The organization of neocortex in mammals: are species differences really so different?

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By examining a variety of mammals, it is possible to determine common features of cortical organization, and from these infer homologies across species. Such analysis also enables differences in the organization of the neocortex to be identified. Species differ in the amount of cortex that is devoted to a particular sensory system, in the size and configuration of a cortical field, in the number of cortical fields, and in the pattern of connections of homologous fields. It is suggested that the plan of organization that is retained is the result of homologous developmental events, and that modifications to this plan are generated by a limited set of mechanisms. These types of changes to the common network might account for the sensory and behavioural diversity that is observed in extant mammals.

THROUGHOUT THE 20TH CENTURY, remarkable advances in techniques for studying the brain have revealed that the neocortex comprises a number of functional parts that interconnect uniquely to form processing networks. While understanding of the functional subdivisions that compose these networks has increased dramatically, studies have focussed on a few species, such as some primates, cats and rats. To some extent, comparative neurobiology has remained in the background of this enormous research front. Yet comparative analyses, from molecular to behavioural levels of organization, create the foundation upon which all studies of living organisms are based. Examination of a variety of species enables us to deduce which features of these neocortical networks were established early in mammalian evolution, and are homologous in all species (Box 1), and to recognize modifications or differences in the neocortex that evolved in different lineages. Such analyses also enable us to appreciate general organizing principles of the neocortex, and potential mechanisms of modification, as well as constraints that limit neocortical evolution and, in turn, function. Thus, comparative neurobiology is an integral part of attempts to understand the functional organization of neocortex and, ultimately, the evolution of more complex functions that are generated by the neocortex, such as perception, cognition and consciousness.

Retained plan of cortical organization

Before differences across species can be understood, it is necessary to determine similarities in the organization of the neocortex in the various lineages. Primary somatosensory, visual and auditory areas (SI, VI and AI, respectively) have been identified in a number of distantly related species (Fig. 1) that represent the three major branches of mammalian evolution, that is, protetherians, metatherians and eutherians[1,19,20] (Box 1). Similarities in topographic organization, relative location, architectonic appearance in both tangential and standard planes of section, patterns of connections with the thalamus and cortex, and stimulus prefer-

ences for neurones in these areas, suggest that they are homologous; that is, inherited from a common ancestor[21] (Box 1). Until recently, it was thought that only these primary areas were common to all mammals, and that additional cortical fields were added independently in different lineages. However, recent work in prototherian mammals, such as the platypus (*Ornithorhyncus anatinus*) and the echidna (*Tachyglossus aculeatus*), as well as studies of several species of metatherian mammals, has led to a re-evaluation of this hypothesis. Additional areas that have been described in representatives of both lineages include the second somatosensory area (SII) or the parietal ventral area (PV), or both, a rostral deep field (R, DS or 3a), a manipulation or motor field (M or MI)[1,3,22–24], a second auditory field (at least one field in addition to AI has been identified in most mammals)[2], and a second visual field, VII[25,26] (L. Krubitzer, unpublished observations). Because these fields have similar patterns of topographic organization, interconnections and consistent architectonic features in all or most mammals investigated, it is most likely that they are homologous, rather than having arisen independently in each lineage. Thus, the plan of organization that is retained from the common ancestor (Fig. 1) appears to have been more complex than was thought previously. However, the individual cortical fields that compose this basic plan or network have clearly undergone their own independent evolution in the various lineages.

These findings of a retained plan are significant, since they indicate that some features of neocortical organization are conserved in all mammals. An appropriate analogy would be the evolution of the body plan in vertebrates. Although it has been possible to modify an existing portion of this plan by reducing or enlarging appendages or changing a forelimb into a wing, or a hindlimb into a flipper, a completely new body plan has not developed. Thus, the body plan, selected very early in vertebrate evolution[27,28], greatly restricts the avenues along which subsequent change can occur.

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Box 1. Homology, homoplasy and analogy[a]

Homology

The term homology refers to characteristics that are inherited from a common ancestor (red lines in Fig.). When examining the neocortex, homology can only be deduced, rather than demonstrated directly. Homologies can be ascertained with varying degrees of confidence, related to the number of species examined, and the number of criteria that is used to define the structure in question. For example, the distinct laminar appearance and position of the hippocampus allows us to identify it readily in all mammals investigated. The hippocampus is proposed to be homologous, rather than having arisen independently in each lineage. Likewise, based on examination of cortical architecture, patterns of connections, position, neural-response properties, and internal organization of a particular cortical field in a variety of mammals, we suggest that the field in question is homologous. The term homologous does not imply similar function (analogy). Indeed, it is highly unlikely that field VI in the platypus and in the macaque monkey has similar functions, since the lineages that gave rise to extant platypuses and primates have evolved independently for over 150 million years.

