GENETIC ANALYSIS OF SIZE-SCALING PATTERNS IN THE MOUSE MANDIBLE

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ABSTRACT

The relationship between multidimensional form of the adult mouse mandible and body size is examined from an ontogenetic perspective. The origin and ontogeny of phenotypic correlations are described in terms of genetic and environmental covariance patterns between adult skeletal morphology and growth in body weight. Different ontogenetic patterns are observed in the genetic correlations, and these can be related to the developmental as well as the functional aspects of mandibular form. The quantitative genetic aspects of craniomandibular growth and morphogenesis are explored, together with an examination of the impact of ontogenetic changes in the genetic variance-covariance structure on morphogenetic integration and evolution by selection.

COMPLEX skeletal structures, such as the mammalian cranium and mandible, are composed of parts that have different embryological origins, are affected by different causal agents, and exhibit different rates of development (ATCHLEY, PLUMMER and RISKA 1985). In spite of this morphogenetic diversity, growth trajectories of the various parts must be cohesively integrated during ontogeny to produce harmoniously functioning morphological structures. Although such morphogenetic integration is important and widespread in development, the actual mechanisms contributing to it are not well understood. As a result, many important problems remain to be resolved, including (1) coordination of growth trajectories, (2) interactions among controlling factors and (3) how selection on both age-specific traits and developmental rates affects coordinated growth patterns.

One aspect of the coordination of growth trajectories is the scaling relationship between skeletal dimensions and body size. Variability in skeletal structures, soft body tissues and physiological processes is often dependent on body size or, at least, is highly correlated with it (ATCHLEY and RUTLEDGE 1980; ATCHLEY 1983, 1984; ATCHLEY *et al.* 1984; PETERS 1983; SCHMIDT-NIELSON 1984; CALDER 1984). Empirical descriptions of the morphological or physiological consequences of variability in body size are available from the literature on allometric growth. Unfortunately, the developmental and genetic bases of these scaling relationships are not well understood, and only recently have realistic models been proposed to explain the underlying processes (*e.g.*, LANDE

1979; ATCHLEY, RUTLEDGE and COWLEY 1981; ATCHLEY *et al.* 1984; CHEVERUD, RUTLEDGE and ATCHLEY 1983; RISKA, ATCHLEY and RUTLEDGE 1984; RISKA and ATCHLEY 1985).

The mammalian mandible is an excellent structure in which to study the genetic and developmental aspects of body-size scaling. The mandible appears to be a single skeletal entity of simple origin, but in actuality is a developmentally complex structure, the phenotypic variability of which stems from the activities of a number of intrinsic and extrinsic factors. Growth patterns involve both intramembranous and endochrondral ossification, as well as surface remodeling (HALL 1978, 1982a,b; MOORE 1981).

In addition to heterogeneity in embryological origin and ossification patterns within the mandible itself, the facial region, in general, continues to grow after the braincase growth has stopped (MOORE and LAVELLE 1974; MOORE 1981). As a result, the skull becomes more and more prolonged during postnatal growth. Thus, one might hypothesize that developmental variability in the mandible would reflect both the basicranial and facial patterns of growth because the mandible articulates with the basal portion of the skull, has masticatory structures common with the facial region and exhibits continuous incisor growth.

The quantitative genetic consequences of heterogeneity in embryonic origin and growth patterns on the form of the adult mandible are unknown. To explore the problem, we have dissected phenotypic correlations between mandible traits and body weight and rate of development in body weight into their underlying genetic and nongenetic components. Mandible traits are available for 70-day-old mice, while body weight and weight gain are available at weekly intervals between 14 and 70 days of age. Hence, we can inquire about how body weight and rate of development influence adult mandible form. In this paper, we deal with four questions: (1) What are the causal factors underlying scaling relationships between mandibular form and body weight in adult randombred mice? (2) Is the heterogeneous embryological origin of various parts of the mandible reflected by different scaling relationships with body weight? (3) Do scaling relationships observed between mandible dimensions and body weight in adults persist between adult mandible dimensions and body weight much earlier in ontogeny? (4) Do parts of the mandible exhibit distinct scaling patterns during ontogeny that can be associated with the basicranial and facial portions of the skull?

MATERIALS AND METHODS

The ICR randombred mice used in these analyses are derived from the more extensive experiment described in the accompanying paper (ATCHLEY, PLUMMER and RISKA 1985); therefore, only a brief outline of the methods and materials used will be given here. The mice were randomly pair-mated, and litters were standardized at birth to eight pups, usually four males and four females. A random half of each litter was cross-fostered between unrelated dams which had pupped on the same day. Pups were weaned at 21 days and were then maintained in single-sex cages each containing less than five mice, as well as unlimited food and water. A total of 510 families of mice consisting of 1803 individuals are included in these analyses.

Body weight was recorded at weekly intervals, beginning at 2 wk of age and continuing until

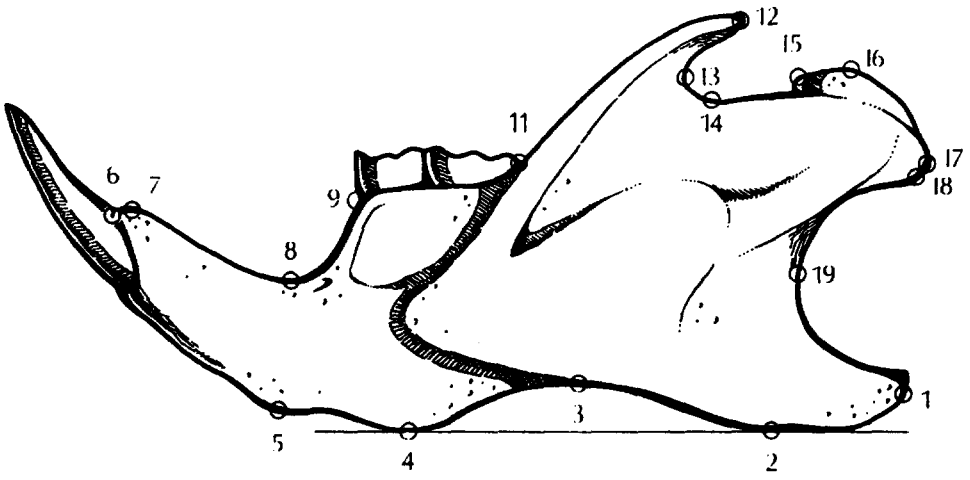

FIGURE 1.—Outline of the mature mouse mandible denoting the position of morphological landmarks used to describe the traits presented in Table 1.

