SELECTION FOR CONSTANCY OF EXPRESSION OF THE *TABBY* GENE IN THE MOUSE*

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Summary

Selection of $Ta/+$ mice for 15 vibrissae caused a reduction in variance of the $Ta/+$ score and a slight increase in the probit width of the 15 class. There was an increase in mean score and variance of the Ta/Ta and Ta/Y sibs and a slight decrease in mean score and increases in variance of the $+/Y$ sibs. Selection of Ta/Ta and Ta/Y mice for 7 vibrissae caused a reduction in variance and an increase in probit width of the 7 class in the two selected genotypes. The mean score of $Ta/+$ sibs declined and their variance increased.

I. INTRODUCTION

A number of selection experiments have been conducted in order to show whether selective breeding can alter the variability of expression of a character about its mean. In many of these experiments the selection routine used did not result in a marked change of variability of the character selected. In a few experiments selection did change the variability (Rendel and Sheldon 1960; Waddington 1960; Kindred 1965). These experiments were carried out on *Drosophila*. Kindred (1967) reported an experiment in which selection was for asymmetry and symmetry of the secondary vibrissae in *Tabby* mice and for the range of toe numbers within litters of luxate mice. She was able to increase and decrease variability of both characters.

Kindred's selection for symmetry and asymmetry of secondary vibrissae in *Tabby* mice was made in a population segregating for the gene *Ta* and selection was for symmetry or asymmetry of $Ta/+$ females and of Ta/Y males in the generations in which this genotype appeared; nevertheless response to selection was confined in both lines to $Ta/+$ females. Indeed, in the line selected for asymmetry Ta/Y males and Ta/Ta females were, if anything, less variable at the end than at the beginning of selection. Kindred pointed out that, in the line selected for symmetry, $Ta/+$ mice with a vibrissa pattern of 7 vibrissae on each side became common. In the generations in which $Ta/+$ were selected, 67% of those born had 14, 15, or 16 vibrissae as against 73% of those selected and 36% as against 46% had 15. This resulted in selection being not only for symmetry but also for a particular number of vibrissae and it occurred to us that the explanation of the failure of the Ta/Y and Ta/Ta classes to respond might be due to effective selection being for a mean of 15 vibrissae. If effective selection has been for control of vibrissa number at 15 (7 on each side and

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one in the middle) rather than for symmetry, then the *Ta*/*Y* and *Ta*/*Ta* genotypes would not be affected since the number of vibrissae in them commonly lies between 6 and 10. If this line of argument is true and it is selection for mean vibrissa number that has been effective, one would expect that selection of *Ta*/*Y* males and *Ta*/*Ta* females with 7 vibrissae should result in canalization of vibrissa number round a mean of 7, which will be feasible in *Ta*/*Y* and *Ta*/*Ta* mice which commonly have such a vibrissa score, but such selection should have no effect on the variability of *Ta*/+ with vibrissa numbers of 10–19.

To test this possibility the line Kindred had selected for symmetry which had acquired some canalization about 15 was continued by selecting *Ta*/+ females with 15 vibrissae; the line selected by Kindred for asymmetry was continued selecting *Ta*/*Y* and *Ta*/*Ta* parents with 7 vibrissae.

II. Materials and Methods

The first line, in which selection in our hands was for *Ta*/+ females with 15 vibrissae, is the one referred to by Kindred as ASL, the second line in which we selected for 7 vibrissae in *Ta*/*Y* males and *Ta*/*Ta* females was Kindred's ASH group (Kindred 1967). In our experiments all secondary vibrissa groups were scored, namely the four paired groups, supraorbital, postorbital, postoral, and ulna–carpal and the single central group of interramals. In normal mice the numbers of vibrissae in these groups are usually 4, 2, 4, 6, 3, respectively, making a total of 19 in all. In *Ta*/+ mice the most common numbers in the five groups are 4, 2, 2, 6, 1, making a total of 15, and in *Ta*/*Y* and *Ta*/*Ta* mice, 2, 0, 2, 2, 1, making a total of 7. In normal mice there is little variation about the mean score of 19 but in the *Tabby* genotypes there is a great spread on either side of the mean so long as this is below 19 (Dun and Fraser 1959). Kindred did not score the interramal group in her lines so scores of 14 for *Ta*/+ mice in her tables correspond to 15 in ours.

