Differential Effects of High-Fat Diets Varying in Fatty Acid Composition on the Efficiency of Lean and Fat Tissue Deposition During Weight Recovery After Low Food Intake

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The energetics of body weight recovery after low food intake was examined in the rat during refeeding for 2 weeks with isocaloric amounts of high-fat (HF) diets providing 50% of energy as either lard, coconut oil, olive oil, safflower oil, menhaden fish oil, or a mixture of all these fat types. The results indicate that for both body fat and protein, the efficiency of deposition was dependent on the dietary fat type. The most striking differences were found (1) between diets rich in n-3 and n-6 polyunsaturated fatty acids (PUFA), with the diet high in fish oil resulting in a greater body fat deposition and lower protein gain than the diet high in safflower oil; and (2) between diets rich in long-chain (LCT) and medium-chain triglycerides (MCT), with the diet high in lard resulting in a greater gain in both body fat and protein than the diet high in coconut oil. Furthermore, the diet high in olive oil (a monounsaturated fat) and the mixed-fat diet (containing all fat types) were found to be similar to the fish oil diet in that the efficiency of fat deposition was greater (and that of protein gain lower) than with the diet high in safflower oil. Neither the efficiency of fat gain nor that of protein gain were found to correlate with fasting plasma insulin, the insulin to glucose ratio, or plasma lipids. The present studies, conducted specifically under conditions of isocaloric refeeding after low food intake, demonstrate that the fatty acid composition of HF diets influences the recovery of both lean and fat tissue compartments—apparently by mechanisms unrelated to plasma insulin and lipid status. The relevance of these findings is discussed in the context of nutritional rehabilitation after undernutrition, as well as in the context of dietary management of obesity relapse.

THE ENERGETICS of body weight recovery following a period of negative energy balance and the extent to which the increased energy supply during refeeding is repartitioned into lean and fat tissue compartments remain poorly understood phenomena. Progress in this field of energy metabolism, with direct implications for the nutritional rehabilitation of malnourished patients and the dietary management of obesity, has been limited by the necessity for precise determinations of body composition and concomitant measurements of energy balance in a dynamic state of weight gain.[1,2] In addition, because differences in the level of energy intake and in energy digestibility tend to obscure effects due to diet composition per se, the impact of various dietary formulations on tissue deposition during weight recovery is often difficult to interpret.

Thus, to gain insight into the energetics of body weight recovery, we have recently described an experimental rat model in which after a period of low food intake the efficiency of energy utilization and energy partitioning are assessed during calorie-controlled refeeding.[3-5] It was demonstrated that during the first 2 to 3 weeks of refeeding with a low-fat (high-carbohydrate) diet, the efficiency of energy utilization is enhanced by nearly twofold and the energy thus saved is directed entirely at fat deposition without increases in the rate of protein gain as compared with weight-matched controls. Subsequent studies indicated that the specific enhancement in the efficiency of fat deposition during refeeding was unaltered by (1) dietary protein levels, (2) dietary carbohydrate types, and (3) diets relatively low in fat (30% by energy) but varying in fatty acid composition.[6] However, the latter study also showed that when refeeding with diets high in fat (ie, >40% of energy intake and consisting of a 1:1 mixture of lard and corn oil), the efficiency of energy deposition was further enhanced, resulting in an accentuation of body fat gain, and again the energy thus economized was not diverted into protein deposition.

Given the common use of high-fat (HF) supplements of widely different fatty acid composition during nutritional rehabilitation, we have extended our previous study[6] examining the effect of diet composition per se on refeeding energetics to investigate the impact of fat types during HF consumption. To this end, energy balance and changes in body composition were assessed during isocaloric refeeding of diets high in fats or oils, namely saturated fats rich in either long-chain triglycerides ([LCT] eg, lard) or medium-chain triglycerides ([MCT] eg, coconut oil), monounsaturated fats rich in oleic acid (eg, olive oil), and polyunsaturated fats (PUFA) either of vegetable origin and rich in linoleic acid (n-6 fatty acids, eg, safflower oil) or of marine origin and hence high in the α-linolenic metabolites eicosapentaenoic acid and docosahexaenoic acid (n-3 fatty acids, eg, menhaden fish oil).

