

Selection under assortative mating in mice

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1. INTRODUCTION

The theory of the effects of assortative mating in panmictic populations was first presented in a classical paper by Wright (1921); he described the effects that such non-random mating should have on parameters such as the variance of the population, the correlation between relatives, homozygosity, etc. Reeve (1953) pointed out that assortative mating could be used to decrease the error variance in estimating population genetic parameters. Over two generations of assortative mating in plants, Breese (1956) found that gene combinations having extreme effects were increased, while those with intermediate effects were decreased in frequency.

McBride & Robertson (1963) combined selection for bristle number with random and non-random mating in *Drosophila*. In all their comparisons, the assortatively mated lines gave a greater response than the line randomly mated, due in part to an increase in heritability and in part to an increase of the selection differential. The greatest response was obtained when individual records were supplemented by family averages so that selection was based on an index. The results were thus nicely in accord with the theory, although the advantages of selecting under assortative mating were not striking.

Wilson, Kyle & Bell (1965) studied the effects of mating system on selection in *Tribolium*. Assortative mating afforded slightly more progress than did random mating in increasing 19-day pupa weight, but the difference was not statistically significant. Furthermore, at the end of six generations of selection the outbred lines showed as much progress as the assortatively mated lines; the randomly mated and inbred lines were intermediate at that time.

The present experiment was designed to evaluate the effectiveness of selection in mammals when combined with assortative or disassortative mating in comparison with random mating. The character studied was 6-week body weight in mice; when selected upward this weight is held to behave as a character approximately 30% heritable, while downward it is reported to be approximately 50% heritable.

2. EXPERIMENTAL METHODS

The base population for this experiment was created by a cross of four highly inbred lines obtained from the Jackson Laboratory, Bar Harbor, Maine. The four-

strain cross generation constituted generation 0. From this base population, mice were chosen at random and then randomly assigned to nine treatment classifications (lines) according to the factorial design in Table 1.

Since generation 1, parents have been selected and mated according to this scheme, each line consisting of fifteen sires and thirty dams plus some half-dozen matings per line to assure population size. Litters were standardized to size 8 at birth and weaned at 3 weeks of age; the young mice were identified, weighed, and caged separately by litter and sex. At 6 weeks of age they were again weighed and the parents of the following generation selected. Mass selection was utilized despite the fairly certain existence of maternal effects on 6-week weight; in this fashion the entire amount of genetic variability was available for selection although admittedly some of it would be hidden by the maternal influence. The diet fed was a standard pellet prepared by a commercial company. To date, in twelve generations of selection, data have been recorded on approximately 25000 mice.

Table 1

Direction of selection	Mating system		
	Assortative	Disassortative	Random
Upward, high 6-week wt	Line 1 (30 litters)	Line 2 (30 litters)	Line 3 (30 litters)
Downward, low 6-week wt	Line 4 (30 litters)	Line 5 (30 litters)	Line 6 (30 litters)
Unselected for body wt	Line 7 (30 litters)	Line 8 (30 litters)	Line 9 (30 litters)

3. RESULTS

(i) *Correlations between mates*

The effectiveness of assortative mating depends on the correlation achieved between the genotypes of the mates, which in turn depends on two quantities: (a) the heritability of the character considered in the assortment, and (b) the phenotypic correlation achieved in the mating system. In the present experiment, consistently high values of the phenotypic correlations between mates were achieved in the assortative and disassortative lines. The arithmetic means and ranges for these correlations over twelve generations are shown in Table 2. As expected, phenotypic variances among the parents in the lines selected for high or low weight were considerably reduced in comparison with randomly selected lines; nevertheless, high correlations were realized in the former lines. Assortment was thus effectively achieved for the phenotypes.

(ii) *Phenotypic variances of 6-week weight*

One of the primary results of mating assortatively based on a character of moderate to high heritability should be a change in the genetic variance; positive assortment should increase the variance while negative assortment should de-

crease it, relative to that obtained under random mating. If the environmental portion of the variance is not greatly affected by the extension or contraction of the genotypic array, then the change in the genotypic array will be expressed as a corresponding change in the phenotypic array; that is, changes in genetic variance should be directly reflected by changes in phenotypic variance. The sum of the variance components for sire effect, dam effect and offspring within dam effect was used to estimate the total phenotypic variance for generations 1-12. (Generation 0 was omitted because of residual stratification of the genetic material from the four-way cross.) The values are shown in Table 3.

