Chapter 1
What Makes the Human Brain Special: Key Features of Brain and Neocortex

Jon H. Kaas and Suzana Herculano-Houzel

Abstract Humans have the largest brain of any primate. While it seems logical to assume that overall size is very important for generating complex behaviours, brain size relative to body size has been considered to be a major factor in predicting overall brain capacity. It turns out, however, that the absolute number of neurons in the cerebral cortex, regardless of body mass, may be a more relevant factor. Here we review the ways in which brains have increased in size, why absolute brain size is sometimes important, and why the size of the human brain allowed us to have cognitive abilities that exceed those of other primates. We suggest that cognitive functions are largely mediated by the neocortex, and because the human brain scales like a typical primate brain, the large neocortex of humans contains more neurons than any other mammal, even those with larger brains such as elephants. Further, as neurons in primary sensory cortex increase in numbers with brain size at a greater rate than the increase in the number of neurons in thalamic relay nuclei, primates with larger brains and more neocortex also have more neurons to analyze these sensory inputs. As numbers of neurons increase, individual neurons are free to specialize in different ways, generating increasing variability in cell size, shape, dendritic arborization and other features. In addition, an expanded cortical sheet contains more cortical areas, thereby increasing the number of computational levels involved in information processing, decision-making, and information storage. Having more cortical areas allows any given area to become more specialized in terms of laminar and sub-laminar organization, modular organization, connectivity and function. Increases in cortical field number also allow for greater variation in the sizes of areas, and thereby different types of functional specializations. Finally, large brains have more areas that are removed from primary sensory inputs and capable of hemispheric specialization. Of course, the costs of a large brain are considerable in terms of gestation time, postnatal vulnerability, and metabolic costs. Thus, it is not surprising that most mammals have relatively small brains that are constrained

UNCORRECTED PROOF

J.H. Kaas (✉) • S. Herculano-Houzel
Department of Psychology, Vanderbilt University, 301 Wilson Hall, 111 21st Ave S, Nashville, TN 37203, USA
e-mail: jon.h.kaas@vanderbilt.edu

© Springer International Publishing Switzerland 2017

I. Opris, M.F. Casanova (eds.), *The Physics of the Mind and Brain Disorders*,
Springer Series in Cognitive and Neural Systems 11,
DOI 10.1007/978-3-319-29674-6_1

in their processing capacity, but are more metabolically efficient, and mature rapidly allowing for early reproduction.

Keywords Areas • Columns • Neurons

1.1 Introduction

Human perceptual and cognitive abilities are so profound that no other species comes close to matching them. Modern humans left Africa more than once, but with a major success only 60,000 years ago as they spread out to dominate most of the world, while two competing hominids, the Neanderthals and the Demisovans, died out after limited admixture. With tools and fire, and sometimes boats or rafts to cover water, early *Homo sapiens* were able to spread out from tropical to temperate to even artic zones and prosper (Fan et al. 2016; Timmermann and Friedrich 2016). Their abilities to learn from each other and pass on cultural innovations, including the domestication of plants and animals, allowed population densities to increase, the advent of cities, the beginning of science and modern medicine. Our various cultures have produced remarkable individuals in many fields, including, art, music, and sport. Modern human created the technology to place humans on the moon, and instruments on Mars. We have also been involved in multiple wars and produced horrible weapons of mass destruction. Our impact on the Earth has been so great that many now consider us to be in a geological epoch called the anthropocene, the epoch remarkably changed by humans.

Why have we been so capable of dominating the Earth and all competing species? Surely there are a number of reasons, starting with the first bipedal steps of our early ancestors as they diverged from the ancestors of present-day chimps and bonobos some five to seven million years ago (mya), with which brains that were no larger than present day chimps. Thus, early evolution was not marked by significant changes in brain structure, but rather the use and specialization of our forelimbs and hands in new ways, allowing advances in tool manufacture and use, and the making of fire. However, we had already inherited a brain from early primate ancestors that had more densely packed neurons than other lines of mammalian evolution (Herculano-Houzel 2016), and this likely favored further dependence on the brain, and ultimately, the evolution of the modern human brain. All of our behavioral and cultural advances depend on our brain. How is our brain different from those of other mammals? This is not fully known, but we are beginning to see some of the ways our brains differ from those of our early ancestors. Here, we briefly review current understanding of how human brains are different, and what the differences mean. Much of our comparisons will be of anatomical features of the brain, as these can be more reliably and productively identified and measured across species. As anatomical features have functional implications, understanding these features also leads to a better understanding of our minds and how they work. We start with something that is easy to measure, brain size, and then consider other features such

UNCORRECTED PROOF

as neuron numbers, neuron distributions and size across brains, brain parts, numbers and types of cortical areas, and laminar and modular specializations of cortical areas.

1.1.1 The Importance of Brain Size

As brains are the source of mental abilities, it seems reasonable to assume that the bigger the brain the better. Thus, it is comforting to know that human brains are the biggest of any primates. Primates vary greatly in brain and body size, with the smallest primates, mouse lemurs of 30 g, having brains of 1.5 g, and the largest of primates, 170 kg gorillas, having brains of 535 g. Because body size is easy to measure, there is a long tradition of relating brain size to body size (e.g., Jerison 1973), but the relationship is only approximate (Herculano-Houzel 2016). Within each mammalian clade, larger animals do tend to have larger brains, although the exact relationship is specific to each clade, such that mammals with similar body sizes may have different brain masses (Herculano-Houzel 2017). The reasons for this trend for larger species to have larger brains are not very clear, but one proposed factor is that a larger body surface requires more somatosensory inputs to the brain, leading to a larger brain (see Kaas 2000). Yet, such an increase in sensory input would seem to impact on only a small part of the brain, the sensory representations, and constitute only a minor factor in adapting brains to a larger body. Indeed, brains gain neurons much more slowly than they gain mass, and clade-specific relationships are particularly clear between body mass and number of neurons in the brainstem structures that interact more closely with the body, which argues that body mass is not a universal determinant of numbers of neurons in the brain (Herculano-Houzel 2017). Similarly, there is only a modest increase in numbers of motor neurons with increasing body mass across both primate and marsupial species, which led to the proposition that larger bodies might allow the survival of larger numbers of neurons during development, rather than require a larger number of neurons to operate larger bodies (Watson et al. 2012).

An alternative view is that, as larger bodies take longer to mature and this delays sexual reproduction, there may have been more selection pressure in larger mammals for those cognitive brain functions that increase life expectancy, thus leading to larger brains (see Allman et al. 1993). In support of this premise, domestic mammals generally have proportionately smaller brains than their wild ancestors (Kruska 2007), suggesting that they have been spared the need for some of the brain functions related to finding food and mates, and avoiding danger. It remains possible, however, that the effect of domestication on the relative size of the brain is rather an indirect consequence of increased body mass, exactly because of the increased abundance of food that comes with domestication.

