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Brain Evolution: Developmental Constraints and Relative Developmental Growth

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Introduction

Components of the brain in mammals enlarge in large part by regular power laws based on the size of the brain overall. To transform the brain of a mouse to the brain of a chimpanzee, we can imagine that the volume or cell number of each brain component (for example, midbrain or cerebellum) or cell class (such as Purkinje cells of the cerebellum or rods in the retina) is each set by its own independent, nonlinear dial. The neocortex and the cerebellum grow with 'positive allometry' with respect to the rest of the brain, so that the larger brains become in absolute size, the progressively greater the proportion of the brain constituting neocortex and cerebellum. Conversely, the proportion that is medulla or midbrain decreases ([Figure 1](#)). The direct mechanistic cause of this conserved pattern of disproportionate but predictable growth is conservation of the order of neurogenesis across species such that structures or cell groups produced last experience the greatest expansion of the numbers of stem cells in their precursor pools in species with extended developmental periods.

Whether this conserved and disproportionate pattern of expansion of brain components is a metabolic and structural load that evolving brains must bear because of a maladaptive uniform application of a developmental program, as the word 'constraint' would suggest, is very suspect. Particularly so in that variation in size is one of the major ways that brains vary! Such conservation might better be interpreted as a mechanism that permits graceful scaling of brain function with brain size. In the same way that components of the body scale nonlinearly with body mass to compensate for the functional requirements of each organ that change lawfully at different body sizes, the brain must also scale appropriately. For example, skeletal mass in terrestrial mammals increases at a greater exponent than total body mass, particularly for supporting limbs (consider the deer, cow, and elephant), not because skeleton production is trapped by a developmental constraint requiring the animal to generate useless volumes of skeleton in supporting limbs at large body sizes, but because proportionately more cross-sectional skeletal mass is required to support the body. For skeletons

and body mass, the reasons for allometric predictability are reasonably self-evident; for the relative scaling of medulla versus cortex, the underlying reasons may not be so clear and are the subject of this article.

The basic phenomena of brain component scaling will be discussed first, and then the properties of conservation and variation in developmental mechanisms that underlie conservation and variation in brain component scaling. Finally, several examples of conserved processes in neuroembryology that have the property of permitting flexible and robust conformation to commonly encountered evolutionary challenges will be considered.

Brain Scaling

Brain versus Body

The brain scales regularly with the size of the body, with an allometric exponent of about 0.75, an exponent whose cause has been the source of numerous academic debates. Therefore, as the body increases in size, the brain also increases in size, but so as to become an even smaller percentage of the body mass. As any cursory examination of office information processing devices will demonstrate that the sizes of a controller and the thing controlled are not obligatorily linked, why is there such a regular relationship in the case of the brain and the body? An obvious peculiarity of biological devices compared with engineered devices is that biological devices are composed of the elemental unit of cells, whose size is limited by diffusion and intracellular transport mechanisms, and not by the size of the body they compose. As the brain's most basic function is to move the body, and the larger bodies will be composed of a larger number of muscle units, an increase in the number of neurons will be necessary to innervate larger musculature (though axonal and dendritic arbors have a considerably greater range in possible size than a cell body does, and account for some of the range of neuromuscular scaling). Similarly, if large animals attempt to maintain the absolute spatial resolution of their skin sensation at some acceptable value (which seems reasonable, as things to be detected and localized, such as insects, cannot be depended on to scale with their prey animal's body size), the number of receptors and associated neurons transmitting information to the brain should scale with body size as well. There is no need whatever, however, to scale other sensory systems, such as eyes, ears, and vestibular organs, with body size, and yet they do scale. Larger organs
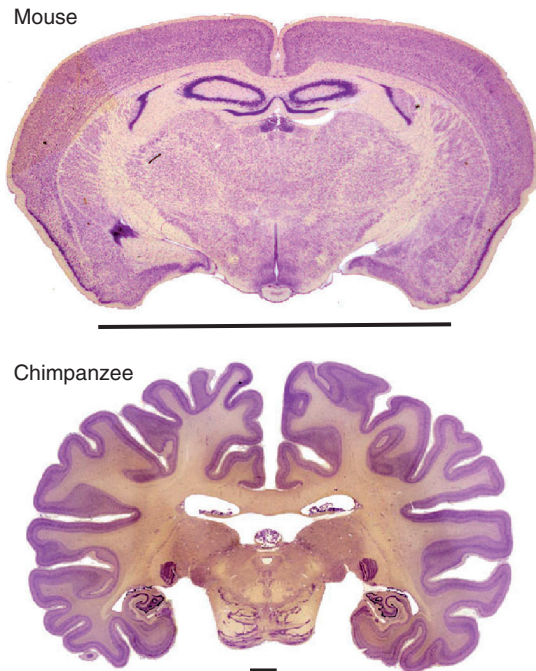
Mouse

Chimpanzee

Figure 1 Comparison of the relative volumes of neocortex and brain stem in mouse (*Mus musculus*) and chimpanzee (*Pan troglodytes*) for comparable coronal brain sections. Scale bar = 0.5 cm for each. From Comparative Mammalian Brain Collections, http://brainmuseum.org.

can permit greater spatial resolution, but that causes improvement, not just maintenance, of quality. This issue will be mentioned again in the section titled 'Employment of "late equals large" to gracefully scale the retina.'