Table 2. *Phenotypic correlations between mates for 6-week weight (mean of twelve generations and range)*

	Assortative mating	Disassortative mating	Random mating
Selection upward	Line 1, 0.95 (0.91 to 0.98)	Line 2, -0.82 (-0.60 to -0.93)	Line 3, 0.01 (-0.17 to 0.28)
Selection downward	Line 4, 0.95 (0.92 to 0.99)	Line 5, -0.84 (-0.49 to -0.98)	Line 6, -0.08 (-0.35 to 0.14)
Unselected	Line 7, 0.95 (0.88 to 0.99)	Line 8, -0.95 (-0.86 to -0.98)	Line 9, 0.00 (-0.25 to 0.18)

Table 3. *Phenotypic variance in 6-week body weight (unweighted mean of the two sexes)*

Line...	Selection upward			Selection downward			Unselected		
	1	2	3	4	5	6	7	8	9
Mating system ...	Ass.	Dis.	Rand.	Ass.	Dis.	Rand.	Ass.	Dis.	Rand.
Gen.									
1	7.1	7.8	8.0	8.4	10.8	7.6	7.6	9.4	7.8
2	4.6	3.8	2.9	3.6	2.8	3.4	4.6	3.2	3.8
3	6.6	7.0	7.9	5.3	5.5	6.1	4.3	6.2	5.5
4	3.9	4.7	4.3	2.4	3.1	3.8	5.3	3.1	4.9
5	5.1	4.7	9.5	3.4	6.2	4.6	6.9	7.1	6.2
6	3.3	4.2	9.2	5.4	5.1	4.9	4.1	7.0	5.5
7	6.1	6.5	11.5	4.0	4.6	5.0	4.4	9.5	9.6
8	8.2	6.5	5.4	3.2	3.6	4.1	6.5	6.7	7.8
9	7.5	4.5	8.6	2.3	4.5	3.5	6.2	6.6	5.9
10	4.4	5.1	5.8	2.4	4.0	2.4	3.9	4.7	3.4
11	4.9	5.5	7.2	1.6	4.1	2.2	3.9	4.4	4.9
12	5.9	5.9	9.0	2.1	4.1	2.6	5.6	4.7	4.5

Comparing lines 1, 2 and 3 ('selection upward'), it can be seen that the assortative line had the highest variance in only 2 of the 12 generations, while the randomly mated line had the highest variance in 9 of the 12 comparisons. The assortative line actually had the lowest variance in 8 of the 12 cases, while the disassortative line had the lowest variance in only 2 comparisons.

Similarly, in lines 4, 5 and 6 ('selection downward'), the positively assortatively mated line 4 showed the highest variance in only 2 of the 12 contrasts and was

lowest in 8 of the 12. Conversely the negatively assorted line was lowest in only 2 and most variable in 7 of the 12 comparisons.

Essentially the same picture holds true in the comparison of lines 7, 8 and 9, which were 'unselected' for 6-week weight. In 3 cases the positive line had the highest variability, and the lowest in 6. The negatively assorted line was most variable in 6 comparisons and lowest in only 2 of the 12. In these randomly selected lines especially, one would have expected results in reasonable conformity with theory.

The results for the variances are indeed so widely at odds with theory that one might almost suspect some consistent effect to be operating. Examination of the data for the sexes separately provides no answer, because essentially the same picture exists in both sexes. The genetic variance is estimated by four times the sire component of variance—this variance is expected to show directly the effect of assortment, but examination of the genetic variance reveals the same discord with theory. Random environmental effects do not seem to be the cause either, in view of the strikingly consistent response of all lines to the general effects operating from generation to generation, as will be discussed below. Thus none of the effects suspected of systematically altering the variances were found to be at fault.

Table 4. *Cumulative selection differentials (g)*

	Assortative mating	Disassortative mating	Random mating
Selection upward	25.5	25.6	26.0
Selection downward	-7.4	-7.6	-8.8
Unselected	5.5	4.8	7.6

(iii) *Selection differentials*

The variability in the population is a fair indicator of the size of the selection differential which might reasonably be expected. Since selection downward (lines 4, 5 and 6) has produced considerably lighter mice, a scale effect should produce phenotypic variances somewhat below those in the lines selected for high 6-week weight (lines 1, 2 and 3); this effect is in fact seen in Table 3, particularly in the later generations when the lines have become differentiated (see Fig. 1). The unselected control lines have shown no consistent change in variability. With these variances, selection differentials were accumulated over twelve generations as indicated in Table 4.

