Acta Genet Med Gemellol 40: 133-146 (1991)

Received 5 October 1990
Final 28 November 1990

A Twin Study Approach Towards Understanding Genetic Contributions to Body Size and Metabolic Rate

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Abstract. The genetic and environmental determinants of a brief assessment of metabolic rate at rest and under psychological stress were studied in 40 pairs of monozygotic and 40 pairs of dizygotic young adult male twins. Height, weight and age were employed as covariates. Univariate analyses showed a high heritability for height and weight and moderate heritability for metabolic rate. Classical twin analyses and multivariate genetic modeling indicated that genetic influences on resting metabolic rate were entirely explained by body weight: there was no independent genetic contribution to resting metabolic rate. Metabolic rate under psychological stress, on the other hand, showed a significant genetic effect. The exponent (3/4) in the power function relating body weight to resting metabolic rate was the same as that found in a wide variety of animal species, a value that has been proposed as defining a body weight set point. We speculate that an adult body weight set point is genetically transmitted. Independent genetic effects on resting metabolic rate would be observed only when the normal equilibrium between body weight and metabolic rate is unbalanced during development, aging or disease. The study illustrates the use of multivariate genetic analyses of twin data which may be readily applied to widely used metabolic rate assessments.

Key words: Metabolic rate, Body weight, Obesity, Heritability, Twins

Genetic factors have recently been shown to influence human obesity and body weight across the spectrum from thin to fat. Classical twin studies have revealed a high heritability for the body mass index [25], and commingling analysis of twin data has found evidence for three distributions of body weight, compatible with genetic transmission

[19]. Adoption studies have shown a relationship between the body mass index of biologic parents [25,18] and siblings [24] with that of adoptees and no relationship between the body mass index of adoptive parents and adoptees.

Genetic influences leading to increased body weight in humans may be transmitted via reduced metabolic rate. Until recently, such a mechanism would have seemed improbable, for, on average, obese persons have elevated metabolic rates [8,17,20]. Longitudinal studies of individual persons, however, have suggested an alternative. Roberts et al [22] have shown that lower energy expenditures in infants at three months predict increased body weight and body fat at two years of age; Ravussin et al [21] have shown that lower metabolic rates among adult Pima Indians predict increased body weight and body fat over a four-year span. Finally, Griffiths et al [6] have found a correlation of 0.77 between intake (and presumably energy expenditure) at age 4 years and body fat in a group of English girls.

There has been surprisingly little investigation of the role of genetics in the determination of metabolic rate and the conclusions from the available studies differ. Family studies by Bogardus et al [1] and by Bouchard et al [2] found only a small familial aggregation of metabolic rate when lean body mass was taken into account. By contrast, classic twin studies by Fontaine et al [4] and by Bouchard et al [2] have shown a high heritability of resting metabolic rate, even when corrected for measures of body size. This result is somewhat surprising given the extensive evidence that, for individuals at a stable body weight, there is a direct relationship between body size and resting metabolic rate.

The importance of the question and the conflicting results led us to examine the role of genetic factors in the determination of metabolic rate in a group of young adult male twins. Classic twin analyses of a brief assessment of metabolic rate at rest and under stress were supplemented with a path analysis to explore the relationship between body mass and metabolic rate. Such analyses are an important extension of the classical twin method and will provide a fuller understanding of the relationship between metabolic rate and its covariates.

METHODS AND MATERIALS

Subjects consisted of 40 pairs of monozygotic (MZ) and 40 pairs of dizygotic (DZ) healthy young adult male twins, mean age ($\pm$ SD) = 19.3 $\pm$ 2.5 years (range 16 to 24), who were recruited from the population-based Birmingham Family Study Register. Zygosity was determined by questionnaire items of the type validated against blood typing by Kasriel and Eaves [10]. Subjects were paid for participation in the study which was part of a wider investigation of genetic determinants of blood pressure and heart rate at rest and under stress [3,27,28]. Testing was carried out in the late afternoon or evening. Subjects were asked to refrain from physical exercise, smoking, drinking tea, coffee or alcoholic beverages for one hour prior to their arrival at the laboratory. Upon arrival, they were asked about compliance with this request and in the rare instances of noncompliance testing was delayed by one hour.

