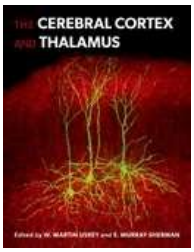

The Cerebral Cortex and Thalamus

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CHAPTER

56. The Coevolution of the Neocortex and Dorsal Thalamus in Mammals: Scaling Relationships Between and Within Structures

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Abstract

Coevolution of the mammalian neocortex and dorsal thalamus occurs within the broader context of diverse mammalian bodies, behavior, lifestyles, and environmental context, the latter of which is composed of unique, complex patterns of sensory stimuli which must be transduced and interpreted by the brain. Natural selection targets behavior and modifies sensory systems to process incoming patterns of input and generate adaptive behavior for a given context. The dorsal thalamus is the primary source of sensory input to the neocortex, and it plays a central role in integrating information from the neocortex to shape motor output. This chapter examines the coevolution of the dorsal thalamus and neocortex in mammals, focusing on studies that have characterized the relative size of primary sensory cortical fields and nuclei of the thalamus that provide their primary inputs. Because most data on scaling of the cortex and thalamus come from work on the visual system, the authors use examples from this system (dorsal lateral geniculate nucleus, pulvinar complex, and primary visual cortex) to demonstrate how species vary in thalamocortical organization more generally. Finally, they consider several theories that propose why thalamocortical relationships vary across lineages.

Keywords: thalamus, cortex, evolution, scaling, allometry

Subject: Neuroscience

Collection: Oxford Medicine Online

Introduction

The neocortex is one of the defining features of mammals, and it differs dramatically in its size and internal organization across species, as does its major source of sensory input, the dorsal thalamus. For example, compared to the smallest present-day primate brain, the mouse lemur, the human brain is over 700 times larger (*Homo*: 1330 cm^3; *Microcebus*: 1.78 cm^3), the human thalamus is 230 times larger (*Homo*: 18.2 cm^3; *Microcebus*: 0.078 cm^3), and the human neocortex is over 1300 times larger (*Homo*: 1006 cm^3; *Microcebus*: 0.74 cm^3) (Stephan et al., 1981). In terms of internal organization, it has been proposed that mammals with a relatively large neocortex have more than one hundred cortical fields, while those with a relatively small neocortex have on the order of 20 cortical fields (Van Essen et al., 2011, 2019; Kaas, 2013). Similarly, mammals with a relatively small dorsal thalamus appear to have substantially fewer nuclei than mammals with a relatively large dorsal thalamus (Jones, 2007).

Despite the dramatic differences in size and internal organization of the neocortex and dorsal thalamus across mammals, it is still possible to identify similar or homologous features of organization in these structures. For instance, the dorsal thalamus is composed of several first-order nuclei—universally shared among extant mammals—that process sensory input from the periphery and ultimately relay that input to the neocortex. These include nuclei associated with visual, somatosensory, and auditory processing; the dorsolateral geniculate nucleus (dLGN), the ventral posterior nucleus (VPN), and the medial geniculate nucleus (MGN), respectively. Like the dorsal thalamus, a number of neocortical fields are highly conserved across species, including (but not limited to) the primary visual (V1), somatosensory (S1), and auditory (A1) areas, which receive inputs from the first-order nuclei noted above. In addition to its inputs from the first-order nuclei of the thalamus, cortical fields other than the primary fields described above have a rich number of connections with higher-order nuclei of the thalamus that both modulate incoming sensory information and drive cortico-thalamocortical circuits (i.e., the trans-thalamic pathway; Sherman, 2016). The ubiquity of some aspects of the functional organization of the neocortex and dorsal thalamus across mammals is remarkable, given how dramatically mammals differ in their absolute brain size and behavioral specializations. However, beyond a constellation of primary sensory cortical fields and first-order thalamic nuclei that have been defined as homologous across all groups of mammals, less is known about the evolution of the higher-order cortical fields and thalamic nuclei, or about their scaling relationships. This is in part due to the difficulties in defining equivalencies across different species.

Defining Homologies in the Cortex and Thalamus

One of the largest problems in making valid comparisons across species is determining the criteria that should be used to determine homologous structures. While many laboratories have traditionally utilized architectonic criteria combined with functional organization and often connections (e.g., Kaas, 1982), modern studies utilize a variety of molecular techniques to define homologous features of the cortex and thalamus. For example, Molnár and colleagues (**Chapter 58 in Section X** of this volume) compare patterns of gene expression across a wide range of vertebrates such as reptiles, birds, and mammals to better understand the origins
p. 586 of the dorsal thalamus and neocortex and corresponding regions within these structures. ↳ These types of studies circumvent the problems that arise when homologous structures take diverse forms (e.g., differ in appearance or relative location) in different lineages, or have different functions and patterns of connectivity.

Despite the difficulties in identifying homologous nuclei of the thalamus and areas of the neocortex across species, decades of comparative studies have shown that mammals share a basic plan of gross brain organization, and that some “new” brain areas may be elaborations of ancestral structures that have been modified, rather than added de novo (Striedter, 2005). Because mammals have been evolving independently for tens of millions to hundreds of millions of years, and have adapted numerous neural, morphological, and behavioral specializations, a central challenge in evolutionary neurobiology is to understand how thalamocortical systems evolve to meet these demands within the constraints imposed by development.

