Lean Body Mass in Twins

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A study of 49 pairs of monozygous (MZ) twins and 38 pairs of same-sexed dizygous (DZ) twins showed that lean body mass (LBM), as determined by potassium 40 counting, is under genetic influence. Intrapair variances for LBM are much smaller than those for body fat, which suggests that LBM has a higher degree of heritability. There is a correlation between the magnitude of intrapair LBM differences and intrapair weight differences for both sets of twins, showing that environment is also an important influence. The effect of weight variation on LBM variation is greater for thin people than for those with appreciable burdens of body fat, an observation previously made on individuals who undergo a nutrition-induced weight change.

LEAN BODY MASS (LBM) is known to vary among individuals of a given age and sex. LBM is also known to change in concert with nutritionally induced changes in body weight.[1,2] Body weight and height are reported to be under genetic control,[3] as is the ratio of weight to height squared (body mass index [BMI][4-9]), which is of interest because of its relationship to adult morbidity and mortality. Although there are several reports about the inheritance of body fat,[4,10] there is only one other study that deals with the major component of body weight, LBM.[11]

Herein, we present data on LBM variability in dizygous (DZ) same-sexed twins compared with monozygous (MZ) twins, using for the first time in twin studies the potassium 40 counting technique. Our results confirm the findings reported by Bouchard et al[11] and Rice et al[12] that this body component is under genetic control. In addition, we now report that the intrapair variability in LBM is a function of intrapair variability in body weight, and further that the magnitude of this effect is inversely related to body fat content.

SUBJECTS AND METHODS

The original group of twins consisted of 51 pairs of MZ twins and 38 pairs of same-sexed DZ twins who were recruited by newspaper advertisement. In addition, there was one set each of MZ and DZ triplets; for purposes of analysis, each was considered as three twin pairs. All who volunteered were accepted for study. The age range was 7 to 85 years.

This study was conducted with the approval of our local institutional review board on human investigation. All participants provided written consent after being informed of the nature and purpose of the study; in the case of children, one or both parents were also asked to consent.

We excluded from consideration three sets of MZ twins, two of a MZ triplet pairing, and three sets of DZ twins because of circumstances that could compromise the size of the LBM in one member of a twin pair. These were the following: a 13-year-old girl who weighed only half as much and was 13 cm shorter than her DZ twin and whose head circumference was 4 cm smaller due to a protracted bout of malabsorption; a 17-year-old MZ boy who weighed only 60% as much as his twin at birth and who had rickets in early life; a 13-year-old MZ boy who had scoliosis and had worn a brace for 4 years; a 15-year-old MZ girl who had a bout of severe anorexia nervosa in the recent past; a 29-year-old woman, the firstborn of MZ triplets, who had spinal curvature, a short left leg, and a history of skeletal muscle surgery; an 85-year-old DZ woman who had two heart attacks and a bout of pneumonia in the recent past and whose twin had kyphosis; and a 17-year-old DZ girl who had a history of recent weight loss and was currently being treated for a kidney infection. The final count was 19 pairs of MZ males, 30 pairs of MZ females, 12 pairs of DZ males, and 26 pairs of DZ females, and these subjects aged 7 to 68 years form the basis of the present report.

The twin pairs came to the laboratory together, where measurements of height and weight were made and an estimate of LBM was determined by potassium 40 counting.[13] This method involves detection and quantitation of gamma rays emanating from naturally occurring potassium 40 in the body. From this, potassium content of the body can be calculated, and since this element is distributed only in lean tissue, it is possible to derive a value for LBM and, by difference, body fat. Birthweight data were provided by the parents.

A sample of venous blood was obtained from each subject, and in most instances from both parents. Genetic marker typing for zygosity determination included ABO, Rh, MNSs, Fy, K, and P blood groups, HLA-A, -B, and -DR, Gm and Km immunoglobulin, properdin factor B, transferrin, group-specific component, phosphoglucomutase, and acid phosphatase. The probability of monozygosity in the marker-type–identical twin pairs, calculated according to methods described by Vogel and Motulsky,[14] was 99.6% or greater for each pair.

