Mammals, birds and non-avian reptiles have signature proportions of numbers of neurons across their brain structures: Numbers of neurons increased differently with endothermy in birds and mammals

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Modern mammals, birds, and non-avian reptiles have shared developmental and evolutionary origins in the ancestral amniotes of 300 million years ago. A previous analysis of a newly completed dataset on the cellular composition of the major parts of the brain of 242 amniote species, generated using the same cell counting method, the isotropic fractionator, argued for changes in the body-brain relationship in amniote evolution (Kverkova et al., 2022), but did not explore how the brains of amniotes diverged in their neuronal composition. Here I show, using the same dataset but focusing instead on the cellular composition of the brains regardless of body mass and phylogenetic relatedness, that the brains of extant mammalian, avian, and non-avian reptile species are characterized by signature proportions of numbers of neurons across the pallium, the cerebellum, and the rest of brain. An increase to a higher, fixed proportion of 4.5 neurons in the cerebellum to every neuron in the rest of brain, with variable numbers of pallial neurons, characterizes the avian brain compared to other reptiles, whereas mammalian brains are characterized by an average 4 neurons in the cerebellum to every neuron in the pallium regardless of numbers of neurons in the rest of brain, which also differs from the proportion in most non-avian reptilian brains of 1.4 neurons in the pallium and 0.5 neuron in the cerebellum to every neuron in the rest of brain. Thus, the independent evolution of endothermy in birds and mammals occurred with dramatic increases in numbers of neurons in all brain structures that differed markedly between birds and mammals. Additionally, there are marked continuities in the scaling of extant amniote brains that allow for the neuronal composition of the brain of

ancestral amniotes to be estimated. Using these similarities in the neuronal scaling rules between living mammals and non-avian reptiles, I provide scaling relationships that allow predicting the composition of early mammaliaform and synapsid brains in amniote evolution, and I propose a simple model of amniote brain evolution that accounts for the diversity of modern mammalian, avian, and non-avian reptilian brains with only a few clade-shifting events in brain connectivity between cerebral cortex and cerebellum in mammals and between the cerebellum and rest of brain in birds, building on the increased availability of energy supply to the brain associated with the evolution of the increased oxidative and cardiovascular capacities that underlie endothermy.

Introduction

Mammals, birds, and non-avian reptiles, which together constitute the amniotes amongst animals, are markedly different in appearance, body size, and life histories. Yet, they derive from common stem amniote ancestors that lived ca. 300 million years ago (Kemp, 2006), and their brains still share a common developmental program (Puelles et al., 2013). The largest amniote brains are all mammalian, but mammalian brains can be as small as those of some lizards; modern bird brains, in turn, are larger than most non-avian reptilian brains, but not larger than those of dog-sized mammals (Kverkova et al., 2022). How did so much diversity in brain size arise, how come the different ranges, and how do they compare in terms of numbers of neurons?

Understanding the evolutionary history of modern amniote brains – those of mammals, birds, and non-avian reptiles – is an enterprise that is necessarily built on the comparative study of these extant brains in order to infer how they arose from evolutionary changes over time in their respective developmental programs. Until the advent of the isotropic fractionator, a method to reliably and rapidly count the neuronal and non-neuronal cells that compose brains without having to painstakingly cut them into thin sections for histological processing, microscopy and stereological analysis (Herculano-Houzel and Lent, 2005; Herculano-Houzel et al., 2015a), comparative studies of vertebrate brains were necessarily focused on the available data on structure size. While any data were better than no data, the limitation to structure size

posed a number of problems. First, the interpretation of comparative studies of brain structure volume required assuming that the underlying scaling rules governing the cellular composition of brain tissues were shared across species and clades, or any results would be meaningless – an assumption that, with data obtained using the isotropic fractionator, was rapidly shown to be invalid (Herculano-Houzel et al., 2006, 2007). Second, absolute and relative measurements often yielded conflicting interpretations (for instance, see Clark et al., 2001 and Sultan, 2002), for they depended on whether or not the size of the whole brain is a relevant reference and normalizer for brain structures. An even more problematic complication is the use of normalization to body mass for comparisons across species, an expedient that became popular once it finally succeeded in setting humans apart from other species (Jerison, 1973). The problem with using body mass as a normalizer is that it assumes a mandatory and universal relationship between body mass and the numbers of neurons, and the mass of the brain structures housing those neurons, that operate the body (Jerison, 1973). In contrast, we have observed repeatedly that body size is largely free to vary across individuals and species without mandatory consequences for the numbers of neurons that compose brain structures or spinal cord (Burish et al., 2010; Herculano-Houzel et al., 2015b, 2015c). Put another way, bodies of a similar size occur with up to 50-fold different numbers of neurons in the spinal cord and brainstem across species. To understand evolutionary changes in brain composition, then, one must look at exactly that, regardless of variations in body mass.

Using the isotropic fractionator, my colleagues and I generated a body of data on the numbers of neuronal and non-neuronal cells that compose the major brain structures of 75 mammalian, 28 bird species, and the Nile crocodile (Herculano-Houzel et al., 2015b; Ngwenya et al., 2016; Olkowicz et al., 2016; Dos Santos et al., 2017; Jardim-Messeder et al., 2017). Those data showed that while similar scaling relationships for each of the major brain parts applied to many mammalian (with the exception of primates) and bird species, there were obviously higher neuronal densities in the telencephalon of songbirds and parrots – even higher than in primates (Olkowicz et al., 2016). While those findings provided an answer to the question of how some birds can be as cognitively capable as primates (answer: because their small brains harbor primate-like numbers of pallial, and particularly associative pallial, neurons; Ströckens et al.,

2022), addressing the question of how bird brain composition came to differ from mammalian brain composition required obtaining data on the third group of amniotes that links them together: non-avian reptiles. That is because while birds are a derived group amongst reptiles, appearing within theropod dinosaurs during the Jurassic (Norell and Xu, 2005), modern reptiles as a whole are a sister group to mammals, with whom they share common ancestors that lived ca. 300 Mya (Kemp, 2006). Thus, comparison of the neuronal scaling rules between non-avian reptiles and mammals might reveal the scaling rules that applied to the brains of ancestral amniotes.

That missing dataset, with the numbers of neurons that compose the brains of 107 non-avian reptilian (hereafter, "reptile") species in 6 major clades and an additional 37 species covering a total of 9 avian (hereafter "bird") clades, was just published (Kverkova et al., 2022). In this dataset, amniote brains were divided into telencephalon/cerebellum/rest of brain (in reptiles and birds, in which case the subpallium is included in the telencephalon, and "rest of brain" is the brainstem plus diencephalon) or cortex/cerebellum/rest of brain (in mammals, in which case the subpallium is included in the rest of brain). In birds, numbers of cells were also available for the two parts of the telencephalon: the pallium (directly equivalent to the mammalian cerebral cortex; Puelles et al., 2013) and subpallium (Olkowicz et al., 2016; Kverkova et al., 2022). While it is unfortunate that the subpallium was not separated from the pallium in the telencephalon of the reptiles examined, the total number of neurons in the reptilian telencephalon is small compared to the "rest of brain" in these species (Olkowicz et al., 2016; Kverkova et al., 2022). With these caveats in mind, the combined dataset allows for the comparison of numbers of cells in the telencephalon/pallium/cortex, cerebellum, and the "rest of brain" (hindbrain to diencephalon in reptiles, hindbrain to subpallium in birds and mammals).

The study that originally reported the reptile and extended bird dataset (Kverkova et al., 2022) focused on the grade shifts in the relationship between brain and body mass that characterize amniote evolution, but did not address a number of fundamental issues in amniote brain evolution, starting with the neuronal scaling rules that apply to each clade specifically that is necessary to shed light on the evolution of the amniote brain. Further, anchoring interpretations of brain evolution on relationships to body mass is a flawed expedient that

assumes a mandatory and universal relationship between brain and body mass that is not there, as attested recently by studies on bird and mammalian brain evolution (Ksepka et al., 2020; Bertrand et al., 2022) and our demonstrations that there is no mandatory, much less a universal, scaling relationship between numbers of brain neurons and body mass (Herculano-Houzel et al., 2015b,c; Ngwenya et al., 2016). Additionally, studies of brain scaling often resort to "correcting" for phylogenetic relationships in the dataset (as done in Kverkova et al., 2022), a procedure that aspires to eliminate sampling bias but glosses over differences in scaling relationships across clades, and contaminates scaling relationships in the raw data with inferences about phylogenetic relations that may or may not be correct. Since the point of the present analysis is understanding the mathematics of the relationship between the size of the brain and of how many cells brain tissue is made across different animal clades, I focus the analysis on the scaling relationships that apply to the raw data; the only phylogenetic information taken into consideration is that pertaining to the nested clades that each animal belongs to.

Here I use the entire dataset of 242 amniote species to determine, regardless of body mass, the cellular scaling relationships that apply to each clade among the three groups of amniote animals – reptiles, mammals, and birds – to then address the following questions. First, non-neuronal cells in the brain include the endothelial cells that compose the brain vasculature, which may or may not scale similarly across endothermic and ectothermic species. Therefore, is the relationship between brain structure mass and number of non-neuronal cells (the so-called non-neuronal scaling rule) that applies universally to mammals (Herculano-Houzel and Dos Santos, 2018) extensive to (ectothermic) reptiles and (endothermic) birds? Second, are the main brain structures of amniotes fundamentally different in their neuronal composition, or do they form a continuum across reptiles, birds and mammals, at least across the more closely related clades, along a single scaling relationship, in which case the brain in these clades could be versions of a same developmental program, simply scaled up for instance in the event of endothermy? Third, if there are such continuums, can the scaling rules that applied to the main divisions of the brain of ancestral amniote species be inferred? In that case, can amniote brain diversity be understood as a simple evolutionary story of continuity with occasional deviations, without major

grade shifts, or are there major grade shifts to be accounted for – for example, associated with the independent evolution of endothermy in birds and mammals (Nespolo et al., 2011)?

Methods

All data on numbers of neurons and mass of the telencephalon, cerebellum and rest of brain for 242 species of reptiles, mammals and birds were taken from Kverkova et al. (2022). All numbers of neurons were obtained with the same method, the isotropic fractionator. For consistency, the olfactory bulbs, which are often not collected whole in brain dissections, are not included in any structure. All power functions were calculated using least-squares regression of log-transformed values in JMP 16 (Carey, NC). Brain mass and body mass values in fossil mammaliaformes and stem amniote species were compiled from the literature (Benoit et al., 2017a,b; Boonstra, 1968; Laas, 2015; Castanhinha et al., 2013; Laass and Kaestner, 2017; Jerison, 1973; Hopson, 1979; Rowe et al., 2011; Sigurdsen et al., 2012; Rodrigues et al., 2014; Quiroga, 1980; Luo et al., 2001; Macrini, 2006; Macrini et al., 2007; Bertrand et al., 2019, 2020, 2022; Cameron et al., 2018; Maugoust and Orliac, 2021), as listed in Table S17.

Results

Across the 242 species of reptiles, mammals, and birds analyzed, whole brain mass (which does not include the olfactory bulb, not always available after dissection) varies almost 500,000 fold, from 0.01 g in the Algerian sand gecko to 4,618.62 g in the African elephant. Across these brains, the total number of non-neuronal cells varies over 100,000 fold, from just under 2 million in the Algerian sand gecko to 216 billion in the African elephant. As a whole, amniote brains vary in mass as an essentially linear power function of their numbers of non-neuronal cells (Figure 1A; power fit, exponent 0.992±0.010, r^2=0.978, $p<0.0001$; linear fit, r^2=0.993, $p<0.0001$). This means that a 1,000 times heavier amniote brain has approximately 1,000 times more non-neuronal cells, with roughly constant densities of non-neuronal cells.

Indeed, reptiles, birds and mammals share the same limited, ca. 2-fold range of densities of non-neuronal cells, concentrated between 50,000 and 120,000 non-neuronal cells/mg of brain, though there is a significant decrease in non-neuronal cell density with increasing brain size in each of the three amniote clades that shows that the relationship between brain mass and

number of non-neuronal cells is actually not linear. Importantly, there are similar densities of non-neuronal cells in (endothermic) bird and mammalian brains that are respectively 100 and 10 times larger in mass than (ectothermic) reptile brains (Figure 1B). At the same time, however, the distributions are shifted between birds and mammals compared to reptiles, such that for brains of a similar mass, for example around 1 g, mammalian brains have systematically more non-neuronal cells per gram of tissue than reptiles; and birds have even more, though there is quite some overlap between bird and mammalian data points (Figure 1B). Thus, the shared, linear scaling of numbers of non-neuronal cells with brain mass across all amniotes in the dataset is only apparent, since densities of non-neuronal cells vary systematically with brain mass; and different scaling relationships apply to each amniote clade, with higher densities of non-neuronal cells in the brains of endothermic species compared to ectothermic reptilian species.

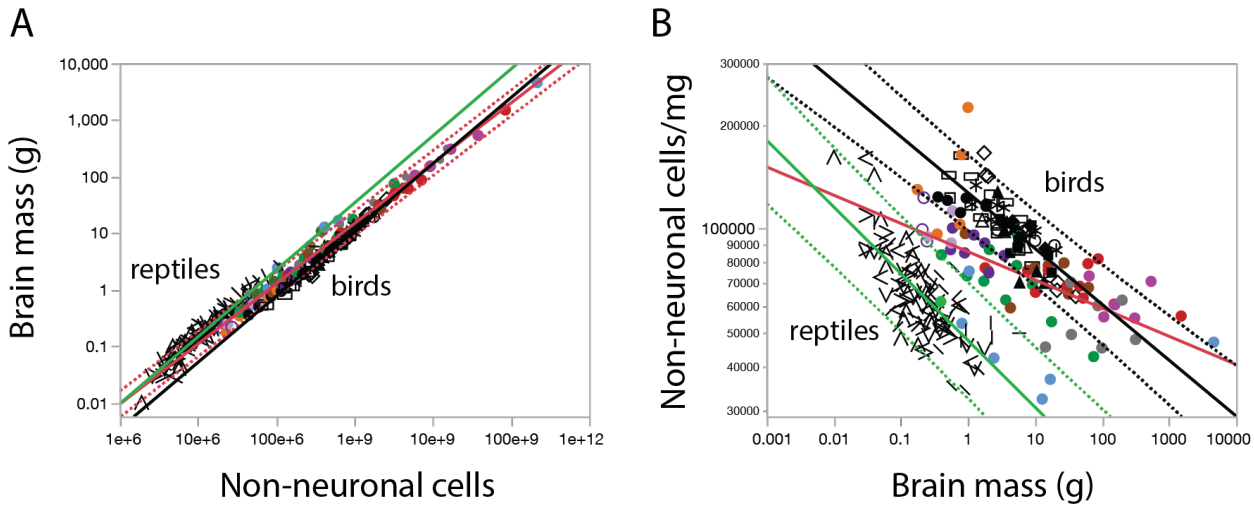

Figure 1. Birds, reptiles and mammals share a nearly linear relationship between brain mass and numbers of non-neuronal cells, although birds and mammals have significantly higher densities of non-neuronal cells than reptiles of similar brain mass. A, scaling of brain mass with non-neuronal cells across 108 species of reptiles (black line symbols), 69 species of mammals (colored circles) and 65 species of birds (black polygons). Power functions are plotted for mammals (in red, with 95% prediction interval: exponent, 1.070±0.013, r^2=0.990, p<0.0001), reptiles (in green; exponent, 1.184±0.026, r^2=0.952, p<0.0001) and birds (in black; exponent, 1.170±0.020, r^2=0.982, p<0.0001). The power function fit across all 242 species has an exponent of 0.992±0.010 (r^2=0.978, p<0.0001). Notice that the prediction interval plotted for mammalian species (in red) includes many reptilian and bird species. **B**, closer inspection of

the ratio between non-neuronal cells and brain mass, which is non-neuronal cell density, reveals that there is a small but highly significant decrease in non-neuronal cell density with increasing structure mass within each clade (power functions plotted), with exponents -0.081±0.014 (mammals, in red, r^2=0.354, p<0.0001), -0.192 (reptiles, in green, r^2=0.556, p<0.0001) and -0.161±0.015 (birds, in black, r^2=0.658, p<0.0001). Non-neuronal cell densities are overlapping between the larger bird and mammalian brains, but for brains around 1 g, birds have consistently higher non-neuronal cell densities than mammals, which are much higher than non-neuronal cell densities in reptiles. All scaling relationships are listed in Table S1.

Separate analysis of the scaling of non-neuronal cell density with the mass of each of the three main divisions of the amniote brains in the dataset reveals that the cortex of mammals aligns with the telencephalon of birds, with roughly twice higher densities of non-neuronal cells compared to reptilian telencephalons of similar mass (Figure S1A,B). Non-neuronal densities in the pallium vary little, are mostly overlapping, and decrease slowly with increasing structure mass across birds and mammals, with exponents barely significantly different from zero, as previously described in mammals (Herculano-Houzel and Dos Santos, 2018; Figure S2, Table S1), but drop rapidly in the telencephalon of reptiles as the mass of structure increases, with an exponent of -0.236±0.020 (p<0.0001, r^2=0.566; Figure S1B, Table S1). In contrast, for the cerebellum, birds and reptiles share similar non-neuronal cell densities, despite the larger mass of the bird cerebellum (Figure S1C,D), with non-neuronal cell densities decreasing faster with increasing cerebellar mass in these species compared to mammals (Figure S1D, Table S1). In the rest of brain, mammals and reptiles share similar non-neuronal cell densities despite the different range in mass of the structure; for a similar mass of the rest of brain, non-neuronal cell densities are higher in mammals than in reptiles, and highest in birds (Figure S1E,F; Table S1).

Neuronal scaling rules

Across the 242 amniote species in the dataset, the total number of brain neurons varies over 100,000 fold, from just under 2 million in the Algerian sand gecko (Kverkova et al., 2022) to 257 billion in the African elephant (Herculano-Houzel et al., 2014a). However, contrary to the fairly homogeneous distribution of non-neuronal cells across brain structures, the distribution of neurons in amniote brains is very heterogeneous across structures in an individual brain, with

neuronal densities that vary by over 1,000 times across brain structures that share non-neuronal densities that vary by less than a factor of 10 (Figure S3). Additionally, the neuronal composition of a given brain structure scales very differently depending on the structure, and also depending on animal clade amongst each group of amniotes. Thus, there is no such thing as the neuronal scaling rules for "the brains of mammals" or "the brains of birds", much less for "the brains of amniotes". Rather, the neuronal scaling rules that apply to the brains of amniote must be determined separately per brain structure and per clade, as below. I then devote special attention to the scaling of numbers of neurons across brain structures in the different mammalian clades, an important feature of quantitative brain anatomy that informs about the scaling of functional relationships between brain structures in evolution (Herculano-Houzel, 2010; Herculano-Houzel et al., 2014b).

Neuronal scaling rules for the telencephalon

It is unfortunate that the study describing the cellular composition of the brains of non-avian reptiles (Kverkova et al., 2022) failed to separate the telencephalon into pallial and subpallial structures, unlike for birds. However, considering that the subpallium contributes only a minority of telencephalic neurons in early derived Palaeognathes and ground-dwelling birds (between 7 and 15%; Olkowicz et al., 2016), and assuming that the same is the case for non-avian reptiles, the neuronal composition of the reptile telencephalon will be considered representative of the reptilian pallium for the purposes of this study, which require a comparison of scaling rules across clades.

Direct investigation of the relationship between the numbers of neurons that compose the reptilian telencephalon and the mammalian cerebral cortex reveals remarkable continuity across all reptilian and mammalian species in the dataset, with the notable exception of primates (Figure 2A, B). Closer examination of each clade in separate reveals that the neuronal scaling rules for the telencephalon are shared across all clades of reptiles examined, with the exception of the Nile crocodile and the Testudines, which have larger telencephalons than predicted for the number of telencephalic neurons in a reptile (Figure S4A). The crocodile telencephalon lies outside the 95% prediction interval for reptilian species, but fits the scaling rules for Testudines

(Figure S4A), a finding that is in line with the evolutionary relatedness of Crocodilia and Testudines (Figure 2C). Combining Testudines and the Nile crocodile yields a scaling relationship with exponent 1.344±0.186 ($p<0.0001$, $r^2=0.743$, 20 species; Table S2), with a scaling relationship for all other reptile telencephalons of exponent 1.309±0.056 ($p<0.0001$, $r^2=0.865$, 88 species; Table S2).

As shown in Figure 2A, reptile telencephalons and non-primate mammalian cerebral cortices of similar mass (which is the case of the smallest mammals in the dataset: eulipotyphlans and bats) are composed of similar numbers of neurons. Beyond that interval of overlap, the reptilian telencephalon/mammalian cerebral cortex scales in mass as a power function of its number of neurons that has statistically indistinguishable exponents between reptiles (1.437±0.064, $p<0.0001$, $r^2=0.827$, 108 species) and non-primate mammals (1.495±0.033, $p<0.0001$, $r^2=0.974$, 56 species), and non-primate mammalian data points fall well within the 95% prediction interval for reptiles (Figure 2A). The continuity in neuronal scaling rules between most reptiles and mammals, with a combined exponent of 1.392±0.020 ($p<0.0001$, $r^2=0.971$, 144 species; Table S2), strongly indicates that these shared scaling rules already applied to the shared common ancestor between the two clades (Figure 2C).

The shared scaling relationship across reptiles and most mammals between numbers of telencephalic neurons and telencephalic (or cerebral cortical) mass with exponents of roughly 1.5 means that as the structure gains 10x more neurons, average neuronal size increases by $10^{0.5}$ = 3.2-fold, causing the measured neuronal density to drop (Mota and Herculano-Houzel, 2014) in a similar manner across reptiles and non-primate mammals. Thus, the mammalian species with the fewest cerebral cortical neurons, which are bats and eulipotyphlans, have similar neuronal densities as many of the reptiles in the dataset with matching numbers of neurons; and as mammalian cortices gain more cortical neurons, their average neuronal density decreases in a way that can be predicted equally well using the power function calculated for non-primate mammals (exponent -0.495±0.033, $p<0.0001$, $r^2=0.803$, 56 species) or for the reptilian telencephalon (with exponent -0.438 ± 0.064, $p<0.0001$, $r^2=0.305$, 108 species; Figure 2B; Table S3). Again, closer examination of the reptilian species shows that Testudines and the Nile

crocodile have lower neuronal densities than predicted for reptilian telencephalons of their numbers of neurons (Figure S4B).

The bird telencephalon, in contrast, gains neurons in a clearly distinct manner from non-avian reptilians – but at least two groups are clearly recognizable (Figure 2). In the first, composed by Palaeognathae and Galliformes, which in this dataset are the earliest derived in avian evolution, arisen prior to the K-Pg extinction event (Brusatte et al., 2015), the telencephalon gains neurons with a pronounced drop in neuronal density, similar to that observed in reptiles and most mammals, with an exponent of -0.386±0.061 ($p<0.0001$, $r^2=0.755$, 15 species; Figure 2B, Figure S4C,D; Table S3). This scaling relationship captures the later arising Columbiformes very well, such that addition of Columbiformes species leaves the scaling exponent virtually unchanged (-0.388±0.061, $p<0.0001$, $r^2=0.697$, 20 species; Figure S4C,D, Table S3). Remarkably, these early-arising birds have neuronal densities on par with those found in reptiles and mammals (Figure 2B), and neuronal scaling rules that appear shifted to the right compared to Testudines and the Nile crocodile, as if the same brain volume now simply accommodated increased numbers of neurons (that is, with increased neuronal density) while maintaining the same allometry across species (Figure S4E). On the other extreme, the later, post-K-Pg-derived Falconiformes, Strigiformes, Passeriformes (including Corvidea) and Psittaciformes, telencephalic neuronal densities are much higher than in the vast majority of reptiles and mammals, and barely decrease with varying numbers of neurons (-0.100±0.044, $p=0.0315$, $r^2=0.136$, 34 species; Figure S4D, Table S3). As a result, early-derived birds have more neurons in the telencephalon than reptiles or non-primate mammals of similar pallial or telencephalic mass; and later-derived birds have even more neurons concentrated in structures of a same mass. Anseriformes and Accipitriformes species lie in between the two clades (Figure S4D).

Mapping these scaling relationships onto the phylogenetic tree of all species in the dataset strongly suggests that the telencephalic scaling rule shared by modern (non-avian) reptiles and non-primate mammals already applied to their common ancestral species (Figure 2c). Birds could have arisen with a shift towards larger neuronal densities that remains in Palaeognathes such as the emu and ostrich, landfowl, and pigeons; and further later shifts

towards even higher neuronal densities at the more recent derivation of songbirds, hawks, owls and parrots (Figure 2C).

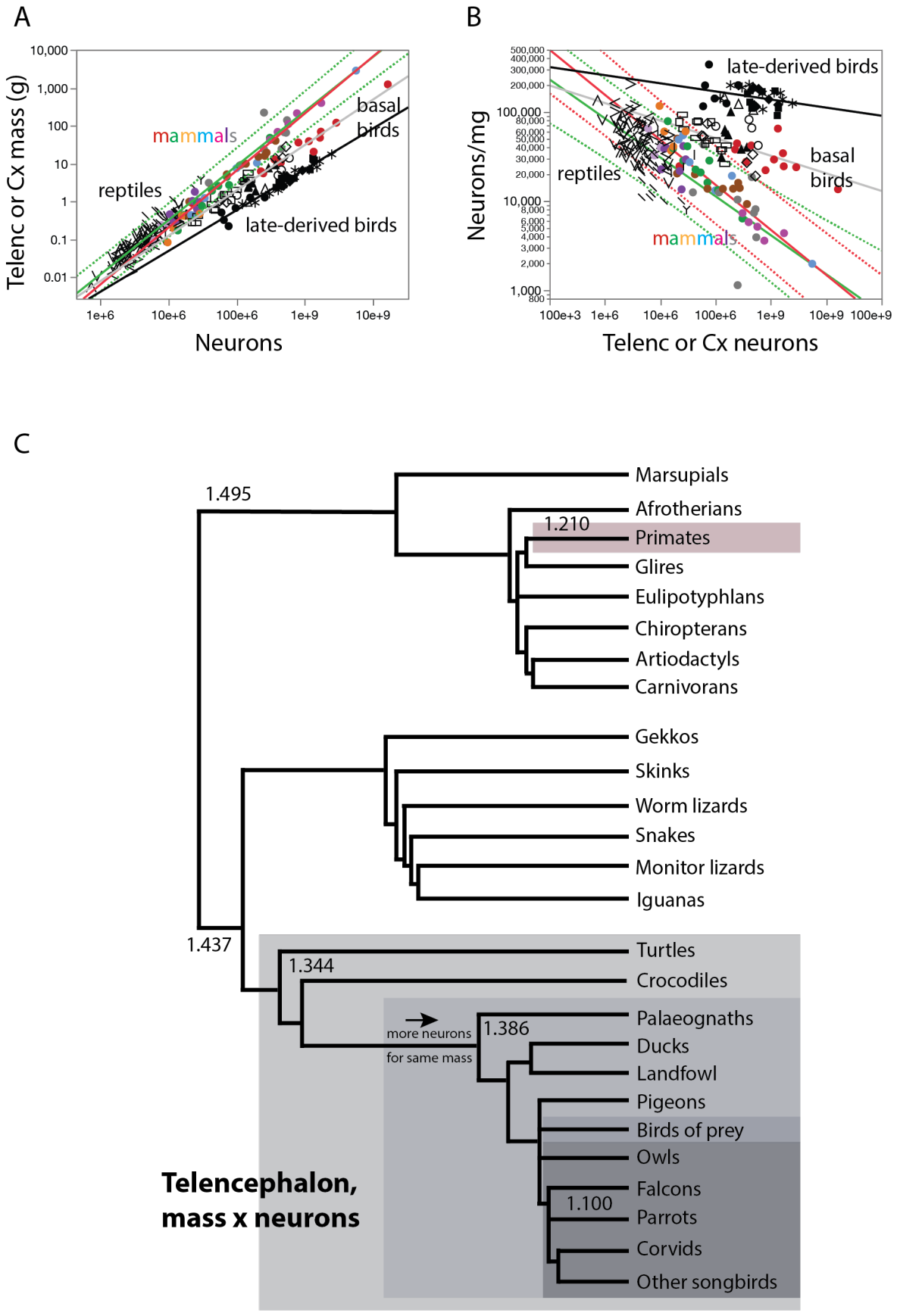
A
Telenc or Cx mass (g)
Neurons
mammals
reptiles
basal
birds
late-derived birds
B
Neurons/mg
Telenc or Cx neurons
late-derived birds
basal
birds
reptiles
mammals
C
1.495
1.210
1.437
1.344
1.386
1.100
Marsupials
Afrotherians
Primates
Glires
Eulipotyphlans
Chiropterans
Artiodactyls
Carnivorans
Gekkos
Skinks
Worm lizards
Snakes
Monitor lizards
Iguanas
Turtles
Crocodiles
Palaeognaths
Ducks
Landfowl
Pigeons
Birds of prey
Owls
Falcons
Parrots
Corvids
Other songbirds
more neurons
for same mass
Telencephalon,
mass x neurons

Figure 2. Reptiles and non-primate mammals share neuronal scaling rules for the telencephalon/pallium, while two different scaling rules apply across birds, and primates conform to one of them. A, scaling of mass of the telencephalon or pallium with numbers of neurons across 108 species of reptiles (black line symbols), 68 species of mammals (colored circles, minus the outlier brown bear; Jardim-Messeder et al., 2017) and 65 species of birds (black polygons). Power functions are plotted for non-primate mammals (in red, with 95% prediction interval: exponent, 1.495±0.033, r^2=0.974, p<0.0001), all reptiles (in green; exponent, 1.437±0.064, r^2=0.827, p<0.0001), early-derived birds (Galliformes, Palaeognathae, Columbiformes, in gray; exponent, 1.386±0.060, r^2=0.967, p<0.0001), and late-derived birds (Falconiformes, Passeriformes, Psittaciformes, and Strigiformes, in black; exponent, 1.100±0.044, r^2=0.950, p<0.0001). For the sake of clarity, the 95% prediction interval is only plotted for reptilian species. Note that non-primate mammalian species conform to the prediction interval for reptiles. All power functions are listed in Table S2. **B**, Neuronal density (the ratio between neurons and telencephalic or pallial mass) decreases steeply with increasing numbers of telencephalic or pallial neurons across reptilian and non-primate mammalian species alike, while early-derived birds have higher neuronal densities, even higher in late-derived birds. Power functions plotted have exponents -0.438±0.064 (reptiles, in green, r^2=0.305, p<0.0001), -0.495±0.033 (non-primate mammals, in red, r^2=0.803, p<0.0001), -0.388±0.061 (early-derived birds, in gray, r^2=0.697, p<0.0001) and -0.100±0.044 (late-derived birds, in black, r^2=0.136, p=0.0315). All power functions are listed in Table S3. **C,** Putative cladogram for the evolution of the exponent that describes the scaling relationship between telencephalic mass and number of neurons, showing a shared exponent across most extant reptilian and mammalian species that can be inferred to have applied to ancestral amniotic species. Shaded areas indicate a shift towards more telencephalic neurons without a change in the scaling exponent at the origin of birds, followed by a shift in scaling exponent at the origin of the recently-derived Passeriformes, Psittaciformes, Falconiformes and Strigiformes.

Neuronal scaling rules for the cerebellum

Differently from the telencephalon, the neuronal scaling rules that apply to the cerebellum are clearly distinct between reptiles and mammals, and overlap across most mammalian and some bird species (Figure 3). Amongst most reptiles, the cerebellum gains mass faster than it gains neurons, in a manner described by a power function of exponent 1.285±0.047

(p<0.0001, 90 species; Figure 3A, green; Table S4) from which snakes are the only clear exception (Figure S5). Thus, across non-serpent reptilian species as a whole, more cerebellar neurons are also on average larger neurons, with decreasing neuronal densities (Figure 3B), although Iguania is the only clade that shows a clear decrease in cerebellar neuronal density as the cerebellum gains neurons across species (Table S5).

A power function with an exponent of 1.257±0.048, statistically indistinguishable from the reptilian exponent, applies to the cerebellum of early derived birds: Accipitriformes, Anseriformes, Columbiformes, Galliformes and Palaeognathae, and also Strigiformes (Figure 3A, grey line; 38 species), although this curve is shifted to the right with respect to reptiles, just as seen in the case of the telencephalon/pallium between Testudine and crocodilian reptiles and early-derived birds. Remarkably, a similar power function to the one that applies to these six bird clades describes the scaling of the non-primate, non-eulipotyphlan mammalian cerebellum (Herculano-Houzel et al., 2007, 2014; Sarko et al., 2009; Jardim-Messeder et al., 2017), with exponent 1.223±0.024 (p<0.0001, 53 species; Figure 3A, red line; Figure S5A,B). Indeed, the scaling relationship that applies to the combination of these two latter groups has an undistinguishable exponent of 1.234±0.021 (p<0.0001, 84 species; Figure S5A,B). Additionally, the scaling exponent that applies to these early-derived birds, plus Strigiformes, is virtually identical to the scaling exponent that applies to reptiles as a whole (1.160±0.047 and 1.159±0.046, respectively), with a distribution that is simply shifted to the right, with more neurons in a same structure mass (Figure S5C; Table S4). Across the other three bird clades (Falconiformes, Passeriformes including corvids, and Psittaciformes), yet another seemingly parallel power function relates cerebellar mass to number of neurons, with exponent 1.223±0.053 (p<0.0001, 27 species), not significantly different from the others (Figure 3A, Figure S5). Strikingly, the neuronal scaling rules that apply to the cerebellum can be further distinguished across Falconiformes and Psittaciformes on the one hand, and Passeriformes on the other, with even higher neuronal densities in the cerebellum of the latter (Figure S5F).