Overall, there is experimental support for the view that absolute brain sizes across mammalian species is related to abilities we associate with intelligence (Byrne and Corp 2004; Dunbar 1998; Barrickman et al. 2008; Deaner et al. 2007; Lefebvre et al. 2004; MacLean et al. 2014). Another possible reason why larger mammals evolve

UNCORRECTED PROOF

with larger brains is that, compared to the small early mammals, the metabolic costs of a larger brain can be more easily met by a larger body (Herculano-Houzel 2015). There is also evidence for development constrains on how brain parts enlarge as brains get bigger, so that the increases in neocortex is greater than other parts of the brain (Finlay and Darlington 1995). These authors suggest that adaptive pressure for an increase in any part of the brain would provoke a coordinated enlargement of other parts of the brain as well. However, there is also clear evidence that adaptive increases in specific sensory representations occur without coordinated increases in other sensory representations (e.g., Krubitzer et al. 2011, 1995; Collins et al. 2005), which is referred to as "mosaic evolution" in contrast to the "concerted evolution" view that all brain structures scale together (Barton and Harvey 2000).

It is in this context that the size of the human brain seems at odds with the size of the human body: human brains vary around 1400 g, nearly three times that of male gorillas, while our body size of around 70 kg is considerably less. Our early Australopithecus ancestors had brains the size of present day chimps. About 2 million years ago (mya), hominids from *Homo habilis* to *Homo erectus* to archaic *Homo sapiens* had increasingly larger brains, showing an overall increase of about three times until reaching modern levels. Although the large size of the human brain relative to the human body was long hailed as the main explanation for our cognitive superiority (Jerison 1973), a simple alternative is that great apes, whose relative brain size is much smaller than that of other primates, cannot afford enough energy to support the larger numbers of neurons (and therefore the larger brains) that they would be expected to have. This metabolic constraint, which must have already applied to our last shared ancestors, was possibly lifted in the human lineage with the advent of tools for modifying foods, that is, cooking (Fonseca-Azevedo and Herculano-Houzel 2012; Herculano-Houzel 2016). Once the constraint that continues to apply to other primates was lifted, the human brain, and it alone amongst primates, quickly evolved to its modern size, with more neurons than any other primate brain.

Yet, brain size clearly is not everything. Brain size in normally functioning humans varies considerably, (Mc Henry 1994; Azevedo et al. 2009). Human females tend to have both smaller bodies and smaller brains than males, while modern academic records suggest that their brains function at least as well as in males, despite long held assumptions (Gould 1981). More to the point, humans do not have the largest of mammalian brains, and yet dominate the planet. African elephants have 5000 g brains, roughly three times larger than ours, and sperm whales have 9000 g brains that are over six times larger than ours (Herculano-Houzel 2016). Obviously, we need to consider other factors than brain size.

1.1.2 The Importance of Neuron Numbers

It came as a great surprise when it turned out that across mammalian taxa, brains of nearly the same size vary greatly in numbers of neurons (Herculano-Houzel 2016).

UNCORRECTED PROOF

Thus, the 16 g brains of a small monkey has 1.5 billion neurons while the 18 g brain of an agouti, a large rodent, has only 0.9 billion neurons (Herculano-Houzel et al. 2006, 2007). Larger primate brains are composed of proportionately larger numbers of neurons, while rodent brains gain mass faster than they gain neurons; this seems to result from an increase in average neuronal cell size in non-primate species, whereas primate neurons maintain a fairly constant average cell size (Herculano-Houzel et al. 2014a). Thus, primates have an advantage over rodents and other mammals in that the former fit larger numbers of neurons in the brain, and the larger the brain, the larger the numeric advantage of primates – to the point where the human brain has ca. 7 times as many neurons than would be expected in a non primate brain of similar mass (Herculano-Houzel 2009). In primates, neuron packing densities remain fairly constant across brain sizes, while they decrease in rodents and other mammals with brain size – an indication that average neuronal cell size increases with brain size in rodents and other mammals, while remaining the same in primates (Mota and Herculano-Houzel 2014).

Because precise but different relationships between brain mass and numbers of neurons apply for primates and rodents, predictions of number of neurons from brain endocasts in extinct rodents and hominids are possible. Thus, the largest rodent that ever lived, at 700 kg, had a brain just over half the size of a human brain, but presumably with less than one tenth the number of neurons. While brain sizes in *Homo erectus* varied, over one million years of evolution, a 963 g brain would have 63 billion neurons, compared to a modern human brain of 1400 g and 86 billion neurons (Herculano-Houzel and Kaas 2011; Herculano-Houzel 2016). Still the, number of neurons in brains as a whole cannot be the only factor. The larger African elephant brain has three times the number of neurons in a human brain, 257 million against our 86 billion neurons (Herculano-Houzel et al. 2014b). However, 98% of neurons in the African elephant brain are found in the cerebellum, which is even more than the typical 80% of all brain neurons found in the cerebellum of other mammals, primates (and humans) included. The cerebellum and cerebral cortex typically gain neurons in tandem, maintaining a fairly fixed average proportion of four neurons in the cerebellum to every neuron in the cortex (Herculano-Houzel et al. 2014a), and the preponderance of neurons in the cerebellum over the cerebral cortex might be a simple consequence of densely packed very small neurons, the granule cells (Herculano-Houzel 2010). Although the cerebellum has traditionally been assigned important functions in motor predictions and error compensation (Stein and Glickstein 1992; Thach et al. 1992), recent models of brain function acknowledge that cerebellum and cerebral cortex work in conjunction (Leiner et al. 1989; Ramnani 2006). Accordingly, there has been a concerted increase in size of the prefrontal cerebral cortex, in prefrontal inputs to the cortico-pontine system, and in prefrontal-projecting cerebellar lobules in primates (Ramnani et al. 2006; Balsters et al. 2010). Thus, while cognitive and perceptual functions and consciousness are traditionally considered to depend on neocortex (e.g., Delacour 1997), it seems that cerebral cortex and cerebellum operate together, and typically gain neurons together (Herculano-Houzel et al. 2014a). The deviation of the elephant cerebellum from the patterned of coordinated scaling of numbers of neurons in the cerebral cortex and

UNCORRECTED PROOF

cerebellum might be associated with massive addition of supernumerary neurons to the elephant cerebellum that are related not to cerebral cortical processing, but to processing of afferent information from the brainstem, possibly related to the trunk or to infrasound communication (Herculano-Houzel et al. 2014a).

The smaller human cerebral cortex has about three times as many neurons (16 billion compared to 5.6 billion) as the twice larger cerebral cortex of the African elephant (2.8 kg compared to 1.2 kg; Azevedo et al. 2009; Herculano-Houzel et al. 2014a). Because it scales as other primate cortices do, the human cerebral cortex is predicted to have more neurons than the cerebral cortex of even the much larger brains of the largest whales (Herculano-Houzel 2016). It seems safe to presume that humans have the most neurons in the cerebral cortex of any species. Thus, although the cerebral cortex generally gains neurons proportionately with the cerebellum, we have proposed that the large number of neurons in the human cerebral cortex is the simplest correlate of our superior cognitive capabilities.

While the cerebral cortex and cerebellum gain neurons proportionately across most species, both gain neurons faster than the remaining brain areas (Herculano-Houzel et al. 2014a). As proportionally more neurons are found in neocortex over the non-cerebellar rest of brain in larger primate brains, the proportional role that neocortex (together with the cerebellum) has in modulating brain functions, including behavior, increases. Early investigators noted that behavioral impairments were greater in humans than in smaller brained mammals after cortical lesions, and called this the "corticalization of function" (e.g., Brodal 1981). For this reason, the subsequent sections of this paper focus on the cerebral cortex.