For analysis of body measurements, intrapair correlation coefficients were calculated by standard methods.[15] Since the subjects had a wide age range and hence a range of body sizes, we chose to express intrapair differences as a fraction of the average value of the twin pairs, twin A being first born: (twin A − twin B)/[(A + B)/2]. Intrapair variances (V) were calculated on this basis, and the coefficient of heritability was determined as $(V_{DZ} - V_{MZ})/V_{DZ}$; the standard deviation of this coefficient was calculated according to a formula set forth by Cavalli-Sforza and Bodmer.[16] Statistical analyses were performed with the CLINFO Software System (BBN Software Products, Cambridge, MA).

The technical error of the ^{40}K-counting procedure was evaluated by making duplicate counts on one to three occasions in 12 individuals who were unrelated to the subjects in this study, for a total of 30 duplicate counts. These individuals ranged in age from 18 to 43 years, in weight from 43 to 112 kg, and in LBM from 36 to 69 kg. The standard deviation of the difference in the two counts divided by the average of the two counts was 0.023, or 2.3%. This is

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Submitted October 1, 1994; accepted March 1, 1995.

Supported by National Institutes of Health Grants No. HD18454, RR00044, and AM35838.

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0026-0495/95/4411-0013$03.00/0

similar to the degree of random variation in radioactive emissions from human burdens of ^{40}K in situations where the gross count from the subject is approximately three times background.[13]

RESULTS

Figure 1 shows frequency distributions of intrapair differences in LBM for MZ and DZ twins, each expressed as a fraction of the average value for the twin pair. Included is a frequency distribution of the difference in duplicate measurements of control subjects, expressed as a fraction of the average value for each subject. The relative variability is greatest for DZ twins, less for MZ twins, and least for duplicate assays on control subjects. This means that MZ twins are not completely concordant with regard to LBM, since their intrapair variability is larger than one would expect from a duplicate assay on the same individual. However, intrapair variability for DZ twins clearly exceeds that for MZ twins.

Table 1 lists correlation coefficients, frequency distributions, and F ratios for weight, height, body fat, and birth weight, as well as LBM. Data for the ratios of LBM to height and weight to height squared (BMI) are also shown. Included are values for measurement error as determined from duplicate measurements on control subjects. In each instance where this was determined, the standard deviation and hence the variance of the frequency distributions was less than for MZ twins, and that for MZ twins was less than for DZ twins. These differences are expressed as variance (F) ratios (Table 1).

Correlation coefficients are higher for MZ twins than for DZ twins for all of the various measurements listed in Table 1, and with one exception, namely birth weight, the standard deviations are lower. Correction for height—the LBM to height ratio and BMI—did not serve to increase the correlations. Leaving birthweight aside for the moment, the standard deviation of intrapair differences is highest for body fat and lowest for height. This may reflect, in part, the difference in precision of these two measurements. Stature can be measured with a precision of less than half of 1%, but body fat determined by the ^{40}K method is obtained by subtracting LBM from weight, and so incurs a larger error.

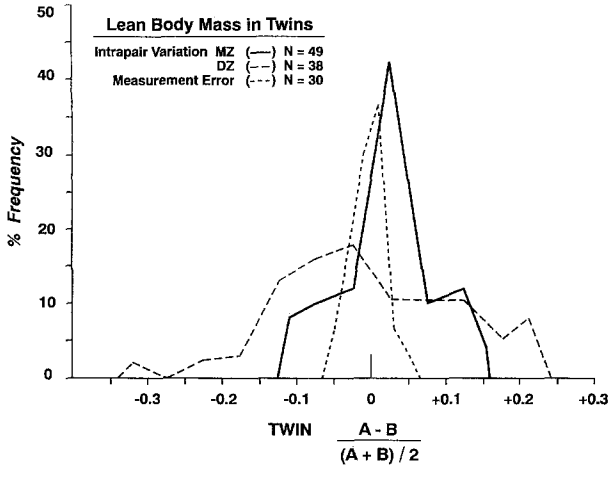

Fig 1. Frequency distributions for intrapair differences in LBM of MZ and DZ twins, expressed as a fraction of the average LBM for each twin pair. Twin A was firstborn. Frequency distribution of measurement error expressed as assay (2) minus assay (1) divided by the average of (1) and (2).

