

A Quantitative and Descriptive Approach to Morphological Variation of the Endocranial Base in Modern Humans

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ABSTRACT The cranial base is one of the major foci of interest in functional craniology. The evolution and morphogenesis of this structure are still poorly known and rather controversial because of multifactorial influences and polyphasic stages. Endocranial dynamics are associated anteriorly with the upper facial structures, laterally with the mandibular system and midsagittally with brain development. In the present study, we investigated the endocranial morphology of modern humans using 3D landmark-based approaches, i.e. geometric morphometrics and Euclidean distance matrix analysis. The structure of endocranial variation is poorly integrated, with only weak reciprocal influences among the three fossae. Some major variations are associated with changes in the posterior

fossa, with possible consequences on the anterior areas. These main patterns of integration are hypothesized to be influenced by the connective tensors of the dura layers. Static allometry and sex differences are largely related to the ontogenetic sequences, characterized by early maturation of the anterior fossa with respect to the middle and posterior regions (i.e., relatively shorter posterior part of the planum sphenoidum and vertical lengthening of the clivus in males). The relative independence between the endocranial fossae, as well as their structural connection through the meningeal tensors, must be carefully considered in studies on the evolutionary dynamics, since they lead to mosaic changes through phylogeny. *Am J Phys Anthropol* 137:30–40, 2008. © 2008 Wiley-Liss, Inc.

For almost two centuries, the study of the skull has focused on single traits and has tried to interpret both its morphogenesis and evolution in terms of variation of individual characters. Each feature was supposed to be the result of character-wise adaptive selection, according to a reductionist application of general Darwinian principles. Although this approach persists in some studies, a very different tendency has emerged in recent decades. Functional craniology is aimed at interpreting the anatomy and morphology of the skull as an integrated structural system in which the final phenotypic product is the result of a genetic background expressed in a given physical context (Moss and Young, 1960). Organs, tendons, bones, and vessels all contribute to form a structural and functional network in which each ontogenetic and phylogenetic change must be balanced according to the overall biological system. The complex nature of genetics was recognized in the General System Theory of Von Bertalanffy (1968) because of the widespread presence of polygenic and pleiotropic networks. In morphology, the importance of structural relationships and constraints was acknowledged even earlier in the approach of D'Arcy Thompson (1942). In terms of phenotype, the result of such biological networks is called morphological integration (Olson and Miller, 1958). This concept refers to the “connections or relationships among morphological elements,” linking developmental, functional, genetic, and evolutionary processes (Cheverud, 1996). In terms of statistics, integration means high levels of covariance, which are investigated by multivariate approaches and shape analysis. Conversely, some anatomical systems may be less constrained by reciprocal influences of their components, and formed by quasi-autonomous units

called modules, or “building blocks of interacting elements that operate in an integrated and relatively autonomous manner” (Schlosser, 2004). Of course, one of the main targets of morphometrics is to localize such modules, and the way they behave in ontogenetic or evolutionary contexts (Klingenberg, 2002). Clearly, the human skull is formed by a hierarchical organization of modules, related through major or minor structural relationships (Ackermann, 2005; Bastir et al., 2006; Polanski and Franciscus, 2006; Bruner, 2007a).

The neurocranial vault represents a relatively linear system in which growth (changes in size) is mainly related to brain expansion while development (changes in shape) is mostly associated with meningeal connective tensors (Moss and Young, 1960). It is worth noting that although sometimes the word “morphogenesis” has been used to delineate just the shape variation along an ontogenetic process (e.g., Hall, 1988), here this term is used to define both the shape and size changes of the ontogenetic

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trajectory. So, brain and endocranial connective tensors drive neurocranial morphogenesis, inducing the neurocranial bones to undergo structural arrangements at the outer and inner surface by deposition and absorption (Enlow, 1990), possibly via soft-tissue mediated signal transduction at the sutural boundaries (Ogle et al., 2004).

In contrast, the cranial base is probably the most controversial topic in functional craniology (see Lieberman et al., 2000a for an extensive review). It is assumed to be the functional and structural interface linking neurocranial and splanchnocranial morphogenesis and evolution, and is also associated with important adaptations ranging from posture to speech. Cranial base flexion during ontogeny and phylogeny is considered one of the major characters involved in primate cranial evolution, mainly in relation to the degree of encephalization and brain globularity (McCarthy, 2001; Ross et al., 2004). This becomes important when neurocranial globularity is assumed to be an autapomorphic trait of the human genus (Lieberman et al., 2002), possibly related to the evolution of cortical brain components like the parietal lobes (Bruner et al., 2003a; Bruner, 2004; Bruner et al., 2004). Nonetheless, the complex geometry and multifactorial variability of the cranial base hamper conclusive and robust hypotheses on the structural and functional relationships involved in growth, development, and evolution.

The cranial base originates embryologically from the neural crests (prechordal elements— anterior to the sella) and the mesoderm (postchordal elements—posterior to the sella), meeting at the sella around the midsphe- noidal synchondroses (Lieberman et al., 2000a; Jeffery and Spoor, 2004). The resulting basal plate is formed by at least 41 ossification centers. Bone deposition begins posteriorly and proceeds rostrally and laterally to form the occipital, temporal, sphenoid, and ethmoid bones (Lieberman et al., 2000a). Structurally, the endocranial base is formed by different functional modules, responsible for the mosaic evolutionary patterns described within the human genus (see Stringer, 2002).

Cranial base flexion is almost complete at 2 years of age (Lieberman and McCarthy, 1999) and is largely influenced by processes at the sphenoccipital, midsphe- noidal, and sphenoccipital synchondroses (Jeffery and Spoor, 2002). In nonhuman primates, the cranial base extends gradually after birth (retroflexion), whereas in humans it extends in association with facial growth in the prenatal period and undergoes rapid flexion after birth (Lieberman et al., 2000a).

