Synergistic improvement of glucose tolerance by sucrose feeding and exercise training

ANDRÉ L. VALLERAND, JEAN LUPIEN, AND LUDWIK J. BUKOWIECKI
Laboratory of Endocrinology, Department of Physiology, Faculty of Medicine, Laval University, Québec, Province of Québec G1K 7P4, Canada

VALLERAND, ANDRÉ L., JEAN LUPIEN, AND LUDWIK J. BUKOWIECKI. *Synergistic improvement of glucose tolerance by sucrose feeding and exercise training.* Am. J. Physiol. 250 (Endocrinol. Metab. 13): E607–E614, 1986.—The interactive effects of exercise training (5–7 wk) and sucrose consumption (ad libitum feeding of a 32% sucrose solution and Purina chow) on intravenous glucose tolerance and plasma insulin levels were investigated using a 2 × 2 experimental design. Rats were divided in Purina-sedentary, Purina-trained, sucrose-sedentary, and sucrose-trained groups. Sucrose feeding of sedentary animals significantly increased basal and glucose-stimulated insulin levels and improved basal glycemia and glucose tolerance. On the other hand, exercise training of Purina-fed animals significantly reduced basal as well as glucose-stimulated insulinemia without altering basal glycemia or glucose tolerance. Such a sparing effect of exercise training on insulin requirements was not as evident in rats consuming sucrose. These animals displayed a reduced basal glycemia ($P < 0.01$) with normal basal insulin levels. Their glucose tolerance was markedly improved ($P < 0.01$) but their insulin response during intravenous glucose tolerance test remained as high as in sucrose-sedentary animals. Results from these studies indicate that *1*) sucrose feeding of sedentary animals leads to hyperinsulinemia without compensatory insulin resistance, resulting in an improvement of glucose tolerance, *2*) exercise training increases the sensitivity of peripheral tissues to insulin, and *3*) the marked improvement of glucose tolerance observed in sucrose-trained animals results from a synergistic combination of the above two factors, i.e., increased insulinemia (induced by diet) and enhanced insulin sensitivity (induced by training).

carbohydrate metabolism; cellularity; nutrition; parametrial; swimming; triglyceride; white adipose tissue

PROFOUND CHANGES in the metabolic regulation of glucose tolerance and insulin secretion are known to take place in animals offered a sucrose-rich diet. It is well established that sucrose feeding markedly increases basal insulin levels as well as glucose-stimulated insulin release (2, 13, 14, 17, 22, 23, 26, 34). However, the influence of this particular type of diet on glucose tolerance is not as clear. Glucose tolerance as well as insulin sensitivity after a period of sucrose feeding have been reported to be either improved (1, 22, 26), unchanged (13, 14, 23), or even deteriorated (2, 17, 34). Explanations for these appearingly conflicting results may lie at the level of differences in total energy intake, in diet composition (proportion of energy derived from carbohydrate or sucrose), in body composition (adiposity), etc.

In contrast to the sucrose diet, exercise training induces a sparing effect on insulin requirements. In Purina-fed rats, it reduces basal and glucose-stimulated insulin levels (3, 21, 24, 30) and decreases the capacity of isolated pancreatic islets for secreting insulin (35). The reduction of circulating insulin is generally counterbalanced by a compensatory increased sensitivity of peripheral tissues to insulin (3, 21). Indeed, in most cases, exercise training does not modify glucose tolerance (3, 21, 30). However, it appears to improve insulin-stimulated glucose uptake in rats in which insulin resistance has been induced by feeding a granulated sucrose diet (34).

Previous studies from our laboratory have shown that when female Wistar rats are offered a sucrose solution in addition to a nutritionally complete diet (Purina laboratory chow), they generally become hyperphagic without gaining excess weight (7, 20). This phenomenon was attributed, at least in part, to an increased capacity for diet-induced thermogenesis in brown adipose tissue (7). In that study, preliminary experiments revealed that sucrose feeding did not deteriorate glucose tolerance, on the contrary, it appeared to improve it. It was therefore decided to reinvestigate the problem and to determine whether exercise training (known to increase insulin sensitivity of peripheral tissues) would amplify the beneficial effect of sucrose feeding on glucose tolerance.

METHODS

Female Wistar rats weighing 180–190 g each (Charles River, St. Constant, Province of Québec, Canada) were divided into four groups of animals: Purina-sedentary, Purina-trained, sucrose-sedentary, and sucrose-trained animals. Animals were housed in individual cages located in a controlled room held at 25°C (12-h light-dark cycle). Two groups of rats (sucrose-sedentary and sucrose-trained animals) were offered ad libitum a 32% (wt/vol) sucrose solution in addition to a nutritionally complete diet (Purina Laboratory Chow; Ralston Purina, St. Louis, MO). These animals were not provided with an additional water bottle (7, 20). Two other groups of rats were only offered water and laboratory chow ad libitum (Purina-sedentary and Purina-trained animals). One group of Purina-fed and one group of sucrose-fed animals (Purina-trained and sucrose-trained animals) were additionally submitted to a strenuous exercise training program. It consisted of daily swimming bouts in fabricated swimming pools containing 0.7 m of continuously

0193-1849/86 $1.50

agitated water held at 36.5 ± 0.5°C. After a week, the animals were swimming 3 h/day, 5 days/wk, for 5–7 wk. This type of exercise has been shown to increase resting oxygen consumption (V_{O_2}) by 300% (19). Thus it compares favorably with treadmill exercise that also increases V_{O_2} by a factor of 3 over resting values when performed at an intensity of 28.7 m/min with 15°C of incline (4). Food and liquid intakes (corrected for losses) and body weights were recorded twice weekly. Spoiled food and liquids (water or sucrose) were collected in a cup or a plastic bag, respectively, which were placed underneath the cage and measured as accurately as possible. The average metabolizable energy content of Purina laboratory chow was 14.2 kJ/g with 28% of energy derived from protein, 60% from carbohydrates (~45% dextrin and 15% sucrose), and 12% from fat (as determined from food composition tables). The sucrose solution had a metabolizable energy content of 5.17 kJ/ml.