Body size does not entirely control brain size, however; at any particular body size, considering all the vertebrates, there is a possible range of about 40 in the ratio of brain to body size, and within the bony fish, birds, reptiles, and mammals, about a factor of 10 in the same ratio. While there is some arguable association of absolute brain size with behavioral complexity, in fact the two can be quite dissociable. For example, while a hummingbird could fly, collect nectar, and conduct social interactions within a space of the size of the brain case of a baleen whale, the length and complexity of the list of behaviors hummingbirds and whales might exhibit somewhat favors the hummingbird. It is relative size of the brain with respect to the body, variously measured as various ratios or statistical residual variance compared with the animal's taxon, that corresponds best to behavioral complexity or intelligence.

Brain Component Scaling

While it is relative brain size, measured best by the 'encephalization quotient,' or residual deviation from the mean brain–body size value from the appropriate

taxonomic group, brain component architecture is best measured with respect to absolute brain size. This was first noted for the relative size of the cortex compared with the rest of the brain; since the cortex has predictable positive allometry with respect to the brain, the larger the brain becomes, the more it comes to be composed of cortex. As humans have the largest encephalization quotient, but not the largest brain, this means that absolutely larger brains, such as the brains of elephants and many cetaceans, are composed of proportionately more cortex than are human brains.

The cortex is not a special case of predictable scaling, however. Each identifiable brain part has its own exponent, as can be seen in the different slopes of each structure in Figure 2, which plots the slopes of six structures versus 'brain core' – medulla, pons, midbrain, and thalamus. In fact, each identifiable region of the cortex, such as visual cortex, other primary sensory cortices, and parietal or frontal cortex has its own exponent as well, which has caused a great deal of confusion about whether components of the human cortex, particularly the frontal cortex, are as large as should be 'expected.' Many would expect a simple ratio, such as the human brain as the chimpanzee brain multiplied by three, and would predict that a deviation from such a ratio should represent special selection or adaptation. A multiplicative ratio, however, is rarely the nature of the relationship between brain parts – in fact, it occurs only in the special case when the ratio of the allometric exponents of the two parts happens to be one. If the frontal cortex has a positive allometry with respect to the cortex overall, as the cortex enlarges in absolute terms, the frontal cortex will come to comprise a greater percentage of the entire cortex. Thus humans have an entirely predictable, but disproportionate, amount of frontal cortex in their brain compared with other primates.

The Limbic Factor

In the various first investigations of brain component scaling of the large data set collected by Stephan and associates, it was observed by many researchers that primates, compared with bats and insectivores, showed a 'grade shift' with respect to the amount of cortex their brains contained, producing more cortex per unit brain but relatively less olfactory bulb, olfactory cortex, and hippocampus, as well as some other components of the extended limbic system. Knowing whole brain volume captures about 94% of the variability in brain component scaling in mammals overall, and adding a second limbic component gains another 4% of the variance. Until recently, it was unclear
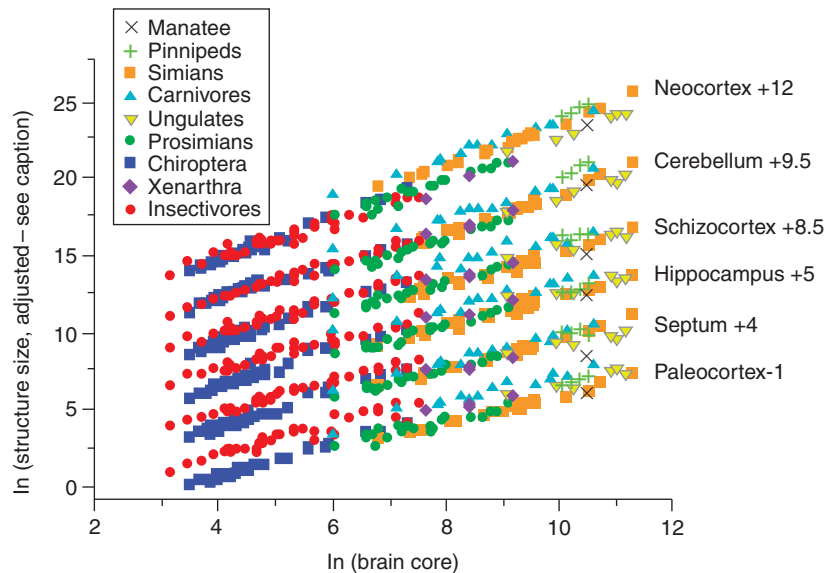
Figure 2 The sizes of six brain structures relative to brain stem and basal ganglia core size, across 160 species in nine taxonomic groups. The six structure sizes have been adjusted by the indicated arbitrary constants (listed on the right of the figure) to separate the six scatterplots visually. Both scales are natural log scales. The regression slopes are paleocortex (olfactory cortex), 0.826; septum, 0.847; hippocampus, 0.912; schizocortex, 0.963; cerebellum, 1.150; and neocortex, 1.441. Natural logarithm, ln. From Reep R, Darlington RB, and Finlay BL (2007) The limbic system in mammalian brain evolution. *Brain, Behavior and Evolution* 70: 57–70.