Subjects visited the laboratory in pairs but were tested individually. Testing took place in a modestly lit, temperature-controlled room and the twins were not permitted to communicate with one another during the experiment.

Upon arrival at the laboratory, subjects were weighed, their height was measured and they were allowed to rest while becoming adjusted to the laboratory. Electrodes were then attached for recording of heart rate. A valve, mouthpiece and noseclip were used in the measurement of the respiratory variables. There followed eight minutes of relaxation and habituation, during the second four minutes of which measurements were made. Oxygen consumption and carbon dioxide production were measured by indirect calorimetry with a Beckman Metabolic Cart. Continuous monitoring of the volume and rate of respiration, oxygen and carbon dioxide concentration in the expired air, temperature and pressure, permitted accurate determination of oxygen consumption (VO_2) and carbon dioxide production (VCO_2) in ml/min. Energy consumption was estimated by use of the equations of Weir relating VO_2 and VCO_2 to energy kj/min [29].

Results are reported for the four minutes of formal relaxation and for the first four minutes of psychological stress. In this study, stress was induced by the active psychological challenge of playing a video game of the "Space Invaders" genre which our previous research had shown to elicit considerable cardiac reactivity in some individuals [3,27,28]. Details of this task and of its influence on heart rate have been reported elsewhere [3].

The first data analyses were descriptive statistics of the samples of MZ and DZ twin pairs followed by calculation of the intrapair correlation coefficients. For each variable, the heritability (h^2) was estimated by two methods. The first is the classic twin method of doubling the difference between the intrapair correlation coefficients of the MZ and DZ twins. The second was a model-fitting method of path analysis applied to the observed variances and covariances for MZ and DZ twins [7,23]. To explore the relationships between variables, the method of maximum likelihood estimation was used with aid of the computer program LISREL-VI [9] to fit a series of multivariate path models to the MZ and DZ covariance matrices for log(Height), log(Weight) and log(Energy), with age as an additional covariate. These analyses were performed separately for metabolic rate at rest and for metabolic rate under stress. The most parsimonious models which fit the data are shown in Figs. 1 and 2. In each case, removing further parameters from the models led to a significantly poorer statistical account of the observations.

RESULTS

Descriptive statistics for the samples of MZ and DZ twins are shown in Table 1 for both observed values and for logarithmically transformed height, weight and body mass index. As befits a sample of healthy young men, these values are within normal limits. Table 1 also shows the intrapair twin correlations for these variables as well as the two estimates of heritability described above. The correlations for MZ twins are approximately twice those for DZ twins, as expected from the fact that MZ twins share all of their genes, while DZ twins share, on average, only half their genes. Doubling the difference between these correlations in the classic twin method yields high estimates. Problems with the classic twin method make it desirable to turn to maximum likelihood estimates of heritability obtained by the model-fitting procedure which take account of the sampling variability inherent in the observations. This approach also yields high estimates of heritability — for height (0.77), weight (0.80) and body mass index (0.87).

Table 1 - Univariate descriptive statistics and heritability (h^2) estimates for body size variables

Variable	MZ twins (N = 40 pairs)			DZ twins (N = 40 pairs)				
	Mean	SD	r	Mean	SD	r	$2(r_{MZ}-r_{DZ})$	h^2
Height (cm)	174.91	7.34	.817*	177.67	6.98	.412*	.81	.77*
$\log_{10}$(Height)	2.24	0.02	.804*	2.25	0.02	.414*	.78	.71*
Weight (kg)	66.14	10.91	.949*	67.70	12.66	.537*	.82	.96*
$\log_{10}$(Weight)	1.81	0.08	.948*	1.82	0.08	.528*	.84	.89*
Body Mass Index (kg/m^2)	21.55	2.95	.855*	21.37	3.27	.541*	.63	.87*

* $p < .01$

Table 2 - Univariate descriptive statistics and heritability (h^2) estimates for resting metabolic rate

