Effect of Mild Exercise Training on Glucose Effectiveness in Healthy Men

YUICHIRO NISHIDA, MS[1]
YASUKI HIGAKI, PHD[2]
KUMPEI TOKUYAMA, PHD[4]
KANTA FUJIMI, MD[3]
AKIRA KIYONAGA, MD, PHD[5]
MUNEHIRO SHINDO, MS[5]
YUZO SATO, MD, PHD[1]
HIROAKI TANAKA, PHD[5]

OBJECTIVE — To detect whether mild exercise training improves glucose effectiveness (S_G), which is the ability of hyperglycemia to promote glucose disposal at basal insulin, in healthy men.

RESEARCH DESIGN AND METHODS — Eight healthy men (18–25 years of age) underwent ergometer training at lactate threshold (LT) intensity for 60 min/day for 5 days/week for 6 weeks. An insulin-modified intravenous glucose tolerance test was performed before as well as at 16 h and 1 week after the last training session. S_G and insulin sensitivity (S_I) were estimated using a minimal-model approach.

RESULTS — After the exercise training, $V\dot{O}_{2max}$ and $V\dot{O}_2$ at LT increased by 5 and 34%, respectively ($P < 0.05$). The mild exercise training improves S_G measured 16 h after the last training session, from 0.018 ± 0.002 to 0.024 ± 0.001 min^{-1} ($P < 0.05$). The elevated S_G after exercise training tends to be maintained regardless of detraining for 1 week (0.023 ± 0.002 min^{-1}, $P = 0.09$). S_I measured at 16 h after the last training session significantly increased (pre-exercise training, 13.9 ± 2.2; 16 h, 18.3 ± 2.4, $\times 10^{-5} \cdot min^{-1} \cdot pmol/l^{-1}$, $P < 0.05$) and still remained elevated 1 week after stopping the training regimen (18.6 ± 2.2, $\times 10^{-5} \cdot min^{-1} \cdot pmol/l^{-1}$, $P < 0.05$).

CONCLUSIONS — Mild exercise training at LT improves S_G in healthy men with no change in the body composition. Improving not only S_I but also S_G through mild exercise training is thus considered to be an effective method for preventing glucose intolerance.

Diabetes Care 24:1008–1013, 2001

Glucose effectiveness (S_G), which is the ability of hyperglycemia to promote glucose disposal at basal insulin, is a component of importance equal to or greater than insulin itself when determining glucose tolerance (1,2). In normal individuals and in insulin-resistant obese individuals, ~50 and ~80%, respectively, of the glucose disposal during an oral glucose tolerance test is attributable to S_G and not to the secreted insulin (2). Welch et al. (3) demonstrated that patients with type 2 diabetes have low S_G as well as low insulin sensitivity (S_I). Moreover, recent reports have shown that Japanese type 2 diabetic patients, offspring with impaired glucose tolerance, and the type 2 diabetic offspring all have a decreased S_G (4–6). These studies suggest that a reduction in S_G is closely associated with an onset of type 2 diabetes. In addition, Martin et al. (7) demonstrated that a reduced S_I and a reduced S_G are both strong predictors of future type 2 diabetes. Improving S_G could, therefore, be important for preventing type 2 diabetes.

Although the effect of exercise training on insulin action has been well documented (8,9), little is known about the effect of exercise training on S_G. Kahn et al. (8) did the first longitudinal study that assessed the effect of physical training on S_G. They studied healthy men (60–82 years of age) before and 6 months after intensive exercise training and found no effects of exercise training on S_G (0.014 ± 0.001 vs. 0.015 ± 0.002 min^{-1}). No change in the S_G of middle-aged men after 14 weeks of moderate to intensive exercise training (0.020 ± 0.002 vs. 0.023 ± 0.002 min^{-1}) was also observed by Houmard et al. (9). On the other hand, we previously reported that young distance runners have a 76% higher S_G than that of the control subjects (10). Based on the findings of these studies, a beneficial effect of exercise on S_G would be expected only in young subjects or in those who are in a very high physically trained state, such as distance runners. We recently demonstrated that mild exercise at the lactate threshold (LT) for 60 min is sufficient to increase S_G in men immediately after the exercise (11). Of note, the increase in S_G immediately after mild exercise is similar to the level in trained subjects. It is therefore of great interest to see whether the repetition of the exercise corresponding to the LT, which can be easily and safely performed, could therefore possibly lead to a long-term improvement in S_G. We therefore investigated whether mild exercise training increases S_G in healthy men. The present results suggest that mild exercise training improves not only S_I but also S_G in healthy men.