TABLE 1

Mandible traits included in these analyses, together with a short descriptive code

1. Posterior mandible length (POSTMANLEN)—Euclidean distance from 1–4
2. Anterior mandible length (ANTMANLEN)—Euclidean distance from 4–6
3. Height at mandibular notch (NOTCHHIGH)—Euclidean distance from 3–14
4. Height at incisor region (INCISHIGH)—Euclidean distance from 5–8
5. Concavity (CONCAVITY)—Vertical distance from 3 to a line computed from 2–4
6. Height of ascending ramus (RAMUSHIGH)—Vertical distance from 2 to a horizontal line at 16 parallel to the line computed from 2–4
7. Condyloid width (CONDYLWID)—Euclidean distance from 15–18
8. Condyloid length (CONDYLLEN)—Euclidean distance from the midpoint of a line from 16–17 to the midpoint of a line from 14–19
9. Coronoid height (CORONHIGH)—Vertical distance (perpendicular to 2–4 line) from 12–14
10. Coronoid area (CORONSIZE)—Area defined by the triangle (11, 12, 14) minus the area of (12, 13, 14)
11. Angular process length (ANGULARLEN)—Euclidean distance of a line segment from the midpoint of 1–2 to the midpoint 3–19
12. Tooth bearing area (TOOTHAREA)—Area of a polygon defined by points (3, 4, 5, 6, 7, 8, 9, 11)
13. Superior incisive process curve (SUPERINCIS)—Shortest distance to 8 from a line from 4–6
14. Inferior incisive process curve (INFERINCIS)—Shortest distance to 5 from a line from 4–6

Figure 1 explains the origin of these measurements.

the mice were 10 wk old. Mice were sacrificed at 10 wk of age, enviscerated, skinned and defleshed by dermestid beetles. The mandibles were then measured by projecting the image of the dentary onto a microcomputer-driven digitizer, and the data from 19 landmark points were recorded in *x-y* space (ATCHLEY, PLUMMER and RISKA 1985). From these 19 landmarks, 14 traits were obtained (Figure 1) which, with a short code, are described in Table 1.

All data were transformed to natural logarithms and were analyzed by analysis of variance and

covariance. The resulting variance compounds were equated with genetic expectations following ATCHLEY *et al.* (1984). The variance and covariance components of body weight and weight gain are described in detail by RISKA, ATCHLEY and RUTLEDGE (1984), while the variance and covariance components for the mandible traits are described by ATCHLEY, PLUMMER and RISKA (1985).

Body weight is equated to body size in these analyses. The relationship between adult mandible dimensions and body weight and body weight gain were determined by estimating the components of phenotypic covariance between log transformed data for the mandibular traits and body weight and weight gain over six postnatal intervals: G1 = gain up to 14 days (including prenatal weight gain), G2 = between 14 and 21 days, G3 = between 21 and 28 days, G4 = between 28 and 35 days, G5 = 35 to 42 days, and G6 = 42 to 70 days. Body weight gain is determined as the difference between natural logs of weights in the respective intervals. Therefore, we are dealing with proportional gain, rather than absolute gain. As pointed out by RISKA, ATCHLEY and RUTLEDGE (1984), body weight at 14 days of age is equivalent to body weight gain up to 14 days of age. Although identical, both values are included in the tables to assist the reader.

RISKA, ATCHLEY and RUTLEDGE (1984) indicate that after an early exponential growth phase, the growth curves for body weight in these mice pass through inflection points for Gompertz growth curves at 22 and 20 days for males and females, respectively. By 42 days of age, growth has begun to level off in a linear phase that persists to the end of the experiment.

Although we have data on the mandibles of the parents, data on their body weight were not available. As a result, the covariances of the mandible traits with body weight are estimated using only the covariances between crossfostered and noncrossfostered full-sibs, rather than the more extensive model described in ATCHLEY *et al.* (1985). Therefore, the model for decomposition of the phenotypic covariance between the ith mandible trait (Y_i) and body weight (X_W) or body weight gain (X_G) is

$$\sigma_{(XY)P} = \sigma_{(XY)G} + \sigma_{(XY)M} + \sigma_{(XY)RE}$$

where $\sigma_{(XY)P}$ = phenotypic covariance; $\sigma_{(XY)G}$ = genetic covariance, including all of the additive and one-half of the dominance effects; $\sigma_{(XY)M}$ = postnatal maternal covariance, including preweaning cage effects; and $\sigma_{(XY)RE}$ = residual environmental covariance after postnatal maternal effects are removed. Genetic covariance was estimated as twice the covariance component for genetic mother; postnatal maternal covariance was equated with the component for postnatal mother; and residual environmental covariance was estimated as the residual, after subtracting the component for genetic mother from the pooled interaction and residual within-cell components.

