Effects of exercise intensity on insulin sensitivity in women with non-insulin-dependent diabetes mellitus

BARRY BRAUN, MICHAEL B. ZIMMERMANN, AND NORMAN KRETCHMER
Department of Nutritional Sciences, University of California, Berkeley 94720; and Department of Pediatrics, University of California, San Francisco, California 94121

Braun, Barry, Michael B. Zimmermann, and Norman Kretchmer. Effects of exercise intensity on insulin sensitivity in women with non-insulin-dependent diabetes mellitus. J. Appl. Physiol. 78(1): 300–306, 1995.—Exercise enhances insulin sensitivity in people with non-insulin-dependent diabetes mellitus (NIDDM), but the intensity of exercise necessary to optimize the effect is unknown. Eight women with NIDDM were studied on a metabolic ward in each of three conditions: 1) low-intensity exercise (LO) that consisted of treadmill walking at 50% of maximal O2 consumption on days 1 and 2, 2) high-intensity exercise (HI) that consisted of walking at 75% of maximal O2 consumption, and 3) no exercise (NX). The duration of exercise was adjusted so that energy expenditure was equal in both exercise conditions. On day 3, glucose, [6,6-2H]glucose, and insulin were infused at fixed rates for 3 h. Insulin sensitivity was determined both by steady-state plasma glucose concentration and rate of glucose disposal per unit plasma insulin. Steady-state plasma glucose concentration and rate of glucose disposal per unit plasma insulin were almost identical after LO or HI; values were significantly greater than after NX. Plasma glucose response to a test meal was the same among the three conditions, but plasma insulin response was lower for HI and LO compared with NX. We conclude that under these conditions LO is as effective as HI in enhancing insulin sensitivity in people with NIDDM.

Exercise recommendations for adults with NIDDM are based on guidelines developed for the general population [20–60 min/day at 50–70% of maximal O2 consumption (VO2 max)] (31). These broad recommendations are designed to facilitate body weight (fat) loss and increase cardiovascular fitness and are not tailored to optimize insulin sensitivity or glucose tolerance in patients with NIDDM. Stimuli for improved insulin sensitivity include depletion of muscle glycogen and/or upregulation of glycogen synthase activity (3, 4, 18) and may explain at least part of the exercise effects. Exercise at high intensities (HI), fueled to a larger extent by muscle glycogen, could enhance insulin sensitivity to a greater extent than low-intensity exercise (LO). In nondiabetic subjects, however, insulin responses to oral glucose were reduced as much by LO as by an equal duration of HI (38). The relationship between exercise intensity and insulin sensitivity, with total energy expenditure held constant, has not been directly studied in humans.

The purpose of this study was to compare insulin sensitivity after several bouts of HI of relatively short duration with LO of longer duration in women with NIDDM. Insulin sensitivity was assessed during a glucose/insulin infusion the day after several bouts of LO or HI and was compared with a no-exercise condition (NX). To determine whether differences found during a nonphysiological test (infusion) were replicated in a more physiological setting, glucose and insulin responses to a mixed meal were compared in the same three conditions.

RESEARCH DESIGN AND METHODS

Subjects. This study was approved by the Human Research Committees at the University of California at Berkeley and at San Francisco. Eight women with NIDDM between the ages of 35 and 50 yr signed informed consent documents and were carefully screened before participation in the study. The inclusion criterion of NIDDM was based on a fasting plasma glucose concentration (FPG) of 7.8–11.1 mM (140–200 mg/dl), which was measured during the screening session. All subjects were obese, with a body fat range of 34.3–48.0%, and nontrained (VO2 max of 23.3–31.8 ml O2·kg⁻¹·min⁻¹). Subjects were excluded from the study if they smoked cigarettes or took insulin. Six subjects were managed with gliburide or glipizide. These medications were discontinued 7 days before each admission. Subjects refrained from exercise for ≥5 days before each admission. Anthropometric and metabolic characteristics of the subjects are shown in Table 1.

Protocol. On the morning of day 1, subjects were admitted to the inpatient facility of the General Clinical Research Center (GCRC) at San Francisco General Hospital. Body composition was assessed by dual energy X-ray absorptiometry (DEXA) (Lunar, Madison, WI). Subjects received a controlled diet that contained energy equal to 1.3 times their basal en-
Energy requirements (13) and was composed of 50% carbohydrate, 20% protein, and 30% fat, with ≥250 g of carbohydrate per day.

