Comparative Study of the Lipogenic Potential of Human and Rat Adipose Tissue

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The reported low activity of lipogenic enzymes (especially adenosine triphosphate [ATP]-citrate lyase) in human adipose tissue led to the general conclusion that in humans lipogenesis occurs primarily in the liver. However, recent studies indicate that the liver plays a minor role in de novo lipogenesis and suggest that adipose tissue may be the principal lipogenic human tissue. In an attempt to resolve these contradictions we reinvestigated the lipogenic potential of human adipose tissue and compared with adipose tissue of rats fed a high-fat diet for 2 weeks and fasted overnight before death. These conditions mimic the nutritional state of patients at the moment of tissue sampling. We found that overnight fasting of the rats maintained previously for 12 days on a high-fat diet caused a decrease of ATP-citrate lyase of about 7-fold. Thus, in human adipose tissue, the mean activity of ATP-citrate lyase was approximately 8 times lower than in rats fed a high-fat diet and fasted overnight, and about 50 times lower than in rats maintained on normal laboratory diet. Unlike ATP-citrate lyase, fatty acid synthase (FAS) activity was only slightly lower in human adipose tissue than in rats maintained on a normal laboratory diet. Comparable FAS activity was found when rats were fed a high-fat diet and fasted overnight. The average activities of human adipose tissue acetyl-coenzyme A carboxylase, malic enzyme, and glucose-6-phosphate dehydrogenase were approximately 3-, 4-, and 6-fold lower than in adipose tissue from rats fed a high-fat diet and fasted overnight before tissue sampling, while the activity of 6-phosphogluconate dehydrogenase in humans was higher than in rat adipose tissue. No significant differences in lipogenic enzyme activities were found between male and female and between lean and obese patients. The rate of fatty acid synthesis in intact pieces of human adipose tissue was approximately 5 times lower than in adipose tissue pieces of rats fed a high-fat diet and fasted overnight before tissue samples were taken. The comparison of the lipogenic potential of humans and rats (maintained on the diet to mimic the nutritional state of patients at the time of tissue sampling) suggests that human adipose tissue is an important site of fatty acid synthesis.

IT IS COMMONLY KNOWN that an excessive provision of carbohydrates in humans results in an anabolic state in which body weight and lipid stores increase. This indicates that de novo fatty acid synthesis from carbohydrates occurs in humans. However, the rate and organ localization of this process is still controversial. Shrago et al[1-4] reported that human adipose tissue, unlike that of the rat, contains little or no adenosine triphosphate (ATP)-citrate lyase activity, an enzyme that catalyzes the reaction considered to be the primary source of acetyl-coenzyme A for fatty acid synthesis. These investigators showed that in human adipose tissue, other enzymes involved in fatty acid synthesis, including fatty acid synthase and acetyl-coenzyme A carboxylase, are also present at negligible levels.[1-4] Starvation-refeeding conditions in rats produce consistently marked adaptative changes in white adipose tissue lipogenic enzyme activity,[5] but no such changes were observed in human adipose tissue.[2,4] Furthermore, the rate of fatty acid synthesis from glucose, as measured in vitro, is much lower in human versus rat adipose tissue.[3,6] Bjorntorp and Sjostrom[6] concluded that healthy subjects on a high-carbohydrate hypercaloric diet convert only 1 to 2 g glucose to fatty acids per day.

These observations led to the general belief that lipogenesis in the human occurs primarily in the liver. However, hepatic catheterization studies of malnourished patients receiving a glucose load demonstrated that only approximately 50% of whole-body lipogenesis occurs in the splanchnic region, suggesting that peripheral adipose tissue makes a substantial contribution to this process.[7] Moreover, other studies have shown that human adipose tissue is capable of readily incorporating the radioactivity of 1,5-^{14}C citrate into fatty acids.[8] Chascione et al[9] reported that the rate of lipogenesis in adipose tissue of rats and humans responds similarly to changes in carbohydrate intake. They showed that in malnourished patients on a high-carbohydrate diet, adipose tissue may account for up to 40% of whole-body lipogenesis.[9] Recent studies indicate that the liver plays a minor role in de novo lipogenesis and suggest that adipose tissue may be the principal lipogenic tissue in humans.[10] In addition, it has been demonstrated recently that glucose utilization, as well as the activity of lipogenic enzymes, are increased by insulin in cultured human adipocytes.[11] Furthermore, it has been demonstrated that insulin increases the transcription rate of the FAS gene in human adipocytes.[12]

