HUMAN BRAIN EVOLUTION
HOW THE INCREASE OF BRAIN PLASTICITY MADE US A CULTURAL SPECIES

Aida Gómez-Robles and Chet C. Sherwood

Why are humans so different from other primate species? What makes us so capable of creating language, art and music? The specializations in human brain anatomy that are responsible for our unique behavioral and cognitive traits evolved over a very short period of evolutionary time (between six and eight million years). Recent evidence suggests that, alongside a reorganization of the brain and an increase in its size, neural plasticity may also play a major role in explaining the evolutionary history of our species. Plasticity is the propensity of the brain to be molded by external influences, including the ecological, social and cultural context. The impact of these environmental influences in shaping human behavior has been long recognized, but it has been only recently that scientists have started discovering the more pronounced plasticity of human brains compared to our close relatives.

Keywords: genes, environment, development, altriciality, epigenetics.

■ INTRODUCTION

Humans and chimpanzees are surprisingly genetically similar, sharing about 98 % similarity in DNA coding sequences. In addition, humans and chimpanzees share in common most of their evolutionary history, having diverged only between six and eight million years ago (Ma). This genetic and evolutionary closeness strikingly contrasts with the clear behavioral and cognitive differences between humans and chimpanzees, which, together with bonobos, are our closest living relatives. These differences are grounded on anatomical modifications that must have evolved after the divergence of chimpanzees and humans from their last common ancestor. However, studying brain evolution in hominin fossil species is challenging because brains do not fossilize. To circumvent this problem, scientists can compare the brains of humans to chimpanzees and other animals to gain insight into the neural features that make our species unique. Such studies have focused on the size and reorganization of the brain, highlighting that human evolution was characterized by a

«NEONATAL BRAIN SIZE IN HUMANS REPRESENTS ONLY ONE QUARTER OF ADULT BRAIN SIZE, WHEREAS IN CHIMPANZEES AND ORANGUTANS NEONATAL BRAIN SIZE IS APPROXIMATELY ONE THIRD OF ADULT BRAIN SIZE»

tripling in overall brain size and a disproportionate expansion of frontal and parietal association areas of the cerebral cortex (Figure 1). More recent studies, however, have shifted this focus to a variety of brain properties. Among them, we consider brain plasticity especially important because it confers individuals the ability to adapt to particular environments, thus providing the grounds for the processes of behavioral and cultural evolution that are so important to our species. In this contribution, we review the available evidence for the evolution of brain plasticity in humans focusing on comparative studies of humans and chimpanzees and on the evaluation of the hominin fossil record, including the paleontological and paleogenetic evidence.

■ COMPARATIVE EVIDENCE FOR THE EVOLUTION OF DEVELOPMENTAL PLASTICITY

In comparison with other mammals, the pace of primate development is considered to be relatively precocial, meaning that neonates are born after a long gestation period with fairly advanced mobility
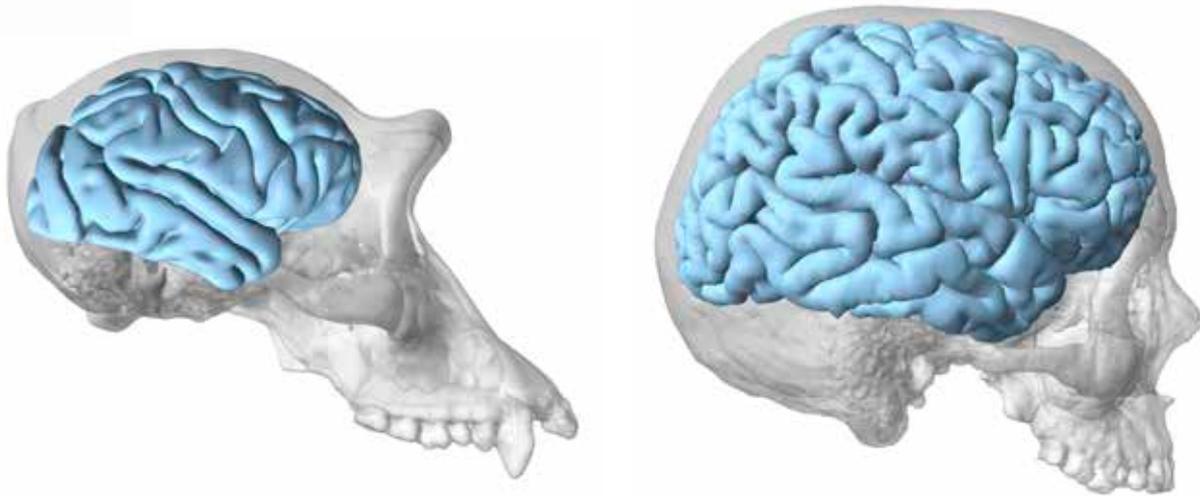
Figure 1. Differences in brain size and anatomy between chimpanzees and humans. Brain size is highly genetically heritable in both species, whereas folding patterns are also genetically heritable in chimpanzees, but not so much in humans.

