Glyceroneogenesis Is Reduced and Glucose Uptake Is Increased in Adipose Tissue from Cafeteria Diet–Fed Rats Independently of Tissue Sympathetic Innervation

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Abstract

The pathways of glycerol-3-P (G3P) generation were examined in retroperitoneal (RETRO) and epididymal (EPI) adipose tissues from rats fed a cafeteria diet for 3 wk. The cafeteria diet induced marked increases in body fat mass and in the plasma levels of insulin and triacylglycerol (TAG). RETRO and EPI from cafeteria diet–fed rats had increased rates of norepinephrine turnover (143 and 60%, respectively) and of de novo fatty acid (FA) synthesis (58 and 98%), compared with controls fed a balanced commercial diet. Cafeteria diet feeding induced marked increases in RETRO and EPI in vivo rates of glucose uptake (52 and 51%, respectively), used to evaluate G3P generation via glycolysis, as well as in glycerokinase activity (119 and 36%) and TAG-glycerol synthesis from glycerol (56 and 71%, respectively). In contrast, there was a marked reduction of glyceroneogenesis in RETRO and EPI from cafeteria diet–fed rats, which was evidenced by the significant decreases of P-enolpyruvate carboxykinase (PEPCK-C) activity (48 and 36%) and TAG-glycerol synthesis from pyruvate (45 and 56%, respectively). Denervation of RETRO from cafeteria diet–fed rats reduced the activity of glycerokinase by 50%, but did not affect glucose uptake or PEPCK-C activity and TAG-glycerol synthesis from pyruvate by the tissue. The data show that glyceroneogenesis can also be inhibited to adjust the supply of G3P to the existing rates of FA esterification and TAG synthesis and suggest that this adjustment is made by reciprocal changes in the generation of G3P from glucose via glycolysis and from glyceroneogenesis, independently from G3P production by glycerokinase.


Introduction

To meet the energy demands of peripheral tissues, white adipose tissue (WAT) needs adequate stores of triacylglycerol (TAG). Preservation of these stores requires a continuous supply of glycerol-3-phosphate (G3P) to esterify newly synthesized or preformed fatty acid (FA). Because WAT has relatively low levels of glycerokinase (GyK), the only generally recognized source of G3P for FA esterification in WAT was, for many years, glucose, via dihydroxyacetone-P in the glycolytic pathway and conversion to G3P by glycerophosphate dehydrogenase (Fig. 1). Although it was demonstrated 4 decades ago (1–4) that pyruvate and glycogenic amino acids can also be converted to TAG-glycerol through glyceroneogenesis at appreciable rates in WAT, the importance of this pathway as a supplier of G3P for lipid metabolism has been fully recognized only recently [see (5) and (6) for recent reviews]. Glyceroneogenesis involves the carboxylation of pyruvate to oxaloacetate, decarboxylation of oxaloacetate to phosphoenolpyruvate by cytosolic phosphoenolpyruvate carboxykinase (PEPCK-C), and, subsequently, the production of G3P through a partial reversal of glycolysis (Fig. 1). The key glyceroneogenic enzyme was determined to be PEPCK-C (1,3), and a number of studies, recently reviewed (7), have been published on the control of its gene transcription.

Although the importance of glyceroneogenesis has been recognized, its contribution to the supply of the G3P used for TAG synthesis in different physiological conditions has not been fully investigated. In the initial studies mentioned above (1,4) it was shown that glyceroneogenesis is increased in WAT from food-deprived and diabetic rats. We demonstrated several years ago that the adaptation of rats to a high protein, carbohydrate-free (HP) diet induces an increase in WAT glyceroneogenic activity, evidenced by an increased activity of PEPCK-C (8) and...
by increased rates of incorporation of nonglucose substrates into TAG-glycerol in vivo (9) and in vitro, by tissue fragments (8) or adipocytes (10). Because the use of glucose in vivo and the glycolytic flux are reduced in WAT from HP diet–adapted rats (11), the increased glyceroneogenesis seemed to represent a compensatory mechanism for the reduced generation of G3P via glycolysis (9). The results in rats adapted to a carbohydrate-free diet are consistent with those obtained in the initial studies mentioned above (1,4) of food-deprived and diabetic rats: situations in which the use of glucose by WAT is reduced. In contrast to food deprivation and diabetes, however, adaptation to the HP diet induces a reduction of WAT lipolytic activity (12,13), a finding that is inconsistent with the hypothesis that glyceroneogenesis acts to restrain an excessive mobilization of FA (2).

