The primate brain connectivity bauplan and human-specific variations

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Abstract

The organization of connectivity in the human brain follows a general primate connectivity ‘bauplan’. Variations specific to the human lineage are mostly found in association fibers. Parietal-frontal connectivity is much more elaborate than seen in other primates, and this is related to the expansion of both these parts of association cortex. Temporal cortex specializations are often underappreciated, but quite prominent. Dorsal longitudinal fibers project deep into temporal cortex and temporal longitudinal tracts have prominent parietal projections. These anatomical specializations are thought to relate to particular behavioral domains, including social cognition and language.

The importance of studying connectivity for comparative neuroscience

The specializations of the human animal have been a fascination of science and philosophy from the very start. While it seems self-evident that humans must possess neural capabilities unique amongst the animal kingdom, specifying what they are and their evolutionary origins has proved elusive. However, advances in our understanding of both the ecological circumstances of early humans and in comparing the architecture of the human brain to that of its nearest relatives in the animal kingdom now make it possible to sketch the neuroecology of the human brain (Mars and Bryant, 2021). Here, we present one aspect of this endeavour by discussing our understanding of human brain connectivity and its relationship to behaviour. We argue that there are three reasons why studying connectivity is particularly useful when trying to understand the origins and organization of the human brain.

The importance of studying connectivity to understand the brain was articulated in a seminal paper by Passingham and colleagues (2002). They argued that each part of the brain has a unique set of connections with the rest of the brain, which they termed the area's 'connectivity fingerprint', echoing the term used by Zilles and colleagues to describe the receptor architecture of brain regions (Zilles et al., 2002). The connections of a brain region constrain the information it has access to and the influence it can exert on the rest of the brain. Therefore, the connectivity fingerprint was argued to be an essential determinant of a region's function. At the time, however, the relationship between connectivity and function could not be conclusively established. When the original paper was revisited 15 years after its publication (Mars et al., 2018a), this relationship was much clearer. Studies on individual differences, development, and lesions all showed a direct relationship between connections, functional activations of brain regions, and behavior. Thus, one major reason for studying connectivity is because it is a level of description of brain organization that has a direct relationship to function.

The second—related—reason for highlighting connectivity in a chapter on human neuroecology is that connectivity is a suitable phenotype when studying diversity in brain organization. Genetic variations set up differences in brain size and organization, but the ultimate phenotype is determined in interaction with the environment and individual experience (Krubitzer and Kaas, 2005). The mammalian neocortex can be said to be particularly underspecified, with developmental and environment influences crucially important in realising its organization at any given time. Connectivity is influenced by all these factors. For instance, comparative studies have shown that connections can differ in a meaningful way between closely related species, such as in frontal-limbic connectivity between chimpanzees and bonobos (Rilling et al., 2012). Connectivity also changes during ontogeny and throughout the lifetime as a factor of environmental exposure, such as when learning to read (Thiebaut de Schotten et al., 2014). Connectivity is also predictive of ability to recover from brain injury and reflects reorganization after developmental or acquired peripheral abnormalities (Forkel et al., 2014; Karlen et al., 2006). Connectivity is therefore a suitable phenotype to study when trying to understand the specializations of the human brain.

The third and most pragmatic reason for studying connectivity is that it is something we can do well. Traditionally, connectivity was studied predominantly in non-human animals, using invasive tracers. Although this provides very detailed and accurate maps, the method is expensive in terms of costs, labour, and sacrificed animals and was available only to few laboratories. For the human brain, post-mortem dissection techniques were all that was available. The rise of non-invasive neuroimaging has dramatically altered this situation. Connectivity can now be studied in-vivo in the human brain, at relatively low costs. Diffusion MRI and associated tractography algorithms allow one to reconstruct the major white matter fibers of the brain. Resting state functional connectivity provides a measure of how strongly the spontaneous activation of different areas correlates, which is related to their connections. Although both measures are indirect and show only partial correlations with tracer data (Donahue et al., 2016; Grandjean et al., 2023), they are nevertheless reliable, replicable, and predictive of other aspects of brain and behaviour, both structural and functional (Mars et al., 2018a; Smith et al., 2009). Connectivity is therefore a measure of brain organization that is both useful and accessible to researchers of many species, including humans.

Both diffusion MRI and resting state fMRI have now been used extensively to compare connectivity across species. Over time, this work has progressed from replicating known patterns of connectivity from monkey tracer studies to the human (Rushworth et al., 2006), establishment of the techniques in non-human animals (Schmahmann et al., 2007; Vincent et al., 2007), and replication of patterns of connectivity across species using the same method (Margulies et al., 2009; Mars et al., 2011). Currently, diffusion MRI and resting state fMRI data are increasingly available in large public databases. Repositories exist that are specific to macaques, mice, and rats (Grandjean et al., 2023, 2020; Milham et al., 2018), as well as those containing larger ranges of species (e.g., Tendler et al. (2022), see Thiebaut et al. (2019) for a list of databases). These data are now complemented with an increasing set of tools for comparison of brain connectivity across species. Connectivity fingerprints are matched across species (Mars et al., 2016; Schaeffer et al., 2020), fiber atlases are constructed using comparable protocols (Warrington et al., 2020), and whole brain connectivity is compared within a single reference frame (Mars et al., 2018b; Suarez et al., 2022).

In this chapter, we will review some of these recent developments, with the aim to understanding their contributions to elucidating the unique specializations of the human brain. Since it is impossible to be exhaustive, the goal here is to provide a framework for the types of questions and answers emerging in the literature, as well as to highlight some of the open questions that currently are only starting to be addressed.

The primate connectivity blueprint: the general plan

The primate brain is a visuomotor brain (Wise, 2006). The first primates are thought to have been tree-dwelling mammals, specialized for a niche foraging in the small branches of angiosperm trees (Fleagle, 2013). They started to rely more on vision, rather than prioritizing hearing and smell as most mammals do. Two forward facing eyes helped with binocular vision and detailed object perception. Adaptations in their shoulders, wrists, and hands helped them manoeuvrer and balance while reaching for the fruits of their home. The primate brain changed along with these modifications in body and behaviour (Mars, forthcoming; Wise, 2024). In this section, we will discuss some of the general trends in connectional organization of the primate brain. Rather than an exhaustive review, this section is meant to present a coarse, general 'bauplan' of primate white matter, the variation and functional implications of which—in particular in the human lineage—we will discuss later in the chapter.

