a0005 # Brain Scaling Laws

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s0005 ## Introduction

p0005 The mammalian brain varies over five orders of magnitude in volume from shrew to whale, and large mammalian brains do not look like small mammalian brains. For example, large neocortices have lower neuron density, are more convoluted, have disproportionately more white matter, and possess a greater number of specialized cortical areas. Knowing the manner in which brains change as a function of size is important in our attempt to understand the fundamental principles governing the brain. In particular, the hope is to find fundamental brain properties that are kept invariant as a function of brain size, the idea being that the brain changes as it does because it has been selected to maintain important invariants. Here, many of the broad ways the neocortex changes as a function of brain size are reviewed, and the principles that may explain these scaling relationships are discussed.

p0010 Before proceeding, note that bigger mammals appear to require bigger brains (brain mass increases as the 3/4 power of body mass), whether or not the animal is any more intelligent. (There is currently no accepted explanation for this brain–body scaling relationship.) Larger but similarly intelligent mammals have bigger brains, and their brains will differ from those found in smaller but similarly intelligent mammals, and therefore these differences are not due to differences in intelligence. The brain scaling relationships discussed here are, for this reason, likely to be explained by fundamental dilemmas encountered by trying to build a larger, highly interconnected brain, not explained by principles for building a 'smarter' brain.

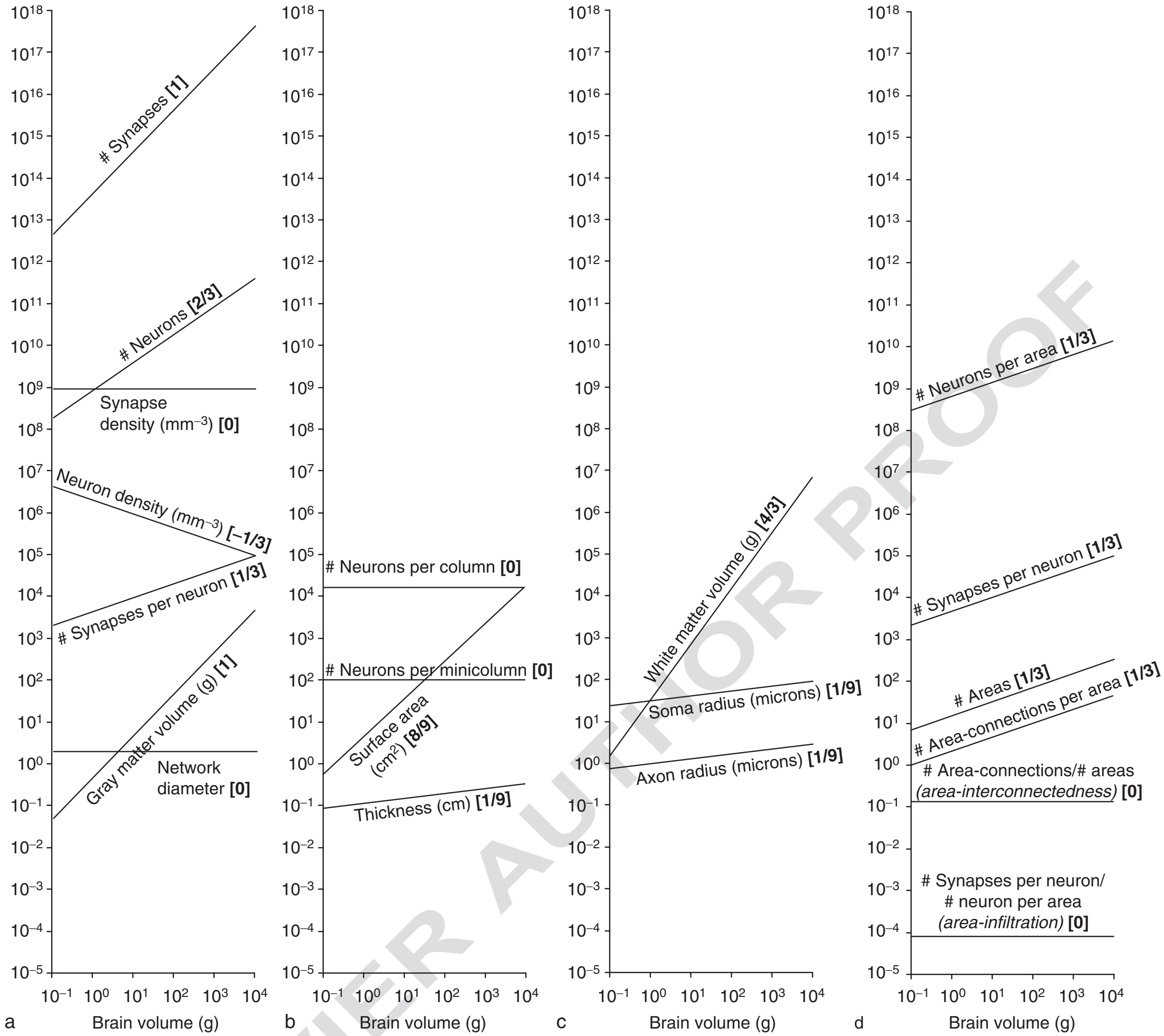
s0010 ## Number of Neurons and Neural Connectivity

