



## A Review on Brain Evolution and Development

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### Abstract

Development of human brain is the essential process in the prenatal period of human growth. The total surface of human brain area is 1820 cm<sup>2</sup>, and the average cortical thickness is 2.7 mm. We reviewed and referred to several articles in this field. Comparative studies of the primate's brain show that there are general architectural basis governing the brain growth and evolutionary development. In this study, it is discussed about the human brain development with highlighting on the main mechanisms in the embryonic stage and early postnatal life as well as the general architectural values in brain evolution from primates to now. It is suggested that neurodevelopment involves some genetic bases in the neural stem cells proliferation, cortical neurons migration, cerebral cortex folding, synaptogenesis, gliogenesis, and myelination of neural fibers.

**Keywords:** Neurodevelopment, Brain Evolution, Prenatal Stage, Primate

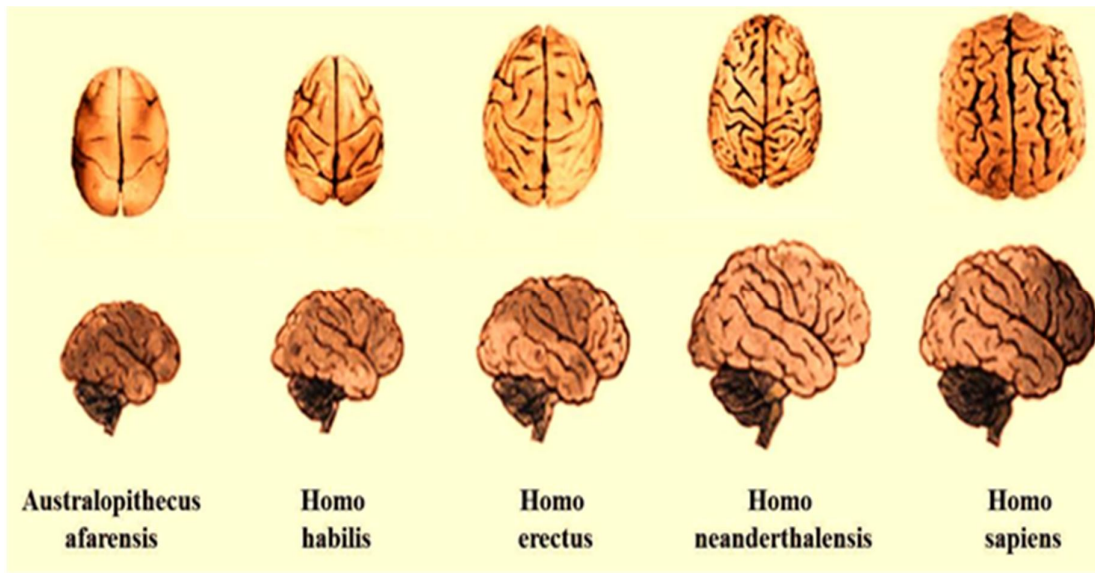
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### 1. Introduction

Studies of the mammal's brain express that there are general principles governing its evolutionary development and growth (Figure 1). The purpose of this review is to collect and discuss about views on the primate brain development in humans as well as some

hypothetical principles that underlie the intricate organization of the brain.

Some physical limits pressured its evolutionary potential and processing power. For example although a brain volume about 3500 cm<sup>3</sup>, equivalent to a brain size two to three times of modern man, looks to reach its great processing capacity, but growing beyond the critical size, makes the brain less efficient (1, 2).



**Fig 1.** Human brain evolution steps. Upper row is a superior view and lower row is a lateral view of the brain in the five species.

## 2. Human brain evolution

The human brain has about 100 billion neurons, more than 100,000 km of interconnections, and an estimated storage capacity of  $1.25 \times 10^{12}$  bytes (3). The boundary to any intelligent system lies in its abilities to process and integrate large volumes of sensory information and to compare these signals with as numerous memory states as possible, and all that in a minimum of time (4). It implies that the practical capacity of a neuronal structure is inherently limited by its neural architecture and signal processing time (5, 6). The average adult modern human brain has a volume of  $1350 \text{ cm}^3$ , a total surface area of  $1820 \text{ cm}^2$ , and an average cortical thickness of 2.7 mm (7, 8).

