Chubby? Blame Those Genes

Heredity plays the pivotal role in weight control

It has long been clear that people's weight is determined by a balance of heredity and life-style. But which exerts the heavier effect? Two reports in last week's *New England Journal of Medicine* tip the scales firmly toward genetic makeup.

In one investigation, researchers from the U.S. and Sweden analyzed weight and height records from the Swedish Adoption/Twin Study of Aging. Reviewing data on 247 identical and 426 fraternal pairs of twins, the team found that siblings end up with similar body weights whether or not they are raised in different families, and that they are much more likely to grow up looking like their natural parents than

their adoptive ones. "If both biologic parents are fat, about 80% of their kids are going to be fat," says Dr. Albert Stunkard of the University of Pennsylvania.

In a separate study, Canadian researchers fed twelve pairs of identical twins 1,000 calories above their normal daily intake for 84 days out of a 100-day period. Weight gains ranged from 4 kg to 13 kg. But the difference in the amount gained was much less between twins than between subjects who were not siblings. Concludes Claude Bouchard, a professor of exercise physics at Quebec's Laval University: "It seems genes have something to do with the amount you gain when you are overfed."

"The results take obesity out of being a moral problem—that obese people have a lack of willpower—and put it more in the realm of metabolism," observes Dr. Theodore VanItallie of Columbia University's College of Physicians and Surgeons. If people are born to be fat, are attempts to slim down doomed? No, say weight specialists. Low-fat diets and exercise can help offset heredity. People may inherit a propensity to obesity, but it need not be their destiny.

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THE RESPONSE TO LONG-TERM OVERFEEDING IN IDENTICAL TWINS

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Abstract We undertook this study to determine whether there are differences in the responses of different persons to long-term overfeeding and to assess the possibility that genotypes are involved in such differences. After a two-week base-line period, 12 pairs of young adult male monozygotic twins were overfed by 4.2 MJ (1000 kcal) per day, 6 days a week, for a total of 84 days during a 100-day period. The total excess amount each man consumed was 353 MJ (84,000 kcal).

During overfeeding, individual changes in body composition and topography of fat deposition varied considerably. The mean weight gain was 8.1 kg, but the range was 4.3 to 13.3 kg. The similarity within each pair in the response to overfeeding was significant (P<0.05) with respect to body weight, percentage of fat, fat mass, and estimated subcutaneous fat, with about three times more variance among pairs than within pairs (r $\approx$ 0.5). After adjustment for the gains in fat mass, the within-pair similarity was particularly evident with respect to the changes in regional fat distribution and amount of abdominal visceral fat (P<0.01), with about six times as much variance among pairs as within pairs (r $\approx$ 0.7).

We conclude that the most likely explanation for the intrapair similarity in the adaptation to long-term overfeeding and for the variations in weight gain and fat distribution among the pairs of twins is that genetic factors are involved. These may govern the tendency to store energy as either fat or lean tissue and the various determinants of the resting expenditure of energy. (N Engl J Med 1990; 322:1477-82.)

THERE are large differences among persons of a given age and sex in body fat content and regional distribution of body fat. The reasons for such differences are not known, but it is increasingly recognized that inheritance is a factor in obesity and regional fat distribution.

One line of research studies biologic relatives and relatives by adoption and relies on the tools of genetic epidemiology to estimate the genetic and nongenetic sources of variation in body fat content and regional fat distribution.[1,2] Another, more experimental, approach requires the study of the differences between people in the response to a well-defined positive or negative energy balance. This strategy allows the amount of weight gained or lost to be determined, as well as the physiologic and biochemical correlates of the response to the change in energy balance. Among studies of the adaptation to short-term and long-term overfeeding, significant differences between people have been found in the response to a regimen of overfeeding.[3-5] Such differences were clearly evident in the Vermont study of overfeeding reported by Sims and his colleagues more than 20 years ago.[5-7]