Homoplasy

Structures that look the same but have arisen independently in different lineages are considered homoplaseous. For example, ocular dominance columns (ODCs) in cats[b] and monkeys[c] are homoplaseous features of field VI, and are likely to have arisen through convergent evolution, since these are very distantly related species, and other intervening lineages to which the common ancestor gave rise do not posses this feature. Thus ODCs in cats and primates are homoplaseous, are not homologous, and might be analogous.

Analogy

Analogy refers simply to the same function. A classic example is the wing of the bat and the wing of a fly.

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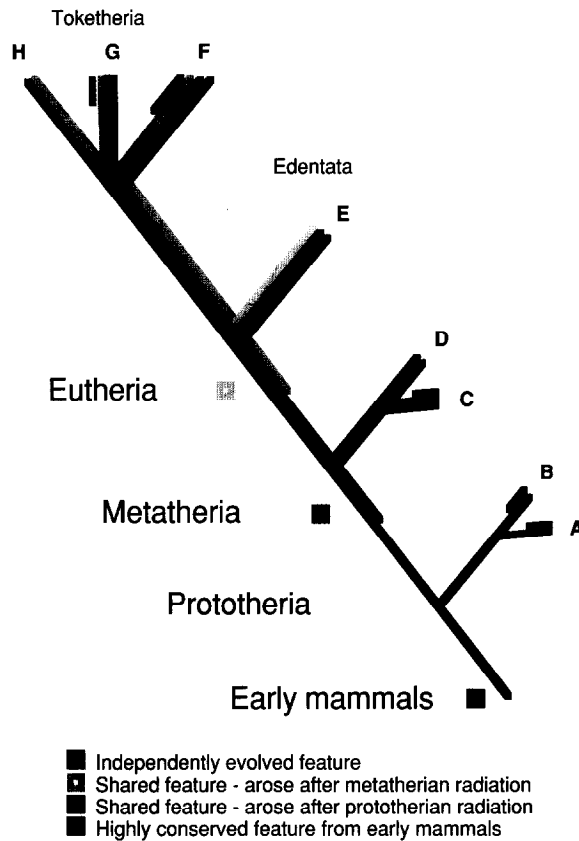
Fig. Evolutionary tree that depicts retained and independently acquired features. This simplified evolutionary tree depicts the three major mammalian radiations: prototherians (for example, platypus and echidna); metatherians (for example, possum and quoll); and eutherians (for example, rats and primates). It illustrates how different features have evolved. Some features are highly conserved, such as cortical fields SI and VI (A–H), and are identified in all extant species (red) and proposed to be homologous. Other features or areas have been added somewhat later in evolution, and are shared only by some groups (green and yellow), such as field SII in metatherian and eutherian mammals (C–H). There are also features that look similar (homoplaseous), such as modules in SI of the platypus and the star-nosed mole, but that have been added independently in several lines of descent (A, B, C, F and G, blue). The Toketherian radiation, which occurred approximately 60 million years ago, includes archontans, ungulates, carnivores and insectivores[d].

While the retained plan of cortical organization has been modified by changes in size, shape and internal organization of cortical fields, or the addition of new fields (Figs 1 and 2), it does not appear possible to eliminate some elements of this plan completely, nor to develop an entirely new plan. For example, visual cortex and the retinogeniculate pathway have been retained in mammals such as the platypus and the insectivorous, star-nosed mole (Condylura cristata; Fig. 2), whose use of vision is minimal, and also in the subterranean blind mole rat (Spalax ehrenberghi), whose vision is almost non-existent[31]. It is possible that genetic pleiotropy, the multiple effects of a single gene on a number of functions or traits, prevents the complete elimination of a particular sensory system or the developmental events that generate that sensory network, because these events are tied genetically to other crucial developmental processes[32]. Cooper and colleagues[31] hypothesized that a 'developmental interdependence within the visual system could explain why, despite large interspecific variation, a common plan of visual organization is universally conserved in vertebrates'. Such interdependence might reflect a set of events that is regulated by a single gene (pleiotropy) or a limited population of genes. Thus, it is not possible to remove one event or function without altering the other events that are encoded by that gene. This type of construction necessarily constrains the evolution of the nervous system. As Miklos and colleagues[33] said: 'Once there is multiple usage for any thing – be it gene, protein, circuit, or organ, compromise is inevitable and specific optimality is unachievable'. Therefore, the retino–geniculo–cortical pathway has not been eliminated, even in animals that do not