After 4 wk of study, animals were cannulated into the right jugular vein according to a modification of a previously described method (28, 30). Briefly, a polyethylene cannula filled with saline (Intramedic PE-50, Clay-Adams, Parsippany, NJ) was inserted under anesthesia into the right jugular vein. The tube exteriorized through a neck incision and sealed. After a period of at least 40 h without exercise, intravenous glucose tolerance tests (IVGTT) were performed during the 5th wk of study in fasted (food and/or sucrose were replaced with water ad libitum for 10 h), unanesthetized, unrestrained, and undisturbed animals. Glucose was slowly injected in the jugular vein at a concentration of 0.5 g/kg and the cannula was immediately rinsed with saline (3, 30). Blood was sampled (0.4 ml) before and after glucose injection and was replaced with equivalent volumes of heparinized saline (50 U/ml). Blood samples were transferred into chilled heparinized tubes, centrifuged at 4°C, and the plasma kept frozen (−80°C) for later insulin and glucose determinations.

Plasma insulin was measured by radioimmunoassay according to the method of Desbuquois and Aurbauch (11) using a rat insulin standard (Novo Research Institute, Denmark). Plasma glucose was estimated by the glucose oxidase method on an automatic glucose analyzer (Beckman Instruments, Fullerton, CA). Glucose fractional clearance rates (K value) and total areas under the curves were calculated as previously described (28). Glucose concentrations declined linearly on a log-linear scale between 2 and 15 min postinjection. This portion of the decay curve was used in conjunction with a linear regression analysis to estimate glucose half-life ($t_{½}$), which was used in the following equation: $K = 0.693/t_{½}$. Total areas were calculated by the trapezoidal rule.

To evaluate the influence of sucrose feeding and exercise training on adipose tissue composition, animals were killed by cervical dislocation, and parametrial white adipose tissue was rapidly removed, freed of all extraneous material, blotted on filter paper, and weighed. Adipocytes were isolated by a method using collagenase and counted (6). Adipose tissue cellularity (total number of adipocytes present in the depot) was determined by dividing the total triglyceride content by the triglyceride content of 10^6 cells, exactly as previously described (6).

Data were statistically analyzed by one-way variance analysis. When the F values proved significant, Duncan's post-hoc test was used to locate significant differences between groups. A two-way analysis of variance was used to evaluate interactions between treatments [Statistical Package for the Social Sciences (SSPS), 1979, Chicago, IL].

RESULTS

Effects of sucrose feeding and exercise training on total energy intake and body weight gain. Both sucrose feeding and exercise training significantly increased total energy intake ($P < 0.01$) without altering body weight gain, in comparison to Purina-sedentary animals (controls) (Fig. 1). The sucrose-induced hyperphagia resulted from a high-sucrose intake that was not completely balanced by a decreased consumption of Purina chow. The proportion of calories taken from carbohydrates, protein, and fat was 60:28:12%, 89.5:7.3:3.2%, and 87.8:8.5:3.7% for the Purina-fed, sucrose-sendentary, and sucrose-trained animals, respectively. Of the carbohydrate calories, 73.8 ±

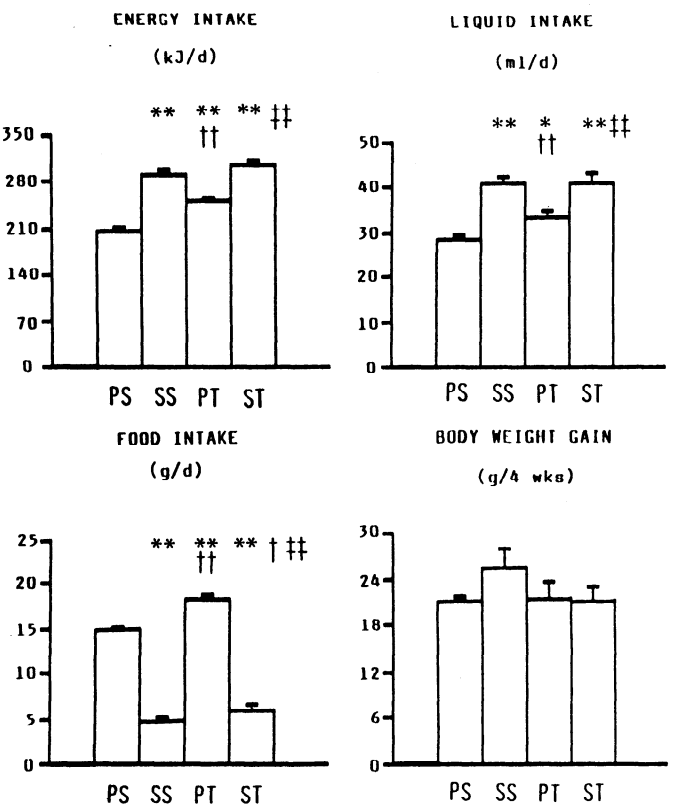

FIG. 1. Influence of sucrose feeding and exercise training on energy, liquid, and food intakes and body weight gain. Four groups of animals were formed: Purina-sedentary (PS) ($n = 10$), sucrose-sedentary (SS) ($n = 7$), Purina-trained (PT) ($n = 9$), and sucrose-trained (ST) ($n = 6$) animals. Sucrose-fed rats were given access to a 32% sucrose solution in addition to a nutritionally complete basal diet (Purina laboratory chow). Purina and sucrose-fed rats were either sedentary or exercise trained. The exercise regimen consisted of daily swimming bouts in continuously agitated water held at 36.5 ± 0.5°C, for 3 h/day, 5 days/wk, for 5–7 wk. Number of animals is same throughout Figs. 1–5. Significant differences from Purina-sedentary (controls) (*), sucrose-sedentary (†), and Purina-trained animals (‡) are indicated by 1 ($P < 0.05$) or 2 *symbols* ($P < 0.01$).

1.9 and 69.5 ± 2.3% were taken from the sucrose solution in sedentary and trained sucrose-fed animals, respectively (the difference was not significant). Thus solubilized sucrose feeding resulted in a diet that was very high in carbohydrate and low in protein and fat.