The primate brain is visually dominated by the neocortex. The neocortex as a six-layered structure is a mammalian invention, homologous to the dorsal cortex in reptiles, but has dramatically expanded in some lineages, especially primates (Kaas, 2011). Most functional studies of the primate brain therefore focus on this part of the brain. However, the neocortex does not receive information from the outside world directly, only via other parts of the central nervous system. Fibers that connect the neocortex with other parts of the forebrain and with the rest of the central nervous system are termed projection fibers. These include the corticospinal tract, optic and acoustic radiations (Fig. 1A), but also thalamocortical connections and cortico-basal ganglia connections. In many cases, these connections show a distinct topography that often takes the form of 'loops', where a series of parallel pathways connects distinct areas of neocortex with distinct areas of non-cortical territory (Behrens et al., 2003; Dum and Strick, 2003; Haber, 2003).

Different parts of the neocortex are connected through an elaborate system of fibers, generally termed association fibers (Fig. 1B). The most prominent association fibers reflect the fact that the primate brain is a visuomotor brain. From the occipital cortex, two major pathways carrying visual information emerge: a ventral pathway through the temporal cortex and a dorsal pathway through the parietal cortex (Mishkin et al., 1983). Although both pathways have proposed subdivisions in different primate lineages (Haak and Beckmann, 2018; Rizzolatti and Matelli, 2003) and their separation can vary, the general architecture is consistent.

The ventral pathway is traditionally labeled the object pathway or the vision for perception pathway. Longitudinal connections run from the early visual areas of the extrastriate cortex throughout the length of the temporal cortex in the inferior longitudinal fascicle (ILF), which is distinct from the nearby optic radiation. From anterior temporal cortex a u-shaped bundle through the extreme capsule, the uncinate fascicle (UF), connects to ventral prefrontal cortex. The presence of a longitudinal bundle parallel to ILF but more medial, running from extrastriate throughout temporal cortex and reaching frontal cortex has long been identified in the human, but its presence in other primates has been controversial. More recent work using blunt dissection in addition to diffusion MRI tractography have identified this bundle in two Old World monkeys (Decramer et al., 2018; Sarubbo et al., 2019). A third longitudinal fiber bundle, the middle longitudinal fascicle, runs more dorsally in the superior temporal gyrus, extending from the inferior parietal cortex to the temporal pole, connecting many multimodal regions of the temporal lobe.

The parietal and the frontal cortex are connected through an extensive set of longitudinal fibers. Recognized subdivisions and terminology of these fibers has changed repeatedly since their first identification (Schmahmann and Pandya, 2006), making a comparison across studies challenging. Nowadays, most authors recognise a set of superior longitudinal fibers, which in larger primates can be separated into three subdivisions organized in a dorsomedial to ventrolateral fashion, namely the SLF1, SLF2, and SLF3. In the human brain, these bundles tend to project to areas in the superior, medial, and inferior superior gyrus (Thiebaut de Schotten et al., 2011). In smaller primates, these bundles might be less easy to separate and some authors have therefore referred to an ‘SLF complex’ (Bryant et al., 2021). The arcuate fascicle is now commonly recognised as a fourth bundle that runs close to the second and third branches of the SLFs but has a distinct projection profile. The terms SLF and AF have long been used synonymously, with some studies referring to ‘SLF/AF’, but the bundles are now seen as separate at least in macaque monkeys and apes (Thiebaut de Schotten et al., 2012).

A separate set of fibers runs from the amygdala along the parahippocampal gyrus, in posterior and dorsal direction along the most medial part of the temporal lobe, curving around the corpus callosum before running anteriorly towards the frontal cortex through the cingulate gyrus (Fig. 1C). This cingulum bundle has been described as a limbic bundle, as it connects parts of the traditional limbic system with the frontal cortex (Catani et al., 2013). However, it is now understood that many brain regions send fibers through only parts of the cingulum bundle, suggesting that the bundle can be segmented into subtracts or zones (Heilbronner and Haber, 2014). More direct connections from the amygdala to the frontal cortex via the amygdalofugal bundle have also been described in a wide range of primates (Folloni et al., 2024, 2019). Another limbic tract often described in primates is the fornix, which runs between the hippocampus and nearby mamillary bodies, but follows a course that starts parallel to the cingulum, curving around the thalamus to reach the mamillary bodies.

Within frontal cortex, we see terminations of fibers from parietal SLF, cingulum, and temporal interiof fronto-occipital fascicle (IFOF) and UF. In addition, a number of shorter fibers within the frontal lobe have been described, including the frontal aslant connecting ventrolateral and dorsomedial parts of the lateral convexity and the orbitopolar tract (Thiebaut de Schotten et al., 2012).

Although the details of endpoints may vary both quantitatively and qualitatively, these categories of fiber bundles can be observed across primates, including humans. Thus, it is likely not an alteration of the bauplan per se, but rather a variation on the theme, that generates uniquely human behaviors and cognition.

The primate connectivity bauplan as a variation of the mammalian

When comparing brain organization across species in an evolutionary context, one can inevitably choose either of two perspectives. The first is to look for general principles of organization, to establish whether there are rules or patterns that all of the biological systems under study abide by (cf. Striedter (2005)). In a way, this is a search for the constraints placed upon phylogenetic diversity, whether they are imposed by physics (for instance, flying animals have to deal with the constraints that gravity places on them) or phylogenetic history (a primate cannot simply turn into an amphibian). The second perspective is to understand each brain in terms of its unique adaptations, to understand how a particular phenotype can help promote fitness in a particular ecological niche. This section and the next will reflect these two extremes. In this section, we will discuss how the primate connectome reflects many aspects of those of other mammalian species. Finding commonalities across the connectomes of most or all mammalian orders presents a strong case for the existence of general rules underlying brain connectivity. In the next section, we will then see how phylogenetic diversity can exist in the context of these rules, by studying the human connectome in relationship to that of other primates.

One prominent way to elucidate general patterns of evolution is to search for scaling rules. By investigating how the size of a brain changes with body size or how the size of parts of the brain scales with whole brain size, we can gain an understanding of the constraints placed upon. A standard example of such allometric scaling is in the size of leg bones. If we should scale the leg bones of a dog to the size of those of an elephant, they would not be strong enough to support the weight of an elephant. The bones need to increase disproportionally to the body size of the animal. For brain connectivity, it has commonly been observed that the volume of white matter outpaces the volume of grey matter when brain increase in size (Rilling and Insel, 1999). However, the size of the cortical surface, which one could argue is the relevant dimension to study when one is interested in the number of computational units of grey matter, outpaces even the white matter (Ardesch et al., 2022; Hofman, 1989). These results mean that connectivity changes with brain size in somewhat surprising ways: cortices with larger numbers of neurons (because of size and cortical folding) are actually less highly connected than would be expected from simple scaling (Herculano-Houzel et al., 2010). However, understanding how these changes manifest themselves requires a close study of the actual pattern of connectivity, the connectome.

