Genetical Studies on the Skeleton of the Mouse

XXIV. Further Data on Skeletal Variation in Wild Populations[1]

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A PILOT experiment by Weber (1950) established the fact that the minor skeletal variations universally present in strains of tame mice are also encountered in wild populations; and that the incidence of individual variants may differ widely from population to population. In the decade since Weber's work many new variants have come to light, and it seemed desirable to repeat his observations on the more extensive range of variants now available. An opportunity to do so presented itself in 1956 when wild mice from various localities in the eastern U.S.A. became available for study.

These animals had been collected for a totally different purpose. As is well known through the work of Dunn and his collaborators, there exists in the mouse a semi-dominant gene (*T*) for Brachyury or short-tail which in $T/+$ heterozygotes shortens the tail to a varying extent. In heterozygotes with a whole series of recessive alleles t^0, t^1, t^2, t^3, . . ., &c., a tailless phenotype is produced. As shown by Dunn and his colleagues (Dunn, 1956, 1957; Dunn & Suckling, 1956), these *t* factors are widely spread in wild mouse populations. Over twenty populations from various parts of the U.S.A. have been tested and, with one exception, were proved to contain such factors. As the *t* factors are recessive, their presence is discovered by a genetical test: wild mice are mated to Brachyuric ($T/+$) mice, and if the progeny includes tailless (T/t^w) individuals which, mated together, give rise to a balanced stock (T/T and most t^w/t^w homozygotes being inviable), the genotype of the tested mouse is considered to be established as $+/t^w$. As this kind of test is laborious and thus restricts the number of individuals which can be tested, it was hoped that the discovery of a suitable skeletal variant diagnostic for t^w might simplify the procedure. This hope has been disappointed. However, the material thus collected has proved useful for population studies.

[1] The material was collected at Nevis Biological Station, Irvington-on-Hudson, N.Y., under contract AT(30–1)–1804, U.S. Atomic Energy Commission; the analysis of the data was completed at the present laboratory.

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[J. Embryol. exp. Morph. Vol. 6, Part 4, pp. 569–574, December 1958]

MATERIAL

A total of 193 skeletons from four wild populations have been studied (Table 1); they were prepared by papain maceration. There were no $+/t^w$ mice in the Gull Island population; the other three included tested $+/t^w$ and $+/+$ mice, as well as some the genotype of which was not known on account of

TABLE 1

The origin of the four wild populations and the number of skeletons examined from each

Name	*Origin*	t^w *factor*	*Skeletons*			
			$+/+$	$+/t^w$	?	*Total*
G.I.	Great Gull Island, N.Y.	none	30	—	—	30
Vt. 1	Norwich, Vt.	t^{w14}	23	1	12	36
Ct. 2	Storrs, Ct.	t^{w11}	15	11	25	51
R–3	N.Y. City ♂ × Philadelphia ♀	t^{w2}	12	28	36	76

sterility, early death, &c. Most of the mice were actually caught in the wild, but some were bred in the laboratory from wild parents. The R–3 population (Levine & Dunn, 1956) was entirely laboratory bred and, as can be seen from Table 1, its origin was mixed. In addition to the papain preparations, twenty alizarin clearances of R–3 mice (10 $+/t^w$; 10 $+/+$) were also used, mainly to examine the bones and skeletal relationships which can be best studied *in situ*.

RESULTS AND DISCUSSION

No obvious differences between the skeletons of $+/t^w$ and $+/+$ mice were discovered in either kind of preparation. While statistical differences between these two groups might be detectable in larger samples, they would be of little value in determining the genotype of a mouse with regard to t^w factors.

The papain preparations were then classified for thirty minor variants which have been extensively used in the study of inbred strains (Deol, Grüneberg, Searle, & Truslove, 1957; Carpenter, Grüneberg, & Russell, 1957). However, not all of these were observed in the wild mice. The following variants were not encountered:

(1) Interfrontal-frontal fusion.
(2) Frontal fontanelle.
(3) Squamosal-parietal fusion.
(4) Foramen ovale open posteriorly.
(5) Periotic-occipital fusion.
(6) Inframaxillary crest.
(7) Interparietal-occipital fusion.
(8) Dyssymphysis of Thoracic I.

(9) Dystopia of processus spinosus of Thoracic II.

(10) Dyssymphysis ischio-pubica.

Most of the above variants have not yet been found outside the C57BL strain, in which they were originally discovered. Another variant, absence of lower third molar, is not mentioned in the tables as it occurred only once: a male in the G.I. population was affected on the right side.