Cranial models are courtesy of José Manuel de la Cuétara.

and behavioral maturity (Figure 2). However, humans have been described as secondarily altricial (Portmann, 1969), which means that humans are born in a relatively immature state in comparison with other primates. Altriciality in humans is evident in terms of relatively slow development of offspring independence and a greater demand for caregiver attention (Figure 3). This initial neonatal underdevelopment can be measured according to different variables. Gestation length in humans is approximately 270 days, which is very similar to the average gestation length observed in gorillas and orangutans (265 and 270 days, respectively) and six weeks longer than the corresponding period in chimpanzees (230 days) (Sacher & Staffeldt, 1974). In absolute terms, human newborns are roughly two times larger than ape newborns both for total body size and brain size (Table 1). Therefore, the claim that humans are secondarily altricial is not based on gestation length, absolute body or brain size. Neonatal body weight in humans is on average 5.6 % of adult body weight, which is also larger than the proportion of neonatal to adult body size observed in great apes: 3.5 % in chimpanzees, 1.2 % in gorillas and 4.1 % in orangutans following data in Sacher and Staffeldt (1974). On the contrary, neonatal brain size in humans represents only one quarter of adult brain size, whereas in chimpanzees and orangutans neonatal brain size is approximately one third of adult brain size, and gorillas are born with approximately half of their adult brain size (Table 1).

Altriciality in relative brain size is further reflected in neurological and behavioral features, which are also immature in humans at birth (Portmann, 1969). Anatomically, it has been demonstrated that

«THE PACE OF PRIMATE DEVELOPMENT IS CONSIDERED TO BE RELATIVELY PRECOCIAL, MEANING THAT NEONATES ARE BORN AFTER A LONG GESTATION PERIOD WITH FAIRLY ADVANCED MOBILITY AND BEHAVIORAL MATURITY»

Steve Hams

Species	Gestation time	Neonatal brain weight	Neonatal body weight	Adult brain weight	Adult body weight	Neonatal/adult brain weight	Neonatal/adult body weight
Gibbon	210 days	65 g	400 g	102 g	5,500 g	63.72 %	7.27 %
Orangutan	270 days	129 g	1,500 g	343 g	36,900 g	37.61 %	4.06 %
Gorilla	265 days	227 g	1,750 g	406 g	140,000 g	55.91 %	1.25 %
Chimpanzee	230 days	128 g	1,560 g	360 g	45,000 g	35.55 %	3.47 %
Humans	270 days	335 g	3,660 g	1,300 g	65,000 g	25.77 %	5.63 %

Data from Sacher and Staffeldt (1974)

Table 1. Variation in neonatal and adult brain and body weight in apes.

major sulcal patterns (the pattern of folds that is characteristic of the brain) are already established at birth, but secondary and tertiary folding, which results in regional patterns of cortical expansion, continue after birth (Hill et al., 2010). At the microstructural level, most cortical neurogenesis (production of neurons) and migration are complete at birth, such that the laminar structure of the cerebral cortex is established at term. The earliest synaptic connections are formed during the first trimester of prenatal development, but these are transient connections that will later give rise to mature circuits (Tau & Peterson, 2009).

«THE SECONDARILY ALTRICIAL NATURE OF HUMANS MEANS THAT GREATER EXPOSURE TO SOCIAL AND ENVIRONMENTAL VARIABILITY DURING THE CRITICAL PERIOD MAY EXERT A STRONG INFLUENCE ON THE ESTABLISHMENT OF BRAIN CONNECTIVITY»

At the time of birth, dendritic arborization and synaptogenesis (the formation of synapses or connections between neurons) are occurring at peak rate, which will extend well into early postnatal life. The excess of neurons and synaptic connections formed during early development is pruned later. Neuronal and synaptic pruning is essential in the reorganization of local and association circuitry that facilitates integration of information across cortical domains. Myelination, the process through which glial cells wrap axons to form multiple layers of glial cell membrane, enhances the speed and fidelity of the transmission of information, and is also essential for enabling synchronized timing of neuronal activity in sensory processing and cognition. At the time of birth in humans, unmyelinated white matter is the predominant brain tissue and the proportion of total brain volume that contains myelinated white matter is only approximately 5 % (Tau & Peterson, 2009). The secondarily altricial nature of human development means that greater exposure to social and environmental variability during the critical period has the capacity to exert a strong influence during the early establishment of connectivity. This may be especially important for the achievement of developmental milestones that typically occur in the initial period of life, such as the onset of join-attention and the first words.

