × RMR) × (time not exercising in min)]), where RMR is resting metabolic rate. The daily energy expenditure has been estimated as 1.5 × RMR for healthy sedentary adults (19). Whole-body fat/triacylglycerol oxidation (g/min) was calculated from VO_2 and VCO_2 measurements using the equations of Frayn (20).

Plasma glucose and insulin area under the curve during the meal tolerance test. Area under the curve (AUC) for plasma glucose and insulin concentration curves during time 0–120 min of the meal tolerance test was calculated using the trapezoidal rule (21).

Hepatic glucose production. Steady-state glucose concentration and TTR were achieved during isotope infusion; therefore, plasma glucose $R_a = R_d$ and could be calculated using the Steele equation for steady-state conditions (22). Exogenous glucose infusion rates were subtracted from glucose R_a calculated during steady state of the hyperinsulinemic-euglycemic clamp.

Insulin sensitivity. Whole-body insulin sensitivity measured using the hyperinsulinemic-euglycemic clamp was calculated as

$$\text{Insulin sensitivity} = \left(\frac{R_d}{SSI}\right),$$

where R_d refers to steady-state whole-body glucose disposal (μmol/min) and SSI refers to steady-state plasma insulin concentration (μU/mL) during the final 20 min of the clamp procedure. Whole-body glucose R_d was calculated as the sum of the total glucose infusion rate (both labeled and unlabeled glucose) and hepatic glucose production during the final 20 min of the clamp.

Fatty acid mobilization and uptake. Steady-state fatty acid concentration and TTR were achieved during isotope infusion; therefore, plasma palmitate $R_a = R_d$ and could be calculated using the Steele equation for steady-state conditions (22). Because palmitate is a reasonable marker for systemic fatty acid kinetics (23), total plasma fatty acid R_a/R_d was calculated by dividing plasma palmitate R_a/R_d by the percent contribution of palmitate to the total plasma fatty acid pool.

Statistical analysis

A repeated-measures two-way (treatment × time) ANOVA was used to test for significant differences in plasma glucose and insulin concentrations at different time points during the meal tolerance test. Repeated-measures one-way ANOVA was used to test for significant differences in all other outcome variables between trials. Tukey post hoc pairwise comparisons were used to examine differences in factor means when significant F values were detected during ANOVA analyses. Pearson product-moment correlation analysis was used to examine the relationship between outcome variables selected a priori. Statistical significance was defined as $P \leq 0.05$. All data are presented as mean ± SEM.

RESULTS

Exercise intensity and energy expenditure

Exercise intensity and the energy expended during exercise were successfully controlled in all exercise sessions as planned (Supplementary Table 1), and all participants were able to complete the exercise sessions. Because exercise intensity was greater during EX65 than EX50 ($P < 0.001$), subjects exercised for ~15 min longer during EX50 than EX65 ($P < 0.001$) in order to successfully match exercise energy expenditure between these trials (Supplementary Table 1). Compared with remaining sedentary (CON), neither resting energy expenditure (main effect $P = 0.28$) nor resting fatty acid oxidation (main effect $P = 0.51$) was different the morning after exercise (data not shown).

Insulin sensitivity after exercise

During the meal tolerance test performed 1 h after exercise, we found that the

glucose and insulin responses to the meals after exercise compared with CON did not quite reach statistical significance (main effects $P = 0.09$ and $P = 0.07$ for glucose AUC and insulin AUC, respectively) (Fig. 2). Insulin sensitivity measured the morning after exercise using the clamp procedure was significantly elevated (~35%) above control levels when measured the morning after EX50 ($P = 0.01$) (Fig. 3*A*); however, the 20% increase above CON the morning after EX65 did not achieve statistical significance ($P = 0.17$). There was no difference in insulin sensitivity between EX50 and EX65 ($P = 0.39$). Importantly, hepatic glucose output during the hyperinsulinemic-euglycemic clamp was suppressed to nearly identical levels among trials (83 ± 5, 88 ± 5, and 84 ± 7% for CON, EX50, EX65, respectively), indicating that the exercise-induced improvement in insulin sensitivity measured during the clamp was the result of enhanced peripheral glucose metabolism.