Our method of selection was as follows. In ASL the mean vibrissa number of all *Ta*/+ females in each litter was calculated; the litters were ranked in order of approximation to 15 vibrissae and 30 females with 15 vibrissae, or the closest approximation to 15, were taken from the top litters; these were mated to *Ta*/*Y* males which were taken at random from top ranked litters. In the ASH line males from litters in which the mean *Ta*/*Y* and *Ta*/*Ta* score was 7 were taken and 15 males with 7 vibrissae were mated to 30 *Ta*/+ females from the top ranked litters. Vibrissae were scored 5 days after birth and again at 10 days.

The effects of this selection procedure were assessed by comparing our results with a base score taken before the start of Kindred's selection and with Kindred's last generation of selection (the 13th) which was the starting point for our selection lines. The base score was calculated for two generations scored prior to the start of Kindred's experiments in both of which the mothers were *Ta*/+ [*Ta*/+ females out of *Ta*/+ mothers have higher vibrissa scores than *Ta*/+ females out of +/+ mothers (Kindred 1967)]. The characters examined were mean vibrissa scores of all genotypes, variances, and probit distances of the 7 class in *Ta*/*Y* and *Ta*/*Ta* mice and the 15 class in *Ta*/+ mice (the 19 class was incomplete in +/*Y* mice so probit distances were not measured for this genotype). The reasons for using these three characters were as follows: If changes in variation are uniform over all vibrissa classes, in any one distribution, all classes will shrink or expand together. Thus if variation is generally reduced, a narrower distribution of vibrissa numbers will result which, nevertheless, still has the same characteristics as before and this will be reflected when the distribution is analysed as an increase in the width of each vibrissa class. If the distribution is roughly normal, probit transformation will show all classes expanding equally. On the other hand, if the character is being controlled at one phenotype the probit width of one class will be expanded, the width of the other classes remaining the same. In our experiment only the 15 and 7 classes changed in width showing that the changes in variance have been brought about by control of the character at a particular phenotype.

III. Results

Table 1 records the history of the ASL line; the distribution of vibrissa frequencies is shown in Figure 1. Kindred's selection for symmetry had little effect on the mean score of the *Ta*/+ phenotype but it reduced its variance; the reduction can be attributed mostly to an increase in the relative importance of the 15 vibrissa class which is indicated by the increase in probit width of this class. The mean and variance of the phenotype of the *Ta*/*Y* and *Ta*/*Ta* genotypes increased at the same time. There was no change in the width of the 7 class and change in variance was due largely to the increase in range of scores which accompanied the increase in mean. In our hands, selection for 15 vibrissae was accompanied at first by an increase in the variance of *Ta*/+ scores, but after two generations selection increased the prominence of the 15 class to a point slightly beyond that reached by Kindred (see Fig. 1). The mean score of the +/*Y* class fell and, as a result, variance increased due to an increase in the number of mice with other than 19 vibrissae, but as there were no mice with more than 19 vibrissae, the width of the 19 class could not be estimated and presumably the degree of control at this class was unchanged.

Table 2 records the history of the ASH line; the distributions of vibrissa frequencies in this line are shown in Figure 2. Kindred's selection for asymmetry decreased the width of the 15 class without much affect on mean or variance; however, the variance of the *Ta*/*Ta*–*Ta*/*Y* phenotype was reduced and the width of the 7 class increased. Selection of *Ta*/*Y* and *Ta*/*Ta* mice for 7 vibrissae continued this trend; the 7 vibrissa class became very prominent whilst the scores in the *Ta*/+ phenotype remained spread out with a small 15 class. There was no change in the +/*Y* phenotype.