We have extended this work by studying the effects of a positive or negative energy balance on pairs of identical twins.[8,9] In these studies, both members of each pair of twins undergo exactly the same treatment in order to determine not only the extent of variation in the individual responses to the experimental situation but also the components of variance within pairs and between pairs, thereby permitting an assessment of the role of inherited characteristics in the response. We previously reported the results of a short-term (22-day) study of overfeeding conducted with six pairs of monozygotic twins.[9-14] The results of that experiment were not conclusive, however, partly because the effect of treatment was small. Therefore, we undertook this long-term study of overfeeding to clarify some of the issues still in doubt. Twelve pairs of male monozygotic twins were overfed by 4.2 MJ (1000 kcal) per day, 6 days a week, over a period of 100 days. We describe the changes in body mass, total body fat, and fat distribution during the period of overfeeding, in which a total energy excess of 353 MJ (84,000 kcal) was administered.

METHODS

Subjects

We studied 24 sedentary young men (mean [±SD] age, 21±2 years) living in the province of Quebec. Each man gave written consent for participation in this study, which was approved by the Laval University Medical Ethics Committee and the Office for Protection from Research Risks of the National Institutes of Health, Bethesda, Md. These men constituted 12 pairs of identical twins.

The youngest pair was 19 years of age, and the oldest pair was 27. The twins had been reared together and had been living together before this study.

The monozygosity of the twins was established on the basis of a questionnaire, their physical appearance, and the similarity of 12 polymorphic red-cell antigens and enzymes, the A, B, and C loci of the HLA-antigen system, and 10 polymorphic adipose-tissue proteins visualized by two-dimensional gel electrophoresis. None of the men had a history of recent illness, obesity, hypertension, diabetes, hyperlipidemia, or endocrinopathy, and each had a normal physical examination and normal fasting serum glucose, triglyceride, and cholesterol concentrations. Men whose parents were obese or had diabetes or lipid disorders were not accepted into the study.

Four pairs of twins were studied at a time over a period of 18 months: one subgroup starting in early August, a second in February, and the third the following August. The results were similar in all three subgroups. The men were housed in a closed section of a dormitory on the campus of Laval University and were under 24-hour supervision by members of the project staff living with them. Each man stayed in the unit for 120 consecutive days — 14 days for base-line testing, 3 days for testing before the period of overfeeding, 100 days for the period of overfeeding, and 3 days for testing after the period of overfeeding. During the base-line testing, body weight was measured daily, skin-fold thickness was measured at 10 sites five times, and body density was measured three times by underwater weighing.

The men were not allowed to drink alcoholic beverages during the study. Five of the pairs of twins were light smokers, but smoking was not permitted during the study. We believe that these men reduced their frequency of smoking to a few cigarettes a day, but did not stop entirely.

Base-Line Test Period

During the base-line period, the men ate freely in a special dining room. The food was prepared by university personnel but was put aside for the men by the dietitians involved in the study. All foods selected by the men were recorded and weighed. All foods not eaten were weighed separately, and their weight was subtracted from that of the food selected so that the net intake could be calculated. The nutrient composition and energy content of the food were derived from a computerized version of the Canadian food-composition tables.[15,16] Each man's habitual daily energy intake under conditions of stable body weight and body composition was calculated from the 14-day record of food intake and was generally based on the entries for the last 12 days, the variations in body weight, and the changes in fat mass or fat-free mass, if any, determined from the body-density measurements. The energy content of body fat was assumed to be 37.8 MJ (9300 kcal) per kilogram, whereas that of lean tissue was assumed to be 4.2 MJ (1020 kcal) per kilogram.[17] The body energy content was the sum of these two components. The average nutrient composition of the food eaten during the base-line period was 52±6 percent carbohydrate, 34±6 percent lipid, and 14±6 percent protein.

Testing before and after the Overfeeding Period

On the first day of the three-day test period before the overfeeding period, we measured the resting metabolic rate and the thermic effect of food. On the third day, underwater weighing, biopsies of adipose tissue, and exercise-tolerance testing were performed. About five days before the overfeeding period, a CT scan of the abdomen was performed. The same studies were repeated during the three-day test period after the overfeeding period.