On the afternoon of day 1, subjects either rested (NX) or performed the first two bouts of exercise at LO or HI. In LO, subjects walked on a motor-driven treadmill (model Q50, Quinton Instruments, Seattle, WA) at 50% of their previously determined VO₂max. In HI, treadmill walking was performed at 75% VO₂max. During exercise, the expired breath of the subjects was diverted by a one-way valve through a calibrated pneumotach and O₂ and CO₂ analyzers (Quinton Q-Plex 1 metabolic cart). Treadmill speed and grade were manipulated so that O₂ consumption (VO₂) was steady at the desired percentage of VO₂max. Duration of each exercise bout was adjusted so that energy expenditure was 523 kJ (125 kcal). There was a 15- to 20-min rest period between the two exercise bouts. Subjects performed two more exercise bouts in the same way on the morning and afternoon of day 2. Target energy expenditure for the six exercise bouts was 3,138 kJ (750 kcal).

Test meal profile. At 1200, 90 min after the morning exercise bouts on day 2, a baseline blood sample was collected via an indwelling catheter inserted into an antecubital vein. Immediately after this procedure, subjects consumed a standard test meal that contained 30% of their calculated daily energy requirements and was composed of 50% carbohydrate, 20% protein, and 30% fat. A representative 2,500-kJ meal consisted of turkey (75 g), wheat bread (60 g), mayonnaise (10 g), lettuce (30 g), tomato (55 g), salad dressing (15 g), apple (100 g), and skim milk (120 g). Subjects were given 20 min to consume the meal. Venous blood samples were collected 30 min after the meal began and every 30 min thereafter for an additional 3 h.

Insulin-suppression test (IST). IST was modified from the procedure initially described by Shen et al. (33). Neither somatostatin nor epinephrine was used to suppress endogenous production of pancreatic hormones (15). A simultaneous infusion of glucose-stable isotope ([6,6-2H]glucose) was added to the procedure so that glucose turnover rate could be assessed. Subjects fasted after 2000 on day 2. At 0430 on day 3, a continuous infusion of [6,6-2H]glucose (70 μg·kg fat-free mass⁻¹·min⁻¹) was started. At 0930, the infusion was stopped and the subject voided. A continuous infusion of insulin and glucose (enriched with 2.5% with [6,6-2H]glucose) was started at rates of 40 mU·m⁻²·min⁻¹ and 4 mg·kg fat-free mass⁻¹·min⁻¹, respectively, and continued for 180 min. Blood samples (5 ml) were obtained every 15 min from an indwelling catheter inserted into a hand vein (the hand and wrist were kept warm with a heating pad to stimulate arteriovenous mixing). Indirect calorimetry by open-circuit spirometry was started 135 min into the infusion and continued for 30 min. A ventilated hood was placed over the subject’s head, and expired breath was directed to the O₂ and CO₂ analyzers of a Delta-Trac metabolic monitor (SensorMedics, Anaheim, CA). The insulin infusion was stopped after 180 min, and urine was collected for determination of glucose concentration. The subjects ate lunch, and intermittent blood samples were taken until blood glucose concentrations were stable. The subjects were then discharged. They reported back to GCRC 4 and 8 wk later (always in the follicular phase of the menstrual cycle) and followed the identical procedures in the other two conditions. The order of the three conditions was randomized across subjects. An overview of the protocols is described below.

NX consisted of rest on day 1 and 2. LO consisted of treadmill walking at 50% VO₂max with 523 kJ (125 kcal)/exercise bout. HI consisted of treadmill walking at 75% VO₂max with 523 kJ (125 kcal)/exercise bout. On day 1, subjects were admitted, body compositions were measured, and exercise bouts 1 and 2 were performed. On day 2, exercise bouts 3 and 4 were performed, followed by a test meal, after which exercise bouts 5 and 6 were performed. On day 3, isotope infusion was done, followed by IST, and then discharge of subjects.

