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HUMAN BRAIN EVOLUTION

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> Nevertheless the difference in mind between man and the higher animals, great as it is, is certainly one of degree and not of kind
>
> ~Darwin, 1871

Following Darwin, the study of human cognition has been properly placed within an evolutionary context. To understand the human mind – how we acquire, process, store, and act on information from the environment – we have to know the long history of our species and the selective pressures that shaped our ancestors. One way of doing this is to compare the differences and similarities among extant species in cognitive processes and the neuroanatomical structures that underlie them. This approach requires understanding the phylogenetic relationships among species to infer the evolutionary changes that occurred in the past. Because the great apes (the primate group that includes chimpanzees, bonobos, gorillas, and orangutans) are the closest living relatives of modern humans, they are an essential basis for comparison. Indirect as it is, the comparative method is one of the most powerful tools we have available, as brains and cognition do not fossilize. Indeed, comparative analysis has provided important insights into the evolution of human behavior and cognition. It has been observed that many behaviors previously thought to be uniquely human are actually present in other species as well, sometimes even to a greater degree (i.e., eusociality in *Hymenoptera*). Tool-making and use, for example, are not restricted to our species alone. When Jane Goodall reported tool-making in chimpanzees, Louis Leakey famously replied: “Now we must redefine ‘tool’, redefine ‘man’, or accept chimpanzees as humans” [1].

Yet, examples of apparent cognitive and behavioral discontinuity between humans and other species abound. Our syntactically rich language, ability to understand mental states of others, and propensity to generate and manipulate symbols are exceptional [2]. What are the possible evolutionary changes in brain structure that allowed these faculties? Here, we offer a brief overview of the evolution of the human brain and the likely neuroanatomical changes associated with our species’ distinctive cognitive abilities. These changes occurred at several levels of brain organization, providing the neuroanatomical hardware for the complexity of human behavior and cognition.

Primates are a very diverse group of mammals of more than 500 living species that includes lemurs, lorises, tarsiers, New World monkeys, Old Word monkeys, and apes. Most comparative neuroanatomical research has focused on a tiny fraction of this variety, concentrating on a few primate model species, including common marmosets (*Callithrix jacchus*), capuchin monkeys (*Cebus apella*), rhesus macaques (*Macaca mulatta*), and chimpanzees (*Pan troglodytes*) [3]. Our closest living relatives are the chimpanzees and the bonobos with whom we share a common ancestor dated to about 4–8 million years ago [4] (Figure 1).

Compared to other primates, including great apes, humans have very large brains. Weighing approximately 1,400 grams, our brains are roughly three times larger than those of other great apes and also significantly larger than expected for a primate of our body size. Fossil evidence of the cranial capacity of our direct ancestors indicates gradual increase in brain size early in hominin evolution with a period of more accelerated growth within the last 2 million years [7]. However, important as it certainly must be for increasing numbers of neurons, synaptic connections, and related processing capacity, brain size expansion alone cannot explain the cognitive complexity of our species for several reasons. Many species, including non-primates such as elephants and whales, have brains larger than ours (although perhaps fewer neocortical neurons) and yet do not approach the cognitive sophistication of humans. Moreover, species may be comparable in brain size yet differ dramatically in behavior and social skills. Chimpanzees and bonobos, for example, have similar brain size but differ in temperament and social behavior. Lastly, there is about 1,000 g normal range of variation among modern humans in brain mass, however all are capable of commanding language and other human-specific capacities. Therefore, much of the answer probably lies in changes to brain development, neuroanatomical reorganization, and modifications at the molecular level. It is likely that the reorganization at these levels, and not solely absolute brain size or total number of neurons, produces species differences in cognition.

The increase in human brain size is due mostly to expansion of the neocortex [8], particularly heteromodal association regions of the frontal, temporal, and parietal lobes. To some extent, evolutionary changes to human association cortex have involved differential enlargement of regions that are homologous in other primates and alterations to cortical connectivity [9]. Notably, many regions of the prefrontal cortex have been shown to be homologous between humans and other great ape and monkey species, including Broca’s language areas (areas 44/45) (Friederici, 2016). Some of the changes to human association cortex, however, might comprise differentiation of novel and functionally distinct areas that perform increasingly fine-grained information processing. For example, data suggest that, compared to rhesus macaques, human intraparietal sulcus (IPS) includes four additional motion-sensitive areas dedicated to processing of three-dimensional form in relation to motion [10]. As a result, human parietal lobe includes more regions dedicated to processing of shape compared to that of rhesus macaques. Addition of these and other posterior parietal areas likely enhanced processing of visual and somatosensory information necessary for complex manipulative abilities required for tool manufacture and manipulation [11,12]. Using combined functional and structural MRI data from the Human Connectome Project, a recent study identified some 180 distinct cortical areas in the human brain based on variation in cortical thickness, myelination, and connectivity patterns [13]. This number far exceeds

estimates of the number of areas for other primate species [14], although such an approach for parcellation has not yet been conducted with brains of non-human species.