A number of comparative studies have been performed that report species differences in cortical anatomy that are thought to correlate with plasticity. These studies have shown some similarities in patterns of postnatal development of neuronal distribution and dendritic morphology in prefrontal areas in chimpanzees and humans. The study of synaptogenesis patterns in developing chimpanzees

EOL

Figure 2. Primate offspring are born with rather advanced mobility. Their developmental pattern is considered relatively precocious in comparison with other mammals. Above, a group of chimpanzees; on the left, a young chimpanzee.

have also shown that, similarly to humans, synapse density peaks in chimpanzees during the juvenile period, which is followed by a subsequent period of environment-dependent synaptic pruning that leads to the establishment of adult neural circuitry and behavior (Bianchi et al., 2013). It has been demonstrated, however, that neocortical myelination is developmentally protracted in humans compared with chimpanzees, such that adult-like levels of myelination are achieved in chimpanzees at the time of sexual maturity, whereas myelination extends in humans beyond late adolescence (Miller et al., 2012). This protracted maturation in humans might be either a byproduct of developmental changes occurring earlier in life, or a particular adaptation to further refine executive and cognitive functions that characterize the transition from adolescence to early adulthood in humans (Miller et al., 2012). While major changes in decision making and emotional regulation are well-known to occur during this life history period in humans, there are not comparable data to determine whether other primates undergo similar developmental changes in cognition at the end of adolescence.

Analyses of large samples of chimpanzee and human brain MRI scans have shown that heritability for cortical organization in humans is low, whereas in chimpanzees is high and similar to the heritability level for brain size, which points to the greater level of environmental influence in cortical organization in humans (Gómez-Robles, Hopkins, Schapiro, & Sherwood, 2015). Low heritability values are observed in association areas, which also show the greatest expansion from birth to adulthood and during primate evolution (Hill et al., 2010). Interestingly, changes in these same areas have been shown to correlate with the outputs of some cognitive tests that are inferred to reflect intellectual function (Fjell et al., 2015).

Although focused on volumetric changes, the study of small longitudinal samples of chimpanzee MRI scans has provided some additional information that is relevant to the study of developmental plasticity (Sakai et al., 2012). It has been observed that increases in brain volume show a protracted course in both chimpanzees and humans, but a much more rapid increase in white matter volume during early infancy characterizes humans (Sakai et al., 2012). This suggests that the dynamic developmental changes observed in human brain tissues, which are driven by the elaboration of neural connections, may have emerged after the split of chimpanzees and humans from their last common ancestor.

SINC / Olmo Calvo

Figure 3. Humans are born in a comparatively immature state that is not observed in other primates, and need extensive parental care during the initial period of life.

«THE DYNAMIC DEVELOPMENTAL CHANGES OBSERVED IN HUMAN BRAIN TISSUES MAY HAVE EMERGED AFTER THE SPLIT OF CHIMPANZEES AND HUMANS FROM THEIR LAST COMMON ANCESTOR»

THE HOMININ FOSSIL RECORD AND THE EVOLUTION OF HUMAN BRAIN PLASTICITY

The study of the evolution of brain plasticity in hominins is challenging due to the fragmentary nature of the fossil evidence and the fact that soft tissues are not preserved. Consequently, paleoanthropology has approached this question through analyses of variation in developmental timing as inferred from changes in endocranial volume and other skeletal indicators of growth. It is generally assumed that the shift towards a more altricial pattern of development observed during hominin evolution is associated with an increased level of neural plasticity due to slower brain growth over a longer period of time (Hublin, Neubauer, & Gunz, 2015), although plasticity itself has not been studied directly from hominin endocasts. Furthermore, the study of developmental patterns in hominins is marked by significant challenges, most notably the lack of agreement concerning when a modern human-like altricial pattern of development arose. This is complicated by the fact that developmental processes, such as the rate and duration of growth, are tremendously difficult to analyze in samples that are not representative of the entire temporal span of development. There are extremely few infant and juvenile endocranial remains from hominins.

Two major types of constraints have been suggested to explain the initial evolution of human altriciality: obstetrical (Rosenberg, 1992) or metabolic (Dunsworth, Warrener, Deacon, Ellison, & Pontzer, 2012). Both types of constraints are related to the evolution of a progressively larger brain. In combination with the narrow birth canal that is typical of fully bipedal hominins, a large brain poses spatial limitations during parturition (Rosenberg, 1992), and will also require large amounts of energy that cannot be supplied by the mother, thus truncating gestation (Dunsworth et al., 2012). Therefore, an altricial pattern of development is expected to characterize hominins as brain size increased. Consequently, australopiths and possible earlier hominins with relatively small brains and non-modern body configurations are likely to have shown a more precocial pattern of development similar to the one that characterizes living great apes.