Effect of sucrose feeding and exercise training on glucose and insulin responses to an IVGTT. Sucrose consumption improved basal glucose levels and the integrated glucose response both in sedentary and trained animals ($P < 0.05$ and $P < 0.01$) (Fig. 2). Exercise training did not significantly modify either basal glucose levels or the integrated glucose response in Purina-fed animals (Fig. 2). However, it markedly enhanced the beneficial effects of sucrose consumption, both on basal glucose levels and integrated glucose response in sucrose-trained animals ($P < 0.01$). To determine whether the combination of exercise training and sucrose consumption improved glucose tolerance in a synergistic manner, glucose fractional clearance rates (K values) were calculated from the data described in Fig. 2 (Fig. 3). Sucrose consumption increased the K value by 33% ($P < 0.05$), whereas exercise training failed to significantly increase this parameter. The fact that the increment in K value of sucrose-trained animals was doubled (66%; $P < 0.01$) in comparison with the increase in sucrose-sedentary rats (33%) strongly indicates that training potentiated synergistically the beneficial effects of sucrose consumption on glucose clearance rates. Factorial analysis of variance (2 × 2 ANOVA) confirmed that the interaction between the effects of exercise and sucrose on K values was indeed significant ($P < 0.05$).

On the other hand, sucrose consumption doubled basal insulin levels in sedentary animals in comparison with controls ($P < 0.01$) and significantly increased the same parameter in trained rats in comparison with Purina-trained animals ($P < 0.05$) (Fig. 4, left). Basal insulinemia of sucrose-trained animals was also similar to controls. Sucrose feeding also markedly increased the insulin response during the IVGTT both in sedentary and trained animals. This resulted in an enhancement of the integrated insulin area by a factor of 2 for sucrose-sedentary animals in comparison with controls and by a factor of 3 for sucrose-trained in comparison with Purina-trained animals ($P < 0.01$) (Fig. 4 right). Exercise training significantly reduced basal insulin levels and the integrated insulin response during the IVGTT in Purina-fed rats ($P < 0.05$) (Fig. 4). However, it failed to alter the latter parameter in sucrose-consuming animals. It therefore appears that the sparing effect of training on glucose-stimulated insulin levels is abolished by sucrose intake.

Effect of sucrose feeding and exercise training on parametrial adipose tissue composition and tissue weights. Sucrose feeding significantly increased parametrial white adipose tissue weight, total tissue triglyceride content, triglyceride content per adipocyte, and total tissue cel-

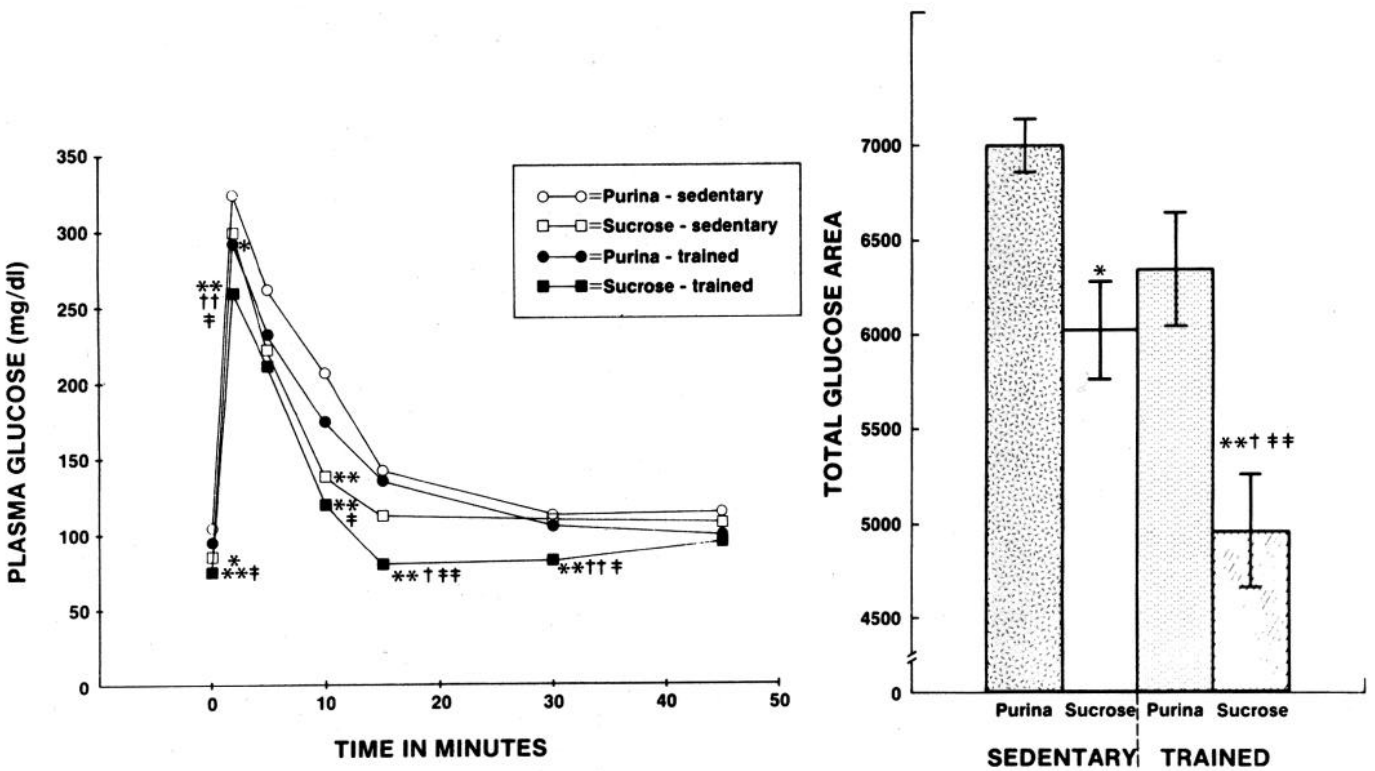

FIG. 2. Plasma glucose responses to intravenous glucose injection (0.5 g/kg) in Purina-sedentary, sucrose-sedentary, Purina-trained, and sucrose-trained animals. Glucose tolerance tests (IVGTT) were performed in precannulated, fasted, conscious, and undisturbed animals. *Figure* on *right* describes total glucose area calculated for data between 0 and stimulated levels of glucose. After IVGTT, rats were returned to their respective treatment conditions before being killed for determination of parametrial white adipose tissue cellularity. *Symbols* for statistical differences are as in Fig. 1.