RESEARCH DESIGN AND METHODS

Subjects.

Eight healthy men (18–25 years of age) who had not performed any regular exercise for at least 2 years were examined. All

From the [1]Research Center of Health, Physical Fitness, and Sports, Nagoya University, Nagoya; the [2]Department of Community Health Science, Saga Medical School, Saga; the [3]Department of Internal Medicine, School of Medicine, Fukuoka University, Fukuoka; the [4]Laboratory of Biochemistry of Exercise and Nutrition, Institute of Health and Sports Science, University of Tsukuba, Ibaraki; and the [5]Faculty of Health and Sports Science Laboratory of Exercise Physiology, Fukuoka University, Fukuoka, Japan.

Address correspondence and reprint requests to Hiroaki Tanaka, PhD, Laboratory of Exercise Physiology, Faculty of Health and Sports Science, Fukuoka University, 8-19-1 Nanakuma Jonan-ku, Fukuoka 814-0133, Japan. E-mail: htanaka@fukuoka-u.ac.jp.

Received for publication 17 October 2000 and accepted in revised form 27 February 2001.

Abbreviations: BIE, basal insulin component of glucose effectiveness; GEZI, glucose effectiveness at zero insulin; HGP, hepatic glucose production; Ib, basal insulin; IVGTT, intravenous glucose tolerance test; K_G, glucose disappearance constant; LT, lactate threshold; S_G, glucose effectiveness; S_I, insulin sensitivity.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

individuals were free of diabetes and none was taking any medications. None of the subjects were smokers. All subjects were asked not to change their normal dietary habits and not to engage in any strenuous physical activity. The study protocol was conducted in accordance with the Helsinki Declaration. Before beginning the study, the nature, purpose, and risks of the study were explained to all subjects, and informed written consent was obtained.

Body composition and physical fitness.
Each subject's percent fat was measured by hydrostatic weighing before training and 2 days after the last training session and was estimated based on the hydrostatic density with a correction for the residual lung volume (12). To measure physical fitness, the graded exercise test on a mechanically braked ergometer (Electric Bicycle Ergometer; Lode's Instrumenten B.V., Groningen, the Netherlands) was performed before training and 2 days after the last training session. The work rate was initially set at 10 W and thereafter was increased every 1 min by 15 W. The test was continued until subjective exhaustion was achieved. V_{O_2} was measured from the mixed expired gas collected in neoprene bags. The volume of the expired gas was quantified with a twin-drum–type respirometer (Fukuda Irika CR-20, Tokyo, Japan), and both the O_2 and CO_2 fractions were analyzed by a mass spectrometer (Perkin-Elmer 1,100, Norwalk, CT). Blood samples from an earlobe were obtained every 30 s to measure the blood lactate levels. The blood lactate concentration was plotted against the exercise workload for each subject; the workload at the first breaking of lactate was used to calculate the exercise training intensity of each subject. The LT was determined for each subject based on a visual inspection, and the average was determined according to the estimations of three experts, who were blinded to the purpose of our study, and was used to establish the exercise intensity for training.

Exercise training program.
Bicycle ergometer training at the LT level (the first 3 weeks, 42.3 ± 2.1% $V_{O_{2max}}$; the latter 3 weeks, 54.2 ± 2.9% $V_{O_{2max}}$) was carried out for 60 min/day, 5 times/week for 6 weeks at our laboratory. Three weeks after the training program started, each subject underwent a submaximal graded exercise test to readjust the training workload. The revised workloads were then used for the next 3 weeks. All participants completed the entire training protocol.