Comparing first-order nuclei of the thalamus and primary cortical fields (e.g., dLGN and V1) can be done with relative ease across wide-ranging groups of mammals, including those with derivations, because their cytoarchitectonic appearance, patterns of connectivity, and functional organization are ubiquitous. Within the thalamus, first-order nuclei ultimately receive their inputs from the skin, muscles, and joints (VPN), the cochlea (MGN), and the retina (dLGN). These homologous nuclei are the easiest to compare

across species, as they are defined by a conserved pattern of cytoarchitecture, inputs from the periphery, outputs to the neocortex, and to some extent, neural response properties. By contrast, it is more difficult to determine homologies of "higher-order" nuclei of the thalamus across species for several reasons. They are often less cytoarchitectonically distinct, their inputs come from a combination of subcortical and cortical sources (the latter of which has changed dramatically in different lineages), their cortical targets are more diverse and diffuse, and in many cases their functional roles remain poorly understood.

The pulvinar nucleus is a perfect case in point (Baldwin et al., 2017; Kaas and Baldwin, 2020). Originally thought to be a thalamic structure that was unique to primates (e.g., Le Gros Clark, 1930), the pulvinar was ultimately shown to have a homolog in non-primate mammals, the product of converging evidence from comparative studies of connectivity, electrophysiology, and histochemistry. In rodents, this nucleus is called the lateral posterior nucleus (LP), which led to confusion because this same terminology had already been applied to an unrelated nucleus in the primate thalamus (e.g., see Schmahmann and Pandya, 1990). Finally, as with many brain structures, more detailed studies have shown that the primate "pulvinar" is not a single nucleus in either function, cytoarchitecture, or connectivity. The inferior and lateral portions of the pulvinar play distinct roles in visual processing (Baldwin et al., 2017; Kaas and Baldwin, 2020), the anterior pulvinar appears to be involved in somatosensation (e.g., Pons et al., 1985; Padberg et al., 2009), and the medial pulvinar is involved in diverse functions such as integrating polymodal information, orienting selective attention, and working memory (see **Chapter 57 in Section X** of this volume). With these complications in mind, in this chapter we use the single term "Pul/LP" to refer to parts of the pulvinar and lateral posterior (LP) nucleus that are thought to be homologous across species, and which have been combined in studies from the literature (e.g., Chalfin et al., 2007, discussed below).

As in the thalamus, establishing homology in the neocortex has been difficult because only a small constellation of cortical fields is unambiguously shared across mammals, including the primary areas (e.g., V1, S1, A1) and a few other areas involved in sensory processing (e.g., second somatosensory area, S2; parietal ventral area, PV; second visual area; V2) or volitional motor control (e.g., primary motor cortex, M1; Krubitzer, 2009; Kaas, 2013). These fields have a unique architectonic appearance, share patterns of cortical and thalamocortical connections, and often share functional features such as topographic organization and magnification of behaviorally relevant sensory receptor arrays.

Comparative data on the relative size of thalamic nuclei and cortical fields are relatively rare, and the majority of studies have focused on structures that compose the visual system. The most widely studied thalamic nucleus is the dorsal lateral geniculate nucleus (dLGN), which can be readily identified in all mammalian species, though it differs in its relative size, the number of layers that compose it, its general morphology, and orientation within the thalamus (Figure 56.1). Figure 56.1 shows matched coronal sections stained for cytochrome oxidase (CO) through the thalamus of 13 mammals, representing 4 mammalian orders (primates, rodents, carnivores, and bats). Even from this limited sample, a number of features are apparent. In anthropoid primates (New and Old World monkeys), the dLGN has a characteristic U-shape, with magnocellular layers located along the ventral aspect of this nucleus (Jones, 2007). In some prosimians such as galagos, the dLGN is ventral with a slight lateral bend, and in some such as mouse lemurs it occupies a more dorsal location (also see McDonald et al., 1993). Within carnivores, the orientation of the dLGN is more variable across species; in the grizzly bear and cat it is laterally oriented, and in ferrets it is lateral to the optic tract. Within rodents, the location and orientation of the dLGN is similar, but there are differences in lamination across species.

