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Multivariate Analysis of Genetic and Environmental Influences for Longitudinal Height and Weight Data

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Abstract. A multivariate analysis of genetic and environmental influences on longitudinal height and weight data from a Swedish twin sample is presented. For height in boys, genetic correlations of all ages with the first time point decrease during puberty and increase afterwards. A more linear pattern is evident for the girls. For weight in boys, genetic and environmental correlations are similar to the ones for height. Genetic correlations for girls are stable with age, while environmental correlations peak at 13.5 years and decrease drastically thereafter. The patterns for height and weight in boys suggest that a new set of genes may be turned on during puberty and turned off again afterwards. The pattern found for weight in girls indicates that a simple additive genetic model is not appropriate. It is necessary, however, to apply the model to actual data from several time points to recognize the inadequacy of the model.

Key words: Height, Weight, Heritability, Longitudinal study, Multivariate analysis

INTRODUCTION

In recent years, growing attention has been paid to issues concerning genetic continuity throughout development [3,5,20,23]. Analyses of the sort suggested by Plomin and DeFries [20] result in matrices of genetic and environmental correlations, which give an indication of whether the same genes and environments, respectively, influence a character at different ages. Phenotypically standardized covariances are measures of the extent to which genetic and environmental factors contribute to the phenotypic correlations among measures of the same character taken at varying time points [20]. These matrices can be examined to address the

issues of whether certain genes turn on and off at various stages, whether they turn off and stay off, etc [4]. In such a way, genetic and environmental contributions to longitudinal stability can be examined. Thus far, only one multivariate genetic analysis of this sort, using longitudinal twin data, has been reported [18]. The present paper reports such an analysis of more extensive longitudinal height and weight data in adolescent Swedish twins from the SLU project [8].

Several aspects of the present material are advantageous for addressing these issues:

1) The physical measurements are strictly longitudinal, in that the same twin pairs have been measured twice a year from age 10 to 16 for the female twins and to age 18 for the male twins.
2) The physical measurements include both height and weight data, and there is reason to believe that genetic and environmental influences will have different impact depending both on type of variable and sex. Fischbein [9] found, for instance, that MZ and DZ within-pair similarity for height changes in a parallel fashion with age, while there tends to be a divergent trend in similarity for weight, especially for the female pairs. This sex difference in the stability of twin similarity with age may reflect environmental factors, changes in the influence of certain genes, or both.
3) The data have been collected at puberty for both boys and girls which means that in addition to within-pair similarity in height and weight growth, comparisons of peak height and weight similarity have been estimated for the twins [7]. The results indicate that onset of puberty is largely genetically regulated. The SLU-material thus gives the opportunity to investigate a possible change in genetic influence at the time of physical maturation.

Three questions can thus be posed:

1) Are the genetic and environmental influences for height and weight at puberty similar to those before and after?
2) Do genetic and environmental factors influence height and weight in the same way?
3) Is the relative impact of genetic and environmental influences on height and weight similar in males and females?

MATERIALS AND METHODS

Subjects

The SLU-project was started in 1964 in order to study longitudinal physical and mental growth of school children from age 9 to 17 [8,13]. Another aim was to look into genetic and environmental influences pertaining to growth during this period.

The total sample was composed of two main groups: pairs of twins, and class-mates to the twins. The twins (about 30% of the total twin population born in Sweden in 1955) and their class-mates were taken from the 40 larger cities and throughout Sweden. The sample is thus not strictly representative for the country as a whole. It is important to note that, because Sweden has a comprehensive school system from grade 1 to grade 9, the sample was not selected for, eg, socioeconomic background.

Height and weight were measured by school nurses using a standard procedure every half year (in April and October) from 1964 (when the subjects were in grade 3 or age 10) to 1970 (when the subjects were in grade 9 or age 16). Because the children were measured during the same month in each school term regardless of their month of birth, individual measure-

ments were interpolated to specific chronological ages. Data on height and weight measurements were also obtained for approximately 50% of the boys who were completing their tenth school year at secondary school level (age 17) and all of the boys at age 18 upon induction into the military service.

