Dietary Arachidonic Acid and Hepatic Desaturation of Fatty Acids in Obese Zucker Rats

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ABSTRACT: The effect of low levels of dietary arachidonic acid (20:4n-6) on Δ6 desaturation of linoleic acid (18:2n-6) and α-linolenic acid (18:3n-3), and on Δ5 desaturation of dihomo-γ-linolenic acid (20:3n-6) were studied in liver microsomes of obese Zucker rats, in comparison with their lean littermates. Fatty acid composition of serum total lipids and of phospholipids from liver microsomes and from total heart and kidney was determined to see whether modifications of desaturation rate, if any, were reflected in the tissue fatty acid profiles. Animals fed for 12 wk on a balanced diet, containing 20:4n-6 and 18:2n-6, were compared to those fed 18:2n-6 only. The low amount of dietary 20:4n-6 greatly inhibited Δ6 desaturation of 18:2n-6 and Δ5 desaturation of 20:3n-6, whereas Δ6 desaturation of 18:3n-3 was slightly increased in obese rats. Inhibition of the biosynthesis of long-chain n-6 fatty acids by dietary arachidonic acid was only slightly reflected in the 20:4n-6 content of liver microsome phospholipids. On the contrary, the enrichment of serum total lipids and heart and kidney phospholipids in this fatty acid was pronounced, more in obese than in lean animals. Our results show that, although the desaturation rate of the n-6 fatty acids in liver microsomes was greatly decreased by the presence of arachidonic acid in the diet, the tissue phospholipid content in arachidonic acid was not depressed. The potentiality of synthesis of eicosanoids of the 2 family from this fatty acid is consequently not lower, especially in obese rats, in which certain tissues are deficient in arachidonic acid, in comparison with their lean littermates.
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KEY WORDS: Dietary arachidonic acid, fatty acid desaturation, liver microsomes, obese and lean Zucker rats, tissue lipids.

The genetically obese Zucker rat (fa/fa), which is characterized by hyperphagia and hyperlipemia (1), is often used as a model for human obesity with regard to lipid metabolism. When compared to its lean littermate (Fa/–), this animal presents enhanced lipogenesis (2,3) and high hepatic Δ9 desaturase activity (4,5), whereas mitochondrial fatty acid oxidation is decreased (6). In addition, increased levels of linoleate (18:2n-6) and dihomo-γ-linolenate (20:3n-6) and decreased levels of arachidonate (20:4n-6) in tissue phospholipids are the abnormalities of the fa/fa rats that are fed *ad libitum* a balanced commercial diet (7–11). The lower arachidonic acid content of tissue phospholipids in obese rats can be deleterious because a high level of this essential fatty acid in body lipids is often associated in humans with low atherogenesis and low thrombogenesis (12).

It is well established that, in animals, 20:4n-6 is biosynthesized from dietary 18:2n-6 through two microsomal desaturation steps and one elongation step. Previous investigations in our laboratory have indicated that, in the obese Zucker rat, the low level of 20:4n-6 resulted mainly from a decreased Δ5 desaturation of 20:3n-6 to 20:4n-6 in liver microsomes, whereas Δ6 desaturation of 18:2n-6 to 18:3n-6 (γ-linolenic acid) was only slightly modified (9). It has also been shown that, after treatment of fa/fa rats with a hypolipidemic drug, such as fenofibrate (13) or simvastatin (14), the proportion of 20:4n-6 in liver microsomes was enhanced concomitantly with enhancement of Δ5 desaturase activity.

