Brain reorganization, not relative brain size, primarily characterizes anthropoid brain evolution

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Comparative analyses of primate brain evolution have highlighted changes in size and internal organization as key factors underlying species diversity. It remains, however, unclear (i) how much variation in mosaic brain reorganization versus variation in relative brain size contributes to explaining the structural neural diversity observed across species, (ii) which mosaic changes contribute most to explaining diversity, and (iii) what the temporal origin, rates and processes are that underlie evolutionary shifts in mosaic reorganization for individual branches of the primate tree of life. We address these questions by combining novel comparative methods that allow assessing the temporal origin, rate and process of evolutionary changes on individual branches of the tree of life, with newly available data on volumes of key brain structures (prefrontal cortex, frontal motor areas and cerebro-cerebellum) for a sample of 17 species (including humans). We identify patterns of mosaic change in brain evolution that mirror brain systems previously identified by electrophysiological and anatomical tract-tracing studies in non-human primates and functional connectivity MRI studies in humans. Across more than 40 Myr of anthropoid primate evolution, mosaic changes contribute more to explaining neural diversity than changes in relative brain size, and different mosaic patterns are differentially selected for when brains increase or decrease in size. We identify lineage-specific evolutionary specializations for all branches of the tree of life covered by our sample and demonstrate deep evolutionary roots for mosaic patterns associated with motor control and learning.

1. Introduction

The brain is central to the adaptive profile of any animal as it underlies the capacity to modify behaviour in a changing environment [1,2]. Mapping the evolutionary changes of the brain across many species helps characterize phylogenetic specialization, providing insight into the various ways in which the neural system has adapted to an organism’s environment [3,4].

The overall size of the brain plays an important part in neural adaptation and has significant implications for patterns of internal organization: as the absolute size of the brain increases, interacting neurons are located further apart and the brain is likely to become more modular in organization [5]. In primates, the evolution of brain size (both in terms of absolute size and relative to body size) shows complex patterns of change involving both increases and decreases along different branches of the primate phylogeny [6,7]. The importance of brain size (in association with size-related allometric scaling of individual brain structures) to species’ adaptation is demonstrated by a comparative correlation between absolute brain size and cognitive ability in non-human primates [8] and between relative brain size and survival in novel environments in different orders across the animal kingdom [2,9,10].

Overall size is, however, not the only way the brain can adapt to an organism’s environment. The relative size of individual brain structures indicates variation beyond purely size-related allometric scaling [3,4]. This (mosaic)...
variation has been shown to reflect anatomical connectivity patterns [11,12] and predict various aspects of behavioural capacity across the animal kingdom [13–16]. In other words, previous work has demonstrated that the neural system adapts in both size-dependent and size-independent ways.

Although the study of primate and mammalian brain evolution has been dominated by research focusing on size-dependent and size-independent adaptations of the neural system, there are three elements that are fundamental to our understanding of these two aspects of brain evolution that have not been established: (i) What is the relative importance of relative brain size and mosaic changes in explaining variation in brain evolution? (ii) Which mosaic changes contribute most to explaining diversity in brain organization across species? and (iii) What are the temporal origin, rate and process underlying evolutionary shifts in mosaic reorganization for individual branches of the primate tree of life?

These factors have not been established for both empirical and methodological reasons. Mosaic studies have mainly focused on allometric scaling trends of particular brain structures [4,17]. Although allometric approaches per se reveal useful information on brain structure evolution, the systemic interaction between different brain structures, in which individual brain structures contribute to different information processing loops to various extents, is better reflected in approaches that allow assessing the extent to which particular variables differentially contribute to explaining different patterns of covariation between all variables in the model (e.g. principal component analysis [3,18]). Allometric approaches further fail to reveal the temporal origin and rate of evolutionary changes taking place on individual branches of the tree of life covered by the sample and confound the different evolutionary scenarios (in terms of patterns of increase/decrease between two traits) that underlie allometric residuals [7]. Finally, comparative data on brain structures that are fundamental to neural processing (prefrontal cortex, frontal motor areas and cerebellar lobules) have not been available until very recently [11,17,19–21], hampering more in-depth insights on the systemic nature of mosaic brain evolution.

We address the questions above by combining novel phylogenetic comparative approaches [7,22] with recently collected data on volumes of cytoarchitectonically delineated brain structures (from post-mortem histologically sectioned brains) across species [11,17,19–21]. The novel comparative approach we employ allows inferring the temporal origin, rate and process of evolutionary changes for all individual lineages of the tree of life covering the sample [7]. The method that underlies this approach [23] infers variable rates of evolution for all individual lineages without a priori parameterization and provides realistic trait value estimates for extinct species. This approach hereby significantly increases the resolution of evolutionary inferences and allows for more detailed interpretations of the evolutionary history of particular biological traits.