For classifying zygosity in the like-sexed twin pairs, a morphological diagnosis based on a special schedule from earlier investigations of similarity diagnosis in twins [6,11] was applied. The teachers were asked if the twins were so similar that they were mistaken for each other by parents, siblings, teachers or friends. The teachers also replied to a question concerning twin similarity in physical appearance (position of the teeth, hair and eye color, shape of external ear, lips and nose and frontal hair line). Finally the teachers, school doctors and school nurses were asked if, in their opinion, the twins were MZ or DZ.

Not more than 10% of the cases are erroneously judged with this type of similarity diagnosis [1]. The reliability of this method can therefore be considered sufficient for group comparisons. A serological analysis has been carried out at the Karolinska Institute, Stockholm, for 71 of the 227 like-sexed SLU twin pairs. Of these, only 3 pairs, or 4%, had been erroneously diagnosed as MZ instead of DZ, and have thus been reclassified.

Table 1 shows the number of SLU twins by sex and zygosity. The proportions of MZ, DZ and unlike-sex DZ pairs are approximately in accordance with the proportions for live-born twins reported in official statistics for Swedish cities and towns [16,17].

In the present study, data from the MZ and like-sexed DZ twins will be used to illustrate the model described below.

Table 1. The twin sample by sex and zygosity

	MZ pairs	DZ pairs
M-M	47	68
F-F	47	65
M-F		97

Model

The path diagram in Fig. 1 (from Plomin and DeFries [20]) provides the basis for the model. P_i is the measured phenotype at one time point and P_m is the same phenotype measured at a later time point. G and E symbolize genetic and environmental deviations, respectively, at the different ages and the path coefficients (h and e) are square roots of heritability and environmentality. The genetic correlation (r_{Gim}) and environmental correlation (r_{Eim}) between the measurements of ages i and m are due to genetic and environmental influences that are salient at both ages. From path analytic theory, the phenotypic correlation (r_{Pim}) can be partitioned into genetic and environmental components as follows:

$$(1)\quad r_{Pim} = h_i\, h_m\, r_{Gim} + e_i\, e_m\, r_{Eim}$$

where $h_i\, h_m\, h_{Gim}$ is the phenotypically standardized genetic covariance and $e_i\, e_m\, r_{Eim}$ is the phenotypically standardized environmental covariance [2].

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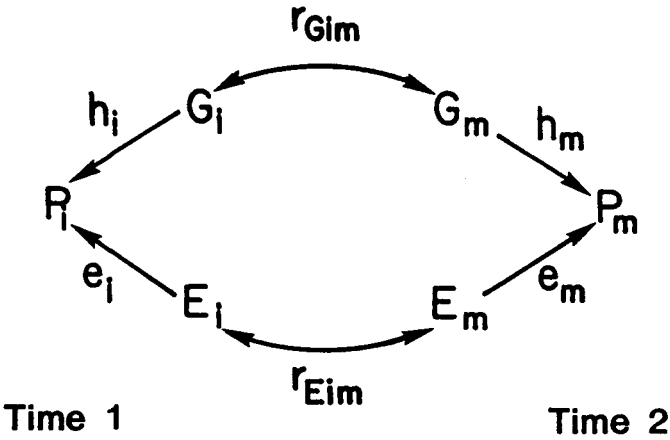

Fig. 1. Path diagram indicating that the phenotype correlation between two times can be mediated genetically and environmentally (Plomin and DeFries, 1981).

Genetic correlations and environmental correlations can be estimated from twin data by methods that are analogous to those used to estimate heritability and environmentality [19]. The heritability of a character at time i is estimated by doubling the difference between the MZ and DZ intraclass correlations:

(2) $h_i^2 = 2\,(r_{MZi} - r_{DZi})$

where r_{MZi} and r_{DZi} are the intraclass identical and fraternal twin correlations at time i. Environmentality is estimated by subtraction:

(3) $e_i^2 = 1 - h_i^2$

In the same manner, $h_i\, h_m\, r_{Gim}$ may be estimated by doubling the difference between the MZ and DZ cross-correlations of measures at different time points:

(4) $h_i h_m r_{Gim} = 2\,(r_{MZim} - r_{DZim})$

Similarly to equation 3, $e_i\, e_m\, r_{Eim}$ may be estimated by subtraction:

(5) $e_i e_m r_{Eim} = r_{Pim} - h_i h_m r_{Gim}$

The phenotypically standardized covariances are relevant for assessing the relative contribution of genetic and environmental influences to phenotypic stability.