As already mentioned, the general belief that lipogenesis in humans occurs primarily in the liver is based mainly on the comparison of lipogenic enzyme activities in human and rat adipose tissue. The normal diet of laboratory rats contains a high concentration of carbohydrate and a low concentration of fat. The human diet contains a much higher level of fat. Considering that a high-fat diet causes a decrease of lipogenic enzyme activities,[13,14] one can suppose that if rats ate a normal human diet, their lipogenic enzyme activities would be significantly reduced. It should also be emphasized that most of the studies have been performed on human adipose tissue taken after an overnight fast, which preceded the surgical removal of the tissue. This could be another reason for the low lipogenic enzyme activities in human adipose tissue.

In an attempt to resolve some of these contradictions, the present study reinvestigated the activity of lipogenic enzymes

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and the rate of fatty acid synthesis in intact pieces of human adipose tissue compared with adipose tissue of rats fed a high-fat diet for 2 weeks and fasted overnight before death. In our opinion, these conditions mimic the nutritional state of patients at the time of tissue sampling, and make the comparison between the activities in rat and human tissue more reliable.

SUBJECTS AND METHODS

Patients

Patients (free of nutritional and metabolic disorders) were admitted to the First Department of Surgery, Medical University of Gdansk, to undergo surgery. The subjects included males and females, lean (body mass index [BMI] < 25 kg/m^2 for men and women) and obese (BMI > 30 kg/m^2 for men and women) individuals aged between 40 and 79 years (56 ± 15). During the preoperative days, patients were allowed a caloric intake of about 2,000 kcal/d, 45% of which was derived from carbohydrate, 35% from fat, and 20% from protein (routine hospital diet). During this period, no significant changes in body weight were observed. Fasting blood glucose was normal in all subjects. The plasma cholesterol concentration was normal in all patients (range, 81 to 188 mg/dL). Plasma triacylglycerol in 70% of the patients was in the normal range (51 to 128 mg/dL). An elevated level (180 to 285 mg/dL) of plasma triacylglycerol was found in 30% of the patients. After an overnight fast, patients were taken to the operating room for elective surgery, at which they donated subcutaneous and omental adipose tissue. The preoperative medication for all patients was dormicum or dolarganum plus relanium. General anesthesia was induced and maintained by a mixture of oxygen (35%), nitrous oxide (65%), and fentanil.

No other medications were used prior to obtaining the specimens. The reason for the surgery for most patients was cholelithiasis (female) and cholelithiasis, cancer of the stomach or colon (at early stages), or hernia (male). The adipose tissue (approximately 1 g) was placed in room-temperature buffered saline and immediately taken to the laboratory.

All studies were approved by the Ethics Committee of the Medical University of Gdansk, Gdansk, Poland, and all patients provided informed consent to participate in the study.

Animals

Male Wistar rats weighing approximately 230 g were used for the experiments. The rats were housed in wire mesh cages at 20°C with alternating 12-hour light/dark and fed ad libitum with a commercially available standard laboratory diet (composition of the diet published recently[5]) and tap water. A randomly selected group of animals were fed for 12 days with a high-fat diet prepared as described previously[14] containing (in wt/wt): 45% lard, 40% casein, 10% cellulose, 1.5% $CaCO_3$, 1.75% KH_2PO_4, 1.25% NaCl, and 0.5% $MgSO_4$.

Control (fed normal laboratory diet) and overnight-fasted (fed normal laboratory diet or a high-fat diet) rats were decapitated. The epididymal white adipose tissue was removed and placed in buffered saline.

Enzyme Activity Assay

Approximately 1 g adipose tissue (either human or rat) was rinsed, blotted dry, weighed, and placed in 8 mL ice-cold 20-mmol/L Tris hydrochloride buffer (pH 7.8) containing 0.2% Triton X-100. The tissue was minced finely with scissors, homogenized manually with a Teflon-pestle homogenizer, and centrifuged at 30,000× *g* for 20 minutes. After removal of the fat cake, the resulting supernatant was decanted, and the pellet was resuspended in 5 mL isolation medium, rehomogenized, and centrifuged as before. The supernatant was combined with that obtained after the first centrifugation step and used for enzyme assay.