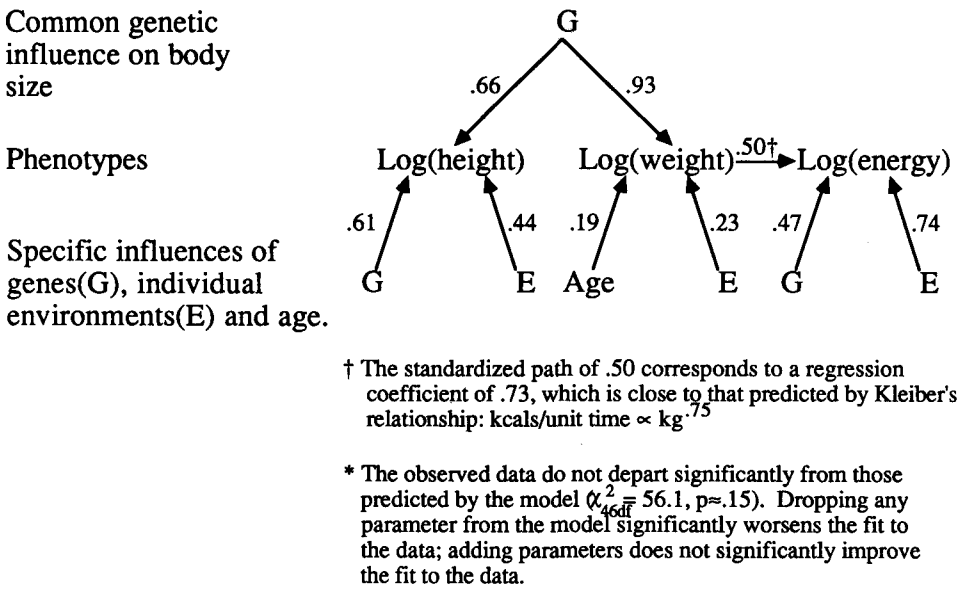
Variable	MZ twins (N = 40 pairs)			DZ twins (N = 40 pairs)				
	Mean	SD	r	Mean	SD	r	$2(r_{MZ}-r_{DZ})$	h^2
Energy (kj/min)	5.25	1.19	.482*	5.25	1.08	.129	.71	.42#
Energy ($100 \times \log_{10}$)	70.90	10.37	.478*	71.04	9.81	.166	.62	.43#
Energy/BMI × 100 ($kj\ min^{-1}/kg\ m^{-2}$)	24.51	5.23	.374*	24.80	5.03	.312	.12	.06
Energy/Surface Area ($kj\ min^{-1}/m^2$)	2.91	0.54	.251	2.86	0.54	.229	.04	.004

* $p < .01$; # $p < .05$

Table 2 shows the intrapair correlation coefficients of MZ and DZ twins for resting metabolic rate, both uncorrected for body size and corrected by two measures designed to take body size into account — surface area and body mass index (weight in kg/height in meters squared). The correlation coefficients of MZ twins were reduced by these corrections for body size, while those of DZ twins were increased. As a result, heritability estimates declined dramatically, from 0.42 to 0.004 and 0.06, respectively. These measures of body size clearly have a strong effect on the estimation of the heritability of metabolic rate.

The effects on heritability of the relationships between the variables was assessed further by the model-fitting procedure described above. The results for the multivariate models are clear. There is a common determinant of height and weight which is entirely

genetic. This genotypic variation, which translates phenotypically to a measure of body size, controls 86% (0.93^2) of the variation in body weight. The remaining variation is attributable to very small increases in weight with age (5%, or 0.23^2), idiosyncratic environmental factors (5%, or 0.23^2) and a small residual component not accounted for by the model (3%). Height is less completely determined by the common genetic factor (44% of the variance), but there appears to be a specific genetic contribution to height independent of weight (37% of the variance) and, also, idiosyncratic environmental variation (19% of the variance).



† The standardized path of .50 corresponds to a regression coefficient of .73, which is close to that predicted by Kleiber's relationship: kcals/unit time $\propto$ $kg^{.75}$

* The observed data do not depart significantly from those predicted by the model ($\chi^2_{46df} = 56.1$, $p \approx .15$). Dropping any parameter from the model significantly worsens the fit to the data; adding parameters does not significantly improve the fit to the data.

Fig. 1. The most parsimonious model for log(height), log(weight) and log(energy consumption at rest).

