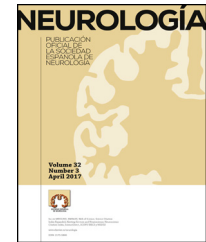




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## REVIEW ARTICLE

# Evolution and genomics of the human brain<sup>☆</sup>

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**Abstract** Most living beings are able to perform actions that can be considered intelligent or, at the very least, the result of an appropriate reaction to changing circumstances in their environment. However, the intelligence or intellectual processes of humans are vastly superior to those achieved by all other species. The adult human brain is a highly complex organ weighing approximately 1500 g, which accounts for only 2% of the total body weight but consumes an amount of energy equal to that required by all skeletal muscle at rest. Although the human brain displays a typical primate structure, it can be identified by its specific distinguishing features.

The process of evolution and humanisation of the *Homo sapiens* brain resulted in a unique and distinct organ with the largest relative volume of any animal species. It also permitted structural reorganisation of tissues and circuits in specific segments and regions. These steps explain the remarkable cognitive abilities of modern humans compared not only with other species in our genus, but also with older members of our own species.

Brain evolution required the coexistence of two adaptation mechanisms. The first involves genetic changes that occur at the species level, and the second occurs at the individual level and involves changes in chromatin organisation or epigenetic changes. The genetic mechanisms include: (a) genetic changes in coding regions that lead to changes in the sequence and activity of existing proteins; (b) duplication and deletion of previously existing genes; (c) changes in gene expression through changes in the regulatory sequences of different genes; and (d) synthesis of non-coding RNAs.

Lastly, this review describes some of the main documented chromosomal differences between humans and great apes. These differences have also contributed to the evolution and humanisation process of the *H. sapiens* brain.

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**PALABRAS CLAVE**

Cerebro humano;  
Genómica del  
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**Evolución y genómica del cerebro humano**

**Resumen** La mayor parte de los seres vivos son capaces de realizar acciones que pueden ser consideradas inteligentes o al menos el resultado de un proceso de reacción adecuado ante las circunstancias cambiantes de su medio ambiente. Sin embargo, la inteligencia o los procesos intelectuales que desarrollan los seres humanos son enormemente superiores a los que logran los organismos de cualquier otra especie. El cerebro humano adulto es un órgano sumamente complejo: pesa aproximadamente 1.500 g, lo que representa solo el 2% del peso corporal pero consume igual cantidad de energía que todo el músculo esquelético en reposo. Aunque el cerebro humano presenta una estructura típicamente primate, revela algunas características que lo distinguen y lo individualizan plenamente.

El proceso de evolución y humanización del cerebro del *Homo sapiens* (*H. sapiens*) lo convirtió en un órgano único y diferente, alcanzando el mayor tamaño relativo entre todas las especies, pero además le permitió una reorganización estructural de tejidos y circuitos en segmentos y regiones específicas. Esto explica las notables capacidades cognitivas del hombre moderno, en comparación no solo con otros miembros de su género, sino con otros miembros más antiguos de su propia especie.

La evolución del cerebro requirió la coexistencia de 2 mecanismos de adaptación. El primero involucra cambios genéticos que ocurren a nivel de especies y el segundo ocurre a nivel individual e involucra cambios en la organización de la cromatina o cambios epigenéticos. Entre los mecanismos genéticos se encuentran: a) cambios en regiones genéticas codificantes que conducen a cambios en la secuencia y actividad de proteínas existentes; b) los procesos de duplicación y delección de genes previamente existentes; c) cambios en la expresión génica a través de modificaciones en las secuencias reguladoras de diferentes genes, y d) síntesis de ARNs no codificantes.

Finalmente, en esta revisión se describen algunas de las más importantes diferencias cromosómicas reportadas entre humanos y grandes simios, que también han contribuido al proceso de evolución y humanización del cerebro del *H. sapiens*.

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**Introduction**

How intelligence should be defined continues to be subject to debate. However, it is widely accepted that the majority of animals, particularly those further up the evolutionary scale, perform a series of actions that may be considered intelligent, or at least the product of an appropriate reaction to a given set of environmental circumstances. In any case, human intelligence and intellectual processes are vastly different from those observed in any other species on the planet.

We know now that the brain is responsible for this capability in humans, although this has not always been the case: the ancient Egyptians extracted the brains from corpses during the process of mummification, while the ancient Greeks believed the brain to be no more than a radiator for cooling the blood flowing from the heart. In his magnum opus *On the origin of species*,<sup>1</sup> Darwin's observations and discussions make little mention of the brain. Likewise, Darwin's contemporary Huxley<sup>2</sup> argued that the human brain fundamentally resembled that of the great apes.<sup>3</sup>

The brain of an adult human is an intricate, complex organ weighing approximately 1500 g and representing 2% of total body weight; however, it consumes the same amount of energy as all the body's skeletal muscle at rest.<sup>4</sup> In general, the human brain is structured similar to a typical primate brain, but with certain distinguishing characteristics.

Despite the enormous body of biological and medical knowledge about the brain, there remain questions which are yet to be completely resolved. What makes the human brain so exceptional, compared even to the brains of the higher primates and ancestral hominids? When did our brain truly become human? How did the human brain evolve?

Initial attempts to answer these questions compared the human brain to those of species with genetic or evolutionary similarities (whether macroscopic or microscopic) in order to identify the similarities and differences. Attempts have also been made to compare the human brain to those of other members of the genus *Homo*, although a detailed comparison is impossible since the only remnants of our ancestors' brains are prints left by contact with the endocranium.<sup>5</sup> This has enabled us to understand the process of encephalisation that led to the development of the complex brain of *Homo sapiens*.

**Brain size and the process of encephalisation**

The human brain is large, with adult brains typically having a volume of approximately 1350 cm<sup>3</sup>, weighing 1500 g, and containing nearly 20 billion neurons.<sup>6</sup> It is therefore much larger than the brain of any extinct primate, and weighs 3 times more than the brain of the chimpanzee, our closest evolutionary relative (Fig. 1).<sup>7</sup>

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