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Evolution of the Brain in Humans – Paleoneurology

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Definition

The evolution of the human brain from hominids existing perhaps 3–5 MYA (million years ago) to the present has been a mosaic process of size increases intercalated with episodes of ►reorganization of the cerebral cortex. The fossil evidence shows that reorganization preceded large-scale brain size increase, whether ►allometric or not, by about 2–3 MYA and again around 1 MYA, involving a reduction of primary visual cortex and cerebral asymmetries, including those within Broca's region. These changes were followed by nearly a tripling of brain size.

Characteristics

What is Paleoneurology?

►Paleoneurology is the study of the fossil evidence for brain evolution and is, at present, the only direct line of evidence as to how different animals' brains have evolved through time. Paleoneurology is not a new branch of paleontological study as earlier publications go back to those of Oken, who found petrified mud in a crocodilian skull in 1819, as mentioned by Owen in 1841. Tilly Edinger wrote a valuable monograph on the evolution of the horse brain and her 1929 [1] and 1949 [2] papers on the history of paleoneurology are an important critique of comparative neurology's mistaken notions of human evolution. Kochetkova's [3] treatise

on ►endocasts is another valuable source, both for history and methods, as well as descriptions of some of the fossil hominids.

What are Endocasts?

The objects studied are called endocasts. These are simply casts that are made from the inside table of bone of crania. It is particularly important to realize that the endocasts are just that; they are *not* casts of brains, because in life, the brain is surrounded by three meningeal layers, the dura mater, arachnoid tissue and cerebrospinal fluid and lastly the pia mater, a thin investing tissue directly overlying the brain. With death, these tissues as well as the brain dissolve, leaving a cranium that will in time fossilize.

How does Paleoneurology Differ from Comparative Neurology?

Comparative neuroscience studies the brains of living animal species and is a particularly rich source of data from a microscopic level to that of whole brains. These data are essential to the understanding of the relationships between structure, function and behavior. In other words, how the brain varies in terms of its cellular makeup, cytoarchitecture, fiber systems, neural nuclei, axons and dendrites and the supporting matrix of glial cells, neurotransmitters and neuroreceptors can hopefully be related to variability of behavior. Paleoneurology is correspondingly exceedingly poor in data, as only the surface features of the once living and pulsating brain can be observed if – and only if – they are imprinted onto the internal table of bone. The drawback of comparative studies is that each species is currently an end product of its own separate line of evolution and therefore cannot provide any real time depth to past evolutionary events that affected the brain. Nevertheless, without comparative studies, there would be no possibility of correctly identifying and interpreting those surface features of the endocast that may have changed during evolutionary time from species to species.

How are Endocasts Made?

First, it is necessary to appreciate that the data obtainable from endocasts depend on the completeness and quality of the endocast and this will be affected by how the endocast has been made. Some endocasts are natural, i.e., made by fine sediments collecting (through the foramina of the cranium) in the cranium of the deceased animal and with time being compacted and eventually turned to stone. Some of these endocasts can obtain an almost jewel-like quality. At least three endocasts of our ancestral hominid australopithecine line of 2–4 MYA were made in this way (e.g., Taung, Sts 60, Sk 1585, Type 2; see [4] for descriptions). Endocasts can also be man-made, by directly covering the surface of the internal bony table with a casting medium, such as latex rubber or various forms of silicon rubber (Figs. 1 and 2). Endocasts can also be made from the data collected during CT scans, which can be rendered as a "virtual" endocast on the computer. This data set, in turn, can be sent to a machine that will literally carve out an endocast from a block of plastic, producing what is called a stereolithic endocast. For example, the recent "hobbit" endocast of the putative *Homo floresiensis* hominid was made this way [5], as was the virtual endocast for Saccopastore, a Neandertal from Italy [6]. Increasingly, CT scans are used for endocranial analyses.

What Data can Endocasts Provide?

Overall Brain Volume

The most useful data gleaned from endocasts is the size of the once living brain, usually determined by either water displacement of the endocast or by a computer algorithm which simply adds sections taken from a CT scan of either the endocast or the cranium. Endocast volumes are somewhat larger, by about 8–12%, than the actual once-living brain, as the endocranial volume (ECV) includes meninges, cerebral fluid (including cisternae) and cranial nerves. Fossil hominids, of which we are the present-day terminal end products, had brain sizes varying from roughly 385 ml to 1700 ml, while the average for our own species is about 1400 ml. If the body weight is known from estimates made from measuring postcranial bones, then it is possible to calculate some derived statistics that may have some epistemological value. For example, "relative brain size" (RBS) would be the weight of the brain divided by body weight. Modern humans have an RBS of roughly 2%, and this value is neither the smallest nor largest in the animal kingdom or even in the primate order. It is also possible, when body and brain sizes are known, to calculate a statistic called the "encephalization quotient" (EQ). An EQ's value depends on the database used to make the calculation. For example, equations derived from two different data sets appear below, with the corresponding modern human value:

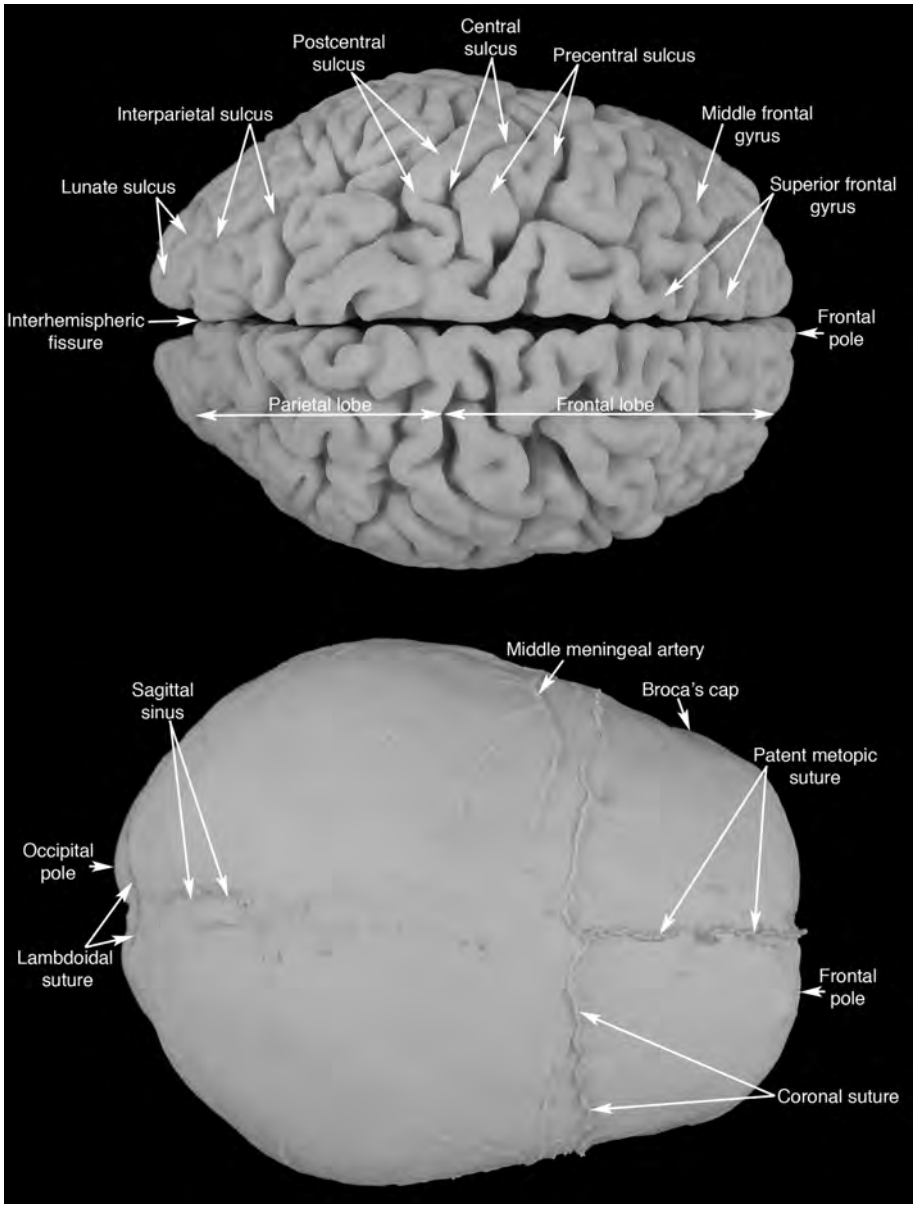
EQ(1) = Brain weight (of any species)/0.12 × Body weight $^{0.66}$ [7]

The human value is 6.91, 4.02 for chimpanzee and 1.8 for gorilla.

EQ(2) = Brain weight/1.0 Body weight $^{0.64}$

This is the "homocentric" equation of Holloway and Post [8], which then expresses each EQ as a direct percentage of the human value, taken as 100%. The chimpanzee EQ is 39.5% and the gorilla 19.1%.

While these values appear very different, the relative position within the primate order is almost static, the rank order correlation being about 0.9 [8].



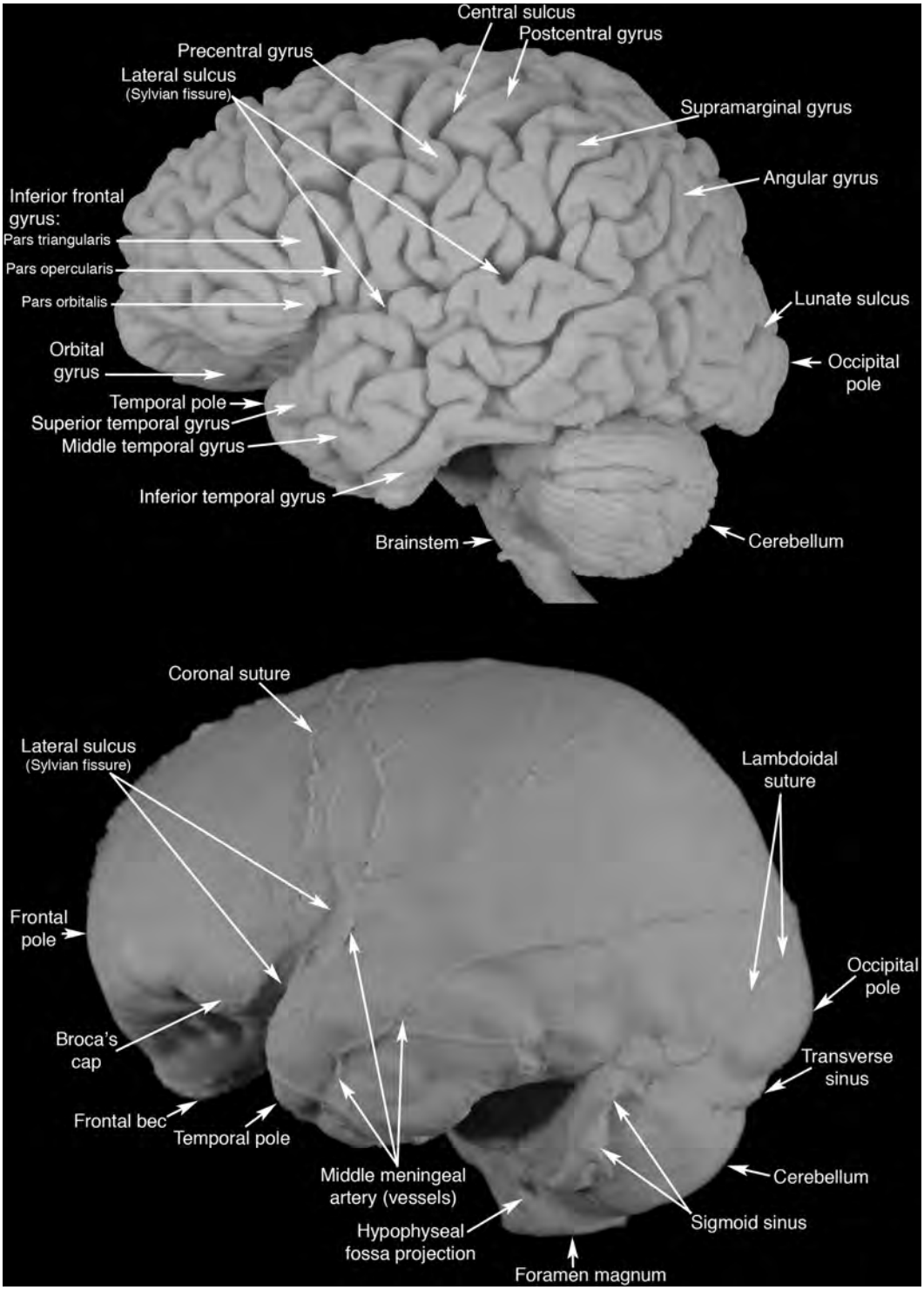
Evolution of the Brain in Humans – Paleoneurology. Figure 1 A dorsal view of a cast of a modern human brain and its accompanying endocast. Note that the left occipital lobe is wider and projects more posteriorly than the right side and that the right frontal lobe width is slightly larger than the left. This is typical of the torque petalial pattern associated with right-handedness.