The mandible is a structure exhibiting high intercorrelations among some of its component parts. To resolve the intercorrelations into patterns of morphogenetic variability, the phenotypic mandible data are analyzed by Varimax-rotated principal components analyses, and a series of principal component scores are produced that position each mouse along an axis of multivariate variability (ATCHLEY, PLUMMER and RISKA 1985). The principal component scores are then treated as typical univariate traits, and their variability is decomposed into genetic and residual environmental fractions. The components of the phenotypic correlation are computed between the Varimax-rotated phenotypic principal components scores and body weight and weight gain.

RESULTS

This section is divided into three main parts to reflect the questions posed in the introductory section of this paper. These parts include (1) results relating to the underlying components of the scaling relationships between adult mandible dimensions and adult body weight, (2) the casual components underlying correlations between adult mandible dimensions and body weight during ontogeny and (3) the relationships between mandible dimensions and rate of gain in body weight.

TABLE 2

Phenotypic correlations of adult mandible dimensions with body weight and with body weight gain at various postnatal intervals

Trait	Days						Postnatal intervals					
	14	21	28	35	42	70	G1	G2	G3	G4	G5	G6
	Body weight						Body weight gain					
POSTMANLEN	43	46	50	52	50	41	43	15	−9	−33	−22	−9
ANTMANLEN	30	34	36	39	43	39	30	13	−9	−21	−9	−1
NOTCHHIGH	34	36	41	41	41	34	34	10	−2	−29	−16	−7
INCISHIGH	12	12	17	26	31	30	12	3	7	−2	−2	2
CONCAVITY	4	10	11	16	21	21	4	12	−1	−3	3	2
RAMUSHIGH	35	37	41	43	45	42	35	13	−6	−27	−12	−1
CONDYLWID	10	12	13	14	15	11	10	6	−2	−9	−4	−5
CONDYLLEN	18	17	17	17	16	16	18	3	−6	−13	−9	2
CORONHIGH	2	5	6	6	8	3	2	7	1	−4	0	−8
CORONSIZE	16	20	23	23	24	18	16	11	−1	−17	−6	−8
ANGULARLEN	25	30	33	38	40	38	25	15	−4	−18	−10	2
TOOTHAREA	47	51	54	58	60	51	47	17	−12	−32	−19	−8
SUPERINCIS	11	14	15	16	18	17	11	9	−5	−8	−3	0
INFERINCIS	3	5	5	9	9	7	3	3	0	2	−4	−1

G1 = gain up to 14 days, G2 = gain between 14 and 21 days, G3 = gain between 21 and 28 days, G4 = gain between 28 and 35 days, G5 = gain between 35 and 42 days and G6 = gain between 42 and 70 days of age. Decimal points have been removed, and standard errors are approximately 3 for all estimates.

Adult mandible dimensions and adult body weight

Phenotypic correlations: Generally speaking, the phenotypic correlations with 70-day body weight (Table 2) are low, ranging from 0.03 for CORONHIGH to 0.51 for TOOTHAREA. The geometric mean of the 14 correlations is only 0.21. Although many phenotypic correlations are significant in a statistical sense due to very large sample sizes, the biological importance of very small correlations can be debated.

The largest phenotypic correlations with adult body weight are found for the major dimensions of the mandible, *i.e.*, TOOTHAREA, POSTMANLEN, ANTMANLEN, RAMUSHIGH and ANGULARLEN. Correlations of 0.2 or less are found for CORONHIGH, CORONSIZE, CONDYLWID, CONDYLLEN, INFERINCIS, SUPERINCIS and CONCAVITY. The first four of these traits are strongly affected by biomechanical factors during prenatal and early postnatal development (ATCHLEY, PLUMMER and RISKA 1985). Therefore, it is not unexpected that these latter traits are lowly correlated with adult body weight. We have shown elsewhere that the correlation between growth up to 14 days of age is lowly correlated with later growth (RISKA, ATCHLEY and RUTLEDGE 1984). Further, there is

TABLE 3

Phenotypic correlations between the scores from a Varimax-rotated principal components analysis of 14 mandible traits and (1) the log of body weight at various ages (in days), and (2) the gain in body weight between various ages

	Days						Postnatal intervals					
Trait	14	21	28	35	42	70	G1	G2	G3	G4	G5	G6
	Body weight						Body weight gain					
P_1	32	36	40	48	53	50	32	15	−6	−19	−11	1
P_2	18	20	24	22	22	14	18	9	0	−19	−8	−12
P_3	5	6	6	5	6	5	5	4	−2	−6	−1	0
P_4	26	28	29	27	25	22	26	8	−8	−23	−13	−3

Decimal points have been removed and all standard errors are approximately three. G1 = gain up to 14 days, G2 = gain between 14 and 21 days, G3 = gain between 21 and 28 days, G4 = gain between 28 and 35 days, G5 = gain between 35 and 42 days and G6 = gain between 42 and 70 days of age.

little reason to believe that the curvature of the incisor (INFERINCIS and SUPERINCIS) should be correlated with adult body weight.

The Varimax-rotated principal components analysis of these 14 traits gave a phenotypic solution with four vectors (ATCHLEY, PLUMMER and RISKA 1985). The first rotated vector has largest coefficients for TOOTHAREA, ANTMANLEN, INCISHIGH, CONCAVITY, ANGULARLEN and RAMUSHIGH. These traits reflect measures of the height of the mandible, particularly at the distal or corpus end. The second rotated vector has largest coefficients for CORONSIZE, CORONHIGH and NOTCHHIGH, traits reflecting the height and area of the middle portion of the mandible between the posterior end of the mandibular tooth row and the mandibular notch. The third rotated vector has large coefficients for SUPERINCIS and INFERINCIS, a pattern of variability reflecting the curvature of the distal portion of the mandible (*i.e.*, the curvature of the incisor). The fact that these coefficients are of opposite sign may stem from correlated measurement error. The fourth rotated vector reflects variability in the ramus, and CONDYLLEN, RAMUSHIGH, CONDYLWID and POSTMANLEN contribute the most to this pattern of variability.