MATERIALS AND METHODS

Animals and Diets

Sprague-Dawley male rats (CMU, Geneva, Switzerland) aged 5 weeks were adapted to the room and cage environments for 2 weeks: ie, they were caged singly in a temperature-controlled room (23°C) with a 12-hour light-dark cycle. They were maintained on a commercial pelleted chow diet (Provimi-Lacta, Cossonay, Switzerland) made from a mixture of wheat, corn, soya extracts, vegetable protein, fish, meat, sweet potato, and molasses, and supplemented

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with minerals and vitamins; this diet consisted (by energy) of 28% protein, 60% carbohydrate, and 12% fat. All animals had free access to tap water during this adaptation period, as well as during the course of the underfeeding and refeeding.

After these 2 weeks of adaptation, 48 of these 7-week-old rats were selected on the basis of body weight within ±5 g of the mean body weight (ie, between 230 and 240 g). They were food-restricted for 2 weeks, during which they received a fixed-ration (15 g) chow diet representing approximately 50% of their spontaneous ad libitum daily food intake. At the end of this underfeeding period, the animals were divided into groups (n = 6) of similar mean body weight (220 g). One group was killed and retained for analysis of body energy content and body composition, and these values were used to estimate individually on a body-weight basis the energy content of animals in the experimental groups at the onset of refeeding. The other groups were refed the various test diets at a level approximately equal in metabolizable energy (ME) content to the normal food intake of nonrestricted animals (~28 g chow daily). The diets were provided in food bowls tightly secured to one side of the cage with metal springs to prevent or minimize food spillage, which was measured. The food bowls were placed into the cages at 4 to 5 PM and removed the next morning at 7 to 8 AM. After 2 weeks of calorie-controlled refeeding, all animals were killed and their carcasses analyzed for energy, fat, and protein content as described below.

The compositions of the low-fat diet and the HF diets varying in fat types are shown in Table 1. The energy digestibility of these test diets was determined during a preliminary study, which involved feeding groups of three animals each of these diets over 14 days (after a period of food restriction as described above), measuring food intake, and collecting feces; any food spilled was collected over blotting paper, dried, and weighed, and suitable corrections were made to the gross food intake. From the energy density of diets and feces measured by a bomb calorimeter,[7] the values for energy digestibility were found to be as follows: low-fat diet, 87.8%; HF lard, 81.1%; HF coconut oil, 86.8%; HF olive oil, 86.2%; HF safflower oil, 86.8%; HF fish oil, 86.5%; and HF mixed, 85.4%. An approximate ME density of each diet was then determined using the formula of Miller and Payne[7] to account for urinary losses of energy. Based on these values, food-restricted groups in the actual experiment reported here were isocalorically refed their various test diets, but this time ME intake was directly determined from the difference between gross energy intake and the energy content of feces, urine, and spillage.

Table 1. Composition of Test Diets

Test Diets	Low-Fat	HF
Basal mixture (g)*	606	606
Added sugars (g)†	394	0
Added fats (g)‡	0	175
Total weight of diets (g)	1,000	781
Total energy content (kJ)§	14,250	14,250
Nutrient composition (%ME)§		
Protein	23	23
Fat	6	53
Carbohydrate	71	24

*The basal mixture contained the following (g/606 g): chow 485, casein 87, DL-methionine 2, choline chloride 1, AIN 76 vitamin mix 5, AIN 76 mineral mix 18, and corn oil 8.

†The added sugars were sucrose and glucose (in equal parts).

‡The added fats were either lard, coconut oil, olive oil, safflower oil, menhaden fish oil, or a mixture of all these fats and oils (in equal parts) and were all supplemented with 0.5% vitamin E.

§In the formulation of test diets, ME density was estimated by computation using values (kJ/g) for ME content as follows: chow 12.133, fat 37.656, carbohydrate 16.736, and protein 16.736. During the actual experiment reported here, ME intake was directly determined as the difference between gross energy intake and the energy content of combined feces, urine, and spillage.

The various food ingredients were purchased from the following sources: ground standard chow and corn starch (Provimi-Lacta); vitamin-free casein, DL-methionine, vitamin E, and fructose (Fluka, Bucks, UK); choline chloride (Sigma, St Louis, MO); glucose (Merck, Lausanne, Switzerland); AIN 76 vitamin mixture, AIN 76 mineral mixture, coconut oil, and refined menhaden oil (ICN, Lausanne, Switzerland); and sucrose, corn oil, olive oil, safflower oil, and lard (Migros, Geneva, Switzerland). Animals used in these studies were maintained in accordance with the institute's regulations and guide for the care and use of laboratory animals.