Intravenous glucose tolerance test.
Intravenous glucose tolerance tests (IVGTTs) were performed before (i.e., pre) and both 16 h and 1 week after the last training session. Because one subject caught a cold, an IVGTT after 1 week of detraining could not be performed on that subject. In the morning (between 0700 and 0900 h) after overnight fasting, the subjects were allowed to rest lying down for at least 30 min before blood sampling commenced. Blood samples were obtained from an antecubital vein in one arm that was kept in a radiant warmer at 70°C to provide an arterialized blood source. Baseline samples for glucose and insulin were obtained, and then glucose was administered in the contralateral antecubital vein (300 mg/kg body wt) within 2 min. Subsequent samples were obtained at frequent intervals until 180 min as previously described (10). Insulin (Humalin; Shionogi, Osaka, Japan) was infused (20 mU/kg) into an antecubital vein from 20 to 25 min after the administration of glucose. On the day before they underwent the IVGTT, all subjects were provided with an evening meal consisting of ≥140 g carbohydrate, ≥30 g fat, and ≥33 g protein.

Data analysis.
The incremental insulin between 0 and 20 min after the administration of glucose was calculated as the area under the curve using the trapezoidal rule. The glucose disappearance constant (K_G) was calculated as the slope of the least-squares regression line related to the natural logarithm of the glucose concentration to the time from samples drawn between 10 and 19 min. The S_I and S_G were estimated using a minimal-model approach (1–11). The S_I index represents the increase in the net glucose disappearance rate, which, in turn, depends on the rise in insulin above the basal level. S_G represents the effect of glucose per se, at basal insulin, to normalize its own concentration independent of the secreted insulin. The basal insulin component of S_G (BIE) can be calculated as the product of basal insulin (Ib) and S_I as follows: BIE = Ib · S_I. The contribution of the noninsulin-dependent component (S_G at zero insulin [GEZI]) is the difference between the total S_G and the BIE: GEZI = S_G – (Ib · S_I). The minimal-model program was written in Pascal (Borland International, Scotts Valley, CA) on a Macintosh IIcx (Apple Computer, Cupertino, CA).

Analytical methods.
The plasma glucose levels were measured in triplicate spectrophotometrically using glucose oxidase (Glucose B-test; Wako Pure Chemical, Osaka, Japan). The immunoreactive insulin levels were measured in duplicate using a Phadeseph insulin radioimmunoassay kit (Shionogi, Osaka, Japan).

Statistics.
All values are shown as means ± SEM. The analyses were performed using Wilcoxon's signed-rank test. To detect the effect of 6 weeks of training on body composition and physical fitness level, the data were compared before and after training. To detect the impact of the 6 weeks of training on metabolic variables, the data were compared before training and 16 h after the last training session (primary end point). Additional comparisons (pre-exercise training vs. 1 week; secondary endpoint were made only when a difference between the data before training and 16 h after the last training session was significant. A P value <0.05 was considered to be statistically significant.

RESULTS

Level of physical training and body composition.
The mild 6-week exercise program produced a training effect as demonstrated by a 5.5% increase in $V_{O_{2max}}$ from 41.6 ± 1.2 to 43.9 ± 1.2 ml · kg^{-1} · min^{-1} ($P < 0.05$). V_{O_2} at LT also increased by 34% ($P < 0.05$) with exercise training. The body weight and the relative percentage of body fat remained unchanged with exercise training (Table 1).

Fasting glucose and insulin levels.
Fasting (arterialized venous) glucose concentration was significantly lower at 16 h after the last training bout (90.5 ± 2.2 mg/dl, $P < 0.05$) than the pretraining level (94.9 ± 1.8 mg/dl) but not 1 week

Table 1—*Characteristics of subjects*

	Before training	After training
Age (years)	21.9 ± 0.8	—
Height (cm)	170.3 ± 1.1	—
Weight (kg)	61.4 ± 2.8	61.0 ± 2.8
Percent fat	12.7 ± 1.3	13.5 ± 1.4
$V\dot{O}_{2max}$ (ml · kg^{-1} · min^{-1})	41.6 ± 1.2	43.9 ± 1.2*
$V\dot{O}_{2max}$ (ml/min)	2551 ± 134	2677 ± 140*
LT-$V\dot{O}_2$ (ml · kg^{-1} · min^{-1})	17.7 ± 1.3	23.7 ± 1.1*

Data are means ± SEM. *$P > 0.05$ vs. before training. LT-$V\dot{O}_2$; $V\dot{O}_2$ at lactate threshold.

after stopping the training regimen (92.9 ± 2.1 mg/dl). The fasting insulin concentrations did not change after exercise training (pre, 28.6 ± 1.3; 16 h, 27.9 ± 3.5; 1 week, 30.2 ± 3.0 pmol/l).

