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QUANTITATIVE GENETIC ANALYSIS OF MULTIVARIATE EVOLUTION, APPLIED TO BRAIN:BODY SIZE ALLOMETRY

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Darwin (1859, pp. 11–14, 143–150) stressed the evolutionary importance of covariation between characters in populations and its "most imperfectly understood" connection with correlated responses to artificial and natural selection. After the turn of the century the discoveries of pervasive pleiotropy and linkage of Mendelian factors revealed the underlying genetic mechanisms. Existing theory on the dynamics of correlated characters has been developed in the limited framework of practical plant and animal breeding. Methods of multivariate analysis, functional analysis and optimality criteria popular among evolutionists, do not account for dynamical constraints imposed by the pattern of genetic variation within populations.

Consideration of phenotypic variation often does not suggest any clear mechanism connecting growth patterns or adult variation to interspecific evolution. When there is individual variation in development, no necessary correspondence exists between ontogenetic and adult variation in a population (Cock, 1966, pp. 148–151). It is also common for the pattern of adult variation within a species to differ from that at higher taxonomic levels (Simpson, 1953, pp. 25–29). An example which will be investigated here is the brain weight:body weight relationship. At various taxonomic levels, brain and body weights tend to follow the allometric equation

$$brain = k(body)^{\alpha}$$

or $$log\ brain = \alpha(log\ body) + log\ k$$

where k and α are constants. In large taxonomic groups, such as an order of mammals, α is near $\frac{2}{3}$ which may reflect an adaptive constraint correlating brain volume with body surfaces. Among adults within a species, or between very closely related forms like subspecies or congeneric species, brain and body weight variation can be fitted by an allometric curve with α between about 0.2 and 0.4. Ontogenetic curves consist of a high prenatal and low postnatal slope, as in Figure 1 (Count, 1947; Bauchot and Stephan, 1964; Jerison, 1973; Gould, 1975).

Similar forms of allometric variation are frequently encountered in comparative morphology and physiology, and in ontogenetic studies (Huxley, 1932; Gould, 1966). Many writers have proposed mechanisms connecting the different levels of variation, the most notorious of which is Haeckel's "ontogeny recapitulates [results from] phylogeny." Others have reversed the causality in this epigram, supposing that phylogeny is simply an extension of adult variation which in turn is produced by differential progress along a single ontogenetic pathway. There often is a *similarity* in the developmental, (adult) individual and evolutionary variation (reviewed by Simpson, 1953; Cock, 1966; Gould, 1977). Huxley (1932, pp. 212–224) observed the frequent close correspondence between individual and interspecific allometries, which he felt would be equivalent when natural selection acted only on general body size. He attributed exceptions, such as the brain:body weight example, to natural selection on both of the characters involved (pp. 215–216). Many modern morphologists also have presumed that selection on body size alone produces an evolution which extrapolates intrapopu-

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lation adult variation (e.g., Kurtén, 1954; Bauchot and Stephan, 1969; Jerison, 1973, pp. 358–362, 392–399; Gould, 1975, pp. 277–280; Marshall and Corruccini, 1978).

The critical factor missing in previous approaches to the problem of evolutionary variation and its connection with intrapopulation adult variation is the application of quantitative genetic methods. By using these techniques, it is demonstrated here that no necessary correspondence exists between individual and evolutionary variation, even when natural selection acts only on body size. Multivariate natural selection and random genetic drift are also analyzed. Methods are described for combining information on evolutionary variation (either from a phylogeny or the static comparison of contemporary species) with experimental data on genetic parameters to reconstruct the forces of directional selection which operated on character complexes. Finally, estimates of genetic parameters of brain and body weights in mice are used to interpret allometric patterns in these characters in natural populations.

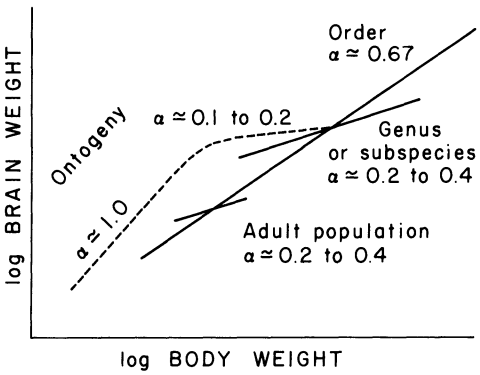

FIG. 1. Allometric curves for brain and body weights at different taxonomic levels among mammals. Closely related forms have a lower slope than distantly related ones. The change of slope in the ontogenetic curve corresponds to the cessation of neuronal cell division around the time of birth (Zamenhof and van Marthens, 1976). Modified from Count (1947) and Gould (1975).

ALLOMETRY DUE TO SELECTION ON ONE CHARACTER

A common hypothesis in the comparison of closely related species is that they diverged morphologically because of natural selection acting only on overall body size and that change in shape is merely a correlated response. One should realize that this hypothesis implies a precise relationship between the coefficients of interspecific allometry and the *genetic* variation of the characters within species. To derive this relationship, let z_b designate the measurement of the character under selection, say body size. The response in the mean of z_b in a population during one generation of selection is

$$\Delta\bar{z}_b = (G_{bb}/\sigma_b^2)S_b = h_b^2 S_b, \qquad (1a)$$

where h_b^2 is the heritability of z_b, that is, the ratio of its additive genetic variance G_{bb} to its total phenotypic variance, σ_b^2 (Falconer, 1960). S_b is the selection differential, the difference in the means of selected and unselected adults. The correlated response in the mean of another character, $\bar{z}_i$, during one generation of selection on z_b is

$$\Delta\bar{z}_i = (G_{ib}/\sigma_b^2)S_b = h_i h_b \gamma_{ib}(\sigma_i/\sigma_b)S_b, \quad (1b)$$

where G_{ib} and γ_{ib} are the covariance and correlation of the additive *genetic* values of z_i and z_b in the population (Falconer, 1960, p. 318). These equations rely on the assumptions that [1] there is no genotype-environment correlation and [2] there is a linear regression of the additive genetic values of z_i and z_b on the phenotypic values of z_b, which is satisfied if these follow a multivariate normal distribution (see next section).