Muscle glycogen

An additional objective of this study was to examine factors that may underlie the improvement in insulin sensitivity in the hours after exercise. Muscle glycogen is known to be a key mediator of the improvement in insulin sensitivity after exercise (14,24). As expected, skeletal muscle glycogen content was lower the morning after exercise compared with remaining sedentary. Glycogen concentration was significantly lower the morning after EX65 compared with CON (343 ± 33 vs. 440 ± 39 mmol/kg dry muscle; $P = 0.007$). Although muscle glycogen concentration was also relatively low the morning after EX50 (377 ± 33 mmol/kg dry muscle), this reduction below CON was not statistically significant ($P = 0.09$). There was no difference in muscle glycogen concentration between EX50 and EX65 ($P = 0.46$).

Lipid metabolism

We have recently demonstrated that altered skeletal muscle lipid metabolism may also be important for the improvement in insulin sensitivity after exercise, particularly when systemic fatty acid availability is elevated (25,26), as is commonly found in obesity (27). Interestingly, despite nearly identical values during CON and EX65 ($P = 0.88$), fatty acid uptake (fatty acid R_d) was lower ($P = 0.02$) (Fig. 3*B*) the morning after exercise during EX50 compared with EX65, but not CON ($P = 0.07$). More importantly, the improvement in insulin sensitivity the morning after exercise (compared with CON) was significantly correlated with the reduction in fatty acid uptake (fatty acid R_d; $r = -0.60$, $P = 0.003$). However, these differences in systemic fatty acid availability did not translate into measurable differences in key skeletal muscle lipid pools or markers of skeletal muscle