Hominin species with an adult brain size comparable to that of modern humans, such as Neanderthals and possibly the last common ancestor of Neanderthals and modern humans, may be inferred to have shown a similarly altricial pattern of brain size growth. However, it has been noted that the pattern of early postnatal development differs substantially between Neanderthals and modern humans, with the latter showing an early globularization phase that is not observed in the former (Gunz, Neubauer, Maureille, & Hublin, 2010). Functional factors related to superior parietal lobe reorganization in modern humans might drive these differences (Bruner, De la Cuétara, & Holloway, 2011; Gunz et al., 2010), but it has been suggested as well that globularization can be the result of pervasive genetic interactions between different elements of the craniofacial complex (Martínez-Abadías et al., 2012).

For species with a brain size between modern humans and great apes, such as *Homo erectus*, it has been more challenging to determine their developmental pattern. Whereas some researchers have estimated the pattern of postnatal brain size development of *Homo erectus* to be intermediate between that of chimpanzees and modern humans, others have suggested that its developmental pattern was within the range of variation of *Homo sapiens* (reviewed in Hublin et al., 2015). Favoring one or the other position is not straightforward because they both have similar drawbacks. First, most inferences concerning *Homo erectus* developmental patterns are based on the study of one single infant, the Mojokerto child. Because brain growth rate is estimated from the proportion of adult brain size reached by this child at death, inferences critically depend on his/her age, which has been estimated to be as young as less than one year old and as old as eight years old. Second, developmental patterns are often estimated from comparisons of infant and adult endocranial size, which provides a crude estimate of the rate and duration of brain size growth and cannot provide insight into the cellular and molecular mechanisms of brain development, including processes of axonal and dendritic growth, synaptogenesis and neuronal and synaptic pruning that underlie the establishment of neural circuitry, myelination, or the folding of the neocortex. Third, another source of discrepancy

> «A NUMBER OF COMPARATIVE STUDIES HAVE BEEN PERFORMED THAT REPORT SPECIES DIFFERENCES IN CORTICAL ANATOMY THAT ARE THOUGHT TO CORRELATE WITH PLASTICITY»

$FOXP2^{hum}$ (coding)
$FOXP2^{hum}$ (regulatory)
$SRGAP2C^{hum}$
Modern humans

$FOXP2^{hum}$ (coding)
$FOXP2^{nonhum}$ (regulatory)
$SRGAP2C^{hum}$

$FOXP2^{hum}$ (coding)
$FOXP2^{nonhum}$ (regulatory)
$SRGAP2C^{hum}$
Neanderthals

Denisovans

$FOXP2^{hum}$ (coding)
$FOXP2^{nonhum}$ (regulatory)
$SRGAP2C^{hum}$

4,000–1,100   600   400   0
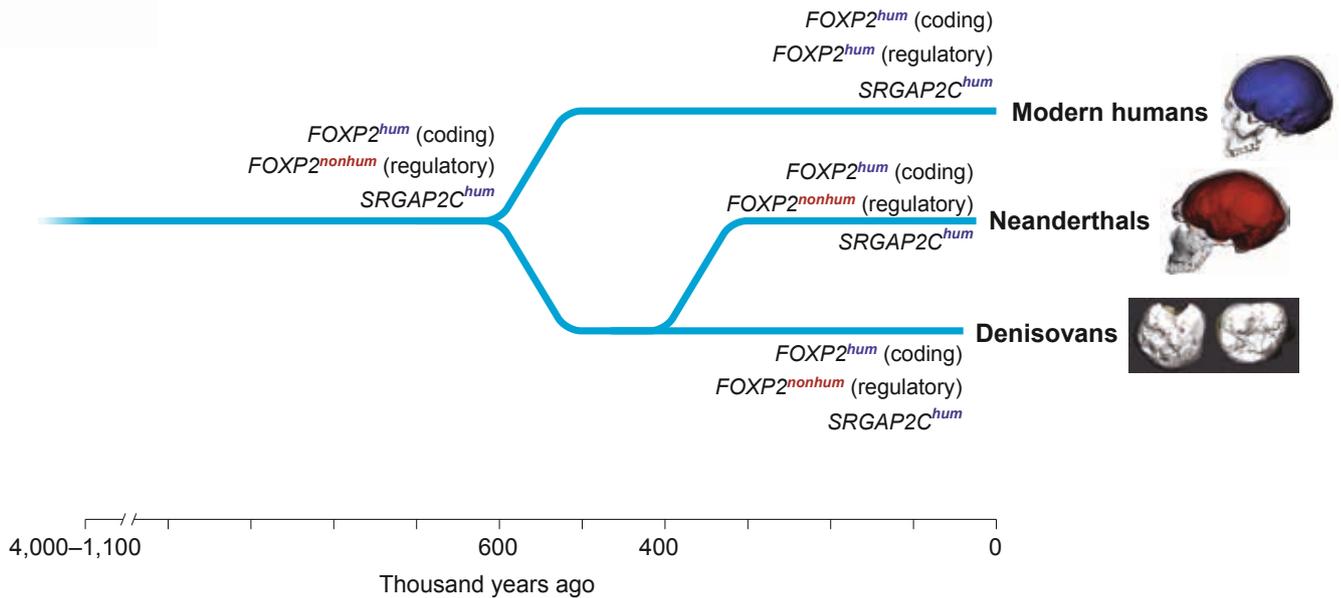
Thousand years ago