Genetic and environmental correlations, r_{Gim} and r_{Eim}, may then be solved by division by the product of the roots of heritabilities and environmentalities, respectively. These correlations are unlike product moment correlations in that they may be greater than 1 or less than -1. The genetic and environmental correlations address the question: do the same genes and environments, respectively, influence a character at ages i and m or are different sets of genes or environmental influences involved at these ages? Because the genetic and environmental correlations are more relevant to the questions posed in the introduction, we will emphasize the correlations rather than the covariances.

RESULTS

Height

Phenotypic correlations (r_p) between the first time point and subsequent time points based on the total sample for height are presented in Table 2.

Table 2. Phenotypic (r_P), genotypic (r_G) and environmental (r_E) correlations between first time point and all other time points for height

Age	Girls			Age	Boys		
	r_P	r_G	r_E		r_P	r_G	r_E
11.0	0.99	1.00	0.97	11.0	NA	NA	NA
11.5	0.97	1.04	0.87	11.5	0.99	1.03	0.95
12.0	0.96	0.99	0.90	12.0	0.98	0.97	0.98
12.5	0.94	0.98	0.87	12.5	0.95	0.86	1.06
13.0	0.92	0.93	0.91	13.0	0.91	0.78	1.11
13.5	0.90	0.94	0.82	13.5	0.88	0.77	1.03
14.0	0.88	0.95	0.80	14.0	0.86	0.76	1.01
14.5	0.85	0.90	0.86	14.5	0.84	0.78	0.92
15.0	0.81	0.85	0.75	15.0	0.84	0.89	0.76
15.5	0.80	0.75	0.96	15.5	0.85	0.92	0.73
16.0	NA	NA	NA	16.0	0.89	0.96	0.79
16.5	NA	NA	NA	16.5	0.90	1.02	0.76
17.0	NA	NA	NA	17.0	0.90	1.18	0.68
17.5	NA	NA	NA	17.5	0.90	1.07	0.71
18.0	NA	NA	NA	18.0	0.88	1.11	0.64

These correlations with the first time point and each of the subsequent measurents give an indication of stability (Fig. 2). A trend of lower correlations at the time of puberty can be seen for both boys and girls, although the "growth spurt effect" is more pronounced for the boys. (The definitions of puberty and growth spurt effect have been discussed earlier [7]).

Intraclass correlations were computed using a double entry technique [22] and pairwise deletion of data. Hence, correlations for some of the later time points are based on somewhat smaller sample sizes than reported in Table 1. Genetic and environmental correlations for height in boys and girls, are also presented in Table 2.

For ease in interpretation, plots of the genetic and environmental correlations between the first time point and each of the later ages are presented in Figs. 3 and 4 for boys and girls, respectively. These plots depict the extent to which genetic and environmental factors relevant prior to puberty are also of importance at the various ages after that point. For the boys, the genetic correlations form a U-shaped curve with low points evident during the time of puberty. The environmental correlations are in an inverted U form. Genetic correlations for the girls are represented by a more linear trend decreasing with age. This is also generally true for the environmental correlations, although an increase is seen at around 15 years of age.

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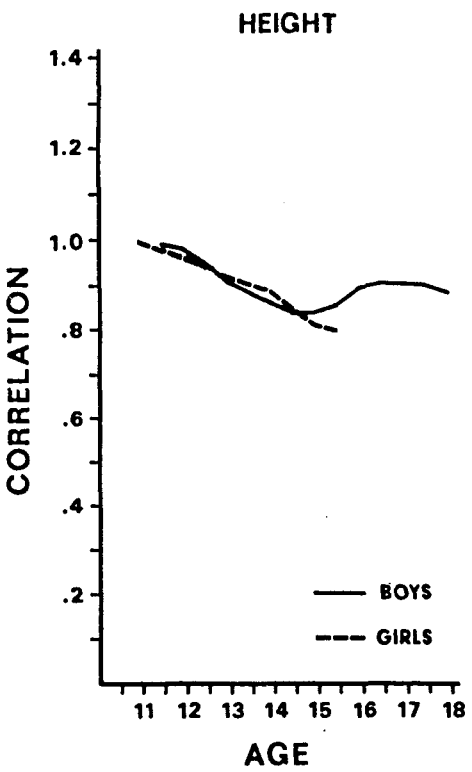