S_G and S_I.

The exercise training significantly increased the S_G measured at 16 h after the last training session (pre, 0.018 ± 0.002; 16 h, 0.023 ± 0.001 min^{-1}, $P < 0.05$, Fig. 1). The elevated S_G after the training tended to be higher than the pretraining level regardless of detraining for 1 week (0.023 ± 0.002 min^{-1}, $P = 0.09$, Fig. 1). Neither GEZI (pre, 0.014 ± 0.002; 16 h, 0.019 ± 0.001 min^{-1}) nor BIE (pre, 0.004 ± 0.001; 16 h, 0.005 ± 0.0003 min^{-1}) changed after exercise training. S_I measured at 16 h after the last training session significantly increased (pre, 13.9 ± 2.2; 16 h, 18.3 ± 2.4, $\times 10^{-5}$ · min^{-1} · pmol/l^{-1}, $P < 0.05$) and still remained elevated 1 week after stopping the training regimen (18.6 ± 2.2, $\times 10^{-5}$ · min^{-1} · pmol/l^{-1} · min^{-1}, $P < 0.05$, Fig. 2). The K_G remained unchanged (pre, 2.4 ± 0.2; 16 h, 2.3 ± 0.2%/min). The incremental insulin response during the first 20 min did not change after training (pre, 3,610 ± 727; 16 h, 3,022 ± 502; 1 week, 3,335 ± 570 pmol · l^{-1} · min^{-1}).

CONCLUSIONS — The main finding of the present study was that mild exercise training for 6 weeks improved S_G in healthy young men. A longitudinal follow-up study showed that a high S_G protected to some degree against the development of type 2 diabetes, whereas a low S_G together with a low S_I produced the greatest cumulative risk of developing the disease (7). Therefore, improving not only S_I but also S_G through mild exercise was thus, for the first time, found to have a preventative effect on glucose intolerance.

By measuring S_G 16 h after the last training bout, we showed exercise training to have a sustained effect on S_G, and this effect was found to occur independently of the metabolic effect of a single bout of exercise. Brun et al. (13) observed an increase in S_G 25 min after 15 min of intensive exercise, whereas no influence on S_G 120 min after 2 h of intensive exercise was reported by Pestell et al. (14). We recently demonstrated that a single bout of mild exercise using the same regimen as that used in the present study increased S_G 25 min after completing the exercise (11). However, improved S_G immediately after the same mild exercise was not ob-