The similar exponents that describe the scaling of cerebellar mass as it gains neurons across reptiles, birds, and most mammalian species stems from the similar slope of the decrease in cerebellar neuronal densities with increasing numbers of neurons across the three groups

described above (Figure 3B, compare green, grey/red, and black lines), with exponents of around -0.25, with parallel power functions that apply to each clade (Figure S5F, Table S5). As described previously (Herculano-Houzel, 2014a), primates and eulipotyphlans are the only groups that clearly depart from these allometric relationships, with no significant change in neuronal density in the cerebellum as it gains neurons (Figure 3B), which translates into cerebellar mass that scales linearly with numbers of neurons (Figure 3A, S5B).

Mapping these scaling relationships onto the phylogenetic tree of all species of amniotes in the dataset indicates that while there has been a major step increase in numbers of cerebellar neurons in the two groups of endotherms compared to reptiles, and apparently two further step increases at the origin of more recently derived birds, the allometric exponent that applies to the scaling of neuronal density with numbers of neurons in the cerebellum only diverged at the origin of primates and eulipotyphlans, amongst mammals; and at the origin of Serpentes, amongst reptiles (Figure 3C).

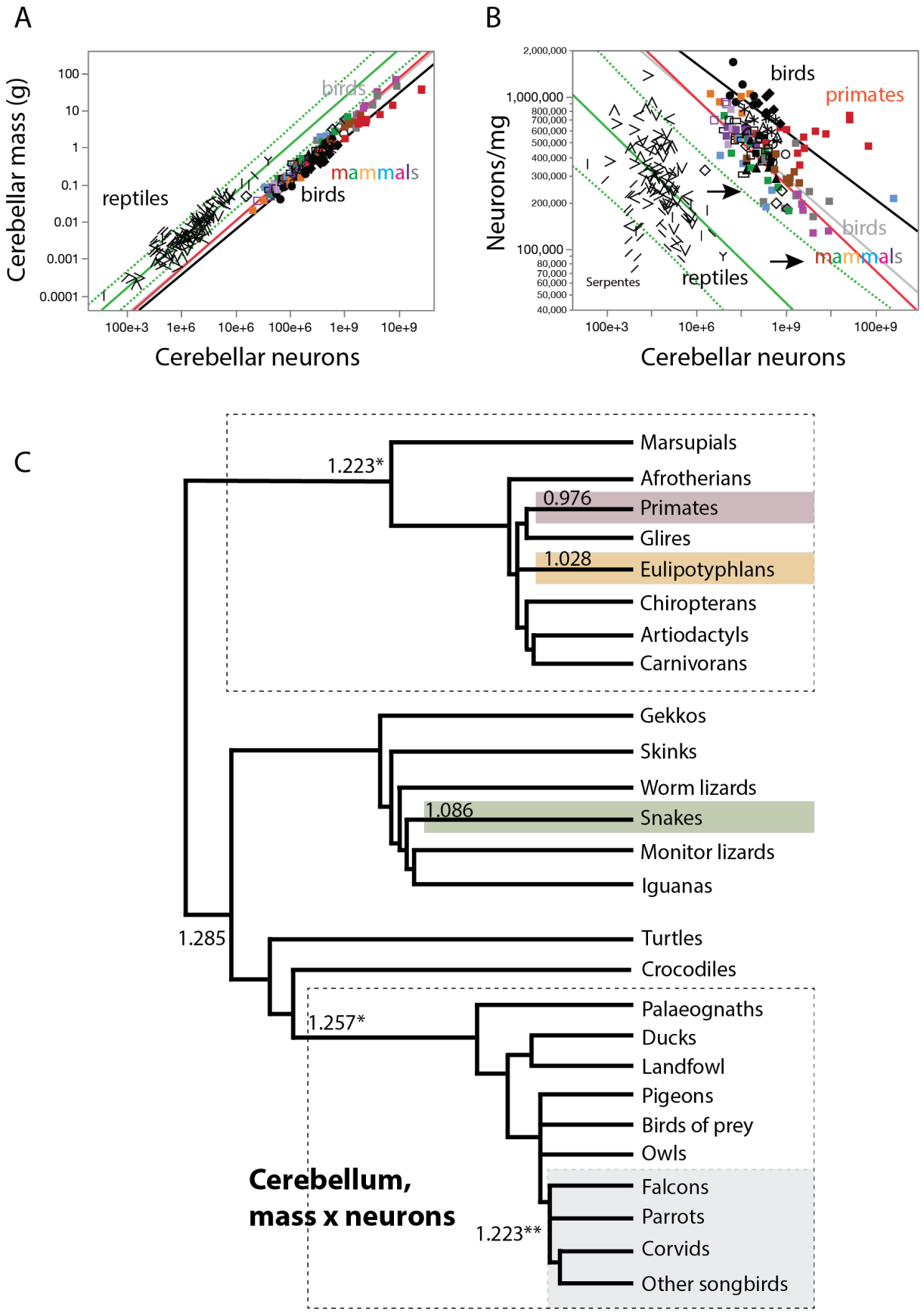
A
Cerebellar mass (g)
100
10
1
0.1
0.01
0.001
0.0001
reptiles
birds
mammals
birds
100e+3
1e+6
10e+6
100e+6
1e+9
10e+9
Cerebellar neurons
B
Neurons/mg
2,000,000
1,000,000
800,000
700,000
600,000
500,000
400,000
300,000
200,000
100,000
80,000
70,000
60,000
50,000
40,000
birds
primates
birds
mammals
Serpentes
reptiles
100e+3
10e+6
1e+9
100e+9
Cerebellar neurons
C
1.223*
Marsupials
Afrotherians
0.976
Primates
Glires
1.028
Eulipotyphlans
Chiropterans
Artiodactyls
Carnivorans
Gekkos
Skinks
Worm lizards
1.086
Snakes
Monitor lizards
Iguanas
1.285
Turtles
Crocodiles
1.257*
Palaeognaths
Ducks
Landfowl
Pigeons
Birds of prey
Owls
Falcons
Parrots
Corvids
Other songbirds
1.223**
Cerebellum,
mass x neurons

Figure 3. Reptiles, birds and non-primate, non-eulipotyphlans mammals share allometric exponents for the neuronal composition of the cerebellum, although relationships are shifted to the right in the two endotherm clades. A, scaling of cerebellar mass with numbers of neurons across 108 species of reptiles (black line symbols), 53 species of mammals (colored circles, minus primates and eulipotyphlans) and 65 species of birds (black polygons). Power functions are plotted for non-primate, non-eulipotyphlan mammals (in red: exponent, 1.223±0.024, r^2=0.981, p<0.0001), all reptiles minus serpents (in green, with 95% prediction interval; exponent, 1.285±0.047, r^2=0.897, p<0.0001), early-derived birds (Galliformes, Palaeognathae, Anseriformes, plus Columbiformes, Accipitriformes and Strigiformes, in gray, with near-perfect overlap with mammals; exponent, 1.257±0.048, r^2=0.950, p<0.0001), and late-derived birds (Falconiformes, Passeriformes, Psittaciformes, in black; exponent, 1.223±0.053, r^2=0.955, p<0.0001). For the sake of clarity, the 95% prediction interval is only plotted for reptilian species. All power functions are listed in Table S4. **B**, Neuronal density in the cerebellum (number of neurons per milligram of cerebellar mass) decreases steeply with increasing numbers of cerebellar neurons in parallel scaling functions across reptilian, non-primate, non-eulipotyphlan mammalian, and early-derived bird species alike, while late-derived birds have higher neuronal densities. Power functions plotted have exponents -0.287±0.046 (reptiles minus serpents, in green, r^2=0.303, p<0.0001), -0.223±0.024 (non-primate, non-eulipotyphlan mammals, in red, r^2=0.628, p<0.0001), -0.257±0.048 (early-derived birds, in gray, r^2=0.440, p=0.0018) and -0.223±0.053 (late-derived birds, in black, r^2=0.414, p=0.0003). For the sake of clarity, the 95% prediction interval is only plotted for reptilian species. All power functions are listed in Table S5. **C,** Putative cladogram for the evolution of the exponent that describes the scaling relationship between cerebellar mass and number of neurons, with a shared exponent across most extant reptilian, basal bird, and mammalian species, with a grade shift towards more neurons in a similar cerebellar mass in the newly endothermic species. The shared exponent between reptilian and mammalian species can thus be inferred to have applied to ancestral amniotic species. Shaded areas indicate clade shifts in the scaling exponent.

Neuronal scaling rules for the rest of brain

Similarly to the telencephalon, the neuronal scaling rules that apply to the rest of brain (brainstem, diencephalon and subpallium in mammals, or brainstem plus diencephalon in

reptiles and birds; Kverkova et al., 2022) overlap across most reptiles and mammals (Table S6), with the exception of primates, which diverge from other mammals as reported previously (Herculano-Houzel et al., 2014a). As shown in Figure 4a, the 95% prediction interval of the scaling relationship for reptiles between the mass of the rest of brain and its number of neurons includes the majority of non-primate mammals, and although the scaling exponents are nominally different, they are not significantly different (non-primate mammals, 1.844±0.076, $p<0.0001$, 57 species; reptiles, 1.569±0.067, $p<0.0001$, 88 species, excluding Testudines and crocodile; combined sample, 1.673±0.035, $p<0.0001$, 145 species). As found for the telencephalon, the rest of brain of Testudines and the Nile crocodile also diverges from the scaling rules that apply to other reptilian species (Figure S6, Table S6). Across reptiles (minus Testudines and the Nile crocodile) and non-primate mammals, increases in numbers of neurons in the rest of brain are accompanied by decreasing neuronal densities as a joint power function across the two clades with exponent -0.672±0.035 ($p<0.0001$, $r^2=0.724$, 145 species; Figure S6B, Table S6). Thus, as for the telencephalon, what differentiates the rest of brain of mammals from the majority of reptiles seems to be simply the vastly larger numbers of neurons in the former, but apparently added in conformity to the same scaling rules.

The conformity of most reptilian and mammalian species to the same scaling relationship between numbers of neurons in the rest of brain and average neuronal density in these structures, with continuity across these species in scaling (Figure 4), indicates that the neuronal scaling rule that they share also applied to their common ancestral amniote species (Figure 4C).

Birds, in contrast, have more neurons in the rest of brain than both reptiles and mammals with similar mass in these structures. The scaling relationship that applies to the bird rest of brain might also be simply shifted to the right compared to reptiles (as found for the cerebellum), with an exponent of 1.346±0.173 ($p<0.0001$, $r^2=0.490$) across the entire bird dataset that is statistically indistinguishable from the reptilian exponent, but is also not significantly different from unity (Figure 4a, black). Accordingly, neuronal densities in the bird rest of brain do not scale significantly with varying numbers of neurons in the rest of brain ($p=0.0505$, $r^2=0.059$, 65 species; Figure 4b). However, separate analysis of the different bird clades shows that different relationships between numbers of neurons and neuronal density apply to the early-derived

Palaeognathae, Galliformes and Collumbiformes versus the later-derived Accipitriformes, Falconiformes and Passeriformes, from which Psittaciformes and Strigiformes also differ (Tables S6 and S7; Figure S6).

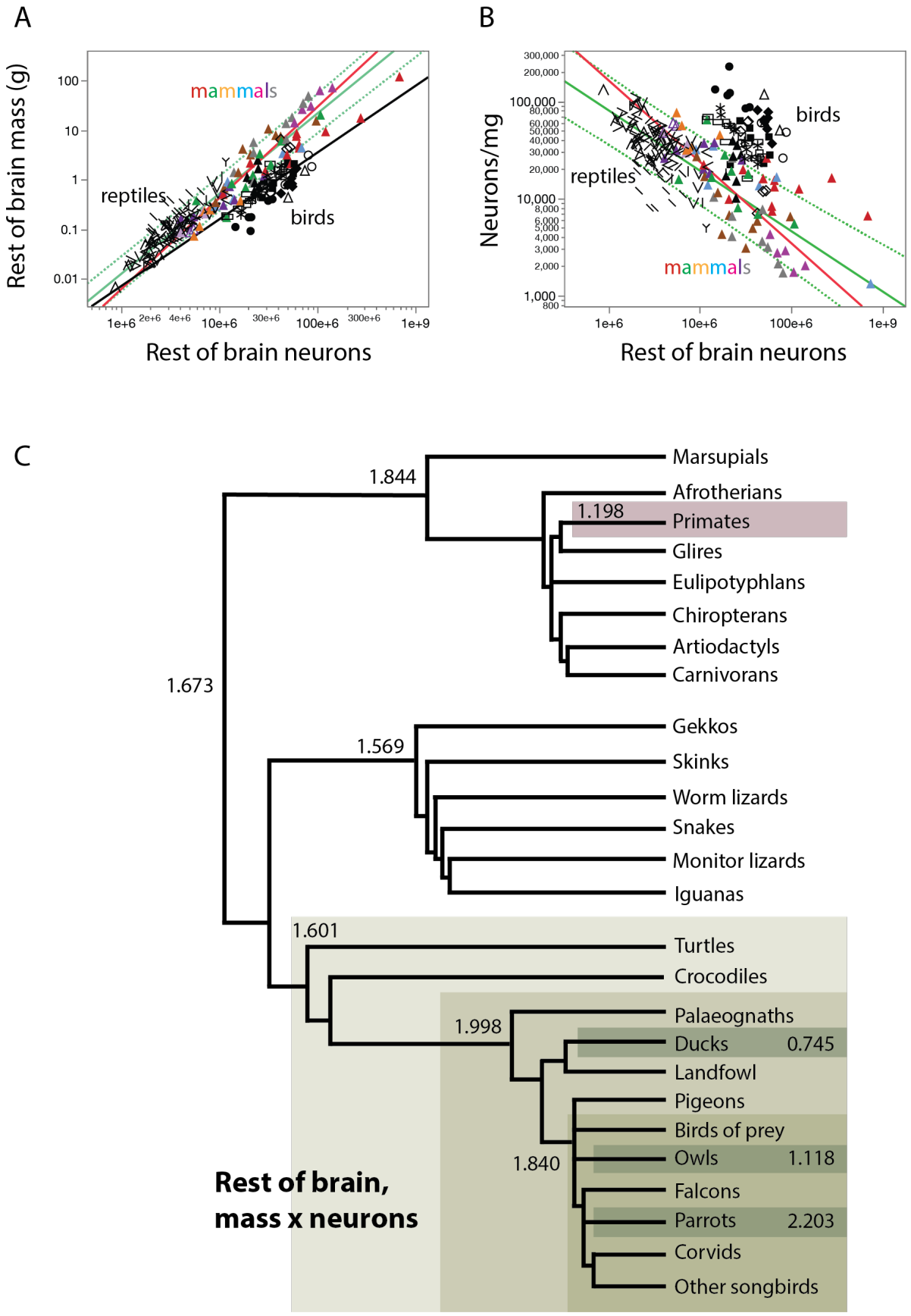
A
Rest of brain mass (g)
mammals
reptiles
birds
Rest of brain neurons
B
Neurons/mg
birds
reptiles
mammals
Rest of brain neurons
C
Marsupials
Afrotherians
Primates
Glires
Eulipotyphlans
Chiropterans
Artiodactyls
Carnivorans
Gekkos
Skinks
Worm lizards
Snakes
Monitor lizards
Iguanas
Turtles
Crocodiles
Palaeognaths
Ducks 0.745
Landfowl
Pigeons
Birds of prey
Owls 1.118
Falcons
Parrots 2.203
Corvids
Other songbirds
1.844
1.198
1.673
1.569
1.601
1.998
1.840
Rest of brain,
mass x neurons

Figure 4. Reptiles and non-primate mammals share allometric exponents for the neuronal composition of the rest of brain, while the scaling relationship for birds is shifted to the right. A, scaling of rest of brain mass with numbers of neurons across 88 species of reptiles (black line symbols, minus Testudines and the Nile crocodile), 57 species of mammals (colored circles, minus primates) and 65 species of birds (black polygons). Power functions are plotted for non-primate mammals (in red interval: exponent, 1.844±0.076, r^2=0.914, p<0.0001), all reptiles minus Testudines and crocodile (in green; exponent, 1.569±0.067, r^2=0.864, p<0.0001), and all birds (in black; exponent, 1.346±0.173, r^2=0.490, p<0.0001). For the sake of clarity, the 95% prediction interval is only plotted for reptilian species. All power functions are listed in Table S6. **B**, Neuronal density in the rest of brain decreases steeply with increasing numbers of rest of brain neurons across reptilian and non-primate mammalian species, while birds have higher neuronal densities. Power functions plotted have exponents -0.573±0.067 (reptiles minus Testudines and crocodile, in green, r^2=0.456, p<0.0001) and -0.845±0.076 (non-primate mammals, in red, r^2=0.690, p<0.0001). Power functions for birds, listed in Table S7, are clade-specific and are not plotted for the sake of clarity. **C,** Putative cladogram for the evolution of the exponent that describes the scaling relationship between rest of brain mass and number of neurons, showing a shared exponent across most extant reptilian and mammalian species that can be inferred to have applied to ancestral amniotic species. Shaded areas indicate clade-specific shifts in birds.

Relationship to body mass

In contrast to the marked continuity in the relationship between structure mass and numbers of neurons across amniote clades pointed out above, the numbers of neurons that compose the telencephalon/pallium (Figure S7A), cerebellum (Figure S7B) and rest of brain (Figure S7C) are not universally related to body mass across all amniotes. Most importantly, it is not the case that there was a simple, one-time grade shift with the advent of endothermy towards more brain neurons for a given body mass, as suggested recently (Kverkova et al., 2022). Instead, different clades have different relationships between body mass and numbers of neurons in each brain structure (Figure S7). Figure S7C demonstrates that the “rest of brain” in particular, which consists of structures directly involved in operating the body, varies in numbers of neurons by about 50-fold across reptiles, birds, and mammals of similar body mass. This discrepancy is consistent with recent reports that body mass and brain mass are quite free to

vary independently of each other in mammalian and avian evolution (Ksepka et al., 2020; Bertrand et al., 2022) and that body mass is not a determinant of numbers of brain neurons (Herculano-Houzel et al., 2015b).

Similarly, neuronal densities in the telencephalon and cerebellum are not universally related to body mass across all amniote clades (Figure S7, right). However, in the rest of brain, all reptiles and small mammals of up to 10 kg body mass share a fairly similar scaling of neuronal densities as body mass increases, with a joint exponent of -0.301±0.010 ($p<0.0001$, $r^2=0.850$, 177 species), suggestive of an increase in average neuronal size proportionately to the length of the body, that is, body mass$^{1/3}$ (Figure S7, Figure S8, Table S8). Amongst birds, however, exact exponents vary. The steepest scaling of neuronal density in the rest of brain with increasing body mass occurs in species of Anseriformes (-0.400±0.045, $p<0.0001$, $r^2=0.941$, 7 species), which overlap with mammals and reptiles (Figure S8). The ensemble of Galliformes, Columbiformes, Psittaciformes and Strigiformes have neuronal densities in the rest of brain which decrease with increasing body mass raised to a much shallower exponent of -0.260±0.026 ($p<0.0001$, $r^2=0.770$, 32 species; Figure S8). Accipitriformes, Falconiformes and Passeriformes, in turn, have higher neuronal densities in the rest of brain for similar body masses, which decrease with increasing body mass raised to an intermediate exponent of -0.297±0.018 ($p<0.0001$, $r^2=0.936$, 20 species; Figure S8, Table S8).

Scaling relationships across structures

The non-telencephalic, non-cerebellar rest of brain comprises the brain structures that operate the body, are readily comparable across clades of amniotes, and provide the anatomical and circuit-related scaffolding on top of which the pallium and the cerebellum function. It is also composed of structures derived from the near entirety of the cranial neural tube, minus the first two neuromeres (Puelles et al., 2013). Thus, I use the rest of brain as an anchor to which I compare the scaling of the other brain structures across clades of amniotes. This procedure allows for a measurement of relative allocation of neurons across brain structures that is completely irrespective of body mass or brain mass.

Despite the 100,000-fold range of variation in the mass of the rest of brain across the 242 species in the dataset, the pallium (or whole telencephalon, in reptiles) scales in mass faster than the rest of brain in a uniform, shared manner across all amniotes, with the notable exceptions of primates and owls (Strigiformes), with a shared exponent of 1.189±0.013, significantly above unity (r^2=0.983, p<0.0001; Figure S9A; Table S9). As a consequence, the mass ratio between pallium (or telencephalon) and rest of brain increases together with the absolute mass of the rest of the brain in a continuous manner across reptiles, mammals, and birds (exponent, 0.189±0.013, r^2=0.592, p<0.0001; Figure S9B; Table S10). Primates and owls show a step increase away from the shared pattern, with a larger pallium than expected for an amniote of similar mass of the rest of brain (Figure S9B).

The cerebellum of mammals and birds, in contrast, shows a marked difference from the scaling relationship in mass with the rest of brain that applies to the non-avian reptiles in the dataset, with ca. 10-fold larger cerebellar mass in the warm-blooded amniotes compared to reptiles of similar rest of brain mass (Figure S9C). As a result, while the cerebellum is on average only about 1/20th the mass of the rest of brain in reptiles, it jumps to a mass equivalent to ca. 1/3 to ½ the mass of the rest of brain in birds and mammals (Figure S9D, Table S10). Strikingly, once more the scaling relationship is shared across avian and mammalian species (Figure S9C-D), although the cerebellum appears relatively smaller in parrots than in mammals of similar rest of brain mass (30% of the mass of the rest of brain in parrots vs. 50% in non-primate mammals and elephant; Table S10). As a consequence, the ratio between the mass of the pallium (or telencephalon) and of the cerebellum is very large in reptiles, whose telencephalons may be from 6 to over 100 times larger than the cerebellum, but this ratio is 4-10 in birds, and only 3-5 in most mammals (Figure S9E-F, Table S10). Thus, examination of the scaling relationships that apply to structure mass across the three main divisions of amniote brains suggests that the vast majority of mammals and birds, while evolutionarily unrelated to each other, share the proportionality with which cerebellar mass is added to the rest of brain; and further share with reptiles the proportionality with which telencephalic mass is added on top of the rest of brain. In terms of scaling of brain structure mass, one might be led to conclude that the main difference in how bird and mammalian brains are built is that there is slightly more pallial mass relative to the rest

of brain in songbirds, parrots and owls than in non-primate mammals (Figure S9F) – but otherwise, bird and non-primate mammalian brains are built to fairly similar proportions across their main structures. These proportions are illustrated in Figure S10.

Strikingly, however, the mass relationships across structures do not inform about the scaling of numbers of neurons across brain structures in amniotes. The shared scaling of pallial (or telencephalic) mass as a function of the mass of the rest of brain across most amniotes in the dataset (Figure S9A,B), with the exception of owls and primates, conceals the fact that artiodactyls, carnivorans and large marsupials, besides owls and primates, have increased numbers of pallial neurons compared to the prediction for an amniote of their numbers of neurons in the rest of brain (Figure 5A,B; Table S11). Similarly, the shared scaling in mass of the cerebellum with the rest of brain across birds and mammals (Figure S9C) contrasts with the very diverse relationships between numbers of neurons in the cerebellum and the rest of brain across birds, small mammals, and large mammals (Figure 5C; Table S12). As a consequence, mammals and birds of similar mass ratios between cerebellum and rest of brain (Figure S9D) have ratios of neurons between the two structures that differ by up to a factor of ten, with much larger and variable ratios in mammals than in birds (Figure 5D). Finally, the much larger mass of the telencephalon relative to the cerebellum in reptiles compared to birds and mammals (Figure S9E,F) is no indication of the fact that the proportion of neurons between the cerebellum and the telencephalon (or pallium) is similar between many reptiles and birds (Figure 5E,F; Table S13).

Despite the enormous diversity in absolute numbers of neurons composing the brains of the different amniotes, striking patterns emerge in how they vary across structures within each group of amniotes. While the scaling of structure mass does not distinguish between bird and mammalian brains, the scaling of numbers of neurons across structures does, as I show next.

All reptiles in the dataset gain neurons coordinately between the telencephalon and the rest of brain, with ratios of numbers of neurons between the structures that vary from just below 1.0 in Iguania to 2.4 neurons in the telencephalon to every neuron in the rest of brain of Testudines and the Nile crocodile (Figure 5A; Table S14). On average, reptiles other than Testudines and the Nile crocodile have 1.4±0.6 neurons in the telencephalon to every neuron in the rest of brain; Testudines and the Nile crocodile have 2.4±0.6 neurons in the telencephalon to

every neuron in the rest of brain (Figure 6, Table S14). Small mammals (eulipotyphlans, chiropterans, rodents, small afrotherians, and South American marsupials) lie in between with ca. 2 neurons in the cerebral cortex for every neuron in the rest of brain, as described before (Herculano-Houzel et al., 2014b). In contrast, large mammals – carnivorans, Australian marsupials, primates, and artiodactyls – have greatly increased ratios of neurons in the cerebral cortex over the rest of brain, which average just over 7 in artiodactyls and carnivorans, and can exceed 20 in primates (Figure 5A, Table S14). These data show that compared to the ancestor shared with modern reptiles, and to small mammals, there has been a marked expansion of cortical neurons over the rest of the neural tube in the evolution of large mammalian species.

Interestingly, the early-derived Galliformes and Columbiformes, along with the smallest Palaeognathes, share with reptiles a low ratio of 1.5 neurons in the pallium to every neuron in the rest of brain. In contrast, most bird species in the dataset have a significantly ratio of ca. 3 neurons in the pallium to every neuron in the rest of brain (Figure 5B, Table S14). Remarkably, owls (Strigiformes) have on average 12 neurons in the pallium for every neuron in the rest of brain, on par with primate species in the dataset (Table S14).

Analysis of the scaling of numbers of neurons across structures reveals that the ratio at which neurons are added to the cerebellum over the rest of brain is particularly well conserved across reptilian species, with on average 1.5 cerebellar neuron in Testudines and the Nile crocodile for every neuron in the rest of brain, and 0.5 neurons in the cerebellum to every neuron in the rest of brain in other reptiles - with the exception of snakes, which have only about 1 neuron in the cerebellum for every 10 neurons in the rest of brain (Figure 5C,D, Table S15). Compared to other reptiles, birds seem to have experienced a step increase to an average of 4.5±2.0 neurons in the cerebellum to every neuron in the rest of brain; the only exception is Psittaciformes, with low ratios of 1 to 3 cerebellar neurons to every neuron in the rest of brain that decrease with increasing numbers of neurons in the latter structure (Table S15).

Across small mammals, there are on average 9 neurons in the cerebellum for every neuron in the rest of brain, whereas larger mammals have increasing ratios of neurons in the cerebellum for every neuron in the rest of brain (Figure 5D, colored data points; Table S15). This scaling parallels the scaling of numbers of neurons in the cerebral cortex against the rest of brain;

as a consequence, mammalian species have a fairly constant average of 3-5 neurons in the cerebellum for every neuron in the cerebral cortex (Figure 5F; Table S16). In contrast, early-derived birds have a predominance of neurons in the cerebellum over the pallium, closer to mammals; Passeriformes have similar numbers of neurons in the cerebellum and pallium; Psittaciformes have a prevalence of cerebellar over pallial neurons; and Strigiformes, like reptiles, have several times more neurons in the telencephalon than in the cerebellum (Figure 5F, Table S16).

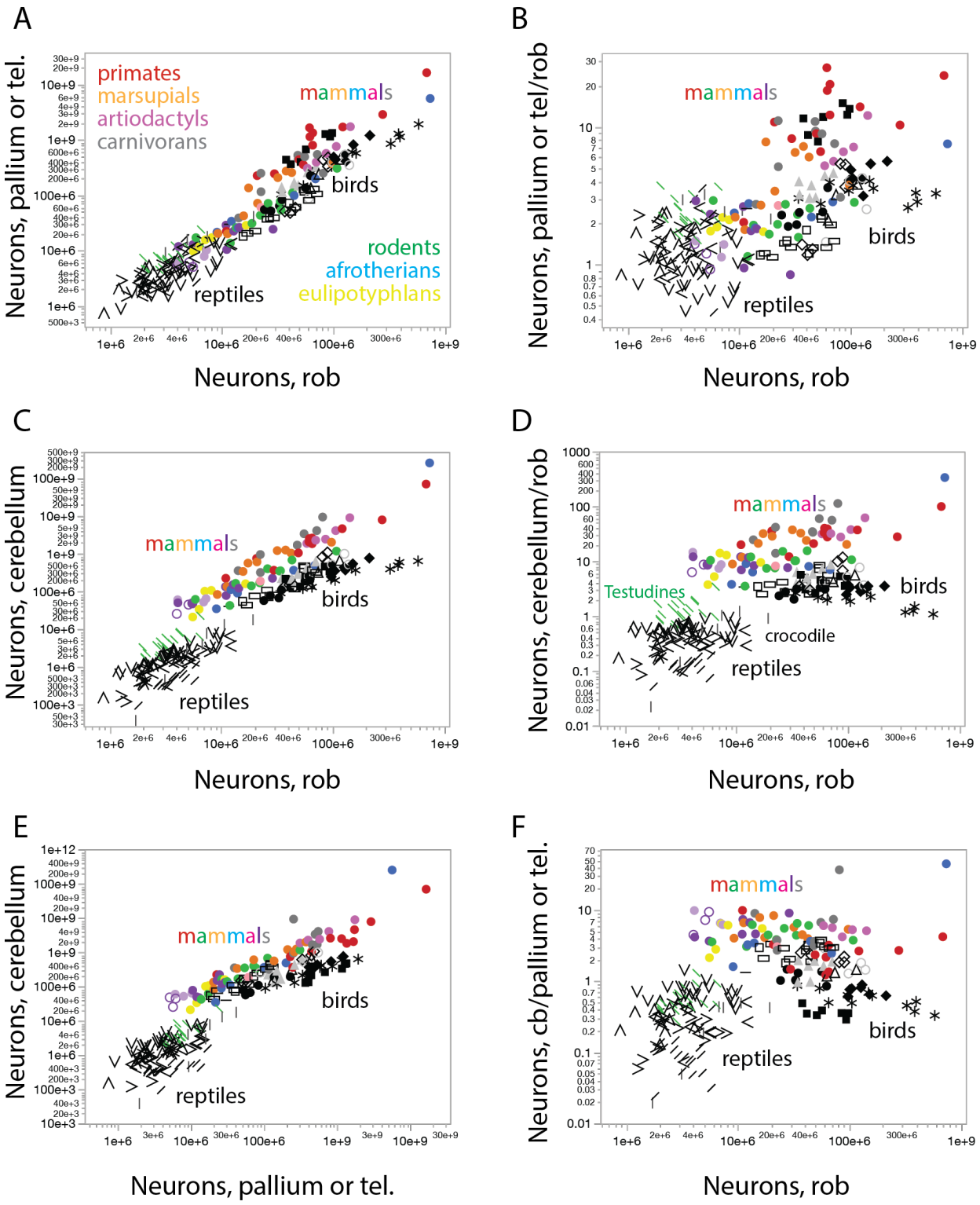

Figure 5. Scaling of numbers of neurons across structures defines clades of amniotes. A, **B,** the pallium or telencephalon gains neurons coordinately with the rest of brain across reptiles, birds, and all small mammals, while some large mammals, with larger numbers of neurons in the rest of brain, have

significantly increased numbers of pallial neurons (primates, red; artiodactyls, lavender; carnivorans, gray; marsupials, orange). Power functions and clade averages are listed in Tables S11 and S14. **C**, **D,** the cerebellum gains neurons in clade-specific relationships with the rest of brain across reptiles, birds, and mammals, while some large mammals, with larger numbers of neurons in the rest of brain, have significantly increased numbers of pallial neurons (primates, red; artiodactyls, lavender; carnivorans, gray; marsupials, orange). Power functions and clade averages are listed in Tables S12 and S15. **E**, **F:** as a result of the parallels between the distributions shown in (A, B) and (C, D), the ratio between cerebellar and pallial (or telencephalic) neurons does not scale significantly with numbers of neurons in the rest of brain across reptiles and birds, and is fairly constant at a higher value across mammalian species. Interestingly, this ratio is higher in early-derived birds than in later-derived birds. Power functions and clade averages are listed in Tables S13 and S16.

Taking all these ratios into consideration, and using the number of neurons in the rest of brain of each species as an equalizer to assess the distribution of neurons across brain structures, reveals that each of the three amniote clades has its signature pattern of distribution of neurons in the brain, illustrated in Figure 6. Modern reptiles have brains that vary by one order of magnitude in numbers of neurons in the rest of brain, with about half as many neurons in the cerebellum; and a fairly steady proportion of neurons between the telencephalon and cerebellum, with a slight (1.4-fold) predominance of neurons in the telencephalon over the rest of brain. The exception are snakes, with a diminutive number of neurons in the cerebellum for their numbers of neurons in the rest of brain; and turtles and crocodilians, with increased numbers of neurons in the cerebellum and telencephalon over the rest of brain (Figure 6, center).