Fig. 2. Phenotypic correlations between the first time point and subsequent time points for height in male and female twins.

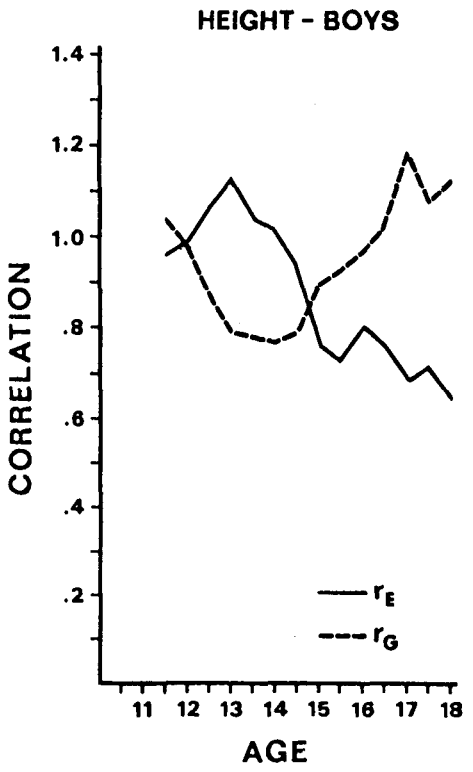

Fig. 3. Genetic and environmental correations between the first time point and subsequent time points for height in male twins.

Weight

Table 3 presents phenotypic correlations for weight in boys and girls. These correlations, depicted in Fig. 5, decrease with age for both sexes.

In Table 3, the genetic and environmental correlations are also presented. At the last time point for the girls, bivariate heritability was greater than one, hence environmentality and the resultant environmental correlations were negative. This indicates that a simple additive genetic model at least for that time point is not appropriate.

Figs. 6 and 7 depict the genetic and environmental correlations for weight with the first time point. The pattern for the boys is similar to that for height. For the girls, however, the genetic correlations are relatively stable with age while the environmental correlations rises to a sharp peak during puberty and drops drastically thereafter.

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Table 3. Phenotypic (r_P), genotypic (r_G) and environmental (r_E) correlations between first time point and all other time points for weight

Age	Girls			Age	Boys		
	r_P	r_G	r_E		r_P	r_G	r_E
11.0	0.99	1.00	0.97	11.0	NA	NA	NA
11.5	0.97	0.96	1.01	11.5	0.98	1.00	1.00
12.0	0.95	0.88	1.07	12.0	0.96	0.91	0.98
12.5	0.93	0.88	1.15	12.5	0.94	0.76	1.02
13.0	0.90	0.98	1.42	13.0	0.91	0.53	1.08
13.5	0.89	0.99	2.11	13.5	0.89	0.56	1.02
14.0	0.88	0.89	1.40	14.0	0.87	0.65	0.95
14.5	0.87	1.04	0.51	14.5	0.85	0.78	0.90
15.0	0.84	0.98	0.29	15.0	0.83	0.86	0.85
15.5	0.80	1.25	-0.25	15.5	0.82	1.09	0.70
16.0	NA	NA	NA	16.0	0.82	0.90	0.89
16.5	NA	NA	NA	16.5	0.81	0.97	0.82
17.0	NA	NA	NA	17.0	0.81	1.15	0.64
17.5	NA	NA	NA	17.5	0.78	1.40	0.39
18.0	NA	NA	NA	18.0	0.76	1.38	0.35