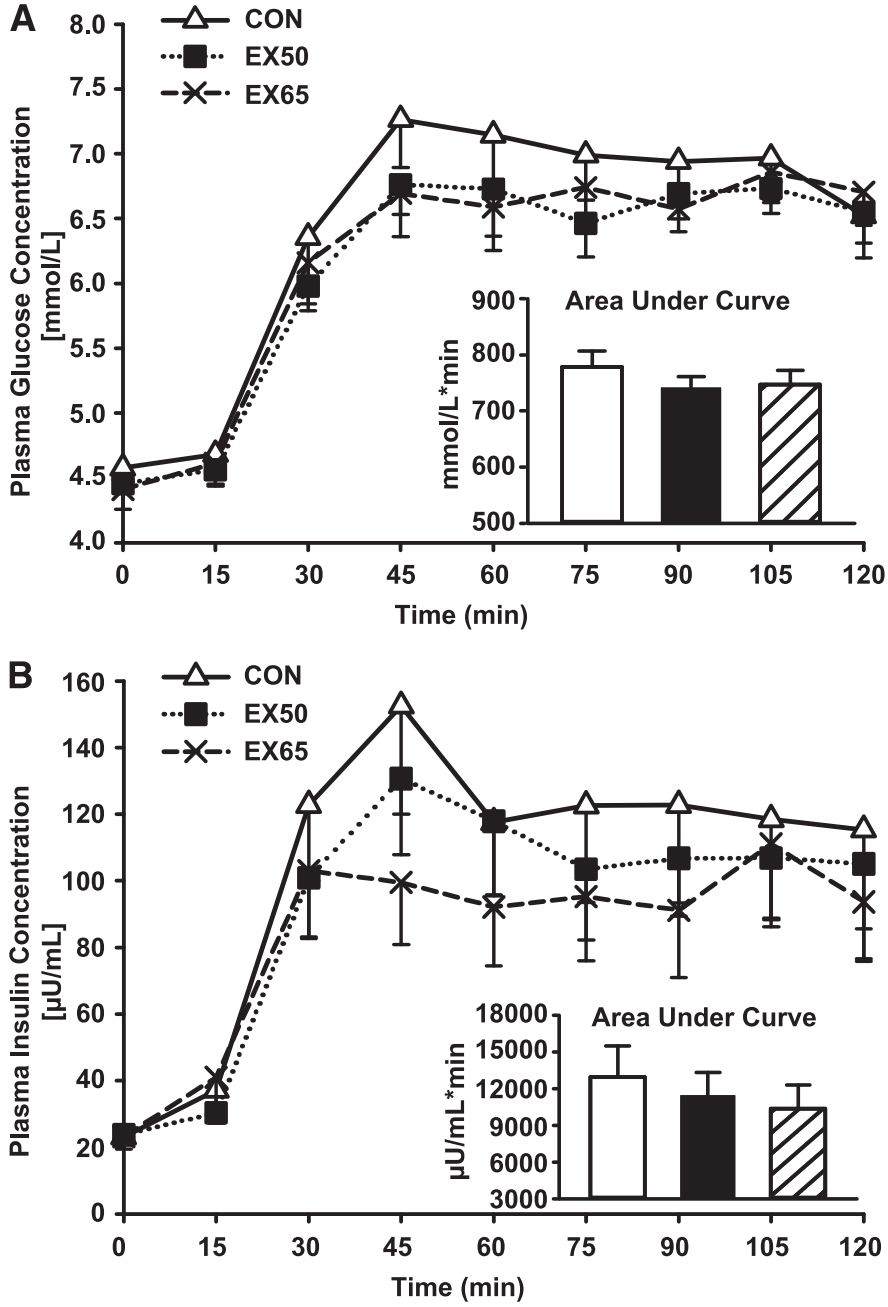

Figure 2—*Plasma concentrations of glucose* (A) *and insulin* (B) *measured during the meal tolerance test conducted 1 h after exercise or remaining sedentary. Inset figures are calculated as mean area under the plasma concentration curve for each trial.* A*: For plasma glucose concentration, the two-way (treatment × time) repeated-measures ANOVA,* P *= 0.17, and the main effect AUC, one-way repeated-measures ANOVA,* P *= 0.09.* B*: For plasma insulin concentration, the two-way (treatment × time) repeated-measures ANOVA,* P *= 0.15, and the main effect AUC, one-way repeated-measures ANOVA,* P *= 0.07.*

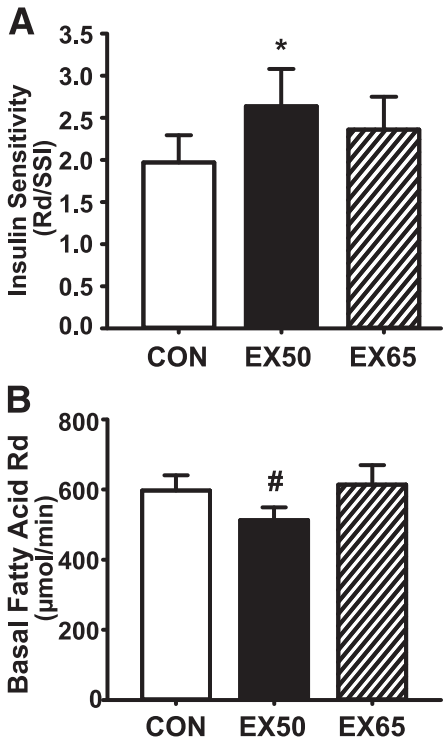

Figure 3—A: *Insulin sensitivity measured via hyperinsulinemic-euglycemic clamp the day after exercise. Data are expressed as clamped whole-body glucose disposal (R_d, μmol/min) per steady-state plasma insulin concentration (SSI, μU/mL).* *P < *0.05 EX50 vs. CON* (P = *0.17 for EX65 vs. CON*). B: *Basal fatty acid rate of disappearance from plasma (R_d) measured the day after exercise.* #P < *0.05 EX50 vs. EX65* (P = *0.07 for EX50 vs. CON*).

proinflammatory stress (Supplementary Figs. 1 and 2, respectively).