Figure 3 illustrates the changes in probit width of the 7 class in ASH and of the 15 class in ASL. Comparison of the results of the two groups show that control of the *Ta*/*Ta*–*Ta*/*Y* phenotype at 7 vibrissae was at all stages more powerful than control of the *Ta*/+ phenotype at 15 vibrissae. The increase in probit distance totals 1·75 in *Ta*/*Y* and *Ta*/*Ta* and 1·25 in *Ta*/+, but one could not claim from the graph that the difference in rate of advance is very significant.

IV. Discussion

This selection experiment shows that stability can be achieved at 15 vibrissae in one line and 7 in the other. Since selection which secures stability of *Ta*/*Y* and *Ta*/*Ta* does not achieve stability in *Ta*/+ sisters and selection which secures stability in *Ta*/+ does not achieve stability in *Ta*/*Y* and *Ta*/*Ta* sibs, it is clear that the genes selected do not act uniformly on all major genotypes and that homozygosity or uniformity of a modifying background cannot be responsible. One is dealing with control of a phenotype at the level of expression about which selection for control has been carried out.

In Kindred's hands, selection for symmetry in *Ta*/+ and *Ta*/*Y* simultaneously resulted in stabilization about 15 vibrissae with reduced variance but reduced stability about 7 in *Ta*/*Ta* and *Ta*/*Y* with increased variance. Her selection for asymmetry apparently resulted in the reverse, although the difference between

TABLE 1

MEANS, VARIANCES, AND PROBIT DISTANCES OF EACH GENOTYPE IN THE LINE SELECTED FOR 15 VIBRISSAE IN *Ta*/+ (ASL)

Probit values marked with an asterisk were for vibrissa classes at the end of the range for that generation

Generation	*Ta*/*Ta*–*Ta*/*Y* Genotype				*Ta*/+ Genotype				+/*Y* Genotype		
	No. of Mice	Mean	σ^2	Probit Width of 7 Class	No. of Mice	Mean	σ^2	Probit Width of 15 Class	No. of Mice	Mean	σ^2
Base	38	7·34	1·37	1·20	54	15·22	5·04	0·76	92	18·97	0·03
Kindred 13	42	8·76	3·42	0·83	41	15·51	1·75	1·57	94	18·90	0·15
1	31	8·53	1·67	1·30*	33	15·29	2·09	1·22	76	18·82	0·17
2	52	8·08	1·65	2·00*	34	15·63	3·52	0·85	33	18·89	0·09
3	82	8·51	1·98	1·42	44	14·84	1·21	1·50	29	18·67	0·31
4	72	8·88	1·58	1·11	40	15·45	1·64	1·60	37	18·65	0·23
5	61	9·21	2·14	1·08*	45	15·20	1·53	1·38	40	18·70	0·32
6	74	9·32	2·33	1·17	43	15·09	1·85	1·26	35	18·80	0·22
7	73	8·96	1·82	1·12*	40	15·18	1·79	1·45	27	18·67	0·31
8	70	8·43	2·02	1·15	62	14·89	1·15	1·57	28	18·68	0·30
9	96	8·64	1·52	1·53	59	14·92	0·77	2·13	49	18·53	0·37
10	104	8·82	2·13	1·63	63	14·86	1·51	1·73	63	18·65	0·39