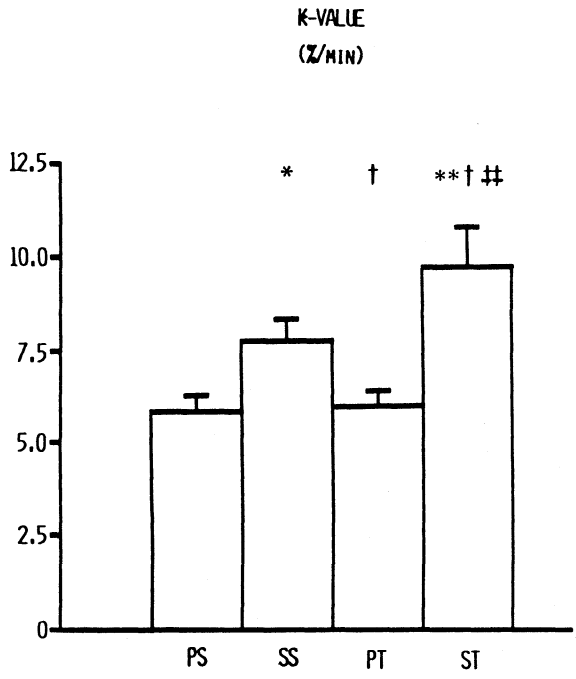

FIG. 3. K values (glucose fractional clearance rates) of Purina-sedentary (PS), sucrose-sedentary (SS), Purina-trained (PT), and sucrose-trained (ST) animals. K values are calculated from values seen in Fig. 2 and are expressed as a percentage of plasma glucose reduction/min. Interaction between effects of exercise training and sucrose feeding was statistically significant. *Symbols* for statistical differences are as in Fig. 1.

lularity in sucrose-sedentary animals in comparison with controls and in sucrose-trained in comparison with Purina-trained rats ($P < 0.05$ and $P < 0.01$) (Fig. 5). In contrast, exercise training significantly reduced adipose tissue weight, total tissue triglyceride content, triglyceride content per adipocyte, and adipocyte number in Purina-fed animals ($P < 0.01$). It should be pointed out that the reduced adipocyte cellularity in trained animals consuming Purina chow most probably resulted from an inhibition of normal adipocyte proliferation in parametrial white adipose tissue of growing animals during the experimental period rather than from an increased adipocyte turnover (8). Furthermore, exercise training entirely inhibited the stimulatory effects of sucrose consumption on adipocyte proliferation in parametrial white adipose tissue (the cellularity of sucrose-trained animals was similar to that of controls). Thus the greater weight of parametrial white adipose tissue of sucrose-trained animals resulted mainly from an increased triglyceride content per adipocyte ($P < 0.01$).

Sucrose feeding also increased the absolute heart weight but decreased the relative kidney weight ($P < 0.01$) (Table 1). On the other hand, exercise training increased the absolute and relative heart weight ($P < 0.01$). Both absolute and relative heart weights were significantly increased in sucrose-trained animals in comparison with all the other groups ($P < 0.05$ and $P < 0.01$). Liver and muscle weights were unaffected by the various treatments.