whether this differential allocation of tissue in the brain was specific to the primate–insectivore contrast or whether it was characteristic of mammalian brain variation more generally. With a sample that included marine mammals, known to have smaller olfactory bulbs, and also some species that would appear to be unusually dependent on chemosensation, such as anteaters, substantial variation along the limbic–cortex tissue allocation axis (**Figure 3**) has been found to be characteristic both between and within mammalian orders. This relationship was not an obligatory reciprocal relationship, however; it is possible for some animals (such as carnivores) to have both a relatively large neocortex and a relatively large olfactory bulb–hippocampus complex with respect to the brain core, or to be reduced in both (like bats), but variation on this dimension dominates the data. Unusually large amounts of variation on this same axis are true of individual variation within species as well, for species as diverse as swine, minks, and mice.

The Developmental Structure of the Observed Species Differences

A basic, conserved pattern of neurogenesis proved to underlie the consistency observed in mammalian brain component scaling. Those structures which became disproportionately large as brains became absolutely larger were the same structures and cell groups whose 'birthdays' were late. That is, those structures whose precursor pools had an extended

time to enlarge before the first of their cells exited the precursor pool and differentiated as neurons were the same ones that became differentially large. We call this relationship 'late equals large,' and it falls directly out of the kinetics of cell proliferation in the developing embryo, which we represent in its most generalized form in **Figure 4**. This figure represents the empirical observation that cell division begins roughly simultaneously in all parts of the neural tube that will give rise to the mammalian brain, but neurogenesis terminates in some parts earlier than others. When neurogenesis is extended from the 21 days or so required to generate a mouse brain to the 100 or so required for a monkey, the consequences for different brain components are not uniform: the regions withdrawing neurons the latest from their precursor pools allow those regions to see more cell divisions and become substantially larger.

The strength of this relationship brings forward some essential regularities about mammalian brain development observed empirically. First, the brain acts as if it is a rate-limiting step in development overall. Early embryos are composed of a large percentage of brain by volume, and the literal bulk of somatic development occurs later, in some species predominantly postnatally. If brain weight is plotted against gestational length in days across diverse eutherian mammalian species, an extremely straight line results, as if a fixed amount of brain can be produced per day. No evidence to date points to locally variable rates of neuron or precursor development; to
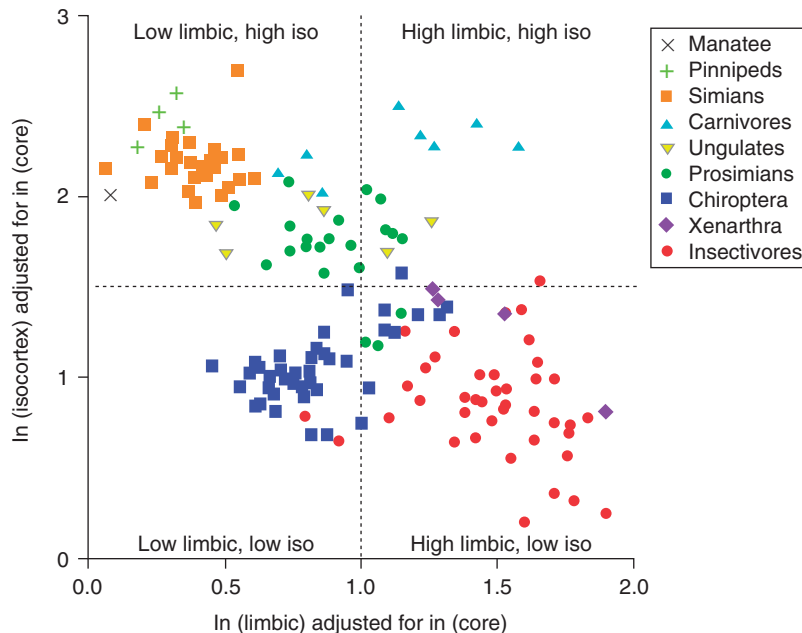
Figure 3 Relationship between limbic and isocortical (neocortical) components of the telencephalon. Plotted are residual variance in the volume of limbic and isocortical components, referenced to brain core volume, for 160 species in nine taxonomic groups. Overall there is a push–pull arrangement between the limbic and isocortical components, indicated by the preponderance of values in the upper left and lower right quadrants. However, some carnivores represent a balanced expansion of both components, and most chiropterans exhibit reduction of both components. iso, isocortex. From Reep R, Darlington RB, and Finlay BL (2007) The limbic system in mammalian brain evolution. *Brain, Behavior and Evolution* 70: 57–70.
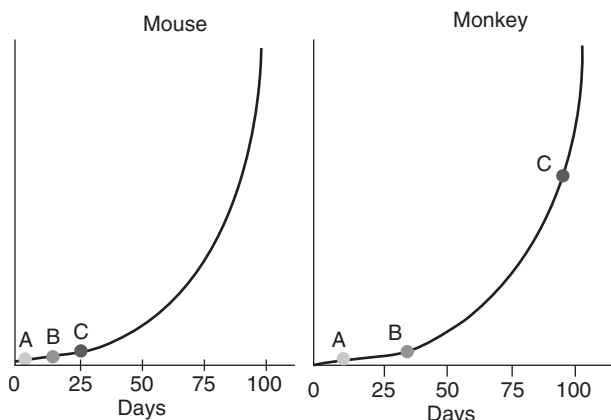