A point of disagreement has been the relative size of the frontal lobes and different prefrontal cortical areas in humans versus other primate species. Regions of the prefrontal cortex play a significant role in language, planning, decision-making, working memory, and other higher-order cognitive functions. Some have argued that change in the absolute and proportional size of the prefrontal cortex is tightly correlated with corresponding changes in other brain areas [15,16], while other analyses show that human prefrontal cortex is enlarged beyond what would be predicted from primate brain scaling trends [17,18]. In this context, direct comparisons of various cytoarchitecturally-defined cortical areas in humans and chimpanzees show that frontopolar cortex (area 10), Broca's area (areas 44/45), and the anterior insular cortex are about six times larger in humans, whereas the primary motor cortex (area 4) and the primary visual cortex (area 17) are much more similar in size between the species [19].

Reorganization of the human brain is also apparent at the level of microstructure, such as the distribution of neurons and glial cells, innervation patterns of neurotransmitters, and expression of genes and proteins. For example, several studies have examined neuron density across different cortical areas in a number of primate [20] and other mammalian species [21]. Results show that neuronal cell density generally decreases with brain size. This decrease in the packing density of neuronal cell bodies seems to be proportionally related to the increase in the space occupied by dendrites, axons, synapses, and glial processes in the surrounding neuropil space, suggesting greater connectivity patterns [22].

Human brains also show specialization in distribution of glial cells. Glial cells are functionally very diverse and, in addition to providing structural and metabolic support to neurons, play an important role in higher cognitive functions, such as learning and memory [23]. These cells are as numerous as neurons – an adult human brain contains an approximately equal number of neuronal and glial cells (about 86 billion each) – and the ratios of these cells vary across cortical and subcortical structures [24]. Comparative analysis of glia-neuron ratios in 18 species of primates showed that human dorsolateral prefrontal cortex (area 9) has a higher ratio (1.65) than other species [25], suggesting a greater glial metabolic support necessary to maintain larger dendritic arborizations and long-range projecting axons of the human brain. Further possible specialization of the human necortex concerns distribution patterns of different subtypes of astrocytes, some of which are absent in non-primate species. These include interlaminar astrocytes that send long processes across upper cortical layers and polarized astrocytes also with long processes that extend vertically and inhabit deeper layers [26]. Moreover, when compared to other species, human astrocytes are both larger in diameter and more elaborate in number of processes [27]. It has been argued that human patterns of glial cell biology not only contribute to our species' complex cognitive abilities but also provide unique vulnerability to neuropathologies compared to other primates [26, 27].

Distribution patterns of neurotransmitters in cortical and subcortical regions are also known to vary between humans and other primates [28,29,30,31]. For example, a recent

examination of basal ganglia showed human-specific increase in dopaminergic innervation of the medial caudate nucleus [32], a highly interconnected region of the striatum that is involved in language production, among other functions. Notably, this increase is evident even in the context of a relatively smaller striatum than predicted for a primate of human brain size, suggesting an evolutionary reorganization in microstructure in the absence of concomitant increase in volume. This finding is interesting in that normal activity patterns within the medial caudate nucleus in humans depend on the presence of the functional copy of *FOXP2* gene [33], suggesting a link between *FOXP2* evolution and distribution of dopamine.

Of particular interest has been the genetic basis of human specialization in brain organization and function. Early analyses revealed a global pattern of increased gene expression in the human brain compared to nonhuman primates, which was not evident in non-brain tissue, such as the heart and the liver [34,35,36]. Examination of these genes revealed an enrichment of those involved in synaptic transmission and plasticity as well as energy metabolism in showing upregulation, supporting the idea that human brain evolution is characterized by molecular modifications to increase levels of neuronal and synaptic activity [37]. Following studies found more examples of genes showing increased levels of expression, such as thrombospondin genes involved in the control of synaptogenesis compared to nonhuman primates [38]. It is important to note, however, that the relationship between mRNA expression and protein abundance is not always straightforward and may depend on biological function. For example, a recent analysis revealed that the relationship between mRNA expression and protein expression in humans and chimpanzees was stronger for some biological functions, such as oxidative metabolism and protein synthesis and modification, and weaker for others [39].