According to the counterpart principle (see Enlow, 1990), contacting elements must keep a biomechanical balance during the morphogenesis, and the final phenotype will be influenced by the integration of their vectorial growth. While the cranial midline structures are relatively independent of the lateral ones, the variations of the latter are associated, through the counterpart principle, with changes in mandibular morphology (Bastir and Rosas, 2005). Size and shape changes are often uncoupled (ontogenetic dissociation) and maturation of the different parts is organized along a sequence in which the earliest structures constrain the following ones. In terms of size, the neurocranium matures first, followed by the midline cranial base and then the lateral cranial base. In terms of shape, the midline cranial base matures first (7–8 years), followed by the midline neurocranium (9–10), the lateral cranial floor (11–12) and the splanchnocranial components (15–16) (Bastir et al., 2006). While the lateral cranial base is constrained by

the mandibular structures, the anterior cranial floor shares many bone components with the face directly through the ethmomaxillary complex (Enlow, 1990). Because of this close contact, and because of the rotation of the face under the neurocranium during morphogenesis, the anterior fossa is largely constrained by the facial block (Lieberman et al., 2000a; Bruner, 2007b). Thus, it can be expected that evolutionary changes of the anterior fossa will be not only associated with neural variation of the prefrontal cerebral cortex, but also with spatial interactions with the underlying facial system.

The patterns of integration/modularisation in this complex structural framework are one of the main topics in functional craniology. Accordingly, the main target of the present analysis is to quantify and to describe the main covariational patterns of the endocranial base morphology in modern humans. The null hypothesis is that the endocranial base is formed by independent components (i.e., no integration at all). Furthermore, taking into account that in modern humans sex and size account for 37 and 54% of cranial variation respectively (Rosas and Bastir, 2002), this survey is aimed at considering the contribution of these factors to the overall morphological relationships of the endocranial base. The null hypothesis is represented by no effect of these variables on the morphological patterns.

MATERIALS AND METHODS

Sample and configuration

The sample consists of 149 crania, which were sectioned transversely in the upper vault to allow complete access to the endocranial cavity. The specimens were collected at the beginning of the 20th century in Italy from anatomical dissections and preparations (see Bruner et al., 2003b). Individuals with pathological traits, marked asymmetries or incomplete endocranial base were not included. The skulls were sexed following Acsadi and Nemeskeri (1970) as males ($N = 40$), undetermined ($N = 41$) and females ($N = 68$). A subsample was also selected including only males ($N = 40$) and females ($N = 50$) to test for sex differences.

The use of a posteriori sexed specimens introduces a sort of circularity in the analysis, being the method of sex-assessment largely based on allometric traits. This must be kept in mind when results are interpreted. Nonetheless, the selection of only full-males and full-females for the sex comparison should minimize this possible bias, unless the sexual morphological signal is extremely low.

A 3D configuration with 19 landmarks was used as a geometric model of the endocranial base (see Fig. 1). The planum sphenoidale was approached using the posteriormost border of the *lamina cribrosa* (PS1) and the posteriormost point of the anterior fossa (PS2). This point is midline between the bases of the anterior clinoid processes (generally linked by a bony ridge), anterior to the *tuberculum sellae*. The internal occipital protuberance is generally sampled at the most projecting point. If the protuberance is too flat, the landmark is sampled at the point most representative of the interhemispheric and cerebro-cerebellar separation. The anterior fossa width is represented by the most projecting point at the base of the third frontal circumvolution (approaching Broca's cap; AF) and by the point at which the posterior border of the anterior fossa fuses with the endocranial lateral wall (PF). This second landmark is located by following the ridge of the border of the sphenoid lesser wings through

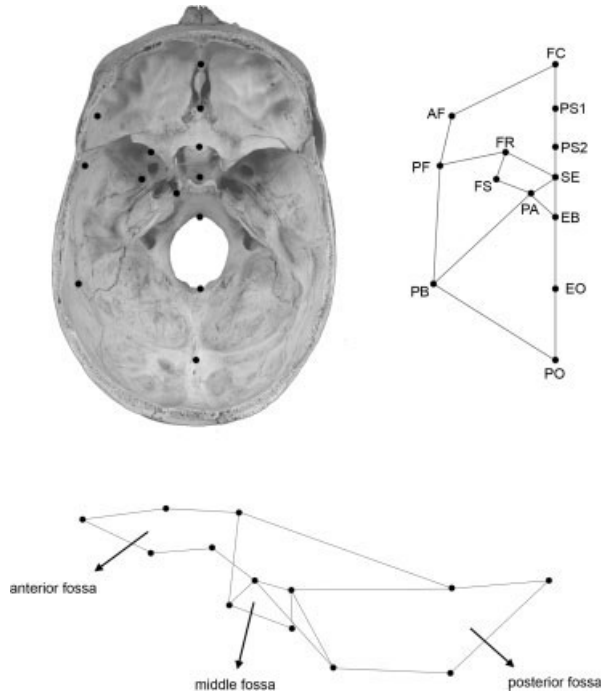


Fig. 1. The analysis was performed using a 3D 13-landmark configuration. The landmarks are shown on an endocranium (top left), together with the resulting geometric wireframe in superior view (top right) and left lateral view (bottom). Labels: AF, anterior frontal; EB, endobasion; EO, endopisthion; FC, foramen caecum; FR, foramen rotundum; FS, foramen spinosum; PA, pyramidal apex; PB, pyramidal base; PF, posterior frontal; PO, internal occipital protuberance; PS1, planum sphenoidum 1; PS2, planum sphenoidum 2; SE, sella (see text for details).

the frontal bone. This point is usually characterised by growth furrows (as longitudinal striae left on the lateral wall of the endocranium along the prolongation of the posterior margins of the anterior fossa) and by the passage of the middle meningeal artery. It is generally more easily recognised on the left side, since the right surface is more gradual and slightly displaced inferiorly. The pyramids are represented by their roots (where the posterior pyramidal ridge meets the temporo-occipital suture) and by their apexes (at the most projecting points contacting the sphenoid bone). The basal foramina (*foramen rotundum*, *foramen spinosum*) are sampled by approaching the centre of the aperture. According to the present sampling, the right *foramen rotundum* seems usually smaller, more anterior and more inferior than the left one.

Coordinates were sampled using a MicroScribe 3DX Digitizer (Immersion Corporation), with an accuracy of 0.23 mm.