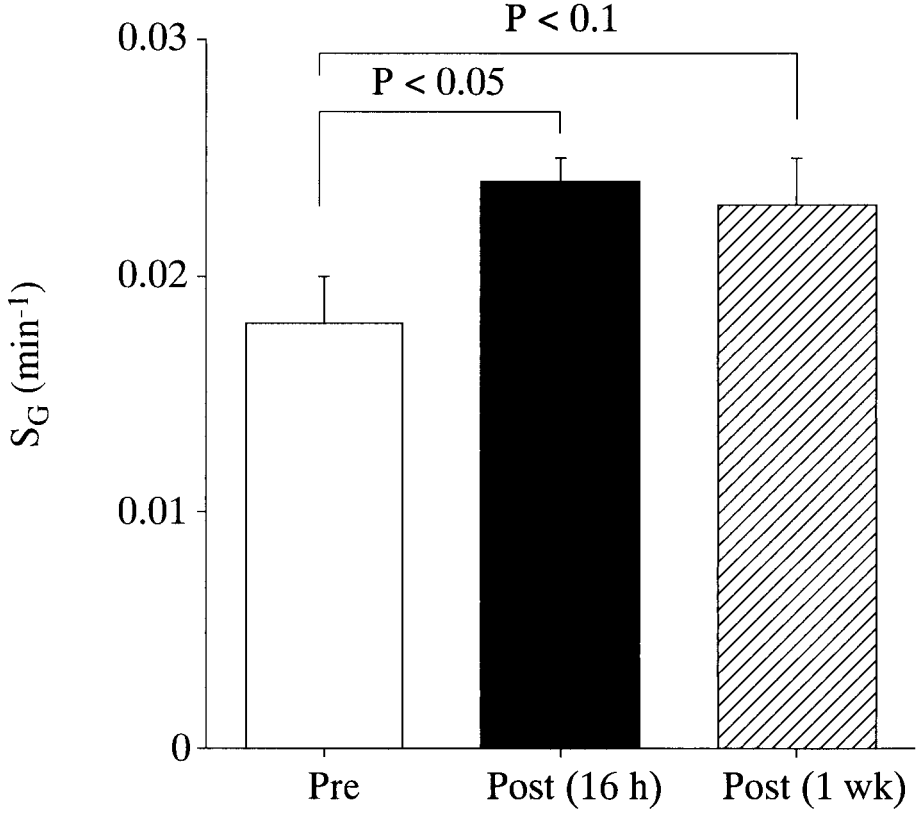

Figure 1—*Changes in S_G with 6 weeks of mild exercise training. Three IVGTTs were performed before (pre,* n = *8) and 16 h* (n = *8) and 1 week* (n = *7) after the last training session.*

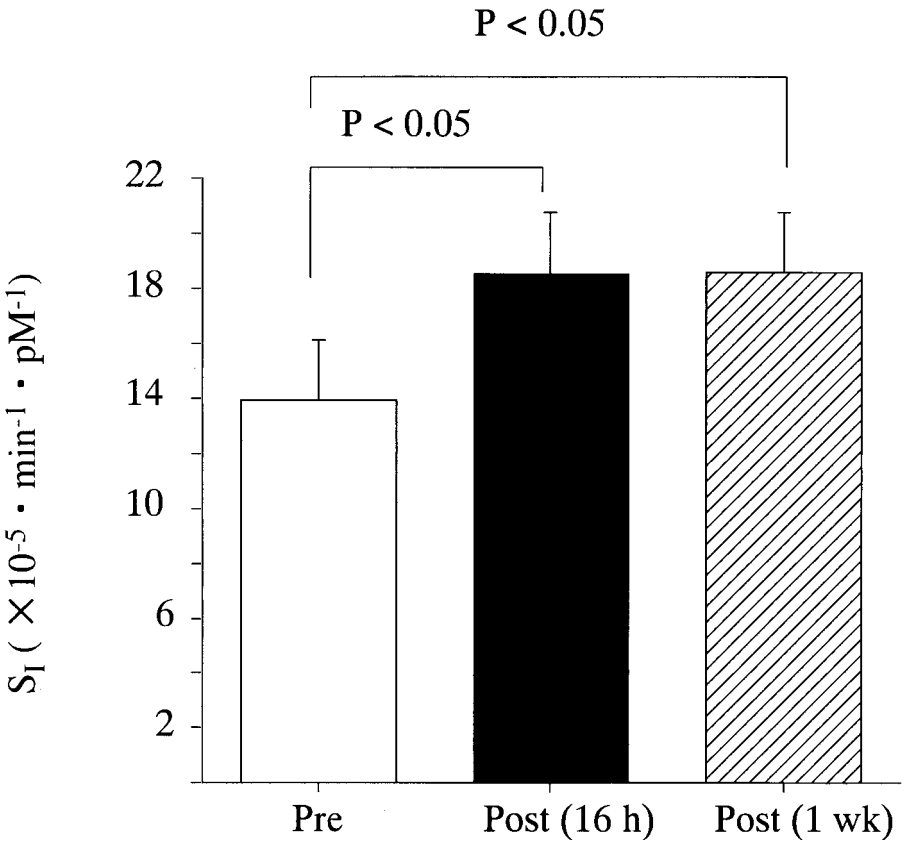

Figure 2—*Changes in* S_I *with 6 weeks of mild exercise training. Three IVGTTs were performed before (pre,* n = *8) and 16 h* (n = *8) and 1 week* (n = *7) after the last training session.*

served 11 h after exercise (15). Taken together, these findings indicated that the effect of a single bout of exercise on S_G could thus rapidly decrease in a time-dependent manner.