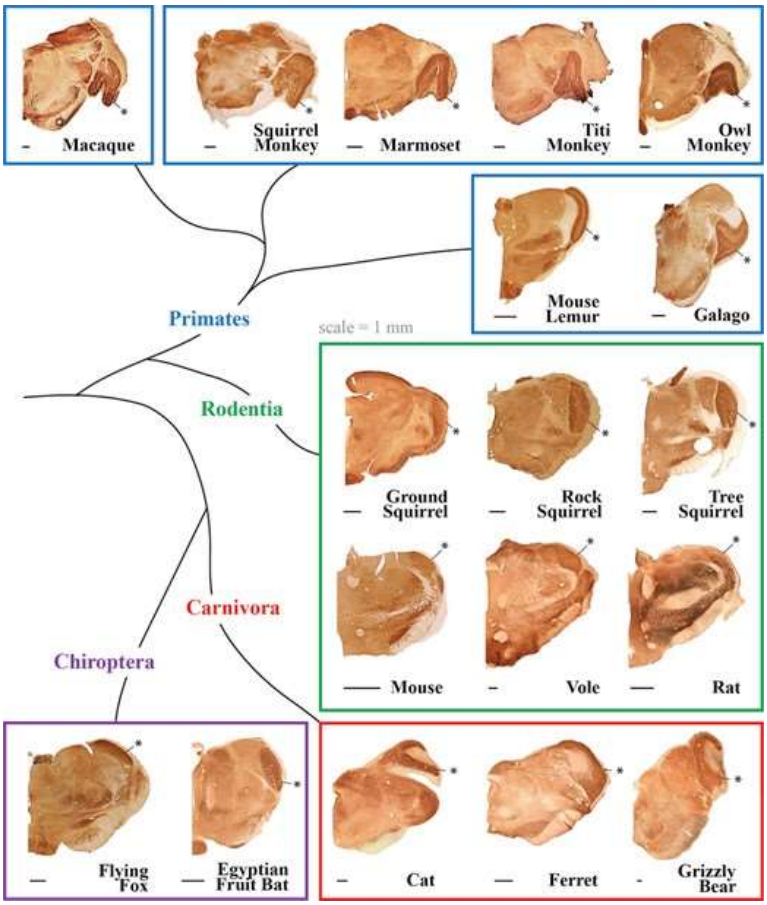

Figure 56.1. **Coronal sections stained for cytochrome oxidase (CO) through the dorsal thalamus at the level of the dorsal lateral geniculate nucleus (dLGN), indicated by a star, in 13 mammalian species, representing Old World monkeys, New World monkeys, prosimians, rodents, carnivores, and bats. Similarities in shape and location within orders are apparent (e.g., rodents), as are some striking differences (e.g., compare mouse lemur to the galago). Despite differences within and across orders, the dorsal lateral geniculate can be readily identified across all mammals. Images of the mouse lemur, galago, and tree squirrel are from unpublished materials provided by the Kaas lab; image of the grizzly bear is from Krubitzer et al. (2018); all other images are from unpublished materials in the Krubitzer lab. Scale bars indicate 1 mm.**

Additional studies have measured elements of the pulvinar/LP complex (Pul/LP) and the primary visual cortex (V1) of the neocortex

p. 587 across species, and these will be described below. Scaling data on other regions of the ↳

p. 588 ↳

dorsal thalamus and neocortex are sparse but will be noted in relation to general trends discovered in the visual system.

Concerted and Mosaic Evolution

Given the diversity in body morphology, behavioral specializations, locomotor styles, and sensorimotor adaptations, mammalian brains have clearly evolved to meet the unique demands of these diverse lifestyles, but it remains unclear how exactly this coevolution of the brain, body, and behavior occurs. First, we might expect that brain structures involved in processing inputs from specialized sensory systems would increase in size relative to other parts of the brain (e.g., more visually specialized species might exhibit enlarged visual structures (e.g., retina, dLGN, and V1)). Theories of *mosaic evolution* propose that specializations in a given sensory system (e.g., visual, somatosensory) are accompanied by changes in the size of brain areas that underlie these adaptations. A classic example in mammals of mosaic brain evolution associated with the overall size of a structure is the expansion of the neocortex in primates (especially monkeys and apes) relative to mammals such as rodents (Barton and Harvey, 2000; Halley and Deacon, 2017). This "neocorticalization" in primates has been proposed to partially explain why primates have more cortical fields than other mammals (Halley and Krubitzer, 2019), and will be discussed below when we compare the size of the neocortex to the size of the structure that provides its primary source of sensory input, the dorsal thalamus (Figure 56.2).

