Inbreeding Effects on Metrical Traits in Northeastern Brazil

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From a geneticist's point of view, relatively little attention has been paid to studies of metrical traits, a fact which is primarily due both to the difficulties intrinsic in their analysis and to their requirements for relatively large samples. Although several investigations in recent years have studied metrical traits in countries with relatively high economic standards, reasonably large samples of "primitive populations" (in the sense of Morton 1964) are practically nonexistent.

The present study is concerned with a trihybrid migrant population from Northeastern Brazil. This population has been intensively surveyed from several aspects (for a review, see Morton 1967), and the comparability between inbreeding groups has been demonstrated (Krieger 1969*a*).

MATERIAL AND METHODS

Data on metrical traits were obtained from a sample of 3,465 children at the Hospedaria de Imigrantes, São Paulo. For details of sampling and other characteristics of this population, see Krieger et al. (1965), Morton (1964), and Yasuda (1966).

In the present study, the subjects were asked questions concerning consanguinity, time of cohabitation, social conditions, and geographical origin. Husband and wife were questioned separately by different interviewers. After this, a final check on the collected information was made by reviewing the two sets of answers in the couple's presence; any discrepancies were resolved on this occasion. During their parents' interview, the children of the couple were submitted to a medical and biometrical examination.

All data on weight and height (in kilograms and centimeters, respectively) were recorded by the same trained nurse throughout the entire project. Dr. E. Azevêdo, the physician of the field team, performed all the medical examinations and recorded arterial tension according to the method of Nance et al. (1965). These procedures eliminated any individual differences in recording techniques. Neither Dr. Azevêdo nor the nurse knew the inbreeding status or other characteristics of the subjects.

After the medical examination, samples of venous blood and saliva were collected from each member of the family. The blood sample was mixed on a rotator for 10

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minutes with EDTA (0.01 ml/3–4 ml of fresh blood), and a capillary sample was taken for a hematocrit determination. The microhematocrit technique was used (McGovern et al. 1955).

Each subject was given a number, which was written on his arm. This number was used to label his data and virtually eliminated incorrect identification. These numbers were used throughout the biometrical and medical examinations and during blood collection.

All the quantitative information was recorded with approximations (when in the middle of the scale) to the next even number. By this procedure the variance of the trait is expected to be increased (since the odd cells will be less numerous), but the mean is unbiased.

The data were analyzed by stepwise multiple regression by the following model:

$$Y = a + b_1F + \sum_{i=2}^{n} b_i x_i \,,$$

where Y is a given metrical trait; a is the multiple intercept; b is the vector of partial regression coefficients with elements $b_1, \ldots, b_n$; x_i is the ith concomitant variable; and F is the individual's inbreeding coefficient.

A stepwise regression was applied after the general model was fitted, and one by one the independent variables were added in decreasing order of their contribution to the regression sums of squares. This was done until the last variable included had a t-test value less than 1.64 (10% level with infinite degrees of freedom). However, a selection of the most economical model (presented here) could be made at any step of the analysis, and this was done when the residual sums of squares of the chosen model were not statistically different from the residual sums of squares of the initial model. Consequently, the introduction of other variables would not increase significantly the regression sums of squares. Under the assumptions of parametric statistics, the partial regression coefficients are expected to deal properly with the problem of stratification, since covariance between independent variables is taken into account.

The stepwise procedure, which provides that no irrelevant variables are included in the model, makes the decision on the most reasonable model by means of selection of variables. "To a large extent the success or failure of a theory is determined by the choice of assumptions—by the extent to which the model accounts for important facts, ignores trivia, and suggests new basic concepts" (J. F. Crow, unpublished notes).

The residual variance among families was used as error, in order to avoid inflation of type-I error by nonbinomial variation (Morton 1965).

RESULTS

Height

The mean body height among the offspring of the interviewed couples was 126.6 cm, with a standard deviation of 9.3 cm, thus giving a coefficient of variation of 7% (table 1). Body height was regressed stepwise on literacy, social level, cohabitation, age, age-squared, sex, race, latitude, longitude, and F. Table 2 shows the final model.

According to the association of height with age and age-squared, the maximum for this function is obtained by setting

$$\frac{d}{dx}(a + bx + cx^2) = b + 2cx$$

equal to zero, and solving for $x = -b/2c = 24.8$ years. This age corresponds approximately, in our population, to the average age of skeletal maturity. The simple correlation of height and F, $r = .0411$ with 3,463 df, is not significant.