Figure 4 'Late equals Large': a schematic of the consequences for eventual size of a structure generated early (A), intermediate (B), or late (C) in the order of neurogenesis for a species with a short period of neurogenesis and a small brain, like a mouse, versus one with a long period of neurogenesis and a large brain. In the long-development species, the precursor pool for late-generated structures has a longer time to multiply and becomes disproportionately large.

produce more brain, precursors are generated, not more quickly, but over a longer time. (In marsupials, noneutherian mammals, however, the overall pace of brain production is considerably slowed compared to placental mammals, so it is possible to change rate wholesale.) Finally, there is a spatial organization, derived from the initial segmental structure of the

neural tube, to the order in which structures enter terminal neurogenesis, and this spatial organization accounts for about half the variation in date of termination of neurogenesis (**Figure 5**). Those areas that are the most anterior in the neural tube, and most lateral with respect to the original neural tube, that is, the alar plate, are the ones that enter terminal neurogenesis the latest. In fact, for two of the three most anterior and lateral division of the neural plate, which give rise to the hippocampus, neocortex, and olfactory bulb, neurogenesis does not terminate at all.

Limbic System Reduction and Amplification

For primates, evidence exists about how the whole-sale reduction of the olfactory bulb, olfactory cortex, hippocampus, and several other nuclear limbic structures, as well as the enlargement of the neocortex, is produced: if the schedule of rodent neurogenesis is appropriately transformed and lined up against the schedule of the rhesus monkey, it is obvious that the distributed limbic structures in the monkey all appear to commence terminal neurogenesis on the same day, and all of them earlier than would have been expected for the same structures in a rat (**Figure 6**). Conversely, all the layers of the cortex begin terminal neurogenesis later in development than would be predicted from the rat schedule. Those structures that do not differ in their expected size – midbrain, basal ganglia,
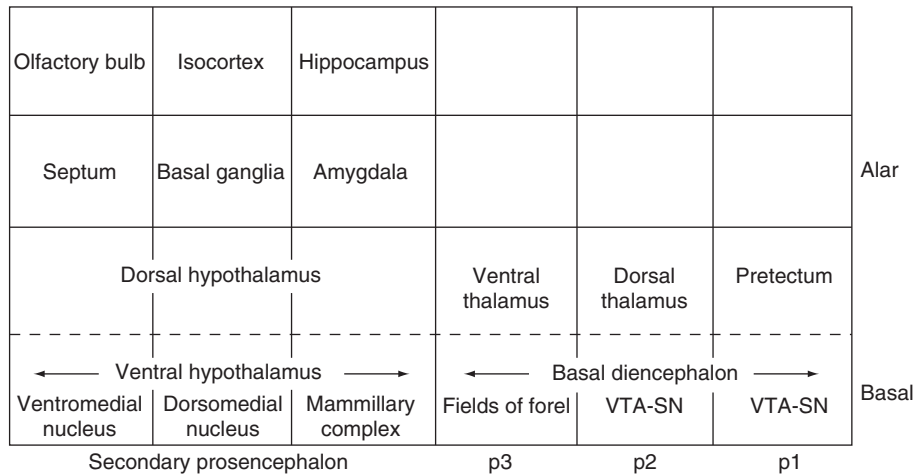
Olfactory bulb	Isocortex	Hippocampus				
Septum	Basal ganglia	Amygdala				Alar
Dorsal hypothalamus			Ventral thalamus	Dorsal thalamus	Pretectum	
← Ventral hypothalamus →			← Basal diencephalon →			Basal
Ventromedial nucleus	Dorsomedial nucleus	Mammillary complex	Fields of forel	VTA-SN	VTA-SN	
Secondary prosencephalon			p3	p2	p1	

Figure 5 Prosomeric model of the forebrain, showing the embryonic spatial relationships of the areas of the brain which undergo the most protracted neurogenesis: olfactory bulb, neocortex, and hippocampus.

and cerebellum – line up at the equivalent times predicted. It is a very interesting research question as to what the genomic alteration might be in monkeys that alters the onset of neurogenesis forward and backward in this distinctive way. It is not yet known whether the other animals that differ on the same axis, like marine mammals, have altered their onsets of neurogenesis in equivalent ways.