To obtain more information about the control of G3P supply for TAG synthesis in WAT, we investigated the state of the pathways of G3P production in WAT from rats fed a cafeteria diet. Unlike food deprivation, diabetes, or a HP diet, the cafeteria diet provides substantial amounts of carbohydrates and induces increased rates of WAT FA and TAG synthesis, with accumulation of body fat. Our main objective was to evaluate the generation of G3P via glycolysis, by direct phosphorylation of glyceraldehyde 3-phosphate dehydrogenase, and via glyceroenogenesis in retroperitoneal (RETRO) and epididymal (EPI) adipose tissues from cafeteria diet–fed rats, and verify the effects of previous unilateral sympathetic denervation of RETRO adipose tissue on these processes. The effects of the diet on in vivo rates of FA synthesis on the activity of lipoprotein lipase (LPL) and on the sympathetic activity of adipose tissue were also investigated.

Materials and Methods

Male Wistar rats weighing 45–55 g were obtained from the Faculty colony, which has remained closed for ~50 y. They were housed in suspended wire-bottom cages in a room kept at 25 ± 2°C with a 12 h light–12 h dark cycle. The rats were fed for 3 wk a cafeteria diet, which consisted of a standard balanced diet [Nuvilab CR1, Nuvital, Brazil (22% protein, 55% carbohydrate, and 4.5% lipid)] supplemented each day with 4 different lipid-rich palatable items selected from a list of 12 (biscuit, chocolate roll, chocolate wafers, nougat, peanut candy, potato chips, and toast). In addition, the water offered to these rats contained 20% sucrose. Control rats were fed the commercial diet only and consumed water ad libitum. The energy intake of the control rats, estimated from the daily intake and composition of the commercial diet, was 209 ± 4 kJ · 100 g body weight (bw)⁻¹ · d⁻¹ (mean ± SEM). In rats fed the cafeteria diet, the energy intake, which included the amount and composition of palatable items and the volume of water consumed, was ~40% higher (293 ± 13 kJ · 100 g bw⁻¹ · d⁻¹) than in controls. In cafeteria diet–fed rats, protein contributed 15 ± 1%, carbohydrate 65 ± 1%, and lipid 20 ± 1% of the energy intake, compared with 25, 63, and 12%, respectively, in rats fed the control diet. The rats weighed 220–240 g when used for the experiments which were always performed in the fed state between 0800 and 1000 h. For tissue removal, the rats were killed by cervical dislocation. Care and treatment of the rats received prior institutional approval by the Ethical Committee of the University of São Paulo.

**RETRO adipose tissue denervation.** The left RETRO adipose tissue depot was surgically denervated as described by Cantu and Goodman (14). The rats were used in the experiments 7 d after surgery, when the tissue norepinephrine (NE) content was reduced to ~30–40% of that in the contralateral, intact tissue, which was used as control.

**WAT NE turnover rates and NE content.** WAT NE turnover rates were estimated from the decline of tissue NE levels after inhibition of catecholamine synthesis with 6-hydroxydopamine and 6-hydroxydopamine (a-MT, Sigma). The procedure used and the technique of NE measurement have been described in detail (15).

**In vivo rates of WAT glucose uptake.** The procedure, based on the method of Sokoloff et al. (16) as modified by Ferre et al. (17), was as previously described (18). Briefly, 2-deoxy-[¹⁴C]glucose (2-DG) 30 μCi (11 Ci/mmol) in 0.5 mL of 0.9% NaCl was injected intravenously and serial blood samples were taken to determine the concentrations of glucose and of 2-DG (in terms of radioactivity). After 60 min, the rats were killed and adipose tissues were removed to measure the content of 2-DG-6-phosphate (2-DG-P) (17). Rates of glucose uptake were calculated from the 2-DG/glucose ratio vs. time curves and tissue 2-DG-P (16).

**Adipocytes isolation.** The rats were killed and EPI and RETRO adipose tissues were removed. Tissues from 4 to 10 rats were pooled and disaggregated with collagenase, according to the method of Robbeld (19), using a previously described medium (13) supplemented with 1 mmol/L of pyruvate or glycerol. After continuous shaking for 25–35 min at 37°C the adipocytes were filtered through a 300-μm nylon mesh and washed 3 times with the same medium.

