Skeletal Variations of the Seventh Cervical Vertebrae in the Mouse with Special Reference to the Foramina Transversaria and the Accessory Foramina

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— Received for Publication, March 18, 1992 —

Key Words: Skeletal variation, Seventh cervical vertebra, Foramen transversarium, Heredity, Mouse

Summary: The formation of foramina transversaria in the seventh cervical vertebra of CBA and C57BL mice and their offspring is found to behave as if it is determined by a single semi-dominant gene.

The accessory foramina of Weber (1950) are investigated in the same material. These foramina are classified into two types and their heredity is evaluated.

In a series of recent papers Johnson and O'Higgins have developed alternative methods for evaluating the differences in bone shape using Fourier analysis (Johnson *et al*, 1985; O'Higgins & Johnson, 1988, Johnson, O'Higgins, McAndrew and Kida, in press). In the course of those studies we noticed some minor variations of mouse cervical vertebra, which are not described in Grüneberg's classic "The pathology of development" (Grüneberg, 1963). Our studies on Grüneberg's material have placed us in a unique situation, and we have taken this opportunity of making the record of these skeletal variations as accurate as possible.

Materials and Methods

The cervical vertebrae used in this study were from two inbred strains (CBA and C57BL), the F1 between them (CB and BC) and the back cross CBA/CB, from the Grüneberg collection of mouse skeletons from the British Museum of Natural History, on permanent loan to one of us (D. R. Johnson). Details of the numbers of each sample are given in

Table 1. The C1-T2 vertebrae were examined under a dissecting microscope and incidences of foramina transversaria and other foramina were recorded.

Results

Foramina transversaria in the seventh cervical vertebra

Eight cases of complete formation and twenty-three cases of incomplete formation of the foramina transversaria (FTI) were observed in the 261 seventh cervical vertebrae of the five groups. A closer observation revealed ninety-seven cases of rudimentary formation of the foramina. Here "incomplete" resembles the gutter formation described in Grüneberg (1950). "Rudimentary" indicates the formation of a shallow groove.

These variations clearly belong to the same trait, the formation of foramina transversaria. In order to summarise our observations four phenotypic categories were defined: perfectly formed (P), imperfectly formed (I), rudimentary (R) and not manifested (N) (Table 2). Sex differences and laterality were not detectable in the five groups observed.

Differences in incidence were not significant between CBA, CB and CBA/CB at the 5% level, but were significant at the 1% level between C57BL and the other groups.

In the cross between CBA and C57BL the incidence of foramina transversaria is consistent with

Table 1. Number of mice observed in each sample.

	CBA	C57BL	CB	BC	CBA/CB
Male	30	25	28	25	25
Female	23	27	24	27	27
Total	53	52	52	52	52

Table 2. Incidence of formation of the foramen transversarium in the seventh cervical vertebra.

	Grade of manifestation of the formation*										NN	Total
	PP	PI	PR	PN	II	IR	IN	RR	RN	(subtotal)		
CBA	0	1	2	0	1	4	8	6	16	(38)	15	53
C57BL	0	0	0	0	0	0	1	0	1	(2)	50	52
CB	0	1	1	1	0	2	0	16	15	(35)	17	52
BC	0	0	0	1	0	1	0	4	14	(20)	32	52
CBA/CB	0	0	1	0	0	2	2	12	20	(37)	15	52

*: The conditions of both sides are expressed by double letters.

Table 3. The foramen transversarium in the seventh cervical vertebra: Observation and expectation for the cross between CBA and CB.

	PP	PI	PR	PN	II	IR	IN	RR	RN	(subtotal)	NN	Total
Obs.	0	0	1	0	0	2	2	12	20	(37)	15	52
Exp.	0.0	1.0	1.5	0.0	0.5	3.0	3.9	10.9	15.3	(36.1)	15.9	52

the hypothesis that it is controlled by a single, semi-dominant gene homozygous in the CBA stock where manifestation is highest and heterozygous in the F1. The observed and expected values for the incidence of foramina transversaria in the backcross (CBA $\times$ CB) shown in Table 3 are in good agreement with this hypothesis ($\chi^2 = 3.57$, d.f. = 9, not significant at the level of 5%).

With regard to the formation of foramina transversaria in the seventh cervical vertebra, the dystopia caudalis of the tuberculum anterius is implicated by Grüneberg (1950a). However in only two cases did FTI coexist with dystopia.

Medial opening of foramina transversaria imperfecta

Two cases of medial opening of foramina transversaria imperfecta of the sixth cervical vertebra were observed in the fifty-two C57BL animals studied by us. Grüneberg (1950a) did not observe this opening in his sample of fifty-two animals of C57BL stock.