DISCUSSION

The present data confirm and extend previous obser-

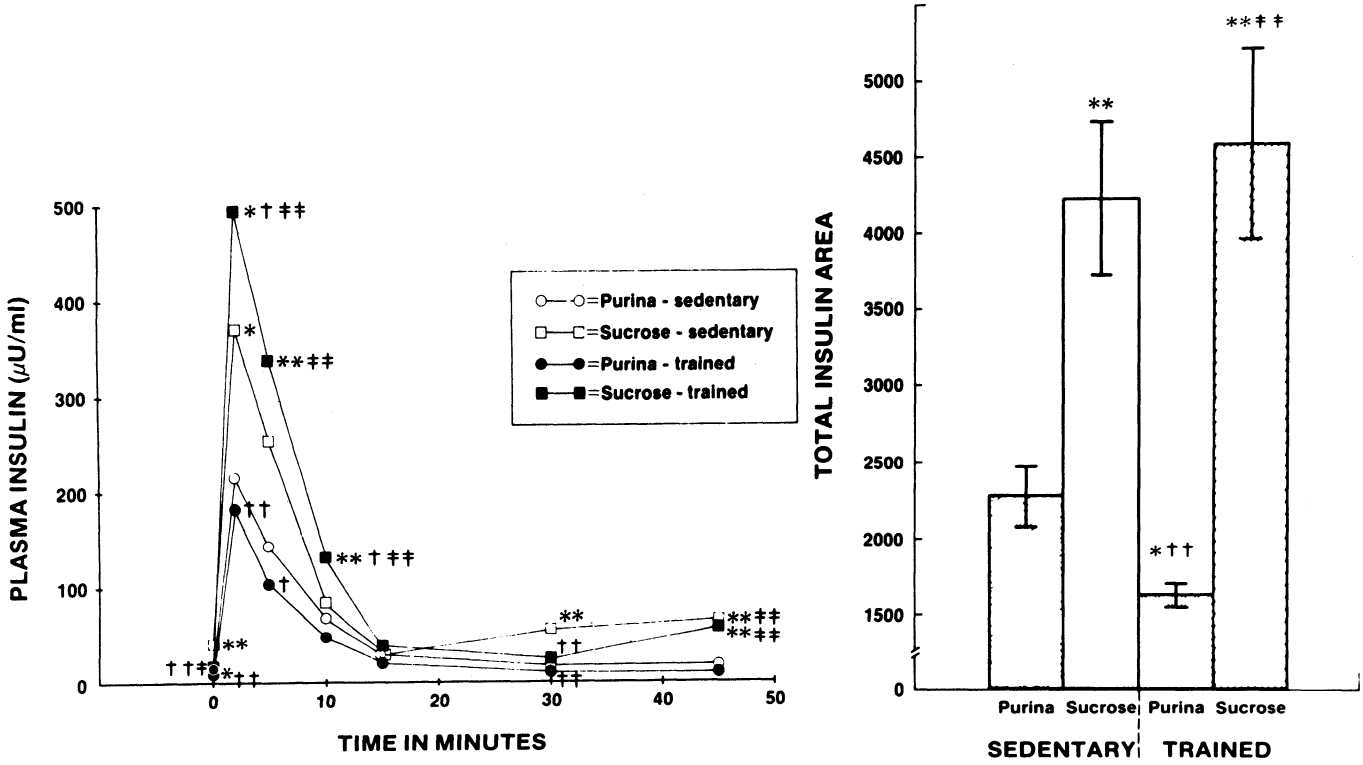

FIG. 4. Plasma insulin responses to intravenous glucose injection (0.5 g/kg) in Purina-sedentary, sucrose-sedentary, Purina-trained, and sucrose-trained animals. Basal insulin levels of these animals are, respectively: 19.5 ± 1.6, 44.7 ± 4.0 **, 9.8 ± 1.0 *‡, and 18.2 ± 2.0 †† ‡ μU/ml. Figure on *right* describes total insulin area calculated for data between 0 and stimulated levels of insulin. *Symbols* for statistical differences are as in Fig. 1.

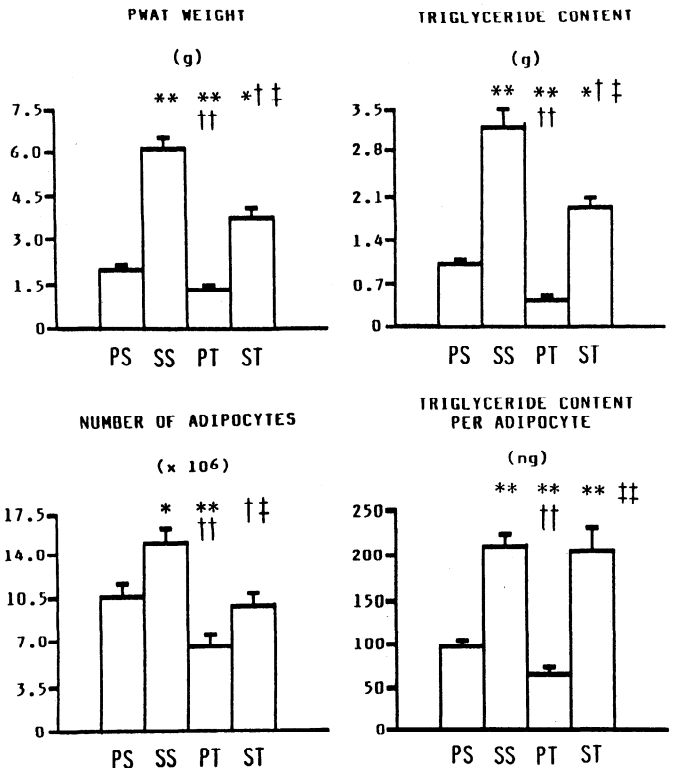

FIG. 5. Influence of sucrose feeding and exercise training on parametrial white adipose tissue cellularity of Purina-sedentary (PS), sucrose-sedentary (SS), Purina-trained (PT), and sucrose-trained (ST) animals. Cellularity of parametrial white adipose tissue is expressed in millions of adipocytes present in both fat pads. It was calculated by dividing its total triglyceride content by that of 1 million isolated adipocytes. Triglyceride content per adipocyte was calculated by dividing total triglyceride content of depot by total number of isolated adipocytes. *Symbols* for statistical differences are as in Fig. 1.

TABLE 1. *Effects of sucrose diet and exercise training on tissue weights*

Groups	*n*	Heart	Liver	Kidney	Soleus	Gastrocnemius
Purina sedentary	13	0.580	6.075	0.616	0.164	1.003
		0.016	0.236	0.021	0.007	0.032
		(0.289)	(3.013)	(0.306)	(0.081)	(0.498)
		(0.008)	(0.094)	(0.008)	(0.004)	(0.014)
Sucrose sedentary	12	0.670*	6.414	0.599	0.151	1.002
		0.014	0.191	0.013	0.005	0.025
		(0.310)	(2.959)	(0.277)*	(0.070)	(0.463)
		(0.006)	(0.064)	(0.005)	(0.002)	(0.010)
Purina trained	13	0.681*	6.293	0.651	0.144	1.012
		0.021	0.214	0.019	0.008	0.021
		(0.333)*	(3.077)	(0.318)‡	(0.071)	(0.495)
		(0.010)	(0.103)	(0.009)	(0.004)	(0.010)
Sucrose trained	12	0.747*	6.590	0.607	0.160	0.994
		0.023†‡	0.156	0.014	0.004	0.026
		(0.360)*	(3.175)	(0.292)§	(0.077)	(0.478)
		(0.012)†‡	(0.068)	(0.006)	(0.002)	(0.011)

Tissue weights and ratio of tissue weights per 100 g of body weight (indicated in parentheses) in Purina-sedentary, sucrose-sedentary, Purina-trained, and sucrose-trained animals. Tissue wet weight is in g and g/100 g body wt. *n* Denotes the number of animals. The data include additional animals of the same study that were only subjected to analysis of adipocyte glucose metabolism (not reported here). * $P <$ 0.01 from Purina-sedentary (controls) animals. † $P < 0.05$ from Purina-trained animals. ‡ $P < 0.01$ from Purina-trained animals. § $P <$ 0.05 from sucrose-sedentary animals.

vations (2, 13, 14, 17, 22, 23, 26, 34) by demonstrating that sucrose feeding increases basal and stimulated insulin levels not only in sedentary but also in trained animals (Fig. 4). Indeed, glucose-stimulated insulin levels of sucrose-trained animals remained as high as those of sucrose-sedentary rats. Thus sucrose feeding obtunds the well-documented (3, 21, 24, 32) sparing effect of exercise training on glucose-stimulated insulin response. Although exercise training normalized basal insulin of sucrose-trained animals, this effect took place at plasma levels significantly higher than those of Purina-trained animals. It has been reported that exercise training reduces pancreatic insulin secretion and simultaneously stimulates hepatic insulin degradation, at least to a certain degree (33, 35). It is therefore possible that sucrose consumption reverses the effects of exercise at the levels of both insulin secretion and degradation, but this still remains to be directly confirmed. However, it is known that prolonged pancreatic glucose stimulation in vivo increases the capacity of isolated islets for secreting insulin in vitro (9) and that exercise training inhibits the same parameter (35). Thus a competition between the stimulatory effects of sucrose consumption and the inhibitory action of exercise training at the level of pancreatic islet secretory mechanisms represents a likely explanation for the reversal of the effects of training by sucrose consumption on stimulated insulin levels.