The improved S_I observed after our program correlated with previous findings using a minimal-model approach performed in middle-aged or older men in which endurance training resulted in a 36–62% increase in S_I (8,9). However, neither of these studies observed any significant effect on S_G (8,9). Kahn et al. (8) studied healthy older men (61–82 years of age) before and 60 h after intensive exercise training for 6 months and found no effects on S_G (0.014 ± 0.001 vs. 0.015 ± 0.002 min^{-1}). In addition, Houmard et al. (9) found no change in S_G in middle-aged men (40–65 years of age) 48 h after moderate to intensive exercise training for 14 weeks (0.020 ± 0.002 vs. 0.023 ± 0.002 min^{-1}). However, there are several possible explanations for the differences between their observations and ours.

First, the participants of their studies were much older than those in our study. Some studies demonstrated that glucose tolerance in older people does not significantly improve regardless of the duration or type of exercise training performed (8,16). These results suggest that aging per se may mask the effect of physical exercise on S_G.

A second possibility may also be due to differences in methodology. Whereas Houmard et al. (9) used venous blood sampling during IVGTT, we used arterialized venous sampling. Although many studies using a minimal-model technique used venous blood sampling (1–7), we believe arterialized sampling to be a more accurate method for measuring S_G. We recently assessed the effect of arterialized sampling on S_G in one subject whose plasma glucose level from venous blood showed a distinctive blunt peak after the rapid injection of glucose throughout the three trials (17). As the arterialized venous blood was sampled, we observed the general response of the plasma glucose, which has a sharp peak immediately after the glucose challenge and an 1.8-fold increase in S_G with no alteration in S_I (17). Because the S_G at least partly depends on the initial state of plasma glucose during the IVGTT, S_G estimated from venous samples may be underestimated. Based on these findings, venous blood sampling may not be suitable for the accurate measurement of S_G.

Martin et al. (18) demonstrated that a prolonged infusion of epinephrine enhanced hepatic glucose production (HGP) and inhibited glucose uptake, thus resulting in a decreased S_G. Although Kahn et al. (8) reported that the catecholamine concentrations obtained in the morning did not change after exercise training, dynamic epinephrine secretion is thus speculated to be secreted in trained subjects a long time after undergoing the intensive exercise training (19). Third, the repetition of epinephrine exposure induced by intensive exercise, such as that reported in the study by Kahn et al., may therefore mask the effect of exercise training on S_G.

Finegood and Tzur (20) showed the minimal-model method to have an artifact that underestimates S_G, particularly when the insulin release decreases. Although Houmard et al. (9) did not show the results of integrated area of insulin after the glucose load, Kahn et al. (8) found a significant decrease in the acute insulin response to glucose after exercise

training. On the other hand, the insulin responses after the glucose load did not change after exercise in this study. A fourth possibility is that the reduced insulin release observed by Kahn et al. could also have masked any increase in S_G after training.

The difference in the timing of IVGTT after the last training bout cannot be the reason for this discrepancy. Kahn et al. (8) and Houmard et al. (9) performed IVGTT 60 and 48 h after the last bout of exercise. The S_G of our participants 48 or 60 h after the last bout of exercise would be higher than the pre-exercise level because we observed both an increase in S_G 16 h after the last bout of exercise and the tendency of increased S_G, despite detraining for 1 week.

We found that exercise training significantly increased S_G, but no statistically significant increase was observed in either BIE or GEZI, which are included in S_G. This is important because if the increase is strictly in BIE, the increase in S_G may thus be due to an increase in S_I, since BIE is determined by multiplying the fasting insulin by S_I. Although the percent increase in GEZI (35%) was similar to that seen in BIE (28%), GEZI, which accounts for 78% of S_G (22% of the remainder is BIE, both before and after exercise), increased after exercise in seven of eight subjects. As a result, these data tend to show that most of the change in S_G occurs in GEZI.