Variation in resting metabolic rates, in as much as it is predictable, is entirely explained by body weight. Once body weight has been taken into account, there is no independent genetic contribution to metabolic rate. The standardized regression of log(Energy) on log(Weight) shown in Fig. 1 is equivalent to an unstandardized regression of 0.77. This value is not significantly different from the 0.75 predicted by Kleiber's rule [5], discussed below.

In contrast to the results for metabolic rate at rest, those for energy expenditure during stress suggest an additional genetic contribution to energy expenditure, over and above that predicted by body weight. Although a model omitting this additional contribution does not fail ($\chi^2_{47} = 61.2$, $p = 0.08$) allowing for this specific genetic contribution significantly improves the fit to the data ($\chi^2_1 = 5.18$, $p < 0.025$). Fig. 2 shows that this specific genetic contribution to metabolic rate may account for 22% (47^2) of the variance in energy expenditure during the task. Note that there is still a sizeable, though somewhat reduced, component of metabolic rate which is predicted from body weight

and, as with resting metabolic rate, the standardized regression coefficient of log(Energy) on log(Weight) corresponds to an unstandardized coefficient of 0.73, again very close to the 0.75 predicted by Kleiber's rule.

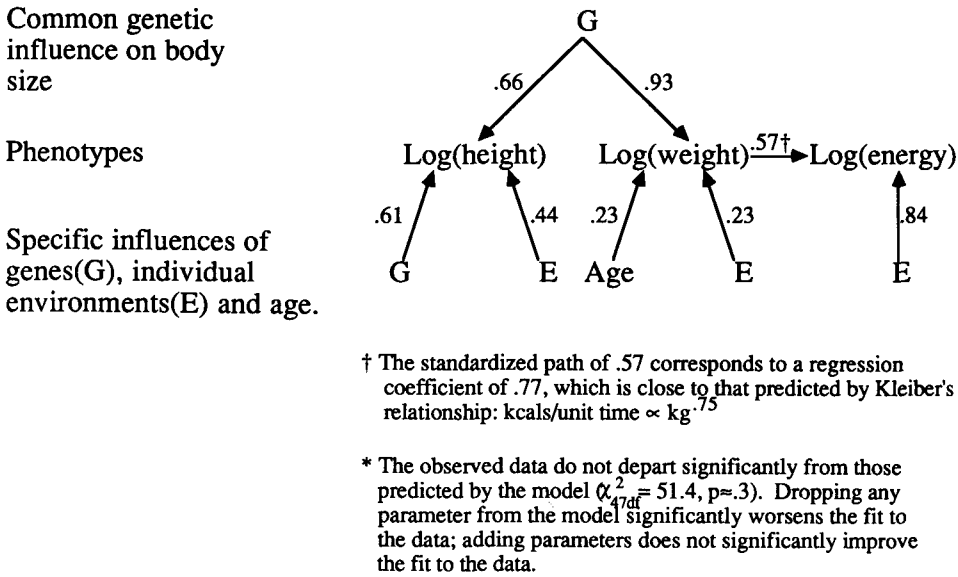


Fig. 2. The most parsimonious model for log(height), log(weight) and log(energy consumption under stress).

DISCUSSION

The results reported here provide a link between recent studies of the heritability of human obesity [18,19,24-26] and those of its pathogenesis [21,22]. It is now clear that obesity is highly heritable. Among the possible intervening mechanisms, metabolic rate is a prime candidate. Studies of English infants by Roberts et al [22], of English girls by Griffiths et al [6], and of adult Pima Indians by Ravussin et al [21], have demonstrated that a low metabolic rate is a risk factor for human obesity. And, as Griffiths and Payne [5] showed several years ago and Bogardus et al [1] more recently, metabolic rate is a familial characteristic. Is it also genetically transmitted?

The evidence bearing on genetic transmission of metabolic rate has been surprisingly limited and, furthermore, inconsistent. It has been confined to two family studies [1,2] and two twin studies [2,4]. In the family studies of both Bogardus et al [1] and Bouchard et al [2], correcting the metabolic rate by a measure of body size left only a very small familial contribution to metabolic rate; the genetic contribution would be, if anything, smaller still. The twin studies by Bouchard et al [2] and by Fontaine et al [4], on the other hand, estimated a substantial heritability for the resting metabolic rate as indicated by the large difference in the intrapair correlation coefficients between MZ and DZ

twins. Furthermore, in contrast to the family studies, correction of metabolic rate by a measure of body size (weight, for example) left a large remaining estimate of heritability — 0.40 in Fontaine's study and 0.80 in Bouchard's.