The sucrose-induced hyperinsulinemia was accompanied by a reduction of basal glucose levels and by an improvement of glucose tolerance in sedentary animals (Figs. 2 and 3). Data from the literature are rather contradictory on this point. Indeed, glucose tolerance and insulin sensitivity have been reported as either improved (1, 22, 26), unchanged (13, 14, 23), or even reduced (2, 17, 34) after sucrose feeding, in spite of significant hyperinsulinemia in most cases. The reason for these apparent discrepancies is not clear but it most probably lies at the level of several different factors such as the relative proportions of carbohydrates, fat, and proteins in the diets, the total carbohydrate concentration, the total sucrose concentration, etc. It may also depend on the palatability of the various diets and on whether they induced hyperphagia, obesity, and/or hyperinsulinemia.

The sucrose diets used in the present studies were extremely rich in carbohydrate and sucrose. They contained as much as 87–89% of carbohydrates, of which 70–74% were taken from dissolved sucrose. A brief survey of recent studies revealed that, in general, very high-carbohydrate diets (70–85%) (or low-fat, low-protein diets) enhance insulin sensitivity of peripheral tissues, increase carbohydrate metabolism, and improve glucose tolerance (5, 18, 25, 32). In contrast, high-fat diets (low-carbohydrate, low-protein diets) lead to glucose intolerance and insulin resistance (1, 12, 24, 29). Thus the ratio of carbohydrates over fat in the diet appears to play a crucial role in modulating carbohydrate metabolism and glucose tolerance. This ratio is relatively high in laboratory chow that contains ~60% of carbohydrates and only 12% of fat (see METHODS). This probably represents one reason why it is so difficult to improve glucose tolerance in sedentary laboratory animals. Perhaps more studies

should be carried out with mixed diets that more closely resemble diets consumed by humans in developed countries.

The concentration of sucrose in the diet (as opposed to the total carbohydrate content) might also represent an important variable controlling insulin sensitivity and glucose tolerance (1). Indeed, laboratories having reported that sucrose consumption deteriorates glucose tolerance and increases insulin resistance generally used a diet that was relatively low in sucrose (32–58%) (2, 17, 34), whereas those finding the opposite used a diet that was very rich in sucrose (65–80%) (1, 22, 26). The present data support the hypothesis that a high-sucrose (and/or high-carbohydrate) diet improves glucose tolerance by causing hyperinsulinemia without compensatory insulin resistance.

The present high-carbohydrate diet can also be considered as a low-protein diet. It is therefore possible that a low-protein intake may have influenced glucose tolerance. However, for a similar low-protein content (8–12%), low-fat high-sucrose diets improve glucose tolerance (Fig. 3), whereas high-fat diets deteriorate it (1, 29). Thus we believe that, for a low-protein content, the principal factor modulating glucose tolerance is the ratio of carbohydrates over fat in the diet.

The mechanism by which sucrose consumption improves glucose tolerance remains to be defined. In unpublished experiments, we observed that if rats were fed granulated sucrose (mixed with Purina chow), there was no hyperphagia (probably because of the lack of palatability of Purina chow), no hyperinsulinemia, and glucose tolerance was not improved. This is in marked contrast to what was observed in the present experiments and might be interpreted as indicating that a hyperphagia leading to a hyperinsulinemia is required to observe the beneficial effects of sucrose consumption on glucose tolerance. However, we recently found that, although palatable high-fat diets lead to a similar hyperinsulinemia (and hyperphagia) as observed with the present high-sucrose diet, high-fat diets deteriorate glucose tolerance (29). Thus alterations of glucose tolerance cannot be explained by hyperinsulinemia alone.

There are many other situations where hyperinsulinemia can be dissociated from an improvement of glucose tolerance. On the one hand, it has been reported that high-carbohydrate and high-sucrose diets improve glucose tolerance in spite of a reduction of basal insulin levels and an unchanged insulin response (1, 5). On the other hand, high-carbohydrate diets have been found to improve glucose tolerance and glucose metabolism with (32) or without hyperinsulinemia (5), even though hyperinsulinemia per se may increase glucose metabolism in peripheral tissues (31). Thus we believe that the nature of the diet and the way it is administered (duration, palatability, etc.) represent the determining factors influencing glucose tolerance (possibly by influencing postinsulin receptor pathways) and that insulin may play a modulatory role that still remains to be defined. It should also be determined whether similar results would be obtained with an oral rather than with an intravenous glucose tolerance test.

Obesity and/or adiposity are often cited as major causes for insulin resistance and glucose intolerance (16). In the present experiments, sucrose-fed animals did not gain excess weight in spite of their high-energy intake (Fig. 1). A possible explanation for this observation is that sucrose feeding increased brown adipose tissue capacity for diet-induced thermogenesis (7). Indeed, it is known that hyperphagia induced by sucrose feeding or cafeteria diets stimulates the activity of the sympathetic nervous system, activates brown adipose tissue growth, increases the calorigenic response to catecholamines, and decreases body weight gain efficiency (6, 7). Although sucrose feeding did not induce obesity in the present experiments, it significantly increased parametrial adipose tissue weight, triglyceride content, and cellularity, apparently without affecting lean body mass (Fig. 5, Table 1). Thus, in spite of a possible increase in total adiposity, sucrose consumption improved glucose tolerance.

Feeding palatable diets rich in sucrose or fat leads to hyperinsulinemia but contrary to high-fat feeding, sucrose feeding generally does not result in insulin resistance (1, 12, 24, 29). This may be explained by a sucrose-induced enhancement of carbohydrate metabolism in peripheral tissues (26, 32). Skeletal muscles and white adipose tissue certainly represent major anatomical sites of glucose uptake (10), but brown adipose tissue might also play an important role in glucose metabolism (27). Considering that sucrose feeding stimulates brown adipose tissue growth and function (6, 7), it appears likely that this thermogenic tissue contributes significantly to the improvement in glucose tolerance found in sucrose-fed animals, although this remains to be directly confirmed.

