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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
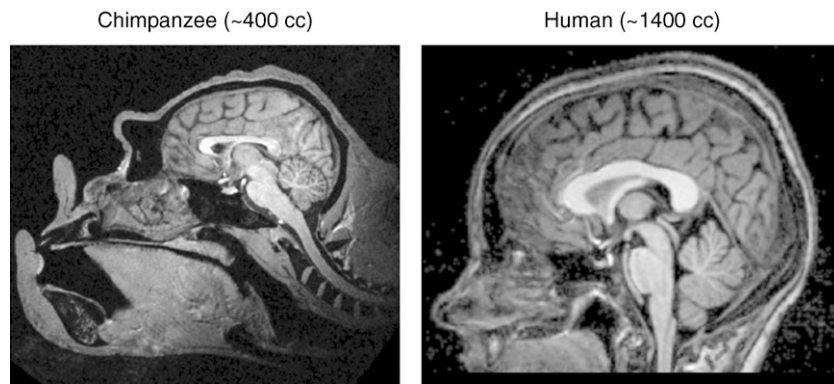
Evolution of the Brain: In Humans – Specializations in a Comparative Perspective. Figure 1 Midsagittal
magnetic resonance image sections of chimpanzee and human heads. In comparison to the chimpanzee, the human
brain is dramatically enlarged relative to other cranial components. From this view, it is 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.

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.

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 sub-
stantially 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 conserva-
tive [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 lateral-
ization in a number of different respects. Humans have a
unique capacity for the generation and communica-
tion of symbolic thinking in the form of language. Con-
comitantly, a majority of humans show left hemisphere
dominance for language functions and display associ-
ated 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
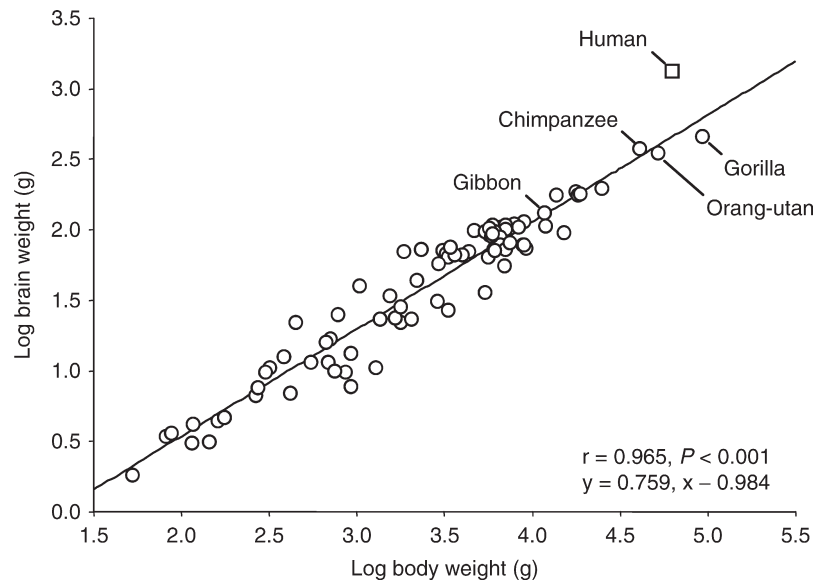
Evolution of the Brain: In Humans – Specializations in a Comparative Perspective. Figure 2 The allometric scaling relationship between mean brain weight and body weight among 85 primate species based on data presented in Holloway [7]. A least-squares regression line is fitted to the nonhuman primate data (y = 0.759x–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.

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]. Although 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, 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.

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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