As expected, considerable pressure has been possible in the upward direction, averaging over 2 g per generation; by contrast, in the downward direction, only about one-third of this much pressure has been exerted. In addition to the scale effect, however, some pressure has had to be exerted against a continuing problem of juvenile diarrhoea which persists in a moderate percentage of the young mice; the positive differentials accrued in the 'unselected' lines (lines 7, 8 and 9) afford a measure of this pressure. Offsetting this amount of pressure in the positively and negatively selected lines renders them much more equivalent, the remaining dif-

ference being easily attributable to scale effect. From the standpoint of mating system applied, however, essentially no difference in selection differential exists; indeed the random mating lines hold a slight edge over both the positively and negatively assorted lines in both directions of selection!

(iv) *Response to selection*

The response shown to the selection pressure has been to date the most satisfying aspect of the project (Fig. 1). The first four generations in the upward direction revealed the same erratic behaviour that has been experienced previously in

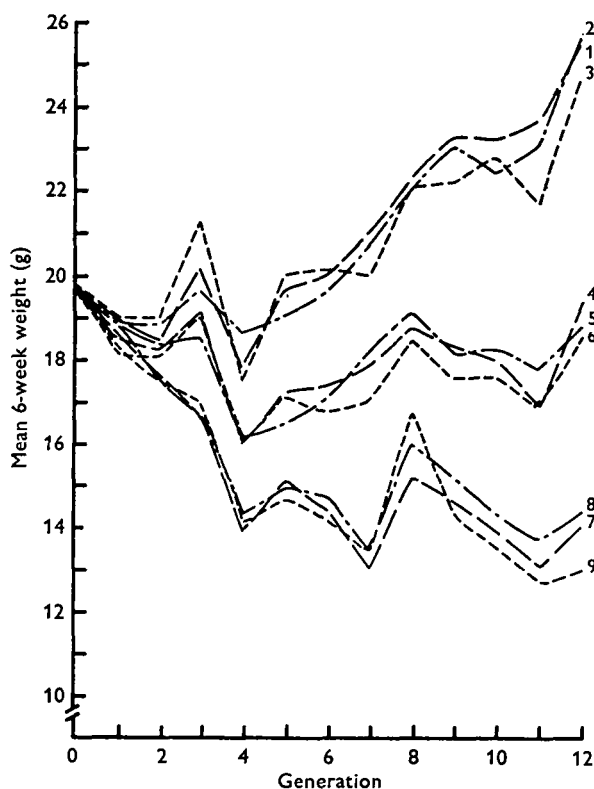


Fig. 1. Responses to selection in the nine lines. —, Assortative; - - -, disassortative; . . ., random.

our laboratory at the beginning of selection experiments, perhaps due to 'sorting out' of the chromosome arrangements introduced in the crossing of four inbred lines. Subsequent progress has been more or less steady and marked; from generation 7 to generation 11 the assortatively mated line actually showed slightly more progress than the disassortative or the random lines, but in the 12th generation was overtaken by the disassortative line. The progress in the randomly mated line has been the most erratic of the three.

In the downward direction, on the other hand, progress was extremely rapid for

the first four generations, after which the behaviour of all three lines has been erratic almost to the exclusion of further advance. By the second generation the lines had begun to pull apart from those in the upward direction, and by the third generation were clearly separate. In generations 6–12, the assortative line stayed ahead of the disassortative, but the greatest progress of all in generations 9–12 was in fact shown by the randomly mated line.

Thus, although exact tests of significance have not yet been applied to the results, it seems from the analyses thus far carried out that mating system has had essentially no effect on the progress from selection in either direction; indeed the most striking feature of the entire experiment has been the similarity of response of all lines, regardless of mating system, in a given direction, and even of *all* lines regardless of direction. For example, in generation 4 all lines suffered a marked general drop of approximately 3 g on average, while generation 8 produced a general rise of some 2 g, followed again in generation 11 by a less marked, and indeed less general, drop. Up to generation 4, the prevailing trend was in a downward direction in all the lines, though of course less so in the lines selected upward; during this period the three lines selected downward were in virtually perfect agreement with each other. This uniform behaviour is in contradiction to the findings of Clayton & Robertson (1957); the only reasonable explanation seems to lie in the effects of the general environment operating over an entire generation, for the probability of genetic drift operating so similarly in all lines is extremely remote. Support for this statement is further provided by the results for the control lines, which have fluctuated between the values of 16 and 20 g for 6-week weight, and which in the 12th generation were still close to the initial value in generation 0.