The present results confirm previous observations (3, 21, 30) that, in Purina-fed animals, exercise training induces a significant reduction of basal and stimulated insulin levels without modifying glucose tolerance, suggesting that it increases insulin sensitivity of peripheral tissues (Figs. 2–4) (3, 21). It should be pointed out that these improvements were accompanied by normal body weight gains (Fig. 1) in spite of the intensive training program to which the female rats were submitted. In contrast to male rats, females generally do not exhibit a reduced growth curve during intensive training because they compensate the extra energy expended during exercise by increasing their food intake (8) (Fig. 1). Nevertheless, exercise training had a strong impact on body composition of female rats because it increased heart weight and decreased parametrial adipose tissue weight, triglyceride content, adipocyte size, and total tissue cellularity (8) (Fig. 5, and Table 1). Most probably, it inhibited the normal proliferation in parametrial white adipose tissue rather than stimulating adipocyte turnover (7, 8). Remarkably, this phenomenon was entirely reversed by sucrose consumption.

One of the most interesting findings of the present studies was that exercise training synergistically amplified the beneficial effects of sucrose consumption, both on basal glucose levels and glucose tolerance, resulting in an increase of 66% of glucose clearance rates (Fig. 3).

This effect of training appears to be specifically linked to a high-sucrose consumption since it generally does not occur when rats are consuming a high-carbohydrate diet such as Purina chow (Fig. 3) or when they are given high-fat diets (24, 30). It is unlikely that the synergistic effect of sucrose consumption and training resulted from an acute effect of either exercise or sucrose deprivation on muscle and liver glycogen levels. First, because the last bout of exercise occurred at least 40 h before the intravenous glucose tolerance test, and, second, because during that resting period, animals were free to eat their usual diet until the 10-h fasting period (water ad libitum only) that preceded the tests.

The marked improvement of glucose tolerance observed in sucrose-trained animals most probably results from a synergistic combination of two factors: an increased insulinemia induced by sucrose consumption occurring without compensatory insulin desensibilization and an enhanced insulin sensitivity of peripheral tissues caused by training (the interaction between sucrose feeding and exercise training on K values was significant) (Fig. 3). To that effect, it is known that exercise increases glucose uptake in skeletal muscles by mechanisms involving insulin-dependent and insulin-independent pathways (the insulinlike effect of exercise) (15). In sucrose-fed animals, these effects of exercise might have been amplified by a sucrose-induced increase of skeletal muscle glucose permeability and metabolism (26, 32), thereby explaining the marked improvement in glucose tolerance. Further studies are required to confirm this hypothesis and to determine whether tissues other than skeletal muscles are significantly involved in the enhancement of glucose disposal in exercised rats consuming sucrose.

These studies were supported in part by grants from the Canadian Diabetes Association and the Medical Research Council of Canada.

A. L. Vallerand and J. Lupien are holders of a Studentship from the Fonds de la Recherche en Santé du Québec.

Received 14 August 1985; accepted in final form 19 January 1986.

