Does Training Spare Insulin Secretion and Diminish Glucose Levels in Real Life?

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Compared with untrained subjects, in trained subjects the increased insulin sensitivity and decreased glucose induced insulin secretion will tend to promote health by decreasing glucose levels and insulin secretion, whereas the increased food intake will tend to increase these variables. To evaluate the net effect of training, we administered oral glucose loads making up identical fractions of daily carbohydrate intake (i.e., same relative glucose loads) to 8 athletes and 7 sedentary subjects (age: 25 ± 1 vs. 24 ± 1 yr [mean ± SE] [NS]; body weight: 76.0 ± 1.3 vs. 79.3 ± 2.3 kg [NS]; maximal oxygen uptake: 76 ± 2 vs. 48 ± 1 ml $O_2 \cdot kg^{-1} \cdot min^{-1}$ [$2P < 0.05$], respectively). Furthermore, 24 h plasma concentration profiles of glucose, C-peptide, and insulin were determined during ordinary living conditions. Daily carbohydrate intake was higher ($2P < 0.05$) in athletes compared with sedentary subjects (678 ± 34 vs. 294 ± 18 $g \cdot day^{-1}$, respectively). In response to same relative oral glucose loads, glucose and C-peptide responses were similar in athletes compared to sedentary subjects. Twenty-four hour integrated glucose and C-peptide concentrations did not differ between athletes and sedentary subjects (7.4 ± 0.2 vs. 7.3 ± 0.6 $mol \cdot L^{-1} \cdot 1440$ min [$2P > 0.05$] and 923 ± 99 vs. 1047 ± 175 $pM \cdot ml^{-1} \cdot 1440$ min [$2P > 0.05$], respectively), and insulin concentrations tended to be lower in athletes compared with sedentary subjects (124 ± 13 vs. 175 ± 38 $pM \cdot ml^{-1} \cdot 1440$ min [$2P > 0.05$]). It is concluded that, during training, adaptations in pancreas and insulin sensitive tissues allow the necessary increase in food intake without harmful hyperglycemia and overloading of β-cells, but sparing of insulin secretion and reductions in glucose levels are only relative to food intake. However, training may be wholesome by increasing hepatic insulin extraction and thereby decreasing arterial insulin levels.

In response to a given glucose load administered orally or as an intravenous bolus, plasma insulin and C-peptide concentrations are lower, whereas glucose concentrations are the same or lower in physically trained than in untrained subjects (1,2). Furthermore, during infusion of glucose at a given rate, lower insulin and C-peptide concentrations in the face of identical glucose concentrations have been found in trained compared with untrained humans (3). These findings reflect that training increases insulin sensitivity of tissue glucose uptake (4) and decreases glucose-stimulated pancreatic β-cell secretion (3). They have given grounds for the general view that training by decreasing the load on the β-cells may decrease the risk of developing type II diabetes (5–7). Less diabetes implies less atherosclerosis. In addition, a training-induced decrease in glucose and/or insulin levels has been speculated independently to protect against development of atherosclerosis, these variables being risk factors (8).

The above mentioned reasoning in favor of beneficial metabolic effects of physical training, however, does not allow for the fact that training necessitates an increased food intake that tends to increase glucose levels, as well as secretion and plasma concentrations of insulin (9). Thus, the sparing effect of training on glucose levels and/or insulin secretion at given glucose loads might under ordinary living conditions be offset by a higher food intake in trained compared with untrained subjects. In order to evaluate this hypothesis, we first compared endurance trained and untrained healthy men both at identical absolute glucose loads and at identical relative glucose loads (i.e., glucose loads making up identical fractions of daily carbohydrate intake in the two groups) (10).

The seven trained subjects had the same age (25 ± 1 vs. 24 ± 1 yr, mean ± SE), body weight (76.0 ± 1.3 vs. 79.3 ± 2.3 kg), and height (187 ± 2 vs. 180 ± 3 cm) as the eight sedentary subjects. However, $\dot{V}O_{2max}$ was higher (76 ± 2 vs. 48 ± 1 ml $O_2 \cdot kg^{-1} \cdot min^{-1}$, $2P < 0.05$) and percent body fat (7 ± 1 vs. 15 ± 2%) and basal heart rate (50 ± 3 vs. 66 ± 3 beats/min^{-1}) lower ($2P < 0.05$) in the trained subjects. Daily energy intake was about 50%

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Table 1—*Integrated glucose, C-peptide, and insulin responses to the same absolute oral glucose load (1 g/kg body wt) in 7 trained and 8 untrained subjects*

	GLUCOSE (MMOL · L^{-1} · 180 MIN)	C-PEPTIDE (PMOL · ML^{-1} · 180 MIN)	INSULIN (PMOL · ML^{-1} · 180 MIN)
UNTRAINED	1277 ± 47*	285 ± 27*	58 ± 4*
TRAINED	1040 ± 29	158 ± 17	24 ± 4

Total areas under concentration vs. time (180 min) curves were calculated. Values are means ± SE.
*$2P < 0.05$.