Overfeeding Period

After the base-line period, the men were fed a diet containing 4.2 MJ (1000 kcal) per day more than their established base-line energy intake from food, 6 days a week for 100 days. On the seventh day of each week they consumed the base-line number of calories. They were thus overfed for 84 of the 100 days, the total excess energy intake being 353 MJ or 84,000 kcal. The food consumed each day had the following prescribed nutrient composition: 50 percent carbohydrate, 35 percent fat, and 15 percent protein. The men ate

three meals per day plus an evening snack tailored to complete the daily prescription for energy intake.

Physical activity was limited during the entire study; the daily schedule included such activities as reading, playing video games, playing cards, and watching television, as well as an outdoor walk for 30 minutes per day. The men were occasionally taken as a group to a play or a movie. They were carefully supervised at all times during all activities, and as far as we could ascertain their compliance with the regimen of dietary intake and the limitations on their activities was perfect. During this period, body weight was measured daily, skin-fold thickness every 5 days, and waist and hip circumference every 25 days.

Body Composition and Regional Fat Distribution

Blood pressure, pulse rate, and body weight were measured (the latter with the men wearing light exercise shorts) each morning before breakfast. The body-mass index was calculated as the body weight (in kilograms) divided by the height (in meters squared). Body density was determined by underwater weighing,[18] and fat mass and fat-free mass were calculated with a standard equation.[19] The volume of air remaining in the lungs was determined while each man was in the water tank, and the pulmonary residual volume was measured by the helium-dilution technique.[20] The data on body weight represent the mean measurements of three days, in each case the day on which the underwater weighing was done and the days before and after. The skin-fold thickness was measured at 10 sites, as were the waist and hip circumferences, according to the procedures recommended at the Airlie Conference.[21] The ratio of the sum of the skin-fold–thickness values for the trunk (subscapular, suprailiac, abdominal, midaxillary, and chest) to the sum of the values for the limbs (biceps, triceps, front midthigh, suprapatellar, and medial calf) was used as one estimate of the regional subcutaneous fat distribution.[22] The ratio of the waist to the hip circumference was used as another estimate of regional fat distribution.[21] For all the anthropometric measurements, two measurements were always made, and the mean was used if the difference between the two measurements was less than 5 percent. If the difference was 5 percent or more, a third measurement was made, and the mean of the two most similar values was used.[21] We also determined the mean adipose-cell mass in the abdominal (umbilicus level) and femoral (midthigh) areas,[23] using data on isolated fat cells obtained by collagenase digestion and the density of triolein to convert the adipose-cell volume to mass.

CT scanning was performed before and after the overfeeding period with a Siemens Somatom DRH scanner (Erlangen, Federal Republic of Germany). The men were examined in the supine position with their arms stretched above their heads.[24] The scans were obtained at the pubic symphysis and at the levels of the disks between the fourth and fifth lumbar vertebrae and between the eighth and ninth thoracic vertebrae. The attenuation interval used in the quantification of the areas of adipose tissue was −30 to −190 Hounsfield units. The total areas of abdominal and abdominal visceral fat were calculated by delineating their surfaces with a computerized pen. The abdominal visceral fat was defined by drawing a line on the inside of the muscle wall surrounding the abdominal cavity. The area of subcutaneous abdominal fat was computed as the total abdominal fat minus the visceral fat. The sum of the three trunk scans was used as an estimate of the response of the trunk fat to overfeeding.

The reproducibility of all the measurements of fat areas by anthropometry, studies of body composition, and CT scanning has been determined by several investigators and is known to be quite high when performed by the same observer, as in this study. The intraclass reliability coefficients for the variables reported were generally above 0.9.[21,24,25]