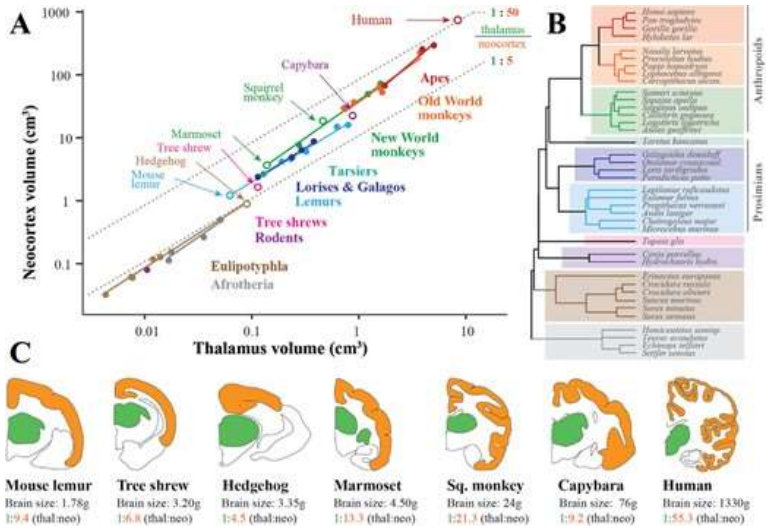

Figure 56.2. Species differ widely in the size of the neocortex relative to the dorsal thalamus, shown here in a comparative dataset. (A). The size of the thalamus plotted against the size of the neocortex across 39 mammalian species. Differences exist both between evolutionary lineages and according to size. Primates are uniquely "neocorticalized" relative to the dorsal thalamus, exhibited by the intercept shift that distinguishes all primates from rodents and shrews. Open circles indicate species whose brains are outlined in coronal section below. (B). The evolutionary relationship between the species included in this plot. (C). Coronal sections through the brain of 7 representative species. An outline of the thalamus is shown in green; an outline of the neocortex is shown in orange. Adapted from Halley and Krubitzer (2019); details in that paper.

Mosaic evolution of the internal organization of a structure has been observed in a wide range of mammals and includes the magnification of the representation of behaviorally relevant sensory receptor arrays in both the neocortex and dorsal thalamus. This
p. 589 magnification or relative enlargement of sensory representations is the ↳ manifestation of multiple factors, including specialized morphology with unique arrays of sensory receptors, behaviors associated with these morphologies, and the unique environmental contexts with different affordances within which mammals live and behave. The best examples are found in mammals with extreme specializations, occupying different niches (e.g., burrowing and aquatic), such as the star nosed mole (Catania and Kaas, 1995) and the duck-billed platypus (Krubitzer et al., 1995). The platypus has a distinctive bill with rows of mechanosensory and electrosensory receptors and uses this bill when engaging in ethologically relevant behaviors such as mating, feeding and navigating (Pettigrew, 1999). Somatosensory cortex in the duck-billed platypus is dominated by the representation of the bill; approximately 90% of S1 is devoted to processing inputs from the bill, and about 60% percent of the entire cortical sheet is dominated by the representation of the bill (see Englund and Krubitzer, 2022, for review). Other examples of cortical magnification in S1 include the representation of

the nose rays in the star nosed mole (Catania and Kaas, 1995), the representation of the incisors in naked mole rats (Catania and Remple, 2002), and the representations of the glabrous hands, and supralaryngeal tract and oral structures in humans (Penfield, 1937; also see Gandhoke et al., 2019). This type of mosaic evolution of cortical fields has been observed to a greater or lesser extent in every mammal examined for all sensory systems.

The magnification of important sensory surfaces is not limited to the cortex, but is also observed in the thalamus. For example, in the platypus, the dorsal thalamus is dominated by the ventral posterior nucleus (VPN) to such an extent that it is difficult to identify other major first-order nuclei (i.e. dLGN, MGN; Ashwell, 2012; Mikula et al., 2008). In the blind mole rat, the dLGN is extremely small and undifferentiated (Rehkämper et al., 1994), and VPN is enlarged. Interestingly, the relative magnification of the pulvinar complex has independently evolved in different mammals that rely heavily on vision, such as primates and carnivores, which both exhibit a relatively larger pulvinar complex compared to rodents (Chalfin et al., 2007).

While there are clear examples of mosaic evolution in the neocortex and dorsal thalamus, much of the variation in the size of brain structures (not necessarily their internal organization) is a reflection of overall brain size. Large comparative datasets measuring the size of brain areas indicate that the absolute size of a given brain is highly predictive of the size of different structures that compose it. This basic size-associated (allometric) effect is called *concerted evolution* and has been described both across species (Stephan et al., 1981) and within species (Charvet et al., 2013). Even within a given brain structure, size has predictable effects on cell density (i.e., larger brains have lower cell density in general across all brain structures; Herculano-Houzel et al., 2015).

In reality, the variation in mammalian brains is the product of both mosaic and concerted evolution. The relative contribution of each form of evolution is largely debated in comparative neurobiology (see Striedter, 2005, for a review), but both are essential for interpreting neuroembryonic data on the expansion of the neocortex (Halley and Krubitzer, 2019). A central proposal to explain concerted evolutionary effects (i.e., the predictability of brain structure size from overall brain size) is that a conserved pattern of neurogenesis during embryonic development—a ventral-to-dorsal and caudal-to-rostral pattern of neurogenic onset from progenitor pools—creates regularities in the size of adult brain areas (Finlay and Darlington, 1995; Finlay et al., 2001). Even though different species develop their brains over variable time periods, they are highly conservative in both the brain growth rate (Halley, 2017) and the schedule of neurodevelopment during this period (Workman et al., 2013), leading to predictable brain structure sizes in adults.