Morphometrics

The statistical framework underlying the analysis of the integration versus modularity patterns is rather delicate, associated with constraints influencing both the computational approaches and the biological organization of the anatomical systems (Mitteroecker and Bookstein, 2007). Methods for considering the degree of integration and the covariation between morphological elements can be basically subdivided in heuristic, theoretical, and experimental ones. Heuristic analyses explore the numerical correlations within a given vari-

ability, while theoretical models test statistically a given expected network onto the observed actual data (see Chernoff and Magwene, 1999, for a detailed synthesis of different approaches). Experimental approaches are based on animal models (such as mice or pigs), providing direct changes in the genetic or biomechanical environments and considering the consequent phenotypic adjustments. The present paper deals with a heuristic description of morphospace structure, that is an eigenanalysis of the correlation/covariation matrix of the endocranial base geometry. The structure of morphospace is directly influenced by modularity and by the independence of the morphological elements (Rasskin-Guttman, 2005). In absence of integration, the multivariate space resulting from a Principal Component Analysis (PCA) must display a smooth and gradually-decreasing value of successive eigenvalues (Wagner, 1984). Such morphospace can be defined “quasi-hyperspheroidal,” suggesting that each single character change rather independently from the other characters. Conversely, if the whole structure is largely integrated, the variation will be mainly organized along few and determinant multivariate vectors, associated with specific covariational patterns. The more the integration, the more the “stretching” of the multivariate space along given components. In cases with one strong factor like generally happens with large allometric variation we can talk about “hyperellipsoidal” spaces. It is worth noting that in some eigenanalysis approaches the allometric component is set apart when the integration patterns are investigated (e.g., Hallgrímsson et al., 2007). Nonetheless, functional and structural size constraints represent the major source of integration between the anatomical elements. And, when it is assumed that the eigenvalues distribution reflects levels of morphological integration, allometry plays a pivotal role in the interpretation of the morphological network (Wagner, 1984).

Apart from eigenvalue analysis, other detailed statistical tools are currently used to describe the nature of the relationship between different morphological structures. For example, partial least-square analysis is extremely useful to quantify and describe the covariation between different anatomical blocks (e.g., Gunz and Harvati, 2007). Nonetheless, such techniques cannot be correctly applied in this case-study, because of the structural continuity between the parts involved. The three fossae share the same boundaries and, in this analysis, even the same landmarks. This introduces a clear bias in the statistical approach, and a “biological tautology” in terms of anatomy. Nonetheless, to perform a preliminary explorative analysis of the covariation between the three fossae, the correlation between the centroid sizes and the first principal components from each single fossa were computed. This can be useful to quantify the allometric component for each districts, and the relationships between their main morphological trends. Of course, future attempts to quantify the partial least-square correlation between the three fossae (with an opportune choice of geometric references) should be surely considered.

The coordinates were registered by using Procrustes superimposition, through translation to a common centroid, scaling to unitary centroid size and rotation by least squares fitting (Bookstein, 1991). Pairwise comparisons between average shapes were performed on the whole bilateral configuration, while multivariate statistics were computed using a 13-landmark unilateral (left side) configuration to increase the ratio between the number of specimens and the number of variables, to improve the statistical power. Multivariate statistics

(principal components analysis, multiple regression) were computed according to the principles of geometric morphometrics (see Zelditch et al., 2004). Pairwise comparisons and permutation tests were carried out using Morphueus et al. (Slice, 2000). Multivariate analyses were conducted using APS 2.41 (Penin, 2001) and Morphologica 2.4 (O'Higgins and Jones, 2006).

Six specimens were sampled twice and the pairs after superimposition were compared to quantify the average within-observer relative error. The error was calculated as the difference between the values of the corresponding specimens divided by the range of the variable. The mean error for the centroid size was 1.8%, while in the morphospace considering the first three principal components it was 3.5%. A cluster analysis was performed using the Procrustes distances, the residuals after superimposition and the first five principal components, by using PAST 1.71 (Hammer et al., 2001). The resampled individuals clustered together in each of these three approaches, suggesting that they are more similar to each other than to any other individual in the sample (data not shown). These data indicate good reliability of the sampling procedure.

The variation between males and females was also analysed by Euclidean Distance Matrix Analysis on the whole bilateral configuration in order to compare the overall form differences without using any criterion of data normalisation (Richtsmeier et al., 1992, 2002). The form difference matrix (FDM, showing all the ratios between the mean male and female values for any interlandmark distance) was used to analyse the distribution of the values, the average difference and the most important diameters (showing ratios exceeding one or two standard deviations from the average value). The average difference indicates the mean size variation, while the distribution of the values shows how the diameters depart (being longer or shorter) from isometric changes. Moreover, the distribution of the ratios for each landmark was considered (influential landmarks, see Cole and Richtsmeier, 1998) to obtain more information about the contribution of each point. In this analysis, bregma (ectocranial) was also included in the configuration to provide information on the neurocranial height. This landmark was not included in the previous analysis because it is rather separate from the rest of the configuration. This may introduce some bias when data are normalized with registration procedures like Procrustes superimposition.

The application of both Procrustes and coordinate-free methods is generally recommended in morphometrics, as complementary heuristic tools. Geometric morphometrics and thin-plate spline probably support a wider and more detailed array of explorative techniques. Nonetheless, the assumptions necessary to their actual computation (like the independent distribution of the residuals) are rarely encountered in real biological case-studies, and bias and artefacts could produce misleading conclusions (see Lele, 1993; Richtsmeier et al., 2002). At the same time, EDMA relies on a more limited set of analyses, but results refer to the actual differences between groups or distributions. Hence, these two approaches should be used simultaneously, to better explore the morphological relationships within a given biological variation (e.g., Lieberman et al., 2002; Hallgrímsson et al., 2004). It is also worth stressing that when the two approaches involve different results, this may be related to bias in one of them, but maybe also to different kind of information and signals captured by the different methods (e.g.,

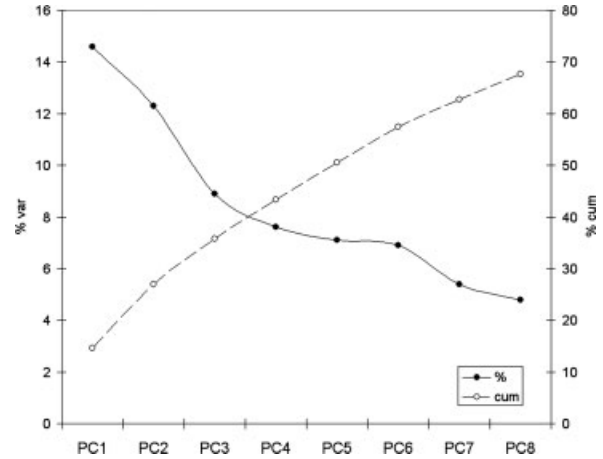


Fig. 2. Scree plot from the principal components analysis of the shape variables, showing the single percentage of variance expressed by the first eight components (filled dots) and the cumulative percentage (open dots).

relative vs. absolute differences, considering they work on shape and form respectively).

