Resistance Training Improves Insulin Sensitivity in NIDDM Subjects Without Altering Maximal Oxygen Uptake

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OBJECTIVE — To examine the effect of resistance training on insulin sensitivity in nonobese NIDDM patients.

RESEARCH DESIGN AND METHODS — Previously sedentary nonobese NIDDM patients were enrolled in a resistance training group (RT; n = 9) or used as sedentary control subjects (SED; n = 8). SED subjects did not perform exercise training because of orthopedic disorders. The training program consisted of two sets of nine exercises with 10–20 repetitions. Subjects trained five times a week for 4–6 weeks. Insulin sensitivity, as assessed by the hyperinsulinemic-euglycemic clamp technique, HbA_{1c}, and body composition, was measured before and after the training period. Maximal oxygen uptake (Vo_{2max}) and quadriceps strength were measured in the RT group.

RESULTS — The two groups did not differ significantly on any variables before participation in the program. The glucose disposal rate during the hyperinsulinemic-euglycemic clamp increased 48% in the RT group (6.85 ± 1.86 to 10.12 ± 3.15 mg · kg^{-1} lean body mass · min^{-1}; $P < 0.05$), but remained unchanged in the SED group (5.95 ± 1.63 to 6.36 ± 1.61 mg · kg^{-1} lean body mass · min^{-1}). There was no significant change in body composition in either group. In the RT group, a 16% increase in quadriceps strength (191.1 ± 45.8 to 216.9 ± 42.8 Nm; $P < 0.05$) but no significant change (27.6 ± 5.0 to 28.6 ± 6.5 ml · kg^{-1} · min^{-1}) in Vo_{2max} was observed.

CONCLUSIONS — Moderate-intensity, high-volume resistance training improves insulin sensitivity in nonobese NIDDM without altering Vo_{2max}.

The effectiveness of exercise as a treatment for NIDDM has been previously recognized. Improvement of insulin sensitivity and maximal oxygen uptake (Vo_{2max}) by an endurance exercise, such as jogging or swimming, has been previously reported (1,2). Recent studies have also indicated that resistance training improves glucose tolerance and/or insulin sensitivity in both diabetic (3) and nondiabetic (3–6) subjects. However, improvement in HbA_{1c}, self-monitored blood glucose in IDDM subjects, and the relationship between plasma glucose and insulin level during a glucose tolerance test provide only indirect assessments of insulin sensitivity. The effect of resistance training on in vivo insulin sensitivity has not yet been examined through direct measurements of insulin sensitivity via the hyperinsulinemic-euglycemic clamp technique. Furthermore, effects of resistance training have not been examined in NIDDM subjects. Our experiment, therefore, examined the effect of resistance training on insulin sensitivity using the hyperinsulinemic-euglycemic clamp technique in 17 previously sedentary nonobese NIDDM subjects.

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Abbreviations: GDR, glucose disposal rate; RT, resistance training group; SED, sedentary control group; Vo_{2max}, maximal oxygen uptake.

RESEARCH DESIGN AND METHODS

— Previously sedentary nonobese NIDDM patients were enrolled in a resistance training group (RT; n = 9) or used as sedentary controls (SED; n = 8). The SED subjects did not perform exercise training because of orthopedic disorders, but had no disability for daily activity. Each subject's age, anthropometric data, HbA_{1c}, fasting plasma insulin, and therapy are shown in Table 1. The two groups did not differ significantly on any variable before the programs. None of the RT subjects had hypertension, cardiovascular disease, or diabetic complications, but two had slight peripheral neuropathy.

All of the subjects were hospitalized and placed on a 30 kcal/kg diet control. The RT subjects trained five times per week for 4–6 weeks. The training program consisted of two sets of the following nine exercises: arm curls, military press, push-ups, squats, knee extensions, heel raises, back extensions, bent knee sit-ups, and upright rowing. Back extensions, push-ups, and bent knee sit-ups were performed with free weights. Resistance loads were 40–50% of one repetition maximum for the other exercises. The subjects performed 10 repetitions per set for all upper-body exercises and 20 repetitions per set for all lower-body exercises. The resting interval between sets was <1 min. Weights were adjusted throughout the training program as strength level increased.

Sensitivity to insulin, HbA_{1c}, and body composition were measured before and after the training period in both groups. The sensitivity to insulin was determined using the hyperinsulinemic-euglycemic clamp technique, as previously described (8).