Distinct types of foramina in the seventh cervical vertebra

Two types of small accessory foramina were observed in the seventh cervical vertebra (Fig. 1),

Fig. 1 The seventh cervical vertebra of CBA male (94 days old) with two accessory foramina of the lateral and medial type on the right side.

one in the lateral side of the base of transverse process (on the lateral side of the superior vertebral notch), and the other more medially. These occurred as frank foramina, pinpoints or dimples. The occurrences and distributions of these foramina in the five groups are tabulated in Table 4.

The incidence of the lateral type was significantly greater in BC than in the other groups ($P < 2\%$). The incidence of the medial type in C57BL was significantly different from that in the others ($P < 2\%$) with the exception of CB (ie. there was a significant difference between the parental stocks). The difference between CB and BC was not significant at the 5% level. The observed and expected values for the incidence of the medial foramen in the backcross

Table 4. Incidence of the two kinds of accessory foramina observed in the seventh cervical vertebra.

	Lateral type					Medial type				
	Bilateral	Right	Left	Total	%	Bilateral	Right	Left	Total	%
CBA	0	7	7	14	26.4	0	5	2	7	13.2
C57BL	0	8	4	12	23.1	0	0	0	0	0.0
CB	5	7	7	19	36.5	0	1	2	3	5.8
BC	13	9	10	32	61.5	0	5	1	6	11.5
CBA/CB	5	5	10	20	38.5	0	1	4	5	9.6

Table 5. The medial accessory foramen in the seventh cervical vertebra: Observation and expectation for the cross between CBA and CB.

	Bilateral	Right	Left	Absent	Total
Observed value	0	1	4	47	52
Expected value	0	3.0	2.0	47.1	52.1

(CBA $\times$ CB) shown in Table 5 again support the hypothesis of a single semi-dominant gene ($\chi^2 = 3.33$, d.f. = 3, no significant difference between observed and expected at the 5% level).

Discussion

In the mouse the foramina transversaria are usually formed in the first to sixth cervical vertebrae. These foramina are likely to be imperfectly formed in some stocks as in man where the foramina are often closed by a ligament. Grüneberg studied this trait widely, and concluded that the foramina transversaria imperfecta behave as if governed by a single semi-dominant gene (Grüneberg, 1950a).

In the same paper he also described the formation of foramina transversaria in the seventh cervical vertebra (CVII) as follows: "Four out of seventy-one mice in the Strong CBA pure line showed a dystopia of the tuberculum anterius (tuberculum anterius accessorius) in a caudal direction, that is, on to CVII. The accessory tuberculum anterius of the two animals has gained double contact with CVII in such a way as to enclose a perfectly normal-sized foramen transversarium. In the other two animals the tuberculum is attached to CVII at one point only; it thus forms the better part of a foramen transversarium. This creates a picture very similar to the foramina transversaria imperfecta condition in C57BL. The resemblance is, however, only superficial. In foramina transversaria imperfecta, a foramen which is part of the normal anatomy is incomplete; in the case under discussion a foramen not normally present is formed, but this process does not always proceed to perfection".

Grüneberg (1950a) explained the formation of foramina transversaria in the CVII in relation to a dystopia of the tuberculum anterius. However, only two cases of coexistence of these traits are observed in this study. This seems to contradict his explanation since the two traits seem to be independent of each other in the cross between CBA and C57BL.

The data presented here on the genetic control of the formation of foramina transversaria in the CVII are compatible with the assumption that the trait in the cross between CBA and C57BL behaves like a single-gene difference with semi-dominance of

the trait.

Our finding that the formation of foramina transversaria in CVII was higher in CB (Table 2) presumably reflects the effects of maternal physiology (a common finding in the study of minor skeletal variation, Grüneberg, 1963).

Grüneberg (1950a) reported that the medial opening had not been observed in C57BL, was common in the F1 between C57BL and Strong A and particularly in the backcross to Strong A, less common in the F2 and least in the backcross to C57BL. He also said that this situation was consistent with the assumption that Strong A carried a semi-dominant gene (or genes). In this study, this trait is observed in C57BL stock itself.

A description of the medial and lateral accessory foramina was given by Weber (1950). He described them in the fifth and sixth cervical vertebrae but did not discriminate between them by location. He also described accessory foramina in CVII, but apparently the lateral type only: "This accessory foramen occurred in all wild populations sampled, but the frequency differs considerably from population to population". He concluded that it seemed most likely that the differences between populations have a genetical basis.

The accessory foramina of the lateral and medial types in the CVII have, to our knowledge, not been reported in CBA and C57BL. The incidence of the lateral type in BC is significantly different from that in the others. This could also suggest the effect of maternal environment. However, the genetic basis of this feature is unknown.

On the other hand, the incidence of the medial type shows a significant difference between the parental stocks. In addition, on the assumption that this trait behaves like a semi-dominant feature and is controlled by a single-gene, the observed and expected values agree with each other, although the penetrance is low (Table 4).

Acknowledgements

We are deeply grateful to Mr. S. Paxton, Department of Anatomy, University of Leeds and Professor Y. Dodo, Department of Anatomy Sapporo Medical College for their useful advice and help.

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