The animals whose schedules of neurogenesis have been examined include rodents, the rhesus monkey, cat, ferret, and possum – not an extensive comparative base, but a corpus that has been examined closely to see whether any other potential units of covariation in brain might be observed in any one species or across species (for example, functional systems, such as visual or auditory systems, or parts of brain geometry such as midbrain or hindbrain). Thus far, no such covarying units that could explain more interspecific variation in brains have been identified.

Developmental Constraint, or a Useful Reservoir of Variation for Brain Evolution?

Many aspects of early brain segmentation and genetic specification are highly conserved across vertebrates. The most reasonable interpretation of the extremely conserved fundamental body plan in vertebrates, one of many examples, is not that it is a crystallized 'constraint' on vertebrate organization, but rather a robust and flexible system that by its nature permits graceful variation. The fundamental mechanisms of the specification of body plan are 'evolvable.' How might this argument be extended to a segmental pattern of neurogenesis that permits by its nature systematic variation in the duration of the genesis of precursor pools for neurons, and that has the further

property of systematically and disproportionately amplifying the numbers of certain populations of precursor pools with respect to each other as neurogenesis is extended? As discussed earlier, if a mammal is to be selected for a larger brain, it must take longer to make it. In mammals, the principal way brains differ in size is across, not within species. Since this type of size variation has happened so commonly, the property of graceful scaling should be viewed as a historical filter on the kinds of developmental programs that can undergo selection and that are preserved today. It should be noted, however, that mammals are unusual with respect to most vertebrates in that most of their neurogenesis is confined to early development. In many other animals, both brain and body grow throughout life and must be scaled 'on line,' coupling scaling of the two structures in the life of an individual animal.

Employment of 'Late Equals Large' to Gracefully Scale the Retina

The retina is a case in which, in order to maintain functionality in a system of different scales, cell groups must (and do) scale with different exponents. Rods and cones must scale at different slopes with eye size in order to hold constant their particular functions. If an eye becomes twice as large in diameter, no change is necessary in the number of cones to retain the same visual acuity; since the retina is flooded with photons in diurnal vision, a single cone will have no difficulty encountering a photon in the visual angle it represents regardless of the angle the cone itself subtends. More cones could of course be added, to improve acuity, but we are discussing here what is required to maintain equivalent, not improved, function over different eye sizes.
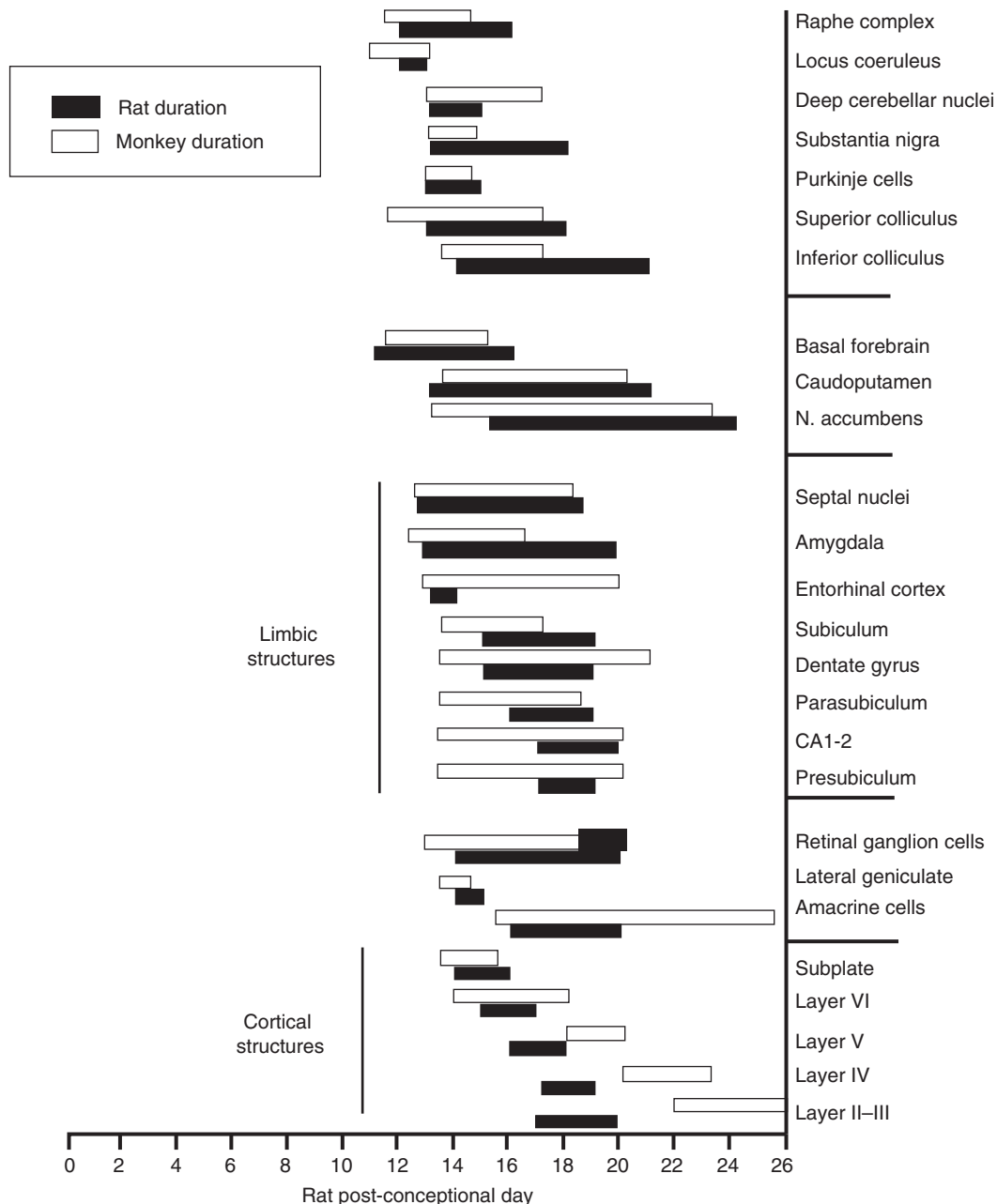
Figure 6 Using the 'translating time' functions described at http://www.translatingtime.net/ (Translating Time Across Developing Mammalian Brains), the schedule of neurogenesis of the monkey is translated to the duration of a rat's for direct comparison. Cessation of neurogenesis for limbic structures begins simultaneously and earlier than expected in the monkey, and the generation of the neocortex later.