Body composition. Body composition was measured three times (once at each admission) with DEXA. Scans were performed with the subject lying comfortably and wearing a hospital gown while low- and high-energy X rays were passed through all regions of the body. A moving detector measures the relative attenuation of the two energies after passing through the body (R value). Contents of bone mineral, other lean tissue, and fat are calculated from standards of known composition with software designed by the manufacturer. The accuracy and precision of DEXA compare very favorably with other methods, including hydrostatic weighing (36). Mean values for the three tests are reported in Table 1. Fat-free mass was used to determine infusion rates for glucose and [6,6-2H]glucose.

Biochemical assays. Immediately after collection, glucocorticoid concentration was measured in whole blood (25 μl) with a Yellow Springs Instruments 23A glucose analyzer (Yellow Springs, OH). Plasma glucose concentration was determined by correcting for hematocrit. After centrifugation, plasma was separated and frozen at −20°C until assays were performed. Concentration of insulin in plasma (200 μl) was measured by radioimmunoassay with Coat-A-Count kits (Diagnostic Products, Los Angeles, CA). Labeled insulin and native insulin were competitively bound to insulin-specific antibodies immobilized to the walls of a polystyrene tube. After overnight incubation, the antibody-bound fraction was isolated and the tube was counted in a gamma counter (model 5500, Beckman Instruments, Fullerton, CA). The concentration of C peptide in plasma samples was determined with the use of a double-antibody radioimmunoassay kit (Diagnostic Products). Plasma (25 μl) was incubated with 125I-labeled C peptide for 4 h, and the antibody-C peptide complex was precipitated and counted as above.

Enrichment of plasma glucose. Plasma samples taken during minutes 150–180 of IST were used for measurement of glucocorticoid enrichment. The samples (350 μl) were deproteinized with 1 N perchloric acid and centrifuged at 1,500 g for 15 min. The supernatant was neutralized by backtitration with 6 N KOH and recentrifuged. The supernatant was passed through anion (AG1-X8) and cation (SOW-X8) exchange resins suspended in Poly-prep chromatography columns (Bio-Rad Life Sciences Group, Hercules, CA). One milliliter of the eluent was lyophilized and reconstituted with acetic anhydride.

<table>
<thead>
<tr>
<th>Table 1. Anthropometric and metabolic characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
</tr>
<tr>
<td>Mean ± SD</td>
</tr>
</tbody>
</table>

BMI, body mass index; FPG, fasting plasma glucose concn; FPI, fasting plasma insulin concn; VO₂ max, maximal O₂ consumption (VO₂) scaled to body wt.
dride/pyridine (2:1) and heated at 60°C for 10 min to derivatize the sample. The sample was dried under a stream of nitrogen and was reconstituted in 100 µl of ethyl acetate. The sample (2 µl) was injected, and mass spectra were recorded on a model 5970 gas chromatography-mass spectrometer (Hewlett-Packard Analytical, Wilmington, DE). Acetate derivatives of glucose were ionized by electron impact ionization. Selected ion monitoring was used to compare the abundance of the unlabeled fragment (mass-to-charge ratio of 331) with that of the deuterated isotopomer (mass-to-charge ratio of 333). Standard curves were calculated from samples of known enrichment to correct for background enrichment (-0.06% in our samples) and interassay variability (3.5%). The abundance of [6,6-^3H]glucose was expressed as a percentage of total glucose species.

Calculations and methodological considerations. Steady-state plasma glucose (SSPG) and insulin (SSPI) concentrations were defined as the mean of the values obtained during minutes 120–180 of IST. Insulin resistance measured with IST correlates extremely well with data obtained by using the euglycemic clamp technique (12, 15). We chose to measure insulin resistance with IST instead of a euglycemic clamp because, since plasma glucose concentration is not maintained at a predetermined level, SSPG may be more indicative of insulin sensitivity at the usual elevation of plasma glucose in people with NIDDM. However, if glucose concentrations rise above ~10 mM, not all glucose filtered by the kidneys is reabsorbed and glucose is excreted in the urine. At high concentrations, glucose leaves plasma via non-insulin-dependent pathways at an increased rate due to mass action effects (1), which results in a lower SSPG than expected in extremely insulin-resistant individuals (1, 27).

The rate of appearance of unlabeled glucose into plasma (Ra) was calculated in the steady state condition (isotopic enrichment and concentration of plasma glucose not changing) by Ra = (isotope infusion rate/isotopic enrichment of plasma glucose) – isotopic infusion rate. In the steady state, Ra = Rd.