p0015 A first question one might reasonably ask is, How fast does the number of neocortical neurons increase as a function of brain size? The number of neurons increases disproportionately slowly as a function of brain volume, increasing approximately proportional to the 2/3 power of brain volume (i.e., number of neurons $\propto V_{\text{brain}}^{2/3}$) or, equivalently, neuron density decreases as the 1/3 power. In other words, brain volume (and also gray matter volume) increases disproportionately quickly as a function of the number of neurons, namely as the 3/2 power of the number of neurons, so that quadrupling the number of neurons requires an eightfold increase in brain size. (See **Figure 1a** for the approximate scaling relationships.)

How does the number of synapses per neuron vary with brain size? It is known that synapse density appears approximately constant as a function of brain size (on the order of $10^9/\text{mm}^3$). Bigger brains, then, have lower neuron density but approximately the same synapse density. Because every synapse, of course, belongs to a neuron, it immediately follows that the number of synapses per neuron is larger in larger brains. In particular, the total number of synapses in the brain increases proportional to brain volume (because synapse density is invariant), and the total number of neurons increases proportional to the 2/3 power of brain volume, from which it follows that the average number of synapses per neuron is proportional to $V_{\text{brain}}/(V_{\text{brain}}^{2/3}) = V_{\text{brain}}^{1/3}$. That is, it follows that the number of synapses per neuron increases approximately as the 1/3 power of brain volume (**Figure 1a**). p0020

Because the number of neurons increases as $V_{\text{brain}}^{2/3}$ and the number of synapses per neuron increases as $V_{\text{brain}}^{1/3}$, it follows that the number of synapses per neuron, δ, increases as the square root of the number of neurons, N; that is, $\delta \propto N^{1/2}$. Assuming that the neocortex is small world (i.e., having sufficiently many axons connecting otherwise separated parts of neocortex that the network diameter can be approximated as that of a random network), the network diameter (i.e., the average number of axons that must be traversed to get from any neuron to another) may be approximated as $\Lambda \approx (\log N)/(\log \delta)$, which can be manipulated into $\Lambda \approx 2 \times [1 + (\log c)/(\log N)]$, where c is the proportionality constant in the equation $\delta = cN^{1/2}$. For sufficiently large brains, then, the network diameter approaches 2. Also, estimates of c are on the order of 1, meaning that perhaps network diameter may be approximately 2 in actual neocortices, despite the number of synapses per neuron scaling up much more slowly than the total number of neurons (namely as a square root of the total number of neurons) (**Figure 1a**). p0025

We have just reported the approximate empirical scaling relationship for the number of neurons, the number of synapses per neuron, and the network diameter but have not given any hint as to why the brain might conform to these scaling relationships. This will be discussed later, where it will be shown that increasing the number of synapses per neuron as the square root of the number of neurons is the slowest rate of increase possible while still allowing high intra-area connectivity and high area–area connectivity. p0030



f0005 **Figure 1** Various neocortical features as a function of brain mass. The number in the square bracket indicates the scaling exponent in each case; for example, for # neurons in a, the '2/3' in square brackets indicates that the number of neurons varies with brain volume to the power of 2/3. The four plots respectively show the scaling relationships concerned with (a) number of neurons and neural connectivity, (b) gray matter convolutedness and thickness, (c) white matter volume and axon caliber, and (d) specialized areas and area–area connectivity.