1.1.3 Cortical Fissures Are of Limited Significance

The human brain has more of neocortex hidden in fissures than any other primate – although less than larger brains, such as elephant and cetacean brains. For animal researchers and neurosurgeons, fissures are often useful landmarks that indicate roughly where cortical areas of interest are located. Of course, cortical fissures have no brain functions, but their existence could be due to some functional advantage imparted by folding. For example, across the crests of folds on the surface of cortex, the gyri, cortex on both sides of the folds of the gyri is interconnected over shorter pathways, increasing the speed of their interactions (Van Essen 1997). In general, the folding of cortex increases with the size of neocortex both across species and during development. There have been a number of explanations of folding patterns, including both functional and mechanical theories, but we now know that only two physical features of neocortex are necessary to account for over 99% of the variation in the amount of folding. In a study across a large sample of mammalian species, Mota and Herculano-Houzel (2015) convincingly demonstrated that cortical folding scales universally with cortical surface area and cortical thickness. Thin cortex folds more easily than thick cortex, and a large cortical sheet tends to have more folds than a small cortical sheet – but the exact degree of folding depends on the product of

UNCORRECTED PROOF

these two variables. Below a certain size, cortex does not fold. The reason for this universal relationship seems to be that the cortex settles into the most energetically favorable conformation as it develops under push-pull tensions, and the degree of folding that imparts the most favorable conformation depends on the combination of surface area and thickness. Local differences within a same cortex also appear to be related to variation in thickness and local surface area. For example, the part of V1 or striate cortex that represents peripheral vision is thinner in primates than the part that represents central vision, and that is where the fissure in V1 of all primates, the calcarine fissure occurs. Additionally, the overall pattern of local connections within a cortical area, or even between areas, is expected to contribute to local variations in push-pull tension that may determine where the first, and therefore main, folds are placed, and thus influence the spatial pattern of folding. In primary somatosensory cortex, for example, there are few local connections between adjoining representations of the face and hand (e.g., Liao et al. 2016; see Welker 1990; Radinsky 1976). As a result, a narrow cell-poor septal zone exists between the representations where a fissure sometimes emerges. Thus, small differences in histological structure and tangential connections do exit and thus they appear to influence the locations of cortical fissures.

1.1.4 The Importance of the Areal Organization of Neocortex

There are four aspects of neocortical organization that are functionally important as we consider human capabilities: the numbers and kinds of cortical areas, laminar and sub-laminar specialization, modular subdivisions, and connection patterns. We start with cortical areas.

By the time Brodmann (1909) published his well known comparative study of areal organization of neocortex of various mammals, the beginnings of understandings of how the cortical sheet is divided into numbers of functionally distinct regions or areas was well underway. For Brodmann, cortical areas were the "organs of the brain", functionally specialized patches of cortex that were specialized like the heart, liver, and lungs of the body. The basic premise of his investigations was that functional specializations are reflected in anatomical specializations, including the ways neurons were arranged and packed into layers and sub-layers of cortex. Differences in the laminar appearance led to the identification of just over 50 proposed areas of the human brain, some of which are well supported, such as area 17 for primary visual cortex, and area 3b for primary somatosensory cortex. But even these areas were not consistently identified across species by Brodmann (1909), largely because laminar differences are not very pronounced for many areas, and for especially some species. Currently, cortical areas are most reliably identified by multiple criteria, including various histological features, patterns of connections, and the physiological properties of neurons. Sometimes, alterations in behavior after the deactivation or lesions of an area provide findings that suggest the main functions of an area, as do behaviors influenced by electrical stimulation of neurons

UNCORRECTED PROOF

in an area. Often, the functions of an area are not totally apparent, as areas are parts of networks of areas and nuclei that function together. More abstractly, one can say that the function of an area is to transform inputs into altered outputs. Thus, revealing this process tells the function or functions (as areas have several types of outputs) of an area. The most easily identified areas are those that systematically represent a sensory surface, the retina, skin or cochlea, or provide a systematic body movement map when micro-stimulated throughout. In general, portrayals of full sets of cortical areas for any mammal are estimates largely based on architectonic evidence, supplemented by various amounts of supportive evidence.

Although the exact numbers of cortical areas in any mammal remain uncertain, major species differences are obvious. Current estimates of the number of cortical areas in the human cortex (one hemisphere) vary (e.g. Kaas 2006), and the most recent estimate is 180 (Glasser et al. 2016). All estimates put the human brain well over the estimates for other primates, and probably all other mammals, including elephants and whales with more neocortex. This is obviously uncertain, given the limited studies on neocortex of most mammals. However, there is great evidence that primate brains with more cortex have more functional areas, while such differences with more cortex appear to be less marked in rodent and brains (Krubitzer et al. 2011; Kaas and Preuss 2014). Early mammals likely had about 20 cortical areas (Kaas 2007), while early primates had nearly 50 areas (Wong and Kaas 2010).

The sizes of cortical areas are typically larger in mammals with more neocortex, which restricts the potential increase in number of areas. Thus, primary visual cortex, V1 or area 17, is only about 4.5 mm^2 in a mouse, but 1200 mm^2 in a macaque monkey, and perhaps 3000 mm^2 in a human (Kaas 2000). However, a chimpanzee has an area 17 of about the same size as in human, although the cortical sheet is over three times as large in a human. As the retinotopic map in V1 contains the information used to locate and identify objects in space, this map is obviously very crude in a mouse, and very precise in a human, although not notably different than in a chimpanzee. This observation suggests that a further increase in the map size in humans would not be that useful, as the resolution limit is set by the eye. However, V1 in humans, as in other primates, has a modular organization that allows an increase in functions that cannot be afforded a mouse. A much smaller V1 than that in a mouse would no longer be capable of retaining an image (Cooper et al. 1993).

The main advantage that comes with increasing the number of cortical areas is that serial processing can produce fantastic outcomes out of a number of simple computational iterations. Each cortical area modifies inputs to create different outputs, but the transformations may be rather slight. It is the number of transformations across numbers of cortical areas that produce astonishing outcomes, and it is the creation of multiple processing networks made possible by large number of cortical areas that makes multiple outcomes possible (Pinker 1997).

UNCORRECTED PROOF

1.1.5 The Importance of Laminar, Sub-laminar, and the Cellular Organization of Neocortex

The neocortex of mammals evolved out of the therapsid cortex, which presumably was something like the dorsal cortex of modern non-avian reptiles (Kaas and Preuss 2014; Kaas 2017). The basics of laminar and cellular organization are similar across most mammals. Like the dorsal cortex of modern non-avian reptiles and possibly of early amniotes, neurons in neocortex consist of pyramidal neurons and star-shaped inhibitory neurons, although some excitatory pyramidal neurons have become modified by losing their apical dendrite and becoming star-shaped stellate or granule cells (Fournier et al. 2015). Instead of having a single row of pyramidal cells as in dorsal cortex, the thicker neocortex is packed with many neurons that are traditionally divided into six layers, and variously into sub-layers. Layer 1 resembles the superficial layer of axons and dendrites in the dorsal cortex of reptiles in that it continues to get widespread axons from subcortical neurons that connect the apical dendrites of many deeper pyramidal cells with a weak, modulating influence. In primary sensory areas, layer 4 is the new target of activating sensory inputs from the dorsal thalamus. Layer 4 is characterized by excitatory stellate neurons or even smaller granular neurons that are often densely packed. Higher order sensory and other areas receive activating inputs from primary sensory areas or earlier areas in processing hierarchies (Felleman and Van Essen 1991). Layer 3 provides feed-forward projections to other cortical areas, while layer 6 provides feedback connections to the thalamus or to other cortical areas. Layer 5 provides most of the projection to subcortical structures in the thalamus, basal ganglia, midbrain, brainstem, and spinal cord. These different connections and functional roles result in various laminar and sub-laminar specializations of neurons (Kaas 2010).