The following sections of this chapter use published data from the literature to shed new light on general scaling principles of the neocortex and dorsal thalamus. Data on the size of the thalamus versus neocortex (Figure 56.2) are taken from Stephan et al. (1981; reproduced from Halley and Krubitzer, 2019). Data on the scaling of thalamic nuclei in apes (Figure 56.3) are taken from a series of papers by Armstrong (1979, 1980a, 1980b, 1981). The datasets on the size of the dLGN, Pul/LP (Figure 56.4) are taken from Stephan et al. (1981); Barton (1998); Chalfin et al. (2007); Finlay et al. (2014); and Armstrong (1979, 1980a, 1980b, 1981). Data on the size of the dLGN, whole thalamus, V1, and neocortex (Figure 56.5A,C) are taken from Stephan et al. (1981); thalamic reconstructions (Figure 56.5B) were made from unpublished coronal sections digitized from the Kaas lab (mouse lemur) and Krubitzer lab (macaque), while neocortical diagrams (Figure 56.5D) were redrawn from published studies (mouse lemur: Saraf et al., 2019; macaque: Krubitzer and Dooley, 2013). Phylogenetic trees across all figures (Figures 56.2, 56.4, 56.5) were made from a mammalian supertree (Bininda-Emonds et al., 2007).

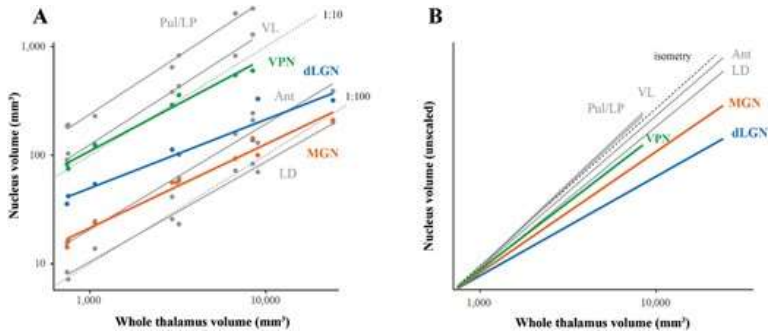

Figure 56.3. The relative size of thalamic nuclei in a sample of apes (gibbon, chimpanzee, gorilla, orangutan, and human) reanalyzed from Armstrong's dataset. (A). The volume of each nucleus is plotted against the total volume of the thalamus across the sample. First-order nuclei are highlighted in color (blue = dLGN; orange = MGN; green = VPN) while higher-order nuclei are collectively shown in gray. (B). The trend lines for this same dataset are aligned at the origin to highlight the different scaling relationships, relative to isometry (black dotted line). The *y*-axis is necessarily unscaled, as the trend lines have been aligned for easier comparison. As ape brains increase in size, the first-order nuclei of the thalamus (VPN, MGN, dLGN) occupy a smaller proportion of the overall thalamus, while higher-order nuclei increase in relative proportions. Data from Armstrong (1979, 1980a, 1980b, 1981).

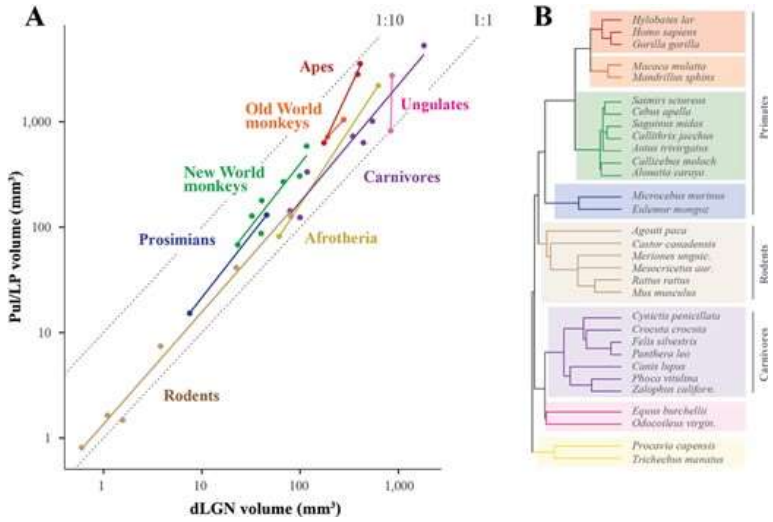

Figure 56.4. The relative size of the pulvinar complex (Pul/LP) and lateral geniculate nucleus (dLGN) in a diverse sample of 31 mammals. In the smallest mammalian brains, the pulvinar and dLGN are relatively similar in size, while in the largest primate brains (e.g., humans and gorillas), the pulvinar can approach 10 times the size of the dLGN. This suggests that in larger brains with larger thalami, first-order nuclei such as the dLGN occupy less space proportionally, while higher-order nuclei such as the pulvinar become exceptionally large. Data are adapted from Chalfin et al. (2007) and Finlay et al. (2014).