Comparisons of insulin sensitivity require equal concentrations of plasma insulin. If there are differences in SSPG, a truer comparison of insulin-mediated glucose disposal is obtained if Rd's are scaled to the ambient plasma insulin concentration (Rd/I) (19, 32). This correction is based on the assumption, which is usually true in the range used for this study, of a linear dose-response relationship between plasma insulin and Rd (1, 7, 19, 24).

To account for differences among conditions in the prevailing glucose concentration, glucose metabolic clearance rate (MCR) was calculated as the ratio of Rd to SSPG. Expression of data as MCR is expected to minimize differences attributable to insulin-independent Rd by mass action and estimate insulin-mediated Rd (1). The calculation assumes that the relationship between plasma glucose concentration and insulin-independent Rd is linear. This is clearly not true at high glucose concentrations (>9–10 mM) when the effectiveness of glucose to enhance its own clearance from plasma is diminished.

Methods of analysis. Data are presented as means ± SD except where noted. Statistical comparisons among condition means were made with repeated measures analysis of variance. Tukey's Studentized range test was used to compare individual timepoints and conditions when significant F ratios were obtained (P < 0.05). Comparisons between the two exercise protocols (Table 2) were made using a paired t-test. Correlation coefficients were calculated and tested for significance with Spearman's rho test.

RESULTS

Body weight and composition. Mean body weights in the three conditions were 84.0 ± 7.9, 83.9 ± 8.3, and 83.9 ± 8.2 kg for NX, LO, and HI, respectively. Mean percentages of body fat were 41.1 ± 4.3, 41.0 ± 4.1, and 41.5 ± 4.2% for NX, LO, and HI, respectively.

Exercise protocols. A comparison of LO and HI is shown in Table 2. Exercise heart rate, VO₂, percentage of VO₂max, and respiratory exchange ratio (RER) were all significantly higher during HI than during LO (P < 0.01). The duration of exercise was longer for LO than for HI (P < 0.01). Total energy expenditure was almost identical between LO and HI. For reference purposes, it was approximately the energy input required to walk 12 km on level ground. On the basis of VO₂ and RER data, total carbohydrate oxidation was approximately two times higher in HI than in LO (P < 0.01).

FPG and fasting plasma insulin concentrations (FPI). FPG was measured 12 h after the last meal and 16–18 h after the most recent bout of exercise. There was a trend toward lower plasma glucose concentrations the morning after HI (10.67 ± 2.63 mM) compared with after LO (11.30 ± 3.16 mM) or NX (11.60 ± 3.38 mM), but the difference between treatment means was not statistically significant (P = 0.065) (time 0; Fig. 1). FPIs were 122.1 ± 29.3, 108.1 ± 15.5, and 102.7 ± 33.9 pM for NX, LO, and HI, respectively. There were no differences among conditions (time 0; Fig. 1).

SSPG during IST. Plasma glucose concentrations rose during the first 30 min of IST and then declined, reaching a steady state after ~90 min in all three conditions (Fig. 1). SSPG was higher after NX (10.64 ± 2.96 mM) than after LO (8.76 ± 3.11 mM) or HI (8.92 ± 3.21 mM) (P < 0.01). There were no differences between LO and HI. Plasma insulin and C peptide concentrations during IST. Plasma insulin concentrations increased rapidly in the first 60 min of IST and then remained relatively constant between minutes 120 and 180 (Fig. 2). SSPI tended to be higher after NX (379 ± 72 pM) than after LO (351 ± 56 pM) or HI (337 ± 59 pM) (P = 0.052). Plasma concentrations of C peptide declined continuously throughout the first 150 min of IST, attaining mean values that were lower by 54 ± 17, 58 ± 18, and 66 ± 21% for NX, LO, and HI, respectively, compared with pre-IST values. The slight rebound from minute 150 to minute 180 in NX was within the variability of the measurement.