Table 1. Summary Data and Variance Ratios

Measurement	No. of Pairs	Correlation Coefficient (twin A v B)	Frequency Distribution (twin A − B)/[A + B]/2)*	F Ratio	P
LBM					
ME	30		−.0034 ± .0233		
MZ	49	.978	+.0158 ± .0693	8.86	<.01
DZ	38	.892	−.0008 ± .125	3.25	<.01
Weight					
ME	27		+.0021 ± .007		
MZ	49	.968	+.0232 ± .0763	119	<.01
DZ	38	.786	+.0323 ± .167	4.79	<.01
Height					
ME	15		+.0037 ± .0031		
MZ	49	.992	+.0028 ± .0147	24	<.01
DZ	38	.908	−.0044 ± .0380	6.69	<.01
Fat					
ME	27		−.0068 ± .2119		
MZ	49	.907	+.0993 ± .655	9.55	<.01
DZ	36	.722	+.171 ± .882	1.81	<.05
Birthweight					
MZ	48	.830	+.0119 ± .153		
DZ	35	.674	+.0165 ± .159	1.08	NS
LBM/Height					
MZ	49	.961	+.0131 ± .0694		
DZ	38	.866	+.0028 ± .108	2.44	<.01
BMI					
MZ	49	.930	+.0176 ± .0737		
DZ	38	.703	+.041 ± .1464	3.95	<.01

NOTE. F ratio for MZ determined as V_{MZ}/V_{ME}, and for DZ, as V_{DZ}/V_{MZ}.

Abbreviation: ME, measurement error as determined from duplicate assays.

*Mean ± SD.

Table 2 presents estimates of heritability; using variances (V) based on data in Table 1, the coefficient of heritability is calculated as $(V_{DZ} - V_{MZ})/V_{DZ}$. The coefficients were high for LBM, as well as for height and weight, but the value for body fat was distinctly lower. For LBM, weight, and height, Student's t values were 7.00, 11.29, and 17.00, respectively ($P < .001$ in each case); the value for fat was 2.368 ($P < .05$), and for birth weight, 0.250 (P NS). Expressing LBM and weight in relation to height did not improve the coefficients.

Table 2. Estimates of Heritability (49 MZ and 38 DZ pairs)

Measurement	Heritability Coefficient (mean ± SD)*
LBM	.70 ± .10
Weight	.79 ± .07
Height	.85 ± .05
Fat	.45 ± .19
LBM/Height	.58 ± .14
BMI	.75 ± .09
Birthweight	.08 ± .32

*$V_{DZ} - V_{MZ}/V_{DZ}$.