It is further assumed here that the characters are measured on scales such that the intraspecific phenotypic variances are roughly constants, independent of the mean values, $\bar{z}_i$ and $\bar{z}_b$. For metrical characters this can usually be accomplished by employing logarithmic scales. If the intraspecific coefficients of variation of the characters are not large (<30%), the stan-

dard deviation of a character on the natural log scale (base e) is approximately equal to the coefficient of variation (=standard deviation/mean) of the raw measurements (Wright, 1968, p. 229) while the heritabilities and correlations, being dimensionless quantities, are approximately invariant under this transformation. When the changes in the mean values of two characters given by equations (1) are graphed, plotting $\bar{z}_i$ against $\bar{z}_j$, the slope of the line (α) is

$$\Delta\bar{z}_i/\Delta\bar{z}_j = G_{ib}/G_{jb} = \gamma_{ib}h_i\sigma_i/(\gamma_{jb}h_j\sigma_j). \quad (2a)$$

When j is b, the selected character, $\gamma_{bb} = 1$ and α equals

$$\Delta\bar{z}_i/\Delta\bar{z}_b = G_{ib}/G_{bb} = \gamma_{ib}h_i\sigma_i/(h_b\sigma_b). \quad (2b)$$

The selection differential, S_b, has cancelled from both of these equations, so the temporal pattern of selection, i.e., fluctuation in the rate and direction of evolution of $\bar{z}_b$, has no influence on the slopes of the lines. If the relative values of the genetic covariances do not change much during evolution, the graphs will tend to be straight lines on logarithmic coordinates, that is, "allometric" in the sense of Huxley (1932).

The coefficients of bivariate evolutionary allometry in formulas (2a) and (2b) differ from the intrapopulation adult allometries, regardless of whether the latter are defined by the regression slope

$$\alpha = P_{ij}/\sigma_j^2 = \rho_{ij}\sigma_i/\sigma_j, \quad (3)$$

where P_{ij} and ρ_{ij} are the phenotypic covariance and correlation of characters i and j among adults within a population; by the major axis slope of the distribution; or by the reduced major axis slope, $\alpha = \sigma_i/\sigma_j$ (Kermack and Haldane, 1950). The reduced major axis may be more appropriate than a regression line for ontogenetic allometry (where the parts of an organism tend to have high positive correlation due to concurrent growth) since it minimizes the squared orthogonal deviations of standardized data from the line rather than just the vertical deviations, but it is clearly inappropriate for many cases of intraspecific adult variation where the correlation between phenotypic characters may be low or negative (e.g., Lerner, 1950, pp. 245–249; Falconer, 1960, pp. 312–316). Another reason for preferring the regression formula (3) over any other to describe bivariate adult allometry is that equation (2b) for evolutionary allometry is itself the regression slope of additive genetic values of z_i on those of z_b within a population, as noted by Reeve (1950). But the genetic and phenotypic regression slopes may differ because of environmental factors, and Falconer (1960, p. 316) gives examples where they are of opposite sign. Thus for selection solely on body size and the correlated response of another character, there is no necessary congruence between the pattern of adult phenotypic variation within populations and the course of evolution. Genetic and phenotypic covariation patterns are often similar, however (next section), so that selection only on body size will produce an allometric slope *resembling* (3); although for two unselected characters genetically correlated with body size, even this similarity cannot be expected because (2a) is not a regression slope.

The multivariate description of selection on a single character according to equations (1) is rectilinear evolution of the mean phenotypes in the direction of the vector (G_{bb}, . . . , G_{ib}, . . .). With three or more characters this vector differs substantially from all of the commonly used lines of multivariate allometry (Sprent, 1972; Blackith and Reyment, 1971), even when genetic and phenotypic covariation patterns are proportional.

Evolution under Multivariate Selection

Evolutionary allometry can arise from natural selection on more than one character. For example, during adaptive size change, selection may be able to adjust ontogeny to keep pace with adaptive allometric constraints on (adult) shape, such as those involved in surface:volume ratios. Multivariate selection can also produce interspecific patterns other than allometric.

If the genetic covariance structure of a character complex is known and remains roughly constant (or in constant proportion) during evolution, it is possible to reconstruct the relative forces of directional selection on the characters, assuming that the phenotypic changes resulted from selection. Approximate constancy of the genetic covariance structure can be inferred from comparison of the genetic variation in related descendant populations, or more indirectly by comparing only the phenotypic pattern of variation in related populations. With additive and independent sets of genetic and environmental factors, the phenotypic covariance between characters is equal to the sum of their genetic and environmental covariances (see below). Hence, constancy of phenotypic covariation is unlikely without constancy of genetic covariation if the latter is a substantial component of the former. Artificial selection experiments (Sen and Robertson, 1964; Bell and Burris, 1973; Cheung and Parker, 1974; papers and refs. in Pollak et al., 1977) and simulation studies (Parker et al., 1970 and earlier) indicate that the mean phenotypes can be shifted considerably without greatly distorting the covariance structure of the characters, particularly in large populations when selection is not very strong. Interspecific comparisons demonstrate, however, that phenotypic (and thus genetic) covariation patterns may evolve over a long period with changing selection pressures, especially if major functional transitions are involved (e.g., Olson and Miller, 1958; Bader and Hall, 1960; Berg, 1960). The genetic basis of changing covariation patterns is that different regimes of selection favor mutations with different pleiotropic effects and/or linked combinations of alleles (Lande, 1979).

The genetic covariance structure in at least one (and preferably more) related population(s) must be known to apply rigorously the present methods. Otherwise further assumptions are necessary concerning the connection between phenotypic and genotypic variation. For many character sets, such as a system of linear skeletal measurements, there are marked similarities between the genetic and environmental (and phenotypic) covariance patterns, indicating that genetic and environmental factors affect the characters through similar physiological pathways (Falconer, 1960, p. 315; Bailey, 1956; Hashiguchi and Morishima, 1969; Hegmann and DeFries, 1970; Leamy, 1977). When this is not likely to be true, or in the absence of genetic information, reasonable caution should be exercised in any attempt to infer past selective forces from observed evolutionary changes and the phenotypic covariation pattern within populations.