Each cortical neuron has 7000 synapse with other neurons on routine, bring a total of 0.15 quadrillion synapses and more than 150,000 km of myelinated nerve fibers (9, 10). A magnetic resonance imaging (MRI) study, furthermore, focusing predominantly on the prefrontal cortex, has displayed that the volume of the humans white matter underlying prefrontal areas is bigger than the other primates (11). It advises that the connectional elaboration of the prefrontal cortex, which mediates such significant behavioral domains as planning, aspects of language, attention, and temporal

and social information processing has played a vital role in human brain development (12).

During development, the human frontal lobe didn't extend, as some areas with important functional correlates are either bigger or smaller in the human brain than expected when compared with the same area in great apes (13, 14). The mammalian brain varies meaningfully in the size, shape, and convolucional complexity, but only marginally in the cortical thickness (15). In a study on anthropoid primates, neuroanatomical information was used to examination the following hypotheses: (1) the neocortex of human is significantly larger than anticipated for a primate of human brain size, (2) the human prefrontal cortex is meaningfully more convoluted than expected for the human brain size, and (3) increase in white matter volume of cerebra gets better results from increases in neocortical gray matter volume between anthropoid primates. The results of this study showed that human brain volume almost tripled in the hominid lineage by demonstrating that the neocortex was modified throughout hominid development (16, 17).

## 3. White matter

The comparative white matter volume raises with the brain size, from 9% in pygmy marmosets (*Cebuella*

pygmaea) to about 35% in humans, the highest value in primates (18). The model predicts a white matter volume of about 1470 cm<sup>3</sup> for an anthropoid primate that has a brain volume of 3000 cm<sup>3</sup> (19). The ratio of white matter rises with brain size, from 22% in a monkey brain of 100 cm<sup>3</sup> to about 65% in a hypothetical primate with a brain size of 10,000 cm<sup>3</sup> (20). These comparative analyses indicate that the evolutionary process of neocorticalization in primates is chiefly due to the progressive growth of the axonal mass that accomplish universal communication, rather than to the rise in the cortical neurons number and the significance of high neural connectivity in the evolution of brain size in anthropoid primates (21).

#### 4. Gray matter

The volume of cortical gray matter which is expressed as a percentage of total brain volume, increases from about 25% for the insectivores to 50% for humans (22). On the other hand, the relative size of the cerebellum remains persistent across phylogenetic groups, occupying about 10–15% of the total brain mass (23). Human brains are twice as large as chimpanzee brains from in 16 weeks of pregnancy already. Although both the humans and chimpanzee show an increase in growth speed at this time, but they diverge abruptly at 22 weeks of gestation, when accelerate the human brain growth, while decelerates the chimpanzee brain growth. Finally, during early infancy, humans experience a very fast increase in white matter volume that significantly exceeds it in chimpanzees (24).

##### 4.1. Folding in the cortex

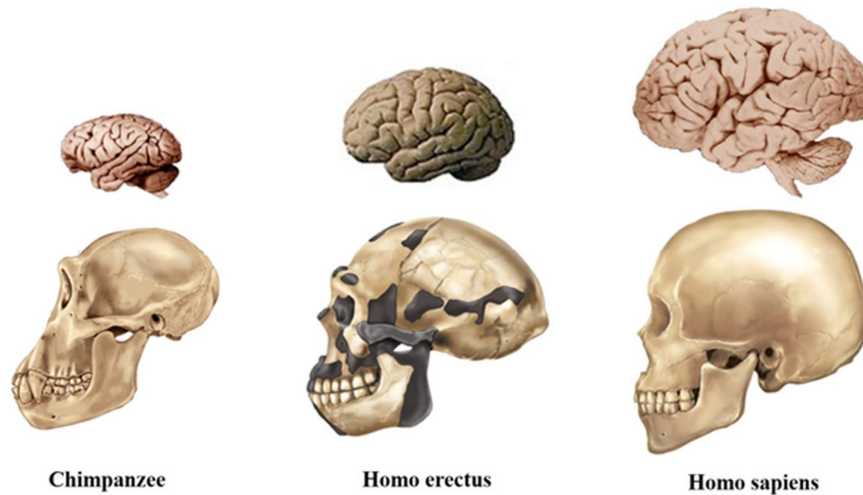
Differences in the duration of neurogenesis, which increases more quickly with the brain size for the cerebral cortex than for subcortical areas, lead to a systematic surge in the ratio of the cortical to the subcortical areas (25, 26). Scientists have found that cortical folding and connectivity are related across species and a simple model based on a white matter-based mechanism may reason for increased cortical folding in the primate cerebral cortex (27-29). They recommend that the degree of tension which is related to the morphological features of the fibers (i.e., axonal