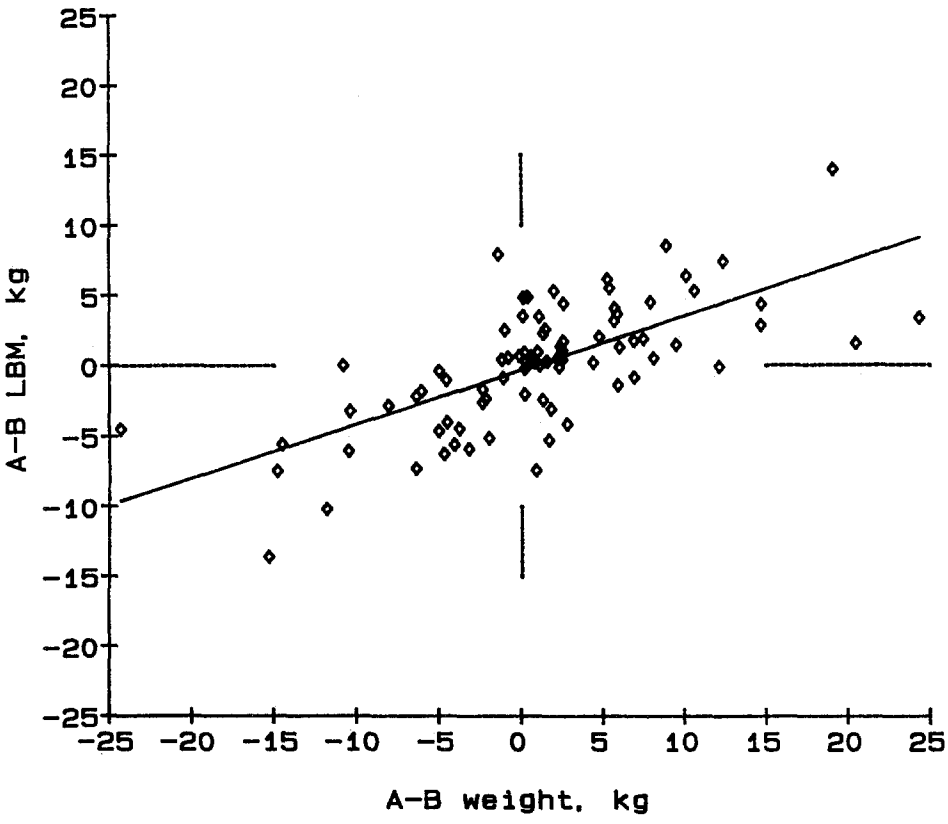

Fig 2. Intrapair LBM variation as a function of intrapair weight variation (n = 87; equation shown in Table 3).

It has been established that a change in body weight resulting from nutritional surfeit or deficit usually involves LBM, as well as body fat.[1,2] It was therefore of interest to determine how much of the intrapair variation in body weight was due to variation in LBM. To this end, we regressed intrapair differences in LBM against intrapair differences in body weight (Fig 2). The observed slope of 0.38 indicates that, on average, 38% of the intrapair weight variation is due to LBM. As shown in Table 3, this relationship is independent of zygosity, the slope being 0.36 for MZ twins and 0.39 for DZ twins despite the larger weight variation for the latter.

The relative contribution of LBM to the total weight change in individuals, be it loss or gain, resulting from nutritional influences is inversely related to body fat content.[1,2,17] Thus, we decided to test for the influence of body fat on the relationship between intrapair differences in LBM and intrapair differences in body weight. Body fat content ranged from zero to 36 kg in our group of twins: those with less than 18 kg (the midpoint) were arbitrarily assigned to the thin group, and those with 18 to 36 kg were classified as heavy. The data in Table 3 show that body fat content did indeed affect the extent to which LBM contributes to intrapair differences in the body weight of twins. The regression slope (ΔLBM/Δweight) for thin individuals is roughly twice that for those with larger fat burdens, and this difference is statistically significant ($t = 3.418, P < .001$).

The possibility of a relationship between intrapair differences in birthweight and intrapair differences in LBM was tested by regressing the latter values against the former values. The difference in birth weight (twin A − twin B) ranged from −900 to +900 g, with a mean of +46 g (P = NS). The correlation coefficient is .12, and the probability of the regression slope being different from zero is .31. We conclude that intrapair differences in LBM are not associated with intrapair differences in birthweight.

DISCUSSION

The only other recorded study of LBM heritability was that reported by Bouchard et al,[11] who assayed a large

Table 3. LBM-Weight Relationships

Subjects	Regression Equation	Δ Weight Range	R^2
All (N = 87)	y = −0.33(±.35) + 0.38x(±.04)	−25, +23	.46
MZ (n = 49)	y = 0.10(±.36) + 0.36x(±.07)	−10, +15	.35
DZ (n = 38)	y = −0.75(±.66) + 0.39x(±.06)	−25, +23	.51
Thin (n = 71; mean fat, 6.9 ± 4.3 kg)	y = −0.11(±.35) + 0.52x(±.06)	−15, +20	.55
Heavy (n = 16; mean fat, 26 ± 5.4 kg)	y = −1.61(±.76) + 0.23x(±.06)	−25, +23	.51