The evolutionary dynamics and a principle of adaptation for the vector of mean phenotypes in a population, $\bar{\mathbf{z}} = (\bar{z}_1, \ldots, \bar{z}_m)^{\mathrm{T}}$, with $^{\mathrm{T}}$ denoting transpose, can be derived as follows. Suppose that on some scale of measurement the vectors of additive genetic effects, $\mathbf{x}$, and environmental effects, $\mathbf{e}$ (including non-additive genetic variation, Hazel 1943, Falconer 1960, p. 313), are each multivariate normal but mutually independent with $\mathbf{z} = \mathbf{x} + \mathbf{e}$,

$$g(\mathbf{x}) = \sqrt{(2\pi)^{-m}\left|\mathbf{G}^{-1}\right|} \cdot \exp\{-\tfrac{1}{2}(\mathbf{x}-\bar{\mathbf{x}})^T\mathbf{G}^{-1}(\mathbf{x}-\bar{\mathbf{x}})\},$$

$$\xi(\mathbf{z}-\mathbf{x}) = \sqrt{(2\pi)^{-m}\left|\mathbf{E}^{-1}\right|} \cdot \exp\{-\tfrac{1}{2}(\mathbf{z}-\mathbf{x})^T\mathbf{E}^{-1}(\mathbf{z}-\mathbf{x})\},$$

where the genetic and environmental covariance matrices, $\mathbf{G}$ and $\mathbf{E}$, are assumed to be non-singular and $\bar{\mathbf{e}} = \mathbf{0}$. The phenotype distribution, $p(\mathbf{z})$, has mean $\bar{\mathbf{z}} = \bar{\mathbf{x}}$ and covariance matrix $\mathbf{P} = \mathbf{G} + \mathbf{E}$. Defining $\int d\mathbf{x} \equiv \int \cdots \int dx_1 \cdots dx_m$,

$$p(\mathbf{z}) = \int g(\mathbf{x})\xi(\mathbf{z}-\mathbf{x})\, d\mathbf{x}$$

implies that $p(\mathbf{z})$ is also multivariate normal,

$$p(\mathbf{z}) = \sqrt{(2\pi)^{-m}\left|\mathbf{P}^{-1}\right|} \cdot \exp\{-\tfrac{1}{2}(\mathbf{z}-\bar{\mathbf{z}})^T\mathbf{P}^{-1}(\mathbf{z}-\bar{\mathbf{z}})\}.$$

Letting the fitness of individuals with

phenotype $\mathbf{z}$ be $W(\mathbf{z})$, the mean fitness in the population can be written either as an average over phenotypes or as an average over genotypes,

$$\bar{W} = \int p(\mathbf{z})W(\mathbf{z})\, d\mathbf{z} = \int g(\mathbf{x})\tilde{W}(\mathbf{x})\, d\mathbf{x}, \tag{4}$$

where

$$\tilde{W}(\mathbf{x}) = \int \xi(\mathbf{z} - \mathbf{x})W(\mathbf{z})\, d\mathbf{z}$$

is the mean fitness of individuals with genotype $\mathbf{x}$. The vector of total selection differentials on adults (before reproduction) is

$$\mathbf{S} = \bar{W}^{-1} \int \mathbf{z}p(\mathbf{z})W(\mathbf{z})\, d\mathbf{z} - \bar{\mathbf{z}}. \tag{5a}$$

The phenotypic response to selection in one generation is determined by the additive genetic variation (Falconer, 1960),

$$\Delta\bar{\mathbf{z}} = \bar{W}^{-1} \int \mathbf{x}g(\mathbf{x})\tilde{W}(\mathbf{x})\, d\mathbf{x} - \bar{\mathbf{x}}. \tag{5b}$$

Defining the gradient operator

$$\boldsymbol{\nabla} = \left(\frac{\partial}{\partial\bar{z}_1}, \cdots, \frac{\partial}{\partial\bar{z}_m}\right)^T = \left(\frac{\partial}{\partial\bar{x}_1}, \cdots, \frac{\partial}{\partial\bar{x}_m}\right)^T,$$

and applying $\boldsymbol{\nabla}$ to equations (4), using (5), produces

$$\boldsymbol{\nabla} \ln \bar{W} = \mathbf{P}^{-1}\mathbf{S} = \mathbf{G}^{-1}\Delta\bar{\mathbf{z}}. \tag{6}$$

These expressions reveal that the evolution of the mean phenotype vector has the dynamics of a modified gradient system,

$$\Delta\bar{\mathbf{z}} = \mathbf{G}\, \boldsymbol{\nabla} \ln \bar{W}, \tag{7a}$$

and also yield the form customary in quantitative genetics, $\Delta\bar{\mathbf{z}} = \mathbf{G}\mathbf{P}^{-1}\mathbf{S}$, (Young and Weiler, 1960; Harvey and Bearden, 1962). The evolution of a particular character, i, is given by

$$\Delta\bar{z}_i = \sum_{j=i}^{m} G_{ij}\partial \ln \bar{W}/\partial\bar{z}_j. \tag{7b}$$

In these equations $\partial \ln \bar{W}/\partial\bar{z}_i$ is the change in the Malthusian mean fitness due to a small change in $\bar{z}_i$ holding fixed all other $\bar{z}_j$ with $j \neq i$, which may be interpreted as the force of directional selection acting on character i. This should be distinguished from the total selection differential, S_i, which includes the correlated phenotypic responses (before reproduction) from selection on other characters (eqs. 5a, 6). The change across one generation, $\Delta\bar{z}_i$, includes the genetic gains both from selection on character i and genetically correlated responses to selection on other characters (7). The *selection gradient,* $\boldsymbol{\nabla} \ln \bar{W}$, contains information only about the directional forces of selection, and not the stabilizing or disruptive aspects of selection which do not alter the mean phenotype.