Statistical Analysis

The study design allowed testing for the presence of similarities within pairs of twins in the response to long-term overfeeding. The effects of overfeeding and the interactions between genotype and overfeeding were assessed with a two-way analysis of variance for repeated measures on one factor (time). The twins were considered nested within the pair, whereas the treat-

ment effect was defined as a fixed variable. The intraclass correlation coefficient for the changes brought about by overfeeding was computed from the between-pairs and within-pair means of squares.[26] This coefficient provides a quantitative estimate of the similarity within pairs in the response to overfeeding. An intraclass correlation coefficient close to 1.0 would indicate a perfect within-pair resemblance in response to overfeeding, whereas a coefficient close to zero would imply that there was no within-pair resemblance in response to the treatment. Similarly, a high F ratio indicates a high ratio of the variance between pairs to the variance within pairs in response to overfeeding, whereas a low F ratio (close to 1) indicates that the variances in response between and within pairs of twins are comparable. In some analyses, the results were adjusted for gains in total fat mass. These adjustments were performed by regression of the variable to be adjusted on the gain in fat mass after overfeeding, with the 24 subjects considered as unrelated persons. P values ≤ 0.05 were considered statistically significant.

RESULTS

Body weight increased significantly ($P<0.001$) during overfeeding, the average gain being 8.1 kg (Table 1). Body composition also changed significantly. Fat mass and fat-free mass increased, but the gain in adipose tissue was greater than the increase in lean tissue, as shown by the changes in the ratio of fat mass to fat-free mass, which increased from 0.13 to 0.22 ($P<0.001$). The sum of the skin-fold–thickness measurements, used to estimate the changes in the amount of subcutaneous fat, increased from 76 to 129 mm, or about 70 percent ($P<0.001$). The mean resting heart rate increased from 58 to 63 beats per minute by the end of the overfeeding period ($P<0.01$). Systolic blood pressure was unaltered, but diastolic blood pressure increased from 66 to 70 mm Hg ($P<0.05$; data not shown).

There were considerable differences between persons with respect to changes in body weight and body composition with overfeeding. Although the mean increase in body weight was 8.1 kg, the standard deviation was 2.4 kg and the range 4.3 to 13.3 kg. The individual differences in body weight and body composition as a result of overfeeding, however, were not distributed randomly among the 24 men. This is demonstrated by the similarity of the absolute changes within pairs shown in Table 1. The F ratios of the variances between pairs to the variances within pairs were about 3, and the intraclass correlation coefficients computed on the basis of the changes resulting from overfeeding were clustered around 0.50. The within-pair similarity was slightly less for fat-free mass (about 0.4). The within-pair similarity for the changes in body weight is illustrated in Figure 1.

Regional fat distribution was estimated by several methods (Table 2). The amount of subcutaneous fat, as estimated on the basis of skin-fold thickness, increased on both the trunk and limbs, but more so on the trunk (about 85 percent vs. 50 percent). Accordingly, the trunk-to-limb ratio of skin-fold thickness increased from 1.26 to 1.60 ($P<0.001$). Both the waist and the hip circumference increased significantly, but the ratio of the waist to the hip circumference also increased ($P<0.001$), indicating that more fat was gained at the waist level than at the hip level. The

Table 1. Effect of 100 Days of Overfeeding in 12 Pairs of Male Twins and Measures of the Similarity within Pairs with Respect to the Absolute Response to Overfeeding.*

| VARIABLE	BEFORE OVERFEEDING	AFTER OVERFEEDING†	SIMILARITY WITHIN PAIRS‡	
			F RATIO	ICC
	mean ±SD			
Body weight (kg)	60.3±8.0	68.4±8.2	3.43	0.55
Body-mass index	19.7±2.0	22.4±2.0	2.85	0.48
Percent fat	11.3±5.0	17.8±5.7	2.92	0.49
Fat mass (kg)	6.9±3.5	12.3±4.5	3.00	0.50
Fat-free mass (kg)	53.4±6.6	56.1±6.7	2.34	0.40
Fat mass/fat-free mass	0.13±0.06	0.22±0.08	3.30	0.53
Subcutaneous fat (mm)§	75.9±21.1	129.4±32.9	2.77	0.47
Body energy (MJ)	497±142	719±176	3.12	0.51

*Statistical significance was determined by a two-way analysis of variance for repeated measures on one factor (time). The F ratio was the ratio of the variance between pairs to that within pairs. The intraclass correlation coefficient (ICC) was used to assess the similarity within pairs in the response to overfeeding.

†$P<0.0001$ for all variables shown in the comparison with the values obtained before overfeeding.