higher ($2P < 0.05$) in trained than in untrained subjects (18,607 ± 835 vs. 12,493 ± 720 kJ/day^{-1}). The difference mainly reflected that carbohydrate intake in trained subjects was 2.3 ± 0.2 times the average for untrained subjects (and in untrained subjects 0.4 ± 0.03 times the average for trained subjects) (678 ± 34 vs. 294 ± 18 g · day^{-1}, $2P < 0.05$). In response to an oral glucose load of 1 g/kg body wt. in trained subjects studied in the postabsorptive state in the morning 12–18 h after their last exercise session, these subjects had markedly lower areas under plasma concentration versus time curves (AUC) for glucose, C-peptide, and insulin than sedentary subjects (Table 1). However, compared with oral glucose loads, which were adjusted for differences between groups in daily carbohydrate intake, glucose and C-peptide responses were identical in athletes and sedentary subjects. This was the case both at identical low (1 g glucose/kg vs. 0.4 g/kg, corresponding to 12% of daily carbohydrate intake) and high (2.3 vs. 1 g/kg, corresponding to 28% of daily carbohydrate intake) relative glucose loads (Table 2). Accepting the general assumption that training does not influence C-peptide clearance (1–3), the latter findings indicate identical responses of insulin secretion at given relative glucose loads in the two groups.

It could be argued that comparisons at identical relative glucose loads might not reflect ordinary living conditions because the amount of carbohydrate given to trained subjects might be too high considering that experiments were conducted in the morning, at a time that is closer to the next rather than to the last exercise bout. However, analysis of the subjects' usual breakfast revealed that, in the morning, trained subjects normally ate more carbohydrates than administered with the high oral glucose load. Furthermore, the usual ratio between morning carbohydrate intake in trained and untrained subjects, respectively, was slightly higher than the experimentally used ratio (10). Thus, the glucose and C-peptide findings suggested that the potentially health promoting effects of physical training on glucose levels and insulin secretion had been overrated in the past. On the other hand, insulin responses tended to be lower in trained compared with untrained subjects also at identical relative glucose loads (Table 2), and this suggested a health benefit such as hyperinsulinemia may be atherogenic and cause hypertension (8). The difference in insulin levels in the face of identical C-peptide levels probably reflected that training increases hepatic insulin extraction (11). An increase in peripheral clearance might also be a factor, but has not been found in studies in which arterial and venous leg catheterizations were conducted (F.D., unpublished observations).

Evidently, the described laboratory experiments did not exactly imitate real life. For instance, glucose is not a major component of usual meals, and acute effects of exercise bouts were not considered. Therefore, we next studied 24-h profiles of glucose, C-peptide, and insulin in plasma under ordinary living conditions (12). The same subjects, who participated in the first study, had blood sampled frequently during their usual daily activities. In the athletes, this included 204 ± 20 min of training (including time for warm up and stretch-

Table 2—*Integrated glucose, C-peptide, and insulin responses to the same relative oral glucose load in 7 trained and 8 untrained subjects*

		GLUCOSE (MMOL · L^{-1} · 180 MIN)	C-PEPTIDE (PMOL · ML^{-1} · 180 MIN)	INSULIN (PMOL · ML^{-1} · 180 MIN)
LOW RELATIVE GLUCOSE LOAD	UNTRAINED (0.4 G/KG)	1066 ± 29	181 ± 23	32 ± 3*
	TRAINED (1.0 G/KG)	1040 ± 29	158 ± 17	24 ± 4
HIGH RELATIVE GLUCOSE LOAD	UNTRAINED (1 G/KG)	1277 ± 47	285 ± 27	58 ± 4
	TRAINED (2.3 G/KG)	1173 ± 47	270 ± 25	44 ± 6

Trained and untrained subjects were compared at oral glucose loads that made out identical fractions of daily carbohydrate intake, 11.8 ± 0.5% (same low relative glucose load) or 27.7 ± 1.1% (same high relative glucose load). Glucose loads are given in parentheses. Total areas under concentration vs. time (180 min) curves were calculated. Values are means ± SE.
*$2P < 0.05$.

Table 3—*Twenty-four-h integrated concentrations in plasma*

	GLUCOSE (MOL · L^{-1} · 1440 MIN)	C-PEPTIDE (PMOL · ML^{-1} · 1440 MIN)	INSULIN (PMOL · ML^{-1} · 1440 MIN)
UNTRAINED	7.3 ± 0.6	1047 ± 175	175 ± 38
TRAINED	7.4 ± 0.2	923 ± 99	124 ± 13

Seven trained and 8 untrained subjects had blood drawn frequently during 24 h of ordinary living conditions. Total areas under concentrations vs. time (1440 min) curves were calculated.
Values are means ± SE.

ing). During the day, plasma glucose concentrations fluctuated more in trained than in untrained subjects, but 24-h integrated glucose concentrations (AUC) did not differ between groups (Table 3). The fact that the concentration of HbA_{1c} did not differ ($2P > 0.05$) between trained and untrained subjects (5.2 ± 0.2 vs. 4.6 ± 0.2%, respectively) indicated that the average glucose concentration had been identical in the two groups for months.