A basic principle of multivariate phenotypic evolution can be represented as an adaptive topography with dimensions $\bar{z}_1, \ldots, \bar{z}_m$ and height $\bar{W}$ (Lande, 1976*a*) by expanding the change in Malthusian mean fitness per generation in a Taylor series,

$$\Delta \ln \bar{W} = (\boldsymbol{\nabla} \ln \bar{W})^T\Delta\bar{\mathbf{z}} + \tfrac{1}{2}\Delta\bar{\mathbf{z}}^T\mathbf{H}\Delta\bar{\mathbf{z}} + \cdots \tag{8a}$$

where $H_{ij} = \partial^2 \ln \bar{W}/\partial\bar{z}_i\partial\bar{z}_j$ is the ij element of the matrix $\mathbf{H}$. With weak selection, the second and higher order terms are negligible. Employing (6) shows that the change per generation in Malthusian mean fitness is approximately equal to the square of the *generalized genetic distance* traversed (on generalized distance see Blackith and Reyment, 1971),

$$\Delta \ln \bar{W} \simeq \Delta\bar{\mathbf{z}}^T\mathbf{G}^{-1}\Delta\bar{\mathbf{z}} \geqslant 0. \tag{8b}$$

The inequality demonstrates that the response of the mean phenotype vector to weak selection in a constant environment always increases the average level of adaptation in a population, $\bar{W}$. But evolution of the vector of mean phenotypes does not proceed in the direction that gives the maximum increase in mean fitness per unit of Euclidean distance in phenotype space, which would be along the selection gradient, $\boldsymbol{\nabla} \ln \bar{W}$. Its direction and speed are determined jointly by the selection gradient and the genetic covariance matrix, $\mathbf{G}$ (eq. 7). As the transformation $\mathbf{z}^* = \mathbf{G}^{-1/2}\mathbf{z}$ carries (7) into gradient form, to the order of (8b) the trajectory of $\bar{\mathbf{z}}$ maximizes

the increase in Malthusian mean fitness per unit of generalized genetic distance.

Consider for instance a Gaussian fitness function

$$W(\mathbf{z}) = \exp\{-\frac{1}{2}(\mathbf{z}-\theta)^{\mathrm{T}}\omega^{-1}(\mathbf{z}-\theta)\},$$

which can approximate many forms of weak directional and stabilizing or disruptive selection. Then $\mathbf{H} = -(\omega + \mathbf{P})^{-1}$ and there are no higher order terms in (8a). Under weak selection (magnitudes of eigenvalues of $\omega + \mathbf{E}$ much larger than those of $\mathbf{G}$) the second order term is small compared to that in (8b), and even with strong stabilizing selection (ω positive definite, θ an optimum), $\Delta \ln \bar{W} \geqslant 0$ because $\Delta\bar{\mathbf{z}}^{\mathrm{T}}\mathbf{G}^{-1}\Delta\bar{\mathbf{z}} > \frac{1}{2}\Delta\bar{\mathbf{z}}^{\mathrm{T}}(\omega+\mathbf{G}+\mathbf{E})^{-1}\Delta\bar{\mathbf{z}} > 0$ if $\Delta\bar{\mathbf{z}} \neq \mathbf{0}$.

Regardless of the pattern of genetic covariation, an optimum phenotype will eventually be attained unless the adaptive topography shifts or additive genetic variation is absent in some selected dimension of the phenotype space, $|\mathbf{G}| = 0$. However, the adaptive topography for each population or species generally has multiple peaks (Simpson, 1953, Ch. 7; Lande, 1976*a*; Wright, 1977 and previous papers). Genetic correlations can alter the long-term result of selection by influencing the direction of evolution at critical periods when a population approaches a threshold (or saddlepoint) between adaptive zones, as by random genetic drift or by environmental fluctuations which directly affect the phenotype or alter the adaptive topography.

The adaptive response in the mean phenotypes can be offset by changes in the genetic covariance matrix from mutation or recombination, and environmental perturbations (as well as frequency-dependent selection, random genetic drift, and directional mutation pressure). But even in a fluctuating environment, $\mathbf{G}$ may usually be near an equilibrium determined by a balance of mutation, selection and recombination (Lande, 1977*b*, 1979). Then the primary mode of adaptation in a population is optimization of the mean phenotypes rather than of the entire genotype or phenotype distribution.

Although the entire vector of mean phenotypes, $\bar{\mathbf{z}}$, obeys this law of local maximization of mean fitness by natural selection, it is important to be aware that no such adaptive principle holds for an arbitrarily chosen character or subset of the selected characters. A particular character, i, may evolve maladaptively, i.e., against the actual force of selection on it, $\partial \ln \bar{W}/\partial\bar{z}_i$, because of genetically correlated responses to selection on other characters (eq. 7b). Adaptive change in the whole organism may therefore entail compromises between genetically correlated characters. Selection acting to change the means of two characters against the sign of their genetic correlation is known as *antagonistic selection,* and results in a kind of genetic "slippage" (Dickerson, 1955). The adaptive cost of antagonistic selection on a population is that, compared to a population with genetically independent characters, more selection is required to produce the same rate and direction of evolution (see last section).

When the phenotypic characters of typical adults among related species follow allometric curves, the vectors of phenotypic differences between species are roughly constant in proportion. If the genetic covariance structure of a character complex, $\mathbf{G}$, remains constant during evolution, the *net selection gradient* in a lineage can be obtained by summing (6) from generations 0 to $t-1$,

$$\sum_{0}^{t-1} \nabla \ln \bar{W} = \mathbf{G}^{-1}[\bar{\mathbf{z}}(t) - \bar{\mathbf{z}}(0)]. \qquad (9)$$

This measure of selection is robust to changes in the rate and direction of evolution, since it is independent of the path taken between the initial and final phenotypes, $\bar{\mathbf{z}}(0)$ and $\bar{\mathbf{z}}(t)$. Treating fitnesses as time-dependent incorporates both natural and sexual selection. The linearity of this equation allows the decomposition of a vector of phenotypic change into arbitrary additive component vectors, and the calculation of the net forces of directional selection corresponding to each. In particular, the selective forces which acted to *differentiate* a related group of contem-

porary species along lines of multivariate allometry (Sprent, 1972), e.g., principal components axes, can be reconstructed without considering other selective forces that may have led to (an often unknown amount of) parallel evolution. This extends the domain of the present analysis beyond strictly phylogenetic changes to the "static" comparison of coexisting forms.