‡$P<0.05$ for all variables except fat-free mass.

§Represents the sum of 10 skin-fold–thickness measurements (see Methods).

within-pair similarity in the response to overfeeding was generally significant with respect to the changes in anthropometric indicators of regional fat distribution, but not with respect to abdominal and femoral fat-cell mass. However, when the data were adjusted for the increase in total fat mass, there was a strong indication that trunk fat and peripheral fat, as well as the descriptors of regional fat distribution — namely, the trunk-to-limb skin-fold–thickness ratio (F = 6.92, $P<0.001$), the waist-to-hip ratio (F = 6.10, $P<0.01$) and the ratio of abdominal-to-femoral fat-cell mass
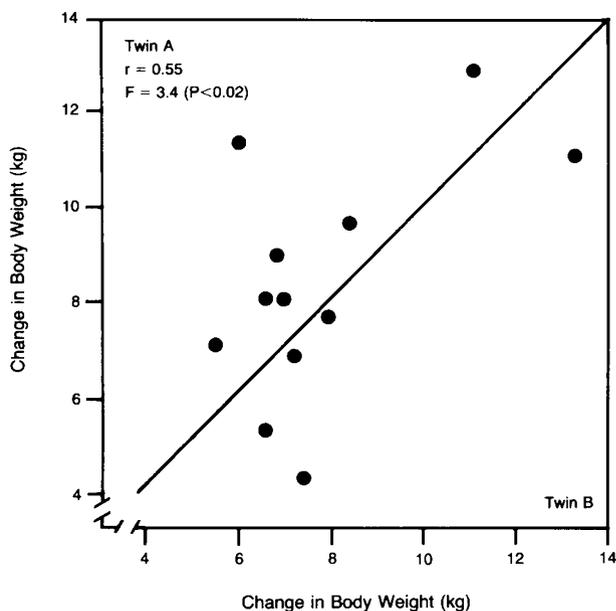
Figure 1. Similarity within Pairs with Respect to Changes in Body Weight in 12 Pairs of Male Twins in Response to 100 Days of Overfeeding.

Each point represents one pair of twins (A and B). The closer the points are to the diagonal line, the more similar the twins are to each other.

(F = 3.11, P<0.05) — were all characterized by a significant similarity within pairs in the response to overfeeding.

The effects of overfeeding on abdominal and trunk fat as measured by CT are shown in Table 3. Overfeeding increased the adipose-tissue surface areas in all the subcutaneous and visceral or deep anatomical sections (P<0.001). Again, however, there were considerable differences between persons with respect to changes in the CT-assessed fat areas, as shown by the percent changes of abdominal visceral fat. In this case, the responses ranged from about zero to an increase of more than 200 percent (data not shown). The within-pair similarity in response was significant with respect to the CT-assessed abdominal visceral fat (P<0.05). When the changes in CT-assessed fat were adjusted for the gain in total fat mass, however, the similarity within pairs became significant with respect to all CT trunk and abdominal measurements. The resemblance was greatest with respect to abdominal visceral fat. The within-pair resemblance in the response of visceral fat, after adjustment for the gains in total body fat, is shown in Figure 2.

We explored the relation among the changes in the various components of body fat by calculating the correlation coefficients of the absolute response values for each of the 24 men (Table 4). As the correlations suggest, the common variance ($r^2 \times 100$) between the gains in body weight or fat mass and the gains in fat on the trunk varied from about 40 to 60 percent. On the other hand, the gains in body weight or fat mass were not significantly correlated with the gains in the two indicators of changes in regional fat distribution — the trunk-to-limb ratio of skin-fold thickness and the ratio of waist to hip circumference. Finally, only the changes in the waist circumference and in the ratio of the waist to the hip circumference were significantly correlated with the gains in the CT-assessed abdominal visceral fat, but the common variance reached only

Table 3. Effect of 100 Days of Overfeeding on CT-Assessed Trunk and Abdominal Fat in 12 Pairs of Male Twins and the Similarity within Pairs in Response to Overfeeding.*