The same solution will not work for rods. Working at low light levels and low photon numbers, a single rod located in a larger absolute retinal angle will fail to detect most photons, even allowing for biologically plausible increases in the size of a single rod. Rods must tile the surface of the retina to maintain sensitivity, increasing in number approximately at the square of change in retinal diameter. The scaling of rods and cones in diurnal primates in fact conforms closely to this functional requirement; for example, the human eye, larger than the marmoset eye, has only about 1.2 times the number of cones and retinal ganglion cells in the marmoset eye but 8 times as many rods (Figure 7). How is this consistent within- and across-species disproportional scaling necessity executed in the schedule of neurogenesis of the
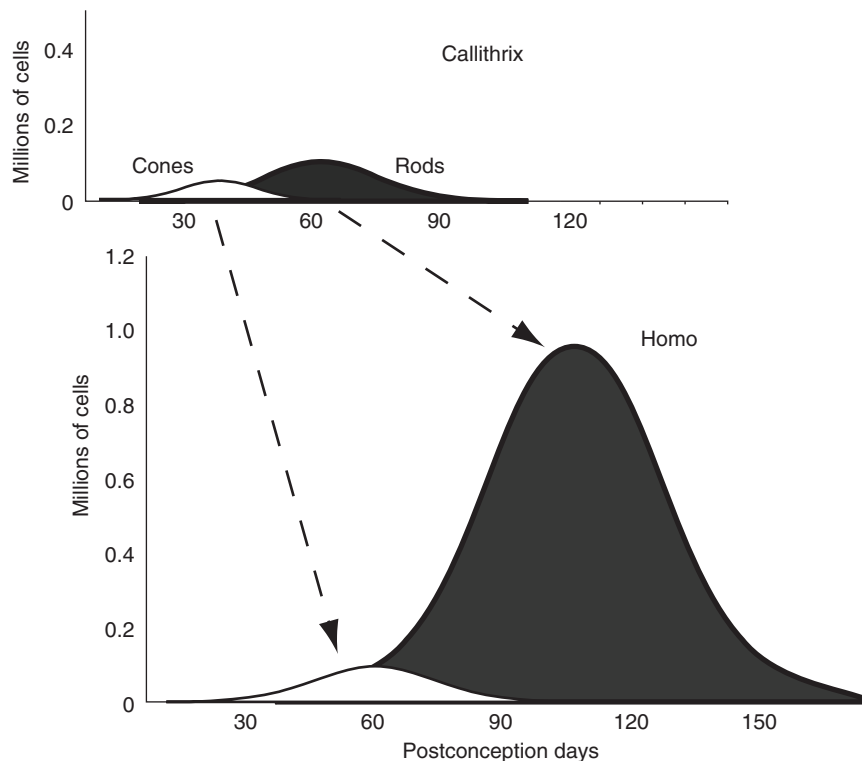
Figure 7 The hypothesized consequences of extended neurogenesis in the retina of *Homo sapiens* versus *Callithrix iacchus* for their relative numbers of cones and rods. The positioning of rod proliferation late in neurogenesis allows dispropotionate proliferation of rods in a larger retina to maintain sensitivity. Areas under the curves for rod and cone numbers are drawn to reflect empirically determined values in each species. Reproduced with permission from figure 2.5 in Finlay BL, Silveira LCL, and Reichenbach A (2005) Comparative aspects of visual system development. In: Kremers J (ed.) *The Structure, Function and Evolution of the Primate Visual System*, pp. 37–72. Chichester: Wiley, Copyright 2005, Copyright John Wiley & Sons Limited.