CONCLUSIONS—The main finding of this study was that expending only 350 kcal during a single session of exercise at a rather mild intensity (50% VO_2peak) was sufficient to significantly improve insulin sensitivity at least into the next day (~19 h after exercise) in obese adults. Importantly, the improvement in whole-body insulin sensitivity was due to enhanced peripheral glucose uptake. Although insulin sensitivity was similar the morning after exercise performed at 50% VO_2peak and 65% VO_2peak, the insulin-sensitizing effects of exercise at 65% VO_2peak did not achieve statistical significance, perhaps as a consequence of the relatively small sample size. We also found that the exercise-induced improvement in insulin sensitivity correlated with the change in fatty acid disappearance from plasma, suggesting that exercise-mediated alterations in fatty acid delivery and uptake may contribute to the improvement in insulin sensitivity during the several hours after exercise. A single session of exercise also tended to improve meal tolerance measured 1 h after exercise.

One of the overarching goals of this study was to determine whether a relatively modest exercise stimulus could have a persistent effect on insulin sensitivity into the next day in adults at risk for developing type 2 diabetes. Several previous studies (4,7), including some from our group (14,26), have reported improvement in insulin sensitivity after a single session of vigorous and/or prolonged exercise. However, the exercise protocols in all of these previous studies were very rigorous (e.g., >65% VO_2peak, >1.5 h duration) and do not reflect realistic expectations for an exercise prescription for most sedentary obese adults. Furthermore, many of these previous studies examining the insulin-sensitizing effect of a single session of exercise have been limited to indirect measures of insulin sensitivity (6,7). Using the "gold standard" for assessing insulin sensitivity in our study (i.e., the hyperinsulinemic-euglycemic clamp), our findings indicate that even fairly modest exercise can significantly enhance insulin sensitivity in obese adults. The exercise stimuli used in our study are generally within the current recommendations for physical activity provided by the American College of Sports Medicine (ACSM) (28), the American Heart Association (AHA) (29), and the Centers for Disease Control and Prevention (CDC) (30). It is important to note that the physical activity/exercise recommendations from the aforementioned societies/agencies were derived with the primary objective of enhancing cardiovascular "fitness" accrued after weeks and months of regular activity. Our findings establish that obese adults can incur metabolic benefits after each session of exercise, even when the exercise is relatively modest (like that recommended by the ACSM, AHA, and CDC). Perhaps most important, these beneficial metabolic effects can clearly be attained prior to any improvement in "fitness." Still, it remains possible that even less of an exercise stimulus than that used in our study (e.g., lower energy expenditure/duration, etc.) may be sufficient to significantly improve insulin sensitivity after only a single session of exercise in sedentary obese individuals and may thus present an even more attractive exercise prescription for the prevention and/or treatment of insulin resistance. We are currently pursuing this exciting possibility.

Moderate- to high-intensity exercise training (i.e., 65–85% VO_2peak) is classically associated with enhanced beneficial cardiovascular and metabolic adaptations compared with lower-intensity exercise (i.e., 40–50% VO_2peak) (31). Based on findings from exercise training studies, it may be logical to presume that a higher intensity of a single session of exercise may also evoke more potent and persistent metabolic effects in the hours after exercise. Our findings provide support for the notion that the insulin-sensitizing effect of a lower-intensity exercise stimulus (EX50) is at least equal to, and perhaps even greater than, an isoenergetic session of exercise performed at a higher intensity (EX65). Mechanisms underlying the possibility of a more robust beneficial metabolic response after mild compared with higher exercise intensity have not been well studied. Because our study was designed to match the energy expended during exercise, this required the participants to exercise ~15 min longer during EX50 compared with EX65. Therefore, we cannot rule out the possibility that something associated with a longer duration of exercise may have influenced the metabolic responses (even though energy expenditure was identical), but what may cause a possible beneficial effect of exercise duration is not clear.