Relative Sizes of Lobes

Endocasts provide a very rough idea of the relative sizes of the lobes of the cerebral cortex. It is rough because all the sulci on a primate endocast, particularly a hominid one, cannot be seen. It is thus not possible to find the central sulcus accurately in order to delineate the frontal lobe or to find the precentral sulcus to delineate the prefrontal lobe.

Convolution Pattern

Endocasts do provide glimpses of the underlying ►convolution (gyri and sulci) pattern, depending both upon the state of preservation of the endocast and the faithfulness of convolutional imprinting on the internal table of bone. Alas, this is seldom complete and such incompleteness often leads to controversy, at least within paleoanthropology. For example, the Taung



Evolution of the Brain in Humans – Paleoneurology. Figure 2 The same brain and endocast in lateral view, showing the difference in details between a cast of the brain and its endocast.

endocast (natural), found with the partial cranium and jaw of *Australopithecus africanus* and described by Raymond Dart in 1925, showed a depression taken by Dart to represent the lunate sulcus or what would have been the approximate anterior limit of primary visual cortex (V1). This appeared to Dart to be in a relatively posterior position, signaling that, even in this early representative of hominids, the brain was organized

differently from that of any ape and was moving toward a more human-like condition (Fig. 3). This depression was in the same region as the lambdoid suture and thus could not be definitively recognized. Putting a lunate in the position expected of an ape such as the chimpanzee or gorilla would violate the existing morphology and the placement of the lunate sulcus even anterior to this would result in a position comparable to an Old World monkey. It was not until 2005 that a description of a posteriorly-placed lunate on the Stw 505 *A. africanus* specimen was made by Holloway et al. [4], effectively settling this controversial issue as to whether the hominid brain had to enlarge before cortical reorganization took place.

Asymmetry

Endocasts, depending on completeness (both halves necessary) and relative lack of distortion, show varying degrees of asymmetry of the once throbbing cerebral hemispheres and these asymmetries become interesting for their relationship to cerebral specializations, including possible handedness and language. For example, when the endocasts show a bulging left hemispheric projection of the occipital lobe posteriorly (and often laterally), combined with a wider right frontal bulge (these bulges are called petalias), this pattern matches what we know from modern human endocasts and radiography to be the result of a torque-like growth pattern. [see 9–11]. Modern humans also show asymmetries in the Broca's cap regions of the third inferior convolution of the frontal cortex. These asymmetries probably differ by handedness as well as by unknown functional relationships. Such asymmetries are present in Neandertals and even earlier on some *Homo erectus* specimens (indeed they are clear on the 1.8 million year-old *Homo rudolfensis* specimen, KNM-ER 1470). They cannot prove that this or that hominid had language, but if these asymmetries are homologous to those found in modern humans, well, why not? What is curious is that scientists speculating about the origins of language never bother to look at the paleoneurological evidence [e.g., 12].

Statistical Analyses

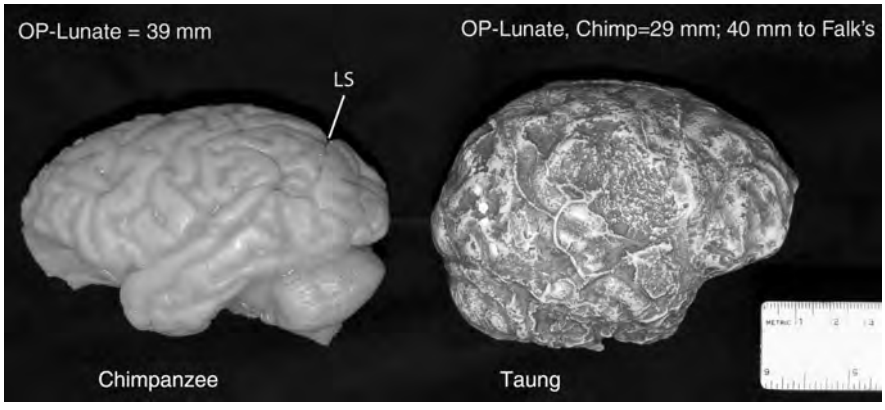
Endocasts have shapes and are thus amenable to measurements that can be taken with calipers or from CT scans. Such data sets can then be statistically analyzed using a variety of multivariate statistical techniques.