The pattern of interspecific variation within higher taxa is influenced both by phenotypic change within lineages and by phenotype-dependent rates of extinction and speciation (Stanley, 1975; Gould and Eldredge, 1977). But branching and extinction of lineages do not in themselves create divergence of character. Barring polyploidy, macromutation, and direct effects of the environment, new forms arise only from the accumulation of genetic variation within lineages. On the hypothesis that phyletic changes were a quantitative genetic response to natural selection, the net forces of directional selection (or components thereof) can be reconstructed for any part of a phylogeny, and in particular those lineages which lead to modern species.

When data are available to provide the time dimension, the magnitude as well as the direction of the net selective forces can be estimated from (9). Another measure of the magnitude of selection is the *minimum selective mortality* necessary to account for an observed rate and direction of evolution. This is obtained by constructing a selection index or discriminant function (Smith, 1936; Hazel, 1943; Harvey and Bearden, 1962) where each character is weighted by the force of directional selection on it, and using (6),

$$I = (\Delta \ln \bar{W})^{\mathrm{T}}\mathbf{z} = \Delta\bar{\mathbf{z}}^{\mathrm{T}}\mathbf{G}^{-1}\mathbf{z}. \quad (10)$$

As the response of any character to selection on I is proportional to its additive genetic covariance with I (eq. 1b), selection on this index produces changes in the direction of $\Delta\bar{\mathbf{z}}$. Calculation of the minimum selective mortality is thus reduced to a consideration of truncation selection on the index (Cochran, 1951), a one-dimensional problem already treated by Lande (1976*a*).

Because the genetic covariance matrix, $\mathbf{G}$, is symmetric, it can be numerically factored by orthogonal rotation of axes (as in principle components analysis) to yield genetically independent characters which are linear combinations of the original measures. If the original characters are multivariate normal so are any linear combinations of them (Kendall and Stuart, 1977, p. 375) such as the index in (10), and all of the foregoing equations again apply. This procedure can reveal the existence of sets of characters which evolve independently in response to selection.

Multivariate Random Genetic Drift

A statistical kind of evolutionary allometry can occur by random genetic drift in characters which are correlated by genes with pleiotropic effects. The extreme case of selectively neutral characters is useful as a null hypothesis in testing for the action of natural selection. At first it will be assumed that the additive genetic variances and covariances are roughly constants or in constant proportions, as may happen over a long period of time when the genetic variation lost from random genetic drift is continually replenished by pleiotropic mutations.

Since the phenotypic change in one generation is determined by the additive genetic values, in the absence of directional mutation pressure the sampling distribution of $\Delta\bar{\mathbf{z}}$ has a mean of $\mathbf{0}$ and covariance matrix equal to $\mathbf{G}/N_e$, the additive genetic covariance matrix in a population divided by the effective population size (Kendall and Stuart, 1977, pp. 245, 250). Starting from a given population the probability distribution of $\bar{\mathbf{z}}$ after t generations, $\Phi(\bar{\mathbf{z}}, t)$, is the t-fold convolution of this sampling distribution, which has a mean equal to that of the initial population and covariance matrix $(t/N_e)\mathbf{G}$. When the additive genetic values in the population are multivariate normal, so is the sampling distribution of $\Delta\bar{\mathbf{z}}$ (Cramér, 1946, p. 405) and hence also $\Phi(\bar{\mathbf{z}}, t)$ because a convo-

lution of normal distributions is again normal. In general for $N_e \gg 1$ the sampling distribution of $\Delta\bar{\mathbf{z}}$ is asymptotically multivariate normal (Cramér, 1946, pp. 364–366). If the genetic matrix $\mathbf{G}$ fluctuates with time, as it must to some degree in a finite population, $\Phi(\bar{\mathbf{z}}, t)$ will have the covariance matrix $(t/N_e)\bar{\mathbf{G}}$, where $\bar{\mathbf{G}}$ represents the time average of $\mathbf{G}$ (Lande, 1977*a*).

A polygenic mutation model with some empirical support is that with a constant rate of production of new additive genetic variance, regardless of the background level of genetic variation. This property follows from the assumption of a wide range of possible allelic effects at each locus, with every allele at a given locus having the same distribution of mutational changes, although mutation rates and magnitudes of change may differ between loci (Kimura, 1965; Lande, 1976*b*, 1979). Other polygenic mutation models with a limited range of allelic effects at each locus may approximate a constant mutational variation for the traits when the mean phenotype of the population is not near the limits of its possible range. The balance of completely additive genetic variation between a constant input from mutation and loss by random genetic drift has been investigated for a single character by Clayton and Robertson (1955) and Latter (1970). To extend this model to multiple characters, let the total rate of production of additive genetic covariance between characters i and j summed over all loci in a diploid, random mating population be U_{ij} per generation. Without selection there is no expected genetic covariance from linkage disequilibrium, and the proportional loss of additive genetic variance and covariance occurs at an expected rate of $1/2N_e$ per generation (Cramér, 1946, pp. 358; Wright, 1951, App. C; Latter and Novitski, 1969). With sampling of adults followed by mutation and reproduction (of a hypothetical large number of offspring), in matrix notation

$$\Delta\mathrm{E}[\mathbf{G}] = -\mathrm{E}[\mathbf{G}]/2N_e + \mathbf{U},$$

where $\mathrm{E}[\cdot]$ denotes expected value in a given generation. In the stationary distribution of genetic variation, the time average, $\bar{\mathbf{G}}$, and state space average, $\mathrm{E}[\mathbf{G}]$, are equivalent, so

$$\bar{\mathbf{G}} = \mathrm{E}[\mathbf{G}] = 2N_e\mathbf{U}. \qquad (11a)$$

The probability distribution of $\bar{\mathbf{z}}$ at time t in a single population may also be interpreted as that among an ensemble of populations with the same initial conditions. The steady state rate of diversification expressed as an increase per generation in the genetic covariance between populations, from (11a) and the penultimate paragraph above is

$$\mathrm{E}[\Delta\bar{\mathbf{z}}(\Delta\bar{\mathbf{z}})^{\mathrm{T}}] = \bar{\mathbf{G}}/N_e = 2\mathbf{U}. \qquad (11b)$$

This reflects the steady flux of pleiotropic mutations and the fact that purely additive genetic (co)variation within a random mating population doubles when converted to (co)variation between populations by random genetic drift (Wright, 1951).