Rd during IST. Total Rd during minutes 150–180 of

<table>
<thead>
<tr>
<th>Measurements</th>
<th>LO</th>
<th>HI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Speed, km/h</td>
<td>3.7 ± 0.1</td>
<td>4.1 ± 0.2*</td>
</tr>
<tr>
<td>Grade, %</td>
<td>6.7 ± 1.4</td>
<td>14.5 ± 1.9*</td>
</tr>
<tr>
<td>Heart rate, beats/min</td>
<td>123 ± 7</td>
<td>147 ± 11*</td>
</tr>
<tr>
<td>VO₂, l/min</td>
<td>1.17 ± 0.15</td>
<td>1.74 ± 0.20*</td>
</tr>
<tr>
<td>VO₂max, %</td>
<td>50.4 ± 1.7</td>
<td>74.4 ± 3.0*</td>
</tr>
<tr>
<td>Duration, min</td>
<td>142.5 ± 23.1</td>
<td>89.6 ± 7.9*</td>
</tr>
<tr>
<td>Total energy expenditure, kJ</td>
<td>3.11 ± 63</td>
<td>3.11 ± 90</td>
</tr>
<tr>
<td>RER</td>
<td>0.79 ± 0.04</td>
<td>0.87 ± 0.02*</td>
</tr>
<tr>
<td>Total CHO oxidation, g</td>
<td>50.8 ± 22.2</td>
<td>100.6 ± 15.8*</td>
</tr>
</tbody>
</table>

Values are means ± SD. Speed and grade refer to treadmill settings. LO and HI, low- and high-intensity exercise protocols, respectively; RER, respiratory exchange ratio; CHO, carbohydrate. * Significantly different from LO according to paired t-tests, P < 0.01.
EXERCISE AND INSULIN SENSITIVITY IN NIDDM

profiles were not different among the three conditions. Postmeal insulin profiles were significantly lower after LO and after HI compared with after NX ($P < 0.05$). Plasma C peptide concentrations were not significantly different among the three conditions despite mean values for NX that appear higher than for LO or HI at 120 and 180 min after the meal.

**Influence of FPG on change in SSPG.** To examine whether degree of fasting hyperglycemia affected the magnitude of the insulin sensitivity change induced by exercise, results for LO and HI were combined. The exercise-induced decrease in SSPG, calculated as $\text{SSPG}_{\text{NX}} - (\text{SSPG}_{\text{LO}} + \text{SSPG}_{\text{HI}})/2$, where SSPG$_{\text{NX}}$, SSPG$_{\text{LO}}$, and SSPG$_{\text{HI}}$ are SSPG for NX, LO, and HI, respectively, was plotted against FPG concentration (measured at the prestudy screening session). There was a significant negative correlation between the percent change in SSPG and fasting glucose concentration ($r = -0.74; P < 0.05$; Fig. 4).

**DISCUSSION**

Several exercise bouts were performed over 2 days to minimize potential effects of chronic exercise training. Body weight and composition, which are known to affect insulin sensitivity (10, 11), were nearly identical among conditions. It is unlikely that six bouts of endurance-type exercise (total of 750 kcal) would induce adaptations associated with chronic training (i.e., greater muscle capillary density and increased capacity to store glycogen in muscle) that could affect uptake and/or utilization of blood glucose. Therefore, changes observed in this study are attributable to recent exercise.

**Insulin sensitivity.** Whether expressed as SSPG, MCR, or Rd/SSPI, the overall pattern is essentially the same. Insulin sensitivity after LO or HI is nearly identical and significantly higher (20, 15, and 30-35% by SSPG, Rd/SSPI, and MCR, respectively) than after NX. With IST,

![Graph](image-url)

**FIG. 1.** Plasma glucose concentration during insulin-suppression test (IST). Glucose and insulin infusions were started immediately after fasting blood sample was drawn (minute 0). Data are means ± SE where indicated (SE omitted from HI for clarity). •, No exercise (NX); ●, low-intensity exercise (LO); ■, high-intensity exercise (HI).

IST was corrected for glucose loss into urine (18 ± 9, 9 ± 4, and 9 ± 5 mg/min for NX, LO, and HI, respectively) to derive tissue Rd. Without accounting for differences in SSPI and SSPG, Rd was similar among the three conditions (266 ± 47, 283 ± 51, and 278 ± 63 mg/min for NX, LO, and HI, respectively). If the differences in plasma insulin concentration are accounted for by scaling Rd to SSPI, glucose disposal rate was 15% lower after NX (0.72 ± 0.18 mg·min$^{-1}$·pM$^{-1}$) than after LO or HI (0.84 ± 0.19 mg·min$^{-1}$·pM$^{-1}$) ($P < 0.05$). If Rd is scaled to the ambient plasma glucose concentration and presented as MCR, the mean value after NX (35.8 ± 13.8 mg·min$^{-1}$·mM$^{-1}$) was 30% lower than after LO (34.8 ± 19.4 mg·min$^{-1}$·mM$^{-1}$) and 50% lower than after HI (34.8 ± 19.4 mg·min$^{-1}$·mM$^{-1}$) ($P < 0.05$). For all measurements, there were no significant differences between HI and LO.