EDMA was computed with WinEdma (Cole, 2002). Univariate and bivariate statistics (distributions, correlations, Shapiro-Wilk t test, Mann-Whitney) were computed using PAST 1.71 (Hammer et al., 2001).

RESULTS

Multivariate statistics

The multivariate shape space does not show a marked polarization along largely determinant axes of covariation, since the variance is gradually explained through the sequence of the principal components (see Fig. 2). The first two components are slightly separated from the following ones (in terms of variance explained), and a further step in the scree plot can be recognized after the sixth component. However, the first six shape axes summarize only 57% of the shape information.

The first component explains just 14.6% of the total variance. According to this first principal component of shape, the posterior fossa becomes deeper (mostly by lengthening of the distance between endopisthion and the internal occipital protuberance, plus a relative lengthening of the clivus), while the anterior fossa tilts upward (Fig. 3a). At the same time, the middle fossa flattens vertically, while the sphenoid height (between sella and *planum sphenoidium*) increases. Conversely, the opposite pole of the multivariate axis includes endocrania with a flattened posterior fossa (shorter cerebellar height), anteriorly flexed anterior fossa, more curved midsagittal profile and deeper middle fossa. It is noteworthy that the curvature of the lateral profile is mainly determined by the flexion/retroflexion of the anterior district as a whole, rotating at the sella. In the coronal plane, the lengthening of the posterior fossa and upward tilting of the anterior fossa are associated with a relative narrowing of the endocranial base, more marked anteriorly than at the pyramidal bases.

The second principal component (12% of the total variance) is associated with vertical flattening and posterior stretching of the posterior fossa, vertical flattening of the midsagittal cranial base at the sella and backward shifting of the posterior lateral border of the anterior fossa

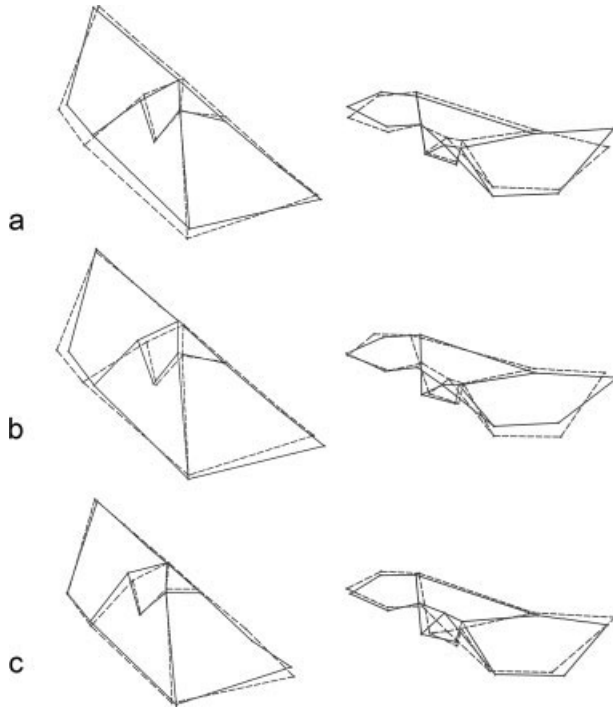


Fig. 3. Shape variation along multivariate axes in superior (left) and left lateral (right) views (**a**: PC1; **b**: PC2; **c**: allometric vector). The superior view is rotated for graphical purposes (the anterior fossa is on the top left, posterior fossa on the bottom right).

(Fig. 3b). In the coronal plane, this pattern is also associated with narrowing of the anterior fossa. At the opposite extreme are endocrania with relatively shorter and deeper posterior fossa, flexion at the sella, and wider and shorter frontal lobes.

There are no differences in the distribution of the sexes along these two principal axes of variation.

A multiple regression of the centroid size onto the principal components shows that the allometric variation is scattered through many different axes. The first principal component is not significantly related to size ($r = -0.14$; $P = 0.10$). That is, the allometric vector is not particularly associated with a principal pattern of covariation, but rather is diagonal (transverse) through the morphospace. The multiple coefficient of determination (R^2) is 0.41 ($P < 0.002$). When adjusted for the degree of freedom to account for random correlation between the dependent and independent variables, this value is reduced to 0.25. This allometric component involves a definite lengthening and heightening of the clivus from smaller to larger size via elevation of the sella (with related deepening of the posterior fossa) and antero-posterior shortening of the frontal fossa (with marked forward shifting of the foramen rotundum) associated with respective lengthening of the middle fossa (Fig. 3c). It is noteworthy that the allometric vector also includes an asymmetrical shifting of the internal occipital protuberance. Although this deformation may simply be a bias of the unilateral configuration, it is not detected in the other multivariate axes. The asymmetry matches the well-known left occipital dominance of the human brain. If confirmed, it means that this trait is size-related, in that it increases in proportion to brain size. Cerebral asymmetries are not the subject of the present paper