A major type of specialization is in neuron size. Small neurons, especially the tiny granular neurons of layer 4 in primary sensory areas, have small dendritic arbors, and are activated by dense synaptic inputs by only a few axons of thalamic or cortical neurons. Thus, layer 4 neurons sum only a few "driving" inputs, and their response properties clearly reflect those of these inputs. Put in another way, layer 4 neurons largely preserve rather than integrate information. In contrast, the large pyramidal neurons of layer 5 have large dendritic arbors and sum the inputs of many axons. Their outputs do not clearly reflect individual inputs, but rather the computational result of many inputs from other areas and subcortical sources, other layers, and local layer 5 influences. Smaller pyramidal neurons likely reflect aspects of these two roles of preserving information, or integrating it, as the result of the summing process to produce an altered output. Thus, different functional roles of cortical layers are reflected in the sizes of neurons in those layers. The smallest neurons are in layer 4, which preserves information for distributions locally to neurons vertically aligned above and below the layer 4 neurons. Layer 3 neurons include the smaller pyramidal neurons that integrate limited local inputs in various ways to provide altered outputs to other cortical areas. Layer 6 neurons integrate local influences with some direct feedforward inputs to provide feedback to the

UNCORRECTED PROOF

input to the thalamic nucleus or cortical area that provides the feedforward input. These anatomical features of neurons in layers and sublayers of cortex are more pronounced in some cortical areas and in some mammals than others, as part of the great diversity of cortical organization that is associated with variations in cortical function. In general, small brained mammals with short life spans have less pronounced laminar and areal specialization, and laminar and areal features are less distinct. As a result, identification of cortical areas in such mammals on the basis of cytoarchitecture can be difficult. With fewer cortical areas and fewer neurons, areas and neurons in these mammals must have general purpose functions and not be anatomically specialized. In mammals with larger brains and more cortical areas, more pronounced specializations of individual neurons may occur sometimes in the same layer. For example, a few very large pyramidal neurons of layer 5 of primary visual cortex of primates are more widely spaced than the adjoining smaller layer 5 pyramidal neurons. These larger neurons sum more inputs as reflected by their larger receptive fields, and they project to visual area MT, part of the visual pulvinar, and the superior colliculus (Fries et al. 1985). Thus, neurons may have different anatomical and functional roles within a cortical layer, and this is another variable across species.

If one considers the differences in neuron packing densities across the cortical sheet, they vary across functional areas in the brains of mice (Herculano-Houzel et al. 2013), and perhaps more so in primates, and especially in primates with more cortex (Collins et al. 2016: Turner et al. 2016; Young et al. 2013). As expected from histological appearance, primary visual cortex (V1, area 17) has neuron packing densities two to four times higher than most cortical areas. This is mainly due to the dense packing of the very small granule neurons in layer 4 (Brodmann 1909), although layer 3 has smaller pyramidal cells that are more densely packed than other cortical areas. The high density of small neurons with small dendritic arbors in V1 the largest of cortical areas in primates is the anatomical framework for an extremely detailed retinotopic map of the visual hemifield. It also allows for the creation of five distinctly different parallel projections from V1 to other visual areas (see following section). It is not known yet if the V1 representation in humans is much different from that in chimpanzees, but the sub-laminar organization of V1 has laminar specializations that may promote detection of visual motion in dim light or other functions (Preuss et al. 1999; Preuss and Coleman 2002).

In addition to V1, areas V2 and V3, and adjacent visual areas also have high neuron packing densities in primates, and this is especially the case in chimpanzees and likely humans. High densities also occur in primary somatosensory cortex, area 3b, and primary auditory cortex. Another region of high packing densities is in dorsomedial prefrontal cortex, a region important in working memory (Goldman-Rakic 1996). The smaller neurons with smaller dendritic fields that reflect this packing density may be important for retaining the details of the retained information. Only primates have a region of frontal granular cortex (Preuss 1995), and we recently found that neuronal densities in frontal cortical areas can be as high as in occipital cortex (Gabi et al. 2016). Other neurons in prefrontal cortex, the layer 3 pyramidal neurons, may have large dendritic arbors comparable with many synaptic inputs

UNCORRECTED PROOF

and proposed executive functions (Elston et al. 2006). As expected, primary motor cortex (M1) and premotor cortex (PM) areas with a very thin or unclear layer 4 (agranular and dysgranular cortex) have large neurons with large dendritic arbors that both sum larger amounts of information, but also have large axons to conduct outputs rapidly to the brainstem and spinal cords. Motor and premotor cortex have larger neurons of lower packing density in primates (Young et al. 2013).

One of the benefits of having a large brain, with a large number of neurons and cortical areas, is that all neurons and areas do not need to have general purpose or broad range functions. This allows some areas and neurons to specialize morphologically and functionally. The study of these specializations in the early stages of development, but relevant observations are accumulating. As an interesting example, spindle cells, named for their spindle shaped cell bodies, are found in anterior cingulate cortex and the anterior insular of human brains (Nimchinsky et al. 1999). Fewer numbers of these neurons, also called von Economo cells, have been found in chimpanzees. There have been various speculations about the functions of spindle cells (see Allman et al. 2005), but functional studies of the cellular level have not been possible. Other differences in the distributions of neuron cell types that favor human brains have been described elsewhere (Spocter et al. 2015: Casanova and Opris 2015).

1.1.6 The Roles of Cortical Columns, Modules, and Domains

Cortical areas have functional subdivisions, in addition to layers and sublayers that have been variously identified as mini-columns, columns, modules, and domains (Kaas 2012; Kaas and Balaram 2015). One of the universal features of neocortex is that narrow, vertical arrays of neurons from surface to white matter are highly interconnected. As a consequence of these restricted vertical connections, the responses of all neurons within the array reflect the information that is sent to layer 4 neurons (or layer 3 in the absence of layer 4), although this information is modified differently in the layers and sublayers. The arrays of the densely interconnected neurons, on the order of 30–50 μm in diameter, are called minicolumns (Mountcastle 1957; Opris et al. 2015). They are sometimes clearly separated from each other by neuropil, and they can be expected to be larger in portions of cortex with larger neurons.

Human minicolumns in many parts of cortex appear to be larger, with more neurons and neuropil, than in other primates (Buxhoeveden et al. 2001; Spocter et al. 2015). In addition, minicolumns are expected to be specialized in different ways, according to the laminar and connectional specializations of cortical areas. The larger cortical sheets of humans provide an advantage in having more minicolumns, and having more functional types of minicolumns.

