

QUANTITATIVE GENETICS DURING THE GROWTH PERIOD OF CHILDREN: METHODOLOGY AND FACTORS

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Abstract: The methodological problems of the quantitative genetics are numerous, especially during the growth period. Many methods are able to give a relative idea of the heritability, based on the study of twins, of sibs, of parent-offspring or of other relatives. But, in the interpretation of these results, one must be careful: the coefficients of heritability are indeed not very adequate to give an accurate prediction of the relative influence of both factors, of genetic or of environmental factors. These coefficients of heritability are specific for a particular population in a particular environment and at a specific time. However, if the population and its environment are good defined, a study of a decreasing order of genetical determination can be useful. These criticisms are also true for the quantitative genetics of growth, supplementary remarks have, however, to be taken into account such as variations of the heritability in function of age and such as difficulties to characterize human growth curve.

Key words: quantitative genetics, growth process, methodology.

The events of growth and development are controlled by a multifactorial system. It is well known that morphological characters are determined by factors of genetical origin and also by factors of environmental origin (SUSANNE 1975, 1977, 1980, DEFRISE 1981). Anthropologists and pediatricians know also that growth is a continuous phenomenon from conception to maturity where the different factors influencing growth are changing in the different periods of growth. The methodological problems in the study of the quantitative genetics during the period of growth are related to the fact that the genetical and environmental factors interact almost invariably and are rarely independent. We intend to develop three different problems of methodological origin: (1) the choice of a tool to study heritability, (2) the problem related to the fact that growth is a continuous phenomenon, and (3) the scarcity of suitable longitudinal data.

Heritability

The concept of heritability h^2 has been defined by plant and animal breeders as the amount of genetic variability which can be used for selective breeding. The heritability is generally defined as the proportion of the total phenotypic variance (V_p) due to additive genetic variation (V_A)

$$h^2 = \frac{V_A}{V_p}$$

This definition corresponds to the heritability in the narrow sense used in selective breeding when the aim is to produce individuals of improved economic quality, when breeders select individuals homozygous for genes related to these qualities, and when environmental correlations are eliminated. Of course, the use of the heritability in the narrow sense is illusory in human populations, where the heritability in a broad sense is mostly used, which is a degree of total genetic determination (V_G) including dominant factors (V_D), epistasis factors (V_i).

$$h^2 = \frac{V_A + V_D + V_i}{V_P} = \frac{V_A + V_D + V_i}{V_A + V_D + V_i + V_E} = \frac{V_G}{V_G + V_E}$$

with V_E , environmental factors.

From this definition, it is apparent that heritability can be change in function of the relative importance of the environmental conditions. In function of a reduced environmental variance or in function of a large environmental variance, the value of the heritability will vary: in these conditions, heritability is inadequate to measure the relative importance of nature versus nurture. These coefficients are only valid for the specific population studied in the specific period and environment of the analysis. The human geneticist cannot control the environments in which people live, these are infinitively variable and very difficult to measure, it is an ever-present source of error.

The additive genetic variance (V_A) refers to the hypothesis that the genes act additively. The regression of this additive genetic value on the phenotypical value gives also a definition of the heritability in the narrow sense. It is only these summed effects of the genes which have a selective value.

The dominant variance (V_D) refers that, for some genes, the phenotypes of the heterozygotes are not exactly intermediate between the two homozygotes. Heterosis would be a very specific example of this deviation to the additivity. The existence of dominance factors will result in a diminution of correlations between relatives, it affects, however, more the correlation between sibs than between parents and children.

The epistasis variance (V_i) results of the interaction between genes, it means that the effects of different genes are not simply summed. In human populations, it is rather impossible to have correct estimations of these effects. The estimation of the importance of linkage between genes and of pleiotropic effects is even difficult.

A genetic factor which can be estimated more easily is the variance due to assortative mating. A positive assortative mating has been observed for different morphological characters (SUSANNE 1967, SPUHLER 1968): it will result in higher frequencies of homozygous genotypes than in panmictic conditions. We must expect also that the effects of assortative mating will be confounded with the additive variance, and that for correlation parent-offspring for instance the existence of a positive assortative mating will increase the value of the coefficients of correlation.