MEASURE OF CT-ASSESSED FAT (cm²)	BEFORE OVER-FEEDING	AFTER OVER-FEEDING	SIMILARITY WITHIN PAIRS		SIMILARITY WITHIN PAIRS ADJUSTED FOR GAIN IN FAT MASS	
			F RATIO	ICC	F RATIO	ICC
	mean ±SD					
Trunk (total)	250±99	448±107†	1.4	0.16	3.8‡	0.58‡
Abdominal						
Total	106±46	199±50†	1.3	0.14	4.1§	0.60§
Subcutaneous	72±40	141±46†	1.0	0.01	3.8‡	0.58‡
Visceral	34±9	58±15†	3.6‡	0.56‡	6.1§	0.72§

*Statistical significance was determined by a two-way analysis of variance for repeated measures on one factor (time). The F ratio was the ratio of the variance between pairs to that within pairs. The intraclass correlation coefficient (ICC) was used to assess the similarity within pairs in the response to overfeeding. CT-assessed abdominal fat was assessed at the L-4–L-5 level. Values for trunk fat represent the sum of three scans obtained at the pubic symphysis and at the levels of the disks between L-4 and L-5 and between T-8 and T-9.

†P<0.001.   ‡P<0.05.   §P<0.01.

20 to 30 percent. The same trends were found when the correlations were computed with the mean changes observed for each pair of twins (12 sets of scores) instead of the 24 individual sets of scores.

There were interesting relations between the gains in the ratio of fat mass to fat-free mass during the overfeeding period and the gains in body weight (r = 0.61, P<0.01), the sum of the five trunk skin-fold–thickness measurements (r = 0.62, P<0.001), and the waist circumference (r = 0.66, P<0.001) (data not shown). There was no correlation, however, between the changes in the ratio of fat mass to fat-free mass and the changes in abdominal visceral fat (r = 0.21) or overall regional fat distribution, as assessed by the trunk-to-limb ratio of skin-fold thickness (r = 0.23) or the waist-to-hip ratio (r = 0.37).

DISCUSSION

Three major components of the obese state can be identified when obesity is considered from the perspective of health — namely, excess total body fat, excess trunk fat or abdominal subcutaneous fat, and excess abdominal visceral fat.[27] These three components were recognized as important at a recent workshop presented by the National Institutes of Health on the clinical implications of regional fat distribution.[28] The results reported here allow assessment of the response of each component to long-term overfeeding.

We found wide differences between individuals in the response to long-term overfeeding. Such heterogeneity was found when only 12 genotypes were exposed to the regimen of positive energy balance. The heterogeneity would probably have been greater if a large number of unrelated subjects had been

Table 2. Effect of 100 Days of Overfeeding on Regional Fat Distribution in 12 Pairs of Male Twins and the Similarity within Pairs in Response to Overfeeding.*

VARIABLE	BEFORE OVERFEEDING	AFTER OVERFEEDING	SIMILARITY WITHIN PAIRS		SIMILARITY WITHIN PAIRS ADJUSTED FOR GAIN IN FAT MASS	
			F RATIO	ICC	F RATIO	ICC
	mean ±SD					
Skin-fold thickness (mm)						
Trunk	42.5±15.1	79.4±24.5†	3.15‡	0.52‡	3.44‡	0.55‡
Limb	33.4±7.4	50.0±11.8†	2.98‡	0.50‡	4.85§	0.66§
Ratio, trunk to limb	1.26±0.26	1.60±0.36†	3.19‡	0.52‡	6.92†	0.75†
Circumference (cm)						
Waist	75±5	84±5†	5.85§	0.71§	6.87†	0.75†
Hip	87±6	93±5†	3.58‡	0.56‡	9.06†	0.80†
Ratio, waist to hip	0.86±0.03	0.89±0.03†	3.64‡	0.57‡	6.10§	0.72§
Fat-cell mass (µg)						
Abdominal	0.20±0.10	0.42±0.16†	2.35	0.40	3.15†	0.52‡
Femoral	0.29±0.13	0.52±0.18†	2.45	0.42	2.24	0.38
Ratio, abdominal to femoral	0.68±0.18	0.81±0.16§	1.12	0.06	3.11‡	0.51‡

*Statistical significance was determined by a two-way analysis of variance for repeated measures on one factor (time). The F ratio was the ratio of the variance between pairs to that within pairs. The intraclass correlation coefficient (ICC) was used to assess the similarity within pairs in the response to overfeeding.