s0015 Convolutedness and Thickness

p0035 One of the most salient differences between small and large brains is that the neocortical surface is smooth in small brains and convoluted in large brains. In fact, the surface area of the gray matter increases as approximately the 8/9 power of brain volume, more quickly than the 2/3 power expected for geometrically similar objects. This difference between 8/9 and 2/3 serves to quantify the rate at which larger brains become increasingly convoluted (**Figure 1b**).

p0040 Given that gray matter surface area increases as the 8/9 of brain volume, and given that gray matter volume obviously equals its surface area multiplied by its thickness, it follows that thickness increases as the 1/9 of brain volume, or very slowly (**Figure 1b**).

From this slow increase in gray matter thickness, it is possible to derive an interesting invariant feature of mammalian brains. Recall that (volumetric) neuron density decreases as the 1/3 power of brain volume. Because linear dimensions are the cube root of volumes, the linear neuron density decreases as the 1/3 power of the volumetric neuron density. Therefore, it follows that the linear neuron density decreases as the 1/9 power of brain volume. In other words, the linear dimensions of some fixed number of neurons along a line will increase as the 1/9 power. p0045

In this light, one can see that the slow increase in gray matter thickness is explained entirely by the neuron density decrease in larger brains, meaning that the number of neurons through the cortical thickness (from pia to white matter) is approximately invariant as a function of brain size. Minicolumns are thin neuroanatomical structures consisting of neurons extending from pia to white matter, and we can conclude – and there is evidence – that the number of neurons per minicolumn does not vary as a function of brain size (**Figure 1b**). (There is also evidence for another invariant-sized computational unit, the module, which includes larger structures such as column, blobs, barrels, and stripes.)

p0050 This suggests an important potential principle underlying why surface area and thickness scale as they do. Namely, gray matter appears to be built out of minicolumns which are repeating computational units of invariant size – that is, computational units possessing a number of neurons that does not vary as a function of brain size – extending through the thickness of the neocortex gray matter. From this principle of invariant-size computational units, and from the neuron density decrease discussed previously, it follows that thickness increases as the 1/9 power of brain volume, entailing, in turn, that surface area scales as the 8/9 power. This explanation for why brains become increasingly convoluted at the rate that they do relies also on the neuron density decrease, and we have not yet provided an explanation for it; this explanation will complete the explanation for why surface area and thickness scale as they do.

s0020 Axon Caliber and White Matter

p0055 For nearly all biological trees, arbors with more leaves possess thicker trunks. The same is true for neurons: Neurons with more synapses tend to have thicker early arbor segments (e.g., the soma or the near-soma axon segment). We have previously seen that larger brains have neurons with a greater number of synapses, and we should not be surprised to find thicker trunked neurons in bigger brains. Although there is large variability in axon caliber, evidence supports that axon caliber tends to slowly increase with brain volume, namely approximately as the 1/9 power (e.g., for white matter axons and for spinal motor neuron somas) (**Figure 1c**).

p0060 White matter consists of axonal wiring connecting disparate parts of neocortex, and its volume depends, in part, on the caliber of the axons. White matter scales disproportionately quickly as a function of brain size, namely approximately with a scaling exponent of approximately 4/3 (**Figure 1c**), although sometimes it has been measured to be as low as approximately 1.2.

What explains these scaling relationships for axon p0065 caliber and white matter volume? Let us start with axon caliber; why an exponent of 1/9, rather than some other positive exponent? This exponent is consistent with a law that appears to apply to neural arbors concerning how the diameter of a parent segment relates to the diameter of the daughter segments downstream. In particular, evidence suggests that the cube of the diameter of the parent is equal to the sum of the cubes of the daughter segments (e.g., $R_{\text{trunk}}{}^3 = R_1{}^3 + R_2{}^3$), which is called Murray's law (and has been found to apply to a variety of kinds of natural arbor), and is the power-efficient diameter setting for laminar flow through pipes and also the optimal setting for simultaneously optimizing volume and transmission speed. The 1/9 exponent is derivable from Murray's law as follows: Each of the terms in the summation of Murray's law is for one daughter segment and can be replaced by the sum of the cubes of that daughter's daughters, and so on, until reaching the synapses so that $R_{\text{trunk}}{}^3 = \delta \times R_{\text{synapse}}{}^3$, where δ is the number of synapses and R_{synapse} is the linear dimensions of synapses. Because synapse density is invariant, R_{synapse} must be invariant, and therefore the equation becomes the proportionality $R_{\text{trunk}}{}^3 \propto \delta$. However, recall that the number of synapses per neuron scales as the 1/3 power of brain volume, and thus $R_{\text{trunk}} \propto V_{\text{brain}}{}^{1/9}$.