In comparison, modern birds have brains characterized by a jump to a steady average of 4.5 neurons in the cerebellum to every neuron in the hindbrain (with the exception of the late-derived Psittaciformes, which have only about half as many neurons in the cerebellum). While the cerebellum/rest of brain proportion remains steady, the ratio between numbers of neurons in the bird pallium and rest of brain are clade-specific, ranging from a reptile-like 1.5 in early-derived birds to 12 in owls, but averaging 3 pallial neurons per neuron in the rest of brain in most bird clades, including Passeriformes and Psittaciformes (Figure 6, bottom). This in in stark contrast to the pattern that defines mammalian brains, where cerebral cortex and cerebellum

gain neurons very rapidly, and coordinately, over the rest of brain, as described previously (Herculano-Houzel, 2010; Figure 6, top).

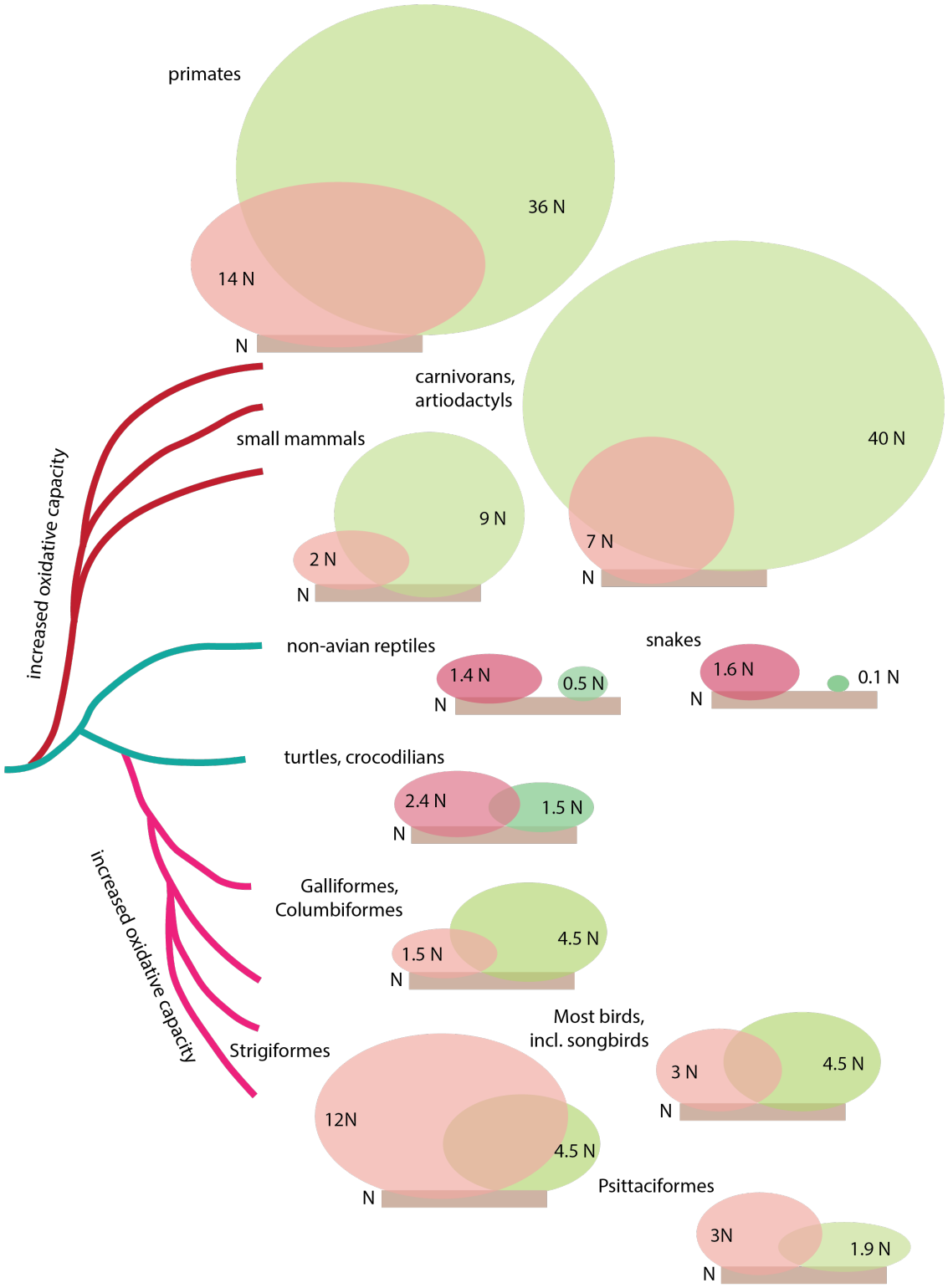

Figure 6. Signature ratios of numbers of neurons across structures describe the brains of different amniote clades. The schematics in varying sizes represent the rest of brain (tan rectangle), telencephalon (red) and cerebellum (green); the surface area of each structure is proportional to its number of neurons (N). All schematics are scaled to a similar number of neurons in the rest of brain; in this way, the surface area of each brain part represents the relative number of neurons in that structure compared to the rest of brain. The schematics illustrate that reptilian brains are characterized by modestly larger numbers of neurons in the telencephalon compared to the rest of brain, and fewer neurons in the cerebellum (green lines). Birds (pink lines), with increased oxidative capacity, diverged away from reptiles with a step increase to a larger ratio of 4.5 neurons in the cerebellum for every neuron in the rest of brain, followed in most bird clades (other than the early derived Galliformes, as well as Columbiformes) by an increase to on average 3 neurons in the pallium to every neuron in the rest of brain, and reaching a peak in Strigiformes. Independently increased oxidative capacity occurred in mammals with a different brain signature of an increased average of 4 cerebellar neurons for every pallial neuron in all extant mammals, while the ratio of pallial/rest of brain neurons remained low at ca. 2 in small species, but increased in carnivorans, artiodactyls, large marsupials, and reached peak values in primates.

Predictions for early reptiles and mammaliaformes

The assumption of parsimony suggests that the similarities and continuities in the neuronal scaling rules observed between most reptilian and mammalian species (Figures 2-4) reflect shared scaling rules that also applied to the common ancestors to these extant species. The data above show that extant reptiles and mammals share not only the neuronal scaling relationships for the telencephalon (Figure 2) and rest of brain (Figure 4), but, importantly for predictive purposes, also the scaling relationship between the mass (Figure S9) and numbers of neurons (Figure 5) in these two structures. Thus, using the present findings, one can predict that the neuronal scaling rules that apply similarly to the telencephalon, and to the rest of brain, of modern mammals and reptiles can be extended to their shared ancestors.

Expressing the neuronal scaling rules that putatively applied to ancestral amniotes as a function of brain mass is informative because the advent of high-resolution 3D computerized tomography has allowed for the size of the brain in fossil species to be estimated from their endocasts (Macrini, 2006). Writing the neuronal scaling rules that apply to ancestral amniotes as a function of brain mass thus allows the estimation of the numbers of neurons that composed

those early brains. Figure S11 shows the neuronal scaling relationships that apply jointly to the cerebral cortex of small extant mammalian species and to the telencephalon of extant reptiles excluding turtles and crocodiles. Across these 122 species in the dataset, the number of cortical (or telencephalic) neurons can be predicted from brain mass according to the equation $N_{tel} = e^{16.609\pm0.040} M_{br}^{0.719\pm0.021}$ ($p<0.0001$) with an r^2 value of 0.906 (Figure S11A). That is, over 90% of the variation in the number of cortical (in mammals) or telencephalic (in reptiles) neurons in extant species as distinct as ectothermic reptiles and endothermic mammals can be predicted from brain mass. Similarly, across the same 122 species, the number of neurons in the rest of brain can be predicted from brain mass according to the equation $N_{rob} = e^{16.087\pm0.030} M_{br}^{0.570\pm0.016}$ ($p<0.0001$) with an r^2 value of 0.913 (Figure S11B).

In contrast, the relationship between numbers of cerebellar neurons and brain mass differs strikingly between ectothermic reptiles and endothermic mammals (as well as birds). Here, two markedly different scaling relationships apply across 70 ectothermic reptiles (minus Serpentes, Testudine and Nile crocodile) and the mammalian clades comprised of 34 small species in the dataset: $N_{cb} = e^{15.593\pm0.133} M_{br}^{0.807\pm0.064}$ ($p<0.0001$, $r^2 = 0.699$) and $N_{cb} = e^{18.294\pm0.052} M_{br}^{0.644\pm0.035}$ ($p<0.0001$, $r^2 = 0.913$), respectively (Figure S11C). The relationship between predicted and measured numbers of neurons across the same species is depicted in Figure S11D-F, which shows that brain mass can be used to make accurate predictions of numbers of neurons in the main divisions of the brain of living reptiles and small mammals.

It follows from the excellent fit between actual numbers of brain neurons and estimates predicted from brain mass using the scaling functions in Figure S11 that the numbers of neurons that composed the telencephalon and rest of brain of early amniotes can be predicted directly from their estimated brain mass from reconstructed endocasts of fossil skulls. As to the cerebellum, however, the clear shift in the neuronal scaling rules that apply between mammals and reptiles means that inferring the neuronal scaling rules that applied to early mammaliaformes requires further evidence from the relationship between body mass and cerebellar mass to infer what neuronal scaling rules applied to early mammaliaform species: whether the allometry that describes ectotherms like the modern reptiles, or endotherms like modern mammals. Importantly, what allometric rules applied to the cerebellum of fossil early

amniote species can be inferred by the different scaling relationship between the mass of the cerebellum and that of the cerebral cortex (or telencephalon) and the rest of brain across extant reptiles and mammals (Figure S9). For the sake of the current estimates, I will use the assumption that early mammaliaformes, with their relatively enlarged cerebella (Kielan-Jaworowska et al., 2004), already had numbers of neurons that conform to the scaling rules that apply to modern, endotherm mammalian species.

Using the equations above, depicted in Figure S11, and applying them to data on estimated brain volume (assumed to equal brain mass, using a specific density of brain tissue of 1 g/cm^3) from endocast reconstructions that excluded the olfactory bulbs in mammaliaformes, or that had barely distinguishable olfactory bulbs in cynodonts and other early Therapsid taxa (Table S17; references therein), I could predict the numbers of neurons that composed the brain of early amniote species. The results are listed in Table S17 and shown in Figure 7, plotted against estimated body mass for each species solely for illustration purposes. Analysis of the estimated numbers of neurons that composed the brains of early amniotes indicate, for a given body mass, a clear shift from modern reptile-like numbers of neurons in the telencephalon, cerebellum and rest of brain of early therapsid species in the Permian and Triassic to modern mammal-like numbers of neurons in the Eocene, with intermediate numbers in species living during the Cretaceous and Paleocene (Figure 7). Of note, *Hadrocodium wui*, considered the earliest mammaliaform (Luo et al., 2001), from the Jurassic period, had an estimated 14.03 million neurons in the brain, 1.6 million neurons of which located in the telencephalon, fewer than in living mammals and on par with the similarly small Sumatran flying dragon (*Draco sumatranus*, which however has far fewer neurons in the cerebellum and thus in the brain as a whole, barely exceeding 5 million; Kverkova et al., 2022). *Morganucodon*, a larger mammaliaform that also lived during the Jurassic, had an estimated 52.32 million brain neurons, 6.9 million of which in the telencephalon, comparable to microbats in the dataset – although *Morganucodon* had a body mass estimated at ca. 5 times the body mass of small bats with similarly small numbers of cortical neurons (Herculano-Houzel et al., 2020). The largest Jurassic mammaliaform in the dataset, *Triconodon mordax*, had the body mass of a hamster but the predicted number of cortical

neurons, 13 million, found in a laboratory mouse of ¼ the body mass (Herculano-Houzel et al., 2006).

In Cretaceous therapsids of known brain volume, the range of numbers of cortical neurons is expanded compared to Jurassic species: while the lower values remain at 6-7 million cortical neurons (in the multituberculate *Kryptobaatar* and the mammal *Kennalestes*), the upper values extend to 118 million cortical neurons in the allotherian *Vintana sertichi*, comparable to the 111 million cortical neurons found in the modern agouti *Dasyprocta primnolopha*, although the Cretaceous animal weighed 6.8 kg and the modern agouti, only 2.8 kg (Herculano-Houzel et al., 2006; Table S17). In the Paleocene, the upper end of the range expanded further to reach 316.5 million cortical neurons in the pantodontan *Leptolambda schmiditi*, of 256 kg body mass (Table S17) – similar to the 306 million cortical neurons found in the much smaller modern capybara, at ca. 47 kg (Herculano-Houzel et al., 2006).

Eocene mammals attained even larger numbers of cortical neurons in bodies that were closer in size, but still larger, than modern mammals of similar numbers of cortical neurons. The largest estimated number of cortical neurons in the dataset belongs to *Tetheopsis ingens*, of the stem mammalian taxon Dinocerata, with 1.1 billion cortical neurons – about 1/5 the number of cortical neurons of the African elephant (Herculano-Houzel et al., 2014) - in a body of 6 tons (Table S17), even larger than the 4-5 tons of the modern African elephant. In contrast, the Eocene mammals with the fewest cortical neurons, the chiropterans *Palaeophyllophora quercyi* and *P. oltina*, had an estimated 8-10 million cortical neurons in bodies of 24-36 g, on par with the modern microchiropteran *Cardioderma cor*, with 11 million cortical neurons in a body of 26 g (Herculano-Houzel et al., 2020). All estimates are listed in Table S17.

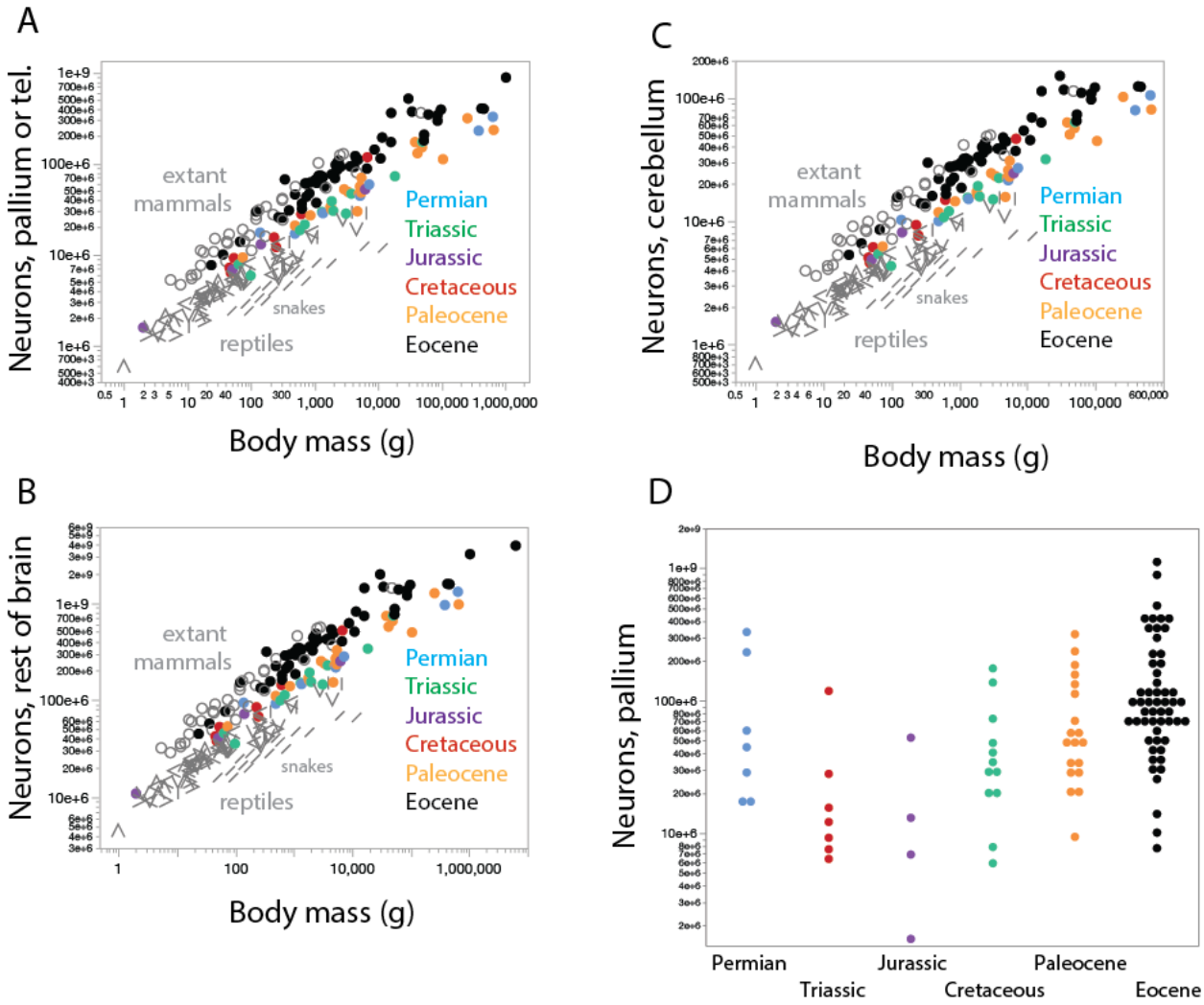

Figure 7. Predicted neuronal composition of the brains of fossil mammaliaform species. Note that for a given body mass, numbers of neurons in all parts of the brain (telencephalon or pallium, **A**; rest of brain, **B**, cerebellum, **C**) increase from the earliest species in the Permian/Triassic to the later species in the Eocene. **D,** In contrast, when body mass is not a confounding variable, the range of the distribution of inferred numbers of pallial neurons in fossil therapsid species appears to decrease from Permian to Jurassic periods, then increase progressively until the Eocene. Data listed in Table S17.

Discussion

Here I show that while there is very little overlap in numbers of brain neurons between ectothermic amniotes (reptiles) and endothermic amniotes (birds and mammals), there is remarkable continuity between reptilian and most mammalian species in the allometric relationship between numbers of neurons in telencephalic and "rest of brain" structures and the mass of these structures, with a shared decrease in neuronal density between the two clades as these structures gain neurons. In the cerebellum, in turn, parallel scaling rules apply between ectothermic and endothermic amniotes, indicative of grade shifts as the cerebellum jumped to larger numbers of neurons in endothermic species while retaining the scaling of neuronal densities, and therefore average neuronal cell size with increasing numbers of neurons (Mota and Herculano-Houzel, 2014).

Under the principle of parsimony, the shared neuronal scaling rules between living mammals and reptiles indicate that those rules already described the neuronal composition of stem amniote species ancestral to synapsids and diapsids. I show that applying those rules, and assuming that stem amniotes were ectothermic (Nespolo et al., 2011) and thus had reptile-like scaling of cerebellar mass with numbers of cerebellar neurons, the neuronal composition of the brains of fossil therapsids, mammaliaforms and early mammals can be inferred from reported brain mass estimates obtained from micro-CT of the cranial cavity. The same scaling rules can be applied in future studies to infer the neuronal composition of the brains of fossil reptile species; in a similar study, I have used the putative ancestral neuronal scaling rules that applied at the origin of birds to estimate numbers of neurons in dinosaur and pterosaur species (Herculano-Houzel, submitted). The numbers obtained here indicate that the earliest mammals of the Jurassic had fewer telencephalic neurons than the smallest modern species, but over time, both the lower and the upper ends of the range progressively increased, reaching modern numbers of neurons for body mass in the Eocene. In comparison, the modern range of mammalian body masses is already found in fossils of the Paleocene, showing that mammalian evolution was characterized by "brawn before brains", and not by a concerted increase in body and brain masses (Bertrand et al., 2022). However, while that study suggested that larger brains evolved later under positive selective pressure because of the cognitive advantage that they posed, I favor

an alternate interpretation, focused on possibilities and opportunities. The analysis of numbers of telencephalic neurons estimated by brain mass untainted by body mass, shown in Figure 7D, indicates that large brains with moderately large numbers of telencephalic neurons similar to those found in modern cats and dogs already occurred in Permian therapsids such as *Moschops* (231 million neurons) and *Struthiocephalus* (329 million neurons; Table S17). The ensuing decrease in brain mass and range of estimated numbers of telencephalic neurons towards an apparent minimum in the Jurassic period (driven by the diminutive Jurassic fossil *Hadrocodium*; Rowe et al., 2011) coincides with the rise of large dinosaurs that came to dominate land habitats in the Mesozoic (Brusatte, 2018). It seems more likely that the factors behind what range of numbers of brain neurons and brain mass were found at any period were first and foremost biological possibility (for instance, depending on rate of energy intake, which increases together with body mass; Fonseca-Azevedo and Herculano-Houzel, 2012) and opportunity (which depends on environmental conditions and competition with other species), before any considerations of "need" or "advantages". Thus, I favor a data-based account of mammalian evolution in which moderately large, modern mammal-like numbers of brain neurons, and thus brain mass, were already possible very early, in large Permian endothermic species that could ingest proportionately large amounts of food; decreased in early therapsids as these species faced the rise of dinosaurs, and as smaller mammals, which could only afford small numbers of brain neurons, had a survival advantage over larger mammals; then increased back once larger-bodied mammals became once again viable after the K-Pg mass extinction that obliterated dinosaurs (Alvarez et al.,1980; Brusatte, 2018). In this scenario, brains with more neurons evolved not because they were advantageous (for species with fewer neurons, that is, reptiles and small mammals, were not replaced), but simply because they were finally possible.

Importantly, the story of increased numbers of brain neurons in mammalian brains after the K-Pg is not simply the story of the evolution of endothermy, one of the defining events at the origin of mammals in the Permian, because endothermy also defines birds, in contrast to other reptiles, and bird brains have very different neuronal scaling rules compared to the similarly endotherm mammals. While birds and mammals share the increased oxidative and cardiovascular capacities that allow endothermy (Nespolo et al., 2011; Hillman et al., 2013), they

do not share the rules that govern the neuronal composition of their brains. Rather, I propose that the "invention" of increased oxidative and cardiovascular capacities, which also allowed endothermy, made larger brains affordable that developed in bigger bodies which in turn allowed for increased energetic intake (Herculano-Houzel, 2015). Thus, I propose that endothermy itself serves not as cause, but as an indicator of the increased oxidative and cardiovascular capacities that created new possibilities for the amniote brain, namely by allowing larger numbers of neurons to be supported during the development of what became mammals and birds, independently (Nespolo et al., 2011).

It is remarkable that, from what was once presumably a single set of neuronal scaling rules that applied to stem amniotes, the shift to endothermy occurred with different changes in the brain of mammals and birds. With endothermy, mammals simply expand the range of numbers of telencephalic and rest of brain neurons compared to reptiles while maintaining the predicted drop in neuronal density and thus progressive increase in average neuronal cell size with larger numbers of neurons. Birds, in contrast, seem to "jump" towards larger numbers of neurons in all brain structures compared to other reptiles, while maintaining the same range of neuronal densities (and thus average neuronal cell size) rather than continuing the trend towards increasing neuronal cell sizes as in mammals. On the one hand, that endothermy was accompanied by larger numbers of brain neurons in extant birds and mammals, compared to reptiles, can be explained by the increased oxidative capacity that seems to power endothermy (Bennett and Ruben, 1979; Hillman et al., 2013). We have recently shown that the energetic economy of the brain is supply-limited, rather than demand-driven, and depends on rates of delivery of oxygen that are constrained by rates of blood flow and capillary density (Herculano-Houzel and Rothman, 2022). Thus, the increased mitochondrial oxidative capacity (Nespolo et al., 2011) that would have allowed for faster heart rates and increased blood flow in endotherms could by way of these mechanisms have sustained brains composed of larger numbers of neurons in both mammals and birds.

How come, then, the distinct patterns of addition of brain neurons to mammals and birds, with decreasing neuronal densities in the former (compared to reptiles) but similar neuronal densities in the latter? The higher densities of non-neuronal cells in all brain structures of birds

compared to mammals raise the possibility that capillary densities have become distinctively larger in the brains of birds. Only further studies will establish whether the difference applies to astrocytes, oligodendrocytes, microglial cells, or vasculature, but any clade-specific increases in capillary densities in the brain, if they happened, would have important consequences for the range of possibilities of brain cellular composition. We recently found that relatively uniform capillary densities in the rat brain make it so that in sites with larger densities of neurons, there is less energy available per individual neuron (Ventura-Antunes et al., 2022). In mammals, the sharply decreased densities of neurons in brain structures that gained more neurons (and thus became larger) offers the advantage, from the viewpoint of single neuron physiology, of increased energy availability per neuron (which may still not be sufficient to compensate for the increased cost of larger neuronal cell size; Ventura-Antunes et al., 2022). With mammal-like capillary densities in the brain, the higher neuronal densities characteristic of bird brains might impose extreme restrictions on neuronal activity and not be viable. I speculate, therefore, that a putative increase in capillary density in the brains of newly-endothermic bird species may have been one of the watershed inventions that originated the densely packed neurons that are characteristic of bird brain structures. Comparative studies of capillary density across reptilian, bird, and mammalian brains of similar mass or similar neuronal densities will be necessary to test this hypothesis.

Another possible source for the difference between brain composition in the independently endothermic mammals and birds is the fact that prenatal development is constrained by a hard shell in birds, but not in most mammals. Strikingly, the neuronal scaling rules that apply to the cerebellum are similar across birds and mammals: in both amniote clades, this structure gains most of its neurons and attains its characteristic circuitry and basic morphology only after birth (Goldowitz and Hamre, 1998), when brain and body mass are no longer constrained by a hard-shelled egg. In contrast, the pallium and rest of brain of birds form inside the egg, presumably strongly constrained by the volume contained by the shell. It thus follows that, all else remaining equal, more neurons formed in bird embryos developing withing those hard bounds will necessarily be smaller neurons compared to mammalian embryos developing similar numbers of neurons in the much less constrained environment of the uterus,

which is a testable hypothesis. Further, I speculate that, simply due to the mechanical constraint imposed by the eggshell, the evolution of altriciality in birds, favoring brain over body development inside the egg and thus the formation of larger and larger numbers of neurons at the cost of leaving body development incomplete, would cause smaller average neuronal cell size and thus higher neuronal densities in the pallium and rest of brain (but not cerebellum) of birds compared to mammals, and to precocial birds. In support of this hypothesis, high neuronal densities in the pallium and rest of brain in the present dataset are found exactly in the most altricial bird clades (Passeriformes, Psittaciformes, and Strigiformes), whereas the lowest neuronal densities are found in the most precocial clades (Galliformes, Palaeognathae, Anseriformes and Columbiformes; Chen et al., 2019). The hypothesis that different tiers of neuronal densities across bird clades are related to different levels of precocial or altricial development can be tested by expanding this dataset to determine for instance whether precocial Gruiformes have the predicted low neuronal densities in the pallium and rest of brain. Similarly, altricial and semi-altricial Strisores are predicted to have high neuronal densities, and the semiprecocial skunk bird *Opisthocomus hoazini*, an outlier amongst altricial Inopinaves, should have the low neuronal densities of other precocial species rather than the high neuronal densities expected for its clade (Chen et al., 2019).

The analysis of scaling of mass and numbers of neurons across structures reveals another key difference in the independent origins of bird and mammal endothermic lineages of amniotes. While the telencephalon gains mass as a uniform function of rest of brain mass across all extant amniotes, both endothermic lineages are distinguished from ectothermic reptiles by their enlarged cerebellum relative to the rest of brain. The concerted increase in relative mass of the cerebellum in both independently arisen endothermic lineages is consistent with the hypothesis postulated above that higher oxygen availability combined with higher oxidative capacity would have allowed for larger brains to be supported in endothermic species. Still, the distribution of mass across brain structures does not distinguish between birds and mammals.

What does clearly distinguish the two clades of endothermic amniotes from each other and from the ectothermic amniotes is the distribution of numbers of neurons across brain structures. Considering the shared relationships in the light of evidence that stem amniotes were

ectothermic (Newham et al., 2022), it is parsimonious to postulate that the scaling rules that apply across brain structures in modern reptiles are conserved from stem amniotes. In this case, birds appeared with a 3-fold step increase in numbers of neurons in the cerebellum for every neuron in the rest of brain compared to the closest living non-avian reptilian relatives, turtles and crocodiles (Figure 6). The new ratio of 4.5 neurons in the cerebellum to every neuron in the rest of brain remains a stable signature of the bird brain, except for Psittaciformes, in which this ratio drops progressively with increasing numbers of neurons, resulting in an average 1.9 neurons in the cerebellum to every neuron in the rest of brain. Developmentally, the cerebellum is part of the hindbrain (Puelles et al., 2013), which is a key component of the "rest of brain". Thus, I propose that birds arose with a modification(s) in the developmental program of the hindbrain that resulted in the generation of 3-fold larger numbers of neurons in the cerebellum. Mechanistically, that could be implemented through two doublings of the numbers of early progenitor cells that give rise to the cerebellum in quantal developmental units, followed by apoptosis (Herrup, 1986). At the same time, the pallium, which originates from the dorsal cap of the second neuromere (Puelles et al., 2013), seems to gain neurons fairly independently from the rest of brain in birds. This freedom in addition of numbers of neurons between pallium and cerebellum in bird species is consistent with the lack of major projections linking the two structures in birds, as the bird cerebellum is predominantly connected to brainstem structures (Gutieérrez-Ibáñez et al., 2018), which, on top of their shared developmental origin, is presumably sufficient to account for the concerted addition of numbers of neurons to the cerebellum and rest of brain across most bird species. It remains to be determined whether the strong link between numbers of neurons formed in the rest of brain and cerebellum of birds is associated with the advent of any major bird-specific neuronal pathways between the two parts of the brain, or simply constitutes a quantitative variation, made possible by increased oxidative and cardiovascular capacity, of a qualitatively similar organization to the rest of brain and cerebellum of reptiles.

The signature proportion of brain neurons in mammals, on the other hand, is a remarkably constant ratio of ca. 4 neurons in the cerebellum for every neuron in the cerebral cortex, both of which gain neurons rapidly and in variable proportions to the numbers of neurons

in the rest of brain (Figure 6; Herculano-Houzel, 2010; Herculano-Houzel et al., 2014a). While the mammalian cerebellum is a hindbrain structure, derived from neuromeres r0-r1 exactly like in birds (Puelles et al., 2013), mammals differ from birds in that the former exhibit massive connectivity between the cerebral cortex and cerebellum, mediated by the pontine nuclei of the hindbrain, and back to the cortex through the ventral thalamus (Ramnani, 2006). I thus propose that a key defining innovation at the evolutionary origin of mammals was the formation of the dominant cortico-pontine-cerebellar pathway, reciprocated by cerebello-thalamo-cortical projections, which, combined with the increased oxidative and cardiovascular capacities that allowed for increased numbers of neurons to be supported (as well as for the evolution of endothermy), led to the concerted scaling of numbers of neurons in the cerebral cortex and cerebellum that I postulate to define mammals. This hypothesis cannot at present differentiate between the possibilities that increased numbers of neurons in the cortex drove increased numbers of neurons in the cerebellum, or that conversely, increased numbers of neurons in the cerebellum drove increased numbers of neurons in the cerebral cortex. However, since numbers of cerebellar neurons are only established after birth, once adult numbers of neurons in the cerebral cortex have already been attained (Goldowitz and Hamre, 1998), it seems more likely that, if numbers of neurons in one structure drive the formation of proportional numbers of neurons in the others, the driver is the cerebral cortex.

The proposition that the advent of a strong anatomical and functional connection between cerebral cortex and cerebellum lies at the origin of mammalian brains is compatible with the finding that while the expansion of the olfactory bulb is a very obvious and diagnostic development in the evolution of modern mammals (Rowe et al., 2011), it is accompanied by expansion of the lateral hemispheres of the cerebellum (Kielan-Jaworowska et al., 2004). Because the predicted increased in numbers of cerebellar neurons in coordination with increased cerebral cortical neurons at the origin of mammals (Figure 5) is accompanied by an increase in cerebellar mass compared to both the mass of the rest of brain and the mass of the cerebral cortex (Figure S9), relative cerebellar mass defined in this manner can be used as a diagnostic feature of endothermic, mammalian brains. The development of segmentation methods that will make it

possible to estimate the volume of the cerebellum in endocasts of fossil species should allow for this new line of investigation to be explored.

While similarities and shared differences across clades reveal patterns that are informative and even diagnostic of what constitutes a reptilian, bird, or mammalian brain, clade-specific features are also enlightening of the mechanisms of biology and evolution. In the present dataset, Serpentes are the obvious outlier group amongst reptiles, with fewer cerebellar neurons than expected for both their body mass and for their numbers of neurons in the rest of brain. The obvious explanation for the fewer cerebellar neurons than expected for body mass is that Serpentes are characterized by their extremely elongated body, in which case the more biologically correct statement would be that Serpentes have larger body mass than expected for their brain structures and numbers of neurons – which seems to be the case for both the cerebellum and rest of brain (Figure S7). However, the finding that Serpentes do have fewer cerebellar neurons than expected for a generic reptile with their numbers of rest of brain and pallial neurons (Figure 5C, E) calls for a clade-specific feature that would have either driven a reduction of numbers of cerebellar neurons or allowed it to suffice. One possibility is the loss of limbs, which should lift the imposition on cerebellar processing that otherwise mediates the stabilization of the sensory surfaces of the limbs through fine motor control. This possibility is consistent with the other extreme in neuronal composition that is the cerebellum of the African elephant, which harbors 12 times the predicted number of neurons for a generic mammal, which we have speculated that might be associated to fine sensorimotor processing of the uniquely large appendage, the trunk (Herculano-Houzel et al., 2014b), mediated by a massively enlarged trigeminal ganglion (Pukart et al., 2022).