Skeletal muscle is the predominant site of insulin-dependent and noninsulin-dependent glucose disposal in humans (21). Recently, Galante et al. (22) demonstrated that acute hyperglycemia induced an increase in the GLUT4 content in the plasma membrane of skeletal muscle independent of insulin in vivo and in vitro. Some studies have reported that physical training increases the GLUT4 protein concentration in human skeletal muscle (9,23). Interestingly, mild exercise training increases the GLUT4 protein concentration to the same extent as that of intensive exercise training in an animal study (24). Phillips et al. (23) reported that the expression of GLUT1 in human skeletal muscle increased after moderate exercise training—training that was somewhat harder than that used in our program (60% $V_{O_{2max}}$ for 1 month). As a result, it is possible that a training-induced augmentation in these proteins in skeletal muscle is one of the reasons for S_G to increase after mild exercise training.

S_G represents the effect of glucose on the net glucose disappearance, i.e., the total sum of glucose's ability to enhance glucose uptake and inhibit HGP. Ader et al. (1) postulate that 54% of S_G could be explained by the effect of glucose on peripheral glucose uptake, whereas 46% results from the glucose-mediated suppression of HGP. Unfortunately, our study was not designed to distinguish between the ability of glucose per se to increase the peripheral glucose uptake and the ability of glucose per se to suppress HGP. Future studies will clarify whether improved S_G is attributable to the ability of glucose per se to increase peripheral glucose uptake and/or suppress HGP using a stable-labeled minimal model.

The present results show, for the first time, direct evidence that physical training induces an increase in S_G in previously sedentary men. Improving not only S_I but also S_G through mild exercise training at LT is thus considered to be an effective method for preventing glucose intolerance.

Acknowledgments— This work was supported by a grant from the Central Research Institute of Fukuoka University and the Japanese Ministry of Education, Science, Sports, and Culture (No. 09480016).

We would like to thank all subjects who participated in this study.

References

1. Ader M, Pacini G, Yang YJ, Bergman RN: Importance of glucose per se to intravenous glucose tolerance: comparison of the minimal-model prediction with direct measurements. *Diabetes* 34:1092–1103, 1985
2. Best JD, Kahn SE, Ader M, Watanabe RM, Ni T-C, Bergman RN: Role of glucose effectiveness in the determination of glucose tolerance. *Diabetes Care* 19:1018–1030, 1996
3. Welch S, Gebhart SSP, Bergman RN, Phillips LS: Minimal model analysis of intravenous glucose tolerance test–derived insulin sensitivity in diabetic subjects. *J Clin Endocrinol Metab* 71:1508–1518, 1990
4. Taniguchi A, Nakai Y, Fukushima M, Kawamura H, Imura H, Nagata I, Tokuyama K: Pathogenic factors responsible for glucose intolerance in patients with NIDDM. *Diabetes* 41:1540–1546, 1992
5. Taniguchi A, Nakai Y, Fukushima M, Imura H, Kawamura H, Nagata I, Florant GL, Tokuyama K: Insulin sensitivity, insulin secretion, and glucose effectiveness in subjects with impaired glucose tolerance: a minimal model analysis. *Metabolism* 43:714–718, 1994
6. Doi K, Taniguchi A, Nakai Y, Kawamura H, Higaki Y, Yokoi H, Tanaka H, Fujitani J, Suzuki M, Tokuyama K, Sakai M, Fukushima M: Decreased glucose effectiveness but not insulin resistance in glucose-tolerant offspring of Japanese non-insulin-dependent diabetic patients: a minimal-model analysis. *Metabolism* 46:880–883, 1997
7. Martin BC, Warram JH, Krolewski AS, Bergman RN, Soeldner JS, Kahn CR: Role of glucose and insulin resistance in development of type 2 diabetes mellitus: results of a 25-year follow-up study. *Lancet* 340: 925–929, 1992
8. Kahn SE, Larson VG, Beard JC, Cain KC, Fellingham GW, Schwartz RS, Veith RC, Stratton JR, Cerqueira MD, Abrass IB: Effect of exercise on insulin action, glucose tolerance, and insulin secretion in aging. *Am J Physiol* 258:E937–E943, 1990
9. Houmard JA, Shinebarger MH, Dolan PL, Leggett-Frazier N, Bruner RK, McCammon MR, Israel RG, Dohm GL: Exercise training increases GLUT-4 protein concentration in previously sedentary middle-aged men. *Am J Physiol* 264:E896–E901, 1993
10. Tokuyama K, Higaki Y, Fujitani J, Kiyonaga A, Tanaka H, Shindo M, Fukushima M, Nakai Y, Imura H, Nagata I, Taniguchi A: Intravenous glucose tolerance test–derived glucose effectiveness in physically trained humans. *Am J Physiol* 265:E298–E303, 1993
11. Sakamoto M, Higaki Y, Nishida Y, Kiyonaga A, Shindo M, Tokuyama K, Tanaka H: Influence of mild exercise at the lactate threshold on glucose effectiveness. *J Appl Physiol* 87:2305–2310, 1999
12. Goldman RF, Buskirk ER: A method for underwater weighing and the determination of body density. In *Techniques for Measuring Body Composition*. Brozek J, Hershel A, Eds. Washington, DC, National Research Council, 1961, p. 78–89
13. Brun JF, Guintrand-Hugret R, Boegner C, Bouix O, Orsetti A: Influence of short-term submaximal exercise on parameters of glucose assimilation analyzed with the minimal model. *Metabolism* 44:833–840, 1995
14. Pestell RG, Ward GM, Galvin P, Best JD, Alford FP: Impaired glucose tolerance after endurance exercise is associated with reduced insulin secretion rather than altered insulin sensitivity. *Metabolism* 42: 277–282, 1993
15. Higaki Y, Kagawa T, Fujitani J, Kiyonaga A, Shindo M, Taniguchi A, Nakai Y, Tokuyama K, Suzuki M, Tanaka H: Effects of a single bout of exercise on glucose effec-