NOTE. y = ΔLBM (kg); x = Δweight (kg). Standard errors are in parentheses.

number of individuals by the method of hydrodensitometry, whereas we used ^{40}K counting. They included adopted and biological siblings, as well as twins. They reported an intrapair correlation coefficient of .53 for DZ twins, which is close to the expected value of .50, and a coefficient of .93 for MZ twins, which is close to our value (Table 1). This circumstance permitted them to express the heritability coefficient as twice the difference between the two correlation coefficients, namely .80.

The relatively high correlation coefficients for all measurements on our DZ twins listed in Table 1 suggests a degree of ascertainment bias in our group of subjects. An incentive for participating in the study was free genetic typing for determination of zygosity. Although we did not specifically inquire about this, it is possible that some parents who volunteered their twin children for the study did so because they were uncertain about their zygosity. If so, there may have been twin pairs who in the parents opinion were neither clearly MZ or DZ.

Although the high correlation coefficients for our DZ twins preclude the use of the formula reported by Bouchard et al[11] in calculating heritability, the intrapair variance (F) ratio for LBM listed in Table 1 together with the frequency distributions shown in Fig 1 clearly demonstrate that LBM is under genetic control.

Since our subjects encompassed a wide age range and both sexes, and since it is known that LBM is age- and sex-dependent, we expressed intrapair differences as a fraction of the average value for that pair. The same maneuver was used to assess measurement error from duplicate assays on control subjects. As an additional check on the possibility of an age effect on LBM variability, we regressed intrapair differences as a fraction of the pair average against age (Table 4). Standard errors of the two regression slopes indicate that neither is significantly different from zero. The mean deviation of the residuals from regression for MZ twins is significantly less than for DZ twins ($P < .05$). Nevertheless, the intrapair variance for LBM in MZ twins (.0048) is almost nine times the variance of the measurement error (.00054); thus, MZ twins are not completely identical with regard to LBM (Fig 1). Since changes in body weight resulting from nutritional deficit or surfeit almost always comprise both LBM and fat,[1,2] we regressed the intrapair difference in LBM against the intrapair difference in weight. The two are indeed correlated, with the result that LBM comprises 38% of the intrapair weight differences (Table 3).

Table 4. Effect of Age on LBM Variation

MZ Twins	DZ Twins
Y = 0.040 + 0.000741X	Y = 0.120 − 0.000914X
(±.011) (±.000486)	(±.022) (±.000828)
r = .22	r = −.18
Residuals from regression (mean ± SE)	
0.0371 ± .0034	0.0536 ± .0079

NOTE. Regression: Y = twin A − B/([A + B]/2); X = age (years). Numbers in parentheses are the standard error.

The R^2 value shown in Table 3 indicates that body weight accounts for 46% of LBM variability, and the datum in Table 2 shows that inheritance accounts for 70% of LBM variability. One may then venture the conclusion that of the total LBM variation, approximately 40% is environmental and 60% is genetic in origin. Bouchard and Pérusse[10] have discussed in some detail the matter of gene-environment interaction in body composition.

Our twin data are consistent with a nutritional influence on LBM in a further respect. It is known that the relative contribution of LBM to the total weight change in individuals, be it loss or gain, resulting from nutritional influences is inversely related to body fat content: LBM comprises a larger proportion of the total weight change in the thin than in the obese, including those who engage in exercise programs.[1,2,17] The data in Table 3 show that body fat content did indeed affect the extent to which LBM contributes to the intrapair difference in the body weight of twins. The regression slope (ΔLBM/Δweight) for thin individuals is roughly twice that for those with larger fat burdens, and this difference is statistically significant.

In summary, MZ twins are more alike than DZ twins with respect to LBM, which for most people is the major component of body weight. Hence, this body component is under some degree of genetic control. Our data also add confirmation to the conclusion derived from other observations that environmental factors, as manifested by variations in body weight, also influence LBM.

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