Figure 4. Evolution of plasticity-related genes as inferred from ancient DNA. *FOXP2* coding changes typical of modern humans are also found in Denisovans and Neanderthals, whereas regulatory changes appear to be unique to modern humans. Changes in *SRGAP2* paralogs are shared by the three species.

corresponds to the geological age of Mojokerto child, estimated to be 1.2-1.8 Ma. Although this variation is itself substantial and has important implications for developmental inferences, it certainly corresponds to an early representative of *Homo erectus*, whose temporal range is estimated to be 1.8 Ma to less than 100 ka. Because a temporal trend to increase brain size exists from earlier to later *Homo erectus*, a gradual modification of developmental patterns across *Homo erectus* evolution cannot be ruled out.

Changes in later development can also have an effect on brain plasticity. The extended period of neural development observed in *Homo sapiens* offers an additional opportunity for environment-dependent brain maturation during adolescence and early adulthood, during which important processes, such as myelination (Miller et al., 2012) and continued developmental pruning of synaptic spines in the prefrontal cortex (Petanjek et al., 2011) are known to occur. This later extended period of brain maturation is expected to have a less critical role in increasing brain plasticity than the initial postnatal period,

«THE STUDY OF DEVELOPMENTAL PATTERNS IN HOMININS IS MARKED BY SIGNIFICANT CHALLENGES, MOST NOTABLY THE LACK OF AGREEMENT CONCERNING WHEN A MODERN HUMAN-LIKE ALTRICIAL PATTERN OF DEVELOPMENT AROSE»

during which major brain size growth and patterning are underway. However, the adolescent period has been suggested to be important in the acquisition of social skills and in the establishment of adult forms of language and communication, as well as in the acquisition of adult foraging skills (Schuppli et al., 2012).

Studies of life history in hominin species mostly rely on inferences made from dental development. Apart from being very abundant and well preserved in the fossil record, teeth are less sensitive to developmental perturbations and to short-term ecological perturbations than other tissues, which makes them useful to infer maturation patterns through dental microstructure and through their timing and sequence of eruption. These dental studies have shown that some aspects of a modern human-like pattern of development may have arisen at ca. 1 Ma (Bermúdez de Castro et al., 2010), but subtle differences seem to remain between Neanderthals and modern humans (Smith et al., 2010), which might be related to differences in brain plasticity.

INSIGHTS FROM ANCIENT DNA

Insights into the evolution of brain plasticity can be also gleaned from the study of ancient DNA through the comparison of the genome of modern humans, Neanderthals and Denisovans. Mitochondrial DNA has also been obtained from some Middle Pleistocene hominins, but paleogenomic information on these hominins is still too limited to be included in this comparison. Among those genes that show human-specific changes, a number of them are involved in brain growth and development. In particular, the human version of *FOXP2*, a gene whose mutation is related to severe speech disabilities, has been shown to increase plasticity in cortico-striatal circuits when expressed in mice (Enard et al., 2009). The human version of this gene, which differs from the chimpanzee's, has been found also in Neanderthals and Denisovans, which indicates that the forms of brain plasticity associated with *FOXP2* mutation during hominin evolution may have been shared by several late hominin species (Figure 4). However, it has been suggested as well that, although coding changes in the *FOXP2* sequence may have evolved before the divergence of the clade including Denisovans, Neanderthals and modern humans, they may have been later followed by regulatory changes unique to modern humans (Maricic et al., 2013). *SRGAP2*, a gene involved in neocortical development, is also a good candidate to be involved in the evolution of human brain plasticity. This gene has undergone two duplications after the divergence of chimpanzees and humans. One of these duplications, designated as *SRGAP2C*, is expressed in the developing human brain, where it dimerizes with ancestral *SRGAP2*, thus inhibiting its function. This inhibition underlies certain human-specific neural developmental changes that are related to brain plasticity, including neoteny during spine maturation. This duplication has been inferred to occur at 2-3 Ma (Dennis et al., 2012), corresponding roughly with the emergence of the genus *Homo,* which is associated with continued neocortical expansion and intensification of widespread manufacture of stone tools. Consistent with this estimate, both Neanderthals and Denisovans have been shown to carry human-specific duplications (Dennis et al.,