**Incorporation of 1-¹⁴C-pyruvate or U-¹⁴C-glycerol into TAG-glycerol.** Aliquots of adipocyte suspension containing ~600,000 cells were incubated for 1 h at 37°C with constant shaking in 1 mL of glucose-free Krebs-Henseleit buffer, pH 7.4, supplemented with 1% FA-free albumin and containing 1-[¹⁴C]pyruvate or U-[¹⁴C]glycerol (1 mmol/L, 1 μCi). The procedures used for lipid extraction, isolation, and counting of ¹⁴C-TAG-glycerol were as previously described (20).

**In vivo rates of FA synthesis.** Fed rats were injected i.p. with 3 H2O (3 mCi in 0.5 mL saline). After 1 h they were killed by decapitation, blood samples were collected for plasma water specific radioactivity determination, and EPI and RETRO adipose tissues were rapidly removed for measurement of label incorporation into TAG. The techniques used for lipid extraction, isolation of the TAG-fatty acids, radioactivity counting, and plasma water specific radioactivity determination have been previously described (21).

**Enzyme activity measurement.** PEPCK-C activity was assayed by the method of Chang and Lane (22) in 100,000 g supernatants, after homogenization of EPI and RETRO adipose tissues in 20 mmol/L triethanolamine buffer, pH 7.5, containing 0.2 mol/L sucrose, 5 mmol/L mercaptoethanol and 1 mmol/L EDTA. The incorporation of [¹⁴C]bicarbonate (2 μCi) into an acid-stable product was determined in an assay mixture of identical composition as that used in a previous study (20). The protein content of homogenates was determined by the bicinchoninic acid method of Sokoloff et al. (16) as modified by Ferre et al. (17), was as previously described (18). Briefly, 2-deoxy-[¹⁴C]glucose (2-DG) 30 μCi (11 Ci/mmol) in 0.5 mL of 0.9% NaCl was injected intravenously and serial blood samples were taken to determine the concentrations of glucose and of 2-DG (in terms of radioactivity). After 60 min, the rats were killed and adipose tissues were removed to measure the content of 2-DG-6-phosphate (2-DG-P) (17). Rates of glucose uptake were calculated from the 2-DG/glucose ratio vs. time curves and tissue 2-DG-P (16).
acid method (23). GyK activity was measured, following the recommendations of Newsholme et al. (24), in 200 g supernatants obtained after homogenization of the tissues in ice-cold 1% KCl in 1 mmol/L EDTA. The composition of the assay mixture, which contained U-[14C]glycerol, and the isolation of labeled glycerol phosphate were previously described (25). LPL activity was assayed by the method of Nilsson-Ehle and Schotz (26) in 17,000 g supernatants of WAT in 0.25 mol/L sucrose, 1 mmol/L EDTA buffer, and 20 kU/L heparin (pH 7.4). The composition of the assay mixture, which contained glycerol tril[1-14C]oleate, and the isolation technique of 14C-FA produced were previously described (27). The protein content of the homogenate used in GyK and LPL assays was determined by the method of Lowry et al. (27).

Other methods of chemical analysis. Plasma glucose and TAG concentrations were determined enzymatically, using commercial kits (Glucose PAP and Triglucérôides) from Labtest. Plasma free FAs levels were determined by the method of Dole and Meineitz (28) and the concentration of plasma insulin by radioimmunoassay was measured using a commercial kit (Coat-a-Count Insulin) from DPC (Diagnostic Products).

Statistical methods. Except for calculated rates of turnover, which were compared using 95% CIs as described by Taubin et al. (29), data are expressed as means ± SEM, and differences between groups were analyzed using unpaired or paired Student’s t test, with P < 0.05 as the criterion of significance.

Results

After 3 wk, the weight of 4 different adipose tissue depots (EPI, RETRO, inguinal, and mesenteric) were 1- to 2-fold greater in cafeteria diet–fed rats than in controls (Table 1). Plasma glucose and free FA concentrations did not differ between cafeteria diet–fed and control rats, but the concentrations of plasma insulin and TAGs were markedly higher in those fed the cafeteria diet (Table 1).

De novo FA synthesis, estimated with 3H2O, was markedly greater in both RETRO and EPI adipose tissue from rats fed the cafeteria diet than in rats fed the control diet (Fig. 2A), a finding consistent with their high plasma insulin concentration. Utilization of preformed FAs incorporated into TAG from circulating lipoproteins also was greater in cafeteria diet–fed rats, as determined from the higher activity of LPL in both tissues (Fig. 2B).

NE turnover rate, an indicator of the sympathetic flux, was higher in both RETRO and EPI from rats fed the cafeteria diet.