We quantify evolutionary changes in brain size and organization for all individual lineages of a phylogenetic tree spanning 17 species of anthropoid primates, including humans, in a hierarchical multivariate model using phylogenetically controlled principal components analysis [22]. Evolutionary changes of specific mosaic patterns are modelled for all individual branches of the tree of life using an approach based on an adaptive peak model of evolution [7,11,23]. Because brain (structure) size scales approximately isometrically as a function of cell number (and therefore computational power) in primates [24,25], we consider mosaic changes in relation to changes in overall brain size. The argument is that as particular mosaic patterns increase or decrease over evolutionary time, the absolute size attributed to each mosaic pattern (and thus its number of cells) will contribute to its computational power.

2. Results

(a) Brain reorganization

Phylogenetic principal components analysis of relative brain size and the relative size of 20 brain structures/areas reveals that seven principal components explain up to 90.4 per cent of neural structure variation observed across 17 primate species (spanning more than 40 Myr of evolution [26]). Principal component 1 (PC1) is dominated by variation in relative brain size and accounts for up to 25.8 per cent of overall variation in brain evolution (table 1). PC1 indicates high inverse loadings of relative brain size and the relative volume of olfactory bulb and medulla. Because olfactory bulb and medulla volume are considered to have experienced the least amount of change across anthropoid evolution, and brain size the most, this component can primarily be interpreted as reflecting changes in relative brain size. Subsequent PCs indicate low loadings for relative brain size, representing patterns of size-independent mosaic changes: PC2 (18.7%) is predominantly associated with prefrontal white matter; PC3 (14.7%) involves the hippocampal formation (hippocampus and entorhinal cortex); PC4 (12.7%) the prefronto-striatal formation; PC5 (7.7%) the paleocortex (a group of structures predominantly related to olfactory function, see electronic supplementary material, S3); PC6 (6%) structures involved in the execution of motor plans (spinocerebellum, mesencephalon and medulla) and PC7 (4.6%) structures associated with motor learning (cerebrocerebellum and frontal motor areas). These patterns of size-independently co-evolving brain structures correspond to brain systems that have been described in electrophysiological and anatomical tract-tracing studies in non-human primates [27–31] and MRI studies in humans [32–35] and can roughly be associated with social reasoning, motor control, learning and memory [36–40].

(b) Phylogenetic mapping

To reveal the temporal origin, rate and processes underlying mosaic patterns of brain reorganization for all individual branches of the tree of life covered by our sample, we employed a novel approach [7] based on the principles of an adaptive peak model of evolution [23]. Results indicate that three mosaic patterns differentiate great apes (and humans) from other primates when considered in conjunction with an overall increase in brain size: prefrontal white matter, prefronto-striatal and cortico-cerebellar (figure 1). Evolutionary investment in these brain systems is shown to originate in the ape ancestral lineage (approx. 30–20 Ma). Other brain formations (prefrontal white matter, hippocampal–entorhinal and descending motor pathway) display significantly increased variation in lineages where brain size decreases compared with those where brain size increases (figure 2; PC2: $F = 0.0037$, $p < 0.0001$; PC3: $F = 0.0066$, $p < 0.0002$; PC6: $F = 0.0395$, $p = 0.0067$).
Table 1. Principal components with respective loadings for the analysis including relative brain size and 20 brain structures/areas. ‘WM’ and ‘GM’ indicate white and grey matter; ‘R’ and ‘L’ indicate right and left hemisphere.

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Figure 1. Phylogenetic mapping of the three principal components that distinguish great apes from other anthropoids (a) PC2 prefrontal white matter, (b) PC4 prefronto-striatal, and (c) PC7 cortico-cerebellar) in relation to absolute brain size. Darker shades (red in colour version) indicate a joint increase in respective PCs and absolute brain size, medium shades (yellow in colour version) an increase in PCs but not in absolute brain size and no shading no increase in either respective PCs or absolute brain size. More detailed figures, including full colour resolution, representing the phylogenetic mapping of each principal component are available in electronic supplementary material, S2. More information on the procedure used to visualize the inferred evolutionary patterns on the phylogeny is provided in electronic supplementary material, S3. (Online version in colour.)
The finding that mosaic changes contribute more to explaining neural system diversity across species than changes in relative brain size confirms that the traditional focus on relative brain size [2,41–43] significantly underestimates the contribution of different neural pathways to primate neural system diversity. We further find that, across more than 40 Myr of anthropoid evolution, different neocortical and cerebellar areas varied in their contributions to different mosaic patterns. Overall, our results indicate that neural adaptation in anthropoid primates primarily involves differential selection on multiple size-independent organizational patterns across different taxonomic groups, and specify the precise evolutionary changes that occurred across evolutionary time and between individual phylogenetic branches.