The first, perhaps obvious, observation of all mammalian connectomes is that they both are not a fully connected network in which all areas are connected to all other areas, and that they are not connected randomly. In the early part of the 21st century, when connectivity data became increasingly available thanks to neuroimaging, a number of groups started applying graph theory and related methods to study brain organization (Bullmore and Sporns, 2009). This work showed that brain networks adhere to a small network architecture, which is characterized by a high clustering coefficient and low shortest path lengths between areas. Given the energetic demands of producing and maintaining connections in the human brain, such an architecture was argued to be an efficient compromise between biological feasibility and efficient communication (Bassett and Bullmore, 2006). Further research nuanced this point, identifying a set of regions that were more interconnected with one another than would be predicted based on their overall number of connections. This group was deemed the 'rich club', a set of areas that show long-distance connectivity, allowing signals from one cluster of regions to be quickly relayed to other clusters (Harriger et al., 2012). As such, quick communication was argued to have gained relative preference to pure economy of wiring in the brain.

Since these constraints should apply to all animals, network analysis of connectomes was quickly employed as a tool in comparative studies. Indeed, one review argued the principles of small worldness with rich clubs to be a ubiquitous feature of connectome wiring, even beyond the mammalian brain (van den Heuvel et al., 2016). The availability of increasingly large datasets allowed such hypotheses to be put to the test. Assaf and colleagues (2020) used diffusion MRI data to test whether the balance between communication speed and wiring costs was conserved across the brains of 123 different species. Across brain volumes, as brain size decreased by four orders of magnitude from 1000 to 0.1 ml, the efficiency of communication as indicated by the mean shortest path between areas only decreased by 40%. They therefore argued that whichever differences there are across brains, there must be accompanying changes that maintain the overall connectivity. They tested this hypothesis for the case of inter- vs intrahemispheric connectivity, showing that in brains with fewer commissural fibers, and therefore likely an increase in the brain's overall mean shortest path length, there is a decrease in the intrahemispheric mean shortest path length. In other words, if there is less connectivity between the hemispheres, there is increased connectivity within hemispheres, which leads to an overall similar lengths of communication paths in the brain. Similar results were obtained by Ardesch and colleagues (2022), who showed that larger brains tend to show more local clustering and fewer long-range connections to maintain the balance of wiring costs and communication efficiency.

Wiring costs thus present an important constraint on the architecture of a connectome at a high level of description. But it does not fully explain the presence or absence of specific connections at the areal level. Goulas and colleagues (2019) investigated the relationship between connectivity and cytoarchitecture in the macaque and marmoset monkeys, the cat, and the mouse. It is well established that feedforward and feedback connection originate in different cortical layers (Rockland and Pandya, 1979), but Goulas *et al.* found that the cytoarchitecture of a region is related to its connectivity profile in additional ways. First, areas with similar cytoarchitecture tended to be connected more than areas with dissimilar cytoarchitecture in most species tested. This effect was independent of the fact that areas that are closer together tend to be more likely to be connected. Second, laminar origin of a connection was better predicted by cytoarchitecture than by topology of the region. Importantly, while all animals in the study showed a connectome with core regions similar to the rich club described above and peripheral regions, the cytoarchitectonic differentiation of these regions differed across species. This complements earlier work showing that regions with high connectivity are not always located in homologous regions across primates (Li et al., 2013). Overall, one can conclude that cytoarchitecture presents another factor constraining connectome architecture across species.

Large comparative datasets can also be used to investigate the constraint of phylogenetic relatedness. Using the same data as the study above, Suarez and colleagues (2022) sought to directly compare connectional architectures across the mammalian order. Each brain was divided into 200 random areas, and the connectivity matrix was calculated. Following the logic of the common space approach, in which different brains are described in terms of an abstract feature space that is comparable across brains even if they differ in size and morphology (cf. Mars et al. (2021)), Suarez and colleagues calculated the Laplacian eigenspectrum of the connectivity matrix. They could then determine the spectral distance between different species' connectomes. Spectral distances within taxonomic orders were significantly lower than those across orders. Importantly, the authors then went on to study what drove some of the differences between different species' connectomes. Local properties of the connectome were more different across species than global measures. This result, the authors argued, shows how conservation and adaptation occur together in the comparative connectome.

Connectivity across brains appears to share fundamental principles of organization, including rich club structure and relationship with cytoarchitecture. These are thus illuminating features about how brains in general evolve, along with giving us some explanations for why and how brains may differ across species.

Human connectivity

The last common ancestor of humans and other great apes lived 6.4 million years ago. Climatological changes meant that in a part of the African continent a group of great apes adapted a lifestyle different from that of the others. Whereas most great apes are forest dwellers, our ancestors adapted to life in the savannah grasslands. In an increasingly volatile climate, they became generalists, capable of foraging in a wide variety of niche, adapting their diet to the ecological circumstances to maximize their overall food return for time and effort invested (Lieberman, 2014; Mars, forthcoming). Over the course of this evolution, our ancestors became more cooperative, building foraging groups that were able to divide tasks and pool resources (Tomasello, 2014). All these new behaviors were associated with changes in our brain.

Following the split between the lineage leading up to humans and the lineage leading to chimpanzees and bonobos, brain size stayed very similar for a long time. Bipedal *Australopithecus* (4.5-1.9 million years ago) had a brain that did not exceed 450 cubic centimetres and even the first members of the genus *Homo* levelled out at 600 cc. Dramatic expansion started to occur during the long lifespan of *Homo erectus* (2-0.1 mya), the later members of which had a brain of about 1250 cc, overlapping with the range of modern humans. It is difficult to access from fossil endocasts which parts of the brain contributed most to this expansion, but comparisons between the human brain and that of living representatives of other lineages is possible. By warping the brain of non-human primates to that of the human, we can assess which areas need to be most expanded to reach human proportions. Using this type of approach, most authors report that expansion has predominantly affected the association cortex, including lateral and medial prefrontal cortex, inferior parietal or temporoparietal junction, and lateral temporal cortex (Chaplin et al., 2013; Van Essen and Dierker, 2007; Vickery et al., 2024).