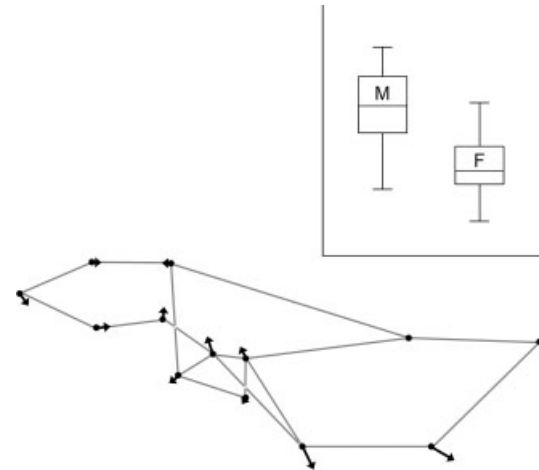


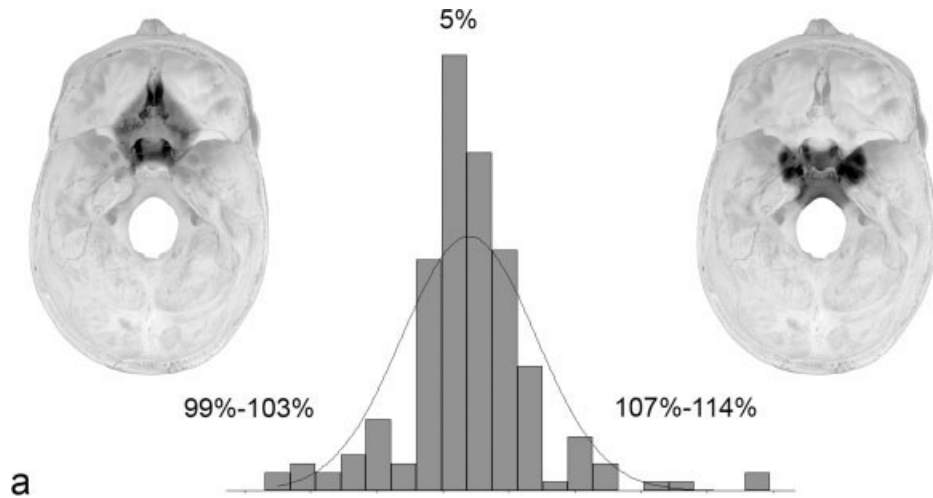
Fig. 4. Shape and size differences between the male and female groups. The arrows show the vectorial difference after Procrustes superimposition between the female mean shape and the male mean shape (magnified $\times 4$). Only the left lateral view is shown, since the superior view did not display any significant change except a very small frontal widening in the male configuration. The boxplots show the distribution (median, interquartile, range) of the centroid size in males (M) and females (F). The undetermined specimens (not shown) display an intermediate figure.

and must be analyzed within a proper statistical framework. Accordingly, this variation along the allometric vector will not be discussed further. Nonetheless, a possible relationship between brain size and degree of hemispheric asymmetry merits further attention.

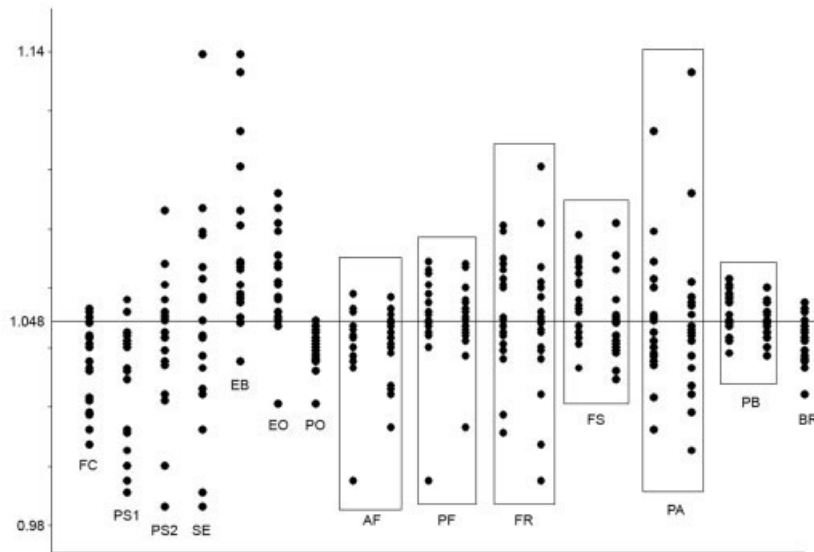
Comparing the three fossae through separated configurations, results differ when size and shape are considered. The centroid sizes of the three districts are correlated, even if only to a minor degree ($R^2 = 0.37$ for contiguous fossae, 0.14 between the anterior and posterior fossae). Only the anterior fossa shows a significant (although extremely feeble) correlation with its centroid size ($R^2 = 0.03$). Comparing the first principal axes of covariation computed independently for the three areas, only the anterior and middle fossae show a significant shape correlation, although again the figure is rather low ($R^2 = 0.16$). Once more it must be taken into account that this analysis is very preliminary, being the single configurations based on few landmarks each, and sharing their boundaries with consequent redundancy of the dataset.

Male versus female: Superimposition and centroid size

The male group shows a larger centroid size than the female one ($P < 0.0001$, using both parametric and non-parametric approaches). The ratio between the mean male and female centroid sizes is 1.048, meaning that the former is about 5% larger than the latter. A permutation test on the Procrustes distances using the male and female subsamples shows a significant shape difference (1000 permutations, $P = 0.016$). The main differences in the male mean are associated with the longitudinal axis and base flexion: the clivus lengthens, the cranial base angle flexes, the anterior fossa displays an antero-posterior relative shortening and the posterior fossa becomes deeper (see Fig. 4).



a



b

Fig. 5. (a) Distribution of the ratios from the male/female Form Difference Matrix (histogram), with the expected normal distribution (curve). The mean value and those exceeding one standard deviation are reported. The areas mainly involved in positive (right) or negative (left) allometric differences are shaded on the endocranium (see Fig. 6 for a detailed report of the diameters). (b) Influential landmarks: the values from each landmark are reported to account for their specific distribution. Paired landmarks are grouped. Labels as in Fig. 1 (BR: bregma).

Male versus female: Euclidean distance matrix analysis

The ratios between the male and female Euclidean distance matrices are not distributed normally (Shapiro-Wilk test: $n = 190$, $W = 0.9156$, $P < 0.0001$), since the curve is based on reduced variation and small tails (Fig. 5a). The mean and median values coincide at 1.048, meaning that the male diameters are on average about 5% larger than the female ones. This value is in perfect agreement with the results for the centroid size. The male values range from a minimum of 99% to a maximum of 114% of those of the females. Figure 5b shows the influential landmarks involved in the distribution of the interlandmark comparison and their average values. Landmarks involved in the smallest male diameters (when compared with the mean sex difference) are the *foramen caecum* and the *anterior planum sphenoidum*, followed by low values for the *posterior planum sphenoidum*, internal occipital protuberance, anterior frontal and bregma. Landmarks involved in the largest male diameters are endobasion and endopisthion. Figure 6

shows the interlandmark distances that exceed one and two standard deviations from the mean distribution in the male/female comparison. The male form is characterized by antero-posterior shortening of the anterior fossa (mostly at its posterior part, associated with the sphenoid) and of the cerebellar length (from endopisthion to internal occipital protuberance), shortening of the endocranial height and enlargement of the structures associated with the clivus (middle fossa, foramen magnum, basal foramina).