Phenotypic correlations between these principal component scores and adult body weight range from 0.5 for the first vector to 0.05 for the third vector (Table 3).

Genetic correlations: Genetic correlations significantly different from zero are found between adult body weight and ANTMANLEN, INCISHIGH, TOOTHAREA, CONDYLLEN, RAMUSHIGH, NOTCHHIGH and CORONSIZE (Table 4). With the exception of CORONSIZE, these are traits associated with the body of the mandible. In all of these traits, except for CORONSIZE, growth occurs by typical bone growth and ossification, rather than by biomechanical stimulation arising from muscle activity.

The Varimax-rotated principal components solution for the genetic correlations produced four vectors. The first rotated vector reflects genetic covar-

TABLE 4

Genetic correlations of adult mandible dimensions with body weight and with body weight gain at various postnatal intervals

Trait	Days						Postnatal intervals					
	14	21	28	35	42	70	G1	G2	G3	G4	G5	G6
	Body weight						Body weight gain					
POSTMANLEN	21	31	43	49	33	12	21	43	19	−33	−54	−54
	±13	±12	±11	±13	±14	±16	±13	±15	±23	±14	±24	±34
ANTMANLEN	33	40	45	61	65	65	33	34	−7	−24	−6	17
	±14	±13	±12	±13	±12	±13	±14	±13	±24	±16	±26	±32
NOTCHHIGH	49	49	58	67	56	40	49	29	1	−43	−48	−34
	±11	±10	±9	±10	±11	±13	±11	±13	±21	±13	±23	±29
INCISHIGH	13	12	36	65	68	67	13	5	72	−1	−12	20
	±17	±16	±15	±16	±15	±16	±17	±18	±29	±19	±29	±36
CONCAVITY	1	5	17	7	18	21	1	8	34	−26	27	15
	±21	±20	±20	±24	±22	±23	±21	±21	±35	±23	±36	±44
RAMUSHIGH	26	33	51	52	52	42	26	29	41	−46	−13	−16
	±14	±12	±11	±13	±13	±14	±14	±14	±25	±14	±25	±31
CONDYLWID	13	16	40	49	24	17	13	14	67	−26	−78	−14
	±17	±16	±16	±19	±19	±19	±17	±18	±32	±19	±34	±36
CONDYLLEN	52	41	43	42	47	48	52	10	−17	−40	0	16
	±14	±14	±14	±17	±16	±17	±14	±16	±25	±16	±26	±33
CORONHIGH	21	24	32	27	25	15	21	20	10	−35	−13	−23
	±17	±15	±16	±19	±18	±19	±17	±17	±27	±18	±28	±35
CORONSIZE	66	58	73	72	57	47	66	25	14	−68	−57	−15
	±23	±21	±22	±24	±23	±24	±23	±23	±36	±25	±41	±47
ANGULARLEN	35	38	44	55	53	35	35	27	−3	−28	−20	−40
	±19	±18	±17	±19	±18	±20	±19	±20	±33	±22	±35	±47
TOOTHAREA	41	45	60	76	74	54	41	33	21	−36	−26	−39
	±11	±10	±9	±8	±8	±11	±11	±12	±21	±13	±21	±29
SUPERINCIS	14	26	30	14	6	5	14	33	−2	−45	−23	−3
	±19	±18	±18	±22	±21	±22	±19	±20	±32	±22	±33	±41
INFERINCIS	−12	−23	−19	13	11	15	−12	−30	30	51	−9	15
	±17	±16	±16	±19	±18	±19	±17	±17	±27	±18	±28	±35

Decimal points have been removed and standard errors given below each value. G1 = gain up to 14 days, G2 = gain between 14 and 21 days, G3 = gain between 21 and 28 days, G4 = gain between 28 and 35 days, G5 = gain between 35 and 42 days and G6 = gain between 42 and 70 days of age.

iation in several measures of height and length of the mandible and has largest coefficients for CONCAVITY, ANTMANLEN, CONDYLWID, TOOTHAREA, RAMUSHIGH and ANGULARLEN. The second vector has largest values for CORONSIZE, POSTMANLEN, NOTCHHIGH, ANGULARLEN and CONDYLLEN. CONDYLLEN varies in the opposite direction as reflected by a negative coefficient. The third vector reflects genetic covariation between incisor shape and condyloid dimensions, with highest coefficients for SUPERINCIS, CONDYLLEN and CONDYLWID. The last ge-

TABLE 5

Genetic correlations between the scores from a Varimax-rotated principal components analysis of 14 mandible traits and (1) the log of body weight at various ages and (2) the various logs of body weight gain

	Days						Postnatal intervals					
Trait	14	21	28	35	42	70	G1	G2	G3	G4	G5	G6
	Body weight						Body weight gain					
P_1	22	28	42	62	67	60	22	24	29	−15	−4	−2
	±15	±13	±13	±12	±11	±13	±15	±15	±25	±17	±26	±33
P_2	42	44	60	62	42	22	42	29	22	−51	−70	−48
	±17	±15	±15	±18	±18	±20	±17	±18	±29	±18	±33	±39
P_3	6	18	18	−8	−12	−19	6	29	−13	−44	−11	−24
	±17	±16	±16	±20	±19	±18	±17	±17	±28	±19	±29	±37
P_4	43	41	54	49	40	27	43	23	15	−54	−36	−27
	±15	±14	±14	±17	±17	±18	±15	±17	±27	±17	±29	±36

Decimal points have been removed and standard errors are given below each value. G1 = gain up to 14 days, G2 = gain between 14 and 21 days, G3 = gain between 21 and 28 days, G4 = gain between 28 and 35 days, G5 = gain between 35 and 42 days and G6 = gain between 42 and 70 days of age.

netic vector has largest coefficients of opposite signs for INCISHIGH and CORONHIGH.