The 1/9 scaling law for axon caliber is key for p0070 understanding white matter volume scaling. The volume of white matter is proportional to the product of the number of white matter-projecting neurons, N_{white}, the length of the average connection, L, and the square of the axon caliber, R; that is, $V_{\text{white}} \propto N_{\text{white}} \times L \times R^2$. Supposing that the number of white matter-projecting neurons scales proportionally with the total number of neurons, and treating the average connection length as proportional to the linear dimensions of the white matter (and recalling that axon caliber scales as the 1/9 power), one may derive that the volume of white matter increases as the 4/3 power of brain volume. If, instead, the average connection length is proportional to the linear dimensions of the brain (rather than to the white matter), white matter volume scales as the 11/9 power of brain volume. White matter volume, then, scales up disproportionately quickly because white matter axon caliber increases as it does, and this, in turn, is due to the increasing number of synapses per neuron and due to Murray's law. If white matter axon caliber were constant (which would require that the number of synapses per neuron be constant), then white matter volume would scale proportionally with brain size. Although we now understand why white matter volume scales the way it does given that the number of synapses per neuron scales as it does, we have not yet addressed why the number of synapses per neuron scales the way it does, something crucial to brain scaling which we discuss later.

s0025 Areas and Area–Area Connectivity

p0075 The neocortex is parceled into specialized areas, and the number of areas increases approximately as the 1/3 power of brain volume. Recalling that the number of neocortical neurons increases as the 2/3 power of brain volume, it follows that the number of areas increases as the square root of the number of neocortical neurons. It immediately follows that the average number of neurons per area increases as the square root of the number of neocortical neurons, or as the 1/3 power of brain volume (**Figure 1d**).

p0080 We are now in position to notice an important invariance. Recall that the number of synapses per neuron increases as the 1/3 power of brain volume, and therefore the number of synapses per neuron scales proportionally with the number of neurons per area. Therefore, when a neuron connects to an area (either to its own area or to another), it is able to connect to a certain fraction of the neurons there (approximately on the order of 10^{-4}), and this fraction does not appear to vary as a function of brain size (**Figure 1d**). This invariance property is referred to as invariant area infiltration because, independent of brain size, neurons have, on average, sufficiently many synapses to 'infiltrate' an invariant fraction of the neurons in an area. Thus, there appears to be strong selective pressure across mammalian neocortices for the average number of synapses per neuron to scale up just fast enough that neuron interconnectedness within areas can remain invariant and that, when an area connects to another area, the average neuron making the connection has sufficiently many synapses to infiltrate an invariant fraction of the neurons in the area.

p0085 Concerning area–area connectivity, evidence suggests that the average number of areas to which an area connects scales proportionally with the 1/3 power of brain volume or, again, as the square root of the number of neurons (**Figure 1d**).

p0090 An important invariance principle follows from this. Recall that the number of areas scales as the 1/3 power of brain volume, and therefore the average number of areas to which an area connects scales proportionally with the number of areas. That is, no matter the size of the brain, each area is able to connect to a certain fraction of the areas in that brain (probably approximately 30%), and that fraction does not appear to vary as a function of brain size (**Figure 1d**). This invariance property is referred to as invariant area interconnectedness. There appears, then, to be strong selective pressure across mammalian neocortices for the number of area connections per area to scale up just fast enough that area networks can maintain an invariant level of area interconnectedness. Equivalently, there is selective pressure for the total number of area–area connections to scale as the square of the total number of areas.