DISCUSSION

Integration and functional craniology

The structural and functional constraints within a biological model (i.e., a species) directly influence the evolutionary patterns, allowing some changes and hampering some others. Statistically, it means that some evolutionary directions are more probable than others. Functional and developmental relationships are supposed to lead towards genetic integration, which in turns leads to evo-

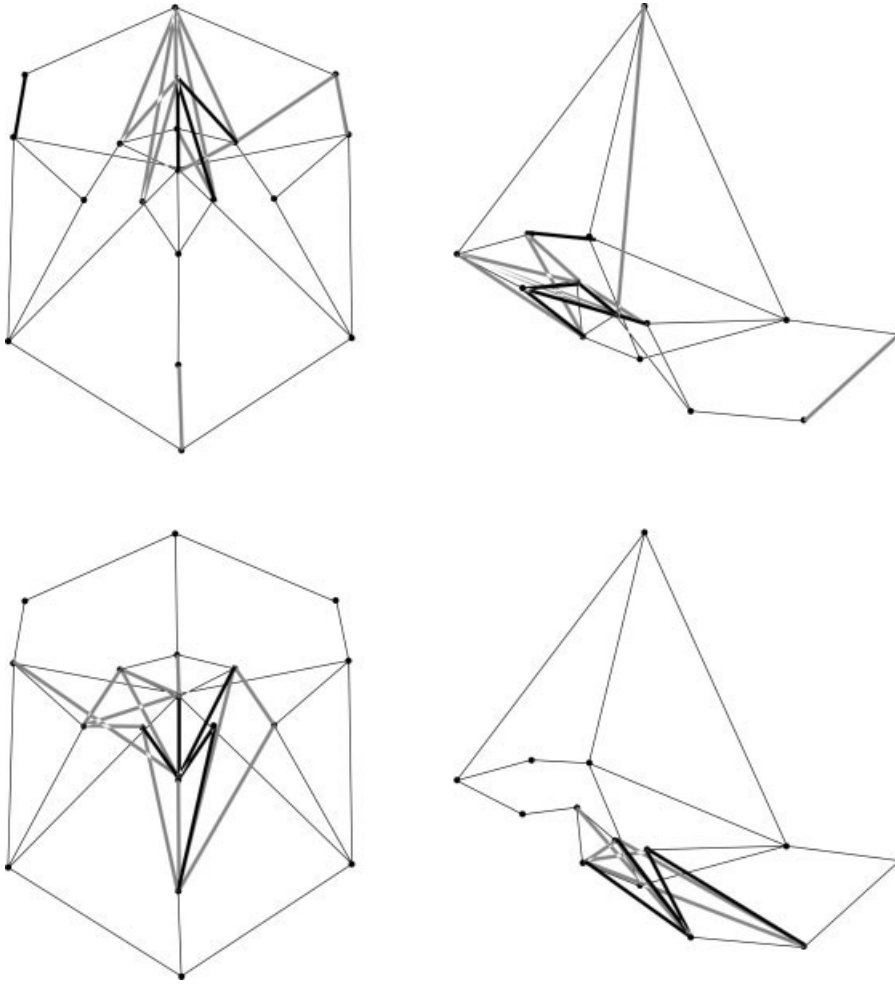


Fig. 6. The diameters exceeding one (bold gray) or two (bold black) standard deviations from the mean male/female EDMA comparison are reported on the wireframe, in superior (left) and left lateral (right) views. (a) diameters showing relative reduction (<103%); (b) diameters showing relative increase (>107%). N.B. the wireframe is slightly changed to accommodate the inclusion of bregma.

lutionary integration (Cheverud, 1996). Hence, evolution can be interpreted not as changes in morphology *per se*, but in terms of changes in the relationship within the anatomical system (Ackermann, 2002, 2005). Accordingly, the knowledge of the intra-specific patterns of covariation is the first step to investigate the nature of the evolutionary substrata. In the analytical framework of integration and modularity, theoretical models generally provide a more solid statistical context, but heuristic approaches are very useful to explore the morphological integration within complex and poorly known anatomical systems (Chernoff and Magwene, 1999). And, although modularity often requires a process-oriented perspective (Schlosser, 2004), morphometrics deals mostly with structural units integrated by developmental and functional constraints (Klingenberg, 2002). The endocranial base is the final result of a complex morphogenetic process, based on polyphasic and multifactorial dynamics and characterized by interactions between genetic influences, functional relationships, and structural constraints (Lieberman et al., 2000a). Its anatomy is organized with large sets of related features, suggesting that different morphological traits must be regarded as single phylogenetic characters for the purposes of cladistic studies (Strait, 2001). Unfortunately, data on endocranial variation in modern humans are often scarce and scattered, hampering robust knowledge and interpretation of the morphological characters. The aim of our

study is then to quantify and describe the main patterns of cohesion within the variation of the human endocranial base, to provide a part of such basic information.

The configuration used in the analysis was chosen to provide a useful geometric wireframe and biologically meaningful model to describe the spatial relationship between the anterior, middle and posterior fossae. These areas are in close contact with the prefrontal cortical volumes (anterior fossa), part of the temporal lobes (middle fossa), subcortical structures (clivus), and cerebellar lobes (posterior fossa), as well as all the vascular systems interposed between the brain and the cranial vault, which are separated by the physical and physiological interface of the meningeal layers. Thus, changes in morphology must be interpreted according to the functional adaptations and structural constraints of these contacting and reciprocally-influencing components.

The structure of the shape space resulting from the principal components analysis of endocranial geometry is only faintly polarized by dominant axes of covariation. The first two principal components are just slightly more important than the following ones in terms of the variation explained. Together, they summarize a quite small proportion of the morphological variability (27%). If we assume that the structure of the morphospace (i.e., the eigenvalues distribution) reveals the degree of integration, therefore the endocranial base morphology shows only minor levels of reciprocal influence between the

three endocranial districts. That is, intra-specific differences in one of the three fossae are only slightly associated with differences in the others, and knowledge of the morphology of one area can hardly predict the morphology of another one. According to this analysis the correlation between the principal patterns of covariation of the three areas is rather low, and limited to a small integration between the anterior and middle fossae. Small levels of integration means that within the anatomical system common factors have a limited influence on the overall morphology, while local factors have a major role. We can therefore hypothesise that if the three endocranial areas are relatively free to arrange themselves reciprocally, certain independence can be assumed not only during morphogenesis but also during phylogeny. As already mentioned, the anterior districts are directly in contact with the upper facial structures and this contact involves many morphogenetic limits. The face rotates downward while the frontal lobes enlarge (Enlow, 1990), and the browridge accounts for a certain percentage of this adjustment working as an interface (Lieberman, 2000). Accordingly, many frontal changes during human evolution probably involved the relationship between the neurocranial and splanchnocranial axes instead of specific morphological variations (Bruner and Manzi, 2005, 2007). It is worth noting that nonallometric changes in the face versus braincase position probably account for about 11% of the human cranial variation, (Zollikofer and Ponce de León, 2002).