Expansion of parts of the brain's grey matter are likely to coincide with changes to the white matter (Krubitzer and Kaas, 2005) (Fig. 2). The simplest case is that an expansion of cortical territory is followed by an expansion in white matter; the existing connections are similar, but there is an increase in their volume, albeit potentially following the rules of allometric scaling. A more elaborate scenario is one where the connections of the expanded area diversify. Instead of all maintaining the same connectivity, expanded territories have different connectivity profiles, associated with distinct functional specializations. Finally, one can imagine an even more elaborate scenario in which completely new connections have invaded part of the expanded territory, substantially changing its connectivity profile. While of course these scenarios present idealised cases, they nevertheless provide useful heuristics to discuss some of the most important differences in connectivity between the human brain and that of non-human primates.

Many of the relative expansions in the human grey matter are in the association areas of the neocortex, but this does not mean there is no effect on connectivity beyond the neocortex. As we have outlined above, a number of subcortical systems form loops of connectivity with parts of the cortex. If parts of the neocortex expand, this will affect these loops. This can be illustrated in the case of cortico-basal ganglia loops, specifically cortico-striatal projections. Balsters and colleagues (2020) used resting state functional MRI to study the connectivity between nucleus accumbens, caudate, and putamen and a series of target regions in the neocortex. While a large part of the human striatum could be classified as having a similar profile of connectivity as either of the three striatal areas in the macaque, parts of the human dorsal striatum could not be classified. Post-hoc analysis showed that this part connected strongly to the inferior parietal lobule and lateral frontal cortex, including the lateral frontal pole. All these areas have expanded in the human compared to the macaque (Van Essen and Dierker, 2007). Similar results were obtained by Liu and colleagues (2021), who showed that for the basal ganglia a part of the human dorsal caudate had the most distinct connectivity compared to the macaque (Fig. 2A). Thus, expanded parts of the human neocortex are connected to the striatum following similar principles as other parts of the cortex, but this leads to a human-unique connectivity pattern in that area. Similar observations have been made for the cerebellum, with lobules projecting to prefrontal cortex showing preferential expansion in the human brain (Balsters et al., 2010).

Most of the unique aspects of brain connectivity described in the human brain concern association fibers. The expansions of both prefrontal and inferior parietal cortex have made the system of fibers connecting the two a prominent object of study. The three branches of the superior longitudinal fascicle (SLF) dominate any image of human brain connectivity, but have been surprisingly hard to reconstruct using diffusion measures, partly because they pass through territory where the rising fibers of the corpus callosum and the corona radiata cross, which makes reconstruction challenging. Nevertheless, modern tractography algorithms can reconstruct these tracts in the human brain (Behrens et al., 2007). However, non-human primates have proven more difficult (Schmahmann et al., 2007). Originally this was seen as a limitation of the tractography method, but now it is more commonly interpreted as a result, namely that the SLFs are much more developed in the human brain. This case was illustrated by a data-driven analysis of the chimpanzee white matter (Mars et al., 2019). While such analyses can identify the SLF in the human, no components capturing the SLF were found in the chimpanzee. Closer inspection of the data showed that the chimpanzee SLF pathways are much more likely to suffer from interruption due to rising crossing fibers (Fig. 2B). Thus, the expansion of the parietal-frontal cortex seems to have been accompanied by an expansion of the superior longitudinal fiber system.

Parietal-frontal connectivity has also been a prominent target of direct between-species comparisons of connectivity. A first such comparison between the human and their closest relative, the chimpanzee great ape, was performed by Hecht and colleagues (2015). They reported that in particular the lateral branches of the SLF were more developed in the human brain, reaching more into prefrontal cortex than is the case in the chimpanzee. A direct comparison of prefrontal connectivity patterns showed similar results, with a dorsal hotpot with stronger SLF2 connectivity, extending earlier results of more elaborate SLF3 connectivity (Bryant et al., 2024). Overall, the results of such comparative studies suggests that, while the general architecture of parietal-frontal connectivity is preserved, the pathways are much more substantial and, in some cases, more extensive in the human.

Although parietal and particularly frontal cortex feature strongly in discussions of human-unique aspects of brain organization, a direct comparison of connectivity profiles across the human and macaque brain identified the middle part of the lateral temporal cortex as the area with the most distinctly human connectivity profile (Mars et al., 2018b). Subsequent investigation showed that this was due to prominent projections of the arcuate fascicle into the temporal lobe in the human brain. The expansion of the arcuate had been identified previously in one of the pioneering studies on comparative connectivity using MRI. Comparing human, chimpanzee, and macaque, Rilling and colleagues (2008) showed that the arcuate fascicle, traditionally identified in the human brain as a tract underlying the human ability for spoken language, projected deeply into the temporal cortex only in humans, but not in any other primate. However, given that the middle temporal cortex and nearby inferior parietal lobule are also areas that have expanded substantially in the human lineages, an alternative hypothesis is that existing connections of the arcuate to the inferior parietal simply follow expanded parts of cortex, therefore making it look like near cortical territory was invaded. These alternative hypotheses were tested in two studies by Eichert and colleagues (2020, 2019). First, they used the macaque-human expansion map of Van Essen and Dierker (2007) to test if such expansions could account for differences in projects of the arcuate to the grey matter across the species. They reported that expanded arcuate projections could not be accounted for by the grey matter expansion map (Eichert et al., 2019). Subsequently, they employed a more elaborate surface-based registration to data of the macaque, chimpanzee, and human to account for both cortical expansion and relocation of areas due to such expansion. Again, arcuate projections in the human could not be accounted for by the grey matter changes alone, indicating that the arcuate indeed projects to areas in the human brain that are not reached in non-human primate species (Eichert et al., 2020) (Fig. 2D). This indicates that the human brain has computational abilities that the other primates do not. Subsequent studies have characterized this result in more detail, showing that the expanded temporal connectivity includes connections to the inferior parietal cortex, and not just to the frontal cortex (Sierpowska et al., 2022).