We have seen that the number of areas and the number of area connections per area each scale as the 1/3 power of brain volume, but we have not yet provided an explanation. Recall that we have also not yet provided any explanation for why neuron density and the number of synapses per neuron scale as they do. The next section discusses how these are connected and how they may be explained. p0095

Economical Well-Connectedness s0030

Previously, we described that neuron density decreases, and the number of synapses per neuron increases, in larger brains; this fact was crucial for understanding why brains become increasingly convoluted (and the principle of invariant computational units was also key), and it was also crucial for comprehending why white matter volume increases disproportionately quickly (and Murray's law was also key). We have not yet provided an explanation for the neuron density and number of synapses per neuron scaling, nor have we provided an explanation for why the number of areas and the number of area connections per area increase. p0100

In the previous section, we noted that the mammalian neocortex maintains two important invariants – invariant area infiltration (or it could have been named invariant area intraconnectedness) and invariant area interconnectedness. The first states that the number of synapses per neuron increases just fast enough that neurons can connect to an invariant fraction of the neurons within a cortical area. In particular, both quantities increase in larger brains, namely as the 1/3 power of brain volume. This means that no matter the brain size (and no matter the size of the areas), each area maintains constant intra-area connectivity; also, when an area sends an axon to communicate to another area, it is able to synapse to some constant fraction of the neurons there. Invariant area interconnectedness, on the other hand, states that the number of area connections per area increases just fast enough that areas can connect to an invariant fraction of the areas in the neocortex. In particular, both quantities increase as the 1/3 power of brain volume. This means that no matter the brain size (and no matter the total number of areas), the neocortex area network maintains a constant area–area connectivity or, equivalently, the number of area–area edges scales as the square of the number of areas. p0105 p0110 That is, the neocortex appears to take a two-tiered approach to high interconnectivity: invariant neural connectivity for the neural network within areas and invariant area connectivity for the entire neocortical area network. It is not understood why the neocortex takes a two-tiered approach of this kind. Why not a one-tiered design in which the number of synapses per neuron scales proportionally with the number of neurons? A one-tiered design would lead to brain size increasing much faster as a function of the number of neurons – and thus a brain of any given size would have to have many fewer neurons – but such a brain would be much more fully connected. It is difficult to state why a one-tiered design would be worse than a two-tiered design, for how does one balance the costs of having fewer neurons against the benefit of having them much more highly interconnected? Alternatively, why not a take a three-tiered design? Again, the advantages of a two-tiered design are not well understood.

p0115 Given that the neocortex follows a two-tiered design, is it possible to explain some of the yet unexplained scaling exponents discussed previously (namely why neuron density decreases and why the number of areas increases as it does)? Invariant area infiltration tells us that $\delta \propto W$, where δ is the number of synapses per neuron and W is the number of neurons per area. Invariant area interconnectedness tells us that $D \propto A$, where D is the number of area connections per area and A is the number of neocortical areas. The problem is that these two proportionalities do not tell us how W relates to A. If we knew that, then we could compute how these variables relate to the total number of neurons (which is the product of W and A). Thus, the answer is "no," the two invariance principles are not sufficient to explain everything. The reason is that there are many ways of implementing a two-tiered design. For example, a two-tiered design could just possess two areas no matter the brain size, in which case the number of neurons per area would increase proportional to the total number of neurons. Alternatively, a two-tiered design could try to keep the number of neurons per area low by compartmentalizing as fast as possible.

p0120 Although there is a continuum of two-tiered designs (parameterized by how quickly the number of neurons per area increases), some designs are more economical than others in terms of the amount of wire required. If the neocortex requires conformance to invariant area infiltration – as it appears to – then the lower the number of neurons per area, the lower the number of synapses per neuron. Fewer synapses per neuron means less arborization for each neuron and thinner wires, which in turn leads to lower distances for the neurons to travel because the brain can be more compactly organized. That is, the lower the number of neurons per area, the less wiring volume is required. Such a 'save wire' desideratum has turned out to be very successful at predicting nervous system organization at many levels, suggesting that it is a key principle for understanding why the neocortex scales as it does. Recall that invariant well connectedness Au2 referred to the pair of invariants: invariant area infiltration and invariant area interconnectedness. Consider now the hypothesis that the neocortex satisfies invariant well connectedness economically, which we may call economical well connectedness for short. As previously mentioned, this hypothesis expects the number of neurons per area to scale up as slowly as possible, which in turn is to say that the number of areas should increase as quickly as possible. The number of areas cannot scale up faster than the number of neurons per area because if it did, then there would not be enough neurons in an area to connect up to an invariant fraction of all the areas, violating invariant area interconnectedness. Thus, the fastest that the number of areas can increase is proportional to the number of neurons per area, or $A \propto W$. However, because $N = W \times A$, where N is the total number of neurons, it immediately follows that W and A each scale as the square root of the number of neurons. But then the number of synapses per neuron, δ, and the number of area connections per area, D, also scale as the square root of the number of neurons. That is, $\delta \propto W \propto A \propto D \propto N^{1/2}$. We see, then, how the area and area connection relationships discussed previously are explained. Also, given that synapse density is invariant, gray matter volume (and brain volume) scales as the total number of synapses, or $\propto \delta \times N$, and this is proportional to $N^{3/2}$, or $N \propto V_{\text{brain}}^{2/3}$. That is, this explains the neural density (and number of synapses per neuron) scaling relationships discussed previously – relationships that were also part of the story in understanding convolutedness, axon caliber, and white matter volume.