Another way to increase the arachidonate content in tissue and serum lipids is to partly bypass the desaturation steps by dietary supplementation of 18:3n-6 or 20:4n-6. Few studies have examined the effects of these fatty acids added to the diet in the obese Zucker rat. Phinney *et al.* (15) have shown that the low level of hepatic phospholipid 20:4n-6 was corrected after gavage with 18:3n-6 (present in black currant oil). However, our previous study had indicated that substitution of 18:3n-6 for part of 18:2n-6 in the diet of obese rats tended to normalize the low Δ6 n-6 desaturase activity but induced a limited correction of the abnormality in tissue 20:4n-6 levels (16). Recently, Niot *et al.* (17) observed that supplementation of the diet with 20:4n-6 was not accompanied by a corresponding enrichment of mitochondrial total lipids with this fatty acid in the obese Zucker rat.

To date, no study has been reported on the influence of dietary arachidonic acid on the biosynthesis of arachidonic acid by Δ6 and Δ5 desaturations and on the level of this essential fatty acid in serum and tissue lipids of the obese Zucker. In other rat phenotypes or species, this acid, when added to the diet, has been reported to increase the 20:4n-6 content of tissue lipids and the *in vivo* and *in vitro* production of eicosanoids (18,19).

Accordingly, this study was undertaken to evaluate the in-

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fluence of dietary arachidonic acid on Δ6 desaturation of linoleic and α-linolenic acid and on Δ5 desaturation of dihomo-γ-linolenic in liver microsomes of obese Zucker rats in comparison with their lean littermates. Additionally, the n-6 and n-3 polyunsaturated fatty acid (PUFA) contents were determined in serum and liver microsome total lipids and in heart and kidney phospholipids to see whether they could reflect modifications of desaturation rates.

MATERIALS AND METHODS

Chemicals. [1-^{14}C]Linoleic acid (50 mCi/mmol, 99% radiochemically pure), [1-^{14}C]α-linolenic acid (56 mCi/mmol, 98% pure) and [1-^{14}C]dihomo-γ-linolenic acid (47 mCi/mmol, 99% pure) were purchased from the Radiochemical Centre (Amersham, Buckinghamshire, United Kingdom). Each substrate was diluted in ethanol with the corresponding unlabeled fatty acid to a specific activity of 10 mCi/mmol (120 nmol/20 μL absolute ethanol solution). Unlabeled fatty acids, coenzymes, and biochemicals were purchased from Sigma Chemical Co. (St. Louis, MO). All other chemicals of analytical grade were purchased from Sigma and Merck (Darmstadt, Germany).

Animals and diets. The two phenotypes of 5-wk-old male rats, obese Zucker (fa/fa) and lean Zucker (Fa/–), were provided by INRA of Jouy en Josas (France). They were fed *ad libitum* for 7 wk a semisynthetic control diet (C diet) that contained (g/kg): sucrose (218), cornstarch (440), casein (220), cellulose (20), vitamin mixture (10.4), salt mixture (40), methionine (1.6), and a control oil mixture (50) (rapeseed oil 52%, sunflower oil 20%, and hydrogenated palm oil 30%, by weight). After this C diet, the animals of each phenotype were randomly divided into two groups of $n = 4$ animals and fed for 12 wk on different diets. The first group of animals continued to receive the C diet, and the second group was fed an arachidonic-supplemented diet (AA diet), the lipids of which consisted of (wt%): rapeseed oil (45), sunflower oil (14), hydrogenated palm oil (35), and 20:4n-6 concentrate (6). This concentrate was isolated from pig livers by preparative high-performance liquid chromatography (HPLC) of the total lipid fatty acid methyl esters (20). Fatty acid composition of dietary oils was determined by gas–liquid chromatography (GLC) of the methyl esters as indicated below. The daily food intake was adjusted to 20 g per rat to prevent hyperphagia of the obese Zucker rats. As shown in Table 1, the two dietary oil mixtures contained the same amount of n-6 and n-3 fatty acids in a ratio close to 6:1. In the AA diet, 16.3% of the n-6 fatty acids were 20:4n-6, whereas 18:2n-6 was the only n-6 fatty acid of the C diet. Under these conditions, each rat ingested the same amount of n-6 fatty acids (258 mg per day). The AA diet contained 42 mg of 20:4n-6.