The activities of fatty acid synthase ([FAS] EC 2.3.1.85), ATP-citrate lyase (EC 4.1.3.8), malic enzyme (EC 1.1.1.40), glucose-6-phosphate dehydrogenase (EC 1.1.1.49), 6-phosphogluconate dehydrogenase (EC 1.1.1.44), isocitrate dehydrogenase (EC 1.1.1.42), lactate dehydrogenase (EC 1.1.1.27), and malate dehydrogenase (EC 1.1.1.37) were measured as described previously.[15-18] All assays were performed in duplicate at 37°C using a Beckman DU 68 spectrophotometer (Beckman Instruments, Fullerton, CA). The absorbance change both against time and against enzyme concentration was linear. Acetyl-coenzyme A carboxylase (EC 6.4.1.2) activity was measured by the $H^{14}CO_3^-$ fixation assay according to the method of Salati and Clarke.[19] The experiments with human and rat adipose tissue were performed at the same time for comparison. If 2 pieces of human adipose tissue were taken separately, the differences in repeat measures did not exceed 10%.

Measurement of Lipogenesis

Samples of adipose tissue (approximately 0.3 g or 1 g in the case of rat and human, respectively) were cut with scissors into small pieces and incubated in 10 mL minimal essential medium containing 1% bovine serum albumin, 5% newborn calf serum, 10 IU/mL penicillin, 100 μg/mL streptomycin, 20 mmol/L HEPES, 26 mmol/L $NaHCO_3$, 5 mmol/L glucose, 100 nmol/L insulin, and 100 μCi ^3H_2O. The incubation was performed in polypropylene flasks in a humidified incubator at 37°C under 5% CO_2 and 95% air for 2 hours. At the end of incubation, tissue samples were removed, rinsed, and placed in 3 mL 30% NaOH. The tissue samples were saponified, and the fatty acid fraction was extracted as described previously.[20] Samples of the incubation medium were also taken for determination of the specific activity of radioactive water. The mass of ^3H_2O incorporated in lipids was calculated as dpm in the lipid fraction/specific activity of the medium ^3H_2O.

The data were analyzed for significance by Student's *t* test. A *P* value less than .05 was considered statistically significant.

Measurement of Plasma Triacylglycerol and Cholesterol Concentrations

Plasma triacylglycerol and cholesterol concentrations were analyzed by a standard enzymatic procedure (Boehringer, Mannheim, Germany). Protein assays were performed according to the method of Peterson.[21]

Chemicals

All nonradioactive substances were obtained from Sigma Chemical (St Louis, MO) or Boehringer. ^3H_2O and $NaH^{14}CO_3$ were obtained from Amersham Buchler (Braunschweig, Germany).

RESULTS

Tables 1 to 3 compare the activities of lipogenic and some other enzymes in human subcutaneous and omental and rat epididymal adipose tissue. The activity of ATP-citrate lyase is low in most human subjects studied. For instance, the mean activity in 10 lean women was 0.74 ± 53 nmol/min/mg protein (range, 0.27 to 1.7). It should be noted that there is great interindividual variation in ATP-citrate lyase (and other lipogenic enzymes) activity. Essentially similar results were obtained in omental adipose tissue.

Neither sex nor body weight markedly affected the ATP-citrate lyase activity. Thus, for comparative purposes (comparison between human and rat enzyme activities), the data were considered altogether regardless of sex and body weight (Tables 1 and 2). Overnight fasting of rats maintained previously on a standard laboratory diet caused a decrease of ATP-citrate lyase by about 2-fold. Approximately a 7-fold reduction of ATP-citrate lyase was observed in overnight-fasted rats maintained

Table 1. Activities of Lipogenic and Some Other Enzymes in Human Subcutaneous Adipose Tissue