When the arcuate fascicle extended into the middle temporal gyrus, it started innervating a part of the neocortex that already showed a lot of variation across different primate lineages. Temporal cortex is difficult to delineate and therefore often gets left out of analyses of the size of relative parts of the brain. Moreover, when compared to the rest of the cortex, which has also expanded, the expansion of temporal cortex does not look very impressive. However, one could argue that the more appropriate comparison is of an area relative to its input, a measure Passingham and Smaers (2014) termed the ‘remapping factor’. If we compare the size of temporal cortex to the striate cortex, human temporal stands out (Braunsdorf et al., 2021). In other words, human temporal cortex has a dramatically increased processing power relative to its input. These differences in size again coincide with changes in the white matter.

As describe above, a number of longitudinal fibers run along the length of the temporal cortex. These include fibers innervating frontal cortex via the IFOF, but also fibers that terminate in the anterior temporal cortex, such as the middle and inferior longitudinal fascicles. Early studies using diffusion MRI tractography in humans highlighted the posterior terminations of this fiber bundle in the inferior parietal lobule (Makris et al., 2009). Similarly, tracer studies in the macaque showed that the inferior longitudinal fascicle (ILF) contains a dorsal section reaching into the posterior parietal cortex (Schmahmann and Pandya, 2006). This latter tract in particular has subsequently been shown to have diversified quite extensively in the different primate lineages. Comparative diffusion MRI tractography works suggests that its parietal extension is an anthropoid specialization (Roumazeilles et al., 2022). In the great ape lineage, the addition of the middle temporal gyrus meant that the ILF split into distinct branches, a dorsolateral branch along the middle temporal gyrus and a ventolateral branch that is likely homologous to the macaque ILF (Roumazeilles et al., 2020) (Fig. 2C. A simplified form of this split can be seen in the gibbon lesser ape (Bryant et al., 2023). In human, this diversified ILF is quite evident, with some authors even recognizing three subdivisions (Latini et al., 2017).

The organization of the major white matter connections of the human brain thus follows the general primate bauplan, but there are significant differences. These differences, in turn, follow understandable patterns, either by showing increased connectivity with or between expanded regions or by invading new cortical territory of know fiber bundles.

Behavioral consequences

The above overview presents a list of specializations of the human brain. However, natural selection is unlikely to act on brain connectivity per se. Rather, the behavioural consequences of these brain changes are the ultimate target of selection. Indeed, it was the relationship with behaviour that firstly motivated us to compare human and non-human connectivity. Unfortunately, it is impossible to study directly which behavioural adaptations related to changes in which white matter architecture over the course of evolution. A more indirect approach, which is feasible, is to investigate the role of areas served by changed connectivity in the current human brain. Bryant and colleagues (2024) explicitly used this approach. They determined the cortical areas with the most divergent connectivity profile in the human brain, when compared to either the chimpanzee or the macaque brain (Fig. 3). They then used a database of functional imaging studies and investigated which behavioural domains are associated with functional activation of these areas, so-called forward inference. Although this method has obvious limitations, being constrained to the behavioural domains categorized in the database and being purely correlational, it can nevertheless provide suggestive evidence on the relationship between structural and behavioural adaptations in the human lineage.

Hotspots of change in the frontal-parietal system driven by the SLF were associated with behavioural domains such as ‘motor learning’, ‘spatial cognition’, and ‘working memory’. Many of these hotspots are part of the so-called multiple demand network, a set of regions that are co-activated when participants are performing a diverse range of cognitively demanding tasks, including selective attention, working memory, task switching, response inhibition, and conflict monitoring. More generally, the network is involved in general problem-solving (Assem et al., 2020). This network has also been identified in the macaque monkey brain (Mitchell et al., 2016), but a direct comparison of the network’s structural connectivity across species shows that the longitudinal connections between these areas are more elaborate in the human brain (Karadachka et al., 2023). In addition, the connections between the multiple demand areas and areas feeding into the network they constitute are more extensive in the human brain. Adopting an evolutionary perspective, Genovesio and colleagues (2014) proposed that the origin of the multiple demand network lies in areas for goal-directed behavior during foraging. Areas of posterior parietal cortex code metrics associated with primate visuomotor foraging, including distance, order, length, and duration. This specialized network then became adapted to support the human capacity for general problem-solving.

Hotspots of divergence between the human and non-human brain were found in both the frontal and temporal termination sites of the arcuate fascicle, showing activation for the behavioral domain ‘language’ for left middle temporal and ventrolateral prefrontal cortex and ‘emotion’ for the right temporal cortex. The association of the arcuate fascicle with language processing dates back at least to the influential model of Norman Geschwind (1970), describing the fiber bundle as connecting Wernicke’s and Broca’s areas, although with already a strong emphasis on connections with the inferior parietal lobule as well. The precise functional role of the arcuate has been a matter of long-standing debate, with the original proposals purely focusing on syntactic processing replaced by models that emphasize distinct processes mediated by subtracts of the larger temporal-parietal-frontal arcuate fiber system (Catani and Bambini, 2014). As a case in point, Janssen and colleagues (2022) correlated interindividual differences in brain activation during two distinct speech production tasks, aimed at isolating sublexical phonological mapping and lexical-semantic mapping, with white matter integrity in different branches of the arcuate fascicle. They showed that the two tasks rely on distinct subparts of the arcuate, innervating the superior and middle temporal gyrus, respectively. Importantly, the role of subtracts of the arcuate fascicle beyond language is increasingly appreciated, including in behaviors that require an integration between the ventral and dorsal visual streams, such as tool use (Ramayya et al., 2010). However, the relative importance of these different behaviors and the order of their reliance on arcuate expansion remains difficult to establish, with the fossil record only providing some clues about the appearance of behaviors such as tool use and language.

Beyond problem-solving, language, and tool use, the cooperative sociality of humans is perhaps their most distinctive behavior; language does not occur if individuals do not rely on sharing information (Tomasello, 2008). The temporal lobe is crucial for many primate social behaviors, containing visual association areas specialized for face and body processing (Tsao et al., 2003) and auditory association areas selective for species-specific vocalizations (Petkov et al., 2009). The temporal visual stream is often described in terms of an increase in abstraction, with areas' receptive fields processivity growing in size and the type of information coded increasingly viewer-independent. The further anterior in the temporal lobe, the less activation is driven by single features of the stimulus and more by feature conjunctions, culminating in conceptual categories in the anterior temporal lobe. Evolutionary models describe this organization in terms of its benefit for foraging (Murray et al., 2016). Braunsdorf and colleagues (2021) argued that the computations underlying this organization are also beneficial for processing social information and that the expanded temporal lobe could be interpreted as applying this organization to the social information domain. This echoes a proposal by Pitcher and Ungerleider (2020) that the lateral temporal cortex in effect contains a separate—social—visual stream, which in turn is consistent with our observation of increasing differentiation of the ILF in the ape lineage (Roumazeilles et al., 2020).