Body Composition Measurements and Determination of Efficiency of Gain

After killing the animals by decapitation, the skull, thorax, and abdominal cavity were incised and the gut was cleaned of undigested food. The whole carcasses were then dried to constant weight in an oven maintained at 60°C, and were subsequently homogenized. Triplicate samples of each homogenized carcass were analyzed for energy content by bomb calorimetry[7] and for fat content by the soxhlet extraction method[8] using light petroleum-ether. Body protein content was determined from a general formula relating energy derived from fat, total energy value of the carcass, and energy derived from protein. The formula is based on the fact that fat and protein are the only energy-yielding components of the carcass, since the contribution from carbohydrates is less than 1% and hence negligible. The calorific values for body fat and protein were 38.6 and 22.7 kJ/g, respectively. Body energy, fat, and protein gain during the 2 weeks of refeeding were obtained as the difference between the final and initial values (with the latter values estimated from values obtained from the group killed at the onset of refeeding). The efficiencies of the body energy, fat, and protein gained during the 2 weeks of refeeding were determined as the percentage of energy, fat, and protein retained per ME intake during the 14-day refeeding period.

Determinations of Plasma Glucose, Insulin, and Lipids

On day 10 of refeeding, the food bowls were removed early in the morning (7 AM). Seven to eight hours later, blood was drained from the tail vein and centrifuged, and the plasma was frozen and stored at −40°C for later assays. The plasma glucose level was measured[9] using a Beckman glucose analyzer (Beckman Instruments, Palo Alto, CA), and the plasma immunoreactive insulin level was measured by radioimmunoassay according to the method of Herbert et al.[10] Enzymatic colorimetric methods were used to measure the levels of plasma triglycerides, nonesterified fatty acids, total cholesterol, and phospholipids.[11-13]

Data Analysis

Data are presented as the mean ± SEM. Statistical analyses were performed using ANOVA, and post hoc comparisons between group pairs were made with the Neuman-Keuls multiple comparison test after ANOVA had established significant differences among the groups.

RESULTS

Influence of Dietary Fat Types on Body Composition and Efficiency of Gain

The final body weight and body composition of animals fed the various test diets are shown in Table 2. Although the mean body weight was higher in groups fed HF lard and HF

Table 2. Final Body Weight, Body Composition, and ME Intake of Groups Refed Either the Low-Fat Diet or Various HF Diets After a Period of Underfeeding

Test Diets	Body Weight (g)	Body Composition			ME Intake (kJ/14 d)
		Water (g)	Fat (g)	Protein (g)	
1. Low-fat	327 ± 3	220 ± 3	35.1 ± 0.9	59.8 ± 1.5	4,839 ± 60
2. HF lard	339 ± 4	222 ± 3	44.7 ± 0.5	58.8 ± 0.6	4,775 ± 56
3. HF coconut oil	331 ± 2	222 ± 2	38.3 ± 1.0	56.0 ± 0.6	4,862 ± 44
4. HF olive oil	329 ± 2	214 ± 2	45.9 ± 1.5	57.3 ± 0.5	4,860 ± 60
5. HF safflower oil	330 ± 5	216 ± 5	38.2 ± 1.2	62.9 ± 1.7	4,873 ± 33
6. HF fish oil	331 ± 3	217 ± 3	44.6 ± 1.5	54.7 ± 1.7	4,864 ± 66
7. HF mixed	339 ± 3	223 ± 2	45.2 ± 1.3	55.6 ± 1.3	4,876 ± 38
Significance of F	NS ($P = .07$)	NS	$P < .001$	$P < .001$	NS
Pairwise comparison			2, 4, 6, 7 *v* 1, 3, 5	3, 4, 6, 7 *v* 5	

NOTE. All values are the mean ± SEM (n = 6). NS indicates no significant difference by ANOVA.

mixed diets than in those fed the other test diets, ANOVA indicates no overall between-group significant differences in body weight or body water. In contrast, marked differences appear in the body energy compartments ($P < .001$) despite the fact that ME intake over the 2-week period was similar in all groups. Compared with the low-fat group, body fat was significantly higher by 25% to 30% in groups fed HF diets rich in lard, olive oil, or fish oil, or the HF mixed diet. On the other hand, groups fed HF diets rich in coconut oil and safflower oil had significantly less (15%) body fat than the other HF-fed groups; they also did not differ significantly in body fat content from the group fed the low-fat diet. These differences among the various test diets on final body fat composition are reflected in the efficiency of fat gain (Fig 1), which is significantly 30% to 35% higher in the lard, olive oil, fish oil, and mixed HF diets