Twenty-four-h integrated plasma C-peptide concentrations did not differ either between trained and untrained subjects (Table 3). Correspondingly, 24-h urinary C-peptide excretion was similar in the two groups (20 ± 4 vs. 22 ± 2 nmol/1440 min^{-1}). These findings support the above mentioned view that training does not influence C-peptide clearance. It appears that glucose and C-peptide findings during ordinary living conditions were in line with findings in our preceding glucose tolerance study. The same was true for insulin findings. Thus, mean insulin concentrations tended to be higher in untrained compared with trained subjects during most of the day, and 24-h AUC for insulin was on an average 41% higher in the former (Table 3). However, the difference in insulin concentrations between the two groups only achieved statistical significance (68% difference, $2P < 0.05$) during a 2-h period late during the night, beginning 514 ± 37 min after start of the last food intake. The fact that trained, compared with untrained subjects, had 2.3 times higher carbohydrate consumption but, nevertheless—as indicated by identical C-peptide AUCs—the same overall insulin secretion shows that, during ordinary living conditions, the effect of insulin in trained subjects enhanced at least as much as suggested by laboratory studies using the hyperinsulinemic, euglycemic clamp technique (4). The increase in insulin sensitivity seems to be more pronounced in peripheral tissues than in the liver, as judged from the tendency to lower average peripheral insulin concentrations, but according to C-peptide concentrations, similar portal insulin levels occurred in trained compared with untrained subjects.

The conclusion from our studies is that the adaptations induced by physical training in secretion and action of insulin seem accurately matched to the increase in fuel turnover that accompanies the training regimen. Trained subjects have, compared with untrained subjects, the same overall insulin secretion and average plasma glucose concentration despite a higher food intake. This means that during training, adaptations in pancreas and insulin-sensitive tissues allow the necessary increase in food intake without potentially harmful hyperglycemia and overloading of β-cells. However, being only relative to food intake, the training-induced sparing of insulin secretion and reduction in plasma glucose concentrations do not indicate a health benefit compared with the untrained state. This is in line with the general finding in insulin-dependent diabetic subjects, who participate in exercise programs, that despite an increase in insulin sensitivity with training, the average plasma glucose concentration and the total insulin requirement do not decline (7). However, training may decrease arterial insulin levels by an increase in hepatic insulin extraction, and this effect may be wholesome. An additional conclusion is that the training-induced reduction in glucose stimulated β-cell secretion is not caused by a diminished average plasma glucose concentration.

Acknowledgments— This study was supported by The Danish Diabetes Association, The Danish Foundation for the Advancement of Medical Science, The Danish Sports Research Council, Jacob and Olga Madsens Foundation, The NOVO Foundation, The P. Carl Petersen Foundation, and The Danish Medical Research Council.

References

1. Björntorp P, Fahlèn M, Grimby G, Gustafson A, Holm J, Renström P, Scherstén T: Carbohydrate and lipid metabolism in middle-aged, physically well-trained men. *Metabolism* 21:1037–44, 1972
2. Wirth A, Diehm C, Mayer H, Mörl H, Vogel I, Björntorp P, Schlierf G: Plasma C-peptide and insulin in trained and untrained subjects. *J Appl Physiol* 50:71–77, 1981
3. Mikines KJ, Sonne B, Tronier B, Galbo H: Effects of training and detraining on dose-response relationship between glucose and insulin secretion. *Am J Physiol* 256:E588–96, 1989
4. Mikines KJ, Sonne B, Farrell PA, Tronier B, Galbo H: Effect of training on the dose-response relationship for insulin action in men. *J Appl Physiol* 66:695–703, 1989
5. Consensus Development Panel: Consensus development conference on diet and exercise in NIDDM. *Diabetes Care* 10: 639–44, 1987
6. Berger M, Kemmer FW: Discussion: exercise, fitness and diabetes. In *Exercise, Fitness and Health: A Consensus of Current Knowledge*. Bouchard C, Shepard RJ,

Stephens T, Sutton JR, McPherson BD, Eds. Champaign, IL, Human Kinetic Publishers, 1990, p. 491–95
7. Galbo H: Exercise and diabetes. *Scand J Sports Sci* 10:89–95, 1988
8. Stout RW: Insulin and atheroma. *Diabetes Care* 13:631–54, 1990
9. Sims EAH, Danforth E Jr, Horton ES, Bray GA, Glennon JA, Salans LB: Endocrine and metabolic effects of experimental obesity in man. *Rec Progr Horm Res* 29:457–97, 1973
10. Dela F, Mikines KJ, von Linstow M, Galbo H: Effect of training on response to a glucose load adjusted for daily carbohydrate intake. *Am J Physiol* 260:E14–20, 1991
11. Wirth A, Holm G, Björntorp P: Effect of physical training on insulin uptake by the perfused rat liver. *Metabolism* 31: 457–62, 1982
12. Dela F, Mikines KJ, von Linstow M, Galbo H: Twenty-four-hour profile of plasma glucose and glucoregulatory hormones during normal living conditions in trained and untrained men. *J Clin Endocrinol Metab* 73:982–89, 1991