The border of posterior temporal and inferior parietal cortex, sometimes referred to as the temporoparietal junction area (TPJ) is often cited as activated in tasks that probe our ability to mentalize or assign belief states to others, a process referred to as Theory of Mind (Saxe, 2006). Once it was established that human TPJ indeed contained a distinct anatomical area involved in these tasks (Mars et al., 2012), functional connectivity was used to search for a similar area in the macaque brain. This work identified the middle part of the macaque superior temporal sulcus as having a similar connectivity profile as human TPJ (Mars et al., 2013). This region had already been implicated in processing social information in macaques, showing increased grey matter on animals living in more complex social networks both in captivity (Sallet et al., 2011) and in the wild (Testard et al., 2022). Recordings from this area showed it to be responsive not to identity, but to the locus of attention of another person, independent of the source of this information (Perrett et al., 1992). Responsiveness to another's locus of attention could be argued to be a precursor or simplified form of humans' ability to attribute beliefs to others. Roumazeilles and colleagues (2021) tested this hypothesis, showing that macaque mid-superior temporal sulcus was responsive to violations of predictions in social scenes, similar to the activation seen in human TPJ in response to violations in predicted behavior by a confederate. This suggests the existence of a precursor for Theory of Mind ability in the last common ancestor of humans and Old World monkeys. Complementing these results, the functional decoding of human regions with distinct connectivity fingerprints by Bryant and colleagues (2024) showed that human TPJ has quite strong innervations of the extended ILF, a tract likely to reach mid-STS in the macaque. Whether these regions are homologous or whether the connectivity profile of human TPJ has extended to include connections similar to macaque mid-STS remains an open question.

In summary, hotspots of connectivity fingerprints that are distinct between the human brain compared to that of closely related non-human primates occur in regions associated mostly with higher-order cognitive functions, including those associated with human ecological adaptations, such as social behavior, language, and general intelligence.

Sources of individual variability

Natural selection operates upon phenotypic variation linked to genetic variation within a population. As discussed above, the behavioral consequences of species-level differences in white matter would allow for selection upon these bundles. Indeed, across humans, there is a great deal of variability in white matter organization, much of which has been linked to behavior. Of course, genetic influences are not the only drivers of white matter variability. Here, we will discuss some of the sources of white matter variation across the population.

As pointed out by Englund and Krubitzer (2022), phylogenetic diversity can be realised at different timescales. Evolutionary changes specified by changes in DNA can occur over millennia or more, while variability related to the changes in the body or environmental input can occur over years, days, or even shorter. As it is known that the course of a particular white matter tract is not prespecified in the DNA, understanding how phylogenetic diversity in brain connectivity appears requires an understanding of how changes are realized at such shorter time scales. For instance, we noted above that the mammalian brain is underspecified at birth, but how mature a brain is at the moment of birth differs across species (Sakai et al., 2012). Furthermore, there species-specific and even brain region-specific constraints on plasticity, meaning some connections are likely more labile than others. As such, influence of different factors varies across brains. In this section, we will illustrate some important lines of research into these factors that are related to the themes discussed above

Like everything else in the brain, white matter is not fully formed at birth. White matter must develop over time. Unfortunately, studying changes in connectivity in early life in humans is challenging, as MRI in young individuals is not always feasible and requires short scans. Although some results are inconsistent, it is clear that projection fibers mature earlier than commissural fibers, and that association fibers mature late (Dubois et al., 2008; Khan et al., 2019). Neonatal brains are dominated by sensorimotor connectivity, with association networks relatively underdeveloped (Larivière et al., 2020). These results are consistent with the notion that areas that mature last are also the ones that show greatest differential expansion between the human and non-human primate (Hill et al., 2010). Thus, ontogeny partly recapitulates phylogeny. This notion was tested by Warrington and colleagues (2022), who compared whole-brain connectivity profiles between adult humans and macaques and between adult and infant humans. The divergence maps in the two comparisons show that indeed there are areas in inferior parietal, precuneus, middle temporal, and anterior lateral prefrontal cortex where both the infant human and adult macaque connectivity profile differs from that of the adult human. However, there also regions where the divergence is not similar. A case in point in ventrolateral prefrontal cortex. Area 45 shows strong innervation by the arcuate fascicle in adult humans, but not in infants or macaques. In contrast, area 44 shows arcuate innervation with humans independent of age, but not in macaques.

Development is not the only time in life when connectivity changes. It is possible to see differences in white matter across adults, as well as changes to white matter within a given individual during adulthood. Although the sources of variability in both cases are likely some combination of genetic and environmental, it is interesting to consider the degree to which white matter can change on the basis of experience during adulthood, and how we know. In general, new long-range connections do not appear during adulthood. However, this does not mean that connectivity is not refined, sometimes quite significantly. White matter itself inside the brain is composed of oligodendrocytes that wrap around axons. Most oligodendrocytes are born early in postnatal development; however, new ones are generated throughout adulthood. These cells can go on to myelinate previously unmyelinated axons and can add myelin to lightly myelinated axons (Wang and Young, 2014). These processes influence velocity of signal transmission, which seems to be one of the fundamental functions of myelin. The process of myelin remodelling likely leads to the adult plasticity observed in macroscale structural measures. Intriguingly, oligodendrocyte generation reduces in later adulthood with aging.

There are many reports of white matter differences associated with experience in adult humans. A swath of studies, for example, has showed enhanced fractional anisotropy and size of the corpus callosum in trained musicians (Schlaug et al., 1995). However, musicians typically begin training in childhood, making it unclear whether these differences truly reflect adult myelin plasticity. Researchers have devised clever ways to circumvent such issues. For example, they trained adults to juggle and observed increases in fractional anisotropy in the intraparietal sulcus (Scholz et al., 2009). Neurofeedback aimed at improving attentional control enhanced fractional anisotropy in multiple bundles, including the SLF. Environmental enrichment, socialization, and exercise are also consistently associated with connectivity changes in the adult brain.