Genetic correlations between adult body weight and the scores from the Varimax-rotated principal components of mandible dimensions range from 0.6 for the first rotated vector to ~0.2 for the remaining three vectors (Table 5). Only the first rotated vector has a significant genetic correlation with body weight at 70 days of age.

Residual environmental correlations: Residual environmental correlations are quite low, and only the correlation between body weight and POSTMANLEN is >0.40 (Table 6). The Varimax-rotated principal components have large coefficients on the first vector measures of the lower dimensions of the ramus, including POSTMANLEN, ANGULARLEN, RAMUSHIGH and CONCAVITY. The second vector has high coefficients for TOOTHAREA, SUPERINCIS, INCISHIGH and ANTMANLEN; the third vector reflects environmental variability in CORONSIZE, CORONHIGH, NOTCHHIGH and CONDYLLEN; and the fourth vector reflects variability in INFERINCIS, CONDYLWID, RAMUSHIGH and ANTMANLEN.

Only the first environmental rotated vector exhibits a correlation with adult body weight significantly different from zero (Table 7).

Adult mandible dimensions and developing body weight

Having described the components of correlation between mandibular form and body weight at 70 days of age, we might inquire about the magnitude and pattern of correlation between mandibular form in adult mice and body weight changes during earlier ontogenetic stages. Different parts of the mandible exhibit different growth patterns, suggesting that they may share different genetic precursors with body weight at various intervals during ontogeny.

TABLE 6

Environmental correlations of adult mandible dimensions with body weight and with body weight gain at various postnatal intervals

Trait	Days						Postnatal intervals					
	14	21	28	35	42	70	G1	G2	G3	G4	G5	G6
	Body weight						Body weight gain					
POSTMANLEN	33	33	36	37	44	42	33	10	−1	−6	1	6
ANTMANLEN	18	21	25	27	28	22	18	9	3	−3	−5	−2
NOTCHHIGH	24	25	28	26	31	29	24	9	0	−9	2	4
INCISHIGH	11	13	11	16	19	17	11	6	−3	4	0	0
CONCAVITY	16	24	22	26	30	26	16	16	−4	−1	0	0
RAMUSHIGH	31	34	27	30	35	34	31	12	−11	−3	1	6
CONDYLWID	14	11	0	3	12	10	14	0	−14	3	11	−1
CONDYLLEN	−5	−8	−7	−2	−5	−5	−5	−5	2	8	−4	−2
CORONHIGH	−1	0	−2	2	4	0	−1	1	−2	4	2	−4
CORONSIZE	2	8	7	9	16	10	2	9	−2	1	6	−4
ANGULARLEN	14	21	28	29	34	36	14	14	6	−4	1	8
TOOTHAREA	37	41	37	41	40	37	37	16	−9	−3	−9	4
SUPERINCIS	11	14	12	21	23	21	11	7	−3	8	−1	1
INFERINCIS	15	20	20	11	8	7	15	11	−2	−15	−5	0

Decimal points have been removed and standard errors are approximately 6 in all instances. G1 = gain up to 14 days, G2 = gain between 14 and 21 days, G3 = gain between 21 and 28 days, G4 = gain between 28 and 35 days, G5 = gain between 35 and 42 days and G6 = gain between 42 and 70 days of age.

TABLE 7

Environmental correlations between the scores from a Varimax-rotated principal components analysis of 14 mandible traits and (1) the log of body weight at various ages and (2) the gain in body weight between various ages

Trait	Days						Postnatal intervals					
	14	21	28	35	42	70	G1	G2	G3	G4	G5	G6
	Body weight						Body weight gain					
P_1	29	36	38	41	43	41	29	18	−1	−5	−6	4
P_2	8	9	7	7	14	10	8	4	−4	−1	7	−2
P_3	0	−1	0	9	12	12	0	−1	1	11	2	2
P_4	11	8	4	7	21	10	11	−1	−6	2	3	2

Decimal points have been removed and all standard errors are approximately 6. G1 = gain up to 14 days, G2 = gain between 14 and 21 days, G3 = gain between 21 and 28 days, G4 = gain between 28 and 35 days, G5 = gain between 35 and 42 days and G6 = gain between 42 and 70 days of age.

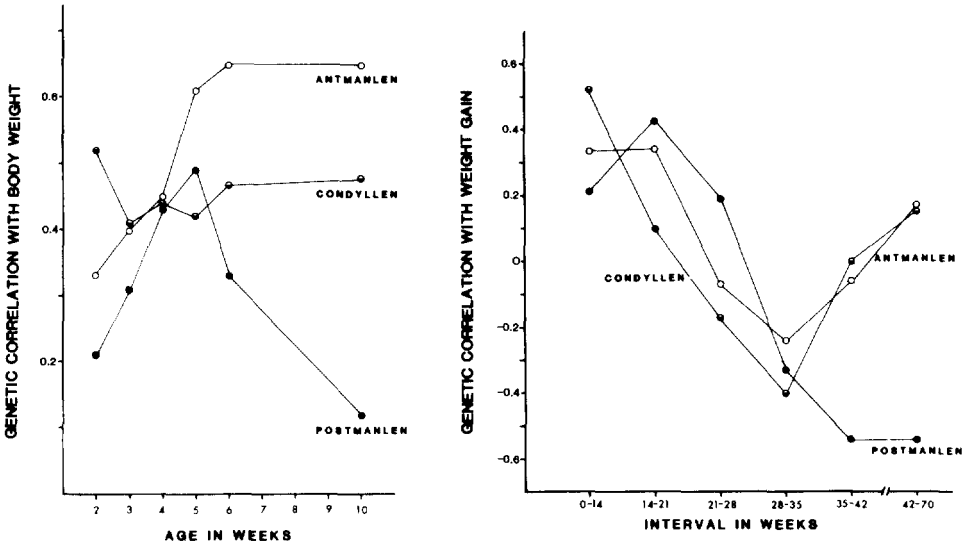

FIGURE 2.—Genetic correlations between anterior mandible length (ANTMANLEN), posterior mandible length (POSTMANLEN) and condyloid length (CONDYLLEN) with body weight at ten intervals and body weight gain at six intervals.