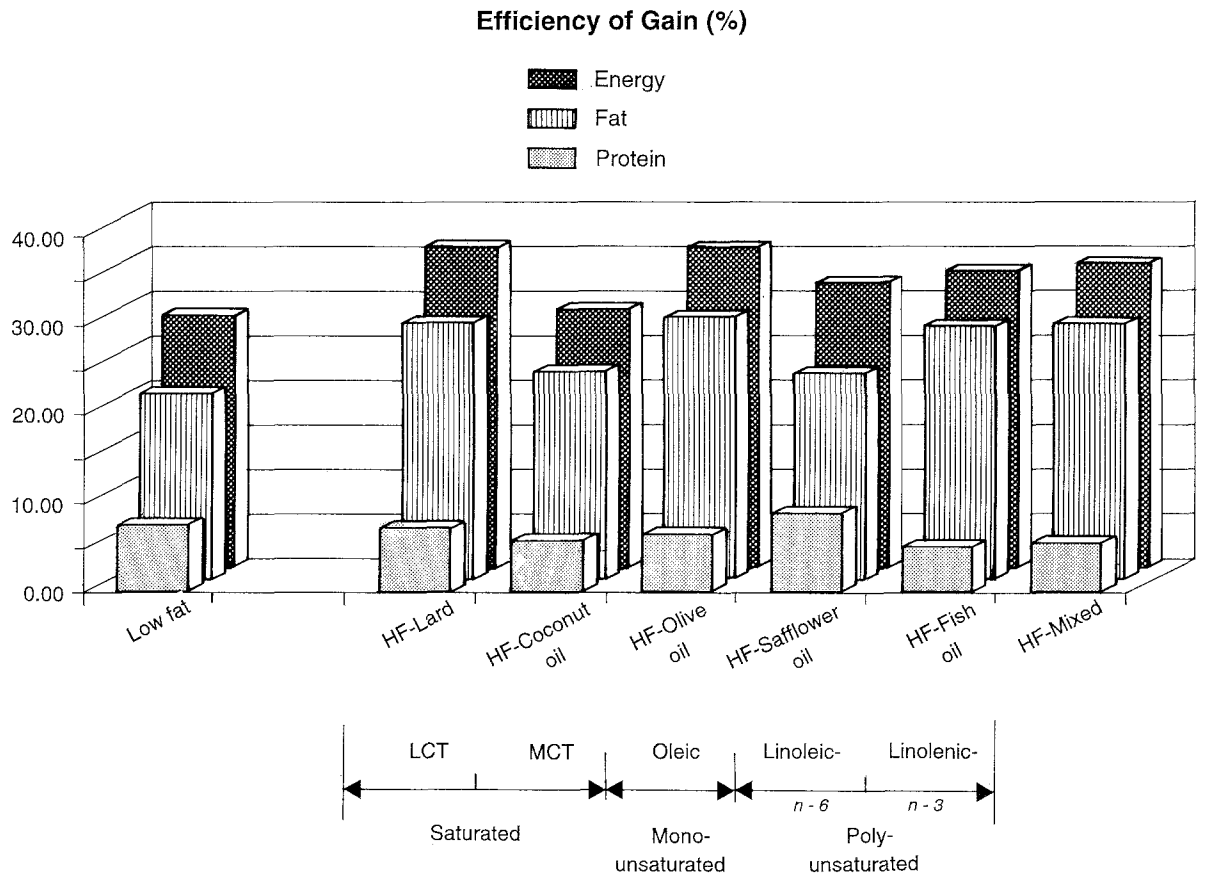

Fig 1. Efficiency (% kJ retained/ME intake) of energy, fat, and protein gain during 2 weeks of refeeding after low food intake. Linolenic refers to α-linolenic metabolites, ie, the n-3 fatty acids eicosapentaenoic acid and docosahexaenoic acid. The data presented are the mean; statistical analysis by ANOVA indicates significant differences ($P < .001$) due to diet in all three parameters. Post hoc multiple pairwise comparison tests indicate the following significant differences: (1) efficiency of protein gain: HF coconut oil, HF olive oil, HF fish oil, HF mixed *v* HF safflower oil; also HF fish oil, HF mixed *v* HF lard, low-fat; (2) efficiency of fat gain: HF lard, HF olive oil, HF fish oil, HF mixed *v* HF coconut oil, HF safflower oil, low-fat; (3) efficiency of energy gain: HF lard, HF olive oil, HF safflower oil, HF fish oil, HF mixed *v* HF coconut oil, low-fat; also HF lard, HF olive oil *v* HF safflower oil.

than in those high in coconut oil and safflower oil. In addition, the latter two diet groups did not differ in this parameter from the group fed the low-fat diet.

