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Influence of Heredity and Environment in Determination of Skinfold Thickness in Children

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Summary

Triceps and subscapular skinfold thicknesses were measured in 222 pairs of like-sex twins (78 monozygotic and 144 dizygotic) aged 3-15 years. Log transformations of the measurements were standardized for age and sex and the results used to estimate heritability—that is, the proportion of total variation determined by genetic factors. The overall contribution of non-genetic familial effects was small. There were appreciable differences in heritability between limb and trunk fat and between the sexes and at different ages. Over the age of 10 heritability was high for both sites in boys and girls. In younger children environmental factors contributed more to the variation.

Introduction

The separation of heredity and environment in the determination of body fat has proved difficult for want of suitable material and sufficient data. The use of weight alone to measure fatness in humans is uninformative, and weight-for-height indices do little to improve the information because of the large differences in body proportions between people of the same height and sex. Skinfold thicknesses correlate well with total body fat in both adults[1] and children.[2]

One study of monozygotic twins brought up together and apart depended only on measurement of weight.[3] Another reported parent/child correlation coefficients of weight and skinfold thickness in children up to the age of 7 years; for weight a higher correlation was found for mother/child than for father/child but for skinfold thickness the correlation coefficients were not significantly different from zero.[4] On the other hand the correlations of skinfold thickness in adult twins suggested that genetic influences were strong but that the influence of sex, heredity, and environment differed for different sites.[5]

We report here the relative contribution of genetic and environmental factors to the variation of skinfold thickness in children of both sexes aged 3-15 years.

Patients and Methods

All twins registered at the Hospital for Sick Children, Great Ormond Street, aged 3-15 years who lived in Greater London were invited to take part. More twins were obtained through an appeal for volunteers at the end of a television programme about twins.[6]

Skinfold thicknesses were measured in the standard manner using a Harpenden skinfold caliper[7] over the mid-point of the triceps muscle on the left arm (representative of limb fat) and under the angle of the left scapula (representative of trunk fat). Since skinfold thicknesses are distributed logarithmically in man,[8] log-transformed scores were used throughout. During childhood the means and standard deviations of skinfold thickness change with age and sex; thus departures from the mean assume different importance at different ages, and standard deviation scores[9] were therefore calculated in all cases using standard control values for each age and sex.[10]

Heritability, defined as the proportion of total variance of a characteristic in a particular population due to genetic causes, was calculated by three different methods from the correlation coefficients of skinfold thicknesses. If the variation of a characteristic is entirely genetically determined the correlation coefficient in monozygotic twins, who have all their genes in common, would be 1·0. In dizygotic twins, who have half their genes in common, the expected correlation coefficient would be 0·5. Accordingly, the estimate of heritability is given by the correlation coefficient in monozygotic twins (r_{MZ}), twice the correlation coefficient in dizygotic twins ($2r_{DZ}$), or twice the difference between the correlation coefficients in monozygotic and dizygotic twins

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TABLE I—*Mean Standard Deviation Scores (± 1 S.E.) of Skinfold Thicknesses in Twins*

	No. of Pairs	Triceps Skinfold	Subscapular Skinfold
Monozygotic male twins	38	−0·32 ± 0·10	−0·01 ± 0·06
Dizygotic male twins	67	−0·28 ± 0·09	−0·14 ± 0·06
Monozygotic female twins	40	−0·29 ± 0·09	−0·07 ± 0·06
Dizygotic female twins	77	−0·24 ± 0·07	−0·06 ± 0·05

$(2(r_{MZ} - r_{DZ}))$.[11] The advantage of the last method is that it minimizes the effects of non-genetic common family environmental factors which would increase the relative likeness between family members.

Product-moment correlation coefficients were calculated in the usual manner.[9] To eliminate bias if the first- or second-born twin were always the fatter, each pair was entered twice in alternate order. The standard errors of the estimates of heritability were derived from the variances of the correlation coefficients.[12] Thus, standard error(s) of:

$$r_{MZ} = \sqrt{\frac{(1 - r^2)^2}{N - 3}}$$

$$2\,r_{DZ} = \sqrt{4\,s^2_{r_{DZ}}}$$

$$2(r_{MZ} - r_{DZ}) = \sqrt{4(s^2_{r_{MZ}} + s^2_{r_{DZ}})}.$$

The method of differences, which gives the best estimate of heritability, also has the highest standard error.

We estimated heritability of skinfold thicknesses separately for triceps and subscapular skinfolds in boys and girls. Because of the effects of puberty and, especially, the preadolescent fat spurt in boys the twins were also divided into those under 10 years and those 10 or over.