Hence, we can inquire whether the various functional parts of the adult mandible exhibit similar correlations with body weight during earlier ontogenetic periods, and whether the correlation between mandible dimensions and body weight increase the nearer the two traits are measured during ontogeny.

Phenotypic correlations between adult mandible dimensions and body weight at 14, 21, 28, 35, 42 and 70 days form a similar pattern for almost all mandible traits. The correlations are never large, and only eight of the 84 correlations are 0.5 or greater. All of these latter correlations occur for two traits, POSTMANLEN and TOOTHAREA.

There is a small but systematic increase in phenotypic correlation between 14 days and 21 days of age, followed by a slight decrease in correlation between 42 and 70 days of age. In several instances, *i.e.*, CONCAVITY, CORONHIGH, INFERINCIS, INCISHIGH, CONDYLWID and SUPERINCIS, the initial correlation is very low and, in at least three instances, not different from zero; however, the correlations increased severalfold for INCISHIGH and CONCAVITY between 14 and 70 days of age.

Residual environmental correlations are generally low, and only five of 84 correlations are 0.4 or greater, and again, these five involve only two traits, POSTMANLEN and TOOTHAREA (Table 6). Further, the environmental correlations are quite stable during ontogeny and in several instances, *i.e.*, INCISHIGH, CONDYLLEN, CONDYLWID, CORONHIGH and CORONSIZE, are almost never different from zero at any time.

The genetic correlations, however, show interesting patterns of ontogenetic change (Table 4). There seem to be three patterns of change in the genetic correlations over this interval (Figure 2). Because of the magnitude of the standard errors, it is not possible to test statistically the validity of these pat-

terns; thus, for the time being, they will have to be considered as qualitative patterns.

The first pattern is found in CONDYLLEN, where there is little change in the genetic correlation throughout the entire measurement period. The initial correlation at 14 days is 0.52, and the final 70-day correlation is 0.48.

In the remaining traits, there is an initial increase in the genetic correlation between body weight from 14 to 35 days of age and adult mandible dimensions. In some traits, the increase is quite marked (TOOTHAREA, INCISHIGH, CONDYLWID and POSTMANLEN), whereas in others the change is rather modest (CORONHIGH and CORONSIZE). However, two patterns of change in correlations become evident after the initial 35-day increase. In the first pattern, found in most traits, there is a decrease, often quite marked, in the genetic correlations (Figure 2). This pattern is most pronounced in CONDYLWID, POSTMANLEN, ANGULARLEN, TOOTHAREA and SUPERINCIS and is less marked, but still present, in CORONSIZE and NOTCHHIGH.

A second pattern is found in ANTMANLEN and INCISHIGH (Figure 2). Here, there is no change in the genetic correlation after 35 days of age. It is possible that RAMUSHIGH might belong to this pattern because there is a 3-week period of stability in the genetic correlations from 28–42 days, followed by a small decrease after 42 days. It is not known at present whether this decrease is simply sampling variability about a stable value.

Earlier, it was pointed out that the basicranium and facial region of the skull exhibit different patterns of growth. Because of its articulation with the basal part of the skull, its integration of the masticatory structures with facial region and its continuous incisor growth, we would hypothesize that developmental variability in the mandible would reflect both the basicranial and facial patterns of growth. Verification of this hypothesis is found in the comparison of genetic correlations with body weight during ontogeny of dimensions of the corpus with those from the ramus region. The genetic correlation between adult ANTMANLEN and INCISHIGH and body weight increase to a peak at about 35 days of age, after which the high correlation changes very little. These traits from the corpus region of the mandible may be reflecting the facial growth pattern.

Correlations with body weight of traits in the ramus region, *e.g.*, CONDYLWID, CORONSIZE and POSTMANLEN, increase also up to 35 days of age; however, the correlations for these traits then decrease, often markedly, after that point. This latter pattern may be reflecting growth of the cranial base as a result of the condylar articulation with the skull and the origin of some of the muscles that insert on the ramus. Braincase volume shows this pattern very clearly (ATCHLEY *et al.* 1984). This latter pattern suggests that the morphological traits have stopped growing at around 35 days of age, or, at least, that any growth after that age is very lowly correlated to growth in body weight.

Discussions about the evolutionary consequences of selection often assume that the genetic covariance structure remains relatively constant during ontogeny. However, ATCHLEY (1984), RISKA, ATCHLEY and RUTLEDGE (1984) and ATCHLEY *et al.* (1984) provide experimental evidence of pronounced ontoge-

TABLE 8

Genetic regression coefficients (= genetic allometry coefficients) of adult posterior and anterior mandible length onto body weight at six intervals during ontogeny

Age in days	POSTMANLEN	ANTMANLEN
14	0.043	0.066
21	0.045	0.056
28	0.074	0.075
35	0.153	0.184
42	0.116	0.218
70	0.039	0.197

netic changes in the genetic variance-covariance structure. These results further document this phenomenon.

Brief examination of the predicted correlated change between the mandible traits and body weight will assist in understanding the consequences of ontogenetic variability in genetic variance-covariance structure. Evolutionary change in mandible traits, such as that which occurs as a result of selection for body size, can be estimated by the genetic regression equation (= genetic allometry coefficients), where the additive genetic covariance between a trait and body size is divided by the additive genetic variance in body size (FALCONER 1981; LANDE 1979). The additive genetic regressions are given in Table 8 for POSTMANLEN and ANTMANLEN with these six body-weight traits. These two traits were chosen as representative of the corpus and ramus regions of the mandible and to reflect the patterns described above for genetic correlations.