The results of the present twin study differ from those of the earlier twin studies; they are more compatible with the results of the earlier family studies. They make it clear that once body size was taken into account, there was no independent genetic contribution to the resting metabolic rate. This conclusion was reached by two different methods of analysis. The first, the classic twin method, showed that estimates of heritability shrank to insignificance when metabolic rate was corrected by two measures of body size. The second, path-analytic, method showed that weight accounted for all of the variance in resting metabolic rate shared by family members.

The very close relationship found in this study between body weight and metabolic rate of a group of healthy young men appears to be an example of a general phenomenon. Kleiber [12] has shown that, when corrected for body size, the metabolic rates of animals ranging in size from mice to elephants are strikingly similar. In these very different species, metabolic rate expressed as kilocalories per day is proportional to body weight in kg raised to the power 0.75.

Keesey [11] has proposed using this powerful between-species relationship as a means of defining a within-species relationship — the body weight "set point". He has shown that in a static, unstressed, state the body weight of rats is related to their metabolic rate according to Kleiber's law, with an exponent of 0.75. Furthermore, when the stability of their body weight is threatened, either by caloric deficit or caloric surplus, the relationship changes in such a way as to defend their usual body weight. Thus caloric deficit leads to a fall in metabolic rate and caloric surplus to a rise. According to Keesey's view, deviations from Kleiber's law indicate a disequilibrium between body weight and metabolic rate. From this point of view, such a disequilibrium existed among those of Roberts' infants [22] and Ravussin's Indians [21] in whom low metabolic rate predicted subsequent weight gain.

Thus, the low metabolic rate of these subjects can be interpreted from two points of view. The traditional viewpoint is that of mechanism. In terms of mechanism, the low metabolic rate can be viewed as the source of the caloric surplus that gave rise to the increase in body weight. However, the significance of the low metabolic rate can also be interpreted from the point of view of regulation.

In terms of regulation, as Keesey [11] has proposed, the low metabolic rate can be viewed as an index of the extent to which body weight is below its "set point", or that level at which it is regulated under ordinary circumstances. The low metabolic rate thus reflects an instability in the equilibrium between body weight and energy expenditure. From this perspective, the increase in body weight can be viewed as a means of reaching a more stable equilibrium. But here is an apparent paradox: the system is not in equilibrium because the body weight is too high for the associated metabolic rate. Why should weight gain bring it into equilibrium? The answer is that, when weight is gained, metabolic rate increases more rapidly than does body weight. Thus, from the regulatory point of view, weight is gained in order to establish a new and more stable equilibrium with a body weight and resting metabolic rate related by Kleiber's law.

In the present study of healthy young men of normal weight, body weight and metabolic rate should be in equilibrium. Our path analysis provides quantitative description

of the way in which genetic influences on resting metabolic rate are mediated by body weight when the system is in equilibrium. As we have noted, the relationship between body weight and metabolic rate found by Roberts [22] and by Ravussin [21] among those subjects who gained weight appears to reflect a (temporary) disequilibrium in the system.

In contrast to the lack of genetic influence on resting metabolic rate when body size is taken into account, we found evidence of a specific genetic effect upon metabolic rate during stress, and, once again, an exponent (0.73) very close to the 0.75 proposed by Kleiber as that relating body weight to metabolic rate. The emergence of a genetic contribution to metabolic rate under stress, independent of body weight, is consistent with other evidence of genetically controlled differences in reactivity to psychological stressors [3].

The model-fitting approach to the estimation of heritabilities and the multivariate genetic analysis provides a powerful and flexible method of analysis. It is based on the method of path coefficients [14] in which variation in observed phenotypes is expressed as a consequence of variation in unobserved, or latent, genotypes and environments [13,15]. Since a genetic model predicts different patterns for MZ and DZ twin resemblance, the maximum likelihood method can estimate path coefficients from the observed phenotypic variances and covariances for the MZ and DZ twins. This method provides not only estimates of the parameters, but also tests of their significance and tests of the overall adequacy of the model. Heritability is a derived summary parameter calculated as the square of the standardized path from genotype to phenotype.