The classical columns of Mountcastle (1957) are another feature of neocortex that is probably universal. Classical columns of two or more types subdivide areas with repeating sets of modules that have neurons with distinctly different response

UNCORRECTED PROOF

properties (see Kaas 2012 for examples). In effect, they allow individual cortical areas to have patchworks of neurons of two or more related, but different functions. For example, the cytochrome oxidase blob and non-blob modules of primary visual cortex of primates divide V1 into regions that process inputs to extract stimulus orientation or color and brightness (Livingstone and Hubel 1988). In a similar manner, cytochrome oxidase dense bands of two types divided by cytochrome oxidase light bands of two types from repeating sets of four different classes of modules in V2 of anthropoid primates, allowing V2 to function as four closely interacting areas (Felleman et al. 2015). The advantage of the human brain with a V2 at least as large as in chimpanzees is that the human V2 has as many or more sets of these modules as any other primate. As many or most cortical areas, especially the larger ones, likely have some type of modular organization that subdivides their functions, and humans have more cortical areas, and some of the largest of cortical area, the subdivision of areas into modules of differing functions likely has the greatest impact in human brains.

Another type of cortical subdivision is one we called domains (Kaas 2012; Kaas and Stepniewska 2016). Domains are functional subdivisions of cortex that are larger and more complex than columns, but still parts of areas. They have many of the characteristics of areas, and can easily be confused with them. Likely, arrangements of columns within an area evolve sometimes into domains, and domains into areas. There has not been much effort to distinguish domains from areas, but the clearest example is in primary motor cortex of primates. M1 has long been recognized as a single area, as it forms a single, crude representation of the movements of parts of the contralateral half of the body. Stimulating with a brief sequence of electrical pulses via microelectrodes at near threshold values evokes different movements from toes to trunk to fingers to face and then tongue in a medial to lateral sequence across M1. However, at a local level, adjacent stimulation sites after evoke different movements, with a site for a wrist movement next to a site for a finger movement for example, and finger, wrist, and arm movement sites repeated and mixed with each other. Thus, M1 has a “mosaic” or “fractured” internal organization of mixed micro-columns rather than a faithful somatotopic map of body parts (see Gould et al. 1986 for early evidence). At a larger scale, a number of these differing micro columns form a larger unit that mediates a specific behavior, such as reaching, grasping, threating, defending, or running. These functional domains were first studied systematically by Graziano and coworkers (see Graziano 2009). The exact number of domains is not yet clear, but for most or all primates it is likely eight or more. Our studies indicate that these M1 domains exist in a wide range of primate species, and there is evidence for them in human M1 (Desmurget et al. 2014), and for a smaller number in rodents (e.g. Brown and Teskey 2014). The main conclusion is that M1 is subdivided with a small number of domains for different behaviorally relevant complex movement. As parts of M1, the domains interact, in often a competitive way, but also cooperate to create more complex movements such as reaching to grasp and retrieve food to the mouth. Thus, M1 is subdivided into domains that mediate different movement goals.

UNCORRECTED PROOF

Matching domains in terms of evoked behaviors are found in premotor cortex (PMC) and in a part of posterior parietal cortex. Depending on the types of movements, domains are either in ventral premotor cortex or dorsal premotor cortex, suggesting that these two "areas" might between considered to be a single area. Likewise, the domains and associated cortex in a portion of posterior parietal cortex, such as previously defined anterior, posterior and medial intraparietal areas (AIP, LIP, and MIP), might be considered as functional divisions within a single area for grasping, looking, reaching, and other behaviors (Kaas and Stepniewska 2016).

The sequence of the three processing stations of posterior parietal cortex (PPC), premotor cortex, and M1 are all parts of a so called dorsal stream of sensorimotor processing (see Ungerleider and Haxby 1994; Goodale and Milner 1992). The domains at all three levels are involved in a decision process that results in a specific type of action over others. As the inputs to PPC are mainly from higher-order sensory areas, mostly visual and somatosensory, and variable across domains, the dominance of one domain over others depends on the mixture and content of ongoing perception. At the next level, premotor cortex domains are under the influence of inputs from the motor thalamus, other motor areas, and prefrontal cortex, so the dominance in the array of the motor domains may change from that in PPC. Likewise, M1 domains are under a different set of thalamic and cortical influences, and the final outcome will largely depend on domain selection process in M1 (Kaas and Stepniewska 2016). Of course, the dominant domain in PPC would selectively activate the functionally matched domains in PMC and M1, and the dominant domain in PMC would selectively activate the matching domain M1.

In the non-primate relatives of primates, rodents and tree shrews, M1 appears to have only a few action specific domains (Baldwin et al. 2016), premotor cortex is poorly developed, and there is little cortex that could be considered to be posterior parietal cortex. Thus, M1 outputs depend on more direct sensory and other inputs. As a result, primates have the advantage over these non-primates of having a large region of PPC where at least eight sub-regions or domains are specialized for specific behaviors, and other parts of posterior parietal cortex are large and participate in further levels of processing sensory information. Additionally, more motor and premotor cortex domains exist, and especially premotor cortex is more developed. All these motor regions are larger in human brains, and posterior parietal cortex is larger in proportion to the rest of cortex (Hill et al. 2010). Most importantly for human brains, additional domains have evolved within the domain structure of PPC. Thus, the contribution of auditory input to the dorsal stream of sensorimotor processing in PPC of primates has resulted in the differentiation of a language production module as domain in PPC of humans (Rauchecker and Scott 2009; Tremblay and Dick 2016). There is also evidence that the domain for grasping and manipulation of PPC in primates has enlarged and differentiated into regions for specialized for tool use in humans (Frey 2008).

UNCORRECTED PROOF

1.1.7 Cortical Asymmetries and the Human Brain

Mammalian brains have two hemispheres that are highly symmetrical in organization. Thus, cortex of the right cerebral hemisphere represents the sensory inputs of the left body surface and the left visual hemifield, and the left ear is more dominant, while motor outputs of the right hemisphere largely control the muscles of the left side of the body. The left hemisphere mirrors this organization. Overall, this appears to be a bad design. As brains get bigger, the connecting axons between the hemispheres get longer, and distance is time in the nervous system. The innovation of the corpus callosum with the advent of placental mammals shortened this pathway and the conduction times, but not enough. The usual way of reducing conduction times is to increase the diameters of axons (Kaas 2000). However, this can be costly in that long, thick axons tend to bulk up the brain so much that after a certain size, one greater than for the brains of present day mammals, a theoretical limit is reached that means that nothing computationally is gained by a further increase in brain size (Cherniak 1990). Another advantage of thick axons is that they are capable of maintaining higher firing rates, and thus a greater rate information transfer (Perge et al. 2012). Yet, the corpus callosum has few large diameter axons, presumably due to space constraints. In macaque monkeys, the largest 15% of axons in the corpus callosum occupies more than half of the cross-sectional area of the callosum. In humans, the corpus callosum has about 300 million axons, most of them small and slowly conducting. Across primates with different sizes of brains, the conduction times for the fastest neurons with the largest axons increases with brain size, indicating that the compensation for the larger conduction distances is not complete (Phillips et al. 2015; Caminiti et al. 2009). There is practically no change in axon diameter in the corpus callosum between humans and chimpanzees with much smaller brains. The large, fast axons connect sensory and motor areas, where the speed of transmission is likely to be the most critical, but the human brain also compensates by having important functions mediated within a single hemisphere (Ringo et al. 1994). Thus, much of language is mediated in the left hemisphere, and manual motor skills are most frequently more effectively mediated in the left hemisphere. While there are functional and structural differences between the two hemispheres in apes, they are much more prominent in humans, where marked cognitive differences in the abilities of the two hemispheres have been revealed in patients with section of the corpus callosum, or with lesions of one hemisphere or the other (e.g. Gazzaniga 2000). Primate brains, and especially larger primate brains, have reduced the need for corpus callosum connections by eliminating the connections from parts of primary somatosensory cortex (area 3b) and most of primary visual cortex (Cusick and Kaas 1986; Doty 2007). Larger primate cortices have a decreasing fraction of their neurons connected through the white matter, with an increasing fraction of their neurons connected within the gray matter (Herculano-Houzel et al. 2010); in contrast, the fraction of neurons connected through the white matter remains constant across rodent species (Ventura-Antunes et al. 2013). The decrease in proportion of long-range connections probably contributes to keeping