The genetic regressions show basically the same pattern as the correlations. The coefficients for POSTMANLEN increase up to 35 days of age and then decrease to approximately the initial value at 70 days of age. ANTMANLEN, on the other hand, has a value similar to POSTMANLEN at 14 days, but increases to a peak at 42 days, with only a slight decrease at 70 days. Thus, change in body weight at any point up to 28 days gives the same approximate change in both traits; however, beyond that point, the results become more disparate. The predicted correlated change of body weight at 42 days of age with ANTMANLEN is twice that of POSTMANLEN and almost five times as great at 70 days of age.

The mechanism for producing this dynamic pattern of changes in genetic correlations is easily seen in the correlation between the adult mandible dimensions and body weight gain.

Adult mandible dimensions and body weight gain

In general, phenotypic correlations with body weight gain are small (Table 2). The largest value is 0.47, and only two correlations are 0.4 or greater. The six traits (TOOTHAREA, POSTMANLEN, RAMUSHIGH, NOTCHHIGH, ANTMANLEN and ANGULARLEN) with highest correlations between 70-day body weight and adult mandible dimensions also have the highest phenotypic correlation

between the mandible dimensions and gain up to 14 days of age. Likewise, the three traits (CORONHIGH, INFERINCIS, and CORONSIZE) with lowest correlations with 70-day body weight also have the lowest correlations with gain up to 14 days of age.

All phenotypic correlations are positive between the mandible dimensions and body weight gain through G2. However, 11 of 14 become zero or negative at G3. These negative values increase in magnitude at G4, but are very small or zero at G6.

All environmental correlations are small (Table 6), with only two values >0.3. After G1, virtually all environmental correlations are not different from zero.

The genetic correlations between body weight gain and adult mandible dimensions show considerable systematic change from 0.7 to −0.8 (Table 4). Within some traits, *e.g.*, CORONSIZE, the correlations range from 0.7 for G1 to −0.7 for G4. Indeed, the most obvious observation in the pattern of genetic correlations in many traits is a change in sign at G4. At this point, the magnitude of the change in genetic correlation with body weight gain is reflected in the pattern of genetic correlations with body weight.

The genetic correlation between body weight and adult mandible dimensions peaks at body weight values about 35 days of age. Traits achieve this peak genetic correlation in two ways. First, high genetic correlations are produced very early in ontogeny, and there is little change up to 35 days of age (*e.g.*, CORONSIZE and CONDYLLEN). Second, there is a lower correlation early in postnatal development that is increased considerably because of a high positive genetic correlation with body weight gain (*e.g.*, INCISHIGH, CONDYLWID and RAMUSHIGH).

The high genetic correlations are then reduced considerably in magnitude in most traits by the change in sign of the genetic correlation between mature mandible size and rate of gain in body weight. This pattern of changes in the genetic covariance also account for the difference in the pattern of the genetic regression coefficients given in Table 8 for POSTMANLEN and ANTMANLEN.

DISCUSSION

The existence of a particular magnitude of correlation between adult traits tells very little about how such a correlation might have arisen during ontogeny; however, the time of the onset of correlation tells a great deal (ATCHLEY *et al.* 1984). Some fundamental questions are as follows: (1) Do high genetic correlations between adult traits suggest that these traits had high correlations throughout ontogeny? (2) If two traits did not share a high correlation early in ontogeny, how do they arrive at a high level of intercorrelation as adults? (3) How do traits with high genetic correlations early in ontogeny come to have low correlations as adults? These are fundamental questions about the origin and ontogeny of pleiotropy patterns and about the coordination of growth trajectories of diverse components into functionally integrated units. These experimental data permit us to begin to ask questions and test hypotheses about these processes in mandibular growth and morphogenesis.

To explore some of these questions, let us examine the distal or corpus portion of the mandible. There is high genetic correlation among the length, width and area of the distal or corpus portion of the mandible and also between these measures and adult body weight. ANTMANLEN, INCISHIGH and TOOTHAREA measure the length and height of the corpus region of the mandible, and coordination of these dimensions is necessary to achieve the correct occlusal relationships with the maxilla. The first two traits probably relate to the dimensions and function of the incisor itself. TOOTHAREA, on the other hand, describes the portion of the mandible occupied by the molars; however, it probably also includes some influence from the incisor, because the incisor passes through this region of the mandible. The three traits have high genetic intercorrelations (0.5–0.8) and cluster together in cluster analyses of the mandible traits (ATCHLEY, PLUMMER and RISKA 1985). Further, these three traits have the highest genetic correlations with 70-day body weight (0.5–0.7).

In spite of their functional relationships and high intercorrelations in adult mice, ANTMANLEN, INCISHIGH and TOOTHAREA exhibit quite different relationships with body weight and rate of gain in body weight during ontogeny. The genetic correlations of adult ANTMANLEN and TOOTHAREA with 14-day body weight are significantly different from zero (0.33 and 0.41, respectively), whereas the genetic correlation for INCISHIGH with 14-day body weight is not different from zero (0.13). With regard to rate of development of body weight, ANTMANLEN and TOOTHAREA have genetic correlations with G1 and G2 of 0.3–0.4. The early correlations are significantly different from zero, but the correlation with weight gain goes to zero or becomes negative from G3 or G4 through G5. However, the negative correlation is only significantly different from zero for TOOTHAREA at G4. INCISHIGH, on the other hand, has a correlation of zero with G1 and G2, after which the correlation increases markedly to 0.7 with G3. After this point, the correlation is never significantly different from zero.

Thus, while these adult traits are, themselves, genetically intercorrelated in the adult mouse, these results suggest that they arrive at high correlations with adult body weight by different mechanisms, in terms of their genetical manipulation of the correlation with rate of development of body weight.