With regard to the temporal fossa, the biomechanical influence of the underlying mandibular ramus is the main source of morphogenetic variation (Bastir and Rosas, 2005): this influence acts rather independently upon the midsagittal basal morphology, which in turn is associated with fine regulation of the whole cranial architecture (Lieberman et al., 2000a) and with its direct contact with the medulla and the subcortical brain structures (Strait, 1999).

Finally, the morphology of the posterior fossa is directly associated with the cerebellar lobes, but is probably integrated with the upper vault via the interaction with the parietal bones (Gunz and Harvati, 2007). Therefore, it is not surprising that the morphology of the endocranial base shows only weak patterns of covariation, as suggested in the present analysis.

Nonetheless, low levels of integration do not mean any integration at all. Integration and modularity are hierarchical concepts referring to larger or smaller degrees of relationship, and any anatomical structure will display certain isolation or a certain linkage with all the others. The first concept is based on the degree of continuity ("grayscale" approach), the second is based on discontinuity ("black and white" approach). Although not so dominant, the two main patterns of covariation showed in the present study should be related to some underlying structural or functional relationships. This is particularly true in intra-specific analysis, being the resulting morphological vectors based on normal distributions associated with the actual random variation of the specimens, and not with adaptations (Martin and Barbour, 1989).

According to the present results, much variation is loaded on the midsagittal than onto the transversal (latero-lateral) plane, which in contrast is rather stable after Procrustes registration. The cranial base width is considered scarcely variable because of its strong influence on the overall cranial architecture, limiting the pos-

sibility of large differences (Lieberman et al., 2000b), and the present data support further this evidence.

The first axis of covariance described in this analysis is associated with a large and local change of the posterior fossa through shortening/lengthening of the lower occipital crest, while the rest of the endocranium seems to undergo only consequent adjustments. The anterior fossa tilts upward as a whole without any significant specific change. The middle fossa becomes relatively flattened, meaning that it does not follow the heightening of the rest of the endocranial base. The first process (tilting of the anterior fossa) can be related to the structural link between the internal occipital protuberance and the *crista galli*, exerted through the *falx cerebri*. This connective layer is considered the major determinant of endocranial tension, mainly influencing the upper vault shape (Moss and Young, 1960). Thus, if this is true any change at one attachment (the occipital protuberance) must be transmitted to the other (the *crista galli*). This rotation of the *planum sphenoidale* changes the relationship between its anterior and posterior components, possibly explaining the difficulties in finding common metrics to analyze these areas (McCarthy, 2001). The position and morphology of the *tuberculum sellae* may be particularly important within this context, meriting further attention. Of course, the principal components of variation of the anterior and posterior fossae show no correlation in the present study but, apart of possible morphological relationships included in the rest of the shape variance, it must once more stressed that the spatial position (topology) more than the shape itself of the anterior fossa could be influenced by the anatomy of the posterior one. That is, the rotation of the anterior plane not necessarily involves a change in its overall morphology. Such rotation of the anterior fossa seems to take place in the area between the sella and the posterior edge of the *planum sphenoidale*. The most important morphogenetic hinge at that level is the midsphenoidal synchondroses (Jeffery and Spoor, 2002, 2004). Considering that in humans this structure is the first to fuse in the anterior fossa, this major arrangement has an effect no later than the late foetal period, thus largely characterizing the subsequent morphogenetic pattern.

In contrast with the large variations of the posterior areas, and the topological arrangements of the anterior district, the lateral morphology of the middle fossa shows certain constancy. Apart from the already mentioned constraints for the latero-lateral variation, the stability of the middle fossa must take into account the relationship with the mandibular ramus (Bastir et al., 2004), which hampers marked phenotypic rearrangements. The independence between its midsagittal and lateral components is further evidenced in the present data, being the lengthening of the former not associated with a similar stretching of the latter.

In sum, it is hypothesized that a primary source of variation of the endocranial base is represented by the morphology of the posterior areas, possibly involving adjustments in the position of the anterior fossa through vectorial strains exerted by hard (clivus) and soft (*falx cerebri*) elements. Interestingly, the position and enlargement of the posterior fossa is mainly determined by the relationship between the supratentorial and infratentorial cerebral structures, related to a negative allometric pattern for the cerebellar volumes (Jeffery, 2002). Furthermore, it is interesting that these endocranial surfaces display a different pattern of osteoblast/osteoclast

organisation (growth fields) in humans compared with non-human primates (Lieberman et al., 2000a).

Remarkably, also the second component is associated mainly with changes in the posterior fossa, which becomes flatter or deeper but without strong differences in the length of the occipital ridge. Interestingly, while the posterior fossa becomes longer and flatter, the anterior one becomes longer and narrower. During the morphogenesis the deepening of the posterior fossa is mainly related to the clivus lengthening and to the dynamics of the occipito-mastoid suture, which fuses very late during the human life-cycle. In terms of general neurocranial architecture, this pattern matches the dichotomy between brachycephalic and dolicocephalic crania.