Results

A total of 222 pairs of like-sex twins were examined. Table I shows the numbers of twin pairs and standard score for their triceps and subscapular skinfold thicknesses. Table II shows the correlation coefficients of skinfold thicknesses according to age and sex.

Table III shows the estimated heritabilities of the triceps and subscapular skinfold thicknesses in the various groups of twins calculated by the method of differences. As expected, the standard errors were large, which explains why some of the estimates exceed 1·0 and why the heritability of triceps skinfold thickness in boys under 10 years of age was negative. For all twins taken together there was an appreciable difference between triceps skinfold thickness and subscapular thickness ($P<0·01$). Even though the standard errors were large most of the variation in trunk fat seemed to be genetically determined compared with only half the variation in limb fat.

Genetic factors seemed to play a major part in the determination of limb fat in girls but environmental influences were more important in boys. The difference in heritability of triceps skinfold thickness between boys and girls was significant ($P<0·001$). For trunk fat estimates of heritability were high in both sexes and the difference was not significantly different. In boys the heritabilities of triceps and subscapular skinfold thicknesses differed significantly ($P<0·001$).

When the twins were divided into older and younger age groups the numbers in each group naturally dropped and the standard errors of heritability increased. In boys under the age of 10 estimates of heritability suggested that environmental influences played a large part in determining the variation in limb fat but not in trunk fat. Over the age of 10 estimates of heritability were high for both sites. In girls estimates of heritability were not significantly different from zero at either site below the age of 10 but in girls over 10 genetic influences were again important.

Table IV shows the estimates of heritability of body fatness derived from combined triceps and subscapular skinfold thicknesses by pooling the correlation coefficients.[9] The estimates calculated by the three methods for twins over the age of 10 agreed well. Below 10 the estimates simply derived from the correlations r_{MZ} and $2r_{DZ}$ were greater than those derived from the method of differences.

TABLE IV—*Estimates of Heritability (± 1 S.E.) of Body Fatness Calculated from Pooled Correlation Coefficients of Triceps and Subscapular Skinfold Thicknesses in Twins*

Method	All Twins	Twins < 10 Years	Twins ⩾ 10 Years
r_{MZ}	0·77 ± 0·05	0·64 ± 0·09	0·91 ± 0·03
$2r_{DZ}$	0·80 ± 0·14	0·76 ± 0·19	0·84 ± 0·22
$2(r_{MZ} - r_{DZ})$	0·74 ± 0·17	0·52 ± 0·26	0·98 ± 0·23

Discussion

Estimates of heritability apply only to the population in which measurements are made and they are not a quantitative measurement of the genetic contribution to the characteristic applicable to an individual. The method of differences has been used to estimate heritability of measurements of height and weight, finger ridge counts, intelligence quotients, and social maturity ratings in the same series of twins,[13] but we used three different methods of estimating heritability of skinfold thickness.

Heritability of skinfold thickness was high in all children over the age of 10. Values were not significantly different from zero in younger children except for subscapular skinfold in boys. By pooling the correlation coefficients of triceps and subscapular skinfold thicknesses the same conclusions could be extended to the determination of total body fat in children, since the sum of these two skinfold thicknesses correlate well with total body fat.[14]

The variation of a characteristic depends on the contributions of genetic factors, external environmental influences, and common family experiences. Similarities between twins depend upon genetic factors and common family environment. The use of differences between correlations of a characteristic in monozygotic and dizygotic twins aims to minimize the contribution of common family environment. If common family factors play no

TABLE II—*Correlation Coefficients (± 1 S.E.) of Skinfold Thickness Standard Deviation Scores in Twins*

	All Twins		Boys						Girls					
			<10		⩾10		Total		<10		⩾10		Total	
	M.Z.	D.Z.	M.Z.	D.Z.	M.Z.	D.Z.	M.Z.	D.Z.	M.Z.	D.Z.	M.Z.	D.Z.	M.Z.	D.Z.
No. of pairs	78	144	20	37	18	30	38	67	24	48	16	29	40	77
Triceps skinfold	0·72 ± 0·05	0·49 ± 0·06	0·48 ± 0·19	0·60 ± 0·11	0·87 ± 0·06	0·45 ± 0·15	0·65 ± 0·10	0·63 ± 0·07	0·55 ± 0·15	0·27 ± 0·34	0·95 ± 0·03	0·50 ± 0·15	0·80 ± 0·06	0·37 ± 0·10
Subscapular skinfold	0·83 ± 0·03	0·34 ± 0·07	0·84 ± 0·07	0·23 ± 0·16	0·95 ± 0·03	0·35 ± 0·17	0·89 ± 0·03	0·33 ± 0·11	0·61 ± 0·14	0·37 ± 0·13	0·86 ± 0·07	0·38 ± 0·17	0·79 ± 0·06	0·41 ± 0·10

M.Z. = Monozygotic. D.Z. = Dizygotic.