Other traits from the corpus region, *e.g.*, incisor curvature, are not genetically correlated with adult body size.

Another important suggestion from these data involves a general pattern of genetic integration in the craniomandibular region. The various genetic correlations with body weight suggest that genetic integration of the entire mandible, and by extension the skull, increases from birth to a particular point in postnatal development, after which it is markedly decreased throughout the craniomandibular region. Thus, if we had measurements of craniomandibular dimensions at a number of points during postnatal ontogeny, would an index of genetic integration (ATCHLEY, PLUMMER and RISKA 1985) increase in magnitude up to a point and then markedly decrease, as seen with the correlations with developing body size? Many studies report that changes occurring from mutation or selection are greater the earlier they occur in ontogeny. This

suggests that the affected processes themselves have a very general mode of action and impact on a number of traits. Alternatively, it might be that a very high level of genetic correlation exists among traits early in development, so that changes in any single trait produces concomitant changes in many others. These two explanations are related, but are not the same.

Growth relationship: There are several additional general observations about the genetic aspects of scaling relationships that are evident from these results.

First, traits that define the general shape of the body or basic functional unit of the mandible should also have highest correlations with early development, because it is early in development that the basic form of the mandible is determined. NOTCHHIGH, ANTMANLEN, TOOTHAREA and CONDYLLEN define large areas of the body of the mandible, and they have their highest genetic correlations with G1 and G2. After G2, the correlation with gain for NOTCHHIGH, ANTMANLEN and CONDYLLEN goes to zero, or becomes slightly negative at G3 and rather strongly negative in G4. In TOOTHAREA, the G3 correlation is 0.21, after which it becomes strongly negative. Posterior mandible length also contributes to some extent here and has significant positive genetic correlations with G1 and G2 and is significantly negative at G4 and beyond.

Second, the level of ossification of the coronoid, angular and condyloid processes depends on muscle development in prenatal and early postnatal ontogeny. Thus, these processes should have high positive genetic correlations with early body-weight gain. Indeed, the highest correlations for coronoid and angular process size and condyloid length is with body weight gain up to 14 days. This is not the case with the width of the condyloid process. The condyloid process continues to develop in mass considerably into postnatal development in response to biomechanical stimulation associated with mastication activities. Therefore, condyloid width probably would not have its highest correlation with the earliest periods of gain, because mastication activities do not become important until around the time of weaning, when the mice begin to take solid food. Indeed, condyloid width is not significantly correlated genetically with G1 or G2, but, rather, has its highest genetic correlation with body weight gain between 21 and 28 days of age for reasons that are described next.

Third, in these mice, the obligatory switch to solid food occurs with forced weaning at 21 days of age. This switch should be paralleled or followed by growth and development of those structures devoted to mastication. INCISHIGH and CONDYLWID have their highest correlations with body weight gain from 21–28 days of age (*i.e.*, 0.72 and 0.67, respectively). TOOTHAREA is another trait strongly involved with mastication, and it has its highest correlation with weight gain in the preceding intervals but the correlation with weight gain is still positive (0.21) during the 21- to 28-day interval.

Fourth, the incisor tooth, which extends back to the neck of the condyloid process, continues to grow throughout postnatal life in rodents. Thus, incisor growth is probably strongly correlated with growth in body weight throughout much of the postweaning life history of the mouse. Although we have no direct measure of incisor growth, we might expect that skeletal dimensions associated

with the incisor might continue to be correlated with later body-weight gain. At the least, these latter traits should not exhibit a strong negative correlation with body weight gain. Figure 2 shows that INCISHIGH, ANTMANLEN and CONDYLLEN have stable genetic correlations with body weight after 5 weeks of age, an observation that reflects the fact that the correlation with body weight gain does not go strongly negative. This latter observation is true for INCISHIGH and ANTMANLEN; however, CONDYLLEN has a correlation of −0.4 with G4.

Selection: Patterns of genetic correlation between POSTMANLEN and ANTMANLEN (Table 8 and Figure 2) and both body weight and body weight gain clarify the role that timing of selection might play in the evolution of morphological form. In nature, selection often operates on body size or rate of development (CALDER 1984). When traits are highly intercorrelated genetically and possess significant additive genetic variance, selection upon one trait, *e.g.*, body size, often has a marked effect throughout the body (ATCHLEY, RUTLEDGE and COWLEY 1982). The impact of selection of skeletal traits is defined by the equation for multivariate selection response (LANDE 1979) as

$$\Delta \mathbf{y} = \mathbf{G}\,\mathbf{P}^{-1}\,\mathbf{s}$$

where **y** is a vector of traits including mandibular dimensions, body weight at various ages and body weight gain, **G** and **P** are the additive genetic and phenotypic covariance matrices for these traits during ontogeny and **s** is a vector of selection differentials. From the results reported here, it is obvious that change in **y** will depend on when during ontogeny the selection occurs, the genetic correlation structure between the mandible traits, body weight and rates of development at different ages. In other words, **y**, **G**, **P** and **s** must contain age-specific traits.

Our results suggest that the effect of selection for body weight or rate of development of size and shape of the mandible may differ depending on when selection occurs during ontogeny, and the genetic variance-covariance structure among traits at that point in time. Selection on body size often occurs on components arising early in ontogeny (RISKA and ATCHLEY 1985), and the genetic correlation between early and late gain in body weight in these mice is low and often negative (RISKA, ATCHLEY and RUTLEDGE 1984). Because of this, accurate prediction of correlated response by mandible traits to selection for body size will depend on the actual correlation structure among the mandible traits themselves early in ontogeny and their genetic correlation with early and later postnatal rates of development. These data suggest that accurate prediction may not be possible if only mandible and body weight data for adults are used.

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