«INSIGHTS INTO THE EVOLUTION OF BRAIN PLASTICITY CAN BE ALSO GLEANED FROM THE STUDY OF ANCIENT DNA THROUGH THE COMPARISON OF THE GENOME OF MODERN HUMANS, NEANDERTHALS AND DENISOVANS»

2012). As in the case of *FOXP2* evolution, specific aspects of brain plasticity related to the evolution of *SRGAP2* paralogs may have been shared by several species within the genus *Homo* (Figure 4).

Epigenetic regulation is influenced by several factors, including stochastic, genetic and environmental effects. Therefore, a new approach that offers a promising window to evaluate the evolution of brain plasticity is the study of the epigenome. Cytosine methylation is one of the best known epigenetic markers, and it is often associated with gene silencing. Recent studies have used the natural degradation process of methylated and unmethylated cytosines to infer methylation maps in Denisovans and Neanderthals (Gokhman et al., 2014), for which high-coverage genome sequences are available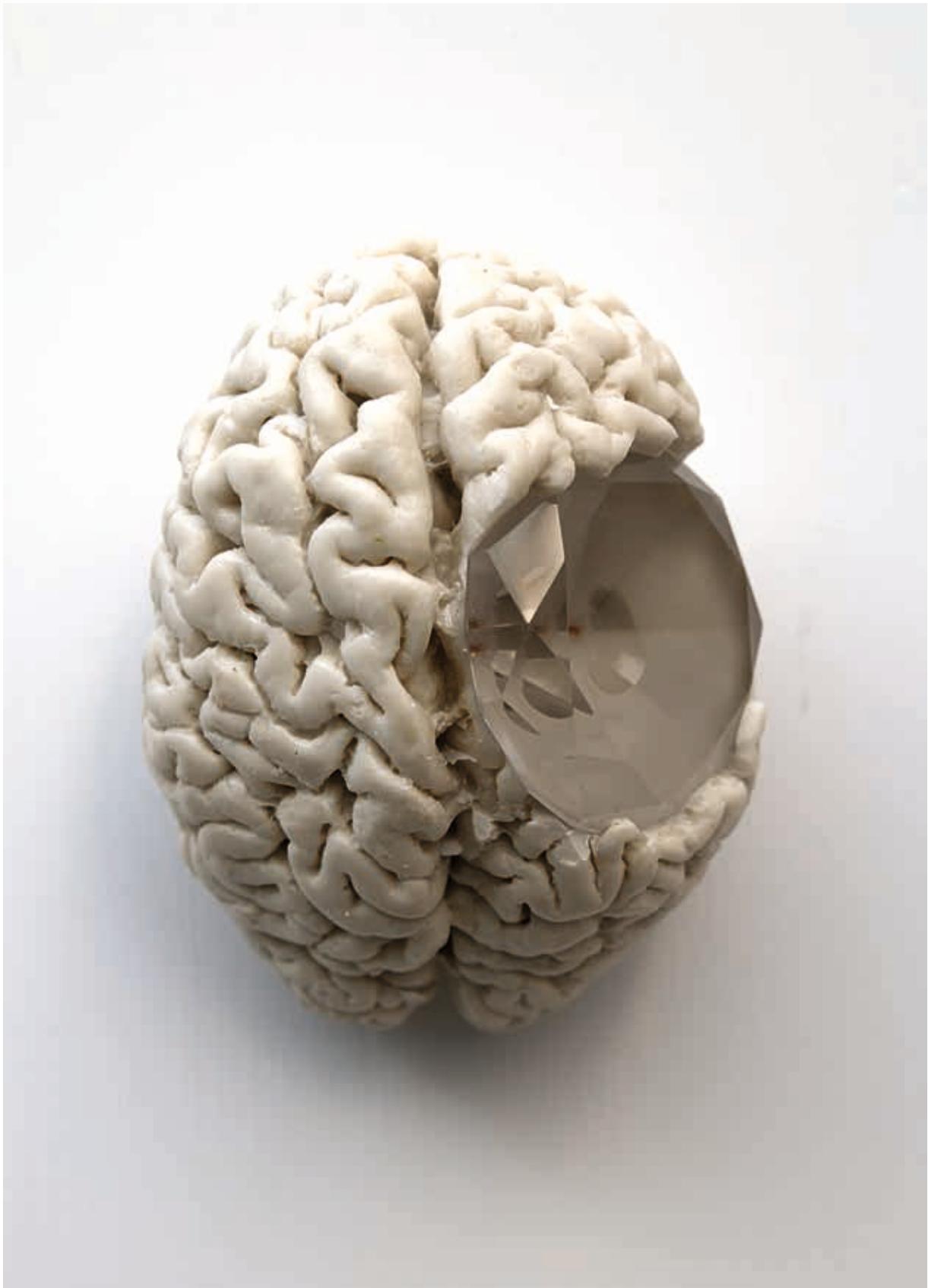. The comparison of the Neanderthal, Denisovan and modern human epigenomes have shown some differentially methylated regions that are especially common in brain-related genes (Gokhman et al., 2014). This observation may initially appear to support the conclusion that there are differences in brain plasticity between the three species. However, these results are difficult to interpret considering the intrinsic difficulties of studying epigenetic variation in a paleoanthropological context. It has been highlighted that DNA methylation patterns are cell type- and developmental stage-specific. Because methylation maps in Neanderthals and Denisovans come from bone tissue, it is difficult to know how the observed epigenetic signature can be extrapolated to developing brain tissue. Neanderthal and Denisovan methylation maps may represent individual and bone-specific epigenetic signatures, but their utility to shed light on the complexity of epigenetic changes across the development of different organs can be limited.