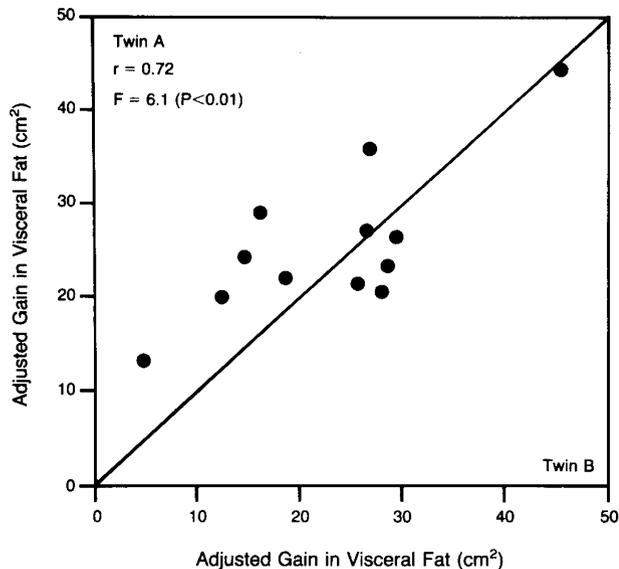†P<0.001.   ‡P<0.05.   §P<0.01.

Figure 2. Similarity within Pairs with Respect to Changes in Abdominal Visceral Fat in 12 Pairs of Male Twins in Response to 100 Days of Overfeeding after Adjustment for Gain in Fat Mass.

When the same analysis was performed with the percent gain in visceral fat as the variable, the intraclass correlation coefficient was 0.90 and the F ratio 18.9 (P<0.001).

studied. The changes in body weight, body composition, trunk fat, and visceral-fat deposition varied between the high and the low weight gainers by at least threefold. Individual differences in weight gain have been found during overfeeding before,[3-5,9,10,29-31] but this study demonstrates them even more clearly, because the degree of overfeeding was identical for each man and the duration was long enough to induce changes in body composition and regional fat distribution reliable beyond any errors in measurement. Thus, a comparable surplus intake of energy over a relatively long period does not cause identical responses with respect to body mass, body composition, or regional fat distribution in sedentary young men.

The average gain in fat mass was 5.4 kg or about 210 MJ (52,220 kcal), whereas the gain in fat-free mass was 2.7 kg or approximately 11.5 MJ (2754 kcal). On average, about 121 MJ (29,000 kcal) did not appear as weight gain when constants were used to convert tissue gains into energy equivalents,[17] and presumably this energy was dissipated in some way. One third of the weight gained by the group as a whole was in the form of fat-free mass, a proportion comparable with that reported previously.[4,9] The man who gained the most weight (13.3 kg) had no evidence of energy dissipation by any mechanism, whereas in the man who gained the least weight (4.3 kg) only about 40 percent of the extra calories were deposited as body tis-

sues. The men who gained more fat than lean tissue tended to gain more weight and to gain more fat in the truncal–abdominal area. On the basis of the correlations we found, 37 to 44 percent of the gains in weight or trunk fat were accounted for by the increments in the proportion of fat and lean tissues.

When the results for all 24 men were analyzed, the correlations between the total energy ingested during the 100-day period (including the 84,000-kcal surplus) and the gains in body weight (r = 0.26), fat mass (r = 0.26), sum of 10 skin-fold–thickness measurements (r = 0.25), and abdominal visceral fat (r = −0.31) were not statistically significant. In addition, the increases in total body fat were correlated with the gains in truncal subcutaneous fat but not with the changes in the distribution of regional fat and particularly abdominal visceral fat (Table 4). In other words, the accumulation of visceral fat cannot be predicted from the increase in body mass or body fat induced by long-term overfeeding. These results demonstrate that people rely on different strategies to cope with long-term overfeeding, even in terms of tissue gained and sites of deposition.