After an overnight fast following the dietary period, all rats were killed by exsanguination between 0700 and 0800 h to avoid any circadian variation in the desaturation activities (21). Blood from aorta was collected in a tube. Livers, hearts and kidneys were withdrawn, blotted on filter paper, and weighed.

TABLE 1
Fatty Acid Composition of Dietary Lipids[a]

Diet	Control (C)	20:4n-6 (AA)
14:0	0.8	0.6
16:0	16.5	16.8
16:1n-7	1.2	—
18:0	4.4	3.9
18:1n-9	43.9	44.7
18:1n-7	3.2	1.8
18:2n-6	25.6	21.6
18:3n-3	4.3	3.9
20:0	0.4	0.4
20:1n-9	0.6	0.7
20:4n-6	—	4.2
22:0	0.3	0.4
22:5n-3	—	0.4
SFA[b]	22.4	22.0
MUFA[c]	47.7	47.2
Total n-6	25.6	25.7
Total n-3	4.3	4.3

[a]The composition of fatty acids is expressed as wt% of total fatty acids in the oil mixture added to the two diets. For 100 g of diet, the n-6 and n-3 fatty acids represented about 1280 mg and 215 mg, respectively.
[b]SFA: saturated fatty acids.
[c]MUFA: monounsaturated fatty acids.

Desaturation assays. Liver microsomes were prepared at 4°C as previously reported (22). Briefly, about 3.5 g of liver was homogenized in a Potter-Elvehjem tube in 6 vol of 0.25 M sucrose and 0.05 M phosphate buffer (pH 7.4). The supernatant of the homogenate centrifugation at 13,000 × *g* for 20 min was recentrifuged at 105,000 × *g* for 60 min. The microsomal fraction was obtained by resuspending the second centrifugation pellet in 0.4 mL of supernatant and 0.8 mL of 0.05 M phosphate buffer (pH 7.4). The protein content of microsomes was measured according to Layne (23).

Microsomal suspension, containing 5 mg of protein, was incubated in an open flask with a high level of substrate solubilized in ethanol: 120 nmol (57 μM) of [1-^{14}C]linoleic acid, 120 nmol (57 μM) of [1-^{14}C]α-linolenic acid, and 80 nmol (38 μM) of [1-^{14}C]dihomo-γ-linolenic acid. Incubations were carried out in a shaking water bath for 20 min in a total volume of 2.1 mL of incubation medium containing (mM): phosphate buffer (pH 7.4) (72), $MgCl_2$ (4.8), CoA (0.5), ATP (3.6), and NADPH (1.2). Incubations were stopped by adding 15 mL of chloroform/methanol (2:1, vol/vol) according to Folch *et al.* (24). After methylation of fatty acids by methanol/BF_3 (25), the conversion of the three labeled substrates into their Δ6 and Δ5 desaturation products (γ-linolenic, stearidonic, and arachidonic acid, respectively) was determined after separation by reversed-phase HPLC (26). Radioactivity was measured with a 1900 TR Tri-Carb (Packard, Rungis, France). Counting efficiency was estimated by comparison with radioactive standards to be at least 95% and generally more.

Lipid analysis. Lipids from dietary oils, serum, liver mi-

crosomes, heart, and kidney were extracted by 15 vol of dimethoxymethane/methanol (4:1, vol/vol) (27). Fatty acids from dietary oils were analyzed by GLC of the lipid extracts without any further separation. Tissue phospholipids were separated by silicic acid column chromatography (28).