Echidna

2 mm

Quoll

1 mm

Squirrel

1 mm

Flying fox

1 mm

Marmoset
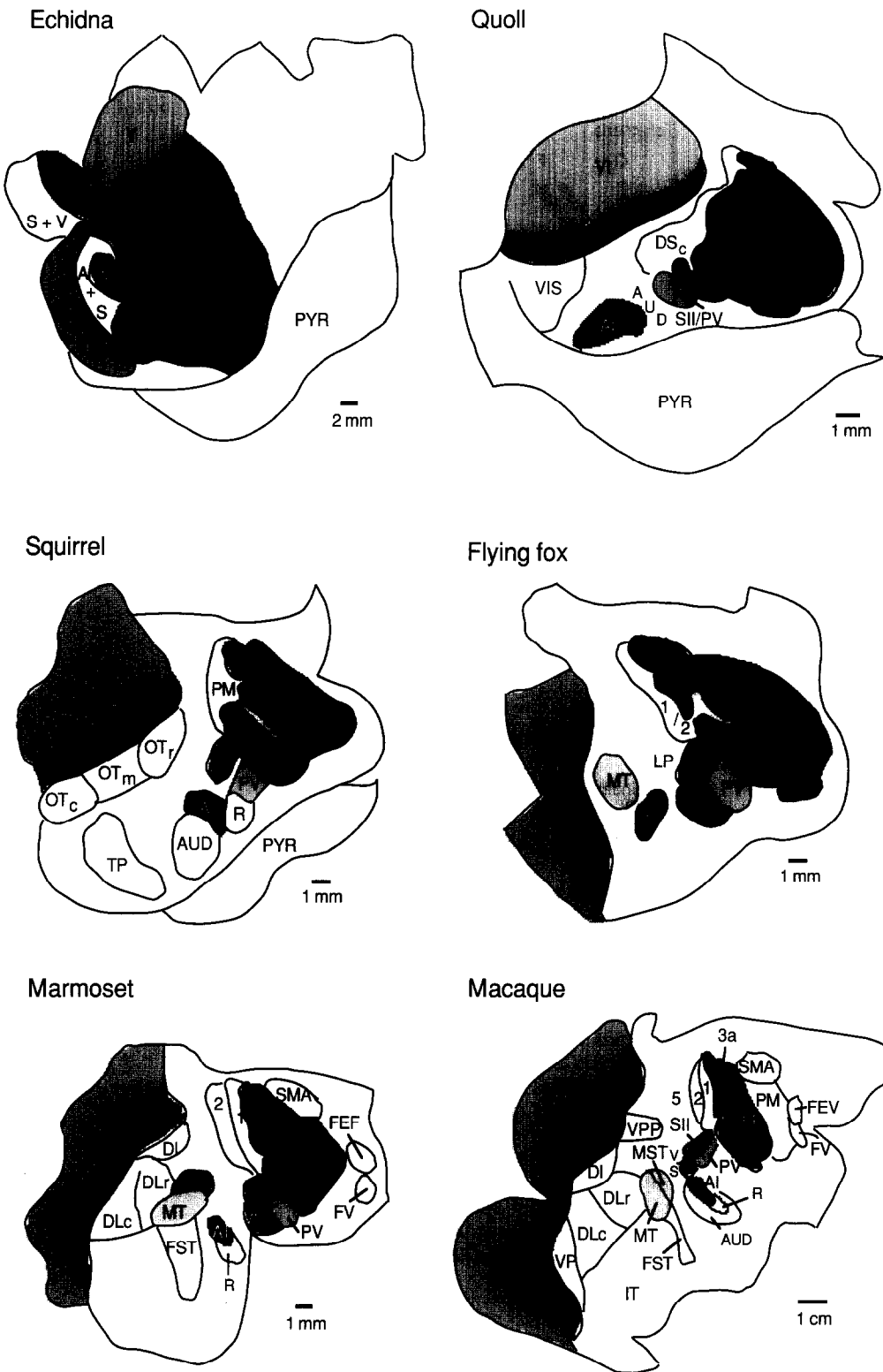

1 mm

Macaque

1 cm

Fig. 1. *Common features of cortical organization in mammals. The organization of cortical fields from six different mammals, as drawn on a flattened cortex. Although the relative size, shape and internal organization of fields has been modified independently in different lineages, homologies can still be identified based on a number of criteria (see Box 1). Similar colours depict homologous fields, although evidence for some of the cortical subdivisions is still preliminary. Subdivisions of echidna cortex are drawn from Ref. 1, while those of the quoll are from Ref. 2 (auditory), and Ref. 3 and L. Krubitzer, unpublished observations (somatosensory visual). Subdivisions of the squirrel neocortex are from Ref. 4 (somatosensory and motor), Ref. 5 (auditory), and Ref. 6 (visual). Subdivisions of the flying fox are from Ref. 7 (visual), Refs 8 and 9 (somatosensory), Ref. 10 (areas 3a and M), and Ref. 11 (auditory). Subdivisions of the marmoset are drawn from Ref. 12 (visual, FEF and FV), Ref. 13 (somatosensory), and Ref. 14, in the closely related tamarin, Saguinus (auditory); VS is estimated from architectonic boundaries and patterns of connections. Subdivisions in the macaque monkey are taken from Ref. 15 (visual), Ref. 16 (anterior parietal fields), Ref. 17 (lateral somatosensory fields and lateral portions of anterior parietal cortex), and Ref. 18 (auditory cortex). Medial is at the top and rostral is to the right. For abbreviations, see Box 2.*

and most species have modified existing sensory apparatuses and systems for enhancing stimulus detection, rather than creating new mechanisms of detection. Although a few species have added new sensory systems (for example, electroreception in the platypus[36], and magnetoreception in the Pacific dolphin[37]), these have interfaced with existing neural systems, and do not claim exclusive cortical territory[1].

Species differences

While there appears to be a retained plan of neocortical organization, this plan has been altered in different lineages. Rodents represent a highly diverse group in terms of morphological and behavioural specializations, and they occupy a variety of niches. Despite common features, their neocortical organization also reflects these specializations. The highly visual, arboreal squirrel (*Sciurus carolinensis*) has a cone-rich retina[38], a relatively large and well-laminated lateral geniculate nucleus[39], and a proportionately large visual cortex that includes areas VI, VII and at least five additional extrastriate areas[6] (Figs 1 and 3A). Much less cortex is devoted to processing somatosensory and auditory information[4,5,40]. Muroid rodents (families: *Cricetinae* and *Muridae*), such as the terrestrial hamster, rat and mouse, rely little on vision but their use of tactile information is extensive. The visual cortex in these species is relatively small and