TABLE 2

Percentage incidence of twenty skeletal variants in four wild populations and four inbred strains

No.	Variant	*Wild populations*				*Inbred strains*			
		G.I.	*Vt. 1*	*Ct. 2*	*R–3*	*CBA*	*A*	*C57BL*	*BALB/c*
1	Lacrimal-maxilla fusion	13·3	2·8	18·6	2·0	0·3	56·3	15·8	5·0
2	Parted frontals	100·0	61·1	43·1	42·1	86·5	31·5	7·2	85·0
3	Fused frontals	20·0	13·9	0·0	13·2	0·0	4·0	4·2	0·0
4	Interfrontal	26·7	22·2	5·9	1·3	86·2	11·7	85·6	0·0
5	Foramen ovale single	40·0	26·4	28·4	14·5	62·3	44·7	3·0	90·0
6	Alae palatinae*	0·0	26·4	14·7	42·8	4·4	0·0	72·1	0·0
7	Presphenoid, preoptic sutures	8·6	27·8	31·3	41·5	95·0	0·5	36·0	57·5
8	Presphenoid, metoptic roots abnormal	6·9	11·1	4·9	25·0	72·5	22·5	1·1	97·5
9	Foramen sphenoidale medium	66·7	33·3	27·5	57·9	12·0	7·3	25·7	35·0
10	Foramen hypoglossi single	48·3	62·5	56·9	62·5	85·4	31·6	75·2	42·5
11	Processus pterygoideus	3·3	16·6	3·9	1·9	0·3	0·0	20·7	2·5
12	Accessory mental foramen	1·7	0·0	1·0	2·6	24·0	25·7	26·4	20·0
13	Foramina transversaria imperfecta of C V	1·7	0·0	0·0	19·1	0·0	0·3	66·2	0·0
14	Tuberculum anterius inflexum	3·3	0·0	0·0	0·7	—	11·9	3·0	17·5
15	Cervical fusions	3·3	0·0	15·7	0·0	0·0	0·2	3·7	0·0
16	Dyssymphysis of processus spinosus of Thoracic II	3·3	0·0	0·0	0·0	0·0	0·0	0·8	0·0
17	Absence of tuberculum anterius of C VI	0·0	0·0	0·0	0·7	6·3	1·1	23·9	0·0
18	Dyssymphysis of Thoracic X	3·3	8·3	0·0	0·0	—	—	4·5	0·0
19	Sacralization of L VI	16·6	0·0	6·9	11·8	—	7·7	5·9	37·5

* This character has so far gone under the name of 'posterior border of the palatine'. It refers to a wing-like flap of bone which may be present on the postero-lateral border of the palatine. The new designation here proposed is both shorter and more descriptive.

The frequencies of various characters in the four populations are given in Table 2. In the case of bilateral characters, the percentage of affected sides rather than animals is taken. Table 3 gives the results of significance tests carried out to compare each of the four wild populations with the rest in turn. The χ^2 method, with Yates's correction where necessary, was used for central characters; and Fisher's 'exact' method if the smallest class was 3 or less. Smith's method (Appendix to Grüneberg, 1955) was used for bilateral characters. In Table 3 a — sign indicates that there is no significant difference between the two values; + means a probability between 0·050 and 0·021; + + a proba-

bility between 0·020 and 0·011; + + + a probability between 0·010 and 0·001; and + + + + indicates a probability smaller than 0·001.

TABLE 3

Results of significance tests carried out to compare each population with the rest in turn. (Explanation of symbols in the text)

No.	Variant	Populations compared					
		G.I. and Vt. 1	*G.I. and Ct. 2*	*G.I. and R–3*	*Vt. 1 and Ct. 2*	*Vt. 1 and R–3*	*Ct. 2 and R–3*
1	Lacrimal-maxilla fusion	+	—	+++	++++	—	++++
2	Parted frontals	++++	++++	++++	—	—	—
3	Fused frontals	—	+++	—	+++	—	+++
4	Interfrontal	—	++	++++	+	++++	—
5	Foramen ovale single	—	—	++++	—	—	—
6	Alae palatinae	++++	++++	++++	—	—	++++
7	Presphenoid, preoptic sutures	++	+++	++++	—	—	—
8	Presphenoid, metoptic roots abnormal	—	—	+++	—	—	+++
9	Foramen sphenoidale medium	+++	++++	—	—	++	++++
10	Foramen hypoglossi single	—	—	—	—	—	—
11	Processus pterygoideus	++	—	—	+++	++++	—
12	Accessory mental foramen	—	—	—	—	—	—
13	Foramina transversaria imperfecta of C V	—	—	++++	—	++++	++++
14	Tuberculum anterius inflexum	—	—	—	—	—	—
15	Cervical fusions	—	—	—	++	—	++++
16	Dyssymphysis of processus spinosus of Thoracic II	—	—	—	—	—	—
17	Absence of tuberculum anterius, C VI	—	—	—	—	—	—
18	Dyssymphysis of Thoracic X	—	—	—	—	+	—
19	Sacralization of L VI	++++	—	—	+	++++	—