Moss (1959) hypothesized that relevant dysmorphologies like craniosynostosis could be the result of a spatial alteration between the cranial base and the connective endocranial tensors of the dura mater. Sagittal synostosis were related to altered tensile stress in the *falx cerebri* versus ethmoid relationships, while coronal synostosis were related to altered tensile stress between the dura attachment at the lesser wings of the sphenoid because of changes in the sphenoid embryological process. These redistributions of the tensile forces and growth vector should induce histological (osteogenic) responses, leading to the altered balance in growth and development. Interestingly, the first axis of covariation described in the present study matches the pattern described by Moss in the first case: tilting of the anterior fossa, lordosis of the orbital roof, midline kyphosis, rotation of the posterior fossa. Hence, the pattern supposed to be associated with the main vectorial alteration of the *crista galli* and *falx cerebri* structural arrangements, is also the main pattern of integration of the endocranial base. Apart from stressing one more the relevance of the *falx cerebri* as morphogenetic determinant of the human neurocranium, and the importance of a functional craniology approach, this correspondence leads to two considerations. First, the connective tensors of the neural capsule are the structures which provide the major integration between the endocranial elements, redistributing the growth forces through the different surfaces. Second, pathologic or subpathologic alterations associated with unbalanced size versus shape changes (like hypo- or hyperostotic traits) may be the result of overexpressed normal structural patterns. It is also interesting that pathologies like craniosynostoses are not associated with brachycephalic versus dolicocephalic figures, which in turns are better described by the second component of covariation of the endocranial (this study) and ectocranial (Zollikofer and Ponce de León, 2002) morphology, which vector does not display any supposed pathological patterns.

Allometry and sexual differences

A further finding suggesting a small degree of integration in the endocranial base is the low and scattered allometric component. Size accounts for only 25% of the shape variation, meaning that brain size influences the cranial base morphology only for one fourth of its morphology. The size of the three fossae is quite correlated (about 37% for the contiguous areas), but the allometric component in each fossa is absent or negligible. Considering the whole configuration, larger endocranial bases have longer and taller clivus, a relatively shorter anterior fossa, and lengthening of the middle fossa. This pat-

tern agrees with the ontogenetic sequences leading to the mature phenotype: the morphogenesis of the frontal area is mainly associated with the midsphenoidal, spheno-ethmoidal, and fronto-ethmoidal synchondroses, which mature with the development of the frontal lobes at about 5–6 years, and growth maturation follows a superior-inferior gradient, starting with the vault and finishing with the mandibular structures and splanchnocranial areas, which reach the last stages of maturation after 16–18 years (Lieberman et al., 2000a; Jeffery and Spoor, 2002; Bastir et al., 2006). Hence, the more the endocranial base enlarges, the more the dimensions of the anterior areas will be exceeded by the heightening of the clivus, lengthening of the middle fossa, and deepening of the posterior fossa.

The comparison of the male and female configurations suggests that allometry explains a large percentage of the sex differences. The lengthening and upward rotation of the clivus in males has already been described taking into account the overall ectocranial variation (Rosas and Bastir, 2002). Analysis of the Euclidean distances adds to this topic. The posterior area of the *planum sphenoidale* is shorter in males, with an estimated mean value of 99% of the female figure. This is clearly associated with the fusion of the midsphenoidal and spheno-ethmoidal synchondroses (Jeffery and Spoor, 2002), which close very early during ontogeny and limit the allometric/sex variation in these areas. The rest of the longitudinal diameters of the anterior fossa follow because of the early maturation of the frontal areas. Conversely, many of the diameters involved in the middle fossa lengthen, with the clivus being 9–14% longer in males than in females. Two points must be stressed. First, the cerebellar length (as measured by the lower occipital crest) is relatively shorter in males, indicating that the deeper posterior fossa is closely associated with the lengthening of the clivus and not with the lengthening of the posterior areas. Lengthening of the clivus, along with relative stability of the length of the occipital crest, necessarily involves a structural rotation of the posterior fossa onto the rest of the endocranial area. Second, the skull height (as shown by the bregma-sella chord) is also relatively reduced in males, suggesting that the vertical elevation of the endocranium is associated with the development of the clivus more than with heightening of the vault. Hence, the positive allometry of the vertical metrics of the skull is related more to the cranial base differences than to the fronto-parietal structures.

As a precautionary note, it must be remembered that the specimens were sexed *a posteriori* using classical morphological indexes. Therefore, they do not represent the mean male and female figures but rather the average of the well-diagnosable phenotypes. This should not be a bias in the male-female comparison, since it influences the mean geometry of the group but not the direction of the differences. On the other hand, this may hamper a reliable separation of the allometric and sexual components. The assessment of sex in cranial remains is largely based on the degree of expression of specific traits (i.e., their general size) or their expression in terms of overproduction of bones (hyperostosis). In both cases, this could bias the variation, leading to a size-biased sex assessment of the variation and thus confounding the two factors. Nonetheless, considering also the limited allometric contribution, these data can be anyway useful to delineate some principal sources of sex differences.

CONCLUSIONS

In 1863, Thomas Henry Huxley, discussing the relationship between humans and nature, suggested that cranial base morphology could represent the principal source of structural information when dealing with the functional aspects of cranial morphogenesis and evolution. His statement followed a basic principle of ontogenetic hierarchy, in which the structures maturing earlier influence the structures maturing later. This approach was pioneering and is still a major law in functional craniology. Even more presciently, he suggested using the cranial base to superimpose the rest of the cranial morphology onto a common system of coordinates in order to compare forms. Almost 150 years after Huxley, we are increasingly recognizing the importance of the cranial base as a common ground for the morphogenesis and evolution of the cranium as a whole. Nonetheless, our knowledge relating to this topic is still poor, and much information is incomplete and controversial.

The present article deals with the patterns of covariation of the three endocranial fossae in modern humans. The structure of the spatial organization suggests a low level of integration among these areas, which are likely to be more involved in changes concerning local functional contexts. This is particularly interesting considering the tendency of modularized anatomical systems to lead to mosaic evolution, as often described in hominid phylogeny (Stringer, 2002). The posterior fossa is the source of a large proportion of the present endocranial variation, both directly and through some structural consequences. The main patterns of covariation evidence once more the importance of the connective tensors of the dura mater as principal source of structural integration between the endocranial elements. Morphogenetic dysfunctions can be related to the over-expression of these normal growth vectors.

Overall allometric constraints are limited, mainly associated with the early maturation of the anterior fossa and later maturation of the middle structures, which are related to the splanchnocranial system. Sex differences are largely allometric. Of course, with such low correlation with size, it is very difficult to assess nonallometric differences between males and females, although perhaps it could be done with very large sample sizes or anatomically localized geometric models. The study of endocranial variation is hampered by the limited availability of true homologous points and the lack of knowledge about the inter-population variation of many morphological traits. Clearly, many biomedical and anatomical issues based on current living variability must be investigated and resolved before providing robust hypotheses on the evolutionary frameworks.

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