After addition of heptadecanoic acid (17:0) as an internal standard, the fatty acid methyl esters were prepared by transmethylation with methanol/BF_3 (25). They were analyzed by GLC in a Becker-Packard Model 417 gas chromatograph, equipped with a laboratory-made 30 m × 0.3 mm i.d. glass capillary column coated with Carbowax 20M (Applied Science, State College, PA). Analyses were carried out at a constant temperature of 180°C with a nitrogen flow rate of 3 mL/min. The Ros injector and the flame-ionization detector were maintained at 220°C. Areas were measured by means of an ICAP 10 calculator–recorder (LTT, Paris, France). The detector response was checked with a standard mixture of methyl esters (Nu-Chek-Prep, Elysian, MN) and results relative to major fatty acids [saturated fatty acids (SFA), monounsaturated fatty acids (MUFA), 18:2n-6, 20:4n-6, and 22:6n-3] were expressed as wt%.

Statistics. Desaturase activities and fatty acid compositions were means ± SD for $n = 4$ animals. After analysis of variance by Duncan's multiple-range test (29), means were compared in the four groups according to the least significant difference and classified according to decreasing order. Values assigned a different superscript letter were significantly different at $P < 0.05$.

RESULTS

Body weight and liver weights. In each type of rat, there was no effect of the AA diet, as compared to the C diet, on the body weight, liver weight, and liver microsomal protein content (data not presented). The liver weight in the two groups of obese rats was about twofold higher than in the two groups of lean rats.

Activity of desaturation in liver. Figure 1 illustrates the specific activity of Δ6 desaturation of linoleic acid (18:2n-6) and α-linolenic acid (18:3n-3) and the specific activity of Δ5 desaturation of dihomo-γ-linolenic acid (20:3n-6), measured in liver microsomes of the two groups of rats fed the C or AA diet. In rats fed the C diet, these activities were lower in obese rats than in the other phenotype, in agreement with what was previously observed (22). After feeding 20:4n-6, the Δ6 n-6 desaturase activities were similar in the two types of rats, showing that the inhibition by 20:4n-6 was higher in lean Zucker rats (−70%) than in obese Zucker rats (−60%). The 20:4n-6 diet also decreased (by 55%) Δ5 desaturase activity in obese rats and, to a somewhat lower extent (by 42.5%), in lean animals, contrary to what was observed with 18:2n-6 as substrate.

The activity of Δ6 desaturation of 18:3n-3 was higher in the lean Zucker rat than in the obese Zucker rat fed the C diet, as observed with Δ6 desaturation of 18:2n-6. The AA diet did not significantly increase the 18:3n-3 desaturation activity in either phenotype.

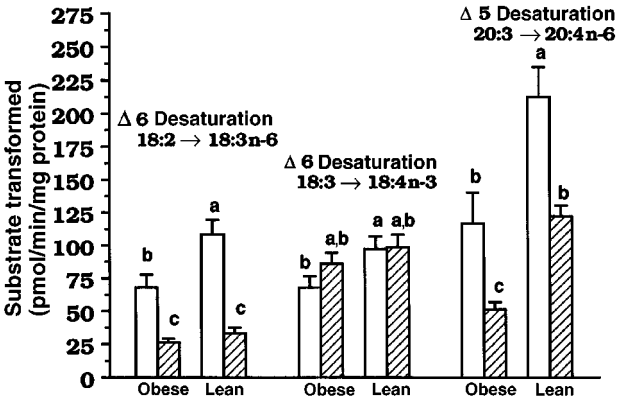

FIG. 1. Δ6- and Δ5-Desaturase-specific activities in liver microsomes from obese and lean Zucker rats fed the control diet (open bars) or the AA diet (hatched bars). Results are means ± SD for four animals in each group. After analysis of variance, means were compared in each type of desaturation. Means assigned different superscript letters were significantly different ($P < 0.05$).

Serum lipid fatty acids. Between obese and lean Zucker rats fed the C diet, the differences in serum total lipids were small, as shown in Table 2. The 18:2n-6, 20:4n-6 and 22:6n-3 contents were only slightly lower in obese than in lean Zucker rats. The presence of 20:4n-6 in the diet resulted in an increase of this fatty acid in both phenotypes (30% in obese and 20.7% in lean rats, respectively), while the percentage of 18:2n-6 was not modified.