length, its mean cross-sectional area, and the proportion of efferent neurons), controls how much the cortical surface folds inwards (30).

The folding of the cortex (gyrification or formation of Gyrus) is detected as a tool to boost the number of brain cortical neurons; intracranial pressure is recognized as a main regulator of the brain development (31). Formation of Gyrus begins in the parieto-occipital and central sulci at the week of 24 (32). Through term, the secondary sulci spread concentrically around the primary sulci. After term, tertiary sulci grow together with short association fibers (33). Gyrification typically begins somewhat earlier in the right hemisphere than the left. The expansion of the cortex is a chief regulator of the brain folding (12).

#### 5. The Relationship between Neanderthal brain size and the evolution of human life history

The primary postnatal brain growth degree of anatomically modern *H. sapiens* (AMHS) and Neanderthals compared to chimpanzees is about double rise of endocranial volume (ECV) during the 1st year of the life. Rates of postnatal brain growth which have developed in *H. erectus*, makes the hypothesis of the beginnings of “modern” human-like patterns of brain growth and life history, which must be sought comparatively early during the evolution of the genus *Homo* (34). The Neanderthal brain growth pattern fits into the hypermorphosis pattern; compared with the *recent* populations of anatomically modern *H. sapiens* (rAMHS), Neanderthals have been shown to reach larger cranial sizes and more shapes, which are progressive within a given period of ontogenetic time (35). Rate hypermorphosis might be an associate of greater average body size in Neanderthals compared with rAMHS, causing brain size reduction in AMHS during the late Pleistocene (36). Otherwise, brain size reduction during the Late Pleistocene could be the result of an evolutionary presentation optimization (37). Proof for the substantial cerebral reorganization comes from Late Pleistocene AMHS and Neanderthals, which had larger cerebral hemispheres relative to cerebellum volume than modern humans (Figure 2) (38, 39).



**Fig 2.** Brain and skull evolution in chimpanzees, *Homo erectus*, and *Homo sapiens*.

### 6. Effective factors on the human brain evolution

Recent comparative genomic studies have recognized a number of mutations in the modern human genome that could underlie the evolution of larger brain size (40). For instance, a deletion of one enhancer of the growth arrest and a DNA-damage-inducible gamma (*GADD45G*) gene, which leads to brain size expansion, is joint with Neanderthals (41). A human-specific duplication of a shortened version of the gene *SLIT-ROBO Rho GTPase activating protein 2* (*SRGAP2*) is anticipated to increase dendritic spine density in the cortex and could have improved signal processing in the hominin brains (42). It is also valued noting that Neanderthals, the extinct hominin species that diverged from the human evolutionary lineages 400–800 (kya), differ from other primates by the same two amino acid changes as modern humans in the gene encoding forkhead box P2 (*FOXP2*) (43).

### 7. Limits to the Human Brain Evolution

Descriptions for the evolution of the human brain are mostly focusing on the selection pressures of the physical environment (climate, diet, food availability) and those of the social environment (group size, coalition formation, parental care) (44). In fact, there are numerals of related factors that interact to limit brain size, factors that can be divided into two categories: 1) energetic constraints and 2) neural processing constraints (3).

### 8. Limits to Information Processing

The limit to any neural system is in its ability to process and integrate large amounts of information in a least of time (45). The development of the cortex does appear to coordinate folding with connectivity in a way that could create smaller and faster brains. The fastest axons have transmission times of 1–5 ms across the neocortex and <1 ms from the eye to the brain, large brains reduce conduction delays and metabolic firing costs at the expense of increased volume. Primates with very large brains (e.g., over 5 kg) may have a decreasing capability for neuronal integration despite their larger number of cortical neurons (46).