Now consider branching and extinction of lineages. The effective population size may differ between lineages, since from (11b) N_e does not influence the steady state rate of random genetic drift. With branching and extinction rates $B(\bar{\mathbf{z}})$ and $D(\bar{\mathbf{z}})$, both $\ll 1$ and possibly time-dependent, the probability distribution of $\bar{\mathbf{z}}$ at generation t, $\Phi \equiv \Phi(\bar{\mathbf{z}}, t)$, in the absence of natural selection obeys the modified diffusion equation (Lande, 1976*a*)

$$\frac{\partial\Phi}{\partial t} = [B(\bar{\mathbf{z}}) - D(\bar{\mathbf{z}}) - \bar{B} + \bar{D}]\Phi + \sum_{i=1}^{m}\sum_{j=1}^{m}\frac{U_{ij}\partial^2\Phi}{\partial\bar{z}_i\partial\bar{z}_j} \qquad (12)$$

where

$$\bar{B} - \bar{D} = \int [B(\bar{\mathbf{z}}) - D(\bar{\mathbf{z}})]\Phi\, d\bar{\mathbf{z}}.$$

The form of the first term is dictated by the condition that $\int \Phi\, d\bar{\mathbf{z}} = 1$. An augmented neutral hypothesis of *random genetic drift in a stochastic phylogeny* can be constructed by letting branching and extinction rates be independent of the mean phenotype in a lineage. Then $B(\bar{\mathbf{z}}) - D(\bar{\mathbf{z}}) \equiv \bar{B} - \bar{D}$, the first term in (12) vanishes, and the solution $\Phi(\bar{\mathbf{z}}, t)$ is the

same as that given above for a single population: multivariate normal with mean at the initial point and covariance matrix $2t\mathbf{U}$. A uniform directional mutation pressure affecting $\bar{\mathbf{z}}$ would only translate the mean of this distribution at a constant rate. With random branching and extinction, any superspecific taxon with a large *effective number of independent lineages* going back to a common ancestor will tend to follow this distribution (cf. Sawyer, 1976, eq. 2.7).

The coefficient of bivariate evolutionary allometry among an ensemble of contemporary populations which diverged from a common ancestor by random genetic drift, defined by the slope of the regression of $\bar{z}_i$ on $\bar{z}_j$, is

$$\alpha = \bar{G}_{ij}/\bar{G}_{jj}. \tag{13}$$

This is nearly the same as the expected regression slope for the additive genetic values of the characters within a population, apart from a factor due to correlated fluctuations in G_{ij} and G_{jj} which should be negligible unless the effective population size is rather small (Avery and Hill, 1977). The allometric slope in (13) for two entirely neutral characters differs from that in the deterministic equation (2a) for two neutral characters genetically correlated with a third selected character. However, if character j is b, the selected character in (2b), virtually the same bivariate allometry is expected from random genetic drift as from natural selection on b alone, in terms of the genetic covariance structure within populations (although this may change with selection).

More generally, a static multivariate *pattern* of interspecific variation can be evaluated against the null hypothesis of random genetic drift by testing for proportionality of $\bar{\mathbf{G}}$ and the covariance matrix between populations. When divergence times and effective population sizes are available, *rate* tests can be performed by noting that on the null hypothesis for the vector $\mathbf{y}$ of net phenotypic change from the centroid of the distribution $\Phi(\bar{\mathbf{z}}, t)$, the scaled square of the generalized genetic distance $(N_e/t)\mathbf{y}^T\bar{\mathbf{G}}^{-1}\mathbf{y}$ is distributed as χ^2 with m degrees of freedom.

Evolutionary Allometry in Brain and Body Weights

It is undoubtedly an oversimplification to study the coevolution of brain and body sizes solely in terms of gross weights, because each are highly structured systems in which the relative sizes of the parts and their internal organization can change (Holloway, 1969; Stephan and Andy, 1970; Jerison, 1976). However, within a group of species which are not too distantly related, the major modes of evolution of brain and body structures are likely to be primarily along the dimensions of overall brain and body sizes. Jerison's (1973, pp. 72–75) multivariate analysis of Bauchot's (1963) data on brain components of insectivores demonstrates that among mammalian species within taxa as large as an order, the great majority of the total variation in the brain is attributable to changes in overall brain size (see also Sacher, 1970; Gould, 1975), and the same is generally true of variation in body parts. The selective significance of body size is well known, affecting metabolic rate, fecundity, lifespan and competitive ability. For discussions of the adaptive value of brain size and its relation to intelligence, consult Rensch (1967), Sacher (1959), Sacher and Staffeldt (1974), Jerison (1973), Roderick, Wimer and Wimer (1976), and Herman and Nagy (1977). Therefore, in the domain of Figure 1, it is not unreasonable to approach the analysis of evolutionary forces producing interspecific allometry in brain and body weights through quantitative genetic studies on the gross measures themselves, rather than using a finer subdivision of parts.