Owls (Strigiformes) are another interesting outlier group, with the largest ratios of pallial neurons per neuron in the rest of brain amongst birds, averaging 12, on par with some primates (Table S14), which seems to be due to an expansion of the pallium that still conforms to the neuronal scaling rules that apply to other late-derived bird clades (Figure 2). As a consequence, the exceptionally large ratio of pallial/rest of brain neurons in Strigiformes is reflected in a similarly exceptionally large ratio of pallial/rest of brain mass (Figure S9). Importantly, whatever the number of rest of brain neurons, the large numbers of neurons mean that the pallium of owls

has a presumably enlarged signal processing capacity that should be on par with that of crows (Kabadayi et al., 2016), which we have recently showed to be associated with large numbers of associative pallial neurons rather than pallial mass (Ströckens et al., 2022). Comparative studies of behavioral flexibility across bird clades beyond Passeriformes should enlighten the issue of whether increased numbers of pallial neurons do bring about increased cognitive capacity.

I have made a point in this study to ignore body mass, even though it is obviously a relevant variable in terms of ecology, energy consumption and physiology. Part of the reason is that the original analysis of the same dataset already focused on relationships between brain mass and numbers of neurons to body mass (Kverkova et al., 2022), and established that birds and mammals evolved with increased numbers of brain neurons for their body mass compared to reptiles and ancestral species. Most importantly to this author, however, is the reiterated demonstration that there is no obligatory scaling relationship between body mass and number of neurons in any brain structure, specially the rest of brain, which directly operates the body (Burish et al., 2010; Herculano-Houzel et al., 2015a,c; Ngwenya et al., 2016). If that is the case, then body mass cannot be used as a universal predictor of brain scaling, and its use as a normalizer is unwarranted and should be discontinued, for there is much more information to be gained in the direct analysis of variables pertaining to brain size and composition without contamination by the confounding factor that is body mass. Naturally, the finding that brain mass increases independently in birds and mammals for a same body size with the advent of endothermy is fundamental to the understanding of how endothermy is transformative; but increased body mass should only be treated as a cause or driver of diversity where mechanistically warranted, such as through the ingestion of more energy per unit time allowed by increased body mass (Fonseca-Azevedo and Herculano-Houzel, 2012; Herculano-Houzel, 2015). Importantly, I have recently showed that body mass is not a direct predictor of life history variables such as age at sexual maturity and maximal longevity across warm-blooded amniotes; numbers of pallial neurons are, and with a much higher r^2 of 0.74 (Herculano-Houzel, 2019). The finding that the pace of life slows down with increasing numbers of pallial neurons offers a new fundamental insight into the evolution of warm-blooded amniotes: namely, that larger numbers of pallial neurons in birds and mammals compensate for the shortening of lifespan that comes

with endothermy (de Magalhães and Costa, 2009), however that happens. In this scenario, what lifespan the increased metabolic capacity of endotherms takes away, it provides back through the now affordable larger numbers of pallial neurons. It will be interesting to work out the mathematical (im)balance of this trade-off.

Finally, the unequivocal continuity shown here between the cousin clades of mammals and reptiles in the relationship between numbers of neurons and structure mass of the telencephalon or cerebral cortex should hopefully put to rest any lingering remnants of the incorrect, unwarranted, yet still popular notion of a "triune brain" with a "mammalian neocortex" expanding over a "reptilian brain" in evolution (MacLean, 1990; Herculano-Houzel, 2016). The pallium, whether organized in visible or in cryptic layers (Stacho et al., 2020), and regardless of how much it proliferates and expands over the rest of the brain, has the same developmental origin from the dorsal cap of the second neuromere in the neural tube across different amniotes (Puelles et al., 2013). Thus, reptiles do have a pallium, which forms as a major part of a telencephalon that I show to be composed according to the same neuronal scaling rules that are shared with mammals. Conversely, the neuronal composition of the supposed "reptilian" rest of brain is also shared between reptiles and mammals. In both cases, the main difference between mammals and reptiles seems to lie in how many neurons the developing body can afford in each structure – and whether it has the increased oxidative capacity that also allows for endothermy seems to be a key factor in determining whether a modern amniote has fewer or more than 10 million neurons in its telencephalon, with all its consequences for cognitive capabilities, energetic economy, and pace of life.

References

Alvarez LW, Alvarez W, Asaro F, Michel HV (1980) Extraterrestrial cause for the Cretaceous-Tertiary extinction. Science 208, 1095-1108.

Álvarez-Carretero S, Tamuri AU, Battini M, Nascimento FF, Carlisle E, Asher RJ, Yang Z, Donoghue PCJ, dos Reis M (2022) A species-level timeline of mammal evolution integrating phylogenomic data. Nature 602, 263-267.

Bennett AF, Ruben JA (1979) Endothermy and activity in vertebrates. Science 206, 649-655.

Benoit J, Fernandez V, Manger PR, Rubidge BS (2017a) Endocranial casts of pre-mammalian therapsids reveal an unexpected neurological diversity at the deep evolutionary root of mammals. Brain Behav Evol 90, 311-333.

Benoit J, Manger PR, Norton LA, Fernandez V, Rubidge BS (2017b) Synchrotron scanning reveals the palaeoneurology of the head-butting Moschops capensis (Therapsida, Dinocephalia). PeerJ 5, e3496.

Benoit J, Legendre LJ, Tabuce R, Obada T, Mararescul V, Manger P (2019) Brain evolution in Proboscidea (Mammalia, Afrotheria) across the Cenozoic. Scientific Reports 9, 9323.

Bertrand OC, Shelley SL, Wible JR, Williamson TE, Holbrook LT, Chester SGB, Butler IB, Brusatte SL (2020) Virtual endocranial and inner ear endocasts of the Paleocene “condylarth” *Chriacus*: new insight into the neurosensory system and evolution of early placental mammals. J Anat 236, 21-49.

Bertrand OC, Shelley SL, Williamson TE, Wible JR, Chester SGB, Flynn JJ, Holbrook LT, Lyson TR, Meng J, Miller IM, Püschel HP, Smith T, Spaulding M, Tseng ZJ, Brusatte SL (2022) Brawn before brains in placental mammals after the end-Cretaceous extinction. Science 376, 80-85.

Bininda-Emonds ORP, Cardillo M, Jonew KE, MacPhee RDE, Beck RMD, Grenyer R et al. (2007) The delayed rise of present-day mammals. Nature 446, 507-512.

Boonstra LD (1968) The braincase, basicranial axis and median septum in the Dinocephalia. Ann S Afr Mus 50, 195-273.

Brusatte SL (2008) The rise and fall of the dinosaurs: A new history of their lost world. New York, HarperCollins.

Brusatte SL, O'Connor JK, Jarvis ED (2015) The origin and diversification of birds. Curr Biol 25, R888-898.

Burish MJ, Peebles JK, Tavares L, Baldwin M, Kaas JH, Herculano-Houzel S (2010) Cellular scaling rules for primate spinal cords. *Brain, Behavior and Evolution* 76, 45-59.

Cameron J, Shelley SL, Williamson TE, Brusatte SL (2018) The brain and inner ear of the early Paleocene "Condylarth" *Carsioptychus coarctatus*: Implications for early placental mammal neurosensory biology and behavior. Anat Rec 302, 306-324.

Castanhinha R, Araújo R, Júnior LC, Angielczyk KD, Martins GG, Martins RM, Chaouiya C, Beckmann F, Wilde F (2013) Bringing dicynodonts back to life: paleobiology and anatomy of a new emydopoid genus from the Upper Permian of Mozambique. PLoS One 8, e80974.

Chen C-K, Chuang H-F, Wu S-M, Li W-H (2019) Feather evolution from precocial to altricial birds. Zool Studies 58, 24.

Clark DA, Mitra PP, Wang SS (2001) Scalable architecture in mammalian brains. Nature 411: 189-193.

De Magalhães JP, Costa J (2009) A database of vertebrate longevity records and their relation to other life-history traits. J Evol Biol 22, 1770-1774.

Dos Santos SE, Porfirio J, Da Cunha FB, Manger PR, Tavares W, Pessoa L, Raghanti MA, Sherwood CC, Herculano-Houzel S (2017) Cellular scaling rules for the brain of marsupials: not as “primitive” as expected. *Brain Behav Evol* 89, 48-63.

Dozo MT, Martínez G (2016) First digital cranial endocasts of late Oligocene Notohippidae (Notoungulata): Implications for endemic South American ungulates brain evolution. J Mammal Evol 23, 1-16.

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 USA 109, 18571-18576.

Goldowitz D, Hamre K (1998) The cells and molecules that make a cerebellum. Trends Neurosci 21, 375-382.

Gutiérrez-Ibáñez C, Iwaniuk AN, Wylie DR (2018) Parrots have evolved a primate-like telencephalic-midbrain-cerebellar circuit. Sci Rep 8, 9960.

Herculano-Houzel S (2010) Coordinated scaling of cortical and cerebellar numbers of neurons. *Frontiers in Neuroanatomy* 4, 12.

Herculano-Houzel S (2015) Decreasing sleep requirement with increasing numbers of neurons as a driver for bigger brains and bodies in mammalian evolution. Proc Biol Sci 282, 20151853.

Herculano-Houzel S (2016) The human advantage: a new understanding of how our brains became remarkable. Cambridge, MIT Press.

Herculano-Houzel S (2019) Longevity and sexual maturity vary across species with number of cortical neurons, and humans are no exception. J Comp Neurol 527, 1689-1705.

Herculano-Houzel S (submitted). Theropod dinosaurs had primate-like numbers of telencephalic neurons.

Herculano-Houzel S, Lent R (2005) Isotropic fractionator: a simple, rapid method for the quantification of total cell and neuron numbers in the brain. J Neurosci 25, 2518-2521.

Herculano-Houzel S, Dos Santos S (2018) You do not mess with the glia. *Neuroglia* 1, 193-219.

Herculano-Houzel S, Rothman DL (2022) From a demand-based to a supply-limited framework of brain metabolism. Front Integr Neurosci 16, 818685.

Herculano-Houzel S, Mota B, Lent R (2006) Cellular scaling rules for rodent brains. *Proceedings of the National Academy of Sciences USA* 103, 12138-12143.

Herculano-Houzel S, Collins C, Wong P, Kaas JH (2007) Cellular scaling rules for primate brains. *Proceedings of the National Academy of Sciences USA* 104, 3562-3567.

Herculano-Houzel S, Avelino-de-Souza K, Neves K, Porfírio J, Messeder D, Calazans I, Mattos L, Maldonado J, Manger PM (2014a) The elephant brain in numbers. *Front Neuroanat* 8, 46.

Herculano-Houzel S, Manger PR, Kaas JH (2014b) Brain scaling in mammalian brain 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, Kaas JH, Miller D, Von Bartheld CS (2015a) How to count cells: the advantages and disadvantages of the isotropic fractionator compared with stereology. *Cell Tissue Research* 360, 29-42.

Herculano-Houzel S, Catania K, Manger PR, Kaas JH (2015b) Mammalian brains are made of these: A dataset on the numbers and densities of neuronal and non-neuronal cells in the brain of glires, primates, scandentia, eulipotyphlans, afrotherians and artiodactyls, and their relationship with body mass. *Brain Behav Evol* 86, 145-163

Herculano-Houzel S, Messeder D, Fonseca-Azevedo K, Araujo Pantoja N (2015c) When larger brains do not have more neurons: Intraspecific increase in numbers of cells is compensated by decreased average cell size. *Front Neuroanat* 9, 64.

Herculano-Houzel S, Cunha F, Reed JL, Kaswera-Kyamakya C, Gillissen E, Manger PR (2020) Microchiropterans have a diminutive cerebral cortex, not an enlarged cerebellum, compared to megachiropterans and other mammals. *Journal of Comparative Neurology* 528, 2978-2993.

Herrup K (1986) Cell lineage relationships in the development of the mammalian CNS: role of cell lineage in control of cerebellar Purkinje cell number. Dev Biol 115, 148-154.

Hillman SS, Hancock TV, Hedrick MS (2013) A comparative meta-analysis of maximal aerobic metabolism of vertebrates: implications for respiratory and cardiovascular limits to gas exchange. J Comp Physiol 183, 167-179.

Hopson JA (1979) Paleoneurology. In Glans C, Northcutt RG, Ulinski P (eds), Biology of the Reptilia. NY, Academic Press, pp 39-146.

Jardim-Messeder D, Lambert K, Noctor S, Marques Pestana F, DeCastro Leal ME, Bertelsen MF, Alagaili AN, Mohammad OB, Manger PR, Herculano-Houzel S (2017) Dogs have the most neurons, though not the largest brain: Trade-off between body mass and number of neurons in the cerebral cortex of large carnivoran species. *Front Neuroanat* 11, 118.

Jerison HJ (1973) Evolution of the brain and intelligence. New York, Academic Press.

Kabadayi C, Taylor LA, von Bayern AMP, Osvath M (2016) Ravens, New Caledonian crows and jackdaws parallel great apes in motor self-regulation despite smaller brains. Roy Soc Open Sci 3, 160104.

Kemp TS (2006) The origin and early radiation of the therapsid mammal-like reptiles: a palaeobiological hypothesis. J Evol Biol 19, 1231-1247.

Kielan-Jaworowska Z, Cifelli RL, Luo ZX (2004) Mammals from the age of dinosaurs: Origins, evolution, and structure. NY, Columbia University Press.

Ksepka DT, Balanoff AM, Smith NA, Bever GS, Bhullar B-AS, Bourdon E et al. (2020) Tempo and pattern of avian brain size evolution. Curr Biol 30, 2026-2036.

Kverkova K, Marhounová L, Polonyiová A, Kocourek M, Zhang Y, Olkowicz S, Stratková B, Pavelková Z, Vodicka R, Frynta D, Nemec P (2022) The evolution of brain neuron numbers in amniotes. Proc Natl Acad Sci USA 119, e2121624119.

Laas M (2015) Virtual reconstruction and description of the cranial endocast of *Pristerodon mackayi* (Therapsida, Anomodontia). J Morphol 276, 1089-1099.

Laas M, Kaestner A (2017) Evidence for convergent evolution of a structure comparable to the mammalian neocortex in a Late Permian therapsid. J Morphol 278, 1033-1057.

Luo ZX, Crompton AW, Sun AL (2001) A new mammaliaform from the Early Jurassic and evolution of mammalian characteristics. Science 292, 1535-1540.

MacLean PD (1990) The triune brain in evolution. New York, Plenum.

Macrini TE (2006) The evolution of endocranial space in mammals and non-mammalian cynodonts. PhD Thesis, University of Texas at Austin.

Macrini TE, Rougier GW, Rowe T (2007) Description of a cranial endocast from the fossil mammal *Vincelestes neuquenianus* (Theriiformes) and its relevance to the evolution of endocranial characters in Therians. Anat Rec 290, 875-892.

Maugoust J, Orliac MJ (2021) Endocranial cast anatomy of the extinct Hipposiderid bats *Pallaeophyllophora* and *Hipposideros* (*Pseudorhinolophus*) (Mammalia: Chiroptera). J Mammal Evol 28, 679-706.

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.

Nespolo RF, Bacigalupe LD, Figueroa CC, Koteja P, Opazo JC (2011) Using new tools to solve an old problem: the evolution of endothermy in vertebrates. Trends Ecol Evol 26, 414-423.

Newham E, Gill PG, Corfe IJ (2022) New tools suggest a middle Jurassic origin for mammalian endothermy. BioEssays 44, 2100060.

Ngwenya A, Patzke N, Manger PR, Herculano-Houzel S (2016) Continued growth of the central nervous system without mandatory addition of neurons in the Nile crocodile (*Crocodylus niloticus*). *Brain Behav Evol* 87, 19-38.

Norell MA, Xu X (2005) Feathered dinosaurs. Annu Rev Earth Planet Sci 33, 277-299.

Olkowicz S, Kocourek M, Lucan RK, Portes M, Fitch WT, Herculano-Houzel S, Nemec P (2016) Birds have primate-like numbers of neurons in the telencephalon. *Proc Natl Acad Sci USA* 113, 7255-7260.

Puelles L, Harrison M, Paxinos G, Watson C (2013) A developmental ontology for the mammalian brain based on the prosomeric model. Trends Neurosci 36, 570-578.

Pukart L, Tuff JM, Shah M, Kaufmann LV, Altringer C, Maier E, Schneeweiss U, Tunckol E., Eigen L, Holtze S, Fritsch G, Hildebrandt T, Brecht M (2022) Trigeminal ganglion and sensory nerves suggest tactile specialization of elephants. Curr Biol 32, 904-910.

Pusch LC, Kammerer CF, Fröbisch J (2019) Cranial anatomy of the early cynodont *Galesaurus planiceps* and the origin of mammalian endocranial characters. J Anat 234, 592-621.

Quiroga JC (1980) The brain of the mammal-like reptile *Probainognathus jenseni* (Therapsida, Cynodontia): a correlative paleo-neoneurological approach to the neocortex at the reptile-mammal transition. J Hirnforsch 21, 299-336.

Quiroga JC (1984) The endocranial cast of the advanced mammal-like reptile *Therioherpeton cargnini* (Therapsida-Cynodontia) from the Middle Triassic of Brazil. J Hirnforsch 25, 285-290.

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

Rodrigues PG, Ruf I, Schultz CL (2014) Study of a digital cranial endocast of the non-mammaliaform cynodont *Brasilitherium riograndensis* (Later Triassic, Brazil) and its relevance to the evolution of the mammalian brain. Pällaontol Z 88, 329-352.

Rowe TB, Macrini TE, Luo Z-X (2011) Fossil evidence on origin of the mammalian brain. Science 332, 955-957.

Sarko DK, Catania KC, Leitch DB, Kaas JH, Herculano-Houzel S (2009) Cellular scaling rules of insectivore brains. *Frontiers in Neuroanatomy* 3, 8.

Sigurdsen T, Huttenlocher AK, Modesto SP, Rowe TB, Damiani R (2012) Reassessment of the morphology and paleobiology of the therocephalian *Tetracynodon darti* (Therapsida), and the phylogenetic relationships of Bauroidea. J Vert Paleontol 32, 1113-1134.

Stacho M, Herold C, Rook N, Wagner H, Axer M, Amunts K, Güntürkün O (2020) A cortex-like canonical circuit in the avian forebrain. Science 369, eabc5534.

Ströckens F, Neves K, Kirchem S, Schwab C, Herculano-Houzel S, Güntürkün O (2022) High associative neuron numbers could drive cognitive performance in corvid species. J Comp Neurol 530, 1588-1605.

Sultan F (2002). Analysis of mammalian brain architecture. Nature 415, 133-134.

Ventura-Antunes L, Dasgupta OM, Herculano-Houzel S (2022) Resting rates of blood flow and glucose use per neuron are proportional to number of endothelial cells available per neuron across sites in the rat brain. Front Integr Neurosci 16, 821850.

Supplementary figures and legends

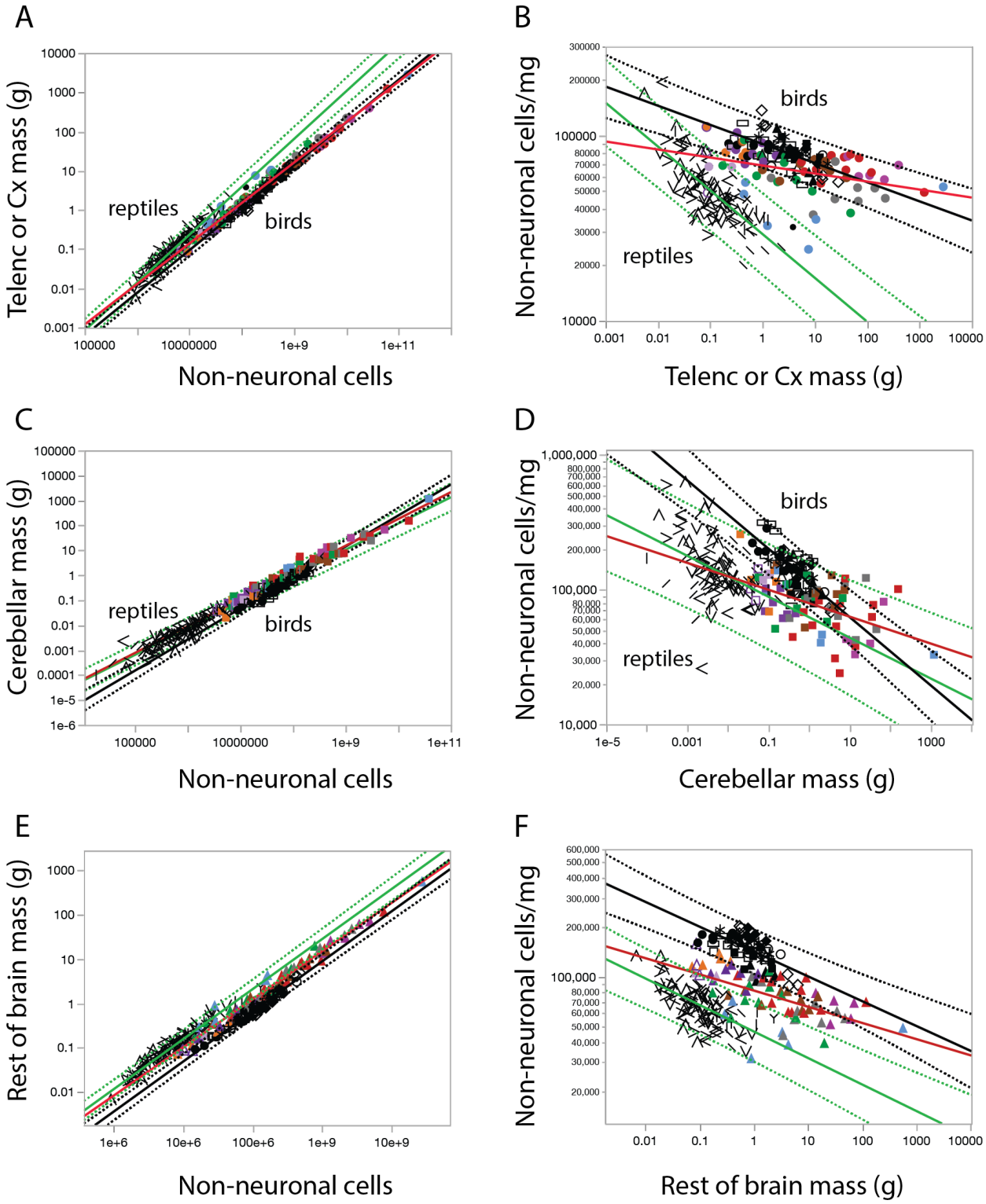

Figure S1. Scaling of density of non-neuronal cells with structure mass differs across brain structures and amniote clades. A, B, telencephalon; **C, D**, cerebellum; **E, F**, rest of brain. **A, C, E**:

scaling of brain structure mass with number of non-neuronal cells in the structure. **B, D, F**: scaling of non-neuronal cell density with structure mass. In all graphs, reptile species are represented with black open line symbols; birds, by black polygons and asterisks; mammals, by colored symbols. Power functions with 95% prediction intervals are plotted for reptiles (green), birds (black), and mammals (red). All power functions are listed in Table S1.

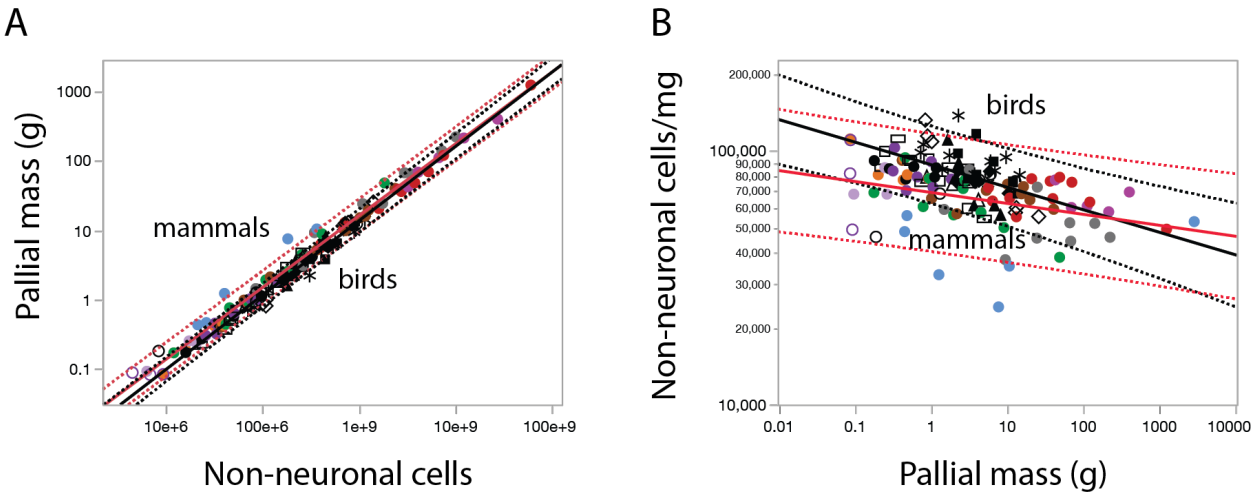

Figure S2. Mammals and birds share the scaling of pallial mass with numbers of non-neuronal cells (A) and of non-neuronal cell density with pallial mass (B). Power functions with 95% prediction intervals are plotted for birds (black) and mammals (red). All power functions are listed in Table S1.

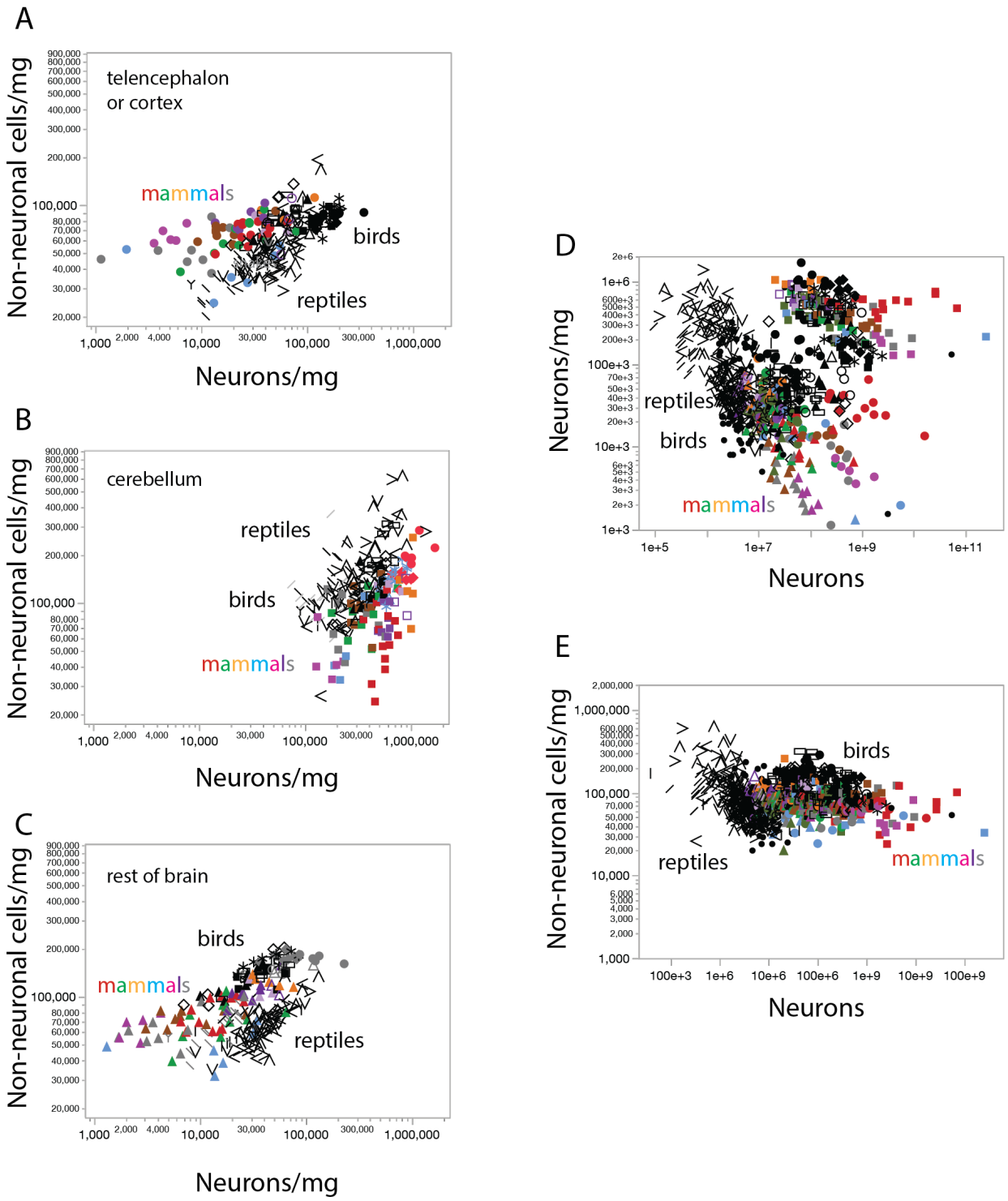

Figure S3. Neuronal cell densities vary 1,000-fold across species and structures, while non-neuronal cell densities vary only ca. 10-fold. A-C, comparison of non-neuronal and neuronal cell densities in the telencephalon or pallium (cerebral cortex; **A**), cerebellum (**B**) and rest of brain (**C**). **D**, **E**, combined dataset contrasting the enormous variation in neuronal densities across

species and structures of variable numbers of neurons (**D**) with the small variation in non-neuronal cell densities in the same structures and species (**E**).

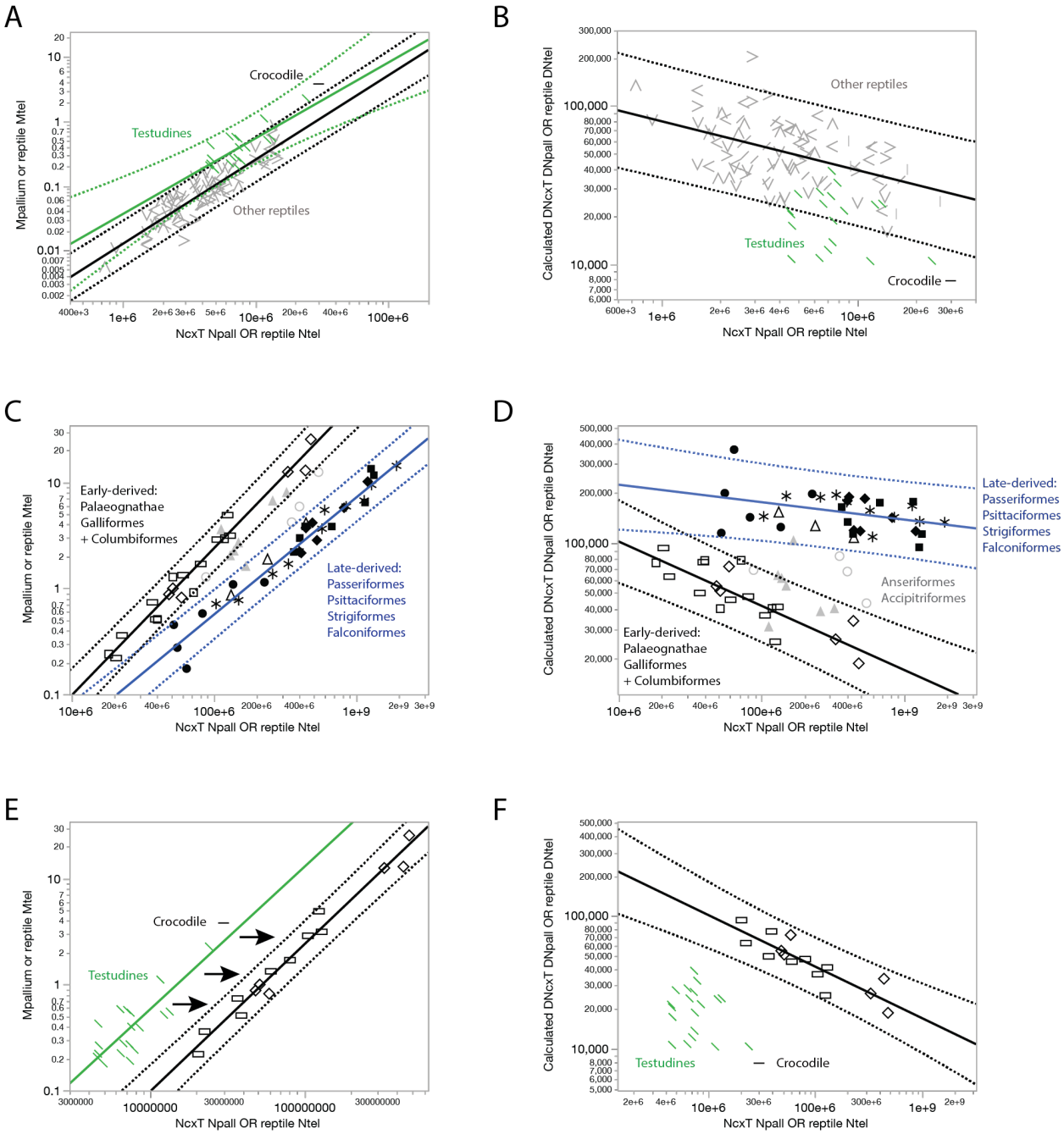

Figure S4. Neuronal scaling rules for the telencephalon of reptiles and birds. A, C, E, scaling of telencephalic mass with numbers of telencephalic neurons. **B, D, F,** scaling of neuronal density in the telencephalon with numbers of telencephalic neurons. **A, B,** Testudines and crocodile have

larger telencephalons for their numbers of neurons, and thus lower neuronal densities, compared to other reptilian species. **C, D,** distinct neuronal scaling rules apply to the telencephalon of different bird clades, with higher neuronal densities and therefore more neurons in a telencephalon of similar mass in late-derived clades compared to early-derived clades. Anseriformes and Accipitriformes do not conform systematically to either scaling relationships. **E, F,** neuronal scaling rules that apply to the telencephalon of early-derived bird species and Testudines plus crocodile have similar exponents, indicative of a grade shift. All power functions are listed in Tables S2 and S3.