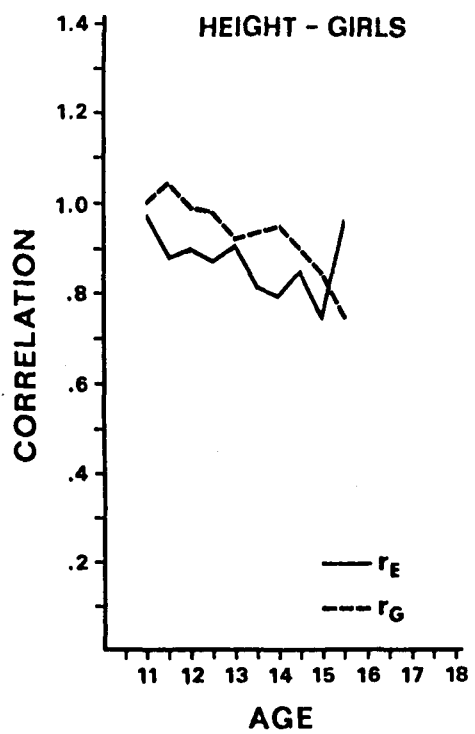

Fig. 4. Genetic and environmental correlations between the first time point and subsequent time points for height in female twins.

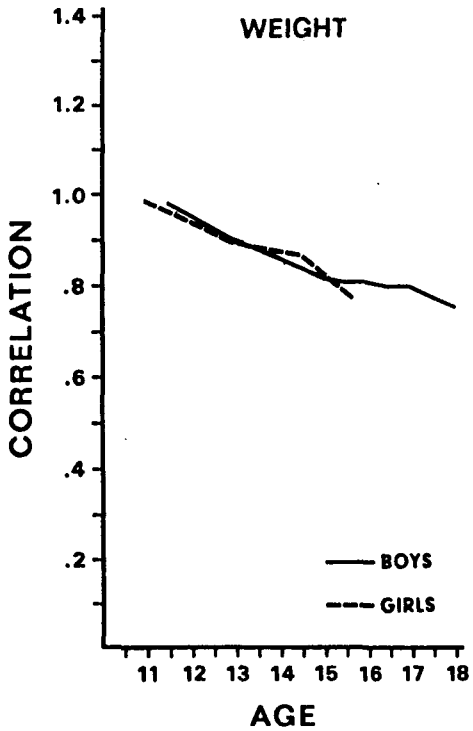

Fig. 5. Phenotypic correlations between the first time point and subsequent time points for weight in male and female twins.

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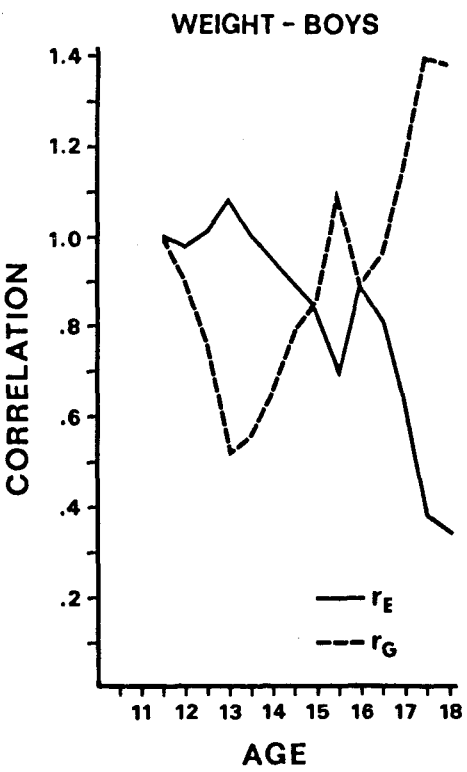

Fig. 6. Genetic and environmental correlations between the first time point and subsequent time points for weight in male twins.