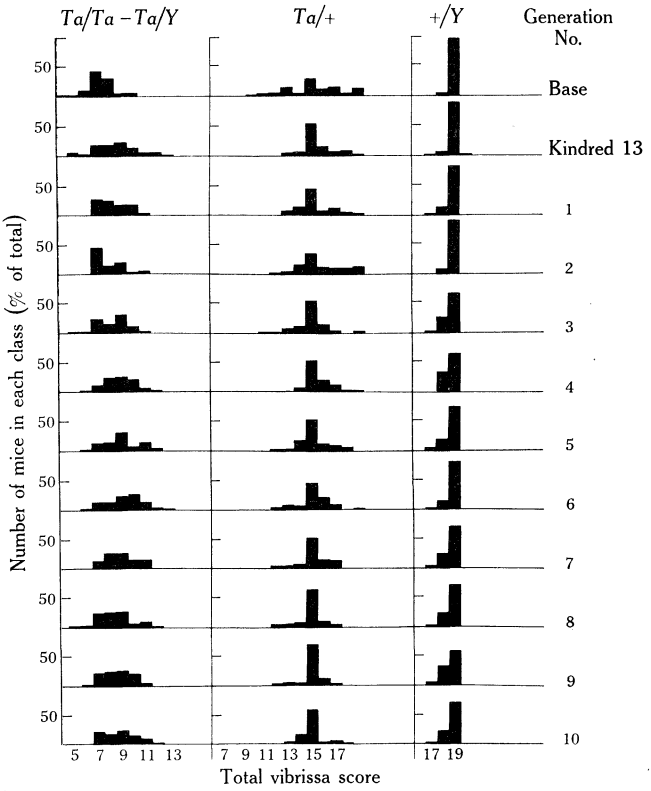

Fig. 1.—Frequency of each vibrissa class in *Ta*/*Ta*–*Ta*/*Y*, *Ta*/+, and +/*Y* mice in the line selected for 15 vibrissae in *Ta*/+ mice (ASL).

TABLE 2

MEANS, VARIANCES, AND PROBIT DISTANCES OF EACH GENOTYPE IN THE LINE SELECTED FOR 7 VIBRISSAE IN *Ta/Y* AND *Ta/Ta* MICE (ASH)

Probit values marked with an asterisk were for vibrissa classes at the end of the range for that generation

Generation	Genotype *Ta/Ta–Ta/Y*				Genotype *Ta/+*				Genotype *+/Y*		
	No. of Mice	Mean	σ^2	Probit Width of 7 Class	No. of Mice	Mean	σ^2	Probit Width of 15 Class	No. of Mice	Mean	σ^2
Base	38	7·34	1·37	1·20	54	15·22	5·04	0·76	92	18·97	0·03
Kindred 13	37	7·76	0·75	1·90*	46	16·50	4·64	0·16	96	18·97	0·05
1	52	7·12	1·47	2·00	29	14·59	6·23	0·53	36	18·91	0·08
2	40	7·38	1·16	1·67	13	12·23	4·36	—	18	18·89	0·28
3	51	7·10	0·37	2·35	66	15·44	6·59	0·08	21	18·95	0·05
4	83	7·43	0·59	2·47	52	13·79	7·43	0·32	31	19·03	0·03
5	57	7·07	0·28	2·72	38	14·18	6·37	0·48	42	18·93	0·07
6	82	7·20	0·41	2·28	33	12·33	8·17	1·12	45	19·00	0
7	83	6·95	0·24	2·78	43	13·23	10·33	0·46	35	19·00	0
8	77	7·13	0·43	2·33	41	12·80	7·16	0·36	34	18·88	0·11
9	93	7·02	0·15	3·13	39	13·21	8·17	0·32	37	18·97	0·03
10	83	7·18	0·22	2·85	36	13·64	5·44	0·38	36	18·94	0·05