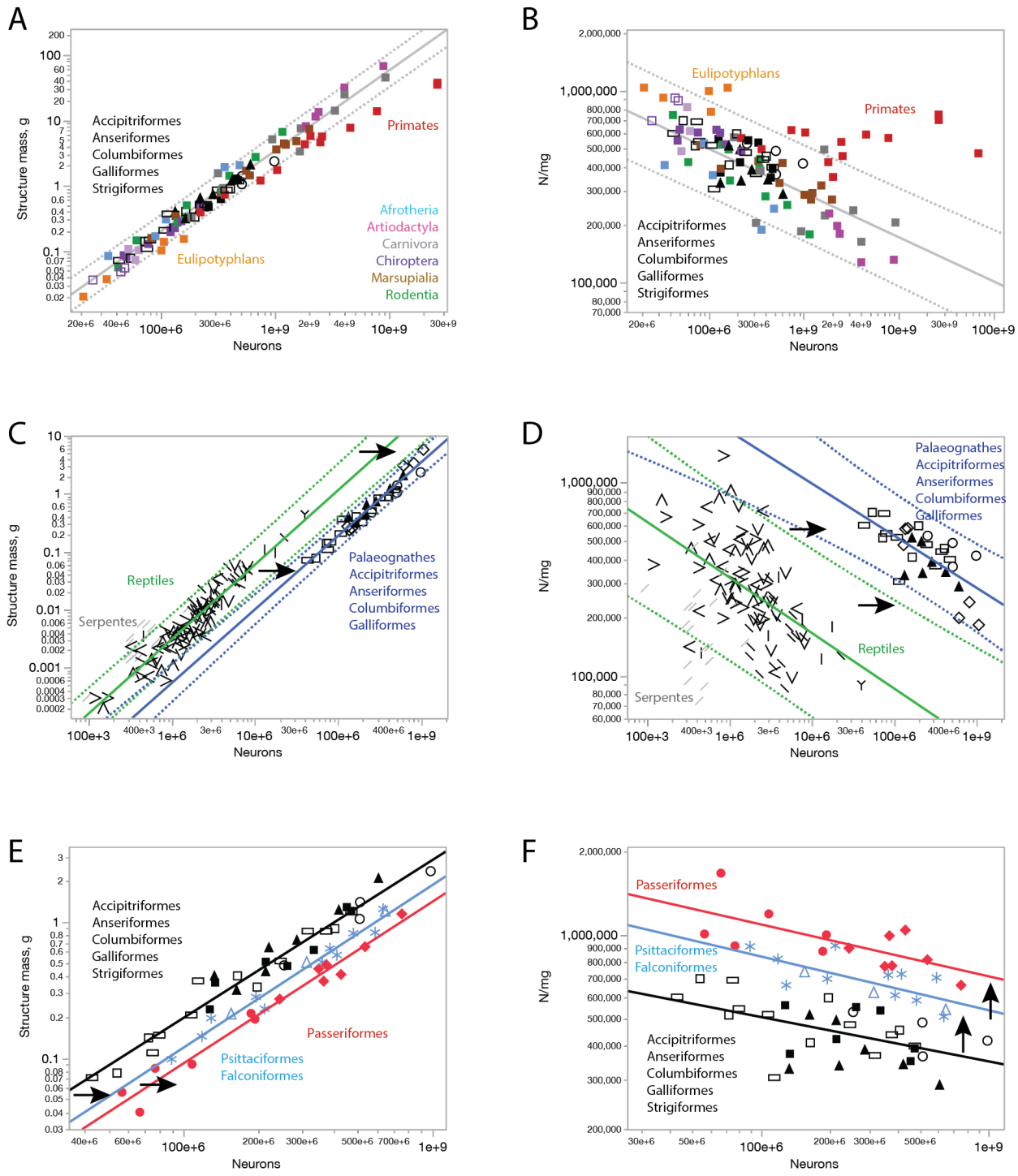

Figure S5. Neuronal scaling rules for the cerebellum of mammals, reptiles and birds. A, C, E, scaling of cerebellar mass with numbers of cerebellar neurons. **B, D, F,** scaling of neuronal density in the cerebellum with numbers of cerebellar neurons. **A, B,** Early-derived birds and mammals other than primates and eulipotyphlans share neuronal scaling rules for the cerebellum. Power

function plotted applies to non-primate, non-eulipotyphlan mammalian species plus the bird clades indicated. **C, D,** neuronal scaling rules for the cerebellum of reptiles (minus Serpentes) and of early-derived bird clades have similar exponents, indicative of a grade shift. **E, F,** neuronal scaling rules for the cerebellum of three different groups of birds, indicated in black, blue and red, have similar exponents, indicative of two grade shifts in bird evolution. All power functions are listed in Tables S4 and S5.

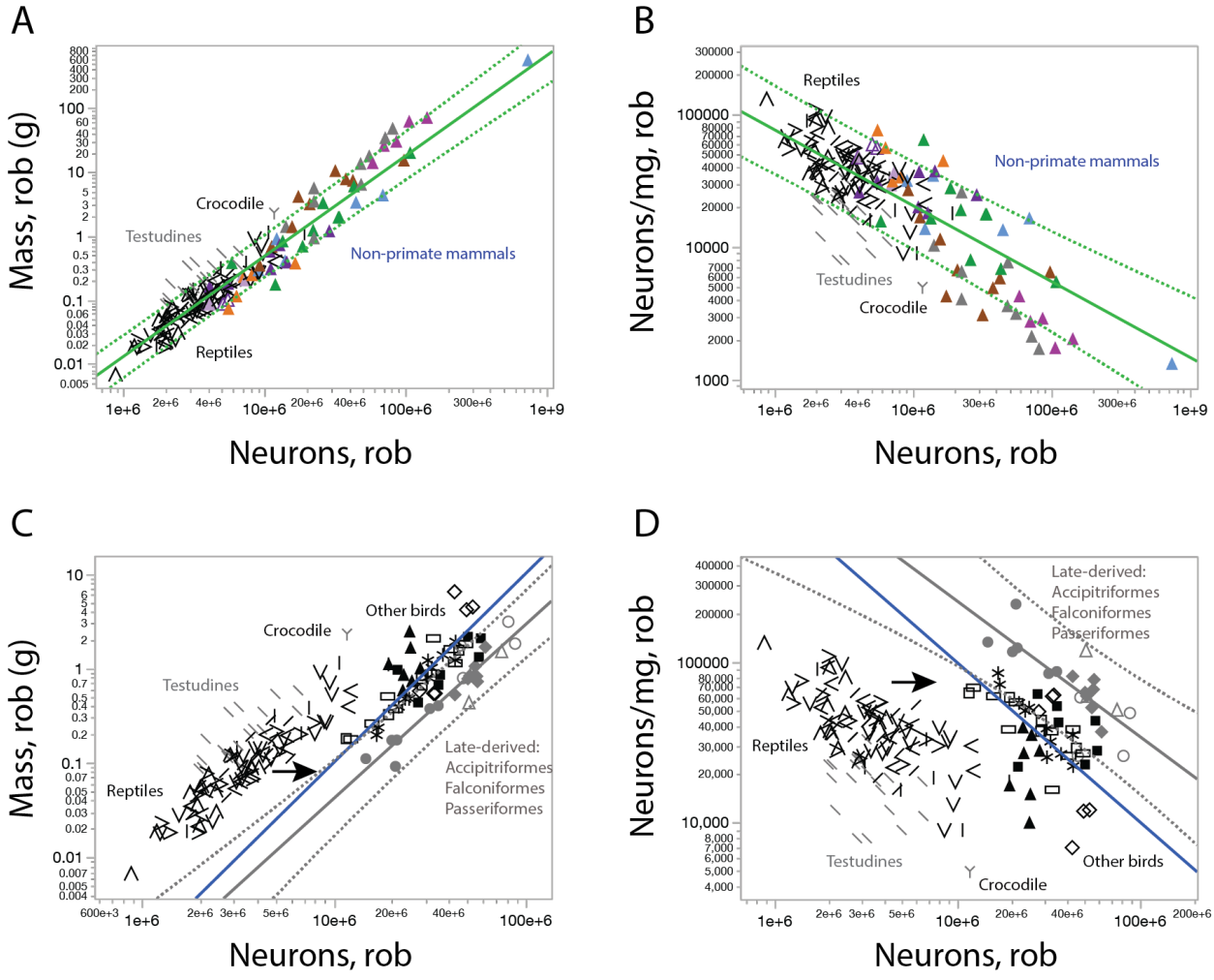

Figure S6. Neuronal scaling rules for the rest of brain of reptiles, mammals and birds. A, C, scaling of rest of brain mass with numbers of rest of brain neurons. **B, D,** scaling of neuronal density in the rest of brain with numbers of rest of brain neurons. **A, B,** Reptiles (minus Testudines and crocodile) and mammals (minus primates) share a single neuronal scaling rule for the rest of brain. **C, D,** parallel neuronal scaling rules with similar exponents apply to the rest of brain of

reptiles and different bird clades, with more neurons, but similar neuronal densities, in late-derived bird clades compared to early-derived bird clades. All power functions are listed in Tables S6 and S7.

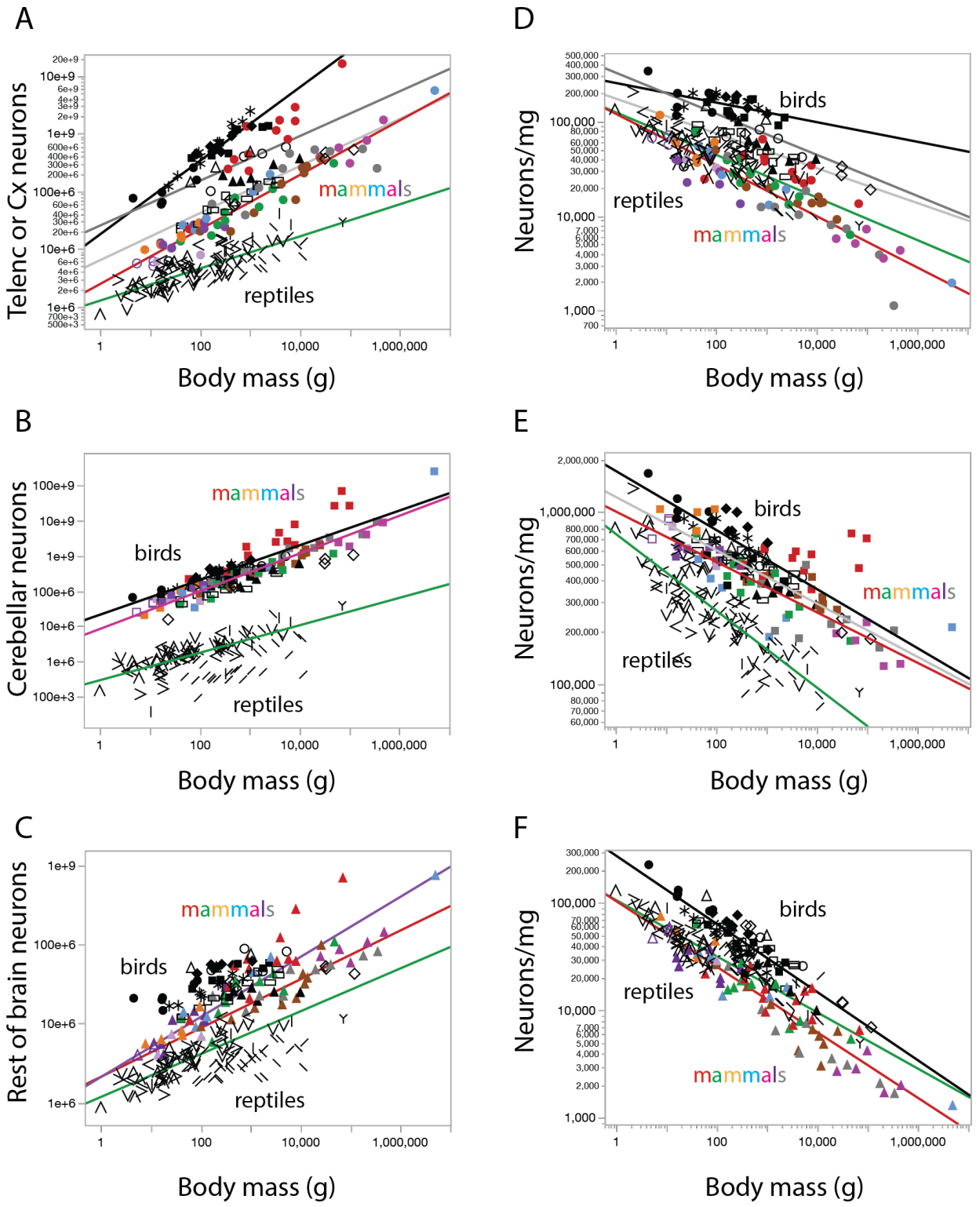

Figure S7. Clade-specific scaling of numbers of neurons and neuronal density in the different brain structures with body mass across mammals, reptiles and birds. A-C, scaling of numbers of neurons in the telencephalon or pallium (**A**), cerebellum (**B**) and rest of brain (**C**) with body mass.

D-F, scaling of neuronal density in the telencephalon or pallium (**D**), cerebellum (**E**) and rest of brain (**F**) with body mass. Power functions plotted apply to reptiles (green), non-primate mammals (red), early-derived birds (gray) and late-derived birds (black). Power functions are listed in Table S8.

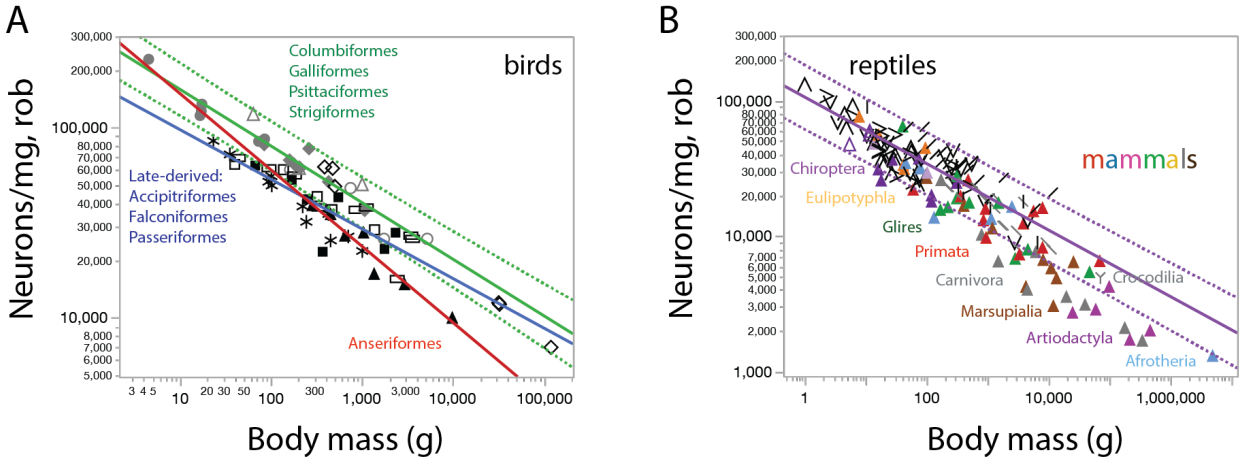

Figure S8. Clade-specific scaling of neuronal density in the rest of brain of birds, but shared across across reptiles and small mammalian species. A, Power functions plotted for the three groups of birds indicated by the colors. **B**, power function plotted across all mammals and reptiles. Power functions are listed in Table S8.

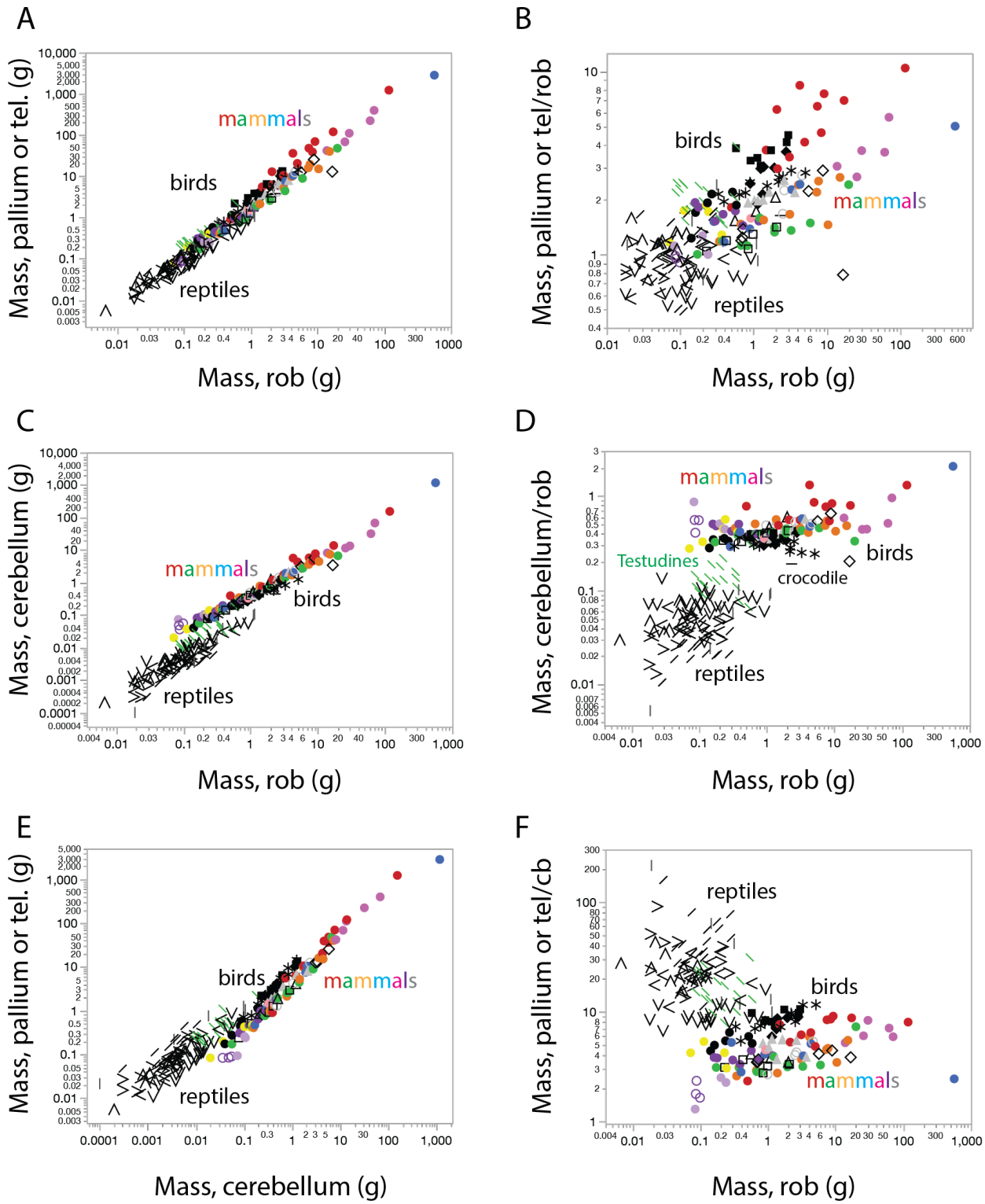

Figure S9. Mass scaling relationships across brain structures in mammals, reptiles and birds. A, C, E, scaling of structure mass across the structures indicated. **B, D, F,** scaling of the mass ratio across the brain structures indicated, as a function of the mass of the rest of brain. In all graphs,

reptile species are represented with black open line symbols; birds, by black polygons and asterisks; mammals, by colored symbols. All power functions, not plotted for clarity, are listed in Tables S9 and S10.

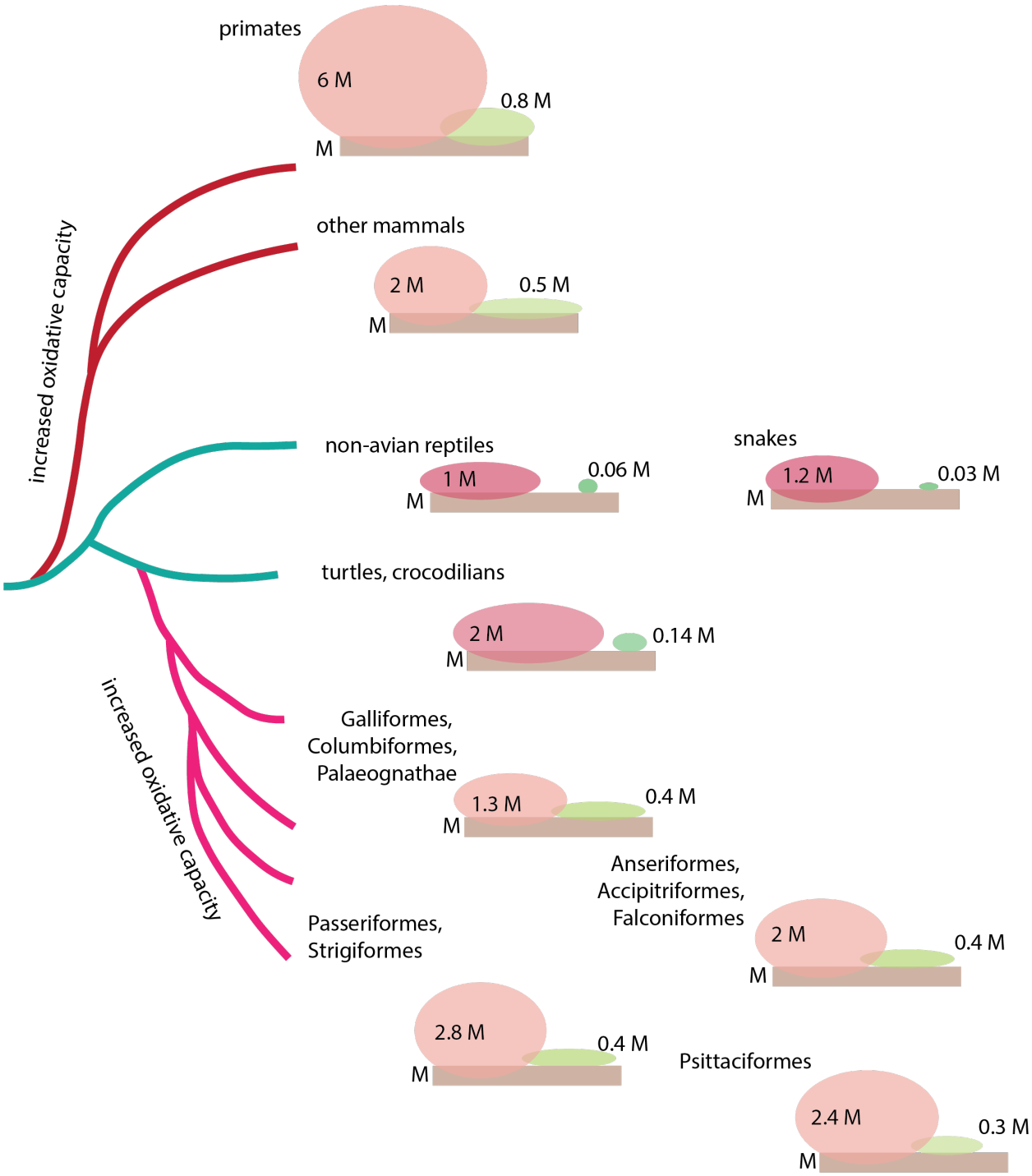

Figure S10. Mass ratios across structures fail to differentiate the brains of different amniote clades. The schematics in varying sizes represent the rest of brain (tan rectangle), telencephalon (red) and cerebellum (green); the surface area of each structure is proportional to its mass (M). All schematics are scaled to a similar unit mass in the rest of brain; in this way, the surface area of each brain part represents the relative mass of that structure compared to the rest of brain. The schematics illustrate that mammalian and avian brains alike are characterized by an increased ratio of telencephalic mass and cerebellum over the rest of brain compared to reptiles.

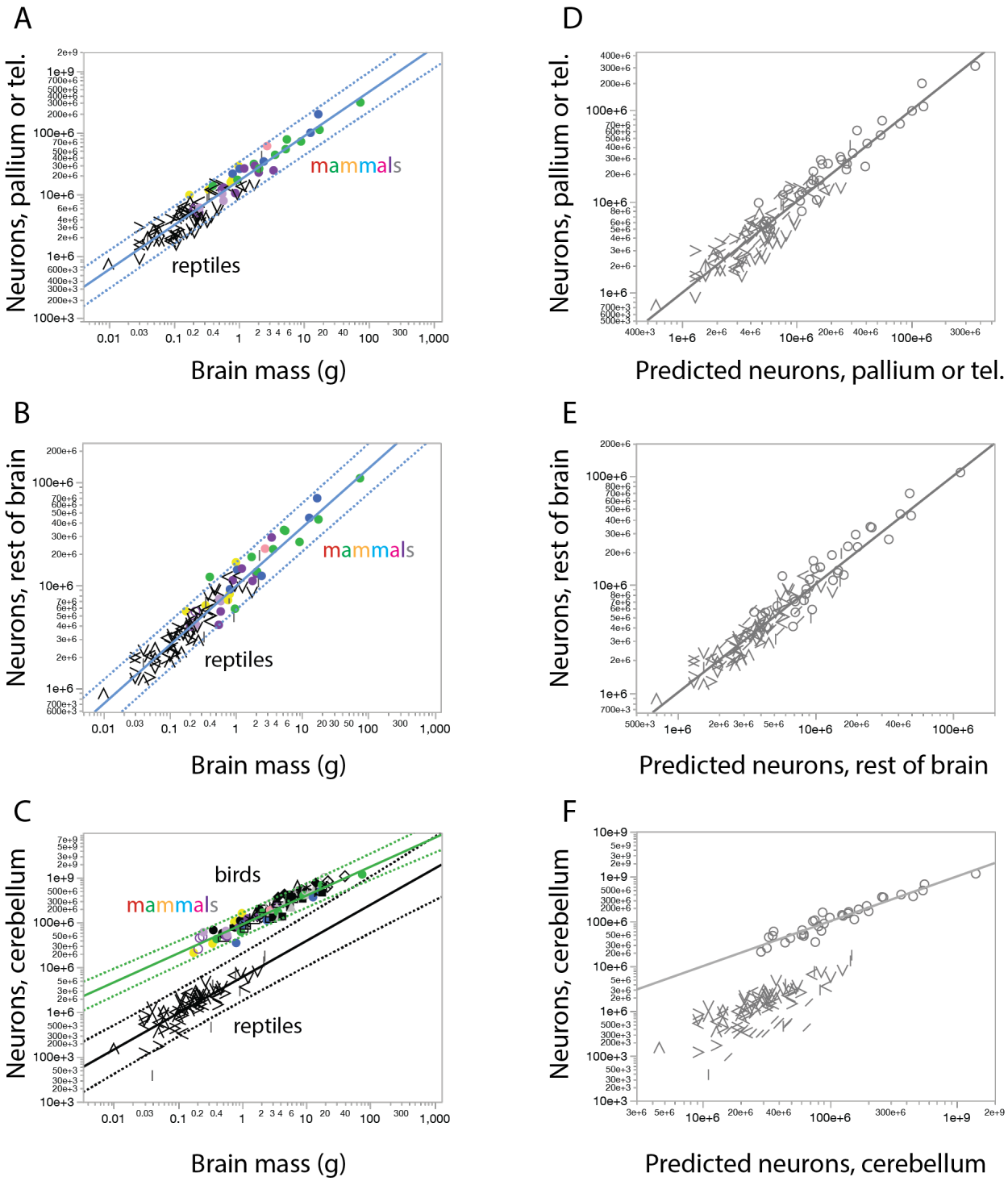

Figure S11. Predictive scaling relationships for numbers of neurons in the different brain structures of ancestral amniotes. A-C, power functions describing numbers of neurons in the telencephalon or pallium (**A**), rest of brain (**B**) and cerebellum (**C**) as a function of whole brain mass (minus the olfactory bulbs). Predictive power functions are $N_{tel} = e^{16.609\pm0.040}\ M_{br}^{0.719\pm0.021}$

(r^2=0.906, p<0.0001), $N_{rob} = e^{16.087\pm0.030} M_{br}^{0.570\pm0.016}$ (r^2=0.913, p<0.0001) and $N_{cb} = e^{15.593\pm0.133} M_{br}^{0.807\pm0.064}$ (across 70 ectothermic reptilian species, excluding Serpentes, Testudine and the Nile crocodile; p<0.0001, r^2 = 0.699) or $N_{cb} = e^{18.294\pm0.052} M_{br}^{0.644\pm0.035}$ (across the 34 small mammalian species in the dataset; p<0.0001, r^2 = 0.913). **D-F,** comparison between measured and predicted numbers of neurons in the telencephalon (D), rest of brain (E) and cerebellum (F, using the scaling rule for small mammalian species). All graphs are fit with linear functions with slope = 1 and intercept = 0.

Supplementary information

Table S1. Non-neuronal scaling rules for the telencephalon of reptiles and the pallium of birds and mammals; the cerebellum; and the rest of brain (hindbrain to diencephalon in reptiles and birds, hindbrain to striatum in mammals). Values correspond to the equations $M_{str} = e^{a\pm SE} O_{str}^{b\pm SE}$ and $O_{str}/M_{str} = e^{a\pm SE} M_{str}^{b\pm SE}$, the p-values for a and b, and the r^2 for the power fit, where M_{str} is structure mass, O_{str} is the number of non-neurons ("other cells") in the structure, and O_{str}/M_{str} is the density of non-neuronal (other) cells in the structure.