	Enzyme Activity (nmol/min/mg protein)				
	Female		Male		
Enzyme	Lean	Obese	Lean	Obese	Altogether
ATP-citrate lyase	0.74 ± 0.53 (0.27-1.7) n = 10	0.51 ± 0.26 (0.17-0.91) n = 8	0.99 ± 0.96 (0.17-4.1) n = 16	2.09 ± 2.88 (0.23-7.0) n = 5	0.97 ± 1.24 (0.17-7.0) n = 39
Fatty acid synthase	0.92 ± 0.67 (0.24-2.5) n = 10	1.14 ± 1.06 (0.23-3.0) n = 8	1.03 ± 0.53 (0.42-2.1) n = 16	0.86 ± 0.49 (0.17-1.4) n = 5	1.00 ± 0.68 (0.17-3.0) n = 39
Acetyl-coenzyme A carboxylase	0.19 ± 0.11 (0.085-0.34) n = 6	0.09 ± 0.10 (0.035-0.31) n = 7	0.14 ± 0.06 (0.071-0.20) n = 4	0.08 ± 0.04 (0.035-0.12) n = 4	0.14 ± 0.09 (0.035-0.34) n = 21
Malic enzyme	12.7 ± 8.1 (4.8-31.0) n = 10	9.84 ± 7.06 (3.0-22.8) n = 8	12.2 ± 5.59 (4.6-26.0) n = 16	12.9 ± 11.1 (4.1-32.0) n = 5	11.9 ± 7.16 (3.0-32.0) n = 39
Glucose-6-phosphate dehydrogenase	2.51 ± 1.35 (0.45-4.3) n = 8	2.18 ± 1.57 (0.52-4.6) n = 7	3.1 ± 1.91 (0.5-8.1) n = 15	5.24 ± 2.73 (2.6-9.7) n = 5	3.09 ± 2.03 (0.45-9.7) n = 35
6-Phosphogluconate dehydrogenase	28.0 ± 9.35 (17.0-43.0) n = 9	21.9 ± 6.18 (12.0-32.0) n = 8	24.5 ± 7.73 (12.5-36.0) n = 15	24.0 ± 12.4 (7.9-42.0) n = 5	24.7 ± 8.48 (7.9-43.0) n = 36
Isocitrate dehydrogenase	40.3 ± 21.7 (15.0-86.0) n = 10	30.7 ± 18.9 (11.7-72.0) n = 8	38.4 ± 14.5 (12.0-59.0) n = 16	47.8 ± 32.2 (17.0-87.0) n = 5	38.5 ± 19.8 (11.7-87.0) n = 39
Lactate dehydrogenase	229 ± 85.0 (104-403) n = 10	196 ± 98.7 (88.0-399) n = 8	215 ± 78.7 (94.0-376) n = 16	175 ± 75.2 (109-265) n = 5	210 ± 83 (88.0-403) n = 39
Malate dehydrogenase	138 ± 78.1 (62.0-280) n = 10	124 ± 68.4 (59.0-280) n = 8	152 ± 66.5 (56.0-312) n = 16	132 ± 60.6 (59.0-204) n = 5	140 ± 68 (56.0-312) n = 39

NOTE. Results are the mean ± SD (range).

previously on a high-fat diet for 12 days. Therefore, the mean activity of ATP-citrate lyase in subcutaneous adipose tissue was approximately 50 times lower versus the rat maintained on a normal laboratory diet, but only approximately 8 times lower versus rats fed a high-fat diet and fasted overnight. It should be noted that in 1 subject, we found activity of ATP-citrate lyase comparable to that found in adipose tissue of rats fed a high-fat diet and fasted overnight (Tables 1 and 3). Unlike ATP-citrate lyase, the activity of FAS was only slightly lower in human adipose tissue than in rat maintained on normal laboratory diet. Comparable FAS activity was found when rats were fed a high-fat diet and fasted overnight (Tables 1 to 3). Acetyl-coenzyme A carboxylase, malic enzyme, glucose-6-phosphate dehydrogenase, and 6-phosphogluconate dehydrogenase activities were present in adipose tissue from all tested patients. No significant differences in acetyl-coenzyme A carboxylase and NADPH-producing enzymes were found between males and females and between control (lean) and obese patients. The mean activity of acetyl-coenzyme A carboxylase in human subcutaneous adipose tissue was approximately 5-fold lower than in adipose tissue from rats maintained on normal laboratory diet. After feeding rats with a high-fat diet for 12 days and fasting them overnight, acetyl-coenzyme A carboxylase activity decreased about 2-fold as compared with rats fed normal