CONCLUDING REMARKS

Increasing evidence demonstrates that one of the key specializations of the human brain is its high degree of plasticity. Comparisons with great apes show that human brains are substantially more plastic than those of our closest living relatives. Paleontological and paleogenetic analyses, however, show that other fossil species within our evolutionary tree, such as

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Lidó Rico. *Brilliant*, 2016. «Genoarchitectures» series. Polyester resin, 12 × 15 × 10 cm.

Neanderthals and Denisovans, may have shared certain aspects of brain plasticity with modern humans. A high level of developmental plasticity can be an indirect result of selection for early parturition in hominin species with increased brain size, which poses strong obstetric and metabolic constraints. These can be relaxed by giving birth to immature offspring whose brain will develop postnatally and under the influence of extensive environmental, social and cultural influences. Different studies have shown that these external influences shape brain anatomy and behavior. A plastic brain is likely more efficient in integrating the external experience with the formation of neural circuits that are responsible for behavior, thus providing a link between biological evolution and cultural evolution. ⊕

REFERENCES

Bermúdez de Castro, J. M., Martinón-Torres, M., Prado, L., Gómez-Robles, A., Rosell, J., López-Polín, L., ... Carbonell, J. L. (2010). New immature hominin fossil from European Lower Pleistocene shows the earliest evidence of a modern human dental development pattern. *Proceedings of the National Academy of Sciences, 107*(26), 11739–11744. doi: 10.1073/pnas.1006772107

Bianchi, S., Stimpson, C. D., Duka, T., Larsen, M. D., Janssen, W. G. M., Collins, Z., ... Sherwood, C. C. (2013). Synaptogenesis and development of pyramidal neuron dendritic morphology in the chimpanzee neocortex resembles humans. *Proceedings of the National Academy of Sciences, 110*(2), 10395–103401. doi: 10.1073/pnas.1301224110

Bruner, E., De La Cuétara, J. M., & Holloway, R. L. (2011). A bivariate approach to the variation of the parietal curvature in the genus *Homo*. *The Anatomical Record, 294*(9), 1548–1556. doi: 10.1002/ar.21450

Dennis, M. Y., Nuttle, X., Sudmant, P. H., Antonacci, F., Graves, T. A., Nefedov, M., ... Eichler, E. E. (2012). Evolution of human-specific neural *SRGAP2* genes by incomplete segmental duplication. *Cell, 149*(4), 912–922. doi: 10.1016/j.cell.2012.03.033

Dunsworth, H. M., Warrener, A. G., Deacon, T., Ellison, P. T., & Pontzer, H. (2012). Metabolic hypothesis for human altriciality. *Proceedings of the National Academy of Sciences, 109*(38), 15212–15216. doi: 10.1073/pnas.1205282109

Enard, W., Gehre, S., Hammerschmidt, K., Hölter, S. M., Blass, T., Somel. M., ... Pääbo, S. (2009). A humanized version of *FOXP2* affects cortico-basal ganglia circuits in mice. *Cell, 137*(5): 961–971. doi: 10.1016/j.cell.2009.03.041

Fjell, A. M., Westlye, L. T., Amlien, I., Tamnes, C. K., Grydeland, H., Engvig, A., ... Walhovd, K. B. (2015). High-expanding cortical regions in human development and evolution are related to higher intellectual abilities. *Cerebral Cortex, 25*(1), 26–34. doi: 10.1093/cercor/bht201