Whole brain						
M_{str} x O_{str}	**n**	**a in e^a**	**b in N_{str}^b**	**p, a**	**p, b**	**r^2**
All amniotes	242	-17.980±0.179	**0.992**±0.010	<0.0001	<0.0001	0.978
All reptiles	108	-20.989±0.424	**1.184**±0.026	<0.0001	<0.0001	0.952
All mammals	69	-19.499±0.264	**1.070**±0.013	<0.0001	<0.0001	0.990
All birds	65	-21.811±0.405	**1.170**±0.020	<0.0001	<0.0001	0.982
O_{str} /M_{str} x M_{str}	**n**	**a in e^a**	**b in N_{str}^b**	**p, a**	**p, b**	**r^2**
All reptiles	108	10.772±0.031	**-0.192**±0.017	<0.0001	<0.0001	0.556
All mammals	68	11.362±0.042	**-0.081**±0.014	<0.0001	<0.0001	0.354
All birds	65	11.754±0.025	**-0.161**±0.015	<0.0001	<0.0001	0.658
Telencephalon or cortex						
M_{str} x O_{str}	**n**	**a in e^a**	**b in N_{str}^b**	**p, a**	**p, b**	**r^2**
All amniotes	242	-17.331±0.175	**0.967**±0.010	<0.0001	<0.0001	0.976
All reptiles	108	-21.137±0.500	**1.221**±0.032	<0.0001	<0.0001	0.932
All mammals	70	-18.617±0.268	**1.033**±0.014	<0.0001	<0.0001	0.988
All birds	65	-19.531±0.424	**1.069**±0.022	<0.0001	<0.0001	0.973
All mammals and birds	135	-18.950±0.232	**1.044**±0.012	<0.0001	<0.0001	0.983
O_{str} /M_{str} x M_{str}	**n**	**a in e^a**	**b in N_{str}^b**	**p, a**	**p, b**	**r^2**
All reptiles	108	10.286±0.049	**-0.236**±0.020	<0.0001	<0.0001	0.566
All mammals	70	11.137±0.037	**-0.043**±0.013	<0.0001	0.0011	0.145
All birds	65	11.388±0.027	**-0.089**±0.019	<0.0001	<0.0001	0.259
All mammals and birds	135	11.258±0.025	**-0.059**±0.011	<0.0001	<0.0001	0.183
Cerebellum						
M_{str} x O_{str}	**n**	**a in e^a**	**b in N_{str}^b**	**p, a**	**p, b**	**r^2**
All amniotes	245	-19.728±0.184	**1.072**±0.011	<0.0001	<0.0001	0.974
All reptiles	108	-20.990±0.424	**1.184**±0.026	<0.0001	<0.0001	0.952

All mammals	72	-19.501±0.444	**1.073**±0.024	<0.0001	<0.0001	0.966
All birds	65	-23.076±0.790	**1.242**±0.044	<0.0001	<0.0001	0.927
All mammals and reptiles	180	-20.053±0.193	**1.100**±0.012	<0.0001	<0.0001	0.978
O_{str} /M_{str} x M_{str}	**n**	**a in e^a**	**b in N_{str}^b**	**p, a**	**p, b**	**r^2**
All reptiles	108	10.772±0.031	**-0.192**±0.017	<0.0001	<0.0001	0.556
All mammals	72	11.281±0.046	**-0.100**±0.020	<0.0001	<0.0001	0.262
All birds	65	11.627±0.035	**-0.254**±0.027	<0.0001	<0.0001	0.592
All mammals and reptiles	180	11.267±0.044	**-0.110**±0.010	<0.0001	<0.0001	0.407
Rest of brain						
M_{str} x O_{str}	**n**	**a in e^a**	**b in N_{str}^b**	**p, a**	**p, b**	**r^2**
All amniotes	242	-17.980±0.179	**0.992**±0.010	<0.0001	<0.0001	0.978
All reptiles	108	-20.050±0.415	**1.129**±0.026	<0.0001	<0.0001	0.946
All mammals	70	-19.804±0.360	**1.087**±0.019	<0.0001	<0.0001	0.980
All birds	65	-21.227±0.546	**1.130**±0.029	<0.0001	<0.0001	0.959
O_{str} /M_{str} x M_{str}	**n**	**a in e^a**	**b in N_{str}^b**	**p, a**	**p, b**	**r^2**
All reptiles	108	10.742±0.048	**-0.162**±0.019	<0.0001	<0.0001	0.394
All mammals	70	11.318±0.034	**-0.099**±0.016	<0.0001	<0.0001	0.364
All birds	65	11.866±0.020	**-0.151**±0.022	<0.0001	<0.0001	0.429

Table S2. Neuronal scaling rules for the telencephalon of reptiles, and the pallium of birds and mammals. Values correspond to the equation $M_{str} = e^{a\pm SE} N_{str}^{b\pm SE}$, the p-values for a and b, and the r^2 for the power fit, where M_{str} is structure mass and N_{str} is the number of neurons in the structure.

M_{str} x N_{str}	**n**	**a in e^a**	**b in N_{str}^b**	**p, a**	**p, b**	**r^2**
Reptiles						
All	108	-24.284±0.988	**1.437**±0.064	<0.0001	<0.0001	0.827
Anguimorpha	7	-24.308±2.212	**1.417**±0.135	0.0001	0.0001	0.957
Crocodilia	1					
Gekkota	14	-21.361±2.904	**1.232**±0.194	<0.0001	<0.0001	0.770
Iguania	20	-24.553±1.196	**1.470**±0.079	<0.0001	<0.0001	0.950
Lacertoidea	15	-22.656±2.038	**1.312**±0.133	<0.0001	<0.0001	0.883
Scincoidea	14	-23.106±2.902	**1.332**±0.189	<0.0001	<0.0001	0.805

Serpentes	18	-22.199±1.749	**1.293**±0.113	<0.0001	<0.0001	0.891
Testudines	19	-19.585±3.618	**1.178**±0.228	<0.0001	<0.0001	0.610
Testudines and Crocodilia	20	-22.193±2.965	**1.344**±0.186	<0.0001	<0.0001	0.743
All minus Testudines and Crocodilia	88	-22.472±0.856	**1.309**±0.056	<0.0001	<0.0001	0.865
Birds						
All	65	-15.245±1.280	**0.840**±0.067	<0.0001	<0.0001	0.715
Accipitriformes	4	-20.574±4.346	**1.134**±0.223	0.0418	0.0366	0.928
Anseriformes	7	-21.727±8.597	**1.209**±0.453	0.0527	0.0446	0.587
Columbiformes	5	-22.941±4.428	**1.284**±0.250	0.0140	0.0142	0.898
Falconiformes	3	-24.320±0.355	**1.293**±0.018	0.0093	0.0090	0.999
Galliformes	9	-26.220±1.904	**1.476**±0.107	<0.0001	<0.0001	0.965
Palaeognathae	6	-25.004±1.876	**1.400**±0.100	0.0002	0.0001	0.980
Passeriformes	13	-20.890±1.692	**1.104**±0.088	<0.0001	<0.0001	0.935
Psittaciformes	11	-20.735±1.199	**1.093**±0.060	<0.0001	<0.0001	0.974
Strigiformes	7	-21.246±3.796	**1.124**±0.186	0.0025	0.0018	0.879
Galliformes, Palaeognathae	15	-24.694±1.111	**1.388**±0.061	<0.0001	<0.0001	0.976
Galliformes, Palaeognathae, Columbiformes	20	-24.679±1.087	**1.386**±0.060	<0.0001	<0.0001	0.967
Falconiformes, Passeriformes, Psittaciformes, Strigiformes	34	-20.799±0.879	**1.100**±0.044	<0.0001	<0.0001	0.950
Mammals						
All (minus bear)	68	-21.938±0.801	**1.275**±0.043	<0.0001	<0.0001	0.929
All non-primates	56	-25.702±0.598	**1.495**±0.033	<0.0001	<0.0001	0.974
Afrotheria	6	-27.188±1.319	**1.565**±0.071	<0.0001	<0.0001	0.992
Artiodactyla	5	-21.576±3.131	**1.303**±0.155	0.0063	0.0035	0.959
Carnivora (minus bear)	7	-20.273±3.869	**1.217**±0.200	0.0034	0.0017	0.882
Chiroptera	13	-26.777±2.641	**1.575**±0.162	<0.0001	<0.0001	0.895
Eulipotyphla	5	-26.451±9.222	**1.518**±0.557	0.0641	0.0721	0.713
Marsupialia	9	-22.703±1.796	**1.329**±0.097	<0.0001	<0.0001	0.964
Primata	12	-18.987±1.513	**1.087**±0.074	<0.0001	<0.0001	0.956
Rodentia	10	-29.369±1.702	**1.699**±0.096	<0.0001	<0.0001	0.975
Scandentia	1					

All non-primate mammals (minus bear), all reptiles	164	-23.441±0.390	**1.377**±0.024	<0.0001	<0.0001	0.954
All non-primate mammals (minus bear), all reptiles minus Testudines and Crocodilians	144	-23.780±0.334	**1.392**±0.020	<0.0001	<0.0001	0.971

Table S3. Scaling of neuronal density with varying numbers of neurons in the telencephalon of reptiles, and the pallium of birds and mammals. Values correspond to the equation $D_{Nstr} = e^{a\pm SE} N_{str}^{b\pm SE}$, the p-values for a and b, and the r^2 for the power fit, where DN_{str} is neuronal density (in neurons/mg) and N_{str} is the number of neurons in the structure.

D_{Nstr} x N_{str}	**n**	**a in e^a**	**b in N_{str}^b**	**p, a**	**p, b**	**r^2**
Reptiles						
All	108	17.390±0.990	**-0.438**±0.064	<0.0001	<0.0001	0.305
Anguimorpha	7	17.354±2.194	**-0.414**±0.134	0.0005	0.0273	0.656
Crocodilia	1					
Gekkota	14	14.423±2.902	**-0.230**±0.194	0.0003	0.2591	0.105
Iguania	20	17.756±1.203	**-0.478**±0.080	<0.0001	<0.0001	0.667
Lacertoidea	15	15.735±2.032	**-0.311**±0.132	<0.0001	0.0352	0.298
Scincoidea	14	16.201±2.905	**-0.332**±0.189	0.0001	0.1050	0.204
Serpentes	18	15.323±1.736	**-0.295**±0.112	<0.0001	0.0184	0.301
Testudines	19	13.104±3.686	**-0.204**±0.233	0.0024	0.3920	0.043
Testudines and Crocodilia	20	15.486±2.997	**-0.356**±0.188	<0.0001	0.0749	0.166
All minus Testudines and Crocodilia	88	15.563±0.858	**-0.309**±0.056	<0.0001	<0.0001	0.262
Birds						
All	65	8.003±1.273	**-0.179**±0.066	<0.0001	0.0089	0.104
Accipitriformes	4	13.794±4.346	**-0.140**±0.223	0.0866	0.5936	0.165
Anseriformes	7	14.721±8.597	**-0.203**±0.453	0.1475	0.6725	0.039
Columbiformes	5	16.826±4.617	**-0.330**±0.260	0.0356	0.2945	0.349
Falconiformes	3	17.404±0.513	**-0.292**±0.027	0.0188	0.0577	0.992
Galliformes	9	19.234±1.899	**-0.472**±0.106	<0.0001	0.0030	0.738

Palaeognathae	6	11.964±7.565	**-0.056**±0.402	0.1889	0.8952	0.005
Passeriformes	13	13.982±1.692	**-0.104**±0.088	<0.0001	0.2615	0.113
Psittaciformes	11	13.827±1.199	**-0.093**±0.060	<0.0001	0.1531	0.213
Strigiformes	7	14.327±3.804	**-0.123**±0.187	0.0131	0.5380	0.080
Galliformes, Palaeognathae	15	13.398±3.092	**-0.386**±0.061	<0.0001	<0.0001	0.755
Galliformes, Palaeognathae, Columbiformes	20	17.795±1.091	**-0.388**±0.061	<0.0001	<0.0001	0.697
Falconiformes, Passeriformes, Psittaciformes, Strigiformes	34	13.895±0.879	**-0.100**±0.044	<0.0001	0.0315	0.136
Mammals						
All (minus bear)	68	15.023±0.803	**-0.274**±0.044	<0.0001	<0.0001	0.375
All non-primates	56	18.793±0.600	**-0.495**±0.033	<0.0001	<0.0001	0.803
Afrotheria	6	20.260±1.332	**-0.564**±0.071	0.0001	0.0014	0.940
Artiodactyla	5	14.668±3.131	**-0.303**±0.155	0.0184	0.1447	0.562
Carnivora (minus bear)	7	13.365±3.870	**-0.217**±0.200	0.0182	0.3258	0.192
Chiroptera	13	19.803±2.656	**-0.571**±0.163	<0.0001	0.0050	0.526
Eulipotyphla	5	19.590±9.296	**-0.521**±0.561	0.1257	0.4217	0.223
Marsupialia	9	15.795±1.796	**-0.329**±0.097	<0.0001	0.0117	0.620
Primata	12	12.094±1.513	**-0.087**±0.074	<0.0001	0.2644	0.123
Rodentia	10	22.415±1.683	**-0.696**±0.095	<0.0001	<0.0001	0.870
Scandentia	1					
All non-primate mammals (minus bear), all reptiles	164	16.526±0.391	**-0.377**±0.024	<0.0001	<0.0001	0.605
All non-primate mammals, reptiles minus Testudines and Crocodilians	144	16.863±0.335	**-0.391**±0.020	<0.0001	<0.0001	0.722

Table S4. Neuronal scaling rules for the cerebellum of reptiles, birds and mammals. Values correspond to the equation $M_{cb} = e^{a\pm SE} N_{cb}^{b\pm SE}$, the p-values for a and b, and the r^2 for the power fit, where M_{cb} is cerebellar mass and N_{cb} is the number of neurons in the cerebellum.

M_{cb} x N_{cb}	**n**	**a in e^a**	**b in N_{cb}^b**	**p, a**	**p, b**	**r^2**
Reptiles						
All	108	-21.597±0.658	**1.159**±0.046	<0.0001	<0.0001	0.856
Anguimorpha	7	-20.551±1.135	**1.099**±0.077	<0.0001	<0.0001	0.976
Crocodilia	1					
Gekkota	14	-22.341±2.108	**1.179**±0.153	<0.0001	<0.0001	0.833
Iguania	20	-27.286±1.536	**1.536**±0.148	<0.0001	<0.0001	0.857
Lacertoidea	15	-21.123±2.516	**1.111**±0.179	<0.0001	<0.0001	0.747
Scincoidea	14	-22.206±2.128	**1.179**±0.155	<0.0001	<0.0001	0.828
Serpentes	18	-20.114±2.679	**1.086**±0.206	<0.0001	<0.0001	0.635
Testudines	19	-19.549±1.908	**1.043**±0.125	<0.0001	<0.0001	0.803
Testudines and Crocodilia	20	-22.828±1.500	**1.128**±0.098	<0.0001	<0.0001	0.881
All minus Serpentes	90	-23.527±0.673	**1.285**±0.047	<0.0001	<0.0001	0.897
Birds						
All	65	-24.549±1.213	**1.229**±0.063	<0.0001	<0.0001	0.859
Accipitriformes	4	-23.486±3.313	**1.178**±0.165	0.0193	0.0191	0.962
Anseriformes	7	-23.887±3.008	**1.214**±0.155	0.0005	0.0005	0.924
Columbiformes	5	-22.998±2.267	**1.156**±0.121	0.0020	0.0024	0.968
Falconiformes	3	-24.558±0.304	**1.220**±0.016	0.0079	0.0081	0.999
Galliformes	9	-23.365±1.703	**1.180**±0.090	<0.0001	<0.0001	0.961
Palaeognathae	6	-30.001±1.405	**1.529**±0.072	<0.0001	<0.0001	0.991
Passeriformes	13	-24.284±1.171	**1.188**±0.061	<0.0001	<0.0001	0.972
Psittaciformes	11	-23.931±1.264	**1.183**±0.065	<0.0001	<0.0001	0.974
Strigiformes	7	-22.131±3.078	**1.114**±0.159	0.0008	0.0009	0.908
Galliformes, Anseriformes, Accipitriformes, Columbiformes, Strigiformes	32	-23.000±0.896	**1.160**±0.047	<0.0001	<0.0001	0.954
Galliformes, Anseriformes, Accipitriformes, Columbiformes,	38	-24.822±0.928	**1.257**±0.048	<0.0001	<0.0001	0.950

Strigiformes, Palaeognathae						
Falconiformes, Passeriformes, Psittaciformes	27	-24.822±1.025	**1.223**±0.053	<0.0001	<0.0001	0.955
Falconiformes, Psittaciformes	14	-24.142±1.039	**1.195**±0.053	<0.0001	<0.0001	0.977
Mammals						
All	71	-22.539±0.553	**1.135**±0.028	<0.0001	<0.0001	0.961
All non-primates	58	-24.586±0.495	**1.245**±0.025	<0.0001	<0.0001	0.977
All non-primates, non-eulipotyphlans	53	-24.111±0.478	**1.223**±0.024	<0.0001	<0.0001	0.981
Afrotheria	6	-21.115±1.027	**1.079**±0.051	<0.0001	<0.0001	0.991
Artiodactyla	5	-26.632±2.588	**1.351**±0.118	0.0020	0.0014	0.978
Carnivora	8	-21.332±2.667	**1.095**±0.126	0.0002	0.0001	0.927
Chiroptera	13	-23.582±1.610	**1.183**±0.089	<0.0001	<0.0001	0.941
Eulipotyphla	5	-21.165±1.520	**1.028**±0.084	0.0008	0.0012	0.980
Marsupialia	10	-23.421±0.746	**1.186**±0.037	<0.0001	<0.0001	0.992
Primata	13	-19.572±0.794	**0.976**±0.036	<0.0001	<0.0001	0.985
Rodentia	10	-26.462±1.406	**1.349**±0.073	<0.0001	<0.0001	0.977
Scandentia	1					
All non-primates, non-eulipotyphlans, Accipitriformes, Anseriformes, Columbiformes, Galliformes, Palaeognathae, Strigiformes	84	-24.283±0.403	**1.234**±0.021	<0.0001	<0.0001	0.978

Table S5. Scaling of neuronal density with varying numbers of neurons in the cerebellum of reptiles, birds and mammals. Values correspond to the equation $D_{Ncb} = e^{a\pm SE} N_{cb}^{b\pm SE}$, the p-values for a and b, and the r^2 for the power fit, where D_{Ncb} is neuronal density in the cerebellum and N_{cb} is the number of neurons in the cerebellum.

D_{Ncb} x N_{cb}	**n**	**a in e^a**	**b in N_{cb}^b**	**p, a**	**p, b**	**r^2**
Reptiles						

All	108	14.685±0.659	**-0.159**±0.046	<0.0001	0.0009	0.100
Anguimorpha	7	13.531±1.117	**-0.092**±0.076	<0.0001	0.2762	0.230
Crocodilia	1					
Gekkota	14	15.756±2.081	**-0.202**±0.151	<0.0001	0.2041	0.131
Iguania	20	20.425±2.176	**-0.539**±0.147	<0.0001	0.0018	0.426
Lacertoidea	15	14.226±2.515	**-0.111**±0.179	<0.0001	0.5448	0.029
Scincoidea	14	15.458±2.127	**-0.190**±0.155	<0.0001	0.2431	0.116
Serpentes	18	12.875±2.662	**-0.061**±0.204	0.0002	0.7687	0.006
Testudines	19	12.631±1.908	**-0.042**±0.125	<0.0001	0.7423	0.007
Testudines and Crocodilia	20	13.914±1.500	**-0.127**±0.098	<0.0001	0.2097	0.086
All minus Serpentes	90	16.651±0.673	**-0.287**±0.046	<0.0001	<0.0001	0.303
Birds						
All	65	17.632±1.214	**-0.228**±0.063	<0.0001	0.0006	0.173
Accipitriformes	4	16.587±3.319	**-0.179**±0.166	0.0378	0.3933	0.368
Anseriformes	7	16.983±3.018	**-0.214**±0.156	0.0025	0.2282	0.274
Columbiformes	5	16.100±2.272	**-0.156**±0.121	0.0058	0.2877	0.357
Falconiformes	3	17.663±0.295	**-0.220**±0.015	0.0106	0.0434	0.995
Galliformes	9	16.451±1.729	**-0.180**±0.092	<0.0001	0.0903	0.355
Palaeognathae	6	23.080±1.405	**-0.528**±0.072	<0.0001	0.0018	0.932
Passeriformes	13	17.363±1.171	**-0.188**±0.061	<0.0001	0.0105	0.463
Psittaciformes	11	17.000±1.256	**-0.182**±0.065	<0.0001	0.0202	0.468
Strigiformes	7	15.248±3.071	**-0.116**±0.159	0.0042	0.4990	0.096
Galliformes, Anseriformes, Accipitriformes, Columbiformes, Strigiformes	32	16.091±0.901	**-0.160**±0.047	<0.0001	0.0018	0.251
Galliformes, Anseriformes, Accipitriformes, Columbiformes, Strigiformes, Palaeognathae	38	17.909±0.930	**-0.257**±0.048	<0.0001	0.0018	0.440
Falconiformes, Passeriformes, Psittaciformes	27	17.900±1.024	**-0.223**±0.053	<0.0001	0.0003	0.414
Falconiformes, Psittaciformes	14	17.218±1.035	**-0.194**±0.053	<0.0001	0.0033	0.526
Mammals						

All	71	15.626±0.554	**-0.134**±0.028	<0.0001	<0.0001	0.256
All non-primates	58	17.688±0.495	**-0.245**±0.025	<0.0001	<0.0001	0.630
All non-primates, non-eulipotyphlans	53	17.210±0.477	**-0.223**±0.024	<0.0001	<0.0001	0.628
Afrotheria	6	14.205±1.017	**-0.079**±0.050	0.0002	0.1904	0.383
Artiodactyla	5	19.724±2.588	**-0.351**±0.118	0.0047	0.0509	0.747
Carnivora	8	14.424±2.667	**-0.095**±0.126	0.0017	0.4771	0.087
Chiroptera	13	16.579±1.625	**-0.178**±0.090	<0.0001	0.0732	0.263
Eulipotyphla	5	14.241±1.452	**-0.027**±0.081	0.0023	0.7633	0.035
Marsupialia	10	16.513±0.746	**-0.186**±0.037	<0.0001	0.0010	0.761
Primata	13	12.578±0.776	**0.028**±0.035	<0.0001	0.4401	0.055
Rodentia	10	19.447±1.376	**-0.343**±0.071	<0.0001	0.0014	0.743
Scandentia	1					
All non-primates, non-eulipotyphlans, Accipitriformes, Anseriformes, Columbiformes, Galliformes, Palaeognathae, Strigiformes	84	17.376±0.403	**-0.231**±0.021	<0.0001	<0.0001	0.608

Table S6. Neuronal scaling rules for the rest of brain of reptiles, birds and mammals. Values correspond to the equation $M_{rob} = e^{a \pm SE} N_{rob}^{b \pm SE}$, the p-values for a and b, and the r^2 for the power fit, where M_{rob} is mass of the rest of brain and N_{rob} is the number of neurons in the rest of brain. In reptiles and birds, rest of brain consists of the brainstem and diencephalon; in mammals, it additionally contains the striatum.

M_{rob} x N_{rob}	**n**	**a in e^a**	**b in N_{rob}^b**	**p, a**	**p, b**	**r^2**
Reptiles						
All	108	-25.833±1.299	**1.568**±0.086	<0.0001	<0.0001	0.757
Anguimorpha	7	-26.920±4.430	**1.640**±0.284	0.0017	0.0022	0.870
Crocodilia	1					
Gekkota	14	-26.507±3.878	**1.603**±0.265	<0.0001	<0.0001	0.753
Iguania	20	-26.795±2.325	**1.619**±0.152	<0.0001	<0.0001	0.863
Lacertoidea	15	-25.422±1.832	**1.519**±0.121	<0.0001	<0.0001	0.924
Scincoidea	14	-24.170±2.686	**1.442**±0.180	<0.0001	<0.0001	0.842
Serpentes	18	-23.542±3.538	**1.411**±0.235	<0.0001	<0.0001	0.692
Testudines	19	-22.191±3.894	**1.371**±0.260	<0.0001	<0.0001	0.621
Testudines and Crocodilia	20	-25.628±3.083	**1.601**±0.205	<0.0001	<0.0001	0.773
All minus Testudines, Crocodilia	88	-26.022±1.012	**1.569**±0.067	<0.0001	<0.0001	0.864
Birds						
All	65	-23.554±2.997	**1.346**±0.173	<0.0001	<0.0001	0.490
Accipitriformes	4	-18.846±6.594	**1.073**±0.362	0.0289	0.0252	0.594
Anseriformes	7	-12.654±5.552	**0.745**±0.320	0.0417	0.0384	0.311
Columbiformes	5	-28.177±2.120	**1.621**±0.125	0.0009	0.0010	0.983
Falconiformes	3	-43.646±25.189	**2.430**±1.409	0.3332	0.3345	0.748
Galliformes	9	-29.695±4.118	**1.717**±0.241	0.0002	0.0002	0.879
Palaeognathae	6	-73.806±19.991	**4.252**±1.144	0.0210	0.0205	0.776
Passeriformes	13	-32.429±2.616	**1.815**±0.150	<0.0001	<0.0001	0.930
Psittaciformes	11	-38.150±2.968	**2.203**±0.173	<0.0001	<0.0001	0.947
Strigiformes	7	-19.472±8.383	**1.118**±0.480	0.0678	0.0673	0.520
Galliformes, Columbiformes, Palaeognathae	20	-34.500±4.266	**1.998**±0.248	<0.0001	<0.0001	0.783
Accipitriformes, Falconiformes, Passeriformes	20	-32.830±2.943	**1.840**±0.167	<0.0001	<0.0001	0.870

Mammals						
All	69	-27.111±1.270	**1.630**±0.074	<0.0001	<0.0001	0.878
All non-primates	57	-30.607±1.290	**1.844**±0.076	<0.0001	<0.0001	0.914
Afrotheria	6	-27.952±2.498	**1.663**±0.142	0.0004	0.0003	0.972
Artiodactyla	5	-30.323±5.553	**1.850**±0.303	0.0121	0.0089	0.925
Carnivora	8	-29.260±4.244	**1.803**±0.243	0.0005	0.0003	0.902
Chiroptera	13	-22.765±2.573	**1.343**±0.162	<0.0001	<0.0001	0.862
Eulipotyphla	5	-22.360±7.566	**1.297**±0.476	0.0598	0.0722	0.712
Marsupialia	9	-26.017±4.666	**1.598**±0.274	0.0008	0.0006	0.829
Primata	12	-19.962±2.087	**1.198**±0.116	<0.0001	<0.0001	0.915
Rodentia	10	-26.202±4.283	**1.568**±0.252	0.0003	0.0003	0.829
Scandentia	1					
All non-primate mammals, all reptiles minus Testudines, crocodile	145	-27.633±0.548	**1.673**±0.035	<0.0001	<0.0001	0.942

Table S7. Scaling of neuronal density with varying numbers of neurons in the rest of brain of reptiles, birds and mammals. Values correspond to the equation $D_{Nrob} = e^{a\pm SE} N_{rob}^{b\pm SE}$, the p-values for a and b, and the r^2 for the power fit, where D_{Nrob} is neuronal density in the rest of brain and N_{rob} is the number of neurons in the rest of brain. In reptiles and birds, rest of brain consists of the brainstem and diencephalon; in mammals, it additionally contains the striatum.

D_{Nrob} x N_{rob}	**n**	**a in e^a**	**b in N_{rob}^b**	**p, a**	**p, b**	**r^2**
Reptiles						
All	108	18.988±1.306	**-0.572**±0.087	<0.0001	<0.0001	0.291
Anguimorpha	7	20.0455±4.455	**-0.641**±0.285	0.0064	0.0744	0.503
Crocodilia	1					
Gekkota	14	19.654±3.864	**-0.605**±0.264	0.0003	0.0409	0.304
Iguania	20	19.971±2.353	**-0.625**±0.154	<0.0001	0.0007	0.479
Lacertoidea	15	18.613±1.844	**-0.526**±0.122	<0.0001	0.0008	0.589
Scincoidea	14	17.280±2.684	**-0.443**±0.180	<0.0001	0.0299	0.336
Serpentes	18	16.789±3.585	**-0.421**±0.238	0.0002	0.0962	0.163
Testudines	19	15.473±3.996	**-0.384**±0.267	0.0012	0.1683	0.109
Testudines and Crocodilia	20	18.854±3.151	**-0.610**±0.209	<0.0001	0.0092	0.321

All minus Testudines, Crocodilia	90	19.168±1.017	**-0.573**±0.067	<0.0001	<0.0001	0.456
Birds						
All	65	16.611±2.991	**-0.344**±0.173	<0.0001	0.0505	0.059
Accipitriformes	4	11.919±6.627	**-0.072**±0.364	0.1222	0.8489	0.007
Anseriformes	7	5.491±5.602	**0.269**±0.323	0.3463	0.4210	0.055
Columbiformes	5	21.172±2.138	**-0.615**±0.126	0.0022	0.0163	0.889
Falconiformes	3	36.340±25.388	**-1.407**±1.420	0.3882	0.5027	0.496
Galliformes	9	22.759±4.091	**-0.715**±0.239	0.0008	0.0202	0.561
Palaeognathae	6	66.530±19.270	**-3.230**±1.102	0.0260	0.0428	0.682
Passeriformes	13	25.522±2.616	**-0.815**±0.150	<0.0001	0.0002	0.728
Psittaciformes	11	31.242±2.968	**-1.203**±0.173	<0.0001	<0.0001	0.843
Strigiformes	7	12.655±8.411	**-0.123**±0.481	0.1928	0.8084	0.013
Galliformes, Columbiformes, Palaeognathae	32	27.464±4.190	**-0.990**±0.244	<0.0001	0.0007	0.479
Accipitriformes, Falconiformes, Passeriformes	20	25.948±2.948	**-0.842**±0.168	<0.0001	<0.0001	0.583
Mammals						
All	69	20.163±1.272	**-0.627**±0.074	<0.0001	<0.0001	0.515
All non-primates	57	23.707±1.290	**-0.845**±0.076	<0.0001	<0.0001	0.690
Afrotheria	6	21.029±2.519	**-0.662**±0.144	0.0011	0.0099	0.842
Artiodactyla	5	23.412±5.552	**-0.850**±0.303	0.0244	0.0677	0.724
Carnivora	8	22.353±4.245	**-0.803**±0.243	0.0019	0.0163	0.646
Chiroptera	13	15.823±2.532	**-0.340**±0.160	<0.0001	0.0564	0.292
Eulipotyphla	5	15.344±7.440	**-0.290**±0.468	0.1312	0.5789	0.114
Marsupialia	9	19.109±4.666	**-0.598**±0.274	0.0046	0.0654	0.405
Primata	12	12.734±2.035	**-0.180**±0.113	<0.0001	0.1413	0.203
Rodentia	10	19.215±4.232	**-0.563**±0.249	0.0019	0.0535	0.390
Scandentia	1					
All non-primate mammals, all reptiles minus Testudines, crocodile	145	20.717±0.549	**-0.672**±0.035	<0.0001	<0.0001	0.724

Table S8. Scaling of neuronal density in the rest of brain of reptiles, birds and mammals with varying body mass. Values correspond to the equation $D_{Ncb} = e^{a\pm SE} M_{bd}^{b\pm SE}$, the p-values for a and b, and the r^2 for the power fit, where D_{Nrob} is neuronal density in the rest of brain and M_{bd} is the average body mass for the species. In reptiles and birds, rest of brain consists of the brainstem and diencephalon; in mammals, it additionally contains the striatum.

D_{Nrob} x M_{bd}	**n**	**a in e^a**	**b in M_{bd}^b**	**p, a**	**p, b**	**r^2**
Reptiles						
All	108	11.570±0.063	**-0.245**±0.012	<0.0001	<0.0001	0.806
Anguimorpha	7	12.045±0.336	**-0.320**±0.051	<0.0001	0.0015	0.887
Crocodilia	1					
Gekkota	14	11.745±0.156	**-0.348**±0.052	<0.0001	<0.0001	0.786
Iguania	20	11.503±0.152	**-0.236**±0.030	<0.0001	<0.0001	0.772
Lacertoidea	15	11.440±0.109	**-0.218**±0.028	<0.0001	<0.0001	0.828
Scincoidea	14	11.563±0.174	**-0.251**±0.046	<0.0001	0.0001	0.716
Serpentes	18	11.820±0.171	**-0.231**±0.028	<0.0001	<0.0001	0.809
Testudines	19	11.825±0.276	**-0.301**±0.039	<0.0001	<0.0001	0.779
Testudines and Crocodilia	20	11.792±0.218	**-0.296**±0.030	<0.0001	<0.0001	0.847
All minus Testudines, Crocodilia	88	11.474±0.067	**-0.215**±0.014	<0.0001	<0.0001	0.732
All minus Serpentes	90	11.582±0.055	**-0.261**±0.011	<0.0001	<0.0001	0.873
Birds						
All	65	12.534±0.110	**-0.317**±0.018	<0.0001	<0.0001	0.837
Accipitriformes	4	12.399±0.562	**-0.270**±0.080	0.0020	0.0774	0.851
Anseriformes	7	12.844±0.322	**-0.400**±0.045	<0.0001	0.0003	0.941
Columbiformes	5	12.040±0.220	**-0.240**±0.039	<0.0001	0.0085	0.927
Falconiformes	3	12.795±0.679	**-0.297**±0.122	0.0337	0.2472	0.857
Galliformes	9	12.184±0.311	**-0.260**±0.048	<0.0001	0.0009	0.810
Palaeognathae	6	12.231±0.111	**-0.372**±0.013	<0.0001	<0.0001	0.995
Passeriformes	13	12.633±0.096	**-0.294**±0.021	<0.0001	<0.0001	0.949
Psittaciformes	11	12.460±0.130	**-0.354**±0.025	<0.0001	<0.0001	0.959
Strigiformes	7	12.037±0.561	**-0.253**±0.091	<0.0001	0.0388	0.608
Anseriformes, Galliformes, Columbiformes,	45	12.239±0.130	**-0.286**±0.020	<0.0001	<0.0001	0.829

Palaeognathae, Psittaciformes, Strigiformes						
Galliformes, Columbiformes, Psittaciformes, Strigiformes	32	12.085±0.154	**-0.260**±0.026	<0.0001	<0.0001	0.770
Accipitriformes, Falconiformes, Passeriformes	20	12.657±0.098	**-0.297**±0.018	<0.0001	<0.0001	0.936
Mammals						
All	70	11.563±0.103	**-0.304**±0.014	<0.0001	<0.0001	0.881
All non-primates	58	11.592±0.099	**-0.315**±0.013	<0.0001	<0.0001	0.913
Afrotheria	6	11.372±0.306	**-0.265**±0.306	<0.0001	0.0020	0.927
Artiodactyla	5	9.726±1.751	**-0.161**±0.150	0.0115	0.3630	0.276
Carnivora	8	10.916±0.385	**-0.271**±0.039	<0.0001	0.0005	0.888
Chiroptera	13	11.256±0.228	**-0.235**±0.062	<0.0001	0.0029	0.570
Eulipotyphla	5	11.689±0.502	**-0.285**±0.144	0.0002	0.1425	0.566
Marsupialia	9	11.628±0.540	**-0.330**±0.065	<0.0001	0.0014	0.788
Primata	12	10.780±0.407	**-0.171**±0.052	<0.0001	0.0085	0.516
Rodentia	10	11.735±0.410	**-0.314**±0.059	<0.0001	0.0007	0.778
Scandentia	1					
All mammals, all reptiles	177	11.725±0.060	**-0.301**±0.010	<0.0001	<0.0001	0.850

Table S9 – Scaling of the mass of the telencephalon or pallium (M_{tel}; reptilian telencephalon or bird or mammalian pallium), mass of the cerebellum (M_{cb}), and mass of the rest of brain (M_{rob}; reptilian or bird brainstem and diencephalon, or mammalian brainstem, diencephalon plus striatum) as a function of one another in the different groups. Values correspond to the equation $M_{structure1} = e^{a\pm SE} M_{structure2}^{b\pm SE}$, the p-values for a and b, and the r^2 for the power fit.