Conclusion s0035

p0125 Despite the large variety of scaling relationships in **Figure 1**, they can be understood in terms of a relatively small number of principles. Economical well connectedness is the principle that the neocortex maintains an invariant two-tiered design (satisfying invariant area infiltration and invariant area interconnectedness) and does so economically. We saw that from this principle the scaling relationships can be derived for the number of neurons, the number of synapses per neuron, the number of areas, the number of neurons per area, and the number of area connections per area. The result for the total number of neurons was crucial for understanding why bigger brains become increasingly convoluted, but also crucial was the principle of invariant computational units (stating that the neocortical gray matter consists of invariant-sized minicolumns), without which the convolutedness (or surface area) scaling relationship would not have followed. Finally, in order to understand why axon caliber and white matter volume scale as they do, it was necessary to understand Murray's law, which governs the rate at which neural arbors become thinner as they near the synapses.

See also: Visual areas in humans (00241); Brain connectivity and brain size (00937); Brain Development: The Generation of Large Brains (00938); Brain Fossils: Endocasts (00941); Allometric analysis of brain size (00944).

Further Reading

Braitenberg V (2001) Brain size and number of neurons: An exercise in synthetic neuroanatomy. *Journal of Computational Neuroscience* 10: 71–77.

Changizi MA (2003) *The Brain from 25,000 Feet: High Level Explorations of Brain Complexity, Perception, Induction and Vagueness*. Dordrecht, The Netherlands: Kluwer Academic.

Changizi MA (2007) Scaling the brain and its connections. In: Kaas JH (ed.) *Evolution of Nervous Systems*. New York: Elsevier.

Haug H (1987) Brain sizes, surfaces and neuronal sizes of the cortex cerebri: A stereological investigation of man and his variability and a comparison with some mammals (primates, whales, marsupials, insectivores, and one elephant). *American Journal of Anatomy* 180: 126–142.

Hofman MA (1985) Size and shape of the cerebral cortex in mammals: I. The cortical surface. *Brain Behavior and Evolution* 27: 28–40.

Jerison HJ (1973) *Evolution of the Brain and Intelligence*. New York: Academic Press.

Kaas JH (2000) Why is brain size so important: Design problems and solutions as neocortex gets bigger or smaller. *Brain and Mind* 1: 7–23.

Prothero J (1997) Cortical scaling in mammals: A repeating units model. *Journal of Brain Research* 38: 195–207.

Prothero J (1997) Scaling of cortical neuron density and white matter volume in mammals. *Journal of Brain Research* 38: 513–524.

Rockel AJ, Hiorns RW, and Powell TPS (1980) The basic uniformity in structure of the neocortex. *Brain* 103: 221–244.

Tower DB (1954) Structural and functional organization of mammalian cerebral cortex: The correlation of neurone density with brain size. *Journal of Comparative Neurology* 101: 9–52.

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Non-Print Items

Abstract:

Bigger brains have lower neuron density, possess a greater number of synapses per neuron, become increasingly convoluted, have disproportionately more white matter, and are compartmentalized into more areas. This article reviews these and many other ways in which large mammalian neocortices differ from small ones. By identifying these allometric scaling laws, we hope to identify fundamental principles that the neocortex obeys across the nearly five orders of magnitude of brain volume change from shrew to whale.

Keywords: Allometry; Areas; Axon caliber; Brain scaling; Brain size; Complexity; Connectivity; Convolutions; Minicolumns; Network diameter; Neuron density; White matter

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