The hyperinsulinemic-euglycemic clamp was performed in the RT group 2 days after the last resistance exercise was done to exclude any acute effect of the exercise on glucose disposal. After a 30-min control period, a priming and continuous infusion of short-acting human insulin (Humulin R; Eli Lilly, Indianapolis, IN) was administered for ~120 min. Plasma glucose concentrations were continuously determined using the glucose oxidase method with an STG-22 instrument (Nikiso, Tokyo). After the

Table 1—*Characteristics of male NIDDM subjects*

	Resistance training	Sedentary
n	9	8
Age (years)	46.8 ± 8.9	51.9 ± 8.2
Body weight (kg)	63.3 ± 8.3	60.3 ± 11.6
BMI (kg/m²)	22.3 ± 2.1	22.2 ± 3.0
HbA_{1c} (%)	9.6 ± 2.8	8.8 ± 2.1
Fasting plasma insulin (μU/ml)	4.6 ± 1.7	5.0 ± 3.2
Treatment		
Diet alone	2	2
Oral hypoglycemic agent	7	6

Data are *n* or means ± SD.

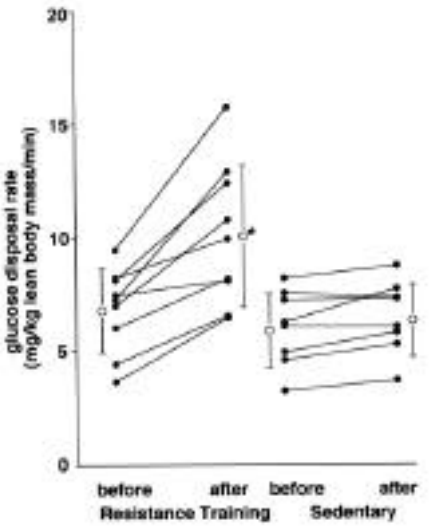

Figure 1—*Changes in GDR before and after the treatment period in RT and SED subjects. P* < *0.05 vs. baseline. Data are means ± SD.*

plasma glucose concentration had declined to 100 mg/dl, an infusion of 10% glucose was adjusted to maintain a constant plasma glucose concentration. The steady-state serum insulin concentration was 80.8 ± 10.7 μU/ml. The glucose disposal rate (GDR) was determined by calculation of the mean glucose infusion rate during the last 15 min and was calculated per kilogram of lean body mass. The body composition was measured by dual-energy X-ray absorptiometry, using the Hologic QDR-2000 (Hologic, Waltham, MA).

In the RT group, $V_{O_{2max}}$ and quadriceps strength were measured before and after the training period; $V_{O_{2max}}$ was measured during a standard incremental exercise test on a cycle ergometer (9). The O_2 and CO_2 fractions were analyzed with the MMC metabolic system (Sensormedics, Anaheim, CA). Quadriceps strength was measured using a KIN-COM 500H (Chattecx, Chattanooga, TN). HbA_{1c} (reference range, 4.3–5.8%) was measured by high-pressure liquid chromatography (Kyoto Daiichi Kagaku, Kyoto, Japan). Plasma insulin concentration was measured by microparticle enzyme immunoassay (Dinabot, Abbotpark, IL).

All data are presented as means ± SD. The effects of resistance training on GDR, HbA_{1c}, and body composition were assessed using a repeated-measures analysis of variance. Where applicable, post hoc analyses were conducted using Scheffé's procedure. Changes in quadriceps strength and $V_{O_{2max}}$ were assessed using paired *t* tests. Statistical calculations were performed using StatView software (Abacus Concepts/Brainpower, Berkeley, CA). $P < 0.05$ was considered statistically significant.

RESULTS — As shown in Fig. 1, the GDR during the hyperinsulinemic-euglycemic clamp increased in the RT group to 10.12 ± 3.15 mg · kg^{-1} lean body mass · min^{-1}, 48% higher than the pretraining level (6.85 ± 1.86 mg · kg^{-1} lean body mass · min^{-1}; $P < 0.05$). However, the GDR did not change significantly in the SED group (5.95 ± 1.63 to 6.36 ± 1.61 mg · kg^{-1} lean body mass · min^{-1}).

There was no significant change in HbA_{1c} in either group (RT, 9.6 ± 2.8 to 7.6 ± 1.3%; SED, 8.8 ± 2.1 to 7.6 ± 1.9%). Body composition measured by dual-energy X-ray absorptiometry before and after the treatment period in both groups is shown in Table 2. There was no significant change in body composition in either group.

In the RT group, a 16% increase in quadriceps strength (191.1 ± 45.8 to 216.9 ± 42.8 Nm; $P < 0.05$) was observed. $V_{O_{2max}}$ did not change significantly (27.6 ± 5.0 to 28.6 ± 6.5 ml · kg^{-1} · min^{-1}).