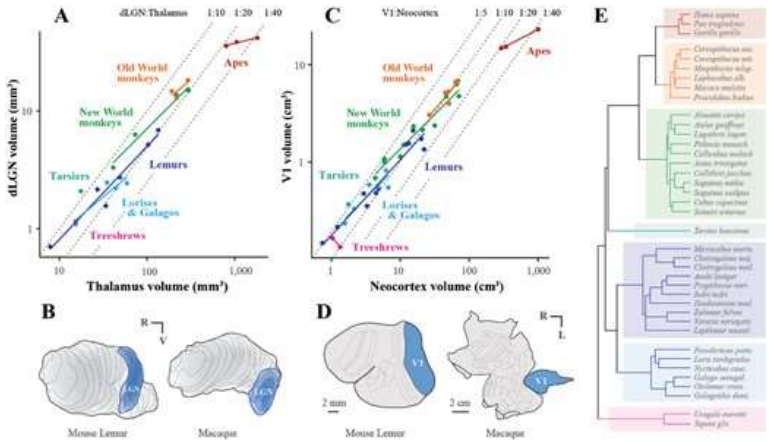

Figure 56.5. **Overall brain size has a major influence on the relative size of both thalamic nuclei and cortical fields, demonstrated here by examining first-order visual structures in a sample of primates and closely related tree shrews. (A). In small primates and tree shrews, the lateral geniculate nucleus (dLGN) is relatively large and constitutes between 5% and 10% of the overall thalamus volume. In large-brained primates (i.e., apes) the dLGN is relatively smaller—between 2% and 5% of the thalamus. (B). 3-D reconstructions of the whole thalamus (gray) and the dLGN (blue) in both the mouse lemur (*Microcebus murinus*) and rhesus macaque (*Macaca mulatta*). The dLGN makes up a larger proportion of the thalamus in the smaller-brained mouse lemur. (C). Similarly, smaller primates have a V1 that occupies a relatively large proportion of the neocortex (10%–20%), while the largest primate brains (i.e., apes) have a relatively smaller V1 (2%–5% of total neocortex). (D). This effect can be seen by comparing the relative size of V1 in flattened neocortex. V1 occupies a larger proportion of the neocortex in the mouse lemur when compared with the rhesus macaque. (E). A phylogenetic tree of the species in (A) and (C). The size-associated effects described above are observed within each primate lineage. Data in (A) and (C) are from a comparative dataset detailed in Stephan et al. (1981). Reconstructions of the thalamus in (B) were created from regularly spaced coronal sections of the forebrain stained for cytochrome oxidase (CO) (Mouse lemur: Kaas Lab, Vanderbilt University; Macaque: Krubitzer Lab, UC Davis). Flattened cortex diagrams were adapted from published studies (Mouse lemur: Saraf et al., 2019; Krubitzer and Dooley, 2013).**

Below, we draw on these large comparative datasets to better understand how the neocortex and thalamus coevolve in mammals. The next section examines the relative size of the dorsal thalamus with respect to the neocortex, followed by a section that examines the size of individual thalamic nuclei relative to the entire dorsal thalamus and the size of individual neocortical fields relative to the whole neocortex; the subsequent section focuses on the visual system, specifically the relative size of the dLGN and Pul/LP relative to the dorsal thalamus, as well as the size of V1 relative to the entire neocortex.

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How Does the Thalamus Scale with Changes in the Size of the Cortical Sheet?: Across-Structure Comparisons

Broadly speaking, the relative size of individual brain structures is associated with absolute brain size—for example, larger brains tend to have a relatively smaller brainstem, and a relatively larger neocortex. But because some mammalian lineages have smaller or larger brains in general, brain structure proportions are also associated with phylogenetic lineages. An important question is: How large is the neocortex relative to the source of its primary sensory inputs, the dorsal thalamus? Figure 56.2 shows the volume of the neocortex compared to the size of the dorsal thalamus in a sample of 39 mammalian species (reproduced from Halley and Krubitzer, 2019). In this overall sample, we can see that the ratio of the thalamus to neocortex varies considerably; from less than 1:5 in the smallest species (the pygmy shrew *Sorex minutus*) to over 1:50 in the largest (humans, *Homo sapiens*). While some of this effect is caused by the expansion of the neocortex in primates specifically (mosaic evolution, e.g., Halley and Deacon, 2017), the general trend of larger mammals having a larger neocortex can be observed within *each* mammalian lineage independent of phylogeny (concerted evolution; see PGLS analysis in Halley and Krubitzer, 2019). Simply put, in larger mammals with larger brains, the neocortex becomes exceptionally large relative to the size of the dorsal thalamus (Figure 56.2).

Scaling of Thalamic Nuclei and Neocortical Fields: Within-Structure Comparisons

Is there a relationship between the overall size of the dorsal thalamus and the size of the individual nuclei that compose it? Is this relationship the same for the neocortex? Data on the relative size of thalamic nuclei compared to the entire dorsal thalamus are limited, and as noted above, are primarily derived from studies of the size of nuclei in the visual system: the dLGN and Pul/LP. Comparative data on the other nuclei of the thalamus are relatively rare; one exception is a unique study on the size of thalamic nuclei from studies on apes (Armstrong, 1979, 1980a, 1980b, 1981). While limited in its species diversity, this unique dataset offers a window into how individual thalamic nuclei scale relative to one another, and to the overall size of the dorsal thalamus. In this section, we will first examine the trends observed in this ape dataset, and then discuss the limited dataset that examines the size of cortical fields relative to the entire cortical sheet.