appear to use it because, under existing genetic constraints, this pathway cannot be eliminated without eliminating other crucial events that are necessary to generate a viable nervous system. Experimental support for this proposal comes from studies on developing monkeys in which bilateral enucleation early in neural development results in a reduction in the size of VI, but not in a complete elimination of this field[34,35].

Similarly, the genetic constraints that make the complete elimination of sensory systems unlikely might also preclude the development of a new sensory system in mammals. Five major senses have been retained and modified from our reptilian ancestors,

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Box 2. Abbreviations

A, primary auditory area defined architectonically; AI, primary auditory area; A+S, auditory + somatosensory area; Aud, acoustically responsive cortex; DI, dorsal intermediate visual area; DLc, dorsal lateral visual area, caudal division; DLr, dorsal lateral visual area, rostral division; DM, dorsal medial visual area; DSc, deep somatosensory area, caudal division; DSr, deep somatosensory area, rostral division; FEF, frontal eye field; FST, fundal superior temporal area; FV, frontal ventral eye movement field; IT, inferior temporal cortex; LP, lateral parietal area; M, motor cortex or manipulation area; MT, middle temporal visual area; MTc, caudal division of the middle temporal visual area; MST, middle superior temporal visual area; OTc, occipital temporal visual area, caudal division; OTm, occipital temporal visual area, middle division; OTr,

occipital temporal visual area, rostral division; PM, premotor cortex in macaque monkeys and parietal medial field in squirrels; PV, parietal ventral area; PYR, pyriform cortex; R, rostral auditory area in squirrels, rostral deep somatosensory area in echidna; SI, primary somatosensory area, architectonic area 3b; SII, second somatosensory area; SMA, supplementary motor area; S+V, somatosensory + visual area; TP, temporal parietal area; V, primary visual area defined architectonically; VI , primary visual area; VII, second visual area; VIS, visual cortex; VP, ventral posterior visual area; VPP, ventral posterior parietal area; VS, ventral somatosensory area; 1, somatosensory area 1; 1/2, somatosensory area 1/2; 2, somatosensory area 2; 3a, somatosensory area 3a; and 5, posterior parietal area 5.