An additional source of individual variability in connectivity in the human brain is disease. Countless studies have demonstrated connectivity abnormalities in the brains of those with psychiatric and neurological disorders. Nearly all brain disorders are not the result of the failure of a single brain region or group of cells; rather, they are rooted in impaired communication within and across brain networks. It could even be that the connectomic structure of the human brain makes it particularly vulnerable to disease. Along those lines, cortical regions with transcription patterns suggestive of rapid evolutionary change in the human lineage are those that appear to underly many mental health conditions (van den Heuvel et al., 2019; Wei et al., 2019). Moreover the 'rich club' structure of connectivity relates to disease vulnerability: hub regions appear to be more impacted in brain diseases than non-hub regions (Crossley et al., 2014).

Neuromodulatory approaches to treating brain disorders, including deep brain stimulation (DBS), rely on rectifying these connectivity deficits. DBS was developed as a treatment for Parkinson's Disease and other movement disorders, it has now been extended to a wide range of other disorders, including mental health conditions. Myelinated white matter is much more easily excited than cell bodies or unmyelinated axons, so we now understand white matter to be the conduit of effective DBS. For Parkinson's Disease, with a target in the subthalamic nucleus, this likely means axons of the hyperdirect pathway (connecting the frontal lobe with the subthalamic nucleus) and the nearby internal capsule. For obsessive-compulsive disorder, with a target embedded in the white matter of the anterior limb of the internal capsule, this likely means fibers connecting medial and orbital prefrontal cortices with the thalamus and brainstem. Finally, for treatment-resistant depression, patients who respond to DBS in the subcallosal cingulate have electrodes intersecting key white matter bundles: the forceps minor of the corpus callosum, the cingulum bundle, and the uncinate fasciculus (Riva-Posse et al., 2014).

Thus, connectivity, although comparable across individuals, is dynamic and subject to changes across life span, expertise and training, and disease and treatment. The connectome is a phenotype that is shaped by many causes.

The future

We have shown that there are many features of connectivity that are shared amongst all primates, which we have termed the bauplan. We have also shown that there are differences across species, including between humans and non-human primates. In our day-to-day lives, it does seem as though humans are fundamentally different from other animals, and that there ought to be some feature of brain organization reflecting this qualitative, rather than quantitative, distinction. Thus far, the evidence suggests that, although human-unique specializations exist, they are in line with a general bauplan of primate connectivity.

An important goal in human neuroecology is to understand how the changes in connectivity relate to behavioural specializations in the human lineage. We have shown that changes in brain connectivity occur in regions that tend to be activated in tasks probing higher-order cognitive functions. However, as we highlighted in the previous section, the relationship between connectivity, behaviour, and other biological factors remains complex.

The coming years are likely to see an increased focus on understanding the relationships between different levels of biological understanding and across time scales. Animal models are an invaluable source of information in this research, but also pose a problem due to the phylogenetic differences across species (Barron et al., 2021). Understanding between-species differences is therefore a two-edged sword, helping to both understand phylogeny itself and improving our knowledge obtained, by necessity, in animal models.

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Figure captions

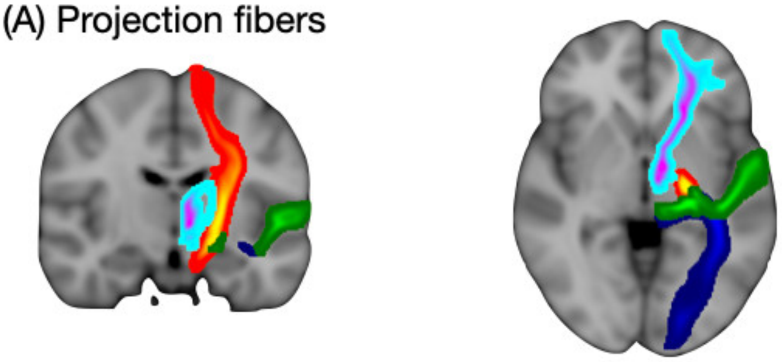
Figure 1. Reconstruction of some major fiber bundles in the human brain. (A) Projection fibers: Corticospinal tract (red-yellow), anterior thalamic radiation (cool), acoustic radiation (green), optic radiation (blue). (B) Association fibers: first (red-yellow), second (blue), and third (green) branches of the superior longitudinal fascicle, the arcuate fascicle (red), the middle longitudinal fascicle (yellow), the inferior longitudinal fascicle (copper), and the inferior fronto-occipital fascicle (dark blue). (C) Limibc fibers: cingulum bundle (cool), fornix (copper). Reconstructions from Warrington et al. (2020). All figures adapted from work published under Creative Commons License (http://creativecommons.org/licenses/by/4.0/).

Figure 2. Heuristics of differences in connectional anatomy across species and examples. (A) Expansion of the cortex can lead to an expansion in white matter that results in an increase in the number of parallel pathways, as is the case for corticostriatal connections to the dorsal caudate (green). Adapted from Balsters et al. (2020). (B) Expansion of the cortex can also lead to more straightforward expansion and elaboration of a pathway, such as in the case of the superior longitudinal fiber system, which is much more extensive in the human (right) than the chimpanzee (left). Adapted from Mars et al. (2019). (C) In the case of such expansions, the pathways can specialize into distinct sub-pathways, as is the case for the inferior longitudinal pathway in apes (right, yellow and red), including humans, compared to macaques (left, yellow). Adapted from Roumazeilles et al. (2020). (D) In addition to expansion, a fiber bundle can also be connected to new cortical territories, such as in the case of the arcuate fascicle connecting to the middle temporal gyrus in the human (right), but not in the macaque (left). Adapted from Roumazeilles et al. (2020). All figures adapted from work published under Creative Commons License (http://creativecommons.org/licenses/by/4.0/).

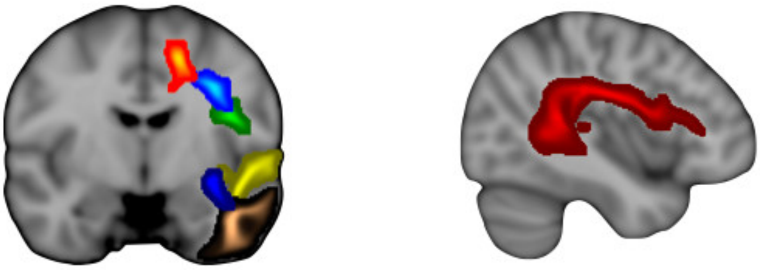
Figure 3. Human-macaque divergence in connectivity profiles and functional roles. Areas with brighter colors (red being the maximum) have a connectivity profile that is most distinct from any profile found in the macaque monkey. The functional labels are behavioral domains associated with functional activations in those areas. Adapted from Bryant et al. (2024). All figures adapted from work published under Creative Commons License (http://creativecommons.org/licenses/by/4.0/).