M_{tel} x M_{rob}	**n**	**a in e^a**	**b in N_{rob}^b**	**p, a**	**p, b**	**r^2**
Reptiles						
All	108	0.341±0.092	**1.112**±0.038	0.0003	<0.0001	0.891
Testudines and crocodile	20	0.614±0.115	**0.952**±0.067	<0.0001	<0.0001	0.918

All minus Testudines and crocodile	88	0.041±0.087	**1.035**±0.034	0.6410	<0.0001	0.917
Mammals						
All	69	0.640±0.051	**1.231**±0.024	<0.0001	<0.0001	0.975
Primates	12	1.137±0.144	**1.294**±0.069	<0.0001	<0.0001	0.972
All minus primates	57	0.533±0.037	**1.193**±0.017	<0.0001	<0.0001	0.988
All reptiles and mammals minus Testudines and crocodiles, and primates	145	0.457±0.032	**1.189**±0.013	<0.0001	<0.0001	0.983
Birds						
Anseriformes, Accipitriformes, Falconiformes	14	0.571±0.049	**1.227**±0.065	<0.0001	<0.0001	0.968
Palaeognathae, Galliformes, Columbiformes	20	0.236±0.059	**1.107**±0.051	0.0009	<0.0001	0.963
Passeriformes, Strigiformes	20	1.020±0.048	**1.301**±0.053	<0.0001	<0.0001	0.971
Psittaciformes	11	0.848±0.016	**1.132**±0.018	<0.0001	<0.0001	0.998
M_{cb} x M_{rob}	**n**	**a in e^a**	**b in N_{rob}^b**	**p, a**	**p, b**	**r^2**
Reptiles						
All	108	-2.225±0.139	**1.318**±0.057	<0.0001	<0.0001	0.835
Testudines and crocodile	20	-1.856±0.172	**1.111**±0.100	<0.0001	<0.0001	0.872
All minus Testudines and crocodile	88	-2.623±0.143	**1.215**±0.056	<0.0001	<0.0001	0.848
Mammals						
All (minus elephant)	67	-0.712±0.038	**1.080**±0.019	<0.0001	<0.0001	0.981
Primates	11	-0.481±0.145	**1.123**±0.067	0.0091	<0.0001	0.969
All minus primates, elephant	56	-0.762±0.035	**1.055**±0.018	<0.0001	<0.0001	0.985

Birds						
All	65	-1.004±0.027	**1.054**±0.028	<0.0001	<0.0001	0.958
All minus Psittaciformes	54	-0.961±0.026	**1.084**±0.027	<0.0001	<0.0001	0.970
Psittaciformes	11	-1.198±0.032	**0.913**±0.036	<0.0001	<0.0001	0.986
M_{tel} x M_{cb}	**n**	**a in e^a**	**b in N_{rob}^b**	**p, a**	**p, b**	**r^2**
Reptiles						
All	108	1.634±0.190	**0.730**±0.036	<0.0001	<0.0001	0.799
Testudines and crocodile	20	1.905±0.275	**0.772**±0.075	<0.0001	<0.0001	0.855
All minus Testudines and crocodile	88	1.407±0.265	**0.694**±0.047	<0.0001	<0.0001	0.719
Mammals						
All (minus elephant)	67	1.444±0.039	**1.143**±0.018	<0.0001	<0.0001	0.983
Primates	11	1.651±0.139	**1.149**±0.066	<0.0001	<0.0001	0.971
All minus primates, elephant	56	1.395±0.040	**1.124**±0.019	<0.0001	<0.0001	0.984
Birds						
Anseriformes, Accipitriformes, Falconiformes	14	1.460±0.066	**1.007**±0.087	<0.0001	<0.0001	0.917
Palaeognathae, Galliformes, Columbiformes	20	1.304±0.023	**1.060**±0.016	<0.0001	<0.0001	0.996
Passeriformes, Psittaciformes, Strigiformes	31	2.280±0.041	**1.226**±0.029	<0.0001	<0.0001	0.984

Table S10 – Scaling of the mass ratios between structures as a function of the mass of the rest of the brain in the different groups. M_{tel}, mass of the reptilian telencephalon or bird or mammalian pallium; M_{cb}, mass of the cerebellum; M_{rob}, mass of the rest of brain, which is the reptilian or bird brainstem and diencephalon, or the mammalian brainstem, diencephalon plus striatum. Values correspond to the equation $M_{structure1} = e^{a\pm SE} M_{structure2}^{b\pm SE}$, the p-values for a and b, and the r^2 for the power fit.

M_{tel} /M_{rob} x M_{rob}	n	a in e^a	b in N_{rob}^b	p, a	p, b	r^2
Reptiles						
All (1.20±0.56)	108	0.341±0.092	**1.112**±0.038	0.0003	0.0037	0.077
Serpentes (1.16±0.43)	18	0.508±0.375	**0.184**±0.155	0.1945	0.2547	0.080
Testudines and crocodile (2.05±0.56)	20	0.614±0.115	**-0.048**±0.067	<0.0001	0.4818	0.028
All minus Testudines and crocodile (1.08±0.33)	88	0.041±0.087	**0.035**±0.034	0.6410	0.3022	0.012
All minus Serpentes, Testudines and crocodile (0.97±0.30)	70	-0.022±0.083	**0.021**±0.032	0.7868	0.4996	0.007
Mammals						
All (2.73±1.98)	69	0.640±0.051	**0.231**±0.024	<0.0001	<0.0001	0.580
Primates (5.57±2.55)	12	1.137±0.144	**0.294**±0.069	<0.0001	0.0017	0.642
All minus primates (2.13±1.18)	57	0.533±0.037	**0.193**±0.017	<0.0001	<0.0001	0.691
All reptiles and mammals minus Testudines and crocodiles, and primates (1.45±0.96)	145	0.457±0.032	**0.189**±0.013	<0.0001	<0.0001	0.592
Birds						
Anseriformes, Accipitriformes, Falconiformes (2.01±0.38)	14	0.571±0.049	**0.227**±0.065	<0.0001	0.0044	0.505
Palaeognathae, Galliformes,	20	0.236±0.059	**0.107**±0.051	0.0009	0.0514	0.195

Columbiformes (1.34±0.47)						
Passeriformes, Strigiformes (2.81±0.90)	20	1.020±0.048	**0.301**±0.053	<0.0001	<0.0001	0.643
Psittaciformes (2.44±0.30)	11	0.848±0.016	**0.132**±0.018	<0.0001	<0.0001	0.860
M_{cb} /M_{rob} x M_{rob}	**n**	**a in e^a**	**b in N_{rob}^b**	**p, a**	**p, b**	**r^2**
Reptiles						
All (0.07±0.05)	108	-2.225±0.139	**0.318**±0.057	<0.0001	<0.0001	0.228
Serpentes (0.03±0.01)	18	-3.199±0.336	**0.193**±0.139	<0.0001	0.1842	0.107
Testudines and crocodile (0.14±0.05)	20	-1.856±0.172	**0.111**±0.100	<0.0001	0.2818	0.064
All minus Testudines and crocodile (0.05±0.03)	88	-2.623±0.143	**0.215**±0.056	<0.0001	0.0002	0.149
All minus Serpentes, Testudines and crocodile (0.06±0.02)	70	-2.471±0.137	**0.223**±0.052	<0.0001	<0.0001	0.211
Mammals						
All (minus elephant) (0.55±0.21)	67	-0.712±0.038	**0.080**±0.019	<0.0001	<0.0001	0.217
Primates (0.80±0.28)	11	-0.481±0.145	**0.123**±0.067	0.0091	0.1006	0.271
All minus primates, elephant (0.50±0.15)	56	-0.762±0.035	**0.055**±0.018	<0.0001	0.0026	0.156
Birds						
All (0.38±0.09)	65	-1.004±0.027	**0.054**±0.028	<0.0001	0.0552	0.057
All minus Psittaciformes (0.39±0.08)	54	-0.961±0.026	**0.084**±0.027	<0.0001	0.0026	0.162

Psittaciformes (0.30±0.04)	11	-1.197±0.032	**-0.087**±0.036	<0.0001	0.0377	0.397
M_{tel} /M_{cb} x M_{rob}	**n**	**a in e^a**	**b in N_{rob}^b**	**p, a**	**p, b**	**r^2**
Reptiles						
All (26.87±27.66)	108	2.566±0.148	**-0.206**±0.060	<0.0001	0.0009	0.099
Testudines and crocodile (16.15±6.31)	20	2.4470±0.177	**-0.160**±0.103	<0.0001	0.1389	0.118
All minus Testudines and crocodile (29.30±30.00)	88	2.664±0.188	**-0.180**±0.073	<0.0001	0.0155	0.066
Mammals						
All (minus elephant) (4.60±1.95)	67	1.338±0.040	**0.162**±0.019	<0.0001	<0.0001	0.515
Primates (6.85±2.09)	11	1.536±0.149	**0.194**±0.069	<0.0001	0.0206	0.466
All minus primates, elephant (4.16±1.61)	56	1.296±0.038	**0.141**±0.019	<0.0001	<0.0001	0.499
Birds						
Anseriformes, Accipitriformes, Falconiformes (4.39±0.91)	14	1.429±0.077	**0.062**±0.102	<0.0001	0.5571	0.029
Palaeognathae, Galliformes, Columbiformes (3.52±0.40)	20	1.243±0.020	**0.062**±0.017	<0.0001	0.0019	0.422
Passeriformes, Psittaciformes, Strigiformes (7.88±1.90)	31	2.033±0.025	**0.231**±0.028	<0.0001	<0.0001	0.702

Table S11 – Scaling of neurons in the reptilian telencephalon or bird/mammalian pallium (N_{tel}) as a function of numbers of neurons in the rest of brain (N_{rob}; reptilian or bird brainstem and diencephalon, or mammalian brainstem, diencephalon plus striatum). Values correspond to the equation $N_{Tel} = e^{a \pm SE} N_{rob}^{b \pm SE}$, the p-values for a and b, and the r^2 for the power fit.

N_{Tel} x N_{rob}	**n**	**a in e^a**	**b in N_{rob}^b**	**p, a**	**p, b**	**r^2**
Reptiles						
All	108	-0.168±1.252	**1.035**±0.083	0.8935	<0.0001	0.594
Anguimorpha	7	-1.508±3.300	**1.145**±0.211	0.6668	0.0029	0.854
Crocodilia	1					
Gekkota	14	-3.634±3.081	**1.271**±0.211	0.2612	<0.0001	0.752
Iguania	20	-1.524±1.977	**1.087**±0.129	0.4508	<0.0001	0.797
Lacertoidea	15	-2.045±2.602	**1.149**±0.172	0.4461	<0.0001	0.775
Scincoidea	14	0.078±2.390	**1.023**±0.160	0.9744	<0.0001	0.772
Serpentes	18	0.846±5.039	**0.970**±0.335	0.8688	0.0106	0.344
Testudines and Crocodilia	20	0.473±1.937	**1.025**±0.129	0.8099	<0.0001	0.779
All minus Serpentes, Testudines, Crocodilia	70	-0.542±1.275	**1.050**±0.084	0.6722	<0.0001	0.694
Birds						
All	65	-5.027±1.826	**1.341**±0.101	0.0077	<0.0001	0.736
Accipitriformes	4	-15.931±12.473	**1.921**±0.677	0.3298	0.1049	0.801
Anseriformes	7	-5.344±4.309	**1.376**±0.244	0.2699	0.0024	0.864
Columbiformes	5	-5.907±3.841	**1.365**±0.222	0.2216	0.0086	0.927
Falconiformes	3	-14.767±8.525	**1.870**±0.468	0.3333	0.1561	0.941
Galliformes	9	-4.157±2.056	**1.259**±0.118	0.0830	<0.0001	0.942
Palaeognathae	6	-28.708±5.017	**2.654**±0.280	0.0046	0.0007	0.957
Passeriformes	13	-7.678±1.235	**1.491**±0.068	<0.0001	<0.0001	0.977
Psittaciformes	11	1.707±0.991	**0.973**±0.053	0.1192	<0.0001	0.974
Strigiformes	7	-4.614±3.495	**1.392**±0.195	0.2440	0.0008	0.911
All minus Strigiformes	58	-5.559±1.220	**1.362**±0.068	<0.0001	<0.0001	0.879
Mammals						
All	70	11.563±0.103	**-0.304**±0.014	<0.0001	<0.0001	0.881
All non-primates	58	11.592±0.099	**-0.315**±0.013	<0.0001	<0.0001	0.913
Afrotheria	6	11.372±0.306	**-0.265**±0.306	<0.0001	0.0020	0.927
Artiodactyla	5	9.726±1.751	**-0.161**±0.150	0.0115	0.3630	0.276

Carnivora	8	10.916±0.385	**-0.271**±0.039	<0.0001	0.0005	0.888
Chiroptera	13	11.256±0.228	**-0.235**±0.062	<0.0001	0.0029	0.570
Eulipotyphla	5	11.689±0.502	**-0.285**±0.144	0.0002	0.1425	0.566
Marsupialia	9	11.628±0.540	**-0.330**±0.065	<0.0001	0.0014	0.788
Primata	12	10.780±0.407	**-0.171**±0.052	<0.0001	0.0085	0.516
Rodentia	10	11.735±0.410	**-0.314**±0.059	<0.0001	0.0007	0.778
Scandentia	1					
All mammals, all reptiles	177	11.725±0.060	**-0.301**±0.010	<0.0001	<0.0001	0.850

Table S12 – Scaling of neurons in the cerebellum (N_{cb}) as a function of numbers of neurons in the rest of brain (N_{rob}; reptilian or bird brainstem and diencephalon, or mammalian brainstem, diencephalon plus striatum). Values correspond to the equation $N_{cb} = e^{a\pm SE} N_{rob}^{b\pm SE}$, the p-values for a and b, and the r^2 for the power fit.

N_{Cb} x N_{rob}	**n**	**a in e^a**	**b in N_{rob}^b**	**p, a**	**p, b**	**r^2**
Reptiles						
All	108	-7.329±2.201	**1.429**±0.146	0.0012	<0.0001	0.475
Anguimorpha	7	-25.867±6.062	**2.597**±0.388	0.0080	0.0011	0.900
Crocodilia	1					
Gekkota	14	-9.390±4.080	**1.587**±0.279	0.0401	0.0001	0.729
Iguania	20	-0.185±1.526	**0.977**±0.100	0.9049	<0.0001	0.842
Lacertoidea	15	-3.750±3.205	**1.172**±0.211	0.2631	<0.0001	0.703
Scincoidea	14	-8.557±3.160	**1.492**±0.212	0.0190	<0.0001	0.805
Serpentes	18	-5.528±4.058	**1.233**±0.270	0.1920	0.0003	0.566
Testudines and Crocodilia	20	-8.934±2.882	**1.612**±0.191	0.0062	<0.0001	0.798
All minus Serpentes, Testudines, Crocodilia	70	-7.008±1.653	**1.405**±0.110	<0.0001	<0.0001	0.708
Birds						
All	65	4.487±1.462	**0.822**±0.081	0.0032	<0.0001	0.620
Accipitriformes	4	-2.245±10.904	**1.209**±0.591	0.8559	0.1776	0.676
Anseriformes	7	-13.063±6.875	**1.837**±0.389	0.1159	0.0053	0.817
Columbiformes	5	-8.072±5.515	**1.549**±0.318	0.2395	0.0166	0.888
Falconiformes	3	-20.443±10.178	**2.196**±0.559	0.2941	0.1586	0.939
Galliformes	9	-5.606±4.027	**1.399**±0.230	0.2065	0.0005	0.841

Palaeognathae	6	-21.326±5.267	**2.287**±0.294	0.0155	0.0015	0.938
Passeriformes	13	-1.796±1.077	**1.160**±0.060	0.1237	<0.0001	0.972
Psittaciformes	11	6.063±1.284	**0.709**±0.068	0.0011	<0.0001	0.923
Strigiformes	7	-1.128±5.866	**1.141**±0.327	0.8551	0.0174	0.709
All minus Psittaciformes	54	-2.085±1.627	**1.196**±0.091	0.2056	<0.0001	0.768
Mammals						
All	70	11.563±0.103	**-0.304**±0.014	<0.0001	<0.0001	0.881
All non-primates	58	11.592±0.099	**-0.315**±0.013	<0.0001	<0.0001	0.913
Afrotheria	6	11.372±0.306	**-0.265**±0.306	<0.0001	0.0020	0.927
Artiodactyla	5	9.726±1.751	**-0.161**±0.150	0.0115	0.3630	0.276
Carnivora	8	10.916±0.385	**-0.271**±0.039	<0.0001	0.0005	0.888
Chiroptera	13	11.256±0.228	**-0.235**±0.062	<0.0001	0.0029	0.570
Eulipotyphla	5	11.689±0.502	**-0.285**±0.144	0.0002	0.1425	0.566
Marsupialia	9	11.628±0.540	**-0.330**±0.065	<0.0001	0.0014	0.788
Primata	12	10.780±0.407	**-0.171**±0.052	<0.0001	0.0085	0.516
Rodentia	10	11.735±0.410	**-0.314**±0.059	<0.0001	0.0007	0.778
Scandentia	1					
All mammals, all reptiles	177	11.725±0.060	**-0.301**±0.010	<0.0001	<0.0001	0.850

Table S13 – Scaling of neurons in the cerebellum (N_{cb}) as a function of numbers of neurons in the telencephalon or pallium (N_{tel}; reptilian telencephalon or bird or mammalian pallium). Values correspond to the equation $N_{cb} = e^{a\pm SE}\ N_{tel}^{b\pm SE}$, the p-values for a and b, and the r^2 for the power fit.

N_{Cb} x N_{tel}	**n**	**a in e^a**	**b in N_{rob}^b**	**p, a**	**p, b**	**r^2**
Reptiles						
All	108	-1.222±1.767	**1.000**±0.114	0.4904	<0.0001	0.419
Anguimorpha	7	-19.526±5.283	**2.091**±0.323	0.0141	0.0013	0.894
Crocodilia	1					
Gekkota	14	-1.849±3.082	**1.047**±0.206	0.5597	0.0003	0.683
Iguania	20	2.548±1.187	**0.809**±0.079	0.0457	<0.0001	0.855
Lacertoidea	15	0.378±2.560	**0.888**±0.167	0.8848	0.0001	0.686
Scincoidea	14	-3.054±4.078	**1.092**±0.266	0.4684	0.0015	0.584

Serpentes	18	7.087±3.523	**0.384**±0.228	0.0614	0.1120	0.150
Testudines and Crocodilia	20	-6.533±2.718	**1.375**±0.171	0.0272	<0.0001	0.782
All minus Serpentes, Testudines, Crocodilia	70	-0.005±1.759	**0.928**±0.115	0.9977	<0.0001	0.490
Birds						
All	65	9.310±1.006	**0.522**±0.052	<0.0001	<0.0001	0.611
Accipitriformes	4	7.638±3.477	**0.637**±0.178	0.1592	0.0703	0.864
Anseriformes	7	-1.860±6.735	**1.120**±0.355	0.7934	0.0253	0.665
Columbiformes	5	-0.881±3.526	**1.107**±0.199	0.8189	0.0114	0.912
Falconiformes	3	-3.120±0.088	**1.176**±0.005	0.0179	0.0025	0.999
Galliformes	9	-1.401±2.108	**1.134**±0.118	0.5277	<0.0001	0.930
Palaeognathae	6	3.352±0.923	**0.865**±0.049	0.0221	<0.0001	0.987
Passeriformes	13	4.395±0.840	**0.767**±0.043	0.0003	<0.0001	0.966
Psittaciformes	11	4.876±1.224	**0.727**±0.061	0.0032	<0.0001	0.940
Strigiformes	7	1.172±2.350	**0.893**±0.115	0.6390	0.0006	0.923
Anseriformes, Accipitriformes, Galliformes, Columbiformes, Palaeognathae	31	3.991±1.100	**0.826**±0.059	0.0011	<0.0001	0.869
Passeriformes, Psittaciformes	24	5.600±0.874	**0.698**±0.044	<0.0001	<0.0001	0.918
Mammals						
All	70	11.563±0.103	**-0.304**±0.014	<0.0001	<0.0001	0.881
All non-primates	58	11.592±0.099	**-0.315**±0.013	<0.0001	<0.0001	0.913
Afrotheria	6	11.372±0.306	**-0.265**±0.306	<0.0001	0.0020	0.927
Artiodactyla	5	9.726±1.751	**-0.161**±0.150	0.0115	0.3630	0.276
Carnivora	8	10.916±0.385	**-0.271**±0.039	<0.0001	0.0005	0.888
Chiroptera	13	11.256±0.228	**-0.235**±0.062	<0.0001	0.0029	0.570
Eulipotyphla	5	11.689±0.502	**-0.285**±0.144	0.0002	0.1425	0.566
Marsupialia	9	11.628±0.540	**-0.330**±0.065	<0.0001	0.0014	0.788
Primata	12	10.780±0.407	**-0.171**±0.052	<0.0001	0.0085	0.516
Rodentia	10	11.735±0.410	**-0.314**±0.059	<0.0001	0.0007	0.778
Scandentia	1					
All mammals, all reptiles	177	11.725±0.060	**-0.301**±0.010	<0.0001	<0.0001	0.850

Table S14 – Scaling of the ratio N_{tel}/N_{rob} between neurons in the telencephalon or pallium (N_{tel}; reptilian telencephalon or bird or mammalian pallium) and in the rest of brain (N_{rob}; reptilian or bird brainstem and diencephalon, or mammalian brainstem, diencephalon plus striatum) as a function of numbers of neurons in the rest of brain (N_{rob}). Values correspond to the equation $N_{tel}/N_{rob} = e^{a\pm SE}\ N_{rob}^{b\pm SE}$, the p-values for a and b, and the r^2 for the power fit. Values in parentheses are the average ratio N_{tel}/N_{rob} for the clade ± standard deviation.

N_{tel}/N_{rob} x N_{rob}	**n**	**a in e^a**	**b in N_{rob}^b**	**p, a**	**p, b**	**r^2**
Reptiles						
All (1.602±0.754)	108	-0.168±1.252	**0.035**±0.083	0.8935	0.6748	0.002
Anguimorpha (2.242±0.775)	7	-1.508±3.300	**0.145**±0.211	0.6668	0.5243	0.086
Crocodilia	1					
Gekkota (1.466±0.493)	14	-3.634±3.081	**0.271**±0.211	0.2612	0.2222	0.121
Iguania (0.864±0.306)	20	-1.524±1.977	**0.087**±0.129	0.4508	0.5112	0.024
Lacertoidea (1.317±0.525)	15	-2.045±2.602	**0.149**±0.172	0.4461	0.4024	0.054
Scincoidea (1.593±0.471)	14	0.078±2.390	**0.023**±0.160	0.9744	0.8884	0.002
Serpentes (1.644±0.784)	18	0.846±5.039	**-0.030**±0.335	0.8688	0.9287	0.001
Testudines and Crocodilia (2.393±0.617)	20	0.473±1.937	**0.025**±0.129	0.8099	0.8505	0.002
All minus Serpentes, Testudines, Crocodilia (1.365±0.621)	70	-0.542±1.275	**0.050**±0.084	0.6722	0.5559	0.005
Birds						
All	65	-5.027±1.826	**0.341**±0.101	0.0077	0.0013	0.153
Accipitriformes (3.073±1.326)	4	-15.931±12.473	**0.921**±0.677	0.3298	0.3067	0.481
Anseriformes (3.721±0.644)	7	-5.344±4.309	**0.376**±0.244	0.2699	0.1836	0.322

Columbiformes (1.561±0.417)	5	-5.907±3.841	**0.365**±0.222	0.2216	0.1980	0.475
Falconiformes (3.040±0.879)	3	-14.767±8.525	**0.870**±0.468	0.3333	0.3142	0.776
Galliformes (1.490±0.363)	9	-4.157±2.056	**0.259**±0.118	0.0830	0.0633	0.410
Palaeognathae (3.045±2.024)	6	-28.708±5.017	**1.654**±0.280	0.0046	0.0041	0.897
Passeriformes (3.546±1.303)	13	-7.678±1.235	**0.491**±0.068	<0.0001	<0.0001	0.825
Psittaciformes (3.329±0.486)	11	1.707±0.991	**-0.028**±0.053	0.1192	0.6162	0.029
Strigiformes (11.536±2.503)	7	-4.614±3.495	**0.392**±0.195	0.2440	0.1002	0.448
Galliformes, Columbiformes (1.515±0.369)	14	-4.436±1.729	**0.277**±0.099	0.0247	0.0163	0.394
Mammals						
All (5.425±5.464)	69	-7.601±1.115	**0.521**±0.065	<0.0001	<0.0001	0.489
All non-primates (3.710±2.873)	57	-5.932±1.118	**0.414**±0.066	<0.0001	<0.0001	0.416
Afrotheria (minus elephant) (2.412±0.415)	5	-0.124±1.869	**0.059**±0.110	0.9514	0.6319	0.086
Artiodactyla (7.349±2.778)	5	-14.592±3.155	**0.904**±0.172	0.0190	0.0135	0.902
Carnivora (7.360±3.339)	8	-1.611±6.173	**0.200**±0.353	0.8028	0.5923	0.051
Chiroptera (1.598±0.665)	13	3.190±3.095	**-0.176**±0.195	0.3248	0.3852	0.069
Eulipotyphla (1.934±0.213)	5	1.733±2.264	**-0.068**±0.142	0.4998	0.6664	0.070
Marsupialia (4.610±2.294)	9	-5.267±4.025	**0.392**±0.236	0.2320	0.1411	0.282
Primata (13.571±7.411)	12	-4.617±2.854	**0.391**±0.158	0.13681	0.0329	0.380
Rodentia (2.164±0.602)	10	-1.015±2.208	**0.103**±0.130	0.65791	0.4509	0.073

Scandentia (2.686)	1					
Small mammals: Afrotheria (minus elephant), Chiroptera, Eulipotyphla, Rodentia, Scandentia (1.965±0.630)	34	-1.405±1.162	**0.124**±0.071	0.2355	0.0908	0.087

Table S15 – Scaling of the ratio N_{cb}/N_{rob} between neurons in the cerebellum (N_{cb}) and in the rest of brain (N_{rob}; reptilian or bird brainstem and diencephalon, or mammalian brainstem, diencephalon plus striatum) as a function of numbers of neurons in the rest of brain (N_{rob}). Values correspond to the equation $N_{cb}/N_{rob} = e^{a\pm SE}\ N_{rob}^{b\pm SE}$, the p-values for a and b, and the r^2 for the power fit. Values in parentheses are the average ratio N_{cb}/N_{rob} for the clade ± standard deviation.

N_{Cb}/N_{rob} x N_{rob}	**n**	**a in e^a**	**b in N_{rob}^b**	**p, a**	**p, b**	**r^2**
Reptiles						
All (0.602±0.572)	108	-7.329±2.201	**0.429**±0.146	0.0012	0.0041	0.075
Anguimorpha (0.646±0.447)	7	-25.867±3.062	**1.597**±0.388	0.0080	0.0092	0.772
Crocodilia	1					
Gekkota 0.487±0.188	14	-9.390±4.080	**0.587**±0.279	0.0401	0.0572	0.269
Iguania (0.598±0.155)	20	-0.185±1.526	**-0.023**±0.100	0.9049	0.8164	0.003
Lacertoidea (0.352±0.157)	15	-3.750±3.205	**0.172**±0.211	0.2631	0.4298	0.049
Scincoidea (0.326±0.130)	14	-8.557±3.160	**0.492**±0.212	0.0190	0.0385	0.310
Serpentes (0.143±0.061)	18	-5.528±4.058	**0.233**±0.270	0.1920	0.4008	0.044
Testudines and Crocodilia	20	-8.934±2.882	**0.616**±0.191	0.0062	0.0050	0.362

(1.463±0.775)						
All minus Serpentes, Testudines, Crocodilia (0.474±0.232)	70	-7.008±1.653	**0.405**±0.110	<0.0001	0.0004	0.167
Birds						
All	65	4.487±1.462	**-0.178**±0.081	0.0032	0.0316	0.071
Accipitriformes (5.196±1.794)	4	-2.245±10.904	**0.209**±0.591	0.8559	0.7576	0.059
Anseriformes (5.779±1.785)	7	-13.063±6.875	**0.837**±0.389	0.1159	0.0843	0.480
Columbiformes (4.469±1.825)	5	-8.072±5.515	**0.549**±0.318	0.2395	0.1831	0.498
Falconiformes (4.083±1.561)	3	-20.443±10.178	**1.196**±0.559	0.2941	0.2781	0.821
Galliformes (4.249±1.886)	9	-5.606±4.027	**0.399**±0.230	0.2065	0.1266	0.300
Palaeognathae (6.439±3.749)	6	-21.326±5.267	**1.287**±0.294	0.0155	0.0119	0.827
Passeriformes (3.037±0.511)	13	12.633±0.096	**0.160**±0.060	0.1237	0.0212	0.396
Psittaciformes (1.898±0.583)	11	6.063±1.284	**-0.291**±0.068	0.0011	0.0021	0.669
Strigiformes (4.235±1.162)	7	-1.128±5.866	**0.141**±0.327	0.8551	0.6834	0.036
All minus Psittaciformes (4.478±2.048)	54	-2.085±1.627	**0.196**±0.091	0.2056	0.0360	0.082
Mammals						
All (26.985±43.398)	68	-6.389±1.078	**0.540**±0.063	<0.0001	<0.0001	0.527
All non-primates (minus elephant) (19.677±19.195)	56	-5.637±1.413	**0.493**±0.084	0.0002	<0.0001	0.390
Afrotheria (minus elephant)	5	-0.990±3.292	**0.170**±0.195	0.7832	0.4461	0.203

(6.869±1.993)						
Artiodactyla (38.321±13.840)	5	-9.891±5.574	**0.737**±0.305	0.1741	0.0941	0.661
Carnivora (47.426±30.782)	8	-9.555±4.646	**0.758**±0.266	0.0854	0.0291	0.576
Chiroptera (9.397±2.471)	13	3.374±1.962	**-0.073**±0.124	0.1135	0.5649	0.031
Eulipotyphla (9.143±4.579)	5	-7.648±11.087	**0.612**±0.697	0.5399	0.4442	0.205
Marsupialia (24.157±9.613)	9	-2.588±3.609	**0.334**±0.212	0.4965	0.1591	0.262
Primata (35.913±23.055)	11	-2.233±2.014	**0.315**±0.112	0.2961	0.0199	0.470
Rodentia (10.301±3.601)	10	-0.892±3.024	**0.186**±0.178	0.7755	0.3271	0.120
Scandentia	1					
Small mammals: Afrotheria (minus elephant), Chiroptera, Eulipotyphla, Rodentia, Scandentia (9.220±3.164)	34	1.171±1.279	**0.060**±0.078	0.3667	0.4459	0.018

Table S16 – Scaling of the ratio N_{cb}/N_{tel} between neurons in the cerebellum (N_{cb}) and telencephalon (N_{tel}; reptilian telencephalon or bird or mammalian pallium) as a function of numbers of neurons in the rest of brain (N_{rob}; reptilian or bird brainstem and diencephalon, or mammalian brainstem, diencephalon plus striatum). Values correspond to the equation $N_{cb}/N_{tel} = e^{a\pm SE}\ N_{rob}^{b\pm SE}$, the p-values for a and b, and the r^2 for the power fit. Values in parentheses are the average ratio N_{cb}/N_{tel} for the clade ± standard deviation.