retina? While the precise kinetics are being worked out, the schedule of neurogenesis in the retina is arranged such that extension of the period of embryogenesis should automatically produce the desired differential scaling, in that cones go into terminal neurogenesis early, and rods late. Those cell types that must change in number with a high exponent with eye diameter, rods and their attendant bipolar cells, are located last in order of differentiation, and those that need not change are produced first. This obligatory, coordinated scaling of retinal cell classes to match functional requirements is an example of the idea of 'evolvability.' The retina offers a potential source of variability in the onset of photoreceptor differentiation by cell class, some of which might gracefully scale with eye size, and some not. Those potential ancestors with perhaps a reversed order of neurogenesis in the retina, rods first, cones last, who might have enjoyed a selective advantage at a larger brain size, but which had ineffective vision in the dark as a result, presumably would enjoy less reproductive success. Common selection points, such as variable body and brain size, will naturally gravitate

to coordinate with predictable aspects of embryogenesis. The retina is a nice example of order of neurogenesis adapted to permit several contrasting functional constraints in a single sensory system.

Using Continuing Neurogenesis to Permit Rapid Memory Acquisition and Loss in the Hippocampus

The hippocampus and the neocortex present another possible example of the siting of a function with respect to a favorable location for continued neurogenesis, the most lateral aspect of the alar plate. Both structures are involved in the integration of multisensory information and in memory but are distinct in that the hippocampus is specialized for immediate short-term memory and the transfer of the short-term store to the long-term storage of the neocortex. New neurons are generated in the hippocampus throughout life, but this unusual maintenance of neurogenesis is well suited to hippocampus function: the 'noise' introduced into the connectivity of a structure whose memories are continually overwritten does not represent a problem for the maintenance of any particular memory and in fact may be useful in

memory erasure. The component of the brain important for short-term memory might function best and survive millions of bouts of selection if the appropriate circuitry and cellular processes were sited in a brain location where the pattern of protracted neurogenesis was favorable.

Why Does the Cortex Get Big and the Spinal Cord and Sensory Thalamus Stay Small? A Network Hypothesis

This argument follows the same lines as that described for the rods and cones of the retina and for the hippocampus: over evolutionary time, important functions in the brain are likely to site themselves where the pattern of neurogenesis is permissive for optimal function, in this case, optimal scaling of its network architecture. The pattern of selective enlargement of the telencephalon and constraint on spinal cord and thalamus contrasts with a type of brain evolution essentially unseen in mammals. Consider that a star-nosed mole, with its specialized end organ for palpation, does not generate a dedicated processing center of cortical proportions for its new sensory system in the spinal cord, but rather in the neocortex, where mouse whiskers, primate hands, and elephant trunks all locate themselves as well. If brain evolution could truly be mosaic, that is, any structure could be the target of differential selection on size, why are integrating structures of the size of the cortex not situated in the spinal cord, the hindbrain, and the midbrain?

The answer to the question of coordination of brain, sensory systems, and body scaling and the preferential enlargement of the cortex may be found in the nature of what is likely to be represented in a larger brain and the particular nature of networks in the brain, particularly the cortex. A common hypothesis about brain evolution is that an animal might specialize or improve function by adding a new 'module,' by which is meant a specialized processing system, relatively encapsulated, like bat echolocation, palpation of the earth by the star nose of the mole, or human language. Minimal consideration of even these systems shows that all must constantly integrate motor output with sensory input, which must then further direct muscle effectors, and even the most committed sensory system has multimodal components. Chemosensory information must be integrated with somatosensory, and in current fMRI studies in human language processing, it has been shown that generating the words for tools activates primary somatomotor cortex. So it is obvious that elaboration of sensory, cognitive, or motor capacities should be situated in locations where multimodal integration is possible.