Dietary fat types also influenced body protein deposition during body weight recovery ($P < .001$). Final body protein contents in groups fed HF diets rich in coconut oil, olive oil, fish oil, and the mixed fats were all lower than those found in the safflower oil, lard, and low-fat groups. Pairwise comparisons showed that these differences were statistically significant when compared with the safflower oil group for final body protein (Table 2), and in addition, the efficiency of protein gain was also significantly lower in groups fed HF fish oil and HF mixed diets as compared with HF lard or low-fat diets (Fig 1).

The overall efficiency of energy gain is also presented in Fig 1, and reflects the additive effects of the efficiencies of fat and protein gain. ANOVA indicates significant differences among dietary treatments ($P < .001$), with the groups fed HF diets rich in lard, olive oil, safflower oil, or fish oil, and the mixed HF diets having significantly higher energetic efficiencies than those fed HF coconut oil or the low-fat diet. In addition, the HF lard and HF olive oil groups had significantly higher energetic efficiencies relative to the HF safflower oil group.

Influence of Dietary Fat Types on Fasting Plasma Insulin, Glucose, and Various Lipids

The effects of the various test diets on fasting blood parameters are presented in Table 3. Plasma glucose was not different with the various test diets, but plasma insulin levels, as well as the ratio of insulin to glucose, were higher in groups fed HF lard and HF mixed diets as compared with the low-fat group and other HF groups fed diets rich in coconut oil, olive oil, safflower oil, and fish oil ($P < .001$).

Relative to the group fed the low-fat diet, plasma cholesterol was higher in the HF lard and HF olive oil groups, similar in the HF coconut oil, HF safflower oil, and HF mixed groups, and lowest in the HF fish oil group. Similarly, the fish oil group had the lowest levels of plasma phospholipids, triglycerides, and nonesterified fatty acids as compared with all the other diet groups (including the low-fat group).

DISCUSSION

The present studies, conducted specifically under conditions of controlled refeeding after low food intake, demonstrate differential effects of various HF diets on the recovery of both lean and fat compartments. Since the ME intake was maintained constant in all groups, these differences in body energy compartments cannot be ascribed to differences in energy intake or in energy digestibilities, but instead to differences in the efficiencies of gaining body fat and protein. Our main findings (Fig 1) are summarized below.

First, the HF mixed diet (consisting of equal proportions of lard, coconut oil, safflower oil, olive oil, and fish oil) enhanced the efficiency of fat gain relative to the low-fat diet. This effect was also observed with HF diets in which the dietary fat was derived principally from either lard, olive oil, or fish oil, but not when either coconut oil or safflower oil was the main source of dietary fat.

Second, our current studies also demonstrate differences among the various HF diets in terms of the lean tissue compartment during weight recovery. In particular, the groups refed HF diets rich in coconut oil, olive oil, or fish oil and the mixed HF diets had a lower efficiency of protein gain versus those fed HF safflower oil. The lowest values were found in groups refed the HF fish oil and HF mixed diets, which were significantly lower not only as compared with the group refed the HF safflower oil diet, but also as compared with groups refed the HF lard diet or low-fat groups.

Differential Effects of Dietary Fat Types During Weight Recovery Versus Spontaneous Weight Gain

To our knowledge, the differences among dietary fat types in the efficiency of protein deposition shown here during refeeding have not been observed during previous studies involving normal feeding,[14-18] thereby underlining differences in the energetics of weight recovery (after food restriction) versus spontaneous weight gain in response to dietary fatty acid composition. In contrast, the ability of diets rich in MCT (like coconut oil) or in n-6, PUFA (like safflower oil or corn oil) to show a lower efficiency of energy utilization and to limit fat accretion during weight recovery has also been reported during spontaneous weight gain in