TABLE 1

DISTRIBUTION OF HEIGHT

Height (cm)	$F=0$	$F>0$
66–70	1	0
71–75	0	0
76–80.........	5	2
81–85.........	29	8
86–90.........	80	7
91–95	117	12
96–100........	232	20
101–105........	171	23
106–110........	186	39
111–115........	215	23
116–120........	229	39
121–125........	230	29
126–130........	248	33
131–135........	188	23
136–140........	205	22
141–145........	188	26
146–150........	235	40
151–155........	168	25
156–160........	157	28
161–165........	90	17
166–170........	46	10
171–175........	12	1
176–180........	3	2
181–185........	1	0

At this point it may be concluded that no appreciable inbreeding effect is present in this population with regard to body height, and, taking the partial regression coefficient at its face value ($b = 11.32 \pm 7.01$) in the initial model, the results are in contradiction to the genetic expectation.

Body Weight

Instead of body weight itself, the natural logarithm of weight was regressed on F and the concomitant variables cited before. This was done in order to avoid scaling effects, as can be seen by the asymmetry of the distribution shown in table 3. The mean weight was 29.07 kg with a standard deviation of 5.43 kg. Although inbreeding, literacy, latitude, latitude-squared, longitude, and sex were present in the initial model for a stepwise regression analysis, these variables were not included in the final model.

The inbreeding effect, taken at its face value in the initial model, was 18 g/10% *F*, which is also in opposition to the genetic expectation. It is clear, however, that this relationship is not significant (table 4).

The positive racial association (see Krieger et al. 1965 for details of racial classification) signifies that weight increases with the increase of skin pigmentation, as is also the case for height (for further discussion of this problem, see Krieger 1969*b*).

TABLE 2

MULTIPLE REGRESSION ANALYSIS OF HEIGHT

x_i	$\bar{x}_i$	b_i	± SE
Social level	0.666	0.5385	0.2453
Race	2.445	0.5115	0.0782
Sex	0.510	0.6909	0.3551
Age (years)	10.649	7.5738	0.1311
Age-squared	139.771	−0.1525	0.0051
Latitude (degrees)	14.124	−0.1765	0.0737
Longitude-squared (degrees)	1698.550	0.0039	0.0010

ANALYSIS OF VARIANCE

Source	df	SS	*F*
Regression	7	1442850	3,686.60
Residual	3,457	193284	

NOTE.—$\bar{Y}$ = body height = 126.56 cm ± 7.4774; intercept = 61.0719. Comparison with the general model: $\chi^2_{[5]} = 6.439$; $.30 > P > .20$.

TABLE 3

DISTRIBUTION OF WEIGHT

Weight (kg)	$F=0$	$F>0$
6–10	10	0
11–15	392	53
16–20	649	90
21–25	500	69
26–30	389	52
31–35	227	24
36–40	191	23
41–45	205	30
46–50	198	42
51–55	143	28
56–60	85	13
61–65	35	4
66–70	8	1
71–75	2	0
76–80	1	0
81–85	1	0

Hematocrit

The average microhematocrit was 37.77% with a standard deviation of 3.75% (see table 5). The multiple regression analysis is shown in table 6. Inbreeding was not significantly associated with hematocrit, although the absolute value of the partial regression in the initial model was in the expected direction ($b = -1.2 \pm 3.5$).

The surprising association of hematocrit with race was retested by including weight in the model to see if the association was consistent. After the inclusion of weight (which had a significant association, $t = 2.19$), the association of hematocrit with race becomes nonsignificant ($t = 1.64$). This problem is analyzed in a different way by Krieger (1969*b*).

Blood Pressure

The diastolic blood pressure in the present population had a mean of 64.15 mm Hg with a standard deviation of 9.89 mm (table 7). The multiple regression analysis,

TABLE 4

MULTIPLE REGRESSION ANALYSIS OF LOGARITHM BODY WEIGHT

x_i	$\bar{x}_i$	b_i	± SE
Social level	0.666	0.0104	0.0061
Cohabitation	18.598	0.0011	0.0008
Race	2.445	0.0088	0.0020
Age	10.649	0.1411	0.0033
Age-squared	139.771	−0.0025	0.0001
Longitude-squared	1698.550	0.00001	0.00002

ANALYSIS OF VARIANCE

Source	df	SS	F
Regression	6	626.349	4,154.5
Residual	3,458	86.892	....

NOTE.—$\bar{Y}$ = log body weight in kilograms = 3.2665 ± .158517; intercept = 2.0384.