The data in Table 3 show that in 80 of the 120 possible comparisons, there were no significant differences. Nine differences of low significance (+ and + +) are probably largely due to accidents of sampling and may be ignored. On the other hand, few, if any, of the thirty-one highly significant differences (+ + + and + + + +) can be ascribed to chance alone. Each one of the four wild populations differs from the rest in the incidence of at least three variants; the average number of highly significant differences between any two populations being five. In turn, 13 out of 20 variants encountered show highly signifi-

cant inter-population differences (all the 20 variants have previously been shown to be, at least partly, under genetic control).

The significant inter-population differences can be expressed in terms of the standard deviation by means of probit transformations. Populations in which a variant was absent have for this purpose been treated as if it had been present in one-half of an individual; and similarly one population with a 100 per cent. incidence has been treated as if one-half of a mouse had failed to show the character. The average of the forty significant differences amounts to 1·14 standard deviations.

The range of percentages of the skeletal variants in the four wild populations is by and large comparable with that in inbred strains of mice (see Table 2; for additional data see Deol, Grüneberg, Searle, & Truslove, 1957; Carpenter, Grüneberg, & Russell, 1957). One exception seems to be the presence of accessory mental foramina. These are uncommon in all four wild populations but very frequent in nearly all tame mice examined; of the 11 inbred strains and sub-strains examined, 9 varied between 20 and 64 per cent., while only 2 showed an incidence of 8 per cent.; an F_1 generation between two inbred strains had 43 per cent. accessory mental foramina. The large difference between wild and tame mice in this respect can hardly be due to chance alone; on the other hand, it is not easy to see why this seemingly trivial variant should be so rare in wild mice.

The foramina transversaria imperfecta are common in the R–3 population (it occurs 7 times on the right, 12 times on the left, and 5 times bilaterally in 76 mice) but do not involve the C VI vertebra. In this respect R–3 differs from various European populations (Weber, 1950), and the C57BL inbred strain (Grüneberg, 1950*a*) in which the C V and C VI vertebrae are about equally affected (C VI is affected more intensely than C V in the presence of the undulated gene; see Grüneberg, 1950*b*).

The variants used in this investigation are partly under genetic control. This is shown by the large inter-strain differences under constant laboratory conditions. On the other hand, it is known that deficient diets can influence the incidence of most of these entities to a considerable extent (Searle, 1954; Deol & Truslove, 1957). As the wild populations have lived under different environmental conditions, it is probable that both sources of variation have contributed towards the inter-population differences. The genetical component could be determined by breeding wild mice for a minimum of two generations under constant laboratory conditions; as the present observations were coincidental to a larger research programme, this was not practicable. However, judging from the general nature of the effects on the skeleton produced by deficient diets, I would regard it as improbable that the inter-population differences reported here are mainly due to differences in the environment. If this is accepted, the question arises of whether the genetical inter-population differences are adaptive and hence the result of natural selection, or whether they

are due to genetic drift (the Sewall Wright effect) and hence purely accidental. The solution of this important question would require elaborate experiments both in the field and in the laboratory.

SUMMARY

Four populations of wild mice (*Mus musculus* L.) derived from different parts of the eastern U.S.A. have been classified for an array of some twenty minor skeletal variants which, from other work, are known to be partly under genetic control. The four populations differed from each other highly significantly in the incidence of, on an average, five of these variants. It is not known whether the genetical component of the inter-population variance is adaptive in nature, or whether it has originated by genetic drift.

ACKNOWLEDGEMENTS

My thanks are due to Professor L. C. Dunn for handing over the material to me, and to Professor H. Grüneberg, F.R.S., for suggestions and criticism of the manuscript.

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(Manuscript received 31 : iii : 58)