Table 3. Fasting Plasma Insulin and Glucose and Plasma Lipids at Day 10 of Refeeding Either a Low-Fat Diet or Various HF Diets After a Period of Underfeeding

Test Diets	Glucose (mg/100 mL)	Insulin (μU/mL)	Insulin to Glucose Ratio	Cholesterol (mmol/L)	Phospholipids (mmol/L)	Triglycerides (mmol/L)	Nonesterified Fatty Acids (mmol/L)
1. Low-fat	127 ± 1	31.5 ± 1.0	0.249 ± 0.01	1.75 ± 0.06	1.64 ± 0.05	0.88 ± 0.07	1.054 ± 0.09
2. HF lard	125 ± 5	40.3 ± 1.0	0.325 ± 0.01	2.14 ± 0.11	1.77 ± 0.07	0.99 ± 0.14	0.921 ± 0.10
3. HF coconut oil	133 ± 4	28.8 ± 1.1	0.216 ± 0.005	1.89 ± 0.11	1.75 ± 0.11	1.15 ± 0.16	1.102 ± 0.07
4. HF olive oil	129 ± 5	29.5 ± 0.5	0.230 ± .008	2.26 ± 0.10	1.85 ± 0.09	1.02 ± 0.16	0.976 ± 0.03
5. HF safflower oil	130 ± 4	33.3 ± 1.1	0.258 ± .012	1.91 ± 0.12	1.52 ± 0.08	0.71 ± 0.08	0.746 ± 0.05
6. HF fish oil	128 ± 2	31.0 ± 0.9	0.244 ± .009	1.30 ± 0.12	1.02 ± 0.06	0.33 ± 0.04	0.580 ± 0.04
7. HF mixed	132 ± 5	37.5 ± 3.2	0.286 ± .022	1.69 ± 0.08	1.46 ± 0.05	0.59 ± 0.03	0.668 ± 0.03
Significance of F	NS	$P < .001$	$P < .001$	$P < .001$	$P < .01$	$P < .01$	$P < .001$
Pairwise comparison		2 *v* 1, 3, 4,5 ,6 7 *v* 1, 3, 4, 6	2 *v* all 7 *v* 3, 4	6 *v* all 2, 4 *v* 1, 6, 7	6 *v* all 7 *v* 4	6 *v* 1, 2, 3, 4, 5 7 *v* 3	5, 6, 7 *v* 1, 3, 4 6, 7*v* 2

NOTE. All values are the mean ± SEM (n = 6). NS indicates no significant difference by ANOVA.

young rodents[14,19-21] but not in older rats,[15,16] thereby raising the possibility that these differences in the efficiency of fat deposition may only be apparent during a rapid phase of tissue deposition.

On the other hand, the present findings showing that the diet rich in fish oil (HF fish oil or HF mixed) induced a higher or similarly high efficiency of fat deposition versus the other fat types during weight recovery contrast with reports that diets high in n-3 PUFA reduced weight gain or decreased fat deposition during normal feeding in rodents.[16-17,22-24] However, as indicated below, the impact of n-3 fatty acids on the efficiency of fat deposition in all the latter studies is difficult to interpret because data on energy balance and body composition are either absent or incomplete, or because of differences in ME intake among the various diet groups, namely:

1. The findings that a decreased weight gain occurred in obese mice[22] fed a diet rich in fish oil as compared with evening primrose oil (rich in n-6 PUFA), or that in rats[23] the addition of n-3 fatty acids (as linseed oil) to a diet rich in saturated fat (beef tallow) resulted in less weight gain than when added to diets rich in monounsaturated fat (olive oil) or n-6 PUFA (safflower oil) despite similar food intake, do not necessarily imply that whole-body energetic efficiency is increased nor that body fat is decreased. The reported reductions in body weight gain could have resulted from reductions in body water and protein or could be due to differences in diet digestibilities.

2. In other studies in rats[16] and hamsters,[17] HF feeding with diets rich in fish oil was found to result in less body fat than feeding with diets rich in other fat types. However, because fish oil also induced the lowest food intake (6% to 15% reductions compared with other diets), the effect of fish oil on fat gain could be merely secondary to reduced energy intake rather than being due to an increase in energy expenditure.