**TABLE 1** Body and adipose tissue depot weights and plasma concentrations of insulin, glucose, free fatty acid, and triacylglycerol from cafeteria diet–fed and control rats

<table>
<thead>
<tr>
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<th>Control diet</th>
<th>Cafeteria diet</th>
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<tr>
<td>Body weight, g</td>
<td>233 ± 6 (10)</td>
<td>234 ± 4 (11)</td>
</tr>
<tr>
<td>Epididymal WAT, g</td>
<td>1.01 ± 0.14 (5)</td>
<td>1.10 ± 0.19 (5)</td>
</tr>
<tr>
<td>Retroperitoneal WAT, g</td>
<td>0.65 ± 0.05 (5)</td>
<td>0.75 ± 0.10 (5)</td>
</tr>
<tr>
<td>Inguinal WAT, g</td>
<td>2.64 ± 0.22 (6)</td>
<td>3.24 ± 0.15 (6)</td>
</tr>
<tr>
<td>Mesenteric WAT, g</td>
<td>1.43 ± 0.06 (6)</td>
<td>1.64 ± 0.10 (6)</td>
</tr>
<tr>
<td>Insulin, pmol/L</td>
<td>216 ± 23 (8)</td>
<td>351 ± 34* (5)</td>
</tr>
<tr>
<td>Glucose, mmol/L</td>
<td>6.66 ± 0.28 (7)</td>
<td>7.05 ± 0.11 (7)</td>
</tr>
<tr>
<td>Free fatty acid, mmol/L</td>
<td>0.41 ± 0.04 (12)</td>
<td>0.49 ± 0.05 (11)</td>
</tr>
<tr>
<td>Triacylglycerol, mmol/L</td>
<td>0.81 ± 0.07 (9)</td>
<td>1.52 ± 0.17* (8)</td>
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1 Values are means ± SEM in all rats used in the biochemical analyses.  
2 In these 2 tissues, similar cafeteria diet–induced weight increases were observed in all rats used in the biochemical analyses.

Figure 2 Effect of cafeteria diet feeding on rates of de novo FA synthesis (A) and on the activity of LPL (B) of RETRO and EPI adipose tissues. Bars represent means ± SEM, n = 7 (A) or n = 12 (B). *P < 0.05 vs. control.

Figure 3 Effect of cafeteria diet feeding on the disappearance of endogenous NE in RETRO (A) and EPI (B) adipose tissues after α-methyltyrosine administration. Values are means ± SEM, n = 10 at each time. Half-time of NE disappearance (t1/2) was 10.7 h in RETRO and 11.2 h in EPI.

than in tissues from the balanced diet–fed controls (Fig. 3 and Table 2). The NE turnover increase induced by the cafeteria diet was more pronounced in RETRO, which had higher NE content and turnover rates than EPI in rats fed the control diet (Table 2).

The results of the experiments on G3P generation pathways (Fig. 4) show that, after 3 wk, rats fed the cafeteria diet had ~50% faster rates of in vivo glucose uptake in both RETRO and EPI than the control group (Fig. 4A). They also had greater GyK activity and capacity to synthesize TAG-glycerol from glycerol in vitro in both adipose tissues (Fig. 4B). Because the enzyme activities in cafeteria diet–fed rats were similar in the 2 tissues and the activity of the enzyme in control rats was higher in EPI than in RETRO, the % increase of GyK activity in the cafeteria diet rats relative to controls was higher in RETRO (Fig. 4B). The capacity to synthesize TAG-glycerol from glycerol in vitro, on the other hand, was greater in EPI than in RETRO in both cafeteria diet–fed and control rats, and the % increase was approximately the same in the 2 tissues (Fig. 4B). In contrast to its effects in the use of glucose, GyK, and TAG-glycerol synthesis from glycerol, the cafeteria diet induced a marked reduction in the activity of PEPPCK-C and the synthesis of TAG-glycerol from pyruvate in vitro by both RETRO and EPI (Fig. 4C). The activity of PEPPCK-C in both RETRO and EPI from rats fed the cafeteria diet was ~50% lower than in controls (Fig. 4C). TAG-glycerol synthesis from pyruvate decreased to almost the same values in RETRO and EPI from cafeteria diet–fed rats, but the % decrease was higher in EPI because, in control rats, this tissue had higher capacity to synthesize TAG-glycerol than RETRO (Fig. 4C).