N_{Cb}/N_{tel} x N_{rob}	**n**	**a±SE in e^a**	**b±SE in N_{rob}^b**	**p, a**	**p, b**	**r^2**
Reptiles						
All (0.403±0.293)	108	-7.161±2.242	**0.394**±0.149	0.0018	0.0093	0.062
Anguimorpha (0.291±0.201)	7	-24.359±4.994	**1.452**±0.320	0.0046	0.0061	0.805
Crocodilia	1					

Gekkota (0.348±0.142)	14	-5.756±4.222	**0.316**±0.289	0.1978	0.2957	0.091
Iguania (0.737±0.226)	20	1.340±1.640	**-0.110**±0.107	0.4247	0.3179	0.055
Lacertoidea (0.286±0.120)	15	-1.705±3.350	**0.024**±0.221	0.6193	0.9162	0.001
Scincoidea (0.228±0.123)	14	-8.635±4.175	**0.470**±0.280	0.0609	0.1195	0.190
Serpentes (0.112±0.092)	18	-6.373±6.778	**0.263**±0.451	0.3611	0.5671	0.021
Testudines and Crocodilia (0.621±0.300)	20	-9.407±2.641	**0.587**±0.175	0.0022	0.0036	0.384
All minus Serpentes, Testudines, Crocodilia (0.416±0.265)	70	-6.466±2.092	**0.355**±0.139	0.0029	0.0126	0.088
Birds						
All	65	9.514±1.920	**-0.520**±0.106	<0.0001	<0.0001	0.274
Accipitriformes (1.859±0.721)	4	13.687±8.180	**-0.712**±0.444	0.2362	0.2499	0.563
Anseriformes (1.567±0.428)	7	-7.719±8.659	**0.461**±0.490	0.4136	0.3909	0.150
Columbiformes (2.834±0.626)	5	-2.165±4.771	**0.184**±0.276	0.6809	0.5523	0.129
Falconiformes (1.316±0.140)	3	-5.676±1.653	**0.326**±0.091	0.1804	0.1725	0.928
Galliformes (2.777±0.641)	9	-1.449±2.764	**0.140**±0.158	0.6163	0.4055	0.101
Palaeognathae (2.295±0.445)	6	7.382±2.368	**-0.367**±0.132	0.0356	0.0501	0.658
Passeriformes (0.940±0.287)	13	5.882±1.353	**-0.331**±0.075	0.0012	0.0010	0.641
Psittaciformes (0.572±0.168)	11	4.356±1.191	**-0.263**±0.063	0.0053	0.0024	0.658
Strigiformes (0.366±0.062)	7	3.486±2.578	**-0.251**±0.144	0.2342	0.1411	0.379
Accipitriformes, Anseriformes, Galliformes, Columbiformes,	31	3.393±2.085	**-0.148**±0.118	0.1145	0.2195	0.052

Palaeognathae (2.301±0.742)						
Passeriformes, Psittaciformes (0.771±0.301)	24	6.313±0.974	-0.360±0.053	<0.0001	<0.0001	0.679
Mammals						
All minus bear, elephant (4.856±2.153)	66	3.304±0.910	**-0.108**±0.053	0.0006	0.0480	0.060
All non-primates (minus bear, elephant) (5.197±1.944)	55	1.756±0.932	**-0.011**±0.055	0.0651	0.8479	0.001
Afrotheria (minus elephant) (2.886±0.846)	5	-0.867±3.581	**0.112**±0.212	0.8244	0.6348	0.085
Artiodactyla (5.276±0.695)	5	4.701±3.804	**-0.166**±0.208	0.3044	0.4818	0.176
Carnivora (minus bear) (5.212±2.469)	7	1.264±6.114	**0.017**±0.352	0.8444	0.9638	0.000
Chiroptera (6.473±2.098)	13	0.184±2.601	**0.103**±0.164	0.9448	0.5425	0.035
Eulipotyphla (4.610±1.986)	5	-9.381±8.832	**0.680**±0.555	0.3661	0.3080	0.333
Marsupialia (5.631±1.676)	9	2.679±2.482	**-0.058**±0.146	0.3163	0.7021	0.022
Primata (3.148±2.424)	11	2.203±3.057	**-0.069**±0.169	0.4893	0.6942	0.018
Rodentia (4.759±1.238)	10	0.123±1.918	**0.083**±0.113	0.9504	0.4839	0.063
Scandentia	1					

Table S17 – Numbers of neurons in the three parts of the brain of fossil Therapsids: telencephalon (N_{tel}), cerebellum (N_{cb}), and rest of brain (N_{rob}), estimated from reported brain mass (M_{br}, minus olfactory bulbs; in grams) inferred from cranial endocasts according to the equations $N_{tel} = e^{16.609\pm0.040} M_{br}^{0.719\pm0.021}$ ($p<0.0001$, $r^2=0.906$), $N_{cb} = e^{18.294\pm0.052} M_{br}^{0.644\pm0.035}$ ($p<0.0001$, $r^2 = 0.913$, calculated for extant mammals) and $N_{rob} = e^{16.087\pm0.030} M_{br}^{0.570\pm0.016}$ ($p<0.0001$, $r^2=0.913$). Brain mass in grams was calculated from endocranial volume (ECV) in cm^3 assuming 1 cm^3 = 1 g. M, million neurons; B, billion neurons. N_{br}, estimated total number of brain neurons, calculated as the sum $N_{tel} + N_{cb} + N_{rob}$.

Permian									
Clade	**Species**	**Body mass**	**ECV, cm^3**	**ECV minus OB, cm3**	**References**	**Estimated N_{tel}**	**Estimated N_{cb}**	**Estimated N_{rob}**	**Estimated N_{br}**
Therapsida, Biarmosuchia	*Lemurosaurus*	5.219 kg	4.02 cm3	4.02 cm3	Benoit et al. (2017a)	44.43 M	215.83 M	18.18 M	281.68 M
Therapsida: Dinocephalia	*Struthiocephalus*	644.088 kg	65 cm3	65 cm3	Boonstra (1968)	328.61 M	1.30 B	104.68 M	1.73 B
Therapsida, Gorgonopsia	*Aelurosaurus*	7.255 kg	6.0 cm3	6.0 cm3	Benoit et al. (2017a)	59.25 M	279.33 M	26.92 M	365.49 M
Therapsida, Dicynodontia	*Pristerodon*	491 g	1.06 cm3	1.06 cm3	Laas (2015)	17.04 M	91.47 M	10.02 M	118.53 M
Therapsida, Dicynodontia	*Niassodon*	139 g	1.10 cm3	1.10 cm3	Castanhinha et al. (2013)	17.50 M	93.68 M	10.24 M	121.41 M
Therapsida, Dicynodontia	*Kawingasaurus*	1.358 kg	2.18 cm3	2.18 cm3	Laass and Kaestner (2017)	28.61 M	145.53 M	15.12 M	189.26 M
Therapsida, Dinocephalia	*Moschops*	385.341 kg	39.85 cm3	39.85 cm3	Benoit et al. (2017b)	231.16 M	945.49 M	79.20 M	1.26 B
Therapsida, Dicynodontia	*Lystrosaurus*	18.511 kg	8.00 cm3	8.00 cm3	Jerison (1973)	72.86 M	336.18 M	31.71 M	440.76 M
Triassic									
Clade	**Species**	**Body mass**	**ECV, cm^3**	**ECV minus OB, cm3**	**References**				

Therapsida, Cynodontia	*Thrinaxodon*	700 g	1.46 cm3	1.46 cm3	Rowe et al. (2011)	21.45 M	112.42 M	12.03 M	145.89 M
Therapsida, Cynodontia	*Trirachodon*	3.125 kg	2.15 cm3	2.15 cm3	Hopson (1979)	28.33 M	144.24 M	15.00 M	187.56 M
Therapsida, Therocephalia	*Tetracynodon darti*	1.317 kg	2.28 cm3	2.28 cm3	Sigurdsen et al. (2012)	29.55 M	149.79 M	15.51 M	194.85 M
Therapsida, Cynodontia	*Diademodon sp.*	50 kg	26.9871 cm3	26.9871 cm3	Rowe et al. (2011)	174.66 M	735.61 M	63.42 M	973.70 M
Therapsida, Therocephalia	*Microgomphodon*	1.797 kg	2.36 g	2.36 g	Benoit et al. (2017a)	30.29 M	153.16 M	15.81 M	199.26 M
Therapsida, Cynodontia	*Brasilitherium riograndensis*	98.57 g	0.378 cm3	0.243 cm3	Rodrigues et al. (2014)	5.91 M	35.43 M	4.33 M	45.66 M
Therapsida, Cynodontia	*Exaeretodon*	46.877 kg	19.19 cm3	19.19 cm3	Quiroga (1980)	136.69 M	590.59 M	52.22 M	779.50 M
Therapsida, Cynodontia	*Massetognathus*	1.865 kg	3.33 cm3	3.33 cm3	Quiroga (1980)	38.80 M	191.18 M	19.24 M	249.22 M
Therapsida, Cynodontia	*Therioherpeton*	64 g	0.36 cm3	0.36 cm3	Quiroga (1984)	7.84 M	45.63 M	5.41 M	58.88 M
Therapsida, Cynodontia	*Probainognathus*	590 g	1.20 cm3	1.20 cm3	Quiroga (1980)	18.63 M	99.08 M	10.76 M	128.46 M
Therapsida, Cynodontia	*Probelesodon*	3.807 kg	4.33 cm3	4.33 cm3	Quiroga (1980)	46.86 M	226.40 M	22.35 M	295.62 M
Jurassic									
Clade	**Species**	**Body mass**	**ECV, cm^3**	**ECV minus OB, cm3**	**References**				
Mammaliaformes	*Hadrocodium wui*	0.002 kg (2 g)	0.045 cm^3	0.039 cm3	Luo et al. (2001), Macrini (2006)	1.59 M	10.91 M	1.53 M	14.02 M
Mammaliaformes, Morganucodonta	*Morganucodon*	51 g	0.33 cm3	0.30 cm3 (assuming	Rowe et al. (2011)	6.87 M	40.57 M	4.88 M	52.33 M

				10% OB)					
Therapsida, Cynodontia	*Tritylodon*	6.278 kg	5.06 cm3	5.06 cm3	Benoit et al. (2017a)	52.42 M	250.30 M	24.43 M	327.14 M
Mammalia	*Triconodon mordax*	0.143 kg	0.82 cm3	0.73 cm3	Bertrand et al. (2022)	13.03 M	71.94 M	8.10 M	93.07 M
Cretaceous									
Clade	**Species**	**Body mass**	**ECV, cm³**	**ECV minus OB, cm3**	**References**				
Theriiformes (stem therian); Cladotheria	*Vincelestes neuquenianus*	0.619 kg	2.37 cm3	2.11 cm3	Macrini et al. (2007)	27.95 M	142.50 M	14.84 M	185.29 M
Multituberculate	*Kryptobaatar dashzevegi*	45.82 g	0.34 cm3	0.32 cm3	Bertrand et al. (2022)	7.20 M	42.30 M	5.06 M	54.56 M
Multituberculate	*Litovoi tholocephalos*	0.248 kg	0.77 cm3 ECV	0.66 cm3	Bertrand et al. (2022)	12.12 M	67.42 M	7.65 M	87.19 M
Mammalia, Asioryctitheria	*Kennalestes gobiensis*	47.89 g	0.30 cm3 ECV	0.27 cm3	Bertrand et al. (2022)	6.37 M	37.91 M	4.60 M	48.88 M
Mammalia, Asioryctitheria	*Asioryctes nemegetensis*	53.76 g	0.50 cm3 ECV	0.45 cm3	Bertrand et al. (2022)	9.20 M	52.68 M	6.15 M	68.03 M
Mammalia, Zalambdalestidae	*Zalambdalestes lechei*	230.73 g	1.02 cm3 ECV	0.93 cm3	Bertrand et al. (2022)	15.51 M	84.08 M	9.30 M	108.89 M
Mammalia, Allotheria	*Vintana sertichi*	6.793 kg	18.30 cm3 ECV	15.64 cm3	Bertrand et al. (2022)	117.99 M	517.69 M	46.47 M	682.16 M
Paleocene									
Clade	**Species**	**Body mass**	**ECV, cm³**	**ECV minus OB, cm3**	**References**				

Multituberculate	*Ptilodus montanus*	0.216 kg	1.48 cm3 ECV	1.32 cm3	Bertrand et al. (2022)	19.95 M	105.35 M	11.36 M	136.65 M
Mammalia, Arctocyonidae	*Loxolophus priscus*	4.734 kg	2.44 cm3 ECV	2.33 cm3	Bertrand et al., 2022	30.01 M	151.90 M	15.70 M	197.61 M
Mammalia, Arctocyonidae	*Claenodon ferox*	38.41 kg	29.17 cm3 ECV	26.71 cm3	Bertrand et al., 2022	173.37 M	730.74 M	63.05 M	967.16 M
Mammalia, Condylarth, Arctocyonidae	*Chriacus baldwini*	1.833 kg	2.7 cm3	2.513 cm3	Bertrand et al. (2020)	31.69 M	159.48 M	16.39 M	207.56 M
Mammalia, Pantodonta	*Pantolambda_bathmodon*	41.919 kg	19.0 cm3 ECV	18.0 cm3	Bertrand et al. (2022)	130.54 M	566.73 M	50.35 M	747.62 M
Mammalia, Pantodonta	*Alcidedorbignya_inopinata*	0.861 kg	2.20 cm3 ECV	2.02 cm3	Bertrand et al. (2022)	27.09 M	138.56 M	14.47 M	180.12 M
Mammalia, Periptychidae	*Ectoconus ditrigonus*	105.644 kg	16.24 cm3 ECV	14.58 cm3	Bertrand et al. (2022)	112.19 M	494.82 M	44.65 M	651.65 M
Mammalia, Periptychidae	*Anisonchus sectorius*	1.789 kg	3.30 cm3 ECV	2.74 cm3	Bertrand et al. (2022)	33.72 M	168.61 M	17.22 M	219.56 M
Mammalia, Taeniodonta	*Onychodectes tisonensis*	5.033 kg	4.83 cm3 ECV	4.37 cm3	Bertrand et al. (2022)	47.17 M	227.75 M	22.47 M	297.39 M
Mammalia, Cimolestidae	*Acmeodon secans*	0.492 kg	1.64 cm3 ECV	1.41 cm3	Bertrand et al. (2022)	20.92 M	109.92 M	11.79 M	142.63 M
Mammalia, Phenacodontidae	*Tetraclaenodon pliciferus*	5.433 kg	5.22 cm3 ECV	4.51 cm3	Bertrand et al. (2022)	48.26 M	232.42 M	22.88 M	303.55 M
Mammalia, Arctocyonidae	*Arctocyon primaevus*	49.28 kg	23.81 cm3 ECV	22.21 cm3	Bertrand et al., 2022	151.83 M	648.87 M	56.76 M	857.47 M
Mammalia, Arctocyonidae	*Arctocyonides arenae*	5.477 kg	8.3 cm3 ECV	7.60 cm3	Bertrand et al., 2022	70.23 M	325.26 M	30.80 M	426.28 M

Mammalia, Pantodonta	*Titanoides primaevus*	664.06 kg	43.65 cm3 ECV	40.79 cm3	Bertrand et al. (2022)	235.06 M	959.80 M	80.26 M	1.28 B
Mammalia, Pantodonta	*Leptolambda schmidti*	256.33 kg	69.00 cm3 ECV	61.70 cm3	Bertrand et al. (2022)	316.53 M	1.25 B	101.62 M	1.67 B
Mammalia, Condylarthra, Perissodactyla	*Pleuraspidotherium aumonieri*	5.208 kg	6.00 cm3 ECV	5.60 cm3	Bertrand et al. (2022)	56.38 M	267.19 M	25.88 M	349.45 M
Mammalia, Apatemyidae	*Labidolemur kayi*	74 g	0.52 cm3 ECV	0.46 cm3	Bertrand et al. (2022)	9.35 M	53.43 M	6.23 M	69.01 M
Mammalia, Plesiadapiforms	*Plesiadapis cookei*	3.387 kg	5.00 cm3 ECV	4.61 cm3	Bertrand et al. (2022)	49.02 M	235.73 M	23.16 M	307.91 M
Mammalia, Plesiadapiforms	*Plesiadapis tricuspidens*	2.925 kg	5.21 cm3 ECV	5.07 cm3	Bertrand et al. (2022)	52.49 M	250.62 M	24.45 M	327.56 M
Eocene									
Clade	**Species**	**Body mass**	**ECV, cm³**	**ECV minus OB, cm3**	**References**				
Mammalia, Pantodonta (stem taxa)	*Coryphodon hamatus*	425.837 kg	93.0 cm3 ECV	87.0 cm3	Bertrand et al. (2022)	405.24 M	1.56 B	123.60 M	2.09 B
Mammalia, Pantodonta (stem taxa)	*Coryphodon elephantopus*	463.837 kg	90.0 cm3	86.0 cm3	Bertrand et al. (2022)	401.88 M	1.55 B	122.79 M	2.08 B
Mammalia, Taeniodonta (stem taxa)	*Ectoganus copei*	53.395 kg	38.95 cm3	34.62 cm3	Bertrand et al. (2022)	208.92 M	863.59 M	73.10 M	1.15 B
Mammalia, Euungulata (stem taxa)	*Hyopsodus miticulus*	0.630 kg	3.20 cm3	3.06 cm3	Bertrand et al. (2022)	36.51 M	181.05 M	18.34 M	235.90 M
Mammalia, Perissodactyla	*Xenicohippus sp.*	16.00 kg	29.40 cm3 ECV	26.71 cm3	Bertrand et al. (2022)	173.37 M	730.74 M	63.05 M	967.16 M
Mammalia, Phenacodontidae (stem taxa)	*Meniscotherium chamense*	6.69 kg	11.03 cm3 ECV	10.50 cm3	Bertrand et al. (2022)	88.60 M	400.52 M	37.03 M	526.16 M

Mammalia, Phenacodontidae (stem taxa)	*Phenacodus wortmani*	10.971 kg	16.19 cm3 ECV	14.99 cm3	Bertrand et al. (2022)	114.45 M	503.73 M	45.36 M	663.54 M
Mammalia, Phenacodontidae (stem taxa)	*Phenacodus primaevus*	52.8 kg	35 cm3	28.20 cm3	Cameron et al. (2018)	180.27 M	756.73 M	65.03 M	1.00 B
Mammalia, Afrotheria	*Prorastomus sirenoides*	98.156 kg	86.87 cm3 ECV	83.79 cm3	Bertrand et al. (2022)	394.43 M	1.53 B	120.98 M	2.04 B
Mammalia, Artiodactyla	*Diacodexis ilicis*	0.830 kg	4.7 cm3	4.38 cm3	Bertrand et al. (2020, 2022)	47.25 M	228.08 M	22.50 M	297.83 M
Mammalia, Palaeoryctidae (stem taxa)	*Eoryctes melanus*	66.98 g	0.96 cm3 ECV	0.80 cm3	Bertrand et al. (2022)	13.92 M	76.31 M	8.54 M	98.76 M
Mammalia, Rodentia	*Paramys copei*	1.030 kg	7.53 cm3 ECV	7.07 cm3	Bertrand et al. (2022)	66.67 M	310.46 M	29.56 M	406.69 M
Mammalia, Plesiadapiforms (stem taxa)	*Ignacius graybullianus*	270.56 g	2.00 cm3 ECV	1.89 cm3	Bertrand et al. (2022)	25.82 M	132.75 M	13.93 M	172.50 M
Mammalia, Euungulata (stem taxa)	*Hyopsodus paulus*	1.068 kg	3.42 cm3 ECV	3.14 cm3	Bertrand et al. (2022)	37.20 M	184.08 M	18.61 M	239.89 M
Mammalia, Euungulata (stem taxa)	*Hyopsodus lepidus*	0.633 kg	2.79 cm3	2.55 cm3	Cameron et al. (2018), Bertrand et al. (2019)	32.03 M	160.99 M	16.53 M	209.54 M
Mammalia, Perissodactyla	*Hyrachyus modestus*	62.220 kg	76.52 cm3 ECV	70.48 cm3	Bertrand et al. (2022)	348.30 M	1.37 B	109.62 M	1.82 B
Mammalia, Artiodactyla	*Agriochoerus sp.*	11.634 kg	33.00 cm3 ECV	31.36 cm3	Bertrand et al. (2022)	194.58 M	810.31 M	69.09 M	1.07 B
Mammalia, Artiodactyla	*Leptotragulus sp.*	8.818 kg	21.42 cm3 ECV	20.46 cm3	Bertrand et al. (2022)	143.13 M	615.47 M	54.16 M	812.77 M

Mammalia, Tillodontia (stem taxa)	*Trogosus hillsii*	86.686 kg	61.02 cm3 ECV	56.59 cm3	Bertrand et al. (2022)	297.45 M	1.19 B	96.73 M	1.58 B
Mammalia, Tillodontia (stem taxa)	*Trogosus grangeri*	86.605 kg	78.60 cm3 ECV	68.82 cm3	Bertrand et al. (2022)	342.38 M	1.34 B	108.14 M	1.79 B
Mammalia, Lepticticida (stem taxa)	*Leptictis sp.*	742.95 g	4.31 cm3 ECV	3.90 cm3	Bertrand et al. (2022)	43.47 M	211.66 M	21.06 M	276.18 M
Mammalia, Palaeanodonta (stem taxa)	*Metacheiromys marshi*	713.36 g	6.64 cm3	6.22 cm3	Bertrand et al. (2022)	60.80 M	285.88 M	27.48 M	374.16 M
Mammalia, Dinocerata (stem taxa)	*Uintatherium anceps*	1,037.06 kg	300.00 cm3 ECV	259.00 cm3	Bertrand et al. (2022)	887.89 M	3.16 B	230.18 M	4.27 B
Mammalia, Dinocerata (stem taxa)	*Tetheopsis ingens*	6,270.20 kg	365.00 cm3 ECV	354.00 cm3	Bertrand et al. (2022)	1.11 B	3.86 B	275.06 M	5.25 B
Mammalia, Hyaenodonta (stem taxa)	*Cynohyaenodon cayluxi*	1.359 kg	8.30 cm3 ECV	7.80 cm3	Bertrand et al. (2022)	71.55 M	330.74 M	31.26 M	433.55 M
Mammalia, Hyaenodonta (stem taxa)	*Sinopa lania*	4.189 kg	11.60 cm3 ECV	11.10 cm3	Bertrand et al. (2022)	92.21 M	415.12 M	38.22 M	545.55 M
Mammalia, Carnivoramorpha	*Miacis sylvestris*	1.157 kg	8.45 cm3 ECV	8.12 cm3	Bertrand et al. (2022)	73.65 M	339.42 M	31.98 M	445.05 M
Mammalia, Carnivoramorpha	*Oodectes herpestoides*	1.172 kg	7.64 cm3 ECV	7.27 cm3	Bertrand et al. (2022)	68.02 M	316.09 M	30.03 M	414.14 M
Mammalia, Carnivoramorpha	*Viverravus minutus*	313.20 g	2.03 cm3 ECV	1.86 cm3	Bertrand et al. (2022)	35.53 M	131.39 M	13.81 M	170.72 M
Mammalia, Carnivoramorpha	*Vulpavus profectus*	2.573 kg	12.07 cm3 ECV	11.16 cm3	Bertrand et al. (2022)	92.57 M	416.56 M	38.34 M	547.47 M
Mammalia, Carnivoramorpha	*Vulpavus ovatus*	3.788 kg	12.36 cm3 ECV	11.30 cm3	Bertrand et al. (2022)	93.40 M	419.92 M	38.61 M	551.94 M

Mammalia, Plesiadapiforms (stem taxa)	*Microsyops annectens*	1.432 kg	5.90 cm3 ECV	5.60 cm3	Bertrand et al. (2022)	56.38 M	267.19 M	25.88 M	349.45 M
Mammalia, Rodentia	*Paramys delicatus*	2.154 kg	12.57 cm3 ECV	11.97 cm3	Bertrand et al. (2022)	97.35 M	435.79 M	39.90 M	573.04 M
Mammalia, Rodentia	*Pseudotomus horribilis*	4.850 kg	15.19 cm3 ECV	14.38 cm3	Bertrand et al. (2022)	111.08 M	490.43 M	44.30 M	645.81 M
Mammalia, Rodentia	*Pseudotomus oweni*	3.666 kg	12.06 cm3 ECV	11.35 cm3	Bertrand et al. (2022)	93.70 M	421.11 M	38.71 M	553.53 M
Mammalia. Rodentia	*Pseudotomus petersoni*	4.386 kg	17.01 cm3 ECV	16.31 cm3	Bertrand et al. (2022)	121.61 M	531.87 M	47.660 M	701.07 M
Mammalia, Rodentia	*Pseudotomus hians*	2.306 kg	13.68 cm3 ECV	12.94 cm3	Bertrand et al. (2022)	102.96 M	458.21 M	41.72 M	602.89 M
Mammalia, Rodentia	*Reithroparamys delicatissimus*	0.749 kg	6.43 cm3 ECV	6.23 cm3	Bertrand et al. (2022)	60.87 M	286.18 M	27.50 M	374.55 M
Mammalia, Rodentia	*Rapamys atramontis*	1.080 kg	6.56 cm3 ECV	6.33 cm3	Bertrand et al. (2022)	61.58 M	289.13 M	27.75 M	378.45 M
Mammalia, Primata	*Rooneyia viejaensis*	341.3 g	7.23 cm3 ECV	7.16 cm3	Bertrand et al. (2022)	67.28 M	313.00 M	29.77 M	410.05 M
Mammalia, Primata	*Notharctus tenebrosus*	2.100 kg	7.62 cm3 ECV	7.47 cm3	Bertrand et al. (2022)	69.36 M	321.66 M	30.50 M	421.52 M
Mammalia, Primata	*Smilodectes gracilis*	1.239 kg	8.37 cm3 ECV	8.23 cm3	Bertrand et al. (2022)	74.37 M	342.37 M	32.23 M	448.97 M
Mammalia, Primata	*Necrolemur antiquus*	0.121 kg	2.36 cm3 ECV	2.31 cm3	Bertrand et al. (2022)	29.83 M	151.06 M	15.62 M	196.51 M

Mammalia, Artiodactyla	*Bathygenys reevesi*	2.390 kg	14.36 cm3 ECV	13.91 cm3	Bertrand et al. (2022)	108.45 M	480.05 M	43.47 M	631.97 M
Mammalia, Artiodactyla	*Robiacina lavergnensis*	0.397 kg	2.50 cm3 ECV	2.41 cm3	Bertrand et al. (2022)	30.75 M	155.24 M	16.00 M	202.00 M
Mammalia, Artiodactyla	*Dichobune leporina*	4.556 kg	15.84 cm3 ECV	14.63 cm3	Bertrand et al. (2022)	112.46 M	495.91 M	44.74 M	653.11 M
Mammalia, Artiodactyla	*Mouillacitherium elegans*	0.864 kg	6.96 cm3 ECV	6.46 cm3	Bertrand et al. (2022)	62.48 M	292.94 M	28.08 M	383.49 M
Mammalia, Artiodactyla	*Tapirulus hyracinus*	2.25 kg	10.71 cm3 ECV	9.91 cm3	Bertrand et al. (2022)	84.99 M	385.88 M	35.83 M	506.70 M
Mammalia, Hyaenodonta (stem taxa)	*Hyaenodon horridus*	34.357 kg	85.00 cm3 ECV	78.00 cm3	Bertrand et al. (2022)	374.64 M	1.46 B	116.14 M	1.95 B
Mammalia, Carnivoramorpha	*Prohesperocyon wilsoni*	30.043 kg	127.63 cm3 ECV	123.12 cm3	Bertrand et al. (2022)	520.17 M	1.96 B	150.65 M	2.63 B
Mammalia, Carnivoramorpha	*Dinictis felina*	16.140 kg	77.10 cm3 ECV	74.41 cm3	Bertrand et al. (2022)	362.16 M	1.41 B	113.06 M	1.89 B
Mammalia, Primata	*Adapis parisiensis*	1.870 kg	8.81 cm3 ECV	8.60 cm3	Bertrand et al. (2022)	76.75 M	352.21 M	33.05 M	462.01 M
Mammalia, Primata	*Microchoerus erinaceus*	0.493 kg	4.26 cm3 ECV	4.22 cm3	Bertrand et al. (2022)	46.00 M	222.68 M	5.33 M	290.71 M
Mammalia, Chiroptera	*Palaeophyllophora quercyi*	23.64 g	0.378 g with OB	0.35 cm3	Maugoust and Orliac (2021)	7.68 M	44.81 M	5.33 M	57.82 M
Mammalia, Chiroptera	*Palaeophyllophora oltina*	36.1 g	0.545 g with OB	0.51 cm3	Maugoust and Orliac (2021)	10.07 M	57.10 M	6.60 M	73.77 M

References

Benoit J, Fernandez V, Manger PR, Rubidge BS (2017a) Endocranial casts of pre-mammalian therapsids reveal an unexpected neurological diversity at the deep evolutionary root of mammals. Brain Behav Evol 90, 311-333.

Benoit J, Manger PR, Norton LA, Fernandez V, Rubidge BS (2017b) Synchrotron scanning reveals the palaeoneurology of the head-butting Moschops capensis (Therapsida, Dinocephalia). PeerJ 5, e3496.

Benoit J, Legendre LJ, Tabuce R, Obada T, Mararescul V, Manger P (2019) Brain evolution in Proboscidea (Mammalia, Afrotheria) across the Cenozoic. Scientific Reports 9, 9323.

Bertrand OC, Shelley SL, Wible JR, Williamson TE, Holbrook LT, Chester SGB, Butler IB, Brusatte SL (2020) Virtual endocranial and inner ear endocasts of the Paleocene "condylarth" *Chriacus*: new insight into the neurosensory system and evolution of early placental mammals. J Anat 236, 21-49.

Bertrand OC, Shelley SL, Williamson TE, Wible JR, Chester SGB, Flynn JJ, Holbrook LT, Lyson TR, Meng J, Miller IM, Püschel HP, Smith T, Spaulding M, Tseng ZJ, Brusatte SJ (2022) Brawn before brains in placental mammals after the end-Cretaceous extinction. Science 376, 80-85.

Boonstra LD (1968) The braincase, basicranial axis and median septum in the Dinocephalia. Ann S Afr Mus 50, 195-273.

Cameron J, Shelley SL, Williamson TE, Brusatte SL (2018) The brain and inner ear of the early Paleocene "Condylarth" *Carsioptychus coarctatus*: Implications for early placental mammal neurosensory biology and behavior. Anat Rec 302, 306-324.

Castanhinha R, Araújo R, Júnior LC, Angielczyk KD, Martins GG, Martins RM, Chaouiya C, Beckmann F, Wilde F (2013) Bringing dicynodonts back to life: paleobiology and anatomy of a new emydopoid genus from the Upper Permian of Mozambique. PLoS One 8, e80974.

Dozo MT, Martínez G (2016) First digital cranial endocasts of late Oligocene Notohippidae (Notoungulata): Implications for endemic South American ungulates brain evolution. J Mammal Evol 23, 1-16.

Hopson JA (1979) Paleoneurology. In Glans C, Northcutt RG, Ulinski P (eds), Biology of the Reptilia. NY, Academic Press, pp 39-146.

Jerison H (1973) Evolution of the brain and intelligence. New York, Academic Press.

Laas M (2015) Virtual reconstruction and description of the cranial endocast of *Pristerodon mackayi* (Therapsida, Anomodontia). J Morphol 276, 1089-1099.

Laas M, Kaestner A (2017) Evidence for convergent evolution of a structure comparable to the mammalian neocortex in a Late Permian therapsid. J Morphol 278, 1033-1057.

Luo ZX, Crompton AW, Sun AL (2001) A new mammaliaform from the Early Jurassic and evolution of mammalian characteristics. Science 292, 1535-1540.

Macrini TE (2006) The evolution of endocranial space in mammals and non-mammalian cynodonts. PhD Thesis, University of Texas at Austin.

Macrini TE, Rougier GW, Rowe T (2007) Description of a cranial endocast from the fossil mammal *Vincelestes neuquenianus* (Theriiformes) and its relevance to the evolution of endocranial characters in Therians. Anat Rec 290, 875-892.

Maugoust J, Orliac MJ (2021) Endocranial cast anatomy of the extinct Hipposiderid bats *Pallaeophyllophora* and *Hipposideros* (*Pseudorhinolophus*) (Mammalia: Chiroptera). J Mammal Evol 28, 679-706.

Pusch LC, Kammerer CF, Fröbisch J (2019) Cranial anatomy of the early cynodont *Galesaurus planiceps* and the origin of mammalian endocranial characters. J Anat 234, 592-621.

Quiroga JC (1980) The brain of the mammal-like reptile *Probainognathus jenseni* (Therapsida, Cynodontia): a correlative paleo-neoneurological approach to the neocortex at the reptile-mammal transition. J Hirnforsch 21, 299-336.

Quiroga JC (1984) The endocranial cast of the advanced mammal-like reptile *Therioherpeton cargnini* (Therapsida-Cynodontia) from the Middle Triassic of Brazil. J Hirnforsch 25, 285-290.

Rodrigues PG, Ruf I, Schultz CL (2014) Study of a digital cranial endocast of the non-mammaliaform cynodont *Brasilitherium riograndensis* (Later Triassic, Brazil) and its relevance to the evolution of the mammalian brain. Pällaontol Z 88, 329-352.

Rowe TB, Macrini TE, Luo Z-X (2011) Fossil evidence on origin of the mammalian brain. Science 332, 955-957.

Sigurdsen T, Huttenlocher AK, Modesto SP, Rowe TB, Damiani R (2012) Reassessment of the morphology and paleobiology of the therocephalian *Tetracynodon darti* (Therapsida), and the phylogenetic relationships of Bauroidea. J Vert Paleontol 32, 1113-1134.