Table 2. Activities of Lipogenic and Some Other Enzymes in Human Omental Adipose Tissue

	Enzyme Activities (nmol/min/mg protein)				
	Female		Male		
Enzyme	Lean	Obese	Lean	Obese	Altogether
ATP-citrate lyase	1.93 ± 1.45 (0.48-4.43) n = 10	0.58 ± 0.34 (0.25-1.27) n = 9	0.89 ± 0.76 (0.03-1.7) n = 17	1.28 ± 0.77 (0.59-2.72) n = 6	1.13 ± 1.01 (0.03-4.43) n = 42
Fatty acid synthase	1.34 ± 0.76 (0.5-1.6) n = 10	0.89 ± 0.49 (0.26-1.7) n = 9	0.8 ± 0.69 (0.03-2.74) n = 17	1.27 ± 0.89 (0.5-2.88) n = 6	1.01 ± 0.72 (0.03-2.88) n = 42
Acetyl-coenzyme A carboxylase	0.09 ± 0.02 (0.064-0.12) n = 4	0.12 ± 0.11 (0.052-0.15) n = 8	0.30 ± 0.12 (0.17-0.41) n = 5	0.11 ± 0.02 (0.094-0.14) n = 4	0.17 ± 0.08 (0.052-0.41) n = 21
Malic enzyme	14.3 ± 6.74 (5.5-27.0) n = 10	8.42 ± 4.3 (2.8-15.0) n = 9	11.0 ± 7.88 (4.2-37.0) n = 17	13.8 ± 8.63 (6.5-30.0) n = 6	11.7 ± 6.99 (2.8-37.0) n = 42
Glucose-6-phosphate dehydrogenase	6.15 ± 5.89 (1.45-21.4) n = 10	4.45 ± 4.77 (0.3-15.0) n = 8	7.24 ± 5.89 (1.8-19.0) n = 12	5.85 ± 4.17 (1.7-10.4) n = 4	6.1 ± 5.34 (0.3-21.4) n = 34
6-phosphogluconate dehydrogenase	31.1 ± 8.31 (12.0-42.0) n = 10	22.0 ± 7.56 (12.0-34.0) n = 8	23.6 ± 6.92 (13.0-33.5) n = 14	35.5 ± 23.2 (21.0-82.0) n = 6	27.2 ± 11.9 (12.0-82.0) n = 38
Isocitrate dehydrogenase	57.2 ± 24.4 (35.0-101) n = 10	40.0 ± 16.2 (22.0-76.0) n = 8	43.7 ± 16.7 (16.0-68.0) n = 15	43.1 ± 15.6 (26.0-61.0) n = 6	46.3 ± 19.2 (16.0-101) n = 39
Lactate dehydrogenase	254 ± 57.3 (188-346) n = 10	223 ± 88.1 (140-267) n = 9	222 ± 58.3 (123-322) n = 17	267 ± 163 (147-571) n = 6	237 ± 84.8 (123-571) n = 42
Malate dehydrogenase	141 ± 47.7 (82.0-233) n = 10	126 ± 44.6 (48.0-192) n = 9	144 ± 54.2 (71.0-250) n = 17	179 ± 123 (65.0-345) n = 6	145 ± 64.5 (48.0-345) n = 42

NOTE. Results are the mean ± SD (range).

Table 3. Activities of Lipogenic and Some Other Enzymes in Rat Adipose Tissue

Enzyme	Enzyme Activities (nmol/min/mg protein)		
	Control (n = 5)	Fasted Overnight (n = 5)	Fed High-Fat Diet/ Fasted Overnight (n = 5)
ATP-citrate lyase	59.8 ± 13.2 (46-79)	27.4 ± 11.3 (12-38)	8.0 ± 2.9 (3.2-11)
Fatty acid synthase	1.58 ± 0.26 (1.3-1.9)	0.9 ± 0.15 (0.83-1.2)	0.51 ± 0.19 (0.27-0.77)
Acetyl-coenzyme A carboxylase	0.74 ± 0.21 (0.55-1.06)	0.57 ± 0.20 (0.45-0.93)	0.39 ± 0.06 (0.28-0.45)
Malic enzyme	87.2 ± 32.1 (43-112)	65.2 ± 3.9 (60-69)	45.8 ± 5.3 (38-51)
Glucose-6-phosphate dehydrogenase	27.6 ± 11.4 (14-40)	21.3 ± 8.9 (12-33)	18.4 ± 2.3 (16-21)
6-phosphogluconate dehydrogenase	21.2 ± 3.6 (18-27)	14.7 ± 2.3 (11-17)	12.4 ± 3.4 (9-16)
Isocitrate dehydrogenase	95.0 ± 12.2 (79-110)	76.6 ± 6.1 (71-86)	80.4 ± 12.9 (70-102)
Lactate dehydrogenase	476 ± 32 (452-512)	334 ± 40 (275-367)	267 ± 56 (217-363)
Malate dehydrogenase	391 ± 79 (297-467)	320 ± 86 (232-441)	295 ± 87 (171-400)