Taken together, these findings show how the human brain is the product of evolutionary changes that occurred over time that underpin the complex cognitive abilities of our species. Human specialization in brain organization and function is apparent at several levels of organization. Changes in overall anatomy, such as increase in absolute and relative size and addition of more cortical areas likely provided the neuroanatomical basis for processing of evermore fine-grained information. Changes in microstructure, such as the distribution patterns of neurons and glial cells and changes in expression of both mRNA and proteins, allowed for plasticity and increased learning capacity that, when coupled with cultural and social forces, shaped human cognition.

Acknowledgments

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HIGHLIGHT

- Human brain shows examples of specialization at several levels of organization
- Increase in absolute brain size
- Increase in relative size of some brain areas (e.g., prefrontal areas 10 and 44/45) but not others (e.g., primary motor (area 4) and primary visual (area 17))
- Addition of novel, functionally distinct cortical areas that process increasingly fine-grained information
- Human-specific changes in distribution of neurons, glial cells, and neuropil space
- Human-specific changes in innervation patterns of neurotransmitters (e.g., dopamine)
- Human-specific changes in gene and protein expression

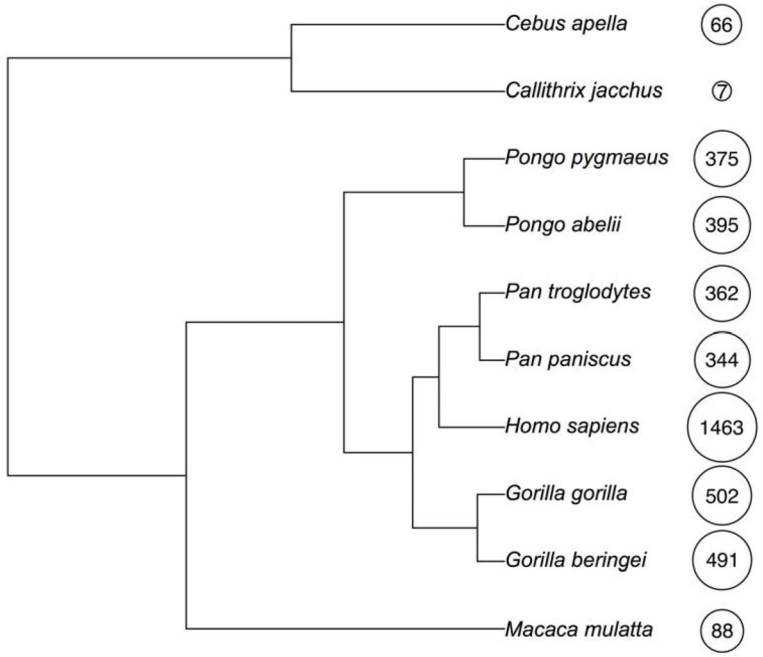

Figure 1. Phylogenetic tree of primates

Phylogenetic relationships among the great apes and other primate species mentioned. The numbers indicate the endocranial volumes (in cm^3, rounded to the nearest whole number) and the size of the circles shows the natural log transformation of the endocranial volumes to demonstrate the diversity in brain size of the primate species. Data from [5,6].

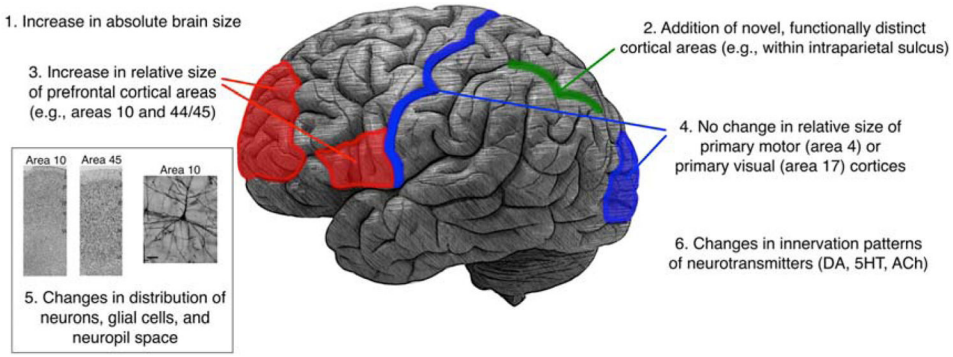

Figure 2. Neuroanatomical changes in human brain evolution

Summary of the neuroanatomical changes in human brain evolution, including macro- and micro-structural changes (see text for more detail).