The size of 7 thalamic nuclei relative to the entire dorsal thalamus in a sample of 5 ape species (gibbon, chimpanzee, gorilla, orangutan, and human) are plotted in Figure 56.3A. To make this raw data easier to compare, we have shown the regression lines for each nucleus aligned at a common origin, with isometry (dotted line) for reference, in Figure 56.3B. This figure shows that all first-order nuclei of the thalamus scale at a low allometric coefficient relative to the overall thalamus, meaning that in larger ape brains,
p. 591 the dLGN, ↳ MGN, and VPN become proportionally the smallest nuclei in the thalamus. By contrast, higher-order nuclei either scale with positive allometry (e.g., Pul/LP; the ventrolateral nucleus, VL), or at higher rates than first-order nuclei (anterior nuclei, Ant; the lateral dorsal nucleus, LD), thereby occupying a larger proportion of the thalamus. Thus, as the thalamus becomes larger, more space is occupied by higher-order nuclei and less space is occupied by first-order nuclei (e.g., Armstrong, 1979, 1980a, 1980b, 1981; Figure 56.3B).

This small dataset, composed of a handful of specimens in 5 species of a highly derived primate lineage—the apes—makes it difficult to draw conclusions about mammals in general. Nevertheless, the Armstrong studies represent the only comparative dataset that measures the relative size of most of the thalamic nuclei. Further, as noted below, this trend is observed in a larger dataset encompassing more species for visual nuclei of the thalamus. Expanding this type of analysis to include more and varied species for more nuclei of the thalamus would greatly inform our understanding of the evolution of the dorsal thalamus, how it changes with alterations in peripheral inputs from the different sensory systems, and how it scales with the neocortex.

Quantitative data on scaling of cortical fields within the neocortex is limited (e.g., Kaskan et al., 2005). However, the basic scaling relationship exhibited in the dorsal thalamus has also been shown for the neocortex. As the cortical sheet increases in size, the primary cortical fields (S1, A1, and V1) become relatively smaller, and a larger proportion of the cortical sheet is devoted to "higher-order" cortical fields involved in multimodal integration and "associative" functions. In mammals with small brains, primary cortical

fields and motor cortex occupy a large proportion of the cortical sheet, while in mammals with larger brains—and especially in primates with expanded neocortices—the neocortex is composed of numerous "higher-order" cortical fields not observed in other lineages (Kaas, 2013; Krubitzer et al., 2011; Seelke et al., 2016; Van Essen et al., 2019; Chaplin et al 2013). There is evidence that these higher-order regions in frontal, posterior parietal, and temporal cortex have differentially expanded in primate evolution (e.g., Chalpin et al., 2013; Van Essen and Dieker, 2007; Goldring & Krubitzer, 2017; Reardon et al., 2018) and that they develop at slower rates in humans compared to primary areas (Reardon et al., 2018), suggesting that they may be more influenced by environmental context, and therefore built over the course of an extended postnatal development.

If we combine the scaling relationships observed in the thalamus and neocortex, a central theme emerges: As brains increase in size, the relative size of first-order thalamic nuclei and the cortical fields they innervate become relatively smaller, the thalamus becomes dominated by higher-order nuclei, and the neocortex becomes dominated by higher-order cortical fields. Thus, larger brains appear to dedicate less space to regions directly processing sensory input, and more space to regions involved in sensory integration and other higher-level functions via cortico-cortical connections, or by the expansion of the trans-thalamic pathway. Thus, small brains with a relatively small neocortex are more sensory bound, while larger brains with a relatively larger neocortex expend more space and energy on within-structure and across-structure communication.

Examples From the Visual System

The studies above describe general trends in scaling across structures and within structures, but are limited in their sample sizes and the species represented. Much more is known about the evolution of visual regions of the thalamus and neocortex, which have been studied extensively both in primates and other mammalian lineages. Here we re-examine larger comparative datasets on the size of dLGN (Stephan et al., 1981; Barton, 1998; Finlay et al., 2014); Pul/LP (Chalfin et al., 2007); dorsal thalamus, V1, and neocortex (Stephan et al., 1981). Importantly, these data on the scaling of visual structures reinforce several findings described above regarding the general scaling principles of the dorsal thalamus and neocortex.

One interesting comparison from the visual system is the size of dLGN relative to the size of Pul/LP. Figure 56.4 shows the volume of the dLGN plotted against Pul/LP in 31 species, including multiple primates, carnivores, rodents, and ungulates. In the smallest mammals, dLGN and Pul/LP are similar in size (see 1:1 isometric line), while in larger species, Pul/LP is many times larger than the dLGN (approaching the 1:10 isometric line). For example, the human Pul/LP is 3560 mm^3, while the dLGN is 406 mm^3. As a lineage, primates appear to have a larger Pul/LP volume, relative to the dLGN, than non-primate mammals—a "grade shift" noted by Chalfin et al. (2007). One potential complication in the Pul/LP measures is that only the inferior (PI) and lateral (PL) portions of the primate pulvinar are predominantly involved in visual processing (Baldwin et al., 2017; Baldwin and Kaas, 2020). If the medial pulvinar and anterior pulvinar were included in the measurements by Chalfin and colleagues, corresponding to nonhomologous structures in their non-primate sample, it would artificially inflate the size of the primate pulvinar to a degree that might affect analysis.