REFERENCES

1. ANDERSON, J. W., R. H. HERMAN, AND D. ZAKIM. Effect of high-glucose and high-sucrose diets on glucose tolerance of normal men. *Am. J. Clin. Nutr.* 26: 600–607, 1973.
2. BECK-NIELSEN, H., O. PEDERSEN, AND N. SCHWARTZ-SORENSEN. Effects of diet on the cellular insulin binding and the insulin sensitivity in young healthy subjects. *Diabetologia* 15: 289–296, 1978.
3. BERGER, M., F. W. KEMMER, K. BECKER, L. HERBERG, M. SCHWENEN, A. GJINAVCI, AND P. BERCHTOLD. Effect of physical training on glucose tolerance and on glucose metabolism of skeletal muscle in anesthetized normal rats. *Diabetologia* 16: 179–184, 1979.
4. BROOKS, G. A., AND T. P. WHITE. Determination of metabolic and heart rate responses of rats to treadmill exercise. *J. Appl. Physiol.* 45: 1009–1015, 1978.
5. BRUNZELL, J. D., R. L. LERNER, W. R. HAZZARD, D. PORTE, JR., AND E. L. BIERMAN. Improved glucose tolerance with high carbohydrate feeding in mild diabetes. *New England J. Med.* 284: 521–524, 1971.
6. BUKOWIECKI, L. J. Regulation of energy expenditure in brown adipose tissue. *Int. J. Obesity* 9, *Suppl.* 2: 31–42, 1985.
7. BUKOWIECKI, L. J., J. LUPIEN, N. FOLLÉA, AND L. JAHJAH. Effects of sucrose, caffeine, and cola beverages on obesity, cold resistance, and adipose tissue cellularity. *Am. J. Physiol.* 244 (*Regulatory Integrative Comp. Physiol.* 13): R500–R507, 1983.
8. BUKOWIECKI, L. J., J. LUPIEN, N. FOLLÉA, A. PARADIS, D. RICHARD, AND J. LEBLANC. Mechanism of enhanced lipolysis in adipose tissue of exercise-trained rats. *Am. J. Physiol.* 239 (*Endocrinol. Metab.* 2): E422–E429, 1980.
9. COLE, E. H., AND J. LOGOTHETOPOULOS. Glucose oxidation ($14CO_2$ production) and insulin secretion by pancreatic islets isolated from hyperglycemic and normoglycemic rats. *Diabetes* 23: 469–473, 1974.
10. CURTIS-PRIOR, P. B., J. TRETHEWEY, G. A. STEWART, AND T. HANLEY. The contribution of different organs and tissues of the rat to assimilation of glucose. *Diabetologia* 5: 384–391, 1969.
11. DESBUQUOIS, B., AND G. D. AURBAUCH. Use of polyethylene glycol to separate free and antibody-bound peptide hormones in radioimmunoassays. *J. Clin. Endocrinol. Metab.* 33: 732–739, 1971.
12. GRUNDLEGER, M. L., AND S. W. THENEN. Decreased insulin binding, glucose transport, and glucose metabolism in soleus muscle of rats fed a high-fat diet. *Diabetes* 31: 232–237, 1982.
13. HALLFRISCH, J., L. COHEN, AND S. REISER. Effects of feeding rats sucrose in a high-fat diet. *J. Nutr.* 111: 531–536, 1981.
14. HALLFRISCH, J., F. L. LAZAR, AND S. REISER. Effect of feeding sucrose or starch to rats made diabetic with streptozotocin. *J. Nutr.* 109: 1909–1915, 1979.
15. IVY, J. L., AND J. O. HOLLOSZY. Persistent increase in glucose uptake by rat skeletal muscle following exercise. *Am. J. Physiol.* 241 (*Cell Physiol.* 10): C200–C203, 1981.
16. JEANRENAUD, B. An overview of experimental models of obesity. In: *Recent Advances in Obesity Research. Proceedings of the Second International Congress on Obesity*, edited by G. A. Bray. Westport CT: Food and Nutrition Press, 1978, Vol. II, p. 111–123.
17. KANAREK, R. B., AND N. ORTHEN-GAMBILL. Differential effects of sucrose, fructose and glucose on carbohydrate-induced obesity in rats. *J. Nutr.* 112: 1546–1554, 1982.
18. KOLTERMAN, O. G., M. GREENFIELD, G. M. REAVEN, M. SAEKOW, AND J. M. OLEFSKY. Effect of a high-carbohydrate diet on insulin binding to adipocytes and on insulin action in vivo in man. *Diabetes* 28: 731–736, 1979.
19. LEBLANC, J., A. LABRIE, D. LUPIEN, AND D. RICHARD. Catecholamines and triiodothyronine variations and the calorigenic response to norepinephrine in cold-adapted and exercise-trained rats. *Can. J. Physiol. Pharmacol.* 60: 783–787, 1982.
20. LUPIEN, J., G. COTÉ, E. CARDINAL, A. L. VALLERAND, AND L. J. BUKOWIECKI. Effects of exercise training and sucrose intake on cellular proliferation in rat parametrial adipose tissue. In: *International Series on Sport Sciences: Biochemistry of Exercise*, edited by H. G. Knuttgen, J. A. Vogel, and J. Poortmans. Champaign, IL: Human Kinetics Publishers, 1983, vol. 13, p. 524–529.
21. MONDON, C. E., C. B. DOLKAS, AND G. M. REAVEN. Site of enhanced insulin sensitivity in exercise-trained rats at rest. *Am. J. Physiol.* 239 (*Endocrinol. Metab.* 2): E169–E177, 1980.
22. PORTHA, B., M.-H. GIROIX, AND L. PICON. Effect of diet on glucose tolerance and insulin response in chemically diabetic rats. *Metabolism* 31: 1194–1199, 1982.
23. REISER, S., AND E. BOHN, J. HALLFRISCH, O. E. MICHAELIS, M. KEENEY, AND E. S. PRATHER. Serum insulin and glucose in hyperinsulinemic subjects fed three different levels of sucrose. *Am. J. Clin. Nutr.* 34: 2348–2358, 1981.
24. RICHARD, D., A. LABRIE, D. LUPIEN, A. TREMBLAY, AND J. LEBLANC. Interactions between dietary obesity and exercise training on carbohydrate metabolism. *Int. J. Obesity* 6: 359–367, 1982.
25. SALANS, L. B., G. A. BRAY, S. W. CUSHMAN, E. DANFORTH, JR., J. A. GLENNON, E. S. HORTON, AND E. A. H. SIMS. Glucose metabolism and the response to insulin by human adipose tissue in spontaneous and experimental obesity: effects of dietary composition and adipose cell size. *J. Clin. Invest.* 53: 848–856, 1974.
26. SALANS, L. B., J. E. FOLEY, L. J. WARDZALA, AND S. W. CUSHMAN. Effects of dietary composition on glucose metabolism in rat adipose cells. *Am. J. Physiol.* 240 (*Endocrinol. Metab.* 3): E175–E183, 1981.
27. TRAYHURN, P. Fatty acid synthesis in vivo in brown adipose tissue, liver and white adipose tissue of the cold-adapted rat. *FEBS Lett.* 104: 13–16, 1979.
28. VALLERAND, A. L., J. LUPIEN, AND L. J. BUKOWIECKI. Interactions of cold exposure and starvation on glucose tolerance and insulin response. *Am. J. Physiol.* 245 (*Endocrinol. Metab.* 8): E575–E581, 1983.
29. VALLERAND, A. L., J. LUPIEN, AND L. J. BUKOWIECKI. Cold

exposure reverses the diabetogenic effect of high-fat feeding. *Diabetes.* In press.

30. VALLERAND, A. L., J. LUPIEN, Y. DESHAIES, AND L. J. BUKOWIECKI. Intensive exercise training does not improve intravenous glucose tolerance in severely diabetic rats. *Horm. Metab. Res.* 18: 77–79, 1986.
31. WARDZALA, L. J., M. HIRSHMAN, E. POFCHER, E. D. HORTON, P. M. MEAD, S. W. CUSHMAN, AND E. S. HORTON. Regulation of glucose utilization in adipose cells and muscle after long-term experimental hyperinsulinemia in rats. *J. Clin. Invest.* 76: 460–469, 1985.
32. WELLE, S. L., AND R. G. CAMPBELL. Improved carbohydrate tolerance and stimulation of carbohydrate oxidation and lipogenesis during short-term carbohydrate overfeeding. *Metabolism* 32: 889–893, 1983.
33. WIRTH, A., G. HOLM, AND P. BJORNTORP. Effect of physical training on insulin uptake by the perfused rat liver. *Metabolism* 31: 457–462, 1982.
34. WRIGHT, D. W., R. I. HANSEN, C. E. MONDON, AND G. M. REAVEN. Sucrose-induced insulin resistance in the rat: modulation by exercise and diet. *Am. J. Clin. Nutr.* 38: 879–883, 1983.
35. ZAWALICH, W., S. MATURO, AND P. FELIG. Influence of physical training on insulin release and glucose utilization by islet cells and liver glucokinase activity in the rat. *Am. J. Physiol.* 243 (*Endocrinol. Metab.* 6): E464–E469, 1982.