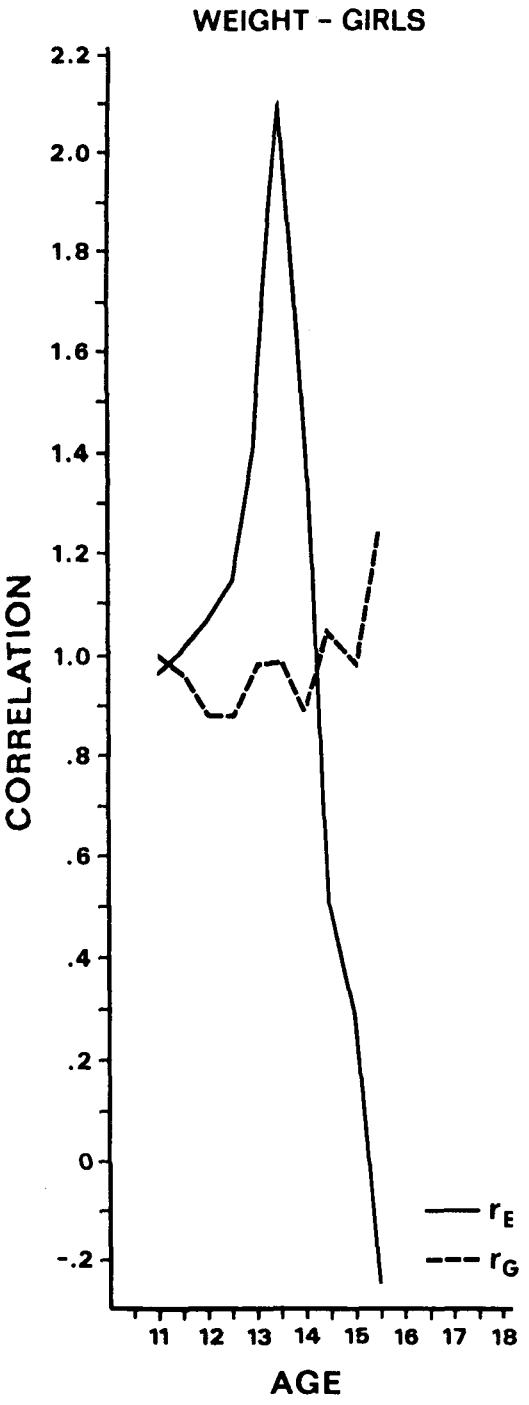

Fig. 7. Genetic and environmental correlations between the first time point and subsequent time points for weight in female twins.

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DISCUSSION

These results represent an attempt at applying one sort of multivariate behavior genetic analysis to longitudinal data. The generally greater variability for height among boys at puberty [14] is reflected in greater fluctuations in the patterns of genetic and environmental correlations in boys than in girls. These patterns suggest that a new set of genes for height may be temporarily turned on during the growth spurt phase, and, at least for boys, turned off again after this period.

The same patterns in genetic and environmental correlations with the first time point are also evident for weight in boys. Perhaps many of the same sort of mechanisms are influencing weight as are influencing height. For the girls, however, quite a different picture develops. Genetic correlations for weight in girls are nearly the same throughout the 5-year period, whereas environmental correlations peak at 13.5 years and drop drastically thereafter. The extreme reduction to a negative environmental correlation after puberty reflects the fact that there is a major divergence in twin similarity with age in the girls, ie, DZ twins appear less similar with age whereas MZ twin similarity remains relatively stable. This type of result indicates that a single additive genetic model is not appropriate for the data.

Fischbein [9] has proposed that this divergence reflects a dynamic GE interaction and correlation whereby certain genotypes respond differently to the specific environments. A similar theory, which is compatible with the present results, has also been presented by Scarr and McCartney [21]. DZ twins, sharing only half of the genetic variance, would be more dissimilar if this type of GE interaction is present. Other explanations for this divergence include nonadditive effects of epistasis and dominance variance, which would tend to reduce the DZ correlation. Alternatively, greater DZ discordance for turning on and off of various sets of genes in a manner analogous to "emergenesis" [15] contribute to DZ divergence. The present data demonstrate, however, that for weight in girls, the genetic correlations are relatively stable, suggesting that the DZ discordance may indeed be a result of dynamic GE interaction and correlation. In the absence of longitudinal adoption data, this hypothesis remains plausible but not confirmed. The presence of nonadditive genetic effects, however, can and will be tested using structural model fitting procedures (eg, with LISREL by Jöreskog and Sörbom [12]).