Liver microsomal phospholipid fatty acids. As shown previously (22), some differences can be observed between the two types of rats fed the C diet (Table 3). When compared to their lean littermates, the obese Zucker rats presented a lower n-6 fatty acid content in their liver microsomal phospholipids, 20:4n-6 being less affected than 18:2n-6. The 22:6n-3 content was not different. Supplementation with dietary 20:4n-6 was not accompanied by an enrichment of microsomal lipids in this fatty acid, either in obese or in lean rats. With regard to n-3 fatty acids, a decreased content in 22:6n-3 (−40 in obese and

TABLE 2
Fatty Acid Composition (wt%) of Serum Total Lipids from the Obese and Lean Zucker Rats Fed the C and the 20:4n-6 AA Diet[a]

Fatty acids	Obese		Lean	
Diet	C	AA	C	AA
Total SFA	25.2 ± 1.4^d	26.4 ± 0.6^d	26.2 ± 0.9^d	23.1 ± 0.6^e
Total MUFA	28.6 ± 3.2^d	25.3 ± 1.1^d	21.9 ± 4.2^{de}	20.9 ± 1.2^e
18:2n-6	6.5 ± 0.8^e	5.1 ± 0.6^e	9.4 ± 1.7^d	10.7 ± 0.9^d
20:4n-6	29.0 ± 4.3^e	37.7 ± 1.9^d	30.9 ± 1.5^e	37.3 ± 0.4^d
22:6n-3	4.5 ± 1.0^e	3.8 ± 0.1^e	5.6 ± 0.2^d	4.5 ± 1.4^{de}
Total n-6[b]	37.7	43.1	42.0	48.0
Total n-3[c]	5.6	4.0	6.6	5.5

[a]Results are expressed as means ± SD ($n = 4$). For each fatty acid (or group of fatty acids), means were compared between the four groups of rats. Means assigned different superscript letters were significantly different ($P < 0.05$). For abbreviations see Table 1.
[b]Also contains 20:2, 20:3, 22:4, and 22:5n-6.
[c]Also contains 18:3, 20:5, and 22:5n-3.

TABLE 3
Fatty Acid Composition (wt%) of Liver Microsomal Phospholipids from Obese and Lean Zucker Rats Fed the C and the 20:4n-6 AA Diet[a]

Fatty acids	Obese		Lean	
Diet	C	AA	C	AA
Total SFA	37.8 ± 1.6[e]	43.1 ± 1.6[d]	33.1 ± 1.8[f]	42.5 ± 1.2[d]
Total MUFA	9.0 ± 0.4[d]	8.2 ± 1.3[d]	9.4 ± 0.8[d]	6.4 ± 1.0[e]
18:2n-6	3.9 ± 0.3[e]	4.0 ± 1.2[e]	7.1 ± 1.0[d]	5.5 ± 1.0[e]
20:4n-6	32.4 ± 0.7[e]	33.6 ± 1.2[de]	35.1 ± 1.4[d]	35.1 ± 1.2[d]
22:6n-3	12.2 ± 0.2[d]	7.3 ± 0.3[e]	11.1 ± 1.4[d]	7.9 ± 1.2[e]
Total n-6[b]	39.1	37.8	43.5	41.2
Total n-3[c]	12.3	7.3	11.8	7.9

[a,b,c]See footnotes in Tables 1 and 2.

–28.8% in lean animals), with a parallel increase in SFA content (+14 and +28.4%, respectively), was observed.

Heart and kidney phospholipid fatty acids. On the C diet, the 20:4n-6 content in heart phospholipids was not significantly different in obese and lean rats, whereas 18:2n-6 was higher in lean rats (Table 4). In both phenotypes, the dietary 20:4n-6 highly increased the 20:4n-6 content of heart phospholipids (+55.9 in obese and +33.5% in lean rats, respectively) and highly decreased the 18:2n-6 content (–65.5 in obese and –50.5% in lean rats, respectively). The 22:6n-3 content was not modified by the dietary arachidonic acid.