It is likely that much, if not all, of the improvement in insulin sensitivity was driven by improved glucose metabolism within skeletal muscle (32). However, it was somewhat unexpected that the exercise-induced improvement in insulin sensitivity did not more closely parallel changes in skeletal muscle glycogen content (i.e., the lowest muscle glycogen after EX65 was not accompanied by the greatest insulin sensitivity). The reason for this is not known, but one possibility may be that a lower rate of fatty acid uptake found the day after exercise during EX50 compared with EX65 may have been an important contributor to the exercise-induced improvement in insulin sensitivity in our obese participants. We (33), and others (34,35), have previously reported systemic fatty acid mobilization and uptake to be a primary determinant of whole-body insulin sensitivity, particularly in obesity-related insulin resistance. In keeping with this hypothesis, here we found the change in insulin sensitivity after exercise compared with control to be correlated with the change in plasma fatty

acid rate of disappearance. Although causality cannot be inferred from this correlation, this finding supports the notion that an exercise-induced reduction in fatty acid uptake in the hours after exercise may be an important mediator of the insulin-sensitizing effect of exercise in obese individuals. One seemingly important beneficial effect of a lower fatty acid uptake is that less intracellular substrate is available for ectopic lipid synthesis in skeletal muscle, thereby limiting the accumulation of lipid intermediates, like diacylglycerol and ceramide, that have been linked with suppressed insulin action (36–38). However, unlike our previous work (25,26), in the current study we were unable to detect any changes in skeletal muscle lipid content after either of the exercise trials compared with control. These discrepancies between our current and previous findings may be partly explained by the difference in subject population used (i.e., obese vs. lean). For example, the high skeletal muscle lipid content commonly observed in obese individuals (39) may limit the ability to detect what might be relatively subtle (but potentially important) changes in muscle lipid content after exercise. Nevertheless, given that we did not find significant changes in muscle triacylglycerol, diacylglycerol, or ceramide concentration after exercise, we must acknowledge the possibility that changes in fatty acid partitioning among the main lipid compartments in skeletal muscle may not be critical for the insulin-sensitizing effect of exercise in obesity.

Summary and clinical relevance

In summary, although exercise is a key component in the treatment of obesity-related metabolic complications, including insulin resistance (1), it is rather surprising that the "dose" of exercise required to improve insulin sensitivity in obese individuals at risk for the development of type 2 diabetes is not more clearly defined. Due to the transient nature of the exercise-induced improvement in insulin sensitivity, we believe it is very important to develop exercise prescriptions aimed at maximizing the beneficial effects of each session of exercise. Here we have demonstrated that expending only a modest amount of energy (350 kcal) during a single session of exercise at a rather mild intensity (50% VO_2peak) was sufficient to significantly improve insulin sensitivity at least into the next day in obese adults. In addition to the effects of lowered muscle glycogen content on insulin sensitivity, evidence from this study also indicates that the insulin-sensitizing effect of exercise in obesity may be mediated in part by attenuated systemic fatty acid mobilization and uptake, although the underlying mechanism(s) for these effects is not known. Finally, the findings from this study carry encouraging clinical implications given that the exercise performed in this investigation represents a substantial reduction in both the energy expenditure and intensity of exercise previously reported to significantly enhance insulin sensitivity in obese adults.

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No potential conflicts of interest relevant to this article were reported.

S.A.N. and J.F.H. designed this study; made substantial contributions to data acquisition, analysis, and interpretation; and wrote the manuscript. A.C.E. and A.H. substantially contributed to data acquisition, analysis, and interpretation and provided critical input for the writing of the manuscript. All authors approved the final version of this manuscript. J.F.H. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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