Univariate models can be readily extended to multivariate ones that include common influences on several variables (such as height and weight) and direct paths between phenotypes (such as weight and energy consumption). The multivariate models thus allow the opportunity to account simultaneously for a complex set of observations in terms of a parsimonious model with few parameters. The present study illustrates how a path model yields a clearer understanding of the interrelationships between the observed variables and their genetic determinants than would a series of classical twin studies carried out one by one.

We readily acknowledge that the metabolic rate at rest that we have measured may differ from resting metabolic rate measured after overnight fasting. However, the conformity of our results to theoretical expectations for the control of our measured metabolic rate at rest, and the apparent change in that control under stress, suggest that our conclusions would hold for a more rigorously defined resting metabolic rate. We are satisfied that the multivariate twin study methodology and techniques of analysis provide important insights in the study of these variables. On the basis of our analyses, we conclude that our results are consistent with the hypothesis that body weight set point is genetically determined and that genetic influences on resting metabolic rate are entirely explained as a consequence of the predicted equilibrium between body weight and resting metabolic rate in healthy young adults. We do not expect to observe independent genetic effects on resting metabolic rate, except when this equilibrium is disrupted during periods of developmental change or disease, or when departures from the set point are induced by caloric deficit or surplus. Metabolic rate during activity or stress, however, may well have independent genetic determinants which could account for differential weight gain or loss if these conditions were sustained.

Aknowledgements: Supported by British Medical Research Council grant G8207495N and in part by HL31010, AG04954, GM30250, AA06781, MH45268 and by a Research Scientist Award from the National Institute of Mental Health to Dr. Stunkard.

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Appendix

A Description of the Model Fitting Procedure

The procedure used to estimate genetic and environmental parameters is a form of linear structural equation modeling. With this procedure, we may account for observed covariation and variation in terms of linear models relating measured, or observed, variables to unmeasured, or latent, genetic and environmental variables [7]. The estimated coefficients, or paths, of the model are equivalent to factor loadings or estimated partial regressions of the observed variables on the latent variables. In our analyses of single variables we consider three independent kinds of latent variation: additive genetic variation, environmental variation which is shared by members of a family, and unique environmental variation not shared by members of a family. To embody our assumptions about the genetic and environmental variables, we specify structural correlations between these latent variables for different members of a family. Thus, the additive genetic variable correlates 1.0 for MZ and 0.5 for DZ twins. The shared family environment correlates 1.0 for both MZ and DZ twins, while the unique environmental effects are assumed to be uncorrelated. We further assume that the paths, or coefficients, of the linear model that relate the latent variables to the measured variables are the same irrespective of birth order or zygosity. Thus, for a particular variable, we estimate three coefficients for the full model: a path from the individual's genotype to the measured variable, h; a path from the shared family environment to the measured variable, c; and a path from the individual's unique environment to the measured variable, e. If the latent variables are assumed to have unit variance, then the squared values of the paths give the estimated contribution of the latent variable to the measured variation. These path coefficients may be standardized so that their squared value gives the proportion of measured variance accounted for by independent latent variables. For example, h^2 will be the estimated heritability of a measured variable; these heritability estimates are reported in Tables 1 and 2.

The coefficients are estimated by maximum likelihood by numerical search for the parameter values which minimize the function:

$$F_i = n_i \, (\ln|\Sigma_i| - \ln|S_i| + \mathrm{tr} \, (\Sigma_i^{-1} S_i) - k)$$

summed over the two zygosity groups, where n_i is the sample size of each group (40 in our case), S_i is the i^{th} observed covariance matrix, Σ_i is the i^{th} expected covariance matrix under the model, and k is the number of observed variables (7 in our case) [9]. This function is twice the difference between the likelihood of the data under our model and the likelihood constant calculated for a perfectly fitting model. Under appropriate distribution assumptions for the original data, this function is distributed as a chi-square with degrees of freedom equal to the number of observed statistics minus the number of estimated parameters [9,16].