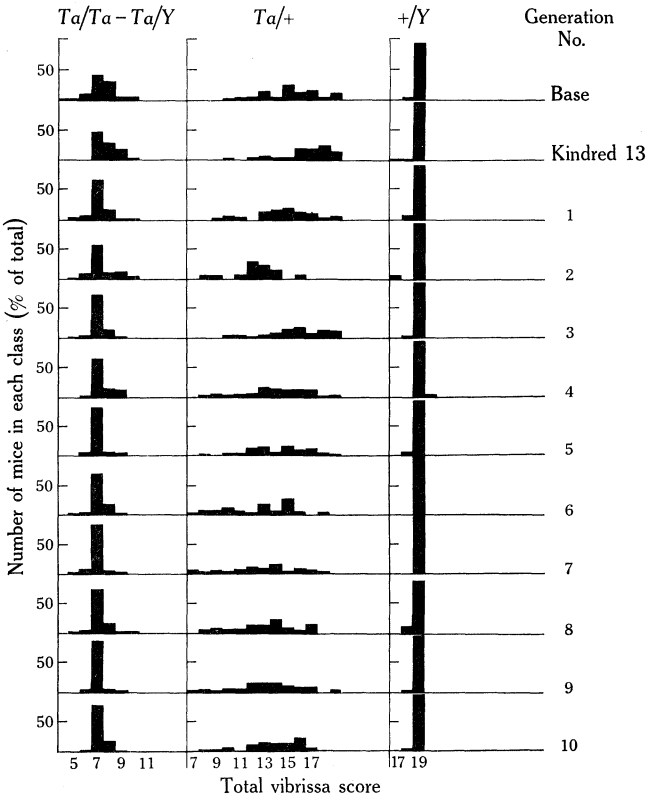

Fig. 2.—Frequency of each vibrissa class in *Ta/Ta–Ta/Y*, *Ta/+*, and *+/Y* mice in the line selected for 7 vibrissae in *Ta/Y* and *Ta/Ta* mice (ASH).

Ta/Ta and *Ta/Y* of the foundation generation and of generation K13 may well be due to small numbers and hence sampling errors. In any event, selection for 7 vibrissae, in contrast to selection for symmetry, did result in control of phenotype in *Ta/Ta* and *Ta/Y* without any corresponding appearance of control in *Ta/+*, as was predicted by the suggestion that the effectiveness of Kindred's selection was the extent to which she in fact selected for 15 vibrissae and not to selection for symmetry.

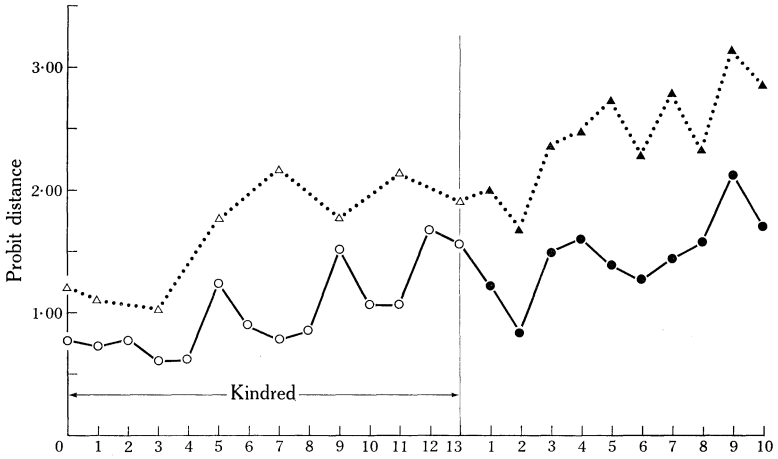

Fig. 3.—Changes in the probit width of the 7 class in the line selected for 7 vibrissae in *Ta/Y* and *Ta/Ta* mice (△, ▲), and changes in the probit width of the 15 class in the line selected for 15 vibrissae in *Ta/+* mice (○, ●).

The results of this trial tend to confirm the suggestion that selection for reduced variability of a phenotype is most likely to be effective when selection is for a particular phenotype or absence of variation about a particular mean.

V. Acknowledgment

Mrs. Margaret McInnes was responsible for maintaining these selection lines throughout the experiment. We should like to thank her for the efficient way in which she did so.

VI. References

Dun, R. B., and Fraser, A. S. (1959).—Selection for an invariant character, vibrissa number, in the house mouse. *Aust. J. biol. Sci.* **12**, 506–23.

Kindred, B. M. (1965).—Selection for temperature sensitivity in *scute Drosophila*. *Genetics, Princeton* **52**, 723–8.

Kindred, B. M. (1967).—Selection for canalization in mice. *Genetics, Princeton* **55**, 635–44.

Rendel, J. M., and Sheldon, B. L. (1960).—Selection for canalization of the *scute* phenotype in *Drosophila melanogaster*. *Aust. J. biol. Sci.* **13**, 36–47.

Waddington, C. H. (1960).—Experiments in canalizing selection. *Genet. Res.* **1**, 140–50.