TABLE 5

DISTRIBUTION OF HEMATOCRIT

Hematocrit (%)	$F=0$	$F>0$
≤15	5	1
16–20	6	1
21–25	16	5
26–30	92	18
31–35	557	74
36–40	1763	237
41–45	506	76
46–50	85	17
51–55	6	0

shown in table 8, detected an effect of inbreeding on blood pressure, significant at the 1% level ($t = 2.98$, with 3,464 df). According to the coefficient of regression, presented in table 8, 10% of inbreeding would increase the diastolic blood pressure approximately 35 mm Hg. Since this inbreeding depression is rather small, either the environmental effect is relatively unimportant (thus not requiring an extremely large sample to show the effect) or we are dealing with a type-I error. To avoid possible sources of error in our model, the interaction of inbreeding with age was

TABLE 6

MULTIPLE REGRESSION ANALYSIS OF HEMATOCRIT

x_i	$\bar{x}_i$	b_i	± SE
Race	2.445	0.1038	0.0372
Age (years)	10.649	0.4768	0.0627
Age-squared	139.771	−0.0060	0.0025
Longitude (degrees)	41.074	1.1140	0.3697
Longitude-squared	1698.550	−0.0178	0.0043
Latitude-squared (degrees)	216.516	−0.0044	0.0013

ANALYSIS OF VARIANCE

Source	df	SS	F
Regression	6	10,998.7	130.285
Residual	3,458	48,654.3	....

NOTE.—$\bar{Y}$ = 37.766% ± 3.7510; intercept = 6.7613. Comparison with the general model: $\chi^2_{[6]} = 7.477$; $.30 > P > .20$.

TABLE 7

DISTRIBUTION OF DIASTOLIC BLOOD PRESSURE

Blood Pressure (mm Hg)	$F=0$	$F>0$
≤30	2	0
31–35	2	0
36–40	88	7
41–45	79	6
46–50	351	38
51–55	263	23
56–60	668	98
61–65	423	54
66–70	531	77
71–75	255	50
76–80	259	55
81–85	82	14
86–90	25	7
91–95	6	0
96–100	1	0
101–105	0	0
106–110	1	0

included in the model and was not related to blood pressure ($F \times$ age; $b = 4.13 \pm 3.97$). Also, to obtain a better prediction of the inbreeding effect, body weight and the interaction term "body weight × age" were included in the model. However, although this term was significantly related to blood pressure, the inclusion of this term of interaction did not change either the partial regression coefficient of F or its significance.

DISCUSSION

The observed lack of inbreeding effect on height, weight, and hematocrit is in agreement with the results reported in the literature. The effect of inbreeding on height and weight, when observed, has been relatively low. Morton (1955), discussing the effect of inbreeding on body weight of live births, found that 10% of inbreeding would decrease the average birth weight by about 43 g and that the common environmental component of the variance was highly important in determining the resemblance among relatives. For height and weight at 10 months of age, Morton (1958) found in two Japanese cities a slight but significant effect of inbreeding (2.8 mm/10% F and 120 g /10% F, respectively).

TABLE 8

MULTIPLE REGRESSION ANALYSIS OF DIASTOLIC BLOOD PRESSURE

x_i	$\bar{x}_i$	b_i	SE
F	0.006	34.6679	11.6373
Cohabitation	18.598	0.0814	0.0398
Sex	0.510	−1.0683	0.4247
Age (years)	10.649	2.0996	0.1564
Age-squared	139.771	−0.0543	0.0062

ANALYSIS OF VARIANCE

Source	df	SS	F
Regression	5	75,329.6	153.984
Residual	3,459	338,432.0	....

NOTE.—$\bar{Y} = 64.149$ mm Hg ± 9.8915; intercept = 48.208. Comparison with the general model: $\chi^2_{[7]} = 11.3603$; $.20 > P > 10$.

Several other studies revealed a similar tendency (Barrai et al. 1964; Schull and Neel 1965; Schork 1964). Morton (1958) concluded that "temporal changes in infant body size . . . must therefore be largely due to nutrition and other environmental factors." Almost all the available data support this conclusion, and the results of the present work are not an exception. According to Meredith and Knott (1962), the change in height in the last 100 years for 12-year-old girls in some localities in the United States was about 10 cm.

There are, however, a few exceptions to this general picture. Steinberg (1963) reported on the results of his joint investigation with Mange on the inbreeding depression of height among the Hutterites in the United States and Canada. According to Steinberg, a pronounced inbreeding depression of about 60 mm/10% F was observed among males. Since the data, in the form presented, do not seem to be corrected for age, no valid interpretation of their results can be made. However, Mange (1964) reported approximately the same order of effect, although the sex effect was different in the two samples.