Blood Supply Patterns

The blood supplies to the meninges show different patterns in different hominid taxa and thus might be useful, in some cases, for identifying hominid phyletic lines [13].

Human Brain Evolution as Seen from Paleoneurology

It is important to keep in mind that roughly 4 MY of evolutionary time has existed for hominid evolution to date and that the number of brain endocasts for hominids that provide reliable data either for size or cerebral organization is very small, numbering no more than about 160, including modern *Homo sapiens* from the end of the Pleistocene (See Holloway et al. [4] Appendix, for a complete listing up to that date). In essence, there is one brain endocast for every 235,000+ years of evolutionary time. Nevertheless, we believe we



Evolution of the Brain in Humans – Paleoneurology. Figure 3 Lateral views of a chimpanzee brain cast, and the hominid Taung *Australopithecus africanus* endocast. The lunate sulcus (LS) of the chimpanzee lies much farther anteriorly than on the Taung endocast. The dots on the Taung endocast show where a typical chimpanzee LS would lie, if Taung showed a typical ape-like pattern. The distance from the occipital pole (OP) to the LS is roughly 30–40 mm on chimpanzee brains. The measurement from OP to Falk's LS line on the Taung endocast is about 40 mm. Both the typical chimpanzee LS placement and that of Falk violate the sulcus morphology on the Taung endocast.

can perceive a mosaic of brain evolutionary events that involve size increases interspersed with elements of cerebral organization, as shown in Tables 1, 2 and 3. At least two important reorganizational events occurred rather early in hominid evolution, (i) a reduction in the relative volume of primary visual striate cortex (PVC, area 17 of Brodmann), which occurred early in australopithecine taxa, perhaps as early as 3.5 MYA and (ii) a configuration of Broca's region (Brodmann areas 44, 45, and 47) that appears human-like rather than ape-like by about 1.8 MYA. At roughly this same time, cerebral asymmetries, as discussed above, are clearly present in early *Homo* taxa, starting with KNM-ER 1470, *Homo rudolfensis*.

The first change suggests that the relative reduction in PVC was accompanied by a relative increase, most

Evolution of the Brain in Humans – Paleoneurology. Table 1 A Table showing the reorganizational changes based on the paleoneurological record of hominid endocasts

Brain changes (Reorganization)	Taxa	Time (MYA)	Endocast evidence
(1) Reduction of primary visual striate cortex, area 17, and relative increase in posterior parietal cortex	*A. afarensis*	3.5–3.0	AL 162–28 endocast
	A. africanus	3.0–2.0	Taung child, Stw 505 endocast
	A. robustus	ca. 2.0	SK 1585 endocast
(2) Reorganization of frontal lobe (Third inferior frontal convolution, Broca's area, widening prefrontal)	*Homo rudolfensis*	2.0–1.8	KNM-ER 1470 endocast
	Homo habilis		Indonesian endocasts
	Homo erectus		
(3) Cerebral asymmetries, left occipital, right-frontal petalias	*Homo rudolfensis*	"	KNM-ER 1470 endocast
	H. habilis, H. erectus		Indonesian endocasts
(4) Refinements in cortical organization to a modern Homo pattern	*? Homo erectusto Present ?*	1.5–10	*Homo* endocasts *(erectus, neanderthalensis, sapiens)*

Changes in the reorganization of the hominid brain based on endocasts (after [14]).

Evolution of the Brain in Humans – Paleoneurology. Table 2 A Table showing the major allometric and non-allometric increases in brain size based on the hominid endocasts

Brain changes	Taxa	Time (MYA)	Evidence
(1) Small increase, Allometric*	*A. afarensis to*	3.0–2.5	Brain size increases from 400 ml to 450 ml., 500+ ml.
	A. africanus		
(2) Major increase, rapid, both allometric and non-allometric	*A.africanus to*	2.5–1.8	KNM-1470, 752 ml (Ca 300 ml)
	Homo habilis		
(3) Small allometric increase in brain size to 800 ml-1000 ml (Assumes habilis was KNM 1470-like)	*Homo habilis to*	1.8–0.5	*Homo erectus* Brain
	Homo erectus		Endocasts and postcranial
			Bones, e.g., KNM-ER 17000
(4) Gradual and modest size increase to archaic homo sapiens mostly non-allometric	*Homo erectus to*	0.5–0.10	Archaic *homo* and
	Homo sapiens		Neandertal endocasts
	neanderthalensis		1200–1700 + ml
(5) Small reduction in brain size among modern homo sapiens, which was allometric	*Homo s. sapiens*	0.015 to present	Modern endocranial capacities

Major size changes in human brain evolution (after [14]).
(* NOTE: Allometric means related to body size increase or decrease, while non-allometric refers to brain size increase without a concomitant body-size increase.)

Evolution of the Brain in Humans – Paleoneurology. Table 3 A table showing the major cortical areas (Brodmann's) involved in reorganization changes

Cortical regions	Brodmann's areas	Functions
Primary visual striate cortex	17	Primary visual
Posterior parietal and anterior occipital (peri- and parastriate cortex)	18, 19	Secondary and tertiary visual integration with area 17
Posterior Parietal, Superior Lobule	5, 7	Secondary somatosensory
Posterior parietal, inferior lobule (mostly right side. left side processes symbolic-analytical)	39	Angular gyrus perception of spatial relations among objects, face recognition
Posterior parietal, inferior lobule (mostly right side. See above)	40	Supramarginal gyrus spatial ability
Posterior superior temporal cortex	22	Wernicke's area, posterior superior temporal gyrus. Comprehension of language.
Posterior Inferior Temporal	37	polymodal integration, visual, auditory. Perception and memory of objects' qualities.
Lateral prefrontal cortex (including mirror neurons)	44, 45, 47	Broca's area (Broca's Cap)
	(also 8, 9, 10, 13, 46)	Motor control of vocalization, language Complex cognitive functioning Memory, inhibiton of impulse, foresight, etc

Major cortical regions involved in early hominid evolution (With major emphasis on the evolution of social behavior, and adapting to expanding environments) (after [14]).