The alterations in body weight, body composition, and body energy content during overfeeding were characterized by about three times more variance between the pairs of twins than within the pairs. The similarity in the response within pairs was a little less than that reported with respect to body weight and indexes of body composition in one study of six pairs of monozygotic twins who were overfed for 22 days.[9,10] The within-pair similarity in the changes during overfeeding was higher with respect to anthropometric indicators of regional fat distribution and abdominal visceral fat after adjustment for the gains in total fat mass. There was a significant resemblance within pairs with respect to the increase in the ratio of abdominal-to-femoral fat-cell mass, but only when individual differences in total fat increases were taken into account. In view of the implications of truncal–abdominal obesity and excessive abdominal visceral fat for insulin metabolism and plasma lipid and lipoprotein levels, and their relations to mortality and morbidity,[28,32-35] the findings that some persons were more prone than others to store fat on the trunk,

Table 4. Correlations between the Gains in Body Fat, Trunk Fat, and Abdominal Visceral Fat in the 12 Pairs of Male Twins during the Period of Overfeeding.*

VARIABLE	FAT MASS	TRUNK SKIN-FOLD THICKNESS	WAIST CIRCUMFERENCE	TRUNK-TO-LIMB RATIO	WAIST-TO-HIP RATIO	CT-ASSESSED ABDOMINAL VISCERAL FAT
Body weight	0.77†	0.63†	0.75†	0.32	0.34	0.32
Fat mass	—	0.78†	0.68†	0.28	0.33	0.28
Trunk skin-fold thickness‡	—	—	0.53§	0.56§	0.22	−0.02
Waist circumference	—	—	—	0.17	0.79†	0.55§
Trunk-to-limb ratio	—	—	—	—	−0.12	−0.04
Waist-to-hip ratio	—	—	—	—	—	0.47¶

*Correlations were computed from the absolute changes measured in the 24 men, considered as independent persons.
†P<0.001.   ‡Represents the sum of five skin-fold–thickness measurements (see Methods).
§P<0.01.   ¶P<0.05.

in the abdominal cavity, or both are of considerable clinical interest.

The most likely explanation for the resemblance between identical twins in the response to overfeeding is that a person's genotype is an important determinant of adaptation to a sustained energy surplus. Since the excess energy intake involved the same composition of macronutrients and was fixed at 84,000 kcal for all the men, and since they kept the same relatively sedentary schedule during the period of overfeeding, differences in the efficiency of weight gain could result either from individual variation in the preferential storage of energy as fat or lean tissue (as shown here) or from variation in the components of energy expenditure during rest.

Our results strongly support the view that there are individual differences in the tendency toward obesity and in the distribution of body fat, and they suggest that these differences are partly related to undetermined genetic characteristics.

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twin pair	1	2	3	4	5	6	7	8	9	10	11	12	
μ:	?	?	?	?	?	?	?	?	?	?	?	?	
α:	?	?	?	?	?	?	?	?	?	?	?	?	
σ:	?	?	?	?	?	?	?	?	?	?	?	?	
w. incr. twin A	13.3	11.1	8.2	6.1	7.9	7.1	6.9	6.5	6.7	7.3	6.5	5.4	ybar: 8.08
w. incr. twin B	11	12.9	9.6	11.4	7.7	6.9	8	8	8.8	4.3	5.3	7.1	var: 5.54
													s.d.: 2.35
ybar(i):	12.15	12	8.9	8.75	7.8	7	7.45	7.25	7.75	5.8	5.9	6.25	var(ybars): 4.44
var(i):	2.645	1.62	0.98	14.05	0.02	0.02	0.605	1.125	2.205	4.5	0.72	1.445	ave(var): 2.49
n(i):	2	2	2	2	2	2	2	2	2	2	2	2	

ANOVA TABLE

Source	$\sum$ Sq	df	Mean Sq	F
B / w Poplns	97.58	11	8.87	3.56
W / n Poplns	29.93	12	2.49	
All	127.51	23	5.54	