Within the visual system, one of the more surprising findings is that the size of visual structures (dLGN, Pul/LP, V1) are not always different in nocturnal and diurnal species, despite differences in the distribution of rods and cones in the retina (Wikler and Rakic,
p. 592 1990; van der Merwe et al., 2018; Finlay et al., 2008) and visual acuity (Ordy and ↳ Smaorajski, 1968). The size of the pulvinar (Chalfin et al., 2007) and of V1 (Krubitzer and Kaas, 1990; Kaskan et al., 2005) do not appear to be associated with nocturnal/diurnal niches. Owl monkeys, which are the only nocturnal anthropoid primate, have a dLGN that is relatively "normal" in size for a New World monkey of its brain size. This lack of variation in visual structure size across diel niche may reflect the fact that within the geniculocortical visual stream, a small number of active neurons can encode sensory information (i.e., sparse coding; Olshausen and Field 1996), making it unnecessary to increase cell numbers or structure size (Finlay et al., 2014). It also seems possible that while nocturnal and diurnal vision involve different *kinds* of processing demands, the information involved in each vision type still requires a similar number of neurons to encode this information.

Another way of looking at scaling within the visual system is to compare the size of dLGN as a proportion of the thalamus, and V1 as a proportion of the neocortex. Importantly, these comparisons (using different datasets) show the same thalamocortical relationships described in sections above: larger brains devote less space to first-order thalamic nuclei and primary neocortical fields.

As noted above for first-order nuclei of the thalamus in apes and in mammals in general, the dLGN scales with negative allometry as the whole thalamus increases in size, composing a smaller proportion of the overall thalamus in larger brains (Figure 56.5A). Note that the overall negative allometric trend is also observed in each mammalian lineage, suggesting an allometric trend that is independent of lineage. Figure 56.5B highlights this trend by showing 3-D reconstructions of the thalamus (dLGN highlighted in blue) in a small- and large-brained primate (*Microcebus* vs. *Macaca*). Similarly, Figure 56.5C shows that V1 scales with negative allometry as the whole neocortex increases in size, composing a smaller proportion of the neocortex in larger brains.

Conclusions

All mammals—from the tiniest rodents to blue whales—have a neocortex that receives its sensory inputs from the first-order nuclei of the dorsal thalamus. Basic features of this thalamocortical system are shared across mammals, irrespective of brain size, sensorimotor specializations, or ecological niche. The thalamus always contains first-order nuclei for processing somatosensory
p. 593 (VPN), auditory (MGN), and ↳ visual (dLGN) inputs, and these nuclei always project to primary sensory fields of the neocortex (S1, A1, V1, respectively). Comparative work on the size of brain structures suggests that in larger brains, less space is devoted to first-order thalamic nuclei and to the primary cortical fields they innervate, and more space is devoted to higher-order cortical fields involved in sensory integration, and to the thalamic nuclei that provide input to these cortical fields. Essentially, brain size has a major influence on the size of primary versus higher-order structures (i.e., concerted evolution).

Where do these size-associated effects come from? One proposal is that the order of neurogenesis in the thalamus—with first-order nuclei undergoing neurogenesis earlier than higher-order nuclei—generates the allometric patterns we observe in adult brains, much as it is thought to underlie broader allometric patterns across the entire brain (Finlay et al., 2001). First-order nuclei like the dLGN, VPN, and MGN could initiate neurogenesis first, cutting off progenitor proliferation earlier than in other nuclei, and thereby producing relatively smaller nuclei.

While some version of this developmental logic likely affects the evolution of neocortex (e.g., cell density across layers; Charvet et al., 2015), it is clear that the interactions between the developing cortex and thalamus are much more complex (see **Chapter 58 in Section X** of this volume). Further, cortical fields appear to be more variable and plastic in their size than subcortical structures are. As noted above, mammals are famously diverse in the relative size and internal organization of somatosensory, visual, and auditory neocortex. This variability may reflect the fact that cortical field specification occurs at the latest stages of neurodevelopment, when arealization is more heavily influenced by activity-dependent mechanisms than by genes intrinsic to the cortex and thalamus associated with specification of these structures. Accordingly, cortical fields can be greatly impacted by manipulations that occur early in development, such as enucleation or congenital deprivation of visual input. Experimental studies have shown that early loss of visual input has profound effects on the size of cortical fields, thalamocortical and corticocortical connectivity, and functional
p. 594 organization (e.g., Chabot et al., 2007; ↳ Charbonneau et al., 2012; Dooley and Krubitzer, 2018; Karlen et al., 2006; Ramamurthy et al., 2021; Englund et al., 2022). These trends are observed in the dorsal thalamus, but are less pronounced (Englund and Krubitzer, 2022). This effect of late-development plasticity should be most extreme in large-brained species with extended neurodevelopmental schedules (Workman et al., 2013), like primates. This may be particularly true for cortical regions that have differentially expanded in primates over the course of evolution, and that have extended periods of development such as frontal, posterior parietal, and inferotemporal cortex (Reardon, 2018). These higher-order regions of the neocortex appear to be built during development based on activity-dependent mechanisms and environmental context, allowing for the generation of adaptive behavior in an ever-changing sensory milieu.

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