For any particular variable, we have six observed statistics: for each zygosity, the variances of twin 1 and twin 2 and the covariance between twin 1 and 2. Estimating three parameters leaves three degrees of freedom to test the adequacy of the model. The fit of the overall model to the data can be assessed by the likelihood ratio chi-square test.

Failure of the assumptions implicit in the structural equation model will lead to a significant chi-square within the resolving power of the data. Furthermore, if parameters are dropped from the model, the resulting more parsimonious model can be tested to establish its adequacy, and a difference chi-square provides a test of the significance of the deleted parameters [16]. Thus, this model fitting procedure can provide maximum likelihood estimates of heritability, the influence of shared family environments and the influence of environments unique to the individual, a test of the assumptions of the genetic and environmental model, and tests of the significance of particular parameters.

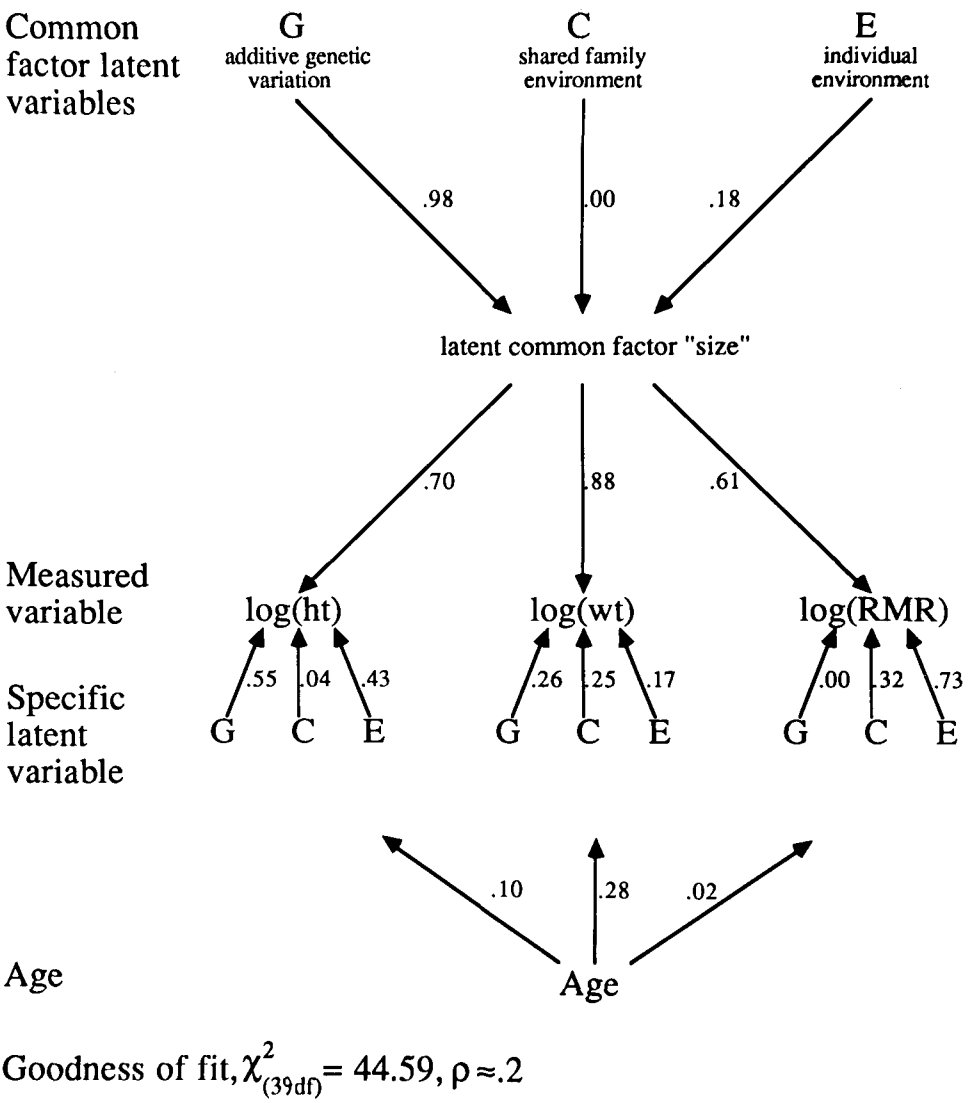

Fig. 3. The factor model for log(height), log(weight) and log(energy consumption at rest).