The effects of the environment which produce such violent changes from generation to generation have not been satisfactorily explained, especially where conditions in the laboratory are maintained stable within narrow limits by air conditioning, constancy of diet, regularity of care, and constant attention to good husbandry in general. One possible explanation is that the effects of the micro-environment in the early stages of growth are subsequently magnified in geometric fashion during the growth process (pre- and post-natally), resulting in a grossly modified phenotype, typical none the less of the generation in which it is produced. The problem is suggested, however, as one meriting a great deal of further study, since it is of very general occurrence in virtually all selection experiments, regardless of organism. Supplementary, more complete analyses are being undertaken in an effort to remove statistically the general effect of environment.

While there is no hint of a limit having been approached yet in the upward direction, the evidence suggests that the lower limit of 6-week body weight may be approximately reached; the latter suggestion agrees with the findings of Roberts (1966), whose lower limit for 6-week body weight in his strains was of the order of 12 g.

(v) *Heritability estimates*

Estimates of the heritability of 6-week body weight based on the covariance of half-sibs were obtained for each line in each generation. These estimates were then averaged over the twelve generations to give the values for 'calculated' heritability shown in Table 5. The 'realized' heritability values are the regressions of generation means on the cumulative selection differential computed within line.

The realized heritabilities, reflecting progress attained relative to that possible from the selection differential, are very much in line with theoretical expectation, except for line 4, where the value is obviously too high. The low values (practically 0) in lines 7, 8 and 9 properly reflect the overall lack of any consistent change in these control lines. The values in the lines selected downward (4, 5 and 6) are considerably higher than those in lines 1, 2 and 3, selected upward, as was expected on the basis of published analyses of other selection experiments dealing with body weight at 6 weeks of age.

Table 5. 'Calculated' and 'realized' heritabilities

Line...	Selection upward			Selection downward			Unselected		
	1	2	3	4	5	6	7	8	9
Mating...	Ass.	Dis.	Rand.	Ass.	Dis.	Rand.	Ass.	Dis.	Rand.
Calculated h^2	0.45	0.24	0.16	0.21	0.42	0.21	1.08	0.36	-0.18
Realized h^2	0.27	0.25	0.18	1.03	0.47	0.70	0.04	0.08	0.01

On the other hand, the values for calculated heritability are not nearly so stable as could be desired; the values shown in lines 4, 5 and 6 are lower than expected, while those in two of the unselected lines (7 and 9) are simply erratic beyond all expectation, based on such large numbers of animals.

The conclusion to be drawn from these results, however, is that the selection aspect of the project has been effective, to about the degree predicted on theoretical grounds, but that the effects of assortment in mating have not been realized—the genetic variation measured from the component analysis has not been consistently increased in the assortative lines and decreased in the disassortative lines relative to the values in the randomly mated lines.

There is a possibility that the inclusion of the respective control line as an independent covariate in the regression of generation mean on cumulative selection differential would clarify the analysis. In this way the general effects of environment would be removed, leaving any effects of the assortment to appear unveiled. Such analyses are under way and will be reported in a future communication.

(vi) *Conclusions*

The present results, obtained on a character of moderate heritability in mammals, complement those previously obtained with *Drosophila* by McBride & Robertson (1963) and by Wilson *et al.* (1965) with *Tribolium*. These workers found a very slight and statistically insignificant advantage for assortative mating over random mating and concluded that only in cases of selection for characters of very

high heritability would there be any economic advantage in using assortative mating. Since few characters at present being selected in domestic animals have a heritability value exceeding that of, for instance, bristle number in *Drosophila*, the evidence suggests that improvement from selection under random mating within a breed will be very nearly as effective as under assortative mating and that therefore the extra trouble involved in arranging assortment within the breed will not be repaid very generously.

SUMMARY

1. Approximately 25000 mice have been produced over twelve generations of selection in nine lines. The experimental design involved a 3×3 factorial arrangement of direction of selection with mating system. The primary character measured was 6-week body weight.

2. Consistently high phenotypic correlations between mates have been achieved, positive in the assortative lines, negative in the disassortative lines. Correlations were low and inconsistent in direction in the random-bred lines. These correlations have had very little, if any, effect in redistributing the genetic variance as estimated from the variance component analysis; the expected higher variances in the assortative lines and expected lower variances in the disassortative lines have not appeared, thus leaving heritability unaffected.

3. Selection differentials likewise show no consistent advantage for the assortative lines, so that the progress from selection has been virtually identical in all three mating systems in each direction.

4. Assortment of mates, either positively or negatively, for characters of even moderate heritability appears to have little influence on the outcome of selection. On the other hand, selection has been singularly effective in modifying the mean 6-week weight, with progress markedly greater in the downward direction; indeed it appears that the lower limit may already have been approximately attained.

5. Environmental effects operating in the various generations have affected all lines in remarkably consistent fashion.

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