In kidney phospholipids (Table 4), contrary to what was observed in heart phospholipids, the 20:4n-6 content was higher in lean than in obese rats fed the C diet. The dietary 20:4n-6 also increased the 20:4n-6 content of kidney phospholipids but to a lesser extent than in the heart (+34.3 in obese and +18.3% in lean rats, respectively). The 18:2n-6 content was also less decreased in the kidney than in the heart (–31.7 in obese and –39.7% in lean rats, respectively). The 22:6n-3 was slightly increased in both phenotypes. The heart phospholipids were also much richer in 22:6n-3 than those from kidneys, whatever the diet, whereas 20:4n-6 was approximately in the same proportion.

DISCUSSION

To evaluate the effect of dietary arachidonic acid on fatty acid composition of tissue lipids and desaturase activities of the liver, the likely influence of hyperphagia in the obese rat must be eliminated. This is why the present work was carried out under pair feeding conditions. All rats received the same amount of diet (20 g) per day. At the beginning of the dietary period, the obese fa/fa rats showed a higher body weight, but the weight gain during the 12 wk of diet was the same in obese and lean rats. So, both groups of rats presented the same food efficiency.

The specific activities of the three desaturations studied were lower, on a per mg protein basis, in obese Zucker rats than in lean rats fed the C diet. The presence of 20:4n-6 in the diet highly decreased Δ6 and Δ5 desaturation-specific activities of n-6 fatty acids in the two types of rats. This effect was observed with only about 0.2% of 20:4n-6 in the diet (42 mg per day). The dietary arachidonic acid was responsible for this effect because the total n-6 fatty acid content was the same in the C diet, but as 18:2n-6 only. Our results could be explained by the fact that high desaturase activities were not needed because a sufficient amount of this acid was available from the diet.

Surprisingly, the presence of 20:4n-6 in the AA diet did not inhibit Δ6 desaturation of 18:3n-3. This finding has also been observed with a fish oil diet that contained long-chain n-3 polyunsaturated fatty acids (22). The differential effect of dietary 20:4n-6 on Δ6 desaturation in the two series of fatty acids (n-6 and n-3) supports the hypothesis for the existence of two different desaturation enzymes or two different forms of the same enzyme for both series of fatty acids.

The mechanism by which dietary 20:4n-6 inhibits *in vitro* desaturation of n-6 fatty acids is not established in this work. One possibility may be that it depresses *in vivo* synthesis of the desaturation enzymes in the same manner as it depresses the synthesis of the enzymes involved in lipogenesis (30,31).

TABLE 4
Major Fatty Acid Composition (wt%) of Heart and Kidney Phospholipids from Obese and Lean Zucker Rats Fed the Control (C) Diet and the 20:4n-6 (AA) Diet[a]