The present sample and those of Morton (1958), Barrai et al. (1964), Schull and Neel (1965), and Schork (1964) are all somewhat different from that of Mange (1964). The sample of Mange has an effect about 10 times larger than the others with respect to height. It is interesting to note, however, that Mange concluded that his results were of the same order of magnitude as those of Schull; nevertheless, Schull (1962) remarked that "they [the anthropometric measurements] appear to be consistent with values reported by Morton (1958) for the decline in live-birth weight with inbreeding." Schull's results seem to be, in fact, consistent with all the other results, except perhaps for body weight.

The results of Mange, on the other hand, are difficult to interpret. It is of interest to note that his results are significant at the .0001 level, with a sample of about 600 women (in contrast with all the other studies).

Hulse (1958) reported a significant effect of endogamy on body weight. Endogamy was defined as marriage between partners born in the same Swiss village, and exogamy, between partners from different villages. Since the difference between inbreeding coefficients is, at the most, of the same order of magnitude as the mean inbreeding coefficient of the "endogamic" population (which seems to be high, but not reaching .015625 [second cousins]), and the genetic component on the determination of the trait is mostly additive, the conclusion of Hulse, that "dans ces conditions l'explication la plus logique de faits observés c'est que l'hétérosis détermine une croissance plus grande chez les descendants de mariages exogames en Suisse," seems open to question.

An interesting fact about Hulse's data is that the height of the endogamic group increased in the following order: *sédentaires*; *migrants*; *californiens*. This also indicates the strong influence of the environment on the claimed effect.

Hematocrit did not show inbreeding depression in the present investigation. The results of Schull and Neel (1965) are in agreement with the present material, since in their data (for sex–cities) only Nagasaki males showed a significant inbreeding depression (at the 5% level). It is suggestive, however, that their four comparisons, using only the inbred groups, are in the same direction; that is, the decrease in hematocrit (nonsignificant) is about 0.2%/10% F, which is similar to the present reported figure, taken at its face value of 0.1%/10% F. This agreement suggests that hematocrit, like body weight and height, may show a small but consistent inbreeding depression, thus requiring large samples for a statistically detectable effect.

On the other hand, the diastolic blood pressure × inbreeding association (see table 8) was significant at the 1% level, suggesting that the dominant component of the determination of blood pressure is large enough to be detected in any reasonable sample size.

Cruz-Coke and Covarrubias (1964), Schull and Neel (1965), and Takkunen (1964) reported somewhat different results in their studies of the association of diastolic pressure × inbreeding. Takkunen, regarding a sample of about 150 pairs of twins in Finland, remarked that "the variability of systolic blood pressure and the pulse rate was found to depend on genetic factors, while the diastolic blood pressure appeared to be dependent on environmental factors." Schull and Neel also failed to detect any significant dominant component in the determination of diastolic blood pressure. On the other hand, Cruz-Coke and Covarrubias, working with a series of about 600 individuals in an endogamic Chilean village, concluded that "in our population the blood pressure phenotype (diastolic) is determined by a strong genetic component of a multifactorial nature. The role played by nongenetic factors in the determination of this phenotype is limited." This conclusion, except for the inference on the role played by environmental factors, is in agreement with the present findings. It is clear that a variety of explanations are possible for these apparent discrepancies with respect to blood pressure; the results of Schull and Neel and my results should be weighted differently, since, although the present sample may be heterogeneous with regard to background noise, the heterogeneity of the Japanese material is a fact, thus biasing to an unknown extent the inbreeding effects (see Krieger 1969*a*; Schull and Neel 1965, chap. 4).

Some support for a strong genetic determination of blood pressure is indicated by the existence of several lines of hypertensive rats (Devine and Smirk 1964) and, for that matter, by some studies of diverse forms of hypertension in man (for a review, see McKusick 1961, pp. 419–420).

Based on the results of the present material, the assumption of selective mechanisms against some homozygotes (in the past, at least) is reasonable in order to account for the observed effect of inbreeding on diastolic blood pressure.

The importance of the genetic component of blood pressure is clearly seen, in connection not only with the present results but also with the results obtained by Nance et al. (1965), who showed that O individuals (ABO system) have a significantly higher blood pressure than their non-O sibs. The conclusions of Nance et al. are consistent with the observations of Maxwell and Maxwell (1955) with regard to hypertension. The inbreeding × blood pressure and the ABO × blood pressure associations deserve further study in order to elucidate their causes.

SUMMARY

An extensive study of inbreeding effect on height, weight, hematocrit, and diastolic blood pressure was performed on a sample of 3,465 children from northeastern Brazil.

There was no significant effect on height and weight, which is in accordance with a small dominant component. There was also a small and nonsignificant effect of inbreeding on hematocrit, but these results are consistent with a very small effect, thus requiring large bodies of data for a sensitive analysis. Diastolic blood pressure, on the other hand, had a relatively large and significant inbreeding effect.

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