The principal component that we find to contribute most to explaining evolutionary changes in primate brain reorganization indicates high loadings for prefrontal white matter (table 1). The prefrontal cortex is a multimodal structure involved in social cognition [44], moral judgements [45], clan mentality [46], introspection [47] as well as goal-directed and stimulus-driven attention [48]. This brain structure is generally considered to provide ‘an infrastructure for synthesizing a diverse range of information that lays the foundation for the complex forms of behaviour observed in primates’ [49, p. 59]. As brains change in size over evolutionary time, multimodal connectivity may be under particular pressure as interacting areas change in distance to each other, affecting the length and thickness (to maintain optimal conduction times) of axons [5,50]. Recent functional connectivity research evidenced the preferential distant connectivity of heteromodal association areas, with some regions in the prefrontal cortex (medial PFC) displaying both high local (evidencing modularity) and high distant (evidencing multimodality) functional connectivity [51]. Because of its combined multimodal and modular nature, the prefrontal cortex is thus likely to be under particular pressure to change the space attributed to its white matter as the size of the brain changes over millions of years of evolution. The identification of prefrontal white matter as a distinct contribution to explaining neural system diversity confirms this view. Phylogenetic mapping of PC2 scores and brain size shows that great apes stand out in their combined investment in both prefrontal white matter and absolute brain size, in that prefrontal white matter keeps track with a substantial increase in brain size, with humans at the extreme of this pattern (figure 1a). The derived pattern of prefrontal white matter evolution in humans aligns with recent work on prefrontal neuropil distribution supporting the conclusion that enhanced connectivity in the prefrontal cortex accompanied the evolution of the human brain [52]. The origin of the great ape grade shift in prefrontal white matter evolution is inferred to date back to the dawn of the ape radiation (at least 20 Ma). In monkeys, investment in prefrontal white matter is mainly displayed in species that have decreased absolute brain size in their lineage (Cebus, Alouatta, Miopithecus; electronic supplementary material, S1), suggesting that, once evolved, patterns of connectivity and modularity associated with larger brains may be maintained when brains undergo secondary reductions in size. This result is in line with the view that changes in prefrontal white matter are, at least in part, owing to the geometric constraints of size on multimodal connectivity.

Considering the high contribution of changes in the prefrontal system to explaining diversity in neural adaptation across primates, further work should aim to investigate the impact of other heteromodal association areas (lateral temporal and inferior parietal). The dissociation of the hippocampus–entorhinal (PC3) and prefronto-striatal (PC4) formations in different principal components (table 1) suggests they have evolved as mosaic patterns, congruent with suggestions that both comprise different memory systems [53,54] involved in forms of learning in which stimulus-response associations or habits are incrementally and sequentially acquired (striatal) [55–57] and more cognitive or declarative memory (hippocampal) [53,58]. Phylogenetic mapping of these two PCs suggests differential evolutionary investment across different species. Great apes stand out in a joint emphasis on the prefronto-striatal formation and absolute brain size; a trend that is inferred to originate with the dawn of the ape radiation (figure 1b). The hippocampus–entorhinal formation does not indicate a clade-specific pattern in combination with an emphasis on absolute brain size (see electronic supplementary material, S2), but displays particular variation in lineages where brain size has decreased (figure 2). Symmetry of brain reorganization in the context of increases versus decreases in absolute brain size has not been extensively studied, but preliminary evidence from the Chiroptera suggests there is asymmetry in the link between brain reorganization and cognitive capacity due to the different ecological niches available to species with different overall sizes [59]. Our primate results also point in this direction.
For physiological reasons, smaller primates tend to be more agile, allowing them to inhabit a more diverse array of physical environments, possibly placing particular pressure on spatial memory.

PC6 indicates high loadings of structures involved in descending motor pathways (spinocerebellum, mesencephalon and medulla) [60], while PC7 loads on structures associated with cortico-cerebellar connectivity (cerebrocerebellum and frontal motor areas) [33,61,62] (table 1). Functionally, these two components can roughly be associated with the execution of motor actions and the acquisition of new complex motor sequences. Phylogenetic mapping of PC6 and PC7 reveals opposite patterns of investment across species with a joint investment in the cortico-cerebellar system and absolute brain size separating the ape from the monkey radiation between 30 and 20 Ma (figure 1c). Specifically, great apes combine increased investment in the cortico-cerebellar system with a decreased investment in the descending motor pathway (see electronic supplementary material, S2). These trends are further extended in humans with an additional investment in absolute brain size (see figure 1c and electronic supplementary material, S2) [63]. In monkeys, Cebus has the highest score for PC7 (see electronic supplementary material, S1), congruent with their increased sensorimotor capacities [64]. PC6 further indicates increased variation when brain size decreases (similar to PC3), further confirming our interpretation that this may be due to smaller primates being confronted with a more diverse array of physical environments placing particular pressure on basic motor execution (such as locomotion).