tiveness. *J Appl Physiol* 80:754–759, 1996
16. Seals DR, Hagberg JM, Hurley BF, Ehsani AA, Holloszy JO: Effects of endurance training on glucose tolerance and plasma lipid levels in older men and women. *JAMA* 252:645–649, 1984
17. Sakamoto M, Nishida Y, Higaki Y, Kiyonaga A, Shindo M, Tokuyama K, Tanaka H: Effects of arterialized versus venous sampling on glucose effectiveness in a case study (Abstract). *Med Sci Sports Exerc* 31 (Suppl. 196):889, 1999
18. Martin IK, Weber KM, Boston RC, Alford FP, Best JD: Effects of epinephrine infusion on determinants of intravenous glucose tolerance in dogs. *Am J Physiol* 255: E668–E673, 1988
19. Gladden LB, Stainsby WN, Macintosh BR: Norepinephrine increases canine skeletal muscle VO_2 during recovery. *Med Sci Sports Exerc* 14:471–476, 1982
20. Finegood DT, Tzur D: Reduced glucose effectiveness associated with reduced insulin release: an artifact of the minimal-model method. *Am J Physiol* 271:E485–E495, 1996
21. Baron AD, Brechtel G, Wallace P, Edelman SV: Rates and tissue sites of non-insulin- and insulin-mediated glucose uptake in humans. *Am J Physiol* 255: E769–E774, 1988
22. Galante P, Mosthaf L, Kellerer M, Berti L, Tippmer S, Bossenmaier B, Fujiwara T, Okuno A, Horikoshi H, Häring HU: Acute hyperglycemia provides an insulin-independent inducer for GLUT4 translocation in C_2C_{12} myotubes and rat skeletal muscle. *Diabetes* 44:646–651, 1995
23. Phillips SM, Han X-X, Green HJ, Bonen A: Increments in skeletal muscle GLUT-1 and GLUT-4 after endurance training in humans. *Am J Physiol* 270:E456–E462, 1996
24. Banks EA, Brozinick JT Jr, Yaspelkis BB III, Kang HY, Ivy JL: Muscle glucose transport, GLUT-4 content, and degree of exercise training in obese Zucker rats. *Am J Physiol* 263:E1010–E1015, 1992