Evolution of the Brain in Humans – Paleoneurology. Table 4 A table showing the average statistics for different hominid taxa

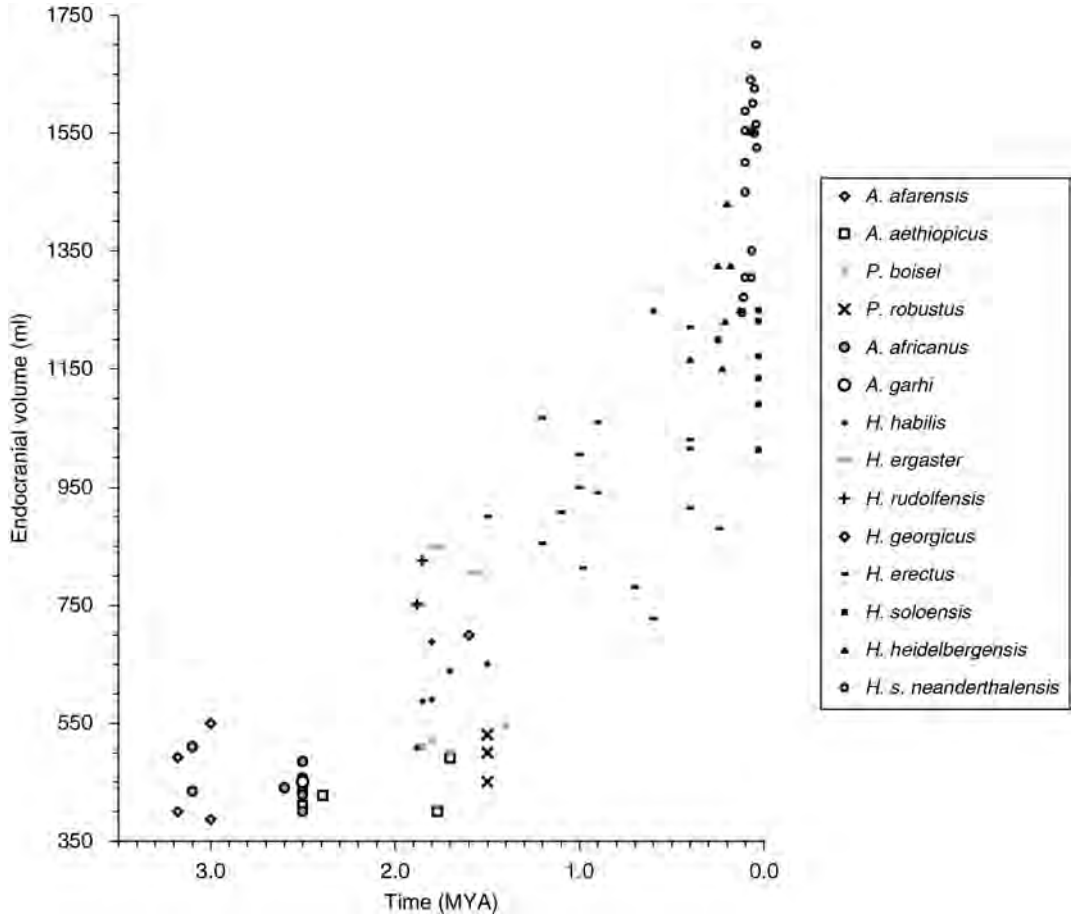
Taxon	Mean volume	Number	Range	Mean MYA	Body mass	EQMARTIN	EQHOMO
A. afarensis	445.80	5.00	387–550	3.11	37.00	4.87	42.79
A. africanus	462.33	9.00	400–560	2.66	35.50	5.21	45.58
P. ethiopicus	431.75	4.00	400–490	2.09	37.60	4.66	41.01
A. garhi	450.00	1.00	450.00	2.50	NA	NA	NA
H. erectus	941.44	20.00	727–1220	0.81	57.80	7.32	67.64
H. ergaster	800.67	2.00	750–848	1.74	57.50	6.25	57.72
H. habilis	610.00	6.00	510–687	1.76	34.30	7.06	61.50
H. heidelbergensis	1,265.75	12.00	1150–1450	0.27	68.70	8.64	81.30
H. rudolfensis	788.50	2.00	752–825	1.87	45.60	7.35	66.08
H. neanderthalensis	1,487.50	28.00	12001700	0.08	64.90	10.60	99.14
H. sapiens	1,330.00	23.00	1250–1730	0.01	63.50	9.63	89.90
H. soloensis	1,155.86	7.00	1013–1250	0.06	NA	NA	NA
P. robustus	493.33	3.00	450–530	1.50	36.10	5.49	48.11
P. boisei	515.00	6.00	475–545	1.65	41.30	5.17	46.02
P. troglodytes	405.00	350–450	NA	0.01	46.00	3.75	33.75
G. gorilla	500.00	400–685	NA	0.01	105.00	2.47	24.39

Average Statistics for Different Hominid Taxa (after [14]).

likely in the inferior parietal and posterior temporal lobes. Exactly what selective forces led to this shift can only be guessed, but following the archaeological record of stone tool development at roughly 2.6 MYA, these changes are perhaps best explained as a response to an expanding ecological niche, where scavenging, some small game hunting and a vegetarian food base necessitated a more complex appreciation of

environmental resources, as well as social behavioral stimuli within foraging hominid groups. A positive feedback model for these and other interacting variables was suggested by Holloway [15,16].