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less complex in organization than that of their distant cousins[41,42], whereas the somatosensory cortex is expanded greatly (Fig. 3B). The vibrissae representation alone assumes approximately one half of the SI representation[43], and a rather large portion of the entire neocortex. The subterranean pocket gopher (*Thomomys*) also has an expanded somatosensory cortex[44]. However, unlike the muroid rodents, the gopher has a large representation of its forepaw, which is specialized for burrowing and making fine tactile discriminations for predator evasion. The representations of the face and cheek pouches, which are specialized for transport of food, are also quite large.

Australian marsupials, like rodents, fill a variety of niches, and examination of their neocortex indicates that modifications to the retained plan of neocortical organization, although evolved independently, have taken the same form as those of rodents (Fig. 3C–F). In the arboreal brush-tailed possum (*Trichosurus vulpecula*), a large region of cortex is devoted to processing

somatosensory information[24], and barrels, similar to the vibrissae representation in some rodents, have been identified[45]. By contrast, the predatory northern quoll (*Dasyurus hallucatus*) and fat-tailed dunnart (*Sminthopsis crassicaudata*) have proportionately more cortex devoted to processing visual information[10]. In the dunnart, architectonically defined area 17 (VI) assumes almost half of the neocortex (Fig. 3D). Finally, the rainforest, canopy-dwelling, striped possum (*Dactylopsila trivirgata*) engages in foraging and other complex behaviours that are somewhat similar to those of the primate aye-aye (*Daubentonia madagascariensis*)[46]. Like the aye-aye, the striped possum possesses a specialized digit that is used for extracting insects from holes gnawed in trees. Volumetric measurements of its brain 'relative to its body size, and corrected for allometry, indicate that it is the largest of all marsupial brains[47]. Initial studies of its somatosensory cortex demonstrate the presence of multiple, highly differentiated representations, and proportionately large, histologically
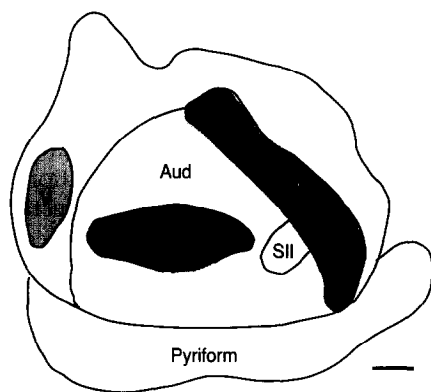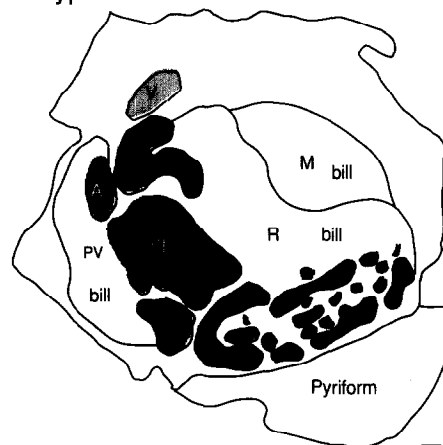
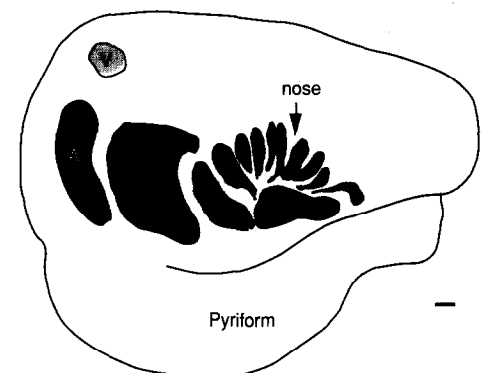## Ghost bat   Platypus   Star-nosed mole