		Obese		Lean	
Fatty acids	Organ	C	AA	C	AA
Total SFA	Heart	39.8 ± 2.6	38.2 ± 1.6	39.9 ± 2.8	39.0 ± 2.1
	Kidney	44.2 ± 1.7[d]	41.9 ± 0.4[e]	42.1 ± 1.7[e]	46.0 ± 0.4[d]
Total MUFA	Heart	14.5 ± 0.5[d]	11.5 ± 0.3[e]	12.5 ± 0.8[e]	11.8 ± 0.5[e]
	Kidney	18.4 ± 0.4[d]	18.1 ± 0.6[d]	14.7 ± 0.5[e]	15.8 ± 0.5[e]
18:2n-6	Heart	7.5 ± 0.3[e]	2.6 ± 0.3[g]	10.9 ± 0.5[d]	5.4 ± 0.4[f]
	Kidney	4.1 ± 0.1[f]	2.8 ± 0.1[g]	8.3 ± 0.2[d]	5.0 ± 0.1[e]
20:4n-6	Heart	22.2 ± 1.9[f]	34.6 ± 0.6[d]	20.6 ± 2.4[f]	31.0 ± 1.0[e]
	Kidney	24.2 ± 1.7[f]	32.5 ± 1.2[d]	27.3 ± 1.2[e]	32.3 ± 0.3[d]
22:6n-3	Heart	7.6 ± 1.8	7.3 ± 1.3	9.3 ± 1.5	8.3 ± 0.3
	Kidney	1.8 ± 0.2[e]	2.5 ± 0.1[d]	2.0 ± 0.2[e]	2.7 ± 0.1[d]
Total n-6[b]	Heart	32.8	40.0	33.1	38.5
	Kidney	29.7	36.9	37.0	38.7
Total n-3[c]	Heart	9.5	10.1	10.7	10.7
	Kidney	2.1	3.1	2.3	2.8

[a,b,c]See footnotes in Tables 1 and 2.

However, the presence of a trace amount of free 20:4n-6 in the isolated microsomes used for the desaturation assays may exert an allosteric product inhibition of both Δ6 and Δ5 desaturases (32,33).

Although AA feeding to obese and lean Zucker rats caused a significant decrease of n-6 fatty acid desaturation, which is likely to cause a decrease of n-6 fatty acid levels in tissue and serum lipids, the 20:4n-6 content of serum lipids was generally higher after the AA diet, although not significantly in obese rats. On the contrary, the fatty acid composition of liver microsomal phospholipids did not show any significant change. The limited influence of dietary 20:4n-6 is likely due to its low level in the experimental diet or to food-restricted conditions. On the other hand, turnover of the microsome phospholipids is probably not rapid enough to completely reflect the rates measured *in vitro*. Another explanation is that arachidonic acid, biosynthesized or originating from the diet, was incorporated preferentially in a neutral lipid class of liver, for instance in cholesteryl esters, as shown by Phinney *et al.* (15). These authors observed an increased 20:4n-6 level in this lipid class in obese Zucker rats, as compared with lean animals, after ingestion of 18:3n-6. The AA diet also caused an increase of SFA and a marked decrease of MUFA contents in the lean rat. This finding suggests an inhibition of Δ9 desaturation by dietary 20:4n-6.

In contrast to what was observed in liver microsomes, heart and kidney phospholipids exhibited an increase of 20:4n-6 during arachidonic acid ingestion, and the effect was more marked in obese than in lean rats. First, this difference can be due to different reasons. In contrast to linoleic acid, arachidonic acid is a poor substrate for β oxidation (34) and, compared to its lean littermate, the obese Zucker rat is known to have a lower rate of hepatic fatty acid oxidation (6), which, additionally, is decreased by dietary arachidonic acid as recently reported (17). Second, heart and kidneys are dependent on plasma lipids for n-6 and n-3 fatty acid supply because Δ6 desaturation is limited in these organs (35). We can thus hypothesize that 20:4n-6 was removed from plasma to organs more efficiently in obese than in lean Zucker rats. This reasoning suggests that the 20:4n-6 content of heart and kidney lipids is regulated by selective incorporation rather than by the availability of this fatty acid provided by desaturation–elongation in the liver.

In vitro results showed that the cardiac tissue of obese Zucker rats fed a chow diet produced smaller amounts of eicosanoids of the 2 family than in the lean littermates. After addition of arachidonic acid *in vitro*, the synthesis of prostaglandins was increased (7). Our results indicate that dietary 20:4n-6 tended to increase the available pool of eicosanoid precursor fatty acid in obese rats. They also suggest that treatment of obese animals or obese humans by dietary arachidonic acid is beneficial by increasing the proportion of this essential fatty acid in tissues because a high level in body lipids is often associated with low atherogenesis and low thrombogenesis (12).

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