Overall, our phylogenetic analysis infers that a clade-specific investment in particular brain formations (prefrontal white matter, prefronto-striatal and higher motor control) in combination with increased absolute brain size differentiates great apes (and humans) from other primates (figure 1). Other brain formations (prefrontal white matter, hippocampal–entorhinal, paleocortex and descending motor pathway) display increased variation in lineages where brain size decreases, suggesting asymmetry in brain reorganization depending on whether the brain increases or decreases in absolute size (see figure 2 and electronic supplementary material, S2). This asymmetrical pattern of brain reorganization may be related to adaptation to different ecological niches available to species with different overall sizes, putative increased pressures on size-independent adaptation in the face of increased energetic constraints on changes in absolute brain size, and/or geometric constraints of size on multimodal connectivity.

In conclusion, our results contribute to explaining primate neural system diversity by quantifying the extent to which variation in anthropoid brain adaptation is principally explained by differential selection on multiple size-independent organizational patterns across different taxonomic groups rather than changes in overall brain size. We also show that different neocortical and cerebellar areas contribute differently to explaining different mosaic patterns in different lineages, that patterns of brain reorganization may indicate different evolutionary pathways across different species depending on whether brain size increases or decreases and that some organizational changes have deep evolutionary roots dating back at least to the divergence of apes and Old World monkeys (between 30 and 20 Ma). Results indicate a high evolvability of mosaic brain reorganization in primates suggesting that putative developmental regularities in the evolution of brain structures in primates [65,66] do not contribute markedly to explaining neural system diversity across species and/or are commonly offset by mosaic reorganization. Overall, our results demonstrate that anthropoid primate brain evolution is primarily characterized by selection on multiple size-independent patterns of brain structure covariation.

4. Material and methods

(a) Data

Brain structure data were collected from serially sectioned post-mortem brains following previously published protocols [11,17,19–21,67] and from the literature [68]. A detailed description of the data is provided in electronic supplementary material, S3. The phylogenetic tree was taken from the 10 k Trees project, v. 3 [69].

(b) Statistical procedure

Phylogenetic reduced major axis regressions with a likelihood fitted lamba model [70] were used to control brain size for body size and brain structure size for brain size. Residuals were used as input for a phylogenetically controlled principal components (PC) analysis [22,70]. PC scores were used to estimate ancestral states and reconstruct lineage-specific evolutionary rates using a variable rates method that is based on the principles of an adaptive peak model of evolution [7,11,23]. A detailed description of the phylogenetic mapping procedures is available in electronic supplementary material, S3. The variation of rates of change for the scores of each PC were compared between lineages that indicate brain size increase (minimum rate of 0.1) versus lineages that indicate brain size decrease (maximum rate of −0.1) using an F-test for equality of variance.

(c) Model accuracy

To test the accuracy of the variable rates method we use to estimate ancestral values and lineage-specific rates of change of PC scores [23], we compare the ancestral values of brain size as estimated by our method to those inferred from the fossil record for three phylogenetic topological locations that characterize the primate radiation: apes versus monkeys, great apes versus lesser apes and humans versus non-human primates. Australopithecus afarensis is considered to be close to the ancestral node of chimpanzees and humans and has an estimated fossil brain size of 434cc [71]; our method estimates this value to be 385cc. Oreopithecus is considered to be derived from the great apes stem lineage, after its divergence from the gibbon lineage, and has an estimated fossil brain size of 383cc [71,72]; our method estimates the value for the great ape last common ancestor (LCA) at 385cc and the LCA of apes at 348cc. Proconsul is most often considered to be derived from the ape stem lineage, after its divergence from the Old World monkey lineage, and has an estimated fossil brain size of 162cc [73]; our method predicts the value for the ape LCA at 348cc and the LCA of Old World monkeys and apes at 225cc. Considering that our sample includes brain size values spanning 40 orders of magnitude (32.8cc for the New World monkey Pithecia monachus and 39.7 for the Old World monkey Mpanthecus talapoin compared with 1419.9cc for our sample of humans), this level of accuracy far exceeds what can be attained with alternative methods and demonstrates the accuracy of our model estimates.

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References