Fig. 2. *The organization of neocortex in highly derived species. Subdivisions of cortex in animals with sensory specializations such as the echolocating ghost bat, the electroreceptive platypus, and the star-nosed mole. More than half of the cortex of the ghost bat is involved in processing auditory information (black + Aud), while approximately two-thirds (including SI, PV, R and M) of cortex in the platypus is involved in processing inputs from the bill (either electrosensory or mechanosensory, or both, red). In the star-nosed mole, visual cortex (V, yellow) is very small, and a large area of cortex is devoted to processing inputs from the nose. Despite the dramatic modifications in terms of size, internal organization, and the addition of modules in these species, components of a common plan of organization can still be identified (depicted in the same colours). Subdivisions of the ghost bat cortex are redrawn from Ref. 29 (somatosensory) and L. Krubitzer (unpublished observations) (visual and auditory). Subdivisions of the platypus cortex are redrawn from Ref. 1, and those of the star-nosed mole cortex are redrawn from Ref. 30. Medial is at the top and rostral is to the right. Scale bars, 1 mm.*
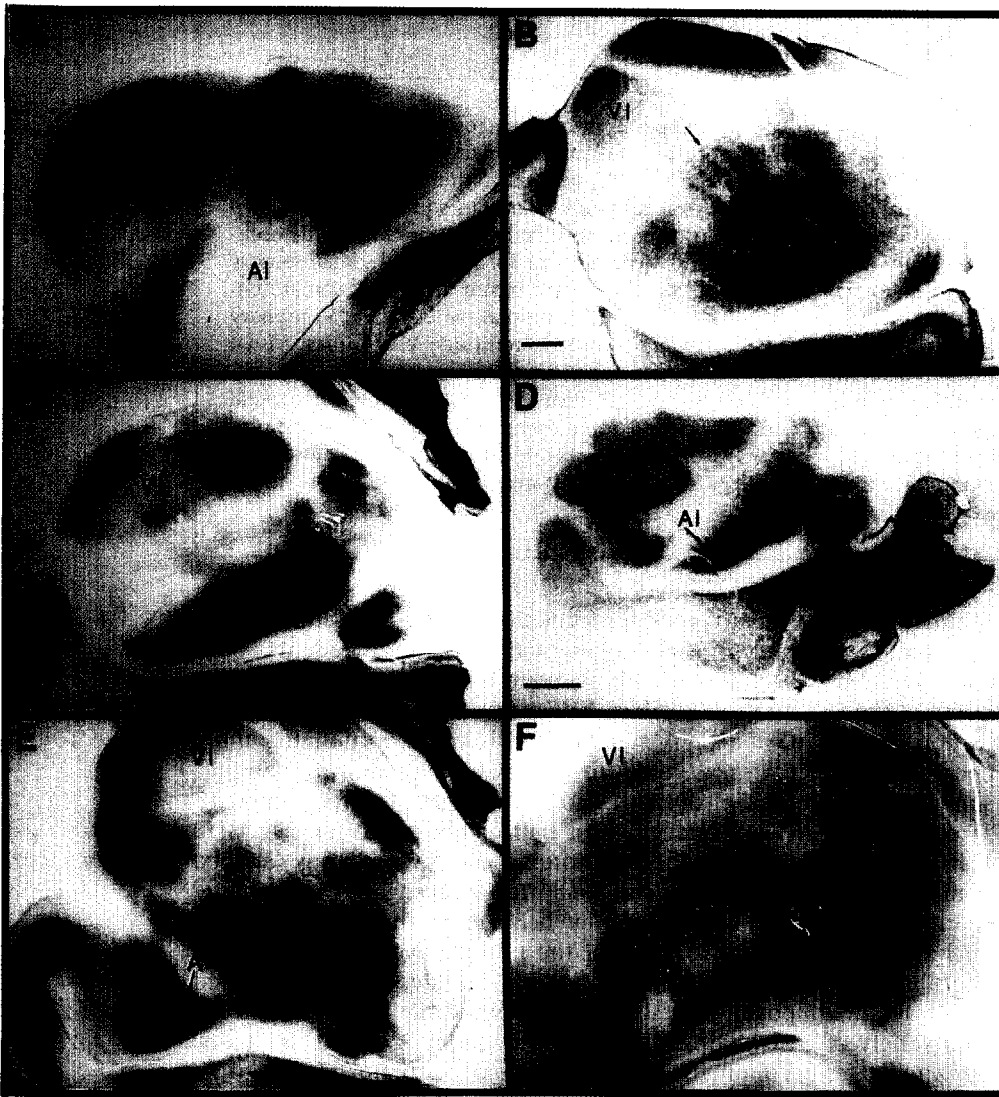
Differences in the size or configuration, or both, of a retained cortical field are observed across mammals and across sensory and motor cortices. For example, SI in raccoons is relatively larger than in other carnivores, and the raccoon has a large expansion of the representation of the hand, such that individual digits are represented on separate gyri[20]. This enlargement is related to the extensive use of tactile information from the glabrous hand for prey capture. The relative size and shape of SI in the flying fox and squirrel (Fig. 4A and C) is significantly different from that of monkeys (Fig. 4B and D). While the architectonic appearance and mediolateral organization of SI is similar across species, details of the internal organization can be quite different. For example, in bats the rostrocaudal organization of the forelimb is reversed from that of most other species: the distal portion of the wing and digits are represented caudally, while more proximal portions of the digits, wing and forelimb are represented more rostrally[29,48]. This is thought to be related to the difference in normal body orientation of bats compared with other animals.