Roderick et al. (1976) performed selection on brain weight in mice and recorded the correlated response in body weight. The results of 16 generations of selection for high and low brain weight and the unselected control in two different experiments are plotted on logarithmic scales in

Figure 2. The average slope of the two lines is 0.77. Because selection was only on brain size, from equation (2b) this slope has the theoretical formula

$$0.77 = \frac{\Delta\bar{z}_{\text{ln brain}}}{\Delta\bar{z}_{\text{ln body}}} = \frac{1}{\gamma}\frac{h_{\text{brain}}\sigma_{\text{ln brain}}}{h_{\text{body}}\sigma_{\text{ln body}}}$$

where γ is the additive genetic correlation between brain and body weights. From the direct response to selection, Roderick et al. (1976) found the average realized heritability of brain weight to be $h^2_{\text{brain}} = 0.64$. From an earlier study by Roderick et al. (1973) I estimated the average value of $\sigma_{\text{brain}}/\bar{z}_{\text{brain}} \simeq \sigma_{\text{ln brain}}$ for the separate sexes in twenty-five *inbred* strains to be about 0.035. Assuming the variance within strains is entirely environmental, an *outbred* population with the above heritability of brain weight would have a variance on the natural log scale of $\sigma^2_{\text{ln brain}} = (0.035)^2/(1-h^2_{\text{brain}})$ or $\sigma_{\text{ln brain}} = 0.058$. This value is consistent with typical coefficients of variation of 6 to 7% for brain weights in small mammals reported by Yablokov (1974, p. 49).

Falconer (1973) carried out extensive selection experiments on body weight in outbred populations of mice and found the mean realized heritability $h^2_{\text{body}} = 0.37$. From Falconer's (1973) data I estimated the average coefficient of variation ($\simeq \sigma_{\text{ln body}}$) for the separate sexes to be $\sigma_{\text{ln body}} = 0.145$ which agrees well with typical coefficients of variation of 12 to 15% for body weight in rodents and insectivores summarized by Yablokov (1974, pp. 66, 72). Substituting these values into the equation above yields an estimate of the additive genetic correlation between brain weight and body weight of $\gamma = 0.68$.

This information can be used to predict the results for the converse of the experiment of Roderick et al. (1976), that is, the allometric slope when selection is only on body weight (eq. 2b),

$$\alpha = \gamma\frac{h_{\text{brain}}\sigma_{\text{ln brain}}}{h_{\text{body}}\sigma_{\text{ln body}}}.$$

Employing the preceding estimates gives $\alpha = 0.36$, which falls in the range 0.2 to 0.4 usually observed between very closely related forms (Bauchot and Stephan, 1964; Jerison, 1973). Assuming that the phenotypic differentiation of subspecies and congeneric species is due to natural selection, this result confirms the hypothesis of previous workers, that the selective forces which acted to differentiate very closely related forms operated predominantly on overall body size and that changes in brain weights were largely a correlated response. Evidence that among breeds of domestic animals α is between 0.2 and 0.4 (Huxley, 1932, p. 215; Weidenreich, 1941) can only be interpreted as circumstantial support for this hypothesis, because breeders select their animals for many characteristics other than size, including features of the head. Since $\alpha = 0.36$ is also the predicted allometric regression of brain weight on body weight among contemporary forms which diverged by random genetic drift (eq. 13), the hypothesis that in some very closely related species these characters evolved by random genetic drift cannot be ruled out on this basis.

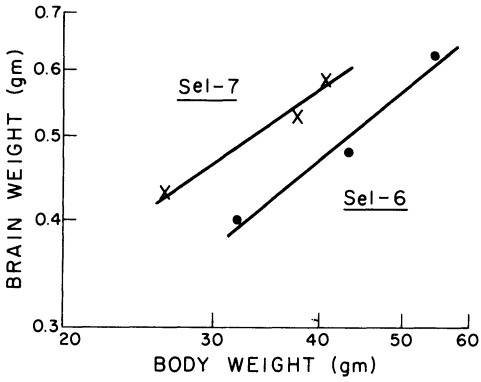

FIG. 2. Correlated response in body weight to artificial selection for high and low brain weight in mice. In each of the two experiments, Sel-6 and Sel-7, there was a high line, a low line and an unselected control. Regression lines were fitted by eye separately for each experiment because the base populations differed in genetic composition, due to segregation in a complex cross. Data are from Roderick et al. (1976).

The estimated brain:body allometry $\alpha = 0.36$ for random genetic drift or direction-

al selection only on body size, differs considerably from α near 0.67 observed for interspecific data among large taxonomic groups (Jerison, 1973; Gould, 1975). If the mouse data are representative for mammals in general, this indicates that neither of these hypotheses can explain the brain:body weight relationships in the larger, older taxonomic groups. That the evolutionary allometric slope for selection only on brain weight, $\alpha = 0.77$, is close to the value of 0.67 for the larger taxa implies that the diversification in brain and body weights at higher taxonomic levels involved a greater net directional selection on brain sizes than on body sizes. These conclusions, being statements about the selective forces which have acted to *differentiate* contemporary species along an allometric line, are robust to parallel evolution which affects all species alike, such as a general trend toward increasing body size (Cope's rule, Rensch, 1959) or increasing encephalization (Jerison, 1973).

Thus it appears that on a time scale typical for subspeciation or speciation, the coevolution of brain and body sizes occurs mainly through natural selection on body size and/or random genetic drift, while on a longer time scale typical for diversification at higher taxonomic levels, natural selection is able to adjust brain size to accumulated changes in body size. It is plausible that in a fluctuating environment the primary short-term adaptation in the brain:body size relation is change of body size, such as that documented by Kurtén (1959, 1960) for mammals during the Pleistocene temperature oscillations. Jerison (1973, pp. 358–360) has shown that for La Brea Pleistocene mammals and their closest living relatives which differ substantially in body size, relative brain sizes scale at α equal about 0.2 to 0.4. The pattern of increased allometric slopes in higher taxa may be partly explained by differential rates of speciation and extinction, e.g., if species which deviate greatly from an ordinal regression with $\alpha \simeq \frac{2}{3}$ usually do not persist or speciate as well as those near the regression line, but this would not alter the foregoing deduction that there must have been a great deal of diversifying selection on brain sizes within mammalian orders (see section on multivariate selection).