Figure 1

(A) Projection fibers



(B) Association fibers



(C) Limbic fibers

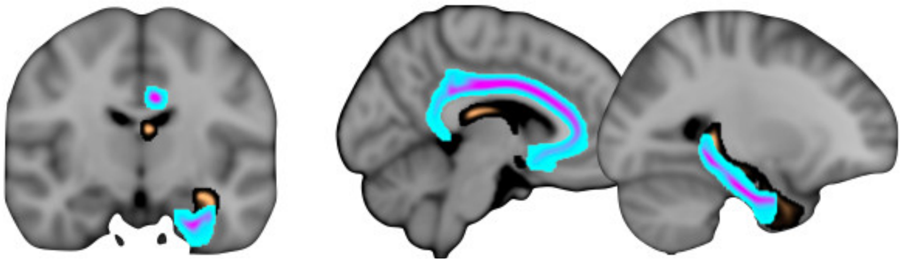


Figure 2

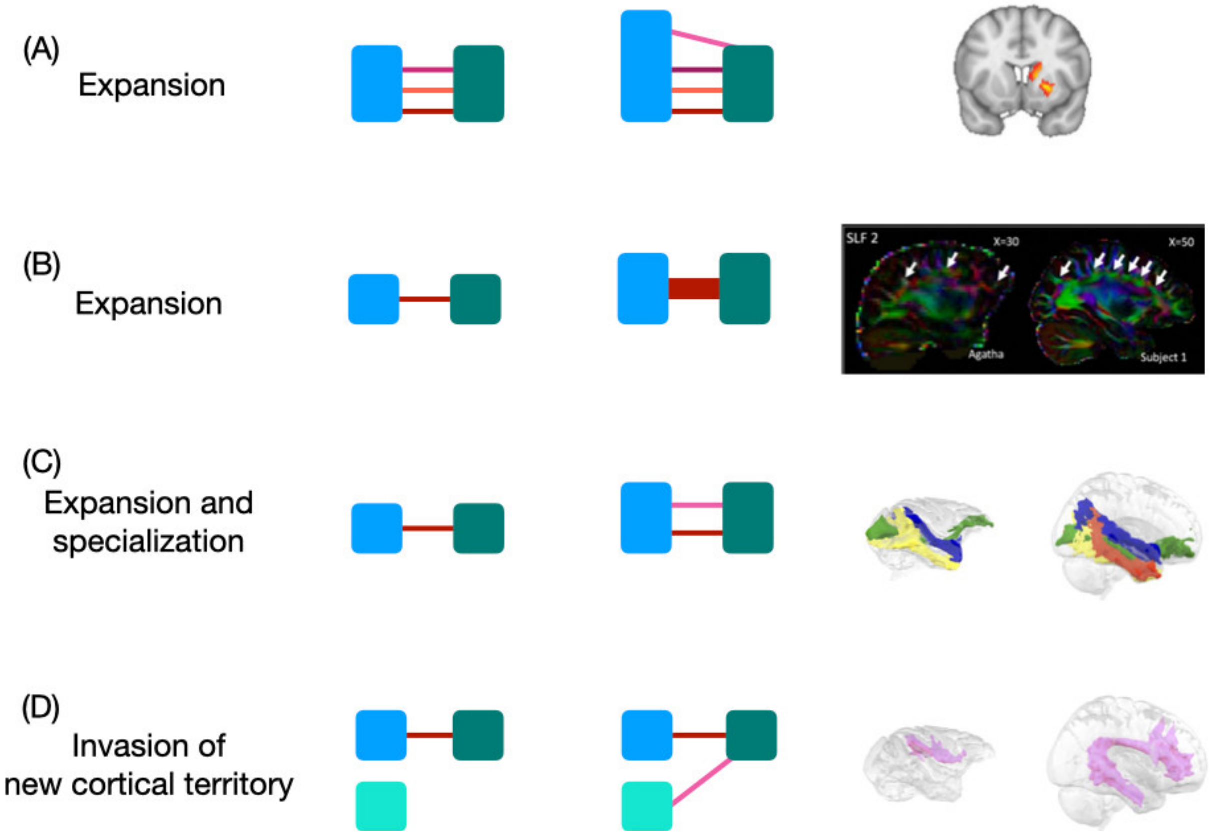
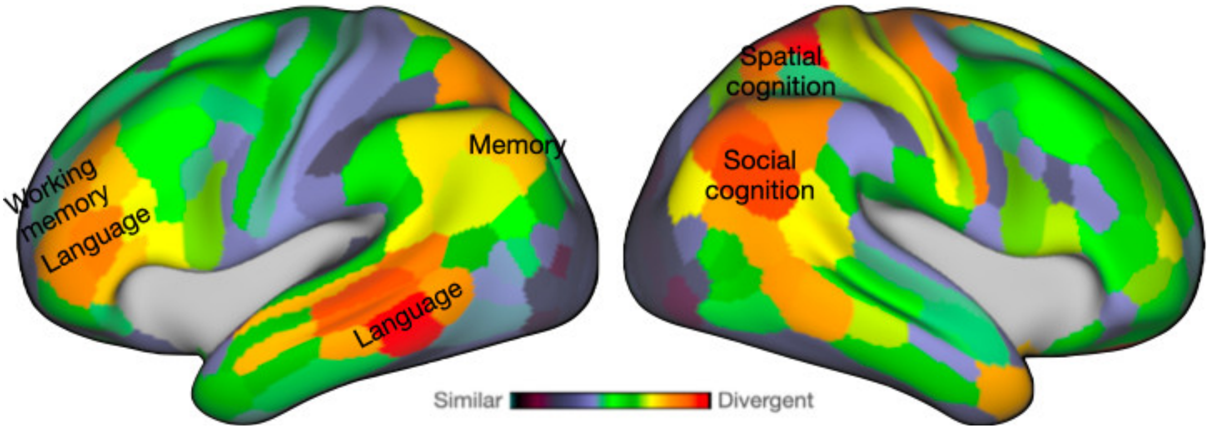

(A)
Expansion
(B)
Expansion
SLF 2
X=30
X=50
Agatha
Subject 1
(C)
Expansion and specialization
(D)
Invasion of new cortical territory

Figure 3


Working memory
Language
Memory
Language
Spatial cognition
Social cognition
Similar
Divergent