**Oxidative glucose disposal (OGD) and non-OGD.** Rates of OGD were estimated from RERs obtained by indirect calorimetry during IST. Mean RER values were 0.84 ± 0.05, 0.84 ± 0.06, and 0.83 ± 0.05 for NX, LO, and HI, respectively. Estimated rates of OGD were 132 ± 49, 123 ± 58, and 119 ± 46 mg/min for NX, LO, and HI, respectively. Rates of non-OGD, estimated as the difference between total Rd and OGD, were 134 ± 27, 160 ± 99, and 165 ± 109 mg/min for NX, LO, and HI, respectively. There were no significant differences among conditions for any of these measurements.

**Test meal profile.** Plasma glucose, insulin, and C peptide concentrations in response to the test meal are shown in Fig. 3. Plasma glucose concentration before the meal tended to be lower after HI compared with after NX ($P = 0.091$). After the meal, plasma glucose
exercise at either intensity enhances insulin sensitivity to an equal extent. The magnitude of the change after exercise is comparable to reports in which euglycemic clamps were used instead of IST. Devlin et al. (8) and Kjaer et al. (20) reported increases in glucose MCR on the order of 20–30% after a single bout of strenuous exercise.

**Test meal.** An aim of this study was to compare postprandial glucose and insulin responses during a physiological test, i.e., a mixed meal, with data derived from an essentially nonphysiological situation (IST). Plasma glucose response to the test meal was not different, but the plasma insulin response was markedly lower after either exercise condition compared with NX. Reinforcing the insulin data, C peptide values in the exercise conditions were lower for every subject at 120–180 min postmeal.

The mixed meal used in this study contained a mean carbohydrate content of 74.1 g, which makes it somewhat comparable to an oral glucose tolerance test (OGTT). Lower glucose and insulin responses were reported in people with NIDDM or impaired glucose tolerance after chronic exercise training (17, 21, 29) or 7 days of exercise (29). After a single exercise bout, Rogers (29) found no change in glucose tolerance and a trend toward lower plasma insulin response to OGTT. Young et al. (38) reported a 40% decrease in plasma insulin response to OGTT in nondiabetic sedentary subjects 40 h after exercise at 40 or 80% VO$_{2\text{max}}$. Shriver et al. (34) compared OGTTs in nondiabetic men and women after two exercise protocols very similar to those used in the present study (equal energy expenditures at 50 and 75% VO$_{2\text{max}}$). They observed no change in glucose response but a significant decrease in insulin response after LO or HI compared with NX. Our results are consistent with those findings and extend them to people with NIDDM.

**FPG and FPI.** FPG tended to be ~10% lower after HI compared with after NX. Given this effect size and eight subjects, we may not have enough statistical power to detect a significant difference. Devlin et al. (8) reported a 17% lower FPG the morning after exercise compared with NX. Reports by Kjaer et al. (20) and Rogers (29), however, showed no differences in FPG 1 day postexercise. The very strenuous protocol used by Devlin et al. (cycle ergometry to exhaustion at 85% VO$_{2\text{max}}$) may have elicited the large change in FPG. Data from the present study lend credence to this explanation as the mean FPG was only 3% lower after LO compared with after NX.

FPI tended to be lower (~15%) after either exercise protocol but was not significantly different from NX. In
Results from the present study have potential clinical relevance. It would be extremely advantageous to patients with NIDDM if they were able to achieve significant metabolic benefits from LO programs. The obesity, diabetic complications, and general lack of fitness that are often attendant in people with NIDDM make prescription of LO safer and more practicable. Data from this study also suggest that exercise enhances insulin sensitivity to a greater extent in people with milder fasting hyperglycemia. This finding supports prior indications that exercise has the strongest influence in people with mild insulin resistance (30). An exercise program may therefore be of greatest utility to obese individuals who have peripheral insulin resistance without severe hyperglycemia.