In quantitative genetic terms there is also an explanation of why the allometric regression slope of brain weight against body weight for adults within a population often falls in the same range of about 0.2 to 0.4 observed between very closely related forms. Data already cited from Yablokov (1974) and further information in Latimer and Sawin (1955, p. 532) and Gjukić (1955) show that for a variety of mammals the intraspecific coefficient of variation of adult brain weight is roughly half (or somewhat less than half) that for body weight, $\sigma_{\ln \text{ brain}}/\sigma_{\ln \text{ body}} \simeq 0.4$ to 0.5. The lower coefficient of variation and higher heritability of brain weight reflect a source of environmental variation in body weight (fatness) not affecting brain weight. Equation (3) shows that the regression slope for intraspecific adult allometry is equal to this ratio multiplied by ρ, the phenotypic correlation of brain and body weights, which is about 0.7 to 0.8 for species of insectivores (Bauchot and Stephan, 1964). The rough correspondence between the adult intrapopulation allometry and the evolutionary allometry of closely related forms apparently results from two conditions: first, closely related forms have usually diverged by selection mainly on body size or by random genetic drift with an allometric slope equal to the genetic regression of brain weight on body weight within populations (eqs. 2b, 13); and second, there is a similarity in the slopes of the genetic and phenotypic regressions of brain weight on body weight within populations.

With major reorganization of the brain it should be anticipated that the population genetic parameters of the brain:body system may also change. There is indirect evidence that the genetic correlation between brain and body weights has decreased with continued encephalization. Among primates the phenotypic correlation between weights of adult body and brain within populations is low, in the

range of 0.1 to 0.3 for various macaques (Sholl, 1948), baboons and pongids (Jerison, 1973, p. 398) and man (Gjukić, 1955; Pakkenberg and Voigt, 1964). On the supposition of no genotype-environment correlation, and granting a rough similarity of genetic and environmental correlations and heritabilities resembling those above, the equation $P_{ij} = G_{ij} + E_{ij}$ (or see eq. 19.1 of Falconer, 1960) implies that the genetic correlation of brain and body weights in primate populations, γ, is also in the neighborhood of 0.2, which is substantially lower than the estimate of $\gamma = 0.68$ for the mouse populations discussed here. This suggests that intrapopulation variation in "extra neurons" is less correlated *genetically* with variation in body parts than is the variation in more primitive brain structures. Evolutionarily, this would mean that size changes in the primate brain are only weakly coupled to changes in body size. Jerison (1973, pp. 344–346, 395–396) has proposed a similar explanation of the pattern of phenotypic variation in closely related primates, based on an added amount of neural tissue which is independent of body size.

Genetic uncoupling of brain and body sizes would facilitate further encephalization, usually defined by Jerison (1973) and others as $\Delta\bar{z}_{\ln\ \text{brain}} - 0.67\Delta\bar{z}_{\ln\ \text{body}} > 0$. For example, Pilbeam and Gould (1974) have estimated that the increase of brain weight and body weight in the human lineage was allometric with a slope of $\alpha \simeq 1.7$. Figure 2 and equation (9) indicate that, in an organism with population genetic parameters similar to those estimated here for mice, any increase of brain size without a relatively large change in body size ($|\alpha| > 1.0$) would require antagonistic selection for larger brains ($\partial \ln \bar{W}/\partial \bar{z}_{\ln\ \text{brain}} > 0$) *and for smaller bodies* ($\partial \ln \bar{W}/\partial \bar{z}_{\ln\ \text{body}} < 0$) to counteract an excessive correlated increase in body size from selection on the brain. Selection on body size would then exert a negative correlated response in brain size thereby hindering encephalization. But if the genetic correlation between size of the brain and that of the body in the human lineage was as low as suggested by the data on primates, the selective forces would have been positive for both characters. Hominids may thus have circumvented the cost of antagonistic selection for increasing brain size and the prevention of gigantism.

Corresponding to the differences in adult brain:body proportions depicted in Figure 1, comparisons of ontogenetic curves tend to follow von Baer's law, that the embryonic stages of related species resemble each other more than do the adults (cf. Gould, 1977, pp. 56, 371–374). This is clearly demonstrated by Count's (1947) graphs of the logarithms of brain and body weights during development in primates and ungulates: the prenatal stages practically coincide within each of these groups. There is more heterogeneity in the early ontogenies of rodents (Holt et al., 1975), although two subspecies of deermice conform to this pattern (King and Eleftheriou, 1960). Von Baer's law is the expected result of selection primarily on the adult stages of characters influenced by many genes of small effect which usually act late in development (Cock, 1966). Body size and brain size are each polygenic characters (Falconer, 1960, 1973; Roderick et al., 1973, 1976) so it is not surprising to find a tendency to obey this law. Exceptions may occur when there is strong selection on young individuals, for example in taxa with both altricial and precocial species (Sacher and Staffeldt, 1974), or with the fixation of (major) genes acting early in development.

Application of quantitative genetic analysis such as that described here, in conjunction with further breeding and selection experiments on a variety of animals, using methods in Falconer (1960) and Cock (1966), would help to resolve these and many similar problems in multivariate phenotypic evolution.

Summary

A basic principle of natural selection on correlated characters is expressed as an adaptive topography for the vector of mean phenotypes in a population. Under

some simple conditions on the pattern of phenotypic and genetic covariation within populations, selection only on body size, certain types of multivariate selection, and random genetic drift in a stochastic phylogeny are each expected to produce allometric evolution, i.e., straight lines or linear regressions on logarithmic coordinates. The orientation of these lines is determined by genetic parameters of the populations. Using this theory, phylogenetic or comparative information can be combined with experimental data on population genetic parameters to test hypotheses about past selective forces.

Data from selection experiments on brain and body weights in mice support the conclusions that [1] the short-term differentiation of brain and body sizes in very closely related mammalian forms resulted either from directional selection mostly on body size with changes in brain sizes largely a genetically correlated response, or from random genetic drift; [2] during the long-term allometric diversification within most mammalian orders there has been more net directional selection on brain sizes than on body sizes. It is suggested that encephalization in primates decreased the genetic correlation between brain size and body size within populations, which facilitated further encephalization in the human lineage by avoiding antagonistic selection on brain and body sizes. The evolution of brain:body ontogeny is briefly discussed.

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