Denervation of RETRO adipose tissue from cafeteria diet–fed rats resulted in a significant (~50%) reduction in the activity of glycerokinase (Fig. 5A), but it did not affect the rates of in
TABLE 2 Fractional (k) and calculated turnover rate (TR) of NE and NE content of RETRO and EPI adipose tissues from cafeteria diet–fed and control rats.

<table>
<thead>
<tr>
<th></th>
<th>k</th>
<th>TR</th>
<th>NE content</th>
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<tbody>
<tr>
<td></td>
<td>% h</td>
<td>pmol · total tissue⁻¹ · h⁻¹</td>
<td>pmol</td>
</tr>
<tr>
<td>Retropitoneal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>6.5 ± 0.6</td>
<td>23 (20–27)</td>
<td>360 ± 23</td>
</tr>
<tr>
<td>Cafeteria</td>
<td>13.4 ± 0.1 *</td>
<td>56 (48–65)</td>
<td>420 ± 12</td>
</tr>
<tr>
<td>Epididymal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>6.2 ± 0.1</td>
<td>15 (14–16)</td>
<td>242 ± 12 **</td>
</tr>
<tr>
<td>Cafeteria</td>
<td>9.1 ± 0.6 *</td>
<td>24 (20–29)</td>
<td>266 ± 35</td>
</tr>
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</table>

1 Values are means ± SEM, n = 10 or 95% CI, n = 10 at each time interval of the turnover experiments (Fig. 3); * P < 0.05 vs. control; ** P < 0.05 vs. retroperitoneal control.

vivo use of glucose (Fig. 5B). Also, neither the activity of PEPCK-C (Fig. 5C) nor the rates of incorporation of 14C-pyruvate into TAG-glycerol (Fig. 5D) were significantly affected by RETRO denervation.

Discussion

Our results can be summarized as follows: 1) the production of G3P by direct phosphorylation of glycerol is activated by the cafeteria diet, as clearly indicated by the increased activity of GyK and the higher rates of TAG-glycerol synthesis from glycerol in both tissues (Fig. 4); 2) the production of G3P from dihydroxyacetone in the glycolytic pathway is also activated by the cafeteria diet, as evidenced by the increased rates of in vivo glucose use (Fig. 4); and 3) in contrast to the increase in the generation of G3P by these 2 pathways, the cafeteria diet induced a reduction of the glyceroneogenic flux in RETRO and EPI adipose tissues, evidenced by the decreased PEPCK-C activity and the lower rates of TAG synthesis from pyruvate (Fig. 4).

Feeding rats a cafeteria diet seems to have produced the first situation in which a decreased glyceroneogenic flux was observed, suggesting that this process can also be inhibited to adjust the supply of G3P in a situation in which the production of this metabolite by the other pathways is activated. This finding supports the hypothesis that the activities of the G3P-generating pathways are regulated to maintain an adequate supply of the G3P needed for FA esterification and storage of TAG. Neither the use of glucose nor the glyceroneogenic activity of RETRO adipose tissue were affected by the marked reduction in GyK activity induced by denervation of the tissue (Fig. 5). It would thus appear that the generation of G3P from glucose and from glyceroneogenesis in WAT of rats can be regulated independently from the G3P production by GyK, which is normally used to recycle the glycerol derived from TAG hydrolysis. If this independent control exists in WAT from rats fed a cafeteria diet, in which the activity of the enzyme is relatively high, it probably also occurs in rats adapted to a carbohydrate-free diet, in which the activity of WAT GyK is even lower than in controls fed a balanced diet (R. H. Migliorini, unpublished data). Therefore, regardless of the availability of carbohydrates, the supply of G3P needed for FA esterification and TAG synthesis in each condition is solely controlled by reciprocal changes in the generation of G3P from glucose via glycolysis and from glyceroneogenesis.

The results of NE turnover measurements (Table 2, Fig. 3) are the first, to our knowledge, to show that cafeteria diet feeding, in addition to its activation of sympathetic flux to brown adipose tissue, also increases WAT sympathetic activity. This increase was probably induced by the high carbohydrate content of the diet (30), especially by the 20% sucrose in the drinking water. It has been recently found (31) that NE turnover rates increases in RETRO but not in EPI adipose tissue after supplementation of a standard rat diet with glucose or fructose for 6 d. After 3 wk, NE turnover rates were also increased in EPI fat from cafeteria diet–fed rats, although the increase was much less marked than in RETRO tissue (Table 2). Further experiments, including analysis of WAT lipolytic activity, are needed to clarify the mechanism

Figure 5 Effect of denervation on the activity of GyK (A); on in vivo rates of glucose uptake (B); on the activity of PEPCK-C (C); and rates of 14C-pyruvate incorporation into TAG-glycerol (D) by RETRO adipose tissue from cafeteria diet–fed rats. Bars represent means ± SEM, n = 12 (A); n = 6 (B); n = 10 (C) or n = 6 (D). * P < 0.05 vs. control.
and physiological importance of these effects of the cafeteria diet.