The generation of modules within cortical fields is another common modification to the retained plan of organization. Modules are defined here very globally as structural and physiological discontinuities within the limits of a classically defined cortical field (see Box 3). This heterogeneity within a field is reflected in architectonic appearance (including visualization using immunohistochemistry), neural-response properties, stimulus preference and connections. In

Fig. 3. *Differences in the proportion of cortex that is devoted to a particular sensory system in different species. Lightfield photomicrographs of cortex that has been flattened, cut parallel to the cortical surface and stained for myelin in the squirrel (A), mouse (B), quoll (C), fat-tailed dunnart (D), and brush-tailed possum (E), and for cytochrome oxidase in the striped possum (F). Although similar fields such as VI, AI and SI can be identified in all of these species, there are clear differences in the relative size, internal organization, and location of these fields. For example, while the mouse has a relatively small VI, its somatosensory cortex is expanded greatly, and the barrel field representation of the vibrissae (arrow) assumes a large portion of the field. In the marsupial quoll (C) and dunnart (D), visual cortex assumes at least a third of the entire cortex. The striped possum (F) has a very large neocortex with multiple somatosensory representations. Within SI, the representations of the specialized digit (top arrow) and gums (bottom arrows) are very large, and distinct architectonically in this preparation. Scale bars, 1 mm. Medial is at the top and rostral is to the right. For abbreviations, see Box 2.*

distinct representations of the specialized gums and fourth digit (L. Krubitzer and J. Nelson, unpublished observations; Fig. 3F).

Cortical-field generation and module formation

Despite the constraints that channel the evolution of the neocortex, there appear to be several consistent modifications to the neocortex in the different lineages. These might account for the diversity that is observed in extant species, and include:

(1) Changes in the size and shape of a cortical field
(2) Changes in the internal organization of a cortical field
(3) Generation of modules in a cortical field
(4) Generation of new cortical fields
(5) Changes in patterns of connections of cortical fields.

the somatosensory system, modules are sometimes related to different morphological specializations in the periphery but are not always related directly to an obvious behaviour (for example, barrels in cortex correspond to vibrissae but not necessarily to whisking behaviour (Fig. 5A and D)[51]. The nose of the star-nosed mole, and the bill of the platypus, has very large heterogeneous representations in the cortex (Fig. 5B and C) that are related to the distribution of inputs from specialized structures at the periphery. In the visual cortex of primates, modular organization for fields VI and VII (Fig. 5E), as well as other extrastriate areas (Fig. 5F), can be defined by patterns of connections, architectonic appearance or electrophysiological properties of neurones[52]. Even in the absence of architectonic or physiological distinctions, connection patterns are patchy in their distribution within a cortical field, and reflect the heterogeneous

nature of the cortex (Fig. 5G and H). We propose that the ubiquity of modules across sensory systems and mammals suggests that they are generated by a set of similar mechanisms, and that the potential to generate modules was present in the common ancestor.

The addition of new cortical fields to the network is another means by which existing patterns of organization change. When comparing the neocortices of different species, a consistent observation is that species differ in the number of cortical fields devoted to a given sense[19]. For example, the cortex of the echidna has several fields that appear to be homologous to fields that are described in macaque monkeys (for example, VI and SI, Fig. 1), however, while the echidna has only two visual areas, the macaque monkey is thought to have over 15 visual areas[53]. The possible mechanisms that underlie addition of cortical fields are discussed below.

Finally, formation of modules, and the addition of new fields, is likely to result in a reweighting of connection patterns of the existing network (Fig. 6). For example, while field VI shows common patterns of connections in rodents and primates, including direct inputs from the lateral geniculate nucleus and outputs to field VII, other patterns of connections are different. Field VI in primates has acquired discrete modules that are related to processing colour, form and motion[52], and a number of extrastriate fields have been added. Unlike in rodents, the interconnections between fields VI and VII in primates arise from discrete modules within the two fields. Furthermore, while field VI in rodents and primates projects to several other extrastriate fields, these areas and connections do not appear to be homologous.