Gokhman, D., Lavi, W., Prüfer, K., Fraga, M. F., Riancho, J. A., Kelso, J., ... Carmel, L. (2014). Reconstructing the DNA methylation maps of the Neandertal and the Denisovan. *Science, 344*(6183), 523–527. doi: 10.1126/science.1250368

Gómez-Robles, A., Hopkins, W. D., Schapiro, S. J., & Sherwood, C. C. (2015). Relaxed genetic control of cortical organization in human brains compared with chimpanzees. *Proceedings of the National Academy of Sciences, 112*(51), 14799–14804. doi: 10.1073/pnas.1512646112

Gunz, P., Neubauer, S., Maureille, B., & Hublin, J. J. (2010). Brain development after birth differs between Neanderthals and modern humans. *Current Biology, 20*(21), R921–R922. doi: 10.1016/j.cub.2010.10.018

Hill, J., Inder, T., Neil, J., Dierker, D., Harwell, J., & Van Essen, D. (2010). Similar patterns of cortical expansion during human development and evolution. *Proceedings of the National Academy of Sciences, 107*(29), 13135–13140. doi: 10.1073/pnas.1001229107

Hublin, J. J., Neubauer, S., & Gunz, P. (2015). Brain ontogeny and life history in Pleistocene hominins. *Philosophical Transactions of the Royal Society B, 370*(1663), 20140062. doi: 10.1098/rstb.2014.0062

Maricic, T., Günther, V., Georgiev, O., Gehre, S., Curlin, M., Schreiweis, C., ... Pääbo, S. (2013). A recent evolutionary change affects a regulatory element in the human *FOXP2* gene. *Molecular Biology and Evolution, 30*(4), 844–852. doi: 10.1093/molbev/mss271

Martínez-Abadías, N., Esparza, E., Sjøvold, T., González-José, R., Santos, M., Hernández, M., & Klingenberg, C. P. (2012). Pervasive genetic integration directs the evolution of human skull shape. *Evolution, 66*(4), 1010–1023. doi: 10.1111/j.1558-5646.2011.01496.x

Miller, D. J., Duka, T., Stimpson, C. D., Schapiro, S. J., Baze, W. B., McArthur, M. J., ... Sherwood, C. C. (2012). Prolonged myelination in human neocortical evolution. *Proceedings of the National Academy of Sciences, 109*(41), 16480–16485. doi: 10.1073/pnas.1117943109

Petanjek, Z., Judaš, M., Šimić, G., Rašin, M. R., Uylings, H. B. M., Rakic, P., & Kostović, I. (2011). Extraordinary neoteny of synaptic spines in the human prefrontal cortex. *Proceedings of the National Academy of Sciences, 108*(32), 13281–13286. doi: 10.1073/pnas.1105108108

Portmann, A. (1969). *Biologische Fragmente zu einer Lehre vom Menschen*. Basel: Benno Schwabe.

Rosenberg, K. R. (1992). The evolution of modern human childbirth. *American Journal of Physical Anthropology, 35*(S15), 89–124. doi: 10.1002/ajpa.1330350605

Sacher, G. A., & Staffeldt, E. F. (1974). Relation of gestation time to brain weight for placental mammals: Implications for the theory of vertebrate growth. *American Naturalist, 108*(963), 593–615.

Sakai, T., Matsui, M., Mikami, A., Malkova, L., Hamada, Y., Tomonaga, M., ... Matsuzawa, T. (2012). Developmental patterns of chimpanzee cerebral tissues provide important clues for understanding the remarkable enlargement of the human brain. *Proceedings of the Royal Society B, 280*(1753), 20122398. doi: 10.1098/rspb.2012.2398

Schuppli, C., Isler, K., & Van Schaik, C. P. (2012). How to explain the unusually late age at skill competence among humans. *Journal of Human Evolution, 63*(6), 843–850. doi: 10.1016/j.jhevol.2012.08.009

Smith, T. M., Tafforeau, P., Reid, D. J., Pouech, J., Lazzari, V., & Zermeno, J. P. (2010). Dental evidence for ontogenetic differences between modern humans and Neanderthals. *Proceedings of the National Academy of Sciences, 107*(49), 20923–20928. doi: 10.1073/pnas.1010906107

Tau, G. Z., & Peterson, B. S. (2009). Normal development of brain circuits. *Neuropsychopharmacology, 35*(1), 147–168. doi: 10.1038/npp.2009.115

«INCREASING EVIDENCE DEMONSTRATES THAT ONE OF THE KEY SPECIALIZATIONS OF THE HUMAN BRAIN IS ITS HIGH DEGREE OF PLASTICITY. HUMAN BRAINS ARE SUBSTANTIALLY MORE PLASTIC THAN THOSE OF OUR CLOSEST LIVING RELATIVES»

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