Other possible complications of the method are the influence of X-linked loci (MATHER et al. 1971).

The most difficult variance to estimate is the environmental variance, different components interact and the variability of environmental conditions is immense. In a quite artificial way, artificial for human populations perhaps

not for breeding conditions, one can distinguish changes of environment between individuals within families, between families, between socio-economical classes, between geographical groups. The quantification of these variances is very difficult, subtle changes can be observed. For instance, the environmental variance within families will not be the same between twins than between sibs, will not be the same between monozygotic twins than between dizygotic twins. The variance between families and the variance between socio-economical classes inflate the covariance between parents and children, they may thus inflate correlations and interact with the correlations due to the genetic variance. The environmental covariance is expected to have a lower influence in parent child comparisons than in comparison of sibs or of twins.

But, even more complex, the interaction between the different factors have to be taken into account. In the familial studies, you can find four different covariances:

- cov. (genotypes parent and child),
- cov. (genotypes parent and environment child),
- cov. (genotypes child and environment parent),
- cov. (environment parent and environment child).

The second and the fourth covariances are in most cases positive.

From all these arguments, it is obvious that the coefficients of heritability are not very adequate to give an accurate prediction of the relative importance of genetic and environmental factors. The estimations of heritability are relative to the studied population, in its specific environment and time (FELDMAN et al. 1975). The coefficients of heritability are specific for a particular gene pool and environment, as well as for a particular interaction between genotypes and environments.

But, in spite of all these criticisms, measurement of the degree of heritability can be useful in defining for a specific population a decreasing order of genetical determination for different anthropological characters. For this kind of approach, different methods of calculation of heritability can be used (for a review, see SUSANNE 1980). But, for a definition of a decreasing order of heritability, not real coefficients of heritability could be used, such as coefficients of correlation parent—child for instance.

Predictions from these measurements of heritability must always be done very carefully. For instance, we know that stature has one of the highest coefficient of heritability, this means that the environmental variance is supposed to be low. However the well-known observation of secular trend of stature is almost certainly the result of environmental conditions. Heritability informs us about the ratio genetical versus environmental variance for one specific environment but cannot be extrapolated to other environments.

Growth as a continuous phenomenon

From conception to maturity, the factors determining growth are changing and are not equivalent for the different periods of growth: as a result, the relative influence of genotype and environment and thus the coefficients of heritability will not be constant during these different periods.

A variation with age is evident in the study of self-correlations, where the correlation is calculated between a measurement at an age x with the

measurement of the same individual at adult age: an increase of these self-correlations is observed from birth to maturity reflecting an increase of the contribution of the child's own genes (TANNER 1960, FURUSHO 1968, ASHIZAWA et al. 1977). A rapid increase is observed during the first year, a slower increase afterwards till the puberty where a relative decrease is observed.

The same kind of observations has been made for correlations parent—offspring, where the correlations are calculated for the height for instance between the value of the adult parents and the value of the growing children and this of course in function of the age.

Longitudinal studies on twins (VANDENBERG et al. 1965, WILSON, 1976) have showed that, starting from a small influence of fetal genetical constitution at birth, a gradual increase of the genetical factors is observed between monozygotic and dizygotic twins for the weight or the length at birth. The varying degrees of vascular anastomosis of the placentas result at birth even in lower correlation between monozygotic twins than between dizygotic twins. But, after birth, the within pair differences of dizygotic twins will gradually increase and the within pair correlation of monozygotic twins will gradually increase too, resulting in terms of heritability in a gradual increase of the genetical component.