Certainly, the second reorganizational pattern, involving Broca's region, cerebral asymmetries of a modern human type and perhaps prefrontal lobe enlargement, strongly suggests selection operating on a more cohesive and cooperative social behavioral repertoire, with primitive language a clear possibility. By *Homo erectus* times, ca. 1.6–1.7 MYA, the body plan is essentially that of modern *Homo sapiens* – perhaps somewhat more lean-muscled bodies but statures and body weights within the modern human range. This finding indicates that relative brain size was not yet at the modern human peak and also indicates that not all of hominid brain evolution was a simple allometric exercise. Again, this pattern reflects the mosaic nature of human brain evolution. Neandertals were present at least 200,000 years ago, and those known from Western Europe, Eastern Europe and the Middle East have brain volumes that on average exceeded those of modern man, yet with bodies that appear more massive (lean body mass). The only difference between Neandertal and modern human endocasts is that the former are larger and more flattened. Most importantly, the Neandertal prefrontal lobe does not appear more primitive. Table 4 provides a brief statistical description of the major hominid taxa and their respective sample sizes, endocranial volumetric means and ranges. The EQ values that accompany this Table were calculated using Holloway and Post's [8] homocentric equation (see Holloway et al. [4] p. 13–14 for a more detailed explanation) as well as Martin's EQ's based on a mammalian sample. Figure 4 presents a plot of endocranial volumes against time.



Evolution of the Brain in Humans – Paleoneurology. Figure 4 Graph showing increase in brain size during the past 3 million years from the fossil hominid endocasts available. While the graph appears smooth and continuous, it should be remembered that each symbol represents several thousand years, and such a graph cannot accurately portray all of the details of brain size changes with time, particularly given the incompleteness of the fossil record. After Holloway et al. [14].

Concluding Comments

Comparative neurology provides neuroscientists with the basic understanding of neural structural variation and correlated behavioral patterns [17]. Paleoneurology provides the direct evidence for hominid brain evolution but is extremely constrained in its evidentiary details, largely thanks to the meninges that surround the surface of the cerebral cortex. In time, growing understanding of molecular neural genetics may help to pinpoint more of the evolutionary differences between modern man and other primates and may even reliably date some of the key organizational and size changes that occurred in mosaic fashion in the human line. It seems that the most essential aspects of human behavior – strong cooperative (and competitive) social behavioral adaptation, far in advance of any ape, centered within and controlled by language and cognitive abilities involving multi-way interactions between predictive prefrontal and analytic parietal/temporal lobes – emerged relatively early in hominid evolution, setting the stage for positive feedback relationships between growing cerebral size and behavioral complexity, which involved a complex interaction between regulatory gene events and changes in the genes themselves.

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Evolution of the Brain in Humans – Specializations in a Comparative Perspective

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Definition

The cognitive and linguistic capacities of humans are exceptional in comparison to other animals. To understand the neural bases of uniquely human behavioral traits, it is necessary to compare brain structure in humans to close primate relatives, particularly the great apes.

Characteristics

The Comparative Approach

Humans express dramatically divergent behavioral attributes compared to other animals in terms of language, social cognition and the manufacture of technology. To discover the human brain specializations that subserve these behavioral capacities, it is necessary to consider neural structure and function in

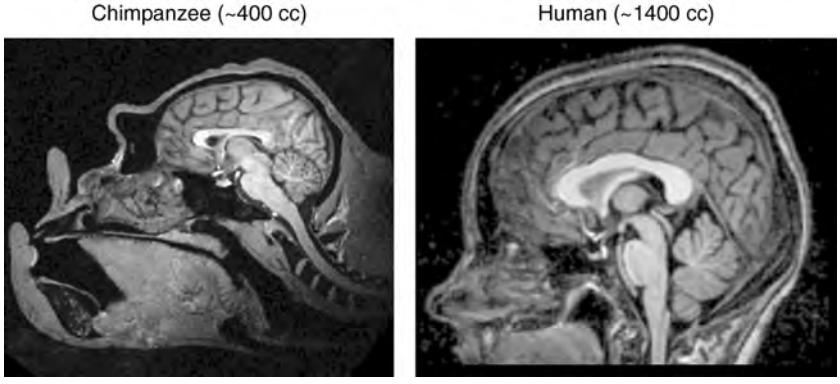
comparison to humanity's closest relatives. Despite pronounced morphological and behavioral differences between humans and other primates, genetic evidence clearly indicates that humans share close phylogenetic affinities with the great apes (orangutans, gorillas, bonobos and chimpanzees). Indeed, humans and chimpanzees are more closely related to each other than either is to gorillas. In light of these phylogenetic relationships, comparisons of human brains to those of chimpanzees and other great apes hold the potential to unveil the neural substrates of human cognitive specializations that have evolved in the 6–8 million years since the last common ancestor (Fig. 1).

Size and Morphology

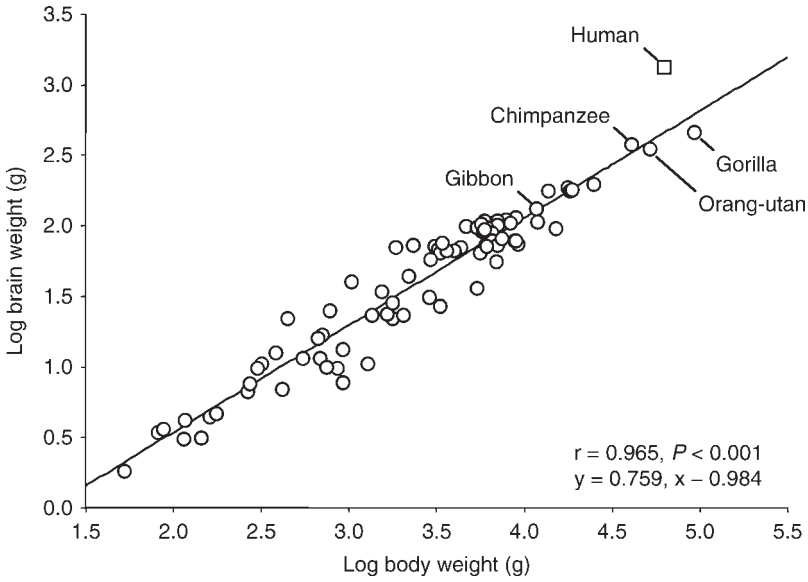
One of the most remarkable features of the human brain is its large size in both absolute and relative terms. Humans have the largest brain of any primate (~1,400 g), being about three times bigger than those of the great apes. Although larger absolute brain sizes can be found among whales and elephants, humans show the greatest deviation among mammals in having exceptionally large brains after controlling for overall body size (Fig. 2) Fossil evidence, furthermore, indicates that the period of most dramatic brain expansion occurred within the human lineage in the last two million years, long after the evolution of other human-specific traits like bipedal walking [1].