The authors thank Drs. Claire Hollenbeck, George Brooks, and Laurie Schumacher for helpful advice; Angela DeCarlo and Judy Randolph for technical assistance; Drs. Rich Neece and Marc Hell-ersten for use of gas chromatography-mass spectrometry; the nursing staff at GCRC for excellent clinical support; and the subjects for their time and effort.

This study was supported by National Institutes of Health Training Grant in Human Nutrition 5-T32-HD-07255-06 at Univ. of California at Berkeley and Research Evaluation and Allocation Committee Cough Fund at Univ. of California at San Francisco.

Address for reprint requests: B. Braun, Dept. of Nutritional Sciences, Morgan Hall, Univ. of California, Berkeley, CA 94720.

Received 23 June 1994; accepted in final form 19 September 1994.

REFERENCES

12. Greenfield, M. S., L. Doberne, L. Kraemer, T. Tobey, and G. Reaven. Assessment of insulin resistance with the insulin...

Two studies, Devlin et al. (8, 9) also saw no significant differences in FPI after a single exercise bout, although in one study the mean was 29% lower than that without exercise (8). Kjaer et al. (20) observed FPIs that were exactly the same before and 24 h after a single exercise bout in men with NIDDM, as did Rogers (29).

FPG and FPI may be lower the day after exercise in people with NIDDM, but the evidence is still weak. Nonsignificant differences among means noted in this study and a study by Devlin et al. (8) suggest that FPGs are lower after HI, but there are also data that are not supportive.

Conclusions. In this study, insulin sensitivity during a glucose/insulin infusion was clearly enhanced after exercise. Results from the test meal are consistent with data from IST, which implies that effects observed during a nonphysiological test also have physiological relevance. For all measurements, LO and HI induced identical changes in postexercise insulin sensitivity.

These data imply that there is no dose-response relationship between the degree of muscle glycogen depletion and the magnitude of the change in sensitivity to insulin. The rate of carbohydrate oxidation during exercise was more than threefold higher and total carbohydrate oxidation was twofold greater for HI compared with LO. Muscle glycogen was not directly measured; thus the actual quantity of oxidized carbohydrate originating as muscle glycogen is unknown. Glucose turnover data obtained with tracer methods suggest that 70–80% of carbohydrate oxidized during exercise is derived from muscle glycogen (5, 38). However, Wahren et al. (57) measured arteriovenous differences across the leg and observed a much greater contribution from blood glucose. Without direct measurement of muscle glycogen concentrations before each IST, we cannot be certain that glycogen in muscle was depleted to a greater extent after HI compared with after LO.

This study was designed to mimic physiological situations as closely as possible; therefore subjects were given an evening meal between the last exercise bout and IST. In other investigations, glycogen depleted during exercise was not replaced by dietary carbohydrate and glycogenesis was minimal before assessment of insulin sensitivity (4, 18). Bogardus et al. (4) included a condition in which subjects were fed 100 g of carbohydrate between a single exercise bout and an euglycemic clamp. Feeding increased muscle glycogen content (although it remained lower than without exercise) and insulin sensitivity was increased to a lesser extent than without refeeding.

There may be stimuli associated with exercise unrelated to glycogen utilization that serve to enhance post-exercise insulin sensitivity. A likely candidate is induction of a negative energy balance. The improvement in sensitivity to insulin after weight loss in obese, insulin-resistant, and NIDDM subjects is well documented (10, 11, 26). Dolkas et al. (10) found that enhanced insulin sensitivity after exercise was diminished after 72 h when rats were in positive energy balance but was retained for 7 days when negative energy balance was maintained. A mechanism by which energy balance influences insulin sensitivity remains to be determined.

The authors thank Drs. Claire Hollenbeck, George Brooks, and Laurie Schumacher for helpful advice; Angela DeCarlo and Judy Randolph for technical assistance; Drs. Rich Neece and Marc Hell-ersten for use of gas chromatography-mass spectrometry; the nursing staff at GCRC for excellent clinical support; and the subjects for their time and effort.

This study was supported by National Institutes of Health Training Grant in Human Nutrition 5-T32-HD-07255-06 at Univ. of California at Berkeley and Research Evaluation and Allocation Committee Cough Fund at Univ. of California at San Francisco.