NOTE. Results are the mean ± SD (range).

laboratory diet. This means that acetyl-coenzyme A carboxylase activity in human subcutaneous adipose tissue was less than 3-fold lower versus adipose tissue from rats fed a high-fat diet and fasted overnight before the tissue sample. It is interesting that in some human subjects, acetyl-coenzyme A carboxylase activity reached the value observed in rats fed a high-fat diet and starved overnight. The mean activity of malic enzyme in human subcutaneous adipose tissue was approximately 7-fold lower versus adipose tissue from rats maintained on normal laboratory diet. After feeding rats with a high-fat diet for 12 days and fasting them overnight, malic enzyme activity decreased about 2-fold as compared with rats fed normal laboratory diet. Thus, malic enzyme activity in human subcutaneous adipose tissue was only 4-fold lower versus adipose tissue from rats fed a high-fat diet and fasted overnight before the tissue sample. In some human subjects, malic enzyme activity reached the value observed in rats fed a normal laboratory diet. The activity of glucose-6-phosphate dehydrogenase was about 9- and 6-fold lower in human subcutaneous adipose tissue than in adipose tissue of rats maintained at normal conditions or fed a high-fat diet and fasted overnight, respectively. In contradiction to the experiments reported previously,[22] we found a relatively high activity of 6-phosphogluconate dehydrogenase in adipose tissue from all patients studied. We also measured the activity of enzymes that are not involved directly in fatty acid synthesis, i.e., isocitrate dehydrogenase, lactate dehydrogenase, and malate dehydrogenase, in human adipose tissue and in adipose tissue from rats fed a normal laboratory diet and high-fat diet. No significant differences in the activities of these enzymes were found between men and women, as well as between normal (lean) and obese patients. As expected, no significant effect of an overnight fast and high-fat diet was found on isocitrate, malate, and lactate dehydrogenase activities in rat adipose tissue. Furthermore, the activities of these enzymes were about 2- to 3-fold lower in human adipose tissue versus the rat tissue.

The rate of fatty acid synthesis in biopsies of human adipose tissue (taken from non-obese male patients) was approximately 5 times lower versus adipose tissue from rats fed a high-fat diet and fasted overnight before tissue sampling (Table 4). This is consistent with the lower activities of most lipogenic enzymes in human adipose tissue. Overnight fasting of rats maintained previously on a standard laboratory diet caused a decrease of fatty acid synthesis. A further reduction of fatty acid synthesis was observed in overnight-fasted rats maintained previously on a high-fat diet for 12 days. These differences were significant ($P < .05$) (Table 4).

DISCUSSION

The present study shows that feeding rats with a high-fat diet and fasting them overnight (dietary conditions that mimic the nutritional state of patients before surgery) resulted in a decrease of lipogenic enzyme activities and lipogenesis in white adipose tissue. Furthermore, these data indicate that the activities of lipogenic enzymes in human adipose tissue are comparable (FAS), higher (6-phosphogluconate dehydrogenase), or lower (acetyl-coenzyme A carboxylase, ATP-citrate lyase, malic enzyme, and glucose-6-phosphate dehydrogenase) versus adipose tissue of rats maintained on the diet that resembles the human diet. The present results also demonstrate that under comparable dietary conditions, lipogenesis is about 5 times lower in pieces of human adipose tissue versus pieces of rat