It has also been observed in domestic animals (DICKERSON 1954) and in man (RAO et al., 1975) that the heritability decreases with the age difference between the sibs. In this case, a higher environmental covariance may explain this observation: the familial environment will be more similar by sibs growing up together than by adult sibs living in different environmental conditions, this results in lower correlations by adult sibs. MUELLER (1977) observed indeed larger correlations between school-aged sibs than between adult sibs when they are studied in the same sample and in a rather limited age cohort. Similarly, when the age differences between the sibs increased, the coefficients of correlation between sibs will decrease, especially for weight, fat and muscle measurements, but not for bone measurements (FURUSHO 1968, MUELLER 1978).

Other difficulties of interpretation are found in the comparison of populations of European origin and the non-European ones, higher correlations being observed in European populations (MALINA et al. 1976, MUELLER 1976, RUSSELL 1976). The existence of a positive assortative mating in these European populations is one explanation of these higher correlations, the other explanation consists in a better expression of the phenotype in absence of malnutrition or of other problems in the standards of living.

The standards of living can influence the level of heritability: authors (CHARZEWSKA et al. 1964, BIELICKI et al. 1966, WELON et al. 1971) have observed, on the contrary of European versus Non European, higher coefficients of correlation in populations with low standards of living and of nutrition (village versus town, poor nourished versus good nourished). A possible explanation is the fact that the environmental component interacts with the genetic variance and inflates the correlations in the poor environmental conditions, children having an environmental component more similar to that of the parents in villages than in towns for instance. In these last cases, children could experience perhaps better environments than the parents have had during their growth period.

Suitable longitudinal data

Heritability of specific characters of human growth curve has been hindered by the difficulties to collect longitudinal data of relatives and also by difficulties to characterize the human growth curve.

Of course, many studies have been published comparing isolated longitudinal curves on sibs, on twins or even triplets. The interpretation of these results is, however, difficult, the curves of growth of monozygotic twins are generally more alike than those of dizygotic twins. It is only recently that human growth curves have been better characterised (HAUSPIE et al. 1980).

BOCK and THISSEN (1978) used a triple logistic curve fitting by unweighted non linear least squares in the study of two sets of triplets, where two were identical and one fraternal. The author showed a clear similarity of the curves of the identical twins and demonstrated also an evident heritable component in the appearance of the adolescent growth spurt.

In another longitudinal study of twins (FISHBEIN et al. 1978), the square root of the sum of squared differences between the deviation points and the intraclass correlation for profiles estimated from an interaction term of an analysis of variance have shown a lower deviation of the profiles of growth curves in monozygotic twins than in dizygotic like sexed twins.

The components of variance analysis model were used to estimate the degree of resemblance of growth patterns in 60 sibs distributed, among 25 families of West Bengal (India) (HAUSPIE et al. 1980). The authors analysed twelve biological parameters derived from the Preece Baines model 1 curve, fitted to the longitudinal data for height growth: a significant added variance component was observed for peak height velocity and the age at peak velocity, for these two parameters the similarity being greater among sibs than among non-related subjects.

These few results are stimulating but more studies on quantitative genetics of the synchronisation of the patterns of growth is suitable.

Conclusion

In this paper, the author has only one object in view, that is to illustrate some of the methodological problems of the quantitative genetics, especially during growth. The fundamental problem is surely the concept of heritability itself. These coefficients of heritability are only valid for the specific population studied at a specific time, it is only relative to the particular environments and genotypes characteristic of this population. If we consider interactions between genotypes and environments, genetic variance depending of the distribution of environments and environmental variance depending of the distribution of genotypes, the interpretation of heritability seems vain. The coefficients of correlation also are the result of genetic variance inflated by the variance between families and between socio-economic groups for instance. This does not mean that quantitative genetics is always useless: in a specific population, the definition of a decreasing (or increasing) order of genetical determination can be useful.

This kind of study when applied to growing children has to taken into account a change with age of the relative influence of the different factors in

the determination of growth status. These changes are related to a gradual increase with age of the contribution of the child's own genes, and to changes in function of the environments of the expression of the phenotypes and thus of the environmental variance interacting with the genetical variance.

Anthropologists, pediatricians, auxologists must be stimulated to studies of quantitative genetics during growth, but specially of the synchronisation of the patterns of growth and of the patterns of maturity.

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