CONCLUSIONS — Recent studies have indicated that resistance training improves glucose tolerance and/or insulin sensitivity in diabetic and nondiabetic subjects. Only one study has reported that resistance training improved glucose tolerance in diabetic patients. Durak et al. (3) reported that heavy resistance training three times per week for 10 weeks improved HbA_{1c} and self-monitored blood glucose in IDDM subjects. In nondiabetic subjects, resistance training has been reported to diminish the plasma insulin response to a glucose load without deterioration in glucose tolerance, suggesting a state of increasing insulin sensitivity (4–7). However, in these studies, the effects of resistance training on insulin sensitivity have been assessed only by indirect methods without the use of the hyperinsulinemic-euglycemic clamp technique. The results of the present study provide direct evidence that the moderate-intensity, high-volume resistance training for 4–6 weeks improved insulin sensitivity by 48% in previously untrained nonobese NIDDM subjects.

Yki-Järvinen and Koivisto (10) reported that glucose metabolism during the euglycemic clamp technique correlated positively with percentage of muscle mass in total body weight, and that the rate of glucose metabolism calculated per kilogram of muscle mass in weight lifters was similar to that in untrained subjects. The results of their study conflict with those of the present study, which demonstrated that resistance training improves glucose metabolism calculated per kilogram of lean body mass. The discrepancy is most likely due to differences in the intensity, volume, and duration of exercise performed. Weight lifters perform high-intensity, low-volume training that requires lifting near the maximal weight for fewer repetitions, with long rest periods between sets. The resulting physiological adaptations are limited to skeletal muscle increase and high-energy phosphate systems and do not influence the growth of muscle capillaries or the improvement of the cardiovascular system (11). The moderate-intensity, high-volume resistance training that RT subjects performed in the present study involved the use of lighter loads, higher repetitions, and shorter resting intervals between sets. With this resistance training, slight increases in capillary-to-muscle fiber ratio were observed (11), as were improvements in the delivery and utilization of insulin and glucose in blood, with the resulting adaptations promoting the

Table 2—*Body composition before and after treatment period in NIDDM subjects*

	Resistance training		Sedentary	
	Before	After	Before	After
BMI (kg/m²)	22.3 ± 2.1	21.7 ± 2.2	22.3 ± 3.0	21.7 ± 3.1
Lean body mass (kg)	47.8 ± 5.8	47.7 ± 5.6	43.7 ± 7.0	43.0 ± 7.3
% fat mass	20.5 ± 2.5	18.3 ± 2.9	23.5 ± 3.4	22.6 ± 3.5

Data are means ± SD.

enhancement of metabolic efficiency in the skeletal muscle system.

The mechanisms for the improvement of insulin sensitivity observed in the present study are unclear. Soman et al. (2) observed that 6 weeks of endurance training (cycle-ergometer exercise) increased insulin sensitivity (as determined by the insulin clamp technique) by 30%, with a 20% increase in $V_{O_{2max}}$ in healthy subjects. Furthermore, the increase in insulin sensitivity correlated directly with the rise in $V_{O_{2max}}$. This mechanism is unlikely to have accounted for the increase in insulin sensitivity in the present study, since $V_{O_{2max}}$ did not change significantly with resistance training.

Although body fat decreased from 20.5 to 18.3% in RT subjects, this decrease also is an unlikely explanation for the improvement in insulin sensitivity. In the SED subjects showing no increase in GDR during the observation period, body fat decreased comparably with that of RT subjects. Furthermore, in the present study, GDR was calculated per kilogram of lean body mass and not per kilogram of total body mass.

In the present study the subjects were lean NIDDM patients without fasting hyperinsulinemia. However, the GDR calculated per kilogram of lean body mass before the observation period was sufficiently low and was comparable with that in obese NIDDM patients. With regard to decreased insulin sensitivity, the present subjects were similar to obese NIDDM patients. Therefore improvement in insulin sensitivity by resistance exercise would be observed in obese NIDDM patients.

Although HbA_{1c} tended to decrease in RT subjects, no significant change was observed in either the RT or SED group. The observation period in this study may not have been long enough to assess the full impact on HbA_{1c}.

Recent studies have indicated that, in NIDDM patients, the major causes of cellular insulin resistance are impaired translocation of GLUT4 and a decrease in the enzyme activity that regulates the storage and oxidation of glucose in skeletal muscle. With aerobic exercise training, an increase in the conversion of low-oxidative type 2b fibers to moderate-oxidative type 2a fibers was observed (12). Because type 2a fibers have a greater capillary density and a higher concentration of GLUT4, they exhibit a greater response to insulin than do type 2b fibers. Furthermore, a significant correlation between glucose clearance during euglycemic clamp and fiber type has been reported (13). There may also have been a change in muscle fiber type with the moderate-intensity, high-volume resistance training performed in the present study. Further examination of the relationship between the improvement of insulin sensitivity observed in resistance training and GLUT4 protein or enzyme activity that regulates the storage and oxidation of glucose in skeletal muscle is required.

In summary, these findings demonstrate that moderate-intensity, high-volume resistance training improves insulin sensitivity in nonobese NIDDM patients without altering $V_{O_{2max}}$.

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