3. Furthermore, the report[24] that long-term feeding of rats with a diet rich in fish oil resulted in lower accretion of perirenal and epididymal fat mass than feeding with a diet rich in lard may only be revealing differential effects of these fat types on regional fat deposition, and does not provide evidence for differences in whole-body efficiency of energy utilization. In fact, a recent study in rats consuming a similar energy intake on diets rich in fish oil concentrate, herring oil, or a mixture of olive oil and beef tallow suggests that n-3 fatty acids from fish oil can influence regional distribution of fat depots without a significant effect on total body fat.[18]

Taken together, the available data based on complete energy balance and body composition analysis in animals fed HF diets suggest that the differences between dietary fat types on efficiency of total body fat deposition during weight recovery (data reported here) are rather similar to those reported during spontaneous weight gain.[14,18-21]

Potential Determinants Underlying Differential Effects of Fat Types on Refeeding Energetics

In our recently reported study on the energetics of body weight recovery in response to various levels of dietary fat consisting of a 1:1 mixture of lard and corn oil (ie, diets rich in both long-chain saturated fat and n-6 PUFA), no differences were apparent when dietary fat contributed between 6 and 30% of total energy intake.[6] However, with higher-fat diets (mixed fat providing 40% to 53% of intake), there was a gradual increase in energetic efficiency, with all the energy thus saved directed at fat deposition and none to protein. By comparing the diets with the extremes of fat content (6% *v* 53%) and assuming that they represent the two extremes of energy cost of fat deposition, it was shown that the energy saved because of the lower obligatory energy cost of incorporating dietary triglycerides into adipose tissue (in the case of HF diets) as compared with the cost involved with de novo lipogenesis from dietary carbohydrates (in the case of low-fat diets) could explain only 50% of the increase in body fat gain induced by HF refeeding. It was concluded that at least during the early phase of refeeding, the HF diet exerts a suppressive effect on energy expenditure that contributes to the higher efficiency of fat gain.[6]

Similar arguments can also be made to explain our current data (Fig 1) showing a higher gain in body fat (without concomitant changes in body protein gain) in the HF lard group than in the low-fat group. However, it is also apparent that other HF diets can also influence protein metabolism and induce a real shift in energy partitioning between protein and fat. This repartitioning of energy available for gain is most prominent with the HF fish oil and HF mixed diet, in which the energy saved from a lower protein gain is shifted to the fat gain. Conversely, it can be argued that the lower fat deposition in the HF safflower group arises at least in part from the fact that energy intake is repartitioned toward the more costly process of protein synthesis and its maintenance, thereby resulting in less energy being available for fat deposition. However, a similar shift in energy partitioning in favor of protein cannot explain the lower efficiency of fat gain in the group refed the HF coconut oil diet, since body protein gain did not increase in this group. It follows therefore that although refeeding with the HF safflower oil and HF coconut oil diets were equally effective in preventing the increase in fat gain found with the other HF diets, at least parts of the underlying mechanisms are likely to be different: safflower oil (rich in n-6 PUFA) will influence energy partitioning in favor of protein, but not coconut oil (rich in MCT), which seems to limit fat accretion mainly by activating thermogenesis.

Increased sympathetic activity has been proposed to underlie the thermogenic effects of diets high in MCT,[20,21] but to date, differential effects of fat types on sympathetic neural activity have not been convincingly demonstrated.[25,26] Similarly, our data cast doubts about the existence of a causative link between insulin resistance and the increased efficiency of fat gain induced by HF feeding. This is because dietary fish oils, which by virtue of their high n-3 fatty acid content are well known to prevent effectively the insulin resistance due to HF feeding,[27] failed to prevent the enhanced efficiency of fat gain in our study, whether fed as a principal or minor component of HF diets (HF fish oil and HF mixed, respectively). This is supported by the lack of

correlation between the efficiency of fat gain (or protein gain) and fasting insulin or the insulin to glucose ratio, and is hence in line with our previous demonstration in the rat that in the absence of differences in food intake, hyperinsulinemia induced by exogenous insulin administration had no impact on energetic efficiency or on body composition.[28]