The discussion of the factors and biochemical mechanisms involved in the regulation of G3P production should start with the control of GyK. Contrary to the notion that the activity of GyK is negligible or nonexistent in WAT, our data show that, despite its relatively low activity in control rats, WAT GyK showed to be controllable, with its activity increasing markedly in cafeteria diet–fed rats (Fig. 4). Previous studies from this laboratory have demonstrated that, in brown adipose tissue, GyK is under direct control by the sympathetic nervous system, with its activity and expression changing in parallel to increases or decreases in the tissue sympathetic flow (23,32). That this control may also exist in WAT is suggested by our present findings that the increased sympathetic activities of RETRO and EPI adipose tissues are accompanied by increased levels of GyK activity, and that denervation of the RETRO tissue reduces the activity of the enzyme (Figs. 4 and 5).

With respect to the biochemical mechanisms involved in the regulation of G3P generation via glycolysis and from glyceroneogenesis, 2 factors, insulin and long chain FA, probably had an important role in WAT from rats fed both cafeteria and carbohydrate-free diets. In addition to its stimulation of adipocyte glucose uptake and of glycolytic flux, insulin inhibits the transcription of the PEPCK-C gene (7), a key enzyme of glyceroneogenesis. FA are potent positive modulators of adipose tissue glyceroneogenesis. Thus, it has been found that the expression of PEPCK-C is strongly stimulated by long chain, unsaturated FA in both 3T3-F442A (33) and normal adipocytes (34). In addition, the transcription factor PPARγ, which is highly expressed in adipose tissue, can be activated by FA and has been found to have an important role in the control of adipose tissue PEPCK-C (35). Our data indicate that insulin is the predominant factor in the control of WAT G3P production in cafeteria diet–fed rats. In these rats, TAG synthesis is very active, with part of the FA originating from insulin-induced increased rates of de novo FA synthesis and part consisting of preformed FA taken from circulating VLDL or chilomicra, as evidenced by the high levels of TAG and increased activity of WAT LPL (Table 1, Fig. 2). Thus, the inhibitory effect of the hormone on PEPCK-C prevailed over the stimulatory effect of preformed FAs; the insulin-induced activation of G3P generation from glucose was more than sufficient to meet the increased demand of the metabolite for FA esterification. Rats adapted to a carbohydrate-free diet, on the other hand, have low levels of plasma insulin, and markedly reduced rates of glucose use and of de novo synthesis of FA by WAT (11,36). Despite the reduced supply of newly synthesized FA, these animals are able to maintain considerable amounts of adipose tissue (37) esterifying preformed FA, most of them derived from the diet, as evidenced by the increased activity of WAT LPL (10). In these rats, the reduced use of glucose is insufficient to maintain an adequate supply of G3P, and both the low levels of insulin and the increased uptake of FA contribute to activate WAT glyceroneogenesis. The importance of FA for the stimulation of WAT glyceroneogenesis has been shown by our recent finding that the administration of Triton WR1339, which blocks the removal of FA incorporated into TAG of lipoproteins, to rats adapted to a carbohydrate-free diet, caused a marked reduction in WAT PEPCK-C activity and in the synthesis of TAG-glycerol from pyruvate (10).

In summary, the data of our present work show that feeding rats a cafeteria diet induces in both RETRO and EPI adipose tissues increases in the generation of G3P from glycerol, by direct phosphorylation by GyK, and from glucose, via glycolysis, that are accompanied by a reduction of the glyceroenogenic flux. RETRO tissue denervation markedly reduced GyK activity but did not affect the use of glucose or glyceroneogenesis. The data suggest that the supply of G3P needed for FA esterification and TAG synthesis is solely controlled by reciprocal changes in the generation of G3P from glucose (via glycolysis) and from glyceroneogenesis. Experiments in vivo are needed to firmly establish this hypothesis.

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Literature Cited


WAT glyceroneogenesis in cafeteria diet–fed rats