Table 4. In Vitro Fatty Acid Synthesis by Human and Rat Adipose Tissue

Species	Experimental Conditions	Rate of Fatty Acid Synthesis (μg ^{3}H/g wet tissue/h)
Human (n = 10)	Fasted overnight before surgery	6.14 ± 2.4 (2.21-9.65)
Rat (n = 5)	Fed high-fat diet and fasted overnight	30.3 ± 8.5 (16.8-37.4)
Rat (n = 5)	Fed normal laboratory diet and fasted overnight	40.5 ± 7.2 (30.0-48.0)
Rat (n = 5)	Fed normal laboratory diet	53.7 ± 12.0 (43.0-73.7)

NOTE. Human subcutaneous adipose tissue from a non-obese male subject was used. Results are the mean ± SD (range). The difference in the rate of fatty acid synthesis observed as the result of fasting is statistically significant compared with animals fed a normal laboratory diet ($P < .05$). The difference in the rate of fatty acid synthesis observed as the result of feeding a high-fat diet and fasting overnight is statistically significant compared with animals fed a normal laboratory diet and fasted overnight ($P < .05$).

adipose tissue. These differences (both in enzyme activities and in the rate of lipogenesis) are not surprising, because the rat is known to be metabolically more active than the human. Studies have shown that the liver (according to many, the main site of lipogenesis in the human) lipogenic capacity is much lower in humans compared with rats.[23] It should be noted that the activities of enzymes not directly involved in lipogenesis are also 2 to 3 times lower in human adipose tissue than in rat tissue (Tables 1 to 3). Thus, the data suggest that adipose tissue could be a significant site of fatty acid synthesis in the human. Therefore, our studies confirm the relative importance of human adipose tissue as a site for de novo synthesis of fatty acid.[24,25]

An estimation of the relative importance of human adipose tissue in fatty acid synthesis may be attempted also by comparing the activity of some human liver lipogenic enzymes versus those reported herein. We have shown previously[23] that the activities of FAS, ATP-citrate lyase, malic enzyme, glucose-6-phosphate dehydrogenase, and 6-phosphogluconate dehydrogenase in human liver (samples were also taken during surgery) were 3.0, 1.5, 6.0, 6.3, and 30.0 nmol/min/mg protein. These values are essentially similar to those presented in Tables 1 and 2. This indicates that on a per-milligram protein basis, the lipogenic capacity of human liver and adipose tissue is very similar. However, when corrected for grams of wet tissue, the activities of liver lipogenic enzymes are approximately 10 times higher due to a higher concentration of protein per gram tissue (approximately 150 and 15 mg in liver and adipose tissue, respectively). However, it should be pointed out that the quantity of adipose tissue in the human is much greater. In non-obese subjects weighing approximately 70 kg, there is about 15 kg adipose tissue as compared with 1.5 kg liver. Therefore, in terms of total organ activity, the lipogenic potential of human adipose tissue equaled that of the liver. However, these calculations on the basis of in vitro determinations are probably overestimated and should be interpreted with caution. Nevertheless, one can assume that the lipogenic capacity of human adipose tissue is much higher than previously estimated. This is in accordance with recent studies demonstrating that in humans adipose tissue may be the principal site for fatty acid synthesis.[10]

As already mentioned, the activities of lipogenic enzymes in human adipose tissue exhibited a large variation. The reason for the patient's surgery is unlikely to be an important factor contributing to the wide range of measured activities, since we selected patients with similar diseases (see the Methods). It should be noted that all of these enzymes fluctuate coordinately, which means that if a human subject exhibited a high activity of one lipogenic enzyme, the activities of other lipogenic enzymes were also high and vice versa.

There are some contradictory data concerning the lipogenic enzyme activities in lean (control) and obese subjects.[2,26,27] Our data indicate that the activities of all lipogenic enzymes studied in adipose tissue of obese patients were not statistically different from the lean control when expressed per milligram of protein. No statistical differences in lipogenic enzyme activities were observed in adipose tissue of women and men (Tables 1 and 2). It also seem that the site from which adipose tissue is taken does not significantly influence the lipogenic enzyme activities.

In conclusion, our data indicate that under comparable dietary conditions, rat adipose tissue exhibits higher lipogenic potential than human adipose tissue. Nevertheless, one can suppose that the human adipose tissue is an important site of fatty acid synthesis.

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