UNCORRECTED PROOF

primate cortices small as they gain neurons, compared to non-primate cortices. But the evolution of hemispheric specializations for human mental functions removed some of the constraints of the need to closely tie the two hemispheres, and allowed human brains to expand by three times, while having colossal connections much like those of a chimpanzee. The major cognitive role of the left hemisphere in humans as the interpreter of one's behavior (Gazzaniga 2000) allows the speaking left hemisphere to feel quite normal in split-brain patients.

1.1.8 The Corticalization of Function

The "corticalization of function" refers to an old concept in neurobiology that reflects the common observation that cortical lesions that appear to be functionally equivalent in humans and other mammals, especially those with small brains, have much greater functional impact in humans (Brodal 1981). Most notably, lesions of the motor cortex in non-primate mammals often did not cause lasting behavioral deficits (Creutzfeldt 1993).

While interpretations of ablation behavioral results across species has been complex and difficult, a "corticalization of function" may in large part be the consequence of the great increase in cortical neurons in comparison with subcortical neurons as cortex disproportionately expands relative to the brain stem and spinal cord with increases in brain size, especially in primates, but also in other mammals. Thus, in a study of primate species, Herculano-Houzel et al. (2016) describe a "cortical takeover of spinal motor control with increasing brain size in primates". These authors propose that cortical and non-cortical motor projections to the spinal cord compete for functional connections on the bases of activity and relative numbers of inputs, so that as cortical inputs become more and more dominant, their loss has more and more impact. Similar consequences likely follow the great increases in numbers of cortical neurons and their descending projections of other cortical areas as a consequence of increasing brain size. Thus, across primates of different brain sizes, primary auditory cortex gains neurons faster than subcortical auditory structures (Wong et al. 2013). This results in proportionately more cortical feedback to subcortical auditory and other structures in primates with bigger brains, increasing the functional dominance of cortex. Similar findings were reported for visual cortex, where primary visual cortex, V1, gains neurons with brain size faster than the superior colliculus and the dorsal lateral geniculate nucleus (Collins et al. 2013). These results suggest that with increasing brain size, and numbers of V1 neurons, V1 gains more control over the sensory and motor functions of the superior colliculus, and more dominating feedback modulation of the lateral geniculate neurons projecting to V1. Faster scaling of cortical than non-cortical neurons for all or nearly all cortical areas is expected, given the results and the finding that cortex overall increases in neuron number with brain size faster than the subcortical brainstem and spinal cord. Thus, the corticalization of function should

UNCORRECTED PROOF

occur for nearly all cortical areas across taxa with increases in brain size, especially in primates, and corticalization of function should be most pronounced in humans.

References

Allman J, McLaughlin T, Hakeem A (1993) Brain weight and life-span in primate species. Proc Natl Acad Sci U S A 90:118–122

Allman JM, Watson KK, Tetreault NA, Hakeem AY (2005) Intuition and autism: a possible role for Von Economo neurons. Trends Cogn Sci 9:367–373

Azevedo FAC, Carvalho LRB, Grinberg LT, Farfel JM, Ferretti REL, Leite REP, Jacob Filho W, Lent R, Herculano-Houzel S (2009) Equal numbers of neuronal and nonneuronal cells make the human brain an isometrically scaled-up primate brain. J Comp Neurol 513:532–541

Balsters JH, Cussans E, Diedrichsen J, Phillips JK, Ramnani N (2010) Evolution of the cerebellar cortex: the selective expansion of prefrontal-projecting cerebellar lobules. NeuroImage 49:2045–2052

Baldwin MKL, Cooke DF, Krubitzer L (2016) Intracortical microstimulation maps of motor, somatosensory, and posterior parietal cortex in tree shrews (tupaia belangeri) reveal complex movement representations. Cereb Cortex 27:1439–1456

Barrickman NL, Bastian ML, Isler K, Van Schaik CP (2008) Life history costs andbenefits of encephalization: a comparative test using data from long-term studies of primates in the wild. J Hum Evol 54:568–590

Barton RA, Harvey PH (2000) Mosaic evolution of brain struture in mammals. Nature 405: 1055–1058

Brodal A (1981) Neurological anatomy, 3rd edn. Oxford University Press, Oxford

Brodmann K (1909) Vergleichende lokalisationslehre der grosshirnride. Barth, Leipzig

Brown AR, Teskey GC (2014) Motor cortex is functionally organized as a set of spatially distinct representations for complex movements. J Neurosci 34:13574–13585

Buxhoeveden DP, Switala AE, Roy E, Litaker M, Casanova MF (2001) Morphological differences between minicolumns in human and nonhuman primate cortex. Am J Phys Anthropol 115:361–371

Byrne RW, Corp N (2004) Neocortex size predicts deception rate in primates. Proc R Soc Lond B 271:1693–1699

Caminiti R, Ghaziri H, Galuske R, Hof PR, Innocenti GM (2009) Evolution amplified processing with temporally dispersed slow neuronal connectivity in primates. Proc Natl Acad Sci U S A 106:19551–19556

Casanova MF, Opris I (2015) Recent advances in the modular organization of the cortex. Springer, New York

Cherniak C (1990) The bounded brain: toward quantitative neuroanatomy. J Cogn Neurosci 2: 58–68

Collins CE, Hendrickson A, Kaas JH (2005) Overview of the visual system of Tarsius. Anat Rec 287A:1013–1025

Collins CE, Leitch DB, Wong P, Kaas JH, Herculano-Houzel S (2013) Faster scaling of visual neurons in cortical areas relative to subcortical structures in primate brains. Brain Struct Funct 218:805–816

Collins CE, Turner EC, Sawyer EK, Reed JL, Young NA, Flaherty DK, Kaas JH (2016) Cortical cell and neuron density estimates in one chimpanzee hemisphere. Proc Natl Acad Sci U S A 113:740–745

Cooper HM, Herbin M, Nevo E (1993) Visual system of a naturally microphthalmic mammal: the blind mole rat, Spalax ehrenbergi. J Comp Neurol 328:313–350