### 9. Energetic Limits

The human brain produces about 15 watts (W) in a well-insulated cavity of about 1500 cm<sup>3</sup>. From an engineering point of view, removal of sufficient heat to prevent thermal overload could be an important problem (1). However, the brain is actively cooled by blood and not basically by heat conduction from the surface of the head. It has been suggested by researchers that the evolution of a “cranial radiator” in hominids aided providing additional cooling systems. It means that natural selection activates on brain size at the cost of growth and reproduction, which could clarify its connection with the life span (47). On the other hand, great brains are energetically costly, and humans expend

a larger amount of their energy budget on brain metabolism than other primates (48). Paleontological evidence shows that rapid brain evolution occurred with the emergence of *Homo erectus* 1.8 million years ago, and was associated with vital changes in diet, body size, and foraging behavior (49).

## 10. Human brain development

Based on biological studies, three different phases contribute to the differential growth: neuronal division and migration, neuronal connectivity, and synaptogenesis and synaptic pruning (50). Growth and folding of the cerebral hemispheres during the fetal life was shown in Figure 3.



**Fig 3.** Growth and folding of the cerebral hemispheres during the fetal life

**10.1. The first phase** of the brain development extends throughout the first half of gestation and is characterized by the creation of new neurons at rates of up to 250,000 neurons per minute followed by their migration toward the outer brain surface (51).

**10.2. The second phase** extends from mid-gestation throughout 2 years postnatal and is dominated by the formation of neuronal connectivity. The new connections induce an extreme tangential expansion of the outer cortex and the cortex begins to fold and at the same time, myelination induces extreme white matter growth (52). During the second half of gestation, axons extend branches to numerous cortical and subcortical targets until each neuron links with thousands of other neurons (50). The most important connective structure in the human brain is the corpus callosum, a bundle of more than 200 million contralateral axons, which connect the left and right cerebral hemispheres (53).

**10.3. The third phase** extends throughout the entire lifetime and is associated with mild synaptogenesis, the formation of a few new connections, mostly with synaptic pruning, and the removal of unnecessary neuronal structures (54). Throughout this phase, the

human cortex remains plastic, locally adapts its thickness, dynamically modifies its stress state, and undergoes secondary and tertiary folding (55). Synaptogenesis which contributes to the greater capacity of the human brain to learn and adapt, contains three phases: first, immature synapses form between axons and dendrites; then, synapses undergo maturation and convert from a quiet to an active state; and finally, the synaptic number is reduced to enhance the neuronal connections within the circuit (56). In humans, synaptic pruning, the process of synapse elimination, starts proximate the time of birth and is completed by the time of sexual maturation (57).

## 11. Role of Glial Cells in the Brain Developing

Astrocytes, a type of glial cells in the central nervous system, play a very important role in synaptic transmission and information processing (58, 59). Human astrocytes are larger and structurally more complex. The ratio of astrocytes to neurons increases with cognitive skills and significantly varies between species and is 1.4 to 1 in humans (60). The first oligodendrocyte progenitor cells are produced in the ventricular and subventricular zones about week 10, and

their formation extends a peak around week 15 (61, 62). They form a myelin sheath around the axon to enable rapid impulse propagation. In humans, myelination mostly occurs after birth, when neuronal migration has ceased and primary and secondary folds have formed (63). Microglial cells help to neuronal proliferation and differentiation, clear debris, and remodel the synapses (64).

### Conclusion

We provided an overview about the cellular, molecular, and genetic basis of brain development and evolution in the species from the primates to modern humans, highlighting the major efficient mechanisms in the normal neural development in the embryonic stage and early postnatal human life. In addition, we discussed about the role of effective factors and limitations related to the human brain evolution. The functional system of the brain benefits from the high synaptic connectivity and short transmission delays. Anatomical differences, which are observed between the human and the chimpanzee brains and the morphological properties in their skulls, present a general image of the evolutionary stages that led to the modern form of the human brain with high cognitive abilities.

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### Conflict of interest

The authors have no conflict of interest in this study.

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