It is less obvious, however, whether brain enlargement in humans has been accompanied by disproportionate increases in particular regions. Some alterations of internal organization may be expected because of developmental, functional or architectural constraints that necessitate redesign with changes in total brain size. For example, in comparison to other primates there is more white matter underneath the neocortex in humans. The proportion of neocortical white matter volume in humans, however, conforms to ►allometric scaling expectations based on the demands for interconnections of gray matter at human brain size [2, 3]. Additionally, the human neocortex (gray and white matter combined) occupies a larger fraction of total brain size than it does in great apes. While much of this extra neocortical growth may be explained by evolutionarily conserved schedules of neurogenesis [4], it is significant that the size of the human neocortex actually exceeds what would be predicted for an anthropoid primate of the same brain size [2].

The neocortex is heterogeneous with respect to architecture and function. Therefore, it is also important to consider whether the human neocortex shows regional modifications in organization. The overall degree of cortical folding or gyrification generally increases with larger brain size in primates and the human brain fits this pattern. Nonetheless, the prefrontal part of the neocortex in humans displays a greater amount of ►gyrification than would be expected for an anthropoid primate of the same size [2]. This suggests that relatively more cortical tissue is buried within sulci in the human prefrontal cortex, which may correlate with enhancement of the cognitive functions mediated by this neocortical region. However, studies that have directly examined whether the prefrontal cortex is enlarged in humans have yielded somewhat contradictory results. While it seems that total frontal cortex size in humans is no greater than expected based on apelike scaling trends for brain size [5], further data may be necessary to resolve whether the prefrontal cortex or any of its constituent cytoarchitectural areas show disproportionate enlargement in humans.



Evolution of the Brain in Humans – Specializations in a Comparative Perspective. Figure 1 Midsagittal magnetic resonance image sections of chimpanzee and human heads. In comparison to the chimpanzee, the human brain is dramatically enlarged relative to other cranial components. From this view, it is also clear that the majority of human brain expansion is due to enlargement of a subset of structures, including the neocortex and cerebellum, whereas others, like the brainstem, are relatively unmodified.



Evolution of the Brain in Humans – Specializations in a Comparative Perspective. Figure 2 The allometric scaling relationship between mean brain weight and body weight among 85 primate species based on data presented in Holloway [7]. A least-squares regression line is fitted to the nonhuman primate data (y = 0.759, x –0.984, r = 0.965, P < 0.001). Note that the value for human brain size is the greatest departure from the allometric scaling trend seen in all other primates.

Beyond the prefrontal cortex, there is evidence of human-specific reorganization of the size of other cortical areas. The primary visual cortex (Brodmann's area 17 or V1) and the primary motor cortex (area 4) are quite similar in absolute volume in humans and great apes, despite vastly different brain size among these species [6]. In fact, the primary visual cortex in humans is substantially smaller than predicted for total brain size [7], probably because it scales closely to the size of the eye rather than the brain. These data suggest that human neocortical enlargement entailed selective expansion of certain "association" areas of the parietal, temporal and prefrontal cortex, whereas primary sensory and motor areas remained more closely correlated with direct inputs and outputs from the periphery. The hypothesis of regional modification in human neocortical evolution is further supported by the observation that human temporal lobes, especially the underlying white matter, are enlarged beyond allometric predictions based on apes [8]. It is also interesting that a subset of thalamic nuclei in humans show differences from apes. After taking scaling into account, humans have more neurons than other hominoids in the anterior principal (anteroventral) nucleus, mediodorsal nucleus and pulvinar, while neuron numbers in sensory relay nuclei are generally conservative [9]. This suggests that the "association" regions of the neocortex have expanded in humans in parallel with the specific thalamic nuclei that furnish them with reciprocal connections. Taken together, the studies reviewed above indicate that some regions within the human neocortex have become selectively modified in size.

The neocortex is not the only brain structure that is uniquely expanded in humans. After the neocortex, the human cerebellum shows the next greatest degree of enlargement relative to body size. This is not surprising given the extensive connections that link neocortex and cerebellum. In fact, the two structures appear to have evolved in tandem as a coordinated system in primates, although fossil endocast data suggest that recent human evolution was characterized by a burst of cerebellar expansion that was unmatched by a parallel increase in neocortex size. Beyond relative cerebellar size, humans also differ from other primates in the size and shape of the cerebellar dentate nucleus. In particular, the ventral portion, believed to send outputs to non-motor regions of the frontal lobe by way of the ventrolateral thalamus, is better developed in humans than in great apes. These connections may be the anatomical substrate supporting the postulated cerebellar involvement in cognition, beyond its traditionally recognized role in motor coordination [8].