Creutzfeldt OD (1993) Cortex Cerebri English edition. Hubent and Co., Gottingen

UNCORRECTED PROOF

Cusick CG, Kaas JH (1986) Interhemispheric connections of cortical sensory and motor maps in primates. In: Lepore F, Ptito M, Jasper HH (eds) Two hemispheres- one brain. Alan R Liss, New York, pp 83–102
Deaner RO, Isler K, Burkart J, van Schaik C (2007) Overall brain size, and not encephalization quotient, best predicts cognitive ability across non-human primates. Brain Behav Evol 70:115–124
Delacour J (1997) Neurobiology of consciousness: an overview. Behav Brain Res 85:127–141
Desmurget M, Richard N, Harquel S, Baraduc P, Szathmari A, Mottolese C, Sirigu A (2014) Neural representations of ethologically relevant hand/mouth synergies in the human precentral gyrus. Proc Natl Acad Sci U S A 111:5718–5722
Doty RW (2007) Cortical commissural connections in primates. In: Kaas JH, Preuss TM (eds) Evolution of nervous systems, vol 4. Primates. Elsevier, London, pp 277–279
Dunbar RIM (1998) The social brain hypothesis. Evol Anthropl 6:178–190
Elston GN, Benavides-Piccione R, Elston A, Zietsch B, Defelipe J, Manger P, Casagrande V, Kaas JH (2006) Specializations of the granular prefrontal cortex of primates: implications for cognitive processing. Anat Rec A Discov Mol Cell Evol Biol 288A:26–35
Fan S, Hansen ME, Lo Y, Tishkoff SA (2016) Going global by adapting local: a review of recent human adaptation. Science 354:54–59
Felleman DJ, Van Essen DC (1991) Distributed hierarchical processing in the primate cerebral cortex. Cereb Cortex 1:1–47
Felleman DJ, Lim H, Xiao Y, Wang Y, Eriksson A, Parajuli A (2015) The representation of orientation in macaque V2: four stripes not three. Cereb Cortex 25:2354–2369
Finlay BL, Darlington RB (1995) Linked regularities in the development and evolution of mammalian brains. Science 268:1578–1584
Fonseca-Azevedo K, Herculano-Houzel S (2012) Metabolic constraint imposes tradeoff between body size and number of brain neurons in human evolution. Proc Natl Acad Sci U S A 109:18571–18576
Fournier J, Muller CM, Laurent G (2015) Looking for the roots of cortical sensory computation in three-layered cortex. Current Opin Neurobiol 3l:119–126
Frey SH (2008) Tool use, communicative gesture and cerebral asymmetries in the modern human brain. Philos Trans R Soc Lond Ser B Biol Sci 363:1951–1957
Fries W, Keizer K, Kuypers HG (1985) Large layer VI cells in macaque striate cortex (Meynert cells) project to both superior colliculus and prestriate visual area V5. Exp Brain Res 58:613–616
Gabi M, Neves K, Masseron C, Ribeiro PFM, Ventura-Antunes L, Torres L, Mota B, Kaas JH, Herculano-Houzel S (2016) No relative expansion of the number of prefrontal neurons in primate and human evolution. Proc Natl Acad Sci U S A 113:9617–9622
Gazzaniga MS (2000) Cerebral specialization and interhemispheric communication: does the corpus callosum enable the human condition? Brain 123(Pt 7):1293–1326
Glasser MF, Coalson TS, Robinson EC, Hacker CD, Harwell J, Yacoub E, Ugurbil K, Andersson J, Beckmann CF, Jenkinson M, Smith SM, Van Essen DC (2016) A multi-modal parcellation of human cerebral cortex. Nature 536:171–178
Goldman-Rakic PS (1996) Regional and cellular fractionation of working memory. Proc Natl Acad Sci U S A 93:13473–13480
Goodale MA, Milner AD (1992) Separate visual pathways for perception and action. Trends Neurosci 15:20–25
Gould HJ, Cusick CG, Pons TP, Kaas JH (1986) The relationship of corpus callosum connections to electrical stimulation maps of motor, supplementary motor, and the frontal eye fields in owl monkeys. J Comp Neurol 247(3):297–325
Gould SJ (1981) Mismeasure of man. Norton, New York
Graziano MS (2009) The intelligent movement machine. Oxford University Press, New York
Herculano-Houzel S (2009) The human brain in numbers: a linearly scaled-up primate brain. Front Hum Neurosci 3:31

UNCORRECTED PROOF

Herculano-Houzel S (2015) Decreasing sleep requirement with increasing numbers of neurons as a driver for bigger brains and bodies in mammalian evolution. Proc R Soc B 282:20151853
Herculano-Houzel S (2016) The human advantage. MIT Press, Cambridge
Herculano-Houzel S (2017) Numbers of neurons as biological correlates of cognitive capability. Curr Opin Behav Sci 16:1–7
Herculano-Houzel S, Mota B, Lent R (2006) Cellular scaling rules for rodent brains. Proc Natl Acad Sci U S A 103:12138–12143
Herculano-Houzel S, Collins CE, Wong P, Kaas JH (2007) Cellular scaling rules for primate brains. Proc Natl Acad Sci U S A 104:3562–3567
Herculano-Houzel S (2010) Coordinated scaling of cortical and cerebellar numbers of neurons. Front Neuroanat 4:12. https://doi.org/10.3389/fnana.2010.00012
Herculano-Houzel S, Mota B, Wong P, Kaas JH (2010) Connectivity-driven white matter scaling and folding in primate cerebral cortex. Proc Natl Acad Sci U S A 107:19008–19013
Herculano-Houzel S, Watson C, Paxinos G (2013) Distribution of neurons in functional areas of the mouse cerebral cortex reveals quantitatively different cortical zones. Front Neuroanat 7:35
Herculano-Houzel S, Manger PR, Kaas JH (2014a) Brain scaling in mammalian evolution as a consequence of concerted and mosaic changes in numbers of neurons and average neuronal cell size. Front Neuroanat 8:77
Herculano-Houzel S, Avelino-de-Souza K, Neves K, Porfírio J, Messeder D, Feijó LM, Maldonado J, Manger PR (2014b) The elephant brain in numbers. Front Neuroanat 8:46
Herculano-Houzel S, Kaas JH, de Oliveira-Souza R (2016) Corticalization of motor control in humans is a consequence of brain scaling in primate evolution. J Comp Neurol 524:448–455
Hill J, Inder T, Neil J, Dierker D, Harwell J, Van Essen D (2010) Similar patterns of cortical expansion during human development and evolution. Proc Natl Acad Sci U S A 107: 13135–13140
Jerison H (1973) Evolution of the brain and intelligence. Academic, New York
Kaas JH (2000) Why brain size is so important: design problems and solutions as neocortex gets bigger or smaller. Brain Mind 1:7–23
Kaas JH (2006) Evolution of the neocortex. Curr Biol 16:R910–R914
Kaas JH (2007) Reconstructing the organization of neocortex of the first mammals and subsequent modifications. In: Kaas JH, Krubitzer LA (eds) Evolution of nervous systems, vol. 3, mammals. Elsevier, London, pp 27–48
Kaas JH (2012) Evolution of columns, modules, and domains in the neocortex of primates. Proc Natl Acad Sci U S A 109(Suppl 1):10655–10660
Kaas JH, Preuss TM (2014) Human brain evolution In: Fundamental neuroscience, 4th ed., Larry R Squire (ed), Elsevier, London, pp 901–918
Kaas JH, Balaram P (2015) The types of functional and structural subdivisions of cortical areas. In: Casanova MF, Opris I (eds) Recent advances on the modular organization of the Cortex. Springer, New York, pp 35–62. https://doi.org/10.1007/978-94-37-9900-3_4
Kaas JH, Stepniewska I (2016) Evolution of posterior parietal cortex and parietal-frontal networks for specific actions in primates. J Comp Neurol 524:595–608
Kaas JH (2017) The organization of neocortex in early mammals. In: Herculano-Houzel S (ed) Evolution of nervous systems, Mammals, vol 2, 2nd edn. Elsevier, London, pp 87–101
Krubitzer L, Campi KL, Cooke DF (2011) All rodents are not the same: a modern synthesis of cortical organization. Brain Behav Evol 78:51–93
Krubitzer L, Manger P, Pettigrew J, Calford M (1995) Organization of somatosensory cortex in monotremes: in search of the prototypical plan. J Comp Neurol 351:261–306
Kruska DCT (2007) The effects of domestication on brain size. In: Kaas JH, Krubitzer LA (eds) Evolution of nervous systems, Mammals, vol 3. Elsevier, London, pp 143–153
Lefebvre L, Reader SM, Sol D (2004) Brains, innovations and evolution in birds and primates. Brain Behav Evol 63:233–246
Leiner HC, Leiner A, Dow RS (1989) Reappraising the cerebellum: what does the hindbrain contribute to the forebrain? Behav Neurosci 103:998–1008