The mechanisms underlying the differential effects of HF types on energy metabolism during refeeding are no doubt complex, given that dietary fatty acids are potentially capable of influencing a wide array of metabolic events—namely (1) by virtue of differences in their oxidation rates, (2) via their central actions of their metabolites or related signals, (3) via their effects in directly altering cell membrane fluidity and hence tissue responsiveness to neurohormonal control of metabolism, or (4) by shifting the balance of eicosanoids, which in turn are potentially capable of influencing both fat and protein metabolism. At the organ/tissue level, differences in the thermogenic capacity of brown adipose tissue have been reported to be influenced by HF feeding, with diets rich in animal fats (rich in saturated LCT) reportedly being more inhibitory than MCT or n-6 PUFA[20,21]—findings compatible with our data showing a higher efficiency of fat accretion with HF lard than with HF coconut or HF safflower oils. There is also evidence for differential effects of fat types on skeletal muscle thermogenesis. Microcalorimetric in vitro studies in our laboratory have recently shown that in muscles of mice fed a HF diet rich in fish oil, the heat production associated with calcium recirculation between sarcoplasmic reticulum and sarcoplasm (the main component of the energy cost of intracellular calcium homeostasis) was lower than in muscles of mice fed HF diets rich in coconut oil or corn oil, or when compared with results obtained with a low-fat diet.[29] Given that the energy dissipation associated with calcium homeostasis amounts to more than 20% of muscle energy expenditure at rest[30] and that skeletal muscle mass accounts for some 40% of body weight, the possibility arises therefore that in the study reported here the suppressing effect of the HF diet rich in fish oil on whole-body energy expenditure (and hence effects on exacerbating body fat accretion) may be due at least in part to a reduction in the energy cost of intracellular calcium homeostasis in skeletal muscles. It remains to be seen whether the modulation of this cellular mechanism underlying muscle thermogenesis is specific to fish oil (and related to its high content of n-3 fatty acids) or could also underlie the equally suppressing effects of lard, olive oil, or the fat mixture on energy expenditure.

Implications

It should be kept in mind that extrapolation across species should be treated with caution. Nonetheless, in the context that these studies were conducted during a period of increased energy availability after a period of low caloric intake, our findings may provide insights vis-à-vis strategies both for nutritional rehabilitation after undernutrition and for the management of weight regain after low-calorie therapy in the obese. Considerable interest focuses on the possibility that diets rich in one particular fat type may be less fattening than another.[2] Our studies examining the influence of various HF diets in a dynamic state of weight gain and characterized by an already elevated efficiency of fat utilization even on low-fat diets,[3-5] show that the exacerbation of fat deposition shown with certain dietary fats does not occur with diets rich in MCT (HF coconut oil) or in n-6 PUFA (HF safflower oil). However, it is also shown here that these differential effects on fat accretion only occur when these oils are fed in very large amounts, and that they are no longer apparent when fed as a minor constituent of the HF diet. One therefore wonders about the therapeutic advantage of one type of fat per se in obesity management.

The current study is also of direct relevance to the issue of whether dietary energy from nonprotein sources can influence nitrogen retention.[31,32] Diets low in carbohydrate and high in fat have been postulated to spare protein in malnourished patients on the basis that (1) increased concentrations of fatty acids in the blood may lead to a preferential increase in the rate of fatty acid oxidation in the muscle and hence a subsequent decrease in glucose utilization, thereby resulting in a reduction in amino acid oxidation; and (2) a high concentration of ketones inhibits the rate of protein degradation in muscle. However, the evidence for a protein-sparing effect of HF as compared with high-carbohydrate supplementary feeding remains highly controversial and has been attributed to several factors including age, duration of treatment, differences in energy intake, and the many different ratios of fat to carbohydrate used in the various studies. Our data here demonstrating important differences in the effects of fat types on body protein retention during weight recovery indicate that at least part of the discrepancy may also reside in the fact that fat types or mixtures of fat types influence both fat oxidation and protein metabolism differently. Further studies directly assessing nitrogen balance in relation to dietary fat types are warranted.

In conclusion, the data presented here demonstrate important different effects among HF diets varying markedly in fatty acid composition on the reconstitution of both lean and fat tissue compartments during the recovery of body weight. In particular, they emphasize striking differences in body protein and fat deposition between n-6 and n-3 PUFA (safflower oil *v* fish oil), as well as between long-chain and medium-chain saturated fats (lard *v* coconut oil). Our study also reveals that fish oil, despite showing all the beneficial effects associated with risks of cardiovascular diseases (ie, low cholesterol, low triglycerides and free fatty acids, and low fasting insulin to glucose ratio), seems to be as effective as lard or olive oil in exacerbating body fat gain, and in addition, it reduces protein gain. However, it would be premature to advocate one type of fat supplement over another during nutritional rehabilitation until the apparently desirable or undesirable effects on energy metabolism and body composition are weighed against changes in muscle function and immune response.

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