In summary, the three questions posed in the introduction may be responded to as follows:

1) Genetic and environmental factors for height and weight appear to change during puberty and,

2-3) The same pattern of genetic and environmental factors is evident for both height and weight for boys, but is different for weight in girls.

Finally, we have learned, by applying the model to actual longitudinal twin data, that:

1) The inadequacy of the model could not be demonstrated without having access to *actual* data for *several* time points;

2) Even if the model does not fit, it has to be tested by using real data.

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REFERENCES

1. Cederlof R, Friberg L, Jonsson E, Kaij L (1961): Studies on similarity diagnosis in twins with the

aid of mailed questionnaires. Acta Genet 11:338-362.
2. DeFries JC, Kuse AR, Vandenberg SG (1979): Genetic correlations, environmental correlations, and behavior. In Royce JR, Mos LP (eds.): Theoretical Advances in Behavior Genetics. Alphen aan den Rijn: Sijthoff & Noordhoff.
3. DeFries JC, Fulker DW (1986): Multivariate behavioral genetics and development: An overview. Behav Genet 16:1-10.
4. Eaves LJ (1983): Modelling the genetics of behavioral change. Paper presented at 4th International Congress on Twin studies, London.
5. Eaves LJ, Last KA, Young PA, Martin NG (1978): Model-fitting approaches to the analysis of human behavior. Heredity 41:249-320.
6. Essen-Möller E (1941): Empirische Ahnlichkeitsdiagnose bei Zwillingen. Hereditas 27:1-50.
7. Fischbein S (1977): Onset of puberty in MZ and DZ twins. Acta Genet Med Gemellol 26:151-158.
8. Fischbein S (1979): Heredity-Environment Influences on Growth and Development During Adolescence. Lund: Liber.
9. Fischbein S (1981): Heredity-environment influences on growth and development during adolescence. In Gedda L, Parisi P, Nance WE (eds.): Twin Research 3, Part B. New York: Alan R. Liss.
10. Henderson ND (1982): Human behavior genetics. Ann Rev Psychol 33:403-410.
11. Husén T (1959): Psychological Twin Research. Stockholm: Almqvist & Wiksell.
12. Jöreskog KG, Sörbom D (1983): LISREL: Analysis of Linear Structural Relationships by the Method of Maximum Likelihood, Version VI. Chicago: International Educational Services.
13. Lindgren G (1979): Physical and Mental Development in Swedish Urban Schoolchildren. Lund: Liber.
14. Ljung BO, Fischbein S, Lindgren G (1977): A comparison of growth in twins and singleton controls of matched age followed longitudinally from 10 to 18 years. Ann Hum Biol 4:405-415.
15. Lykken DT (1982): Research with twins: the concept of emergenesis. Psychophysiol 19:361-373.
16. Medlund P, Cederlöf R, Floderus-Myrhed B, Friberg L, Sörensen S (1977): A new Swedish twin registry. Acta Med Scand Suppl 600.
17. Official Statistics of Sweden (1958): Befolkningsrörelsen, Ar 1955 (Vital statistics 1955). Stockholm: Central Bureau of Statistics.
18. Plomin R (1986): Multivariate analysis and developmental behavioral genetics; Developmental change as well as continuity. Behav Genet 16:25-43.
19. Plomin R, DeFries JC (1979): Multivariate behavioral genetic analysis of twin data on scholastic abilities. Behav Genet 9:505-517.
20. Plomin R, DeFries JC (1981): Multivariate behavioral genetics and development: Twin studies. In Gedda L, Parisi P, Nance WE (eds.), Twin Research 3, Part B. New York: Alan R Liss.
21. Scarr S, McCartney K (1983): How people make their own environments: A theory of genotype-environment effects. Child Dev 54:424-435.
22. Snedecor GW, Cochran WG (1967): Statistical Methods. Amens, Iowa: Iowa State University Press.
23. Wilson RS (1979): Analysis of longitudinal twin data: basic model and applications to physical growth measures. Acta Genet Med Gemellol 28:93-105.

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