Why body, brain, and sensory systems should covary so regularly, even though neural tissue is metabolically expensive, may have its answer in the distributed nature of neuronal connections. Particularly in the cortex, each neuron receives thousands of synapses, none of which has a 'command' nature; not only that, there are small assemblies of neurons, such as the cortical column, with high local interconnectivity and which almost certainly participate in multiple disparate computations, such as in the language example above. In modeling studies, if the size of just one component of a multicomponent system is increased differentially, the excessive input–output (I/O) requirements of the single larger component when communicating with other system components propagates itself throughout the neural net, leaving the remaining systems with far fewer computational resources than they would have if the large system had simply been deleted from the resources of the net. It is a peculiar and not much noticed fact that the primary sensory and motor nuclei are the first-generated ones in the thalamus, causing them to scale with negative allometry with respect to the rest of the thalamus. The primary sensory nuclei and their inputs act as a significant bottleneck on input to the cortex – for example, the human retina has only about 6 times as many retinal ganglion cells contributing optic nerve axons to the thalamus as a gerbil's! The primary sensory and motor areas of the cortex are also the ones that appear to be the most specified in terms of location and size in the developing brain. Further, in all the primary sensory areas, if an animal develops a specialization, such as an auditory, acoustic, or somatosensory 'fovea,' the increased allocation of cortical area to the specialization takes its place within the primary cortex and does not appear to enlarge it. Rather, the effect of the specialization is seen primarily in the proliferation of new cortical areas. It is interesting that the two large neural systems that show evidence of decoupling, the neocortical and limbic, do not directly combine primary sensory inputs in the thalamus, which may be permissive for diverging allometric scaling that these two systems show (Figure 4).

These anatomical observations, initial modeling studies, and hypotheses are here combined to suggest that the fundamental kinetic of cytogenesis described as 'late equals large' may be employed repeatedly as a natural substrate for graceful scaling in vertebrate development and evolution, whether to defend the functional requirements of rods versus cones in sensitivity or acuity, respectively, or the I/O requirements of an associative net with multiple separate inputs. Thus, the conservation seen in the scaling of body, sensory, and motor inputs and brain components does probably represent a constraint, although not a constraint that development places on function but rather functional constraints that exploit to best purpose the intrinsic nonlinearities of neurogenesis.

See also: Brain Asymmetry: Evolution; Brain Connectivity and Brain Size; Brain Development: The Generation of Large Brains; Brain Evolution: The Radiator Theory; Brain Modules: Mosaic Evolution; Brain Scaling Laws.

Further Reading

Catania KC and Kaas JH (1997) Somatosensory fovea in the star-nosed mole: Behavioral use of the star in relation to innervation patterns and cortical representation. *Journal of Comparative Neurology* 387: 215–233.

Finlay BL and Brodsky PB (2006) Cortical evolution as the expression of a program for disproportionate growth and the proliferation of areas. In: Kaas JH (ed.) *Evolution of Nervous Systems*, pp. 73–96. Boston, MA: Elsevier.

Finlay BL, Darlington RD, and Nicastro N (2001) Developmental structure of brain evolution. *Behavioral and Brain Sciences* 24: 263–308.

Finlay BL, Hersman MN, and Darlington RB (1998) Patterns of vertebrate neurogenesis and the paths of vertebrate evolution. *Brain, Behavior and Evolution* 52: 232–242.

Finlay BL, Silveira LCL, and Reichenbach A (2005) Comparative aspects of visual system development. In: Kremers J (ed.) *The Structure, Function and Evolution of the Primate Visual System*, pp. 37–72. Chichester, UK: Wiley.

Gerhart J and Kirschner M (1997) *Cells, Embryos and Evolution*. Malden, MA: Blackwell.

Jerison HJ (1997) Evolution of prefrontal cortex. In: Krasnegor NA, Lyon GR, and Goldman-Rakic PS (eds.) *Development of the Prefrontal Cortex: Evolution, Neurobiology and Behavior*, pp. 9–26. Baltimore, MD: Brookes.

Pascual-Leone A, Amedi A, Fregni F, and Merabet LB (2005) The plastic human brain. *Annual Review of Neuroscience* 28: 377–401.

Pulvermuller F (2001) Brain reflections of words and their meaning. *Trends in Cognitive Sciences* 5: 517–524.

Ragsdale CW and Grove EA (2001) Patterning the mammalian cerebral cortex. *Current Opinion in Neurobiology* 11: 50–58.

Reep R, Darlington RB, and Finlay BL (2007) The limbic system in mammalian brain evolution. *Brain, Behavior and Evolution* 70: 57–70.

Schmidt-Nielsen K (1984) *Scaling: Why Is Animal Size So Important?* Cambridge, UK: Cambridge University Press.

Stephan H, Baron G, and Frahm HD (1981) New and revised data on volumes of brain structures in insectivores and primates. *Folia Primatologica* 53: 1–29.

Relevant Websites

http://brainmuseum.org – Comparative Mammalian Brain Collections.

http://www.translatingtime.net – Translating Time Across Developing Mammalian Brains.