UNCORRECTED PROOF

Liao CC, Reed JL, Kaas JH, Qi HX (2016) Intracortical connections are altered after long-standing deprivation of dorsal column inputs in the hand region of area 3b in squirrel monkeys. J Comp Neurol 524:1494–1526

Livingstone M, Hubel D (1988) Segregation of form, color, movement, and depth: anatomy, physiology, and perception. Science 240:740–749

MacLean EL et al (2014) The evolution of self-control. Proc Natl Acad Sci U S A 111:E2141–E2148

McHenry HM (1994) Tempo and mode in human evolution. Proc Natl Acad Sci U S A 91:6780–6786

Mota B, Herculano-Houzel S (2014) All brains are made of this: a fundamental building block of brain matter with matching neuronal and glial masses. Front Neuroanat 8:127

Mota B, Herculano-Houzel S (2015) Cortical folding scales universally with surface area and thickness, not number of neurons. Science 349:74–77

Mountcastle VB (1957) Modality and topographic properties of single neurons of cat's somatic sensory cortex. J Neurophysiol 20:408–434

Nimchinsky EA, Gilissen E, Allman JM, Perl DP, Erwin JM, Hof PR (1999) A neuronal morphologic type unique to humans and great apes. Proc Natl Acad Sci U S A 96:5268–5273

Opris I, Popa IL, Casanova MF (2015) Prefrontal cortical microcircuits for executive control of behavior. In: Casanova MF, Opris I (eds) Recent advances on the modular organization of cortex. Springer, New York, pp 157–179

Perge JA, Niver JE, Margraini E, Balasubramanian V, Sterling P (2012) Why do axons differ in caliber? J Neurosci 32:626–638

Phillips KA, Stimpson CD, Smaers JB, Raghanti MA, Jacobs B, Popratiloff A, Hof PR, Sherwood CC (2015) The corpus callosum in primates: processing speed of axons and the evolution of hemispheric asymmetry. Proc Biol Sci 282(1818):282. 20151535

Pinker S (2009) How the mind works. W W Norton and Company, New York

Preuss TM, Qi H, Kaas JH (1999) Distinctive compartmental organization of human primary visual cortex. Proc Natl Acad Sci U S A 96:11601–11606

Preuss TM (1995) Do rats have prefrontal cortex? The rose-woolsey-akert program reconsidered. J Cogn Neurosci 7:1–24

Preuss TM, Coleman GQ (2002) Human specific organization of primary visual cortex: alternating compartments of dense cat 301 and calbindin immunoreactivity in layer 4A. Cereb Cortex 12:671–691

Radinsky L (1976) Cerebral clues. Nat Hist 85:54–59

Ramnani N (2006) The primate cortico-cerebellar system: anatomy and function. Nat Rev Neurosci 7:511–522

Ramnani N, Behrens TE, Johansen-Berg H, Richter MC, Pinks MA, Andersoon JL, Rudebeck P, Ciccarelli O, Richter W, Thomson AJ, Gross CG, Robson MD, Kastner S, Matthews PS (2006) The evolution of prefrontal inputs to the cortico-pontine system: diffusion imaging evidence from macaque monkeys and humans. Cereb Cortex 16:811–818

Rauschecker JP, Scott SK (2009) Maps and streams in the auditory cortex: nonhuman primates illuminate human speech processing. Nat Neurosci 12:718–724

Ringo JL, Doty RW, Demeter S, Simard PY (1994) Time is of the essence: a conjecture that hemispheric specialization arises from interhemispheric conduction delay. Cereb Cortex 4:331–343

Spocter MA, Raghanti MA, Butti C, Hof PR, Sherwood CC (2015) The minicolumns in comparative cortex. In: Casanova MF, Opris I (eds) Recent advances on the modular organization of the cortex. Springer, New York, pp 63–80

Stein JF, Glickstein M (1992) Role of the cerebellum in visual guidance of movement. Physiol Rev 72:967–1017

Thach WT, Goodkin HP, Keating JG (1992) The cerebellum and the adaptive coordination of movement. Annu Rev Neurosci 15:403–442

Timmermann A, Friedrich T (2016) Late Pleistocene climate drivers of early human migration. Nature 538:92–95

UNCORRECTED PROOF

Tremblay P, Dick AS (2016) Broca and Wernicke are dead, or moving past the classic model of language neurobiology. Brain Lang 162:60–71

Turner EC, Young NA, Reed JL, Collins CE, Flaherty DK, Gabi M, Kaas JH (2016) Distributions of cells and neurons across the cortical sheet in old world macaques. Brain Behav Evol 88:1–13. https://doi.org/10.11591000446762

Ungerleider LG, Haxby JV (1994) 'What' and 'where' in the human brain. Curr Opin Neurobiol 4:157–165

Van Essen D (1997) A tension-based theory of morphogenesis and compact wiring in the central nervous system. Nature 385:313–318

Ventura-Antunes L, Mota B, Herculano-Houzel S (2013) Different scaling of white matter volume, cortical connectivity and gyrification across rodent and primate brains. Front Neuroanat 7:3

Watson C, Provis J, Herculano-Houzel S (2012) What determines motor neuron number? Slow scaling of facial motor neuron numbers with body mass in marsupials and primates. Anat Rec 295:1683–1691

Welker WI (1990) Why does cerebral cortex fissure and fold? In: Jones EG, Peters A (eds) Cerebral cortex, vol 8B. Plenum Press, New York, pp 3–136

Wong P, Kaas JH (2010) Architectonic subdivisions of neocortex in the galago (*Otolemur garnetti*). Anat Rec 293:1033–1069

Wong P, Peebles JK, Asplund CL, Collins CE, Herculano-Houzel S, Kaas JH (2013) Faster scaling of auditory neurons in cortical areas relative to subcortical structures in primate brains. Brain Behav Evol 81:209–218

Young NA, Szabo CA, Phelix CF, Flaherty DK, Balaram P, Foust-Yeoman KB, Collins CE, Kaas JH (2013) Epileptic baboons have lower numbers of neurons in specific areas of cortex. Proc Natl Acad Sci U S A 110:19107–19112

UNCORRECTED PROOF