https://doi.org/10.1017/S0001566000002567 Published online by Cambridge University Press

Table 3 - The variances (in parentheses) and correlations for log(height), log(weight), log(energy consumption at rest) and age

Variable	MZ twins							Variable	DZ twins						
Log(Height)	twin A	(3.73)						Log(Height)	twin A	(3.38)					
	twin B	.80	(3.16)						twin B	.41	(2.53)				
Log(Weight)	twin A	.56	.72	(53.99)				Log(Weight)	twin A	.74	.38	(38.53)			
	twin B	.55	.73	.95	(60.28)				twin B	.28	.54	.53	(74.59)		
Log(Energy)	twin A	.44	.59	.64	.62	(141.99)		Log(Energy)	twin A	.26	.08	.37	-.01	(81.36)	
	twin B	.42	.60	.53	.58	.48	(75.99)		twin B	.06	.40	.24	.53	.17	(113.09)
Age		.05	.05	.24	.25	.08	-.08	(6.09)	Age		.12	.14	.32	.32	-.08	.13	(6.19)

Table 4 - The variances (in parentheses) and correlations for log(height), log(weight), log(energy consumption under stress) and age

Variable	MZ twins							Variable	DZ twins						
Log(Height)	twin A	(3.73)						Log(Height)	twin A	(3.38)					
	twin B	.80	(3.16)						twin B	.41	(2.53)				
Log(Weight)	twin A	.56	.72	(53.99)				Log(Weight)	twin A	.74	.38	(38.53)			
	twin B	.55	.73	.95	(60.28)				twin B	.28	.54	.53	(74.59)		
Log(Energy	twin A	.28	.35	.53	.49	(185.56)		Log(Energy	twin A	.19	-.20	.46	.14	(75.19)	
w/stress)	twin B	.24	.33	.45	.46	.48	(180.11)	w/stress)	twin B	.31	.29	.40	.51	.17	(81.28)
Age		.05	.05	.24	.25	.07	.08	(6.09)	Age		.12	.14	.32	.32	.15	.15	(6.19)

The procedure readily generalizes to the multivariate case [7], where we can test hypotheses about the genetic or environmental independence of variables. Here we employ the same basic ingredients: additive genetic variation, shared family environmental variation, and individual environmental variation. Now, however, we can define a model which postulates, for example, a common factor which influences height, weight and resting metabolic rate, as well as specific influences on each variable separately. Fig. 3 shows the standardized coefficients for such a model fitted to the variance-covariance matrices for log(Ht), log(Wt), log(Resting metabolic rate), and age. For each zygosity, we observed the variances for twin 1 and twin 2 for each of the three measured variables and age, and we observed the covariances between these seven variables. The observed data are given in Tables 3 and 4.

Thus, for each zygosity we had 28 observed statistics, yielding 56 in all. If we estimate 18 parameters, we have 38 degrees of freedom to test the fit of the model; in fact, for the model to be "identified" [9,16], one of our parameters must be arbitrarily fixed, thereby increasing the degrees of freedom by one [7]. The likelihood ratio chi-square indicates that this model is quite adequate. Clearly, a number of the parameters are small or nonsignificant and may be dropped from the model without significantly reducing the likelihood of the observations. For example, there is no shared family environmental influence on the factor common to the three variables or on height specifically, no genetic effects specific to resting metabolic rate, and very little influence of age on height or metabolic rate.

We can examine alternative, more parsimonious models. Data on MZ and DZ twins make it possible to examine causal relationships between variables. Consider an example in which variable A is highly genetic while variable B is strongly influenced by the shared family environment. If variation in A causes variation in B, then the cross-twin cross-trait correlation of twin 1 variable A with twin 2 variable B will show a pattern of genetic determination. If variation in B causes variation in A, then the cross-twin cross-trait correlation will show a pattern of shared environmental determination. This simple method can be used to examine causality wherever variables show different patterns of genetic and environmental determination. The final model for height, weight and resting metabolic rate (Fig. 1) gives the most parsimonious account of these variables after dropping nonsignificant parameters and exploring the possible alternative causal models.