TABLE III—*Estimated Heritabilities of Skinfold Thickness in Twins; Values of 2 (rMZ − rDZ) ± 1 S.E.*

	All Twins	Boys			Girls		
		<10	⩾10	Total	<10	⩾10	Total
Triceps skinfold	0·46 ± 0·17	−0·25 ± 0·43	0·81 ± 0·34	0·04 ± 0·25	0·56 ± 0·41	0·90 ± 0·30	0·85 ± 0·23
Subscapular skinfold	0·98 ± 0·16	1·23 ± 0·35	1·20 ± 0·34	1·12 ± 0·34	0·47 ± 0·37	0·96 ± 0·36	0·76 ± 0·23

part in the determination of a characteristic estimates of heritability derived from values of ^{r}MZ, ^{2r}DZ, and 2 (^{r}MZ — ^{r}DZ) will be the same (see methods). The reverse is also true: if estimates of heritability calculated by the three methods are similar the contribution of common family environment must be small. The heritabilities calculated by the three methods were similar in older twins, but the discrepancies between them in the younger twins indicate that the influence of common family environment is strongest at this age. Parental influence over food intake is greatest in younger children, and we presume this accounts for the high contribution of family environment to the variation of total body fatness in younger children which overrides the genetic contribution observed in older children.

There were few obese twins in our series and no special study was made of them. Nevertheless, our findings have implications for the aetiology of obesity. The part played by over-nutrition in infancy in the subsequent development of obesity has been much debated. Our results suggest that in younger children environmental influences largely determine the variation in body fatness and imply that body fatness can be readily affected by changes in diet. In older children, however, the alteration of a characteristic so strongly genetically determined will be much more difficult and will demand great environmental adjustments. Our results may go some way towards explaining why the treatment of obesity in older children is so difficult and so often unsuccessful.

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Probabilistic Application of Plasma Carcinoembryonic Antigen Assay in Cancer Patients

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Summary

Plasma carcinoembryonic antigen (C.E.A.) levels in inpatients proved at necropsy to be cancer free were used to assess the ability of the C.E.A. assay to distinguish benign and malignant disease. The patients had a mean C.E.A. level significantly greater than that for young healthy people. In view of the considerable overlap of the ranges of plasma C.E.A. concentration in cancer patients and patients with non-malignant disease a probabilistic interpretation is advocated rather than the use of a simple cut-off between positive and negative. On the basis of the cancer-free control group, 19 out of 64 untreated patients with various solid tumours had plasma C.E.A. levels considered to correspond to a greater than 95% probability of cancer.

Introduction

Despite encouraging early results[1] the assay of plasma or serum carcinoembryonic antigen (C.E.A.) is now known to be non-specific as a test for cancer of the digestive tract. Raised plasma C.E.A. levels are associated with various non-gastrointestinal malignancies, chronic liver disease, and inflammatory diseases of the bowel and lung.[2-5] Since C.E.A. which is immunologically identical with that from tumour tissue is present in the plasma of normal healthy adults[6] it cannot be considered tumour-specific, and further refinement of the assay reagents may not eliminate these "false-positive" results.

If the C.E.A. assay is to be useful for the diagnosis of cancer, then it will be necessary to use it quantitatively and in relation to appropriate control groups, rather than by setting an arbitrary division between normal and abnormal based on levels in young healthy people. In an attempt to establish a more appropriate control group we set out to use C.E.A. levels in inpatients proved after death to be cancer free as the basis against which to compare levels in cancer patients.

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SAMPLE COLLECTION AND SELECTION

Blood was collected in 10-ml tubes containing 15 mg dipotassium EDTA, and cells were removed by gentle centrifugation within four hours. Plasma samples were frozen and stored at −20°C.

Plasma samples from 114 people in the following three groups were assayed. (1) A control group of healthy young adults consisting of 27 laboratory workers and medical students with a mean age of 24·1 ± 1·0 years and a male to female ratio of 1·1 : 1. (2) A second control group consisting of 23 patients selected from 220 inpatients with various potentially lethal conditions. These patients were chosen because they subsequently died and were shown at necropsy to be free from malignant disease. The causes of death were circulatory disease (8), multiple trauma (5), pneumonia (5), viral encephalitis (2), alcoholic cirrhosis (1), alcoholic hepatitis (1), and benign gastric ulcer (1). The mean