Asymmetry

Human brains exhibit structural and functional lateralization in a number of different respects. Humans have a unique capacity for the generation and communication of symbolic thinking in the form of language. Concomitantly, a majority of humans show left hemisphere

dominance for language functions and display associated anatomical asymmetries of the brain. Human brains are especially asymmetric in the region of cortex along the sylvian fissure [10]. In most human brains, the left sylvian fissure is longer and more superiorly oriented than the right. In addition, the ►planum temporale, located on the superior temporal plane between Heschl's gyrus and the termination of the sylvian fissure, is larger on the left in most human brains. These asymmetries may be significant for language lateralization because this region of posterior temporal cortex corresponds to cytoarchitectural area Tpt, a site that has been identified as a major component of Wernicke's area. Whether or not these asymmetries can be considered human evolutionary specializations can only be determined in reference to great apes. Notably, the sylvian fissure and planum temporale have been demonstrated to display humanlike left dominant asymmetry in chimpanzees, gorillas and orangutans [11]. The full extent to which these gross anatomical asymmetries in great apes reflect underlying microstructural differences in circuitry between the left and the right is not yet clear. However a comparative study of area Tpt cytoarchitecture demonstrated that humans have left dominance in terms of greater spacing between minicolumns and more overall neuropil volume, allowing for interconnectivity among cells [12]. It is interesting that these histological asymmetries are absent in macaque monkeys and chimpanzees.

The gyri of the inferior frontal cortex in the location of Broca's area exhibit morphological asymmetries in humans. Although it has been claimed that similar anatomical asymmetries of the inferior frontal gyrus exist in African great apes (gorillas, bonobos and chimpanzees), the poor correspondence between cytoarchitectural boundaries and the location of sulci makes it difficult to asses the significance of external landmarks for revealing asymmetries of Brodmann's areas 44 and 45 [13]. At the histological level, Broca's area in humans displays lateralization of pyramidal neuron dendritic arborization and overall neuron packing densities. However, it is not yet known whether comparable microstructural lateralization exists in the homologous areas of great apes.

A further aspect of human cerebral asymmetry can be observed as greater width and protrusion of the left occipital pole and right frontal pole, called ►petalias [7]. In humans, this typical petalia torque pattern is most strongly observed in right-handed individuals. The characteristic humanlike pattern of left occipital-right frontal petalias is not expressed in great apes to the same degree.

Histology and Connectivity of the Neocortex

More subtle alterations of histological architecture in the absence of large-scale volumetric reorganization also have occurred in the course of human brain evolution. For example, the human primary visual cortex shows modifications of dendritic compartments and interneurons in layer IVA relative to great apes, which might relate to changes in the way that humans process motion information [6]. The anterior cingulate and paracingulate cortex have also undergone modifications in histological organization at various times along the evolutionary lineage leading to humans. Very large ►spindle-shaped neurons, also known as Von Economo neurons, located in layer Vb are present in the anterior cingulate cortex of humans and great apes, but not that of any other primates [14]. In comparison to other species, in humans these unusual neurons are especially large in size, more numerous and aggregated in clusters. Because their distinctive morphology derives from the presence of thick singular apical and basal dendrites, these neurons might be specialized to transmit rapid outputs to subcortical targets. In addition to the spindle-shaped neurons, great apes and humans are also unique among primates in displaying calretinin-containing pyramidal cells in layer V of anterior cingulate cortex [15]. The location of these two classes of specialized neurons in the anterior cingulate cortex suggests that great ape and human brains are adapted for the integration of emotion and cognition. In particular, it is possible that these connections are involved in the rapid processing of judgments in circumstances of social uncertainty. Furthermore, it is interesting that calretinin-containing pyramidal neurons are also found in the anterior paracingulate cortex (area 32) only in humans, but not great apes. This area is implicated in "theory of mind," a cognitive capacity that is exceptionally well developed in humans.

Finally, although there are extremely few comparative data on connectivity patterns in humans and great apes, a set of intriguing results from axon degeneration studies suggest that the human brain is distinguished among primates in having direct projections from neurons in the primary motor cortex to the motoneurons of the larynx in the nucleus ambiguus [16]. These direct cortico-motoneuron connections would be situated to provide enhanced voluntary motor control for speech production. Additionally, a recent comparative study used diffusion tensor imaging to show that the arcuate fasciculus language tract has a much larger projection to the middle and inferior temporal cortex in humans compared with chimpanzees or macaques.

Evidence from Gene Expression and Gene Sequence Evolution

Distinctive aspects of the human brain phenotype arise from alterations to the genes that direct processes involved in neural development, physiology and

structure. Several genes that participate in orchestrating brain development show evidence of natural selection in the lineage leading to humans [17]. For example, the genes *ASPM* and *MCPH1* have undergone high rates of nonsynonymous amino acid substitution at different branch points in the evolutionary history of apes, including a marked upsurge in humans since the last common ancestor with chimpanzees. Because the proteins encoded by these genes are involved in neuroblast proliferation during embryonic development and mutations within these genes can cause pathological reduction in brain volume (microcephaly), these data suggest that some part of human brain enlargement may be related to their evolution. The transcription factor *FOXP2* also displays evidence of sequence changes in human evolution [18]. Specific linguistic impairment, intellectual deficits, orofacial dyspraxia and structural abnormalities of language-related brain areas have been shown to occur in members of a single human family that share a point mutation in the *FOXP2* gene. The FOXP2 transcription factor is highly conserved across mammals, with identical amino acid sequences in rhesus macaques, gorillas and chimpanzees. Humans however, have mutations that yield two amino acid substitutions in comparison to other primates, suggesting that this gene may be involved in the evolution of language and speech.

Several studies of gene expression in the brain using microarray techniques broadly agree in showing that the human cortex is distinguished from that of chimpanzees and other primates in displaying up-regulation of the expression of many genes related to neuronal signaling, plasticity, and activity [19]. These observations are further supported by findings that genes that encode various subunits of the mitochondrial electron transport chain show evidence of natural selection in the human lineage [20]. These changes would presumably enhance the aerobic energy producing capabilities of cells that have high metabolic rates, such as neurons.

Conclusions

Research efforts directed at understanding the human brain in comparative perspective are still in their infancy. As more data accumulate to articulate the phenotypic differences between human brains and those of humanity's close relatives, greater insights will be gained into how neuroanatomical and genetic changes translate to human behavioral specializations.

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