Although cortical fields can be defined as homologous in different lineages, using the criteria that are outlined in Box 3, the types of modifications that are described above make it unlikely that they are strictly analogous (Box 1). Indeed, despite the rigidity of some developmental events that produce common networks, such modifications appear to be capable of changing the retained network to such an extent that a wide range of diversity in sensory, perceptual, behavioural and cognitive abilities is possible. How are such changes accomplished? What are the mechanisms that are involved in module formation, and changes in cortical-field configuration and number?

Theories of cortical evolution

There is a number of theories to explain the addition of cortical fields in evolution. Lende[54] proposed
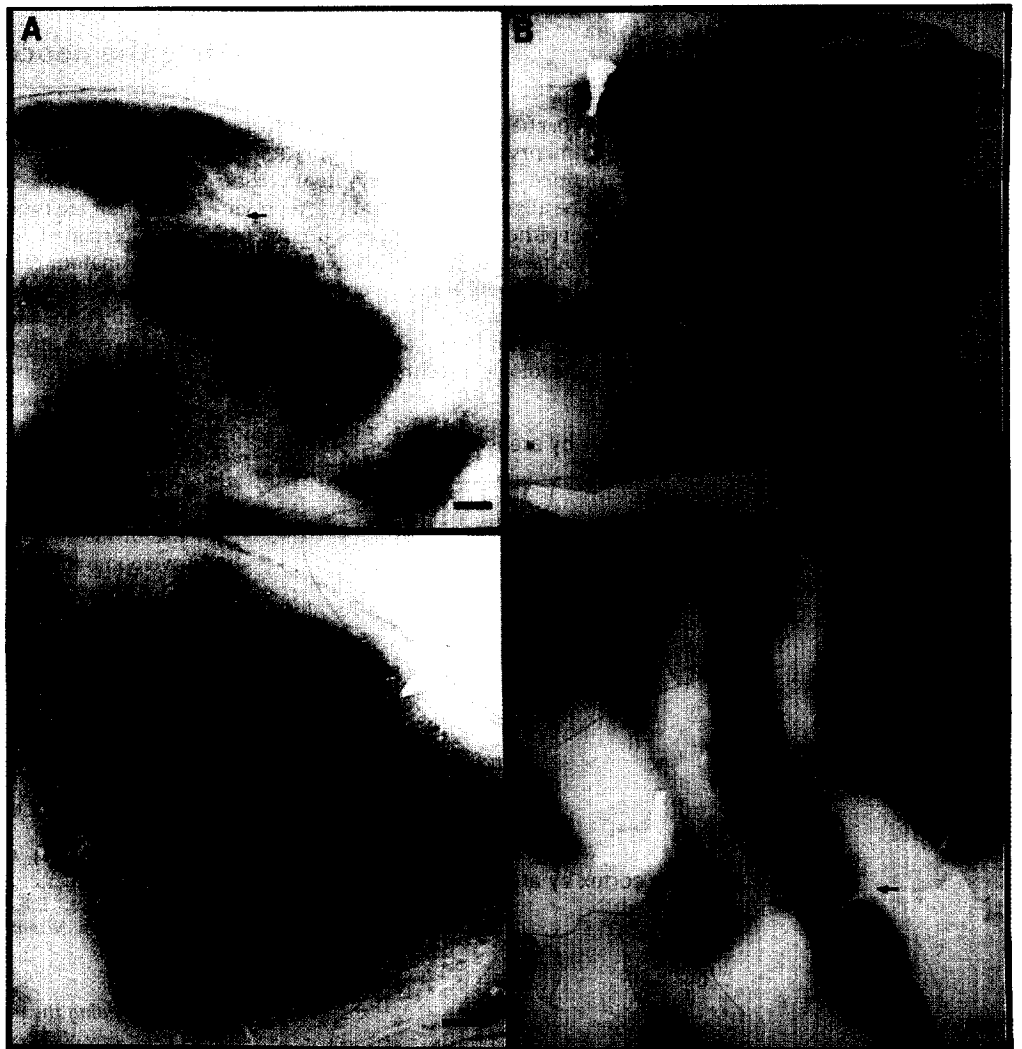

Fig. 4. *Differences in the relative size and shape of SI in different mammals.* Lightfield photomicrographs of cortex that has been flattened, cut parallel to the cortical surface, and stained for myelin in the flying fox (**A**), marmoset (**B**), squirrel (**C**), and macaque monkey (**D**). In all species, SI stains densely for myelin relative to surrounding cortex, and is composed of myelin dark regions and myelin light regions that separate major body-part representations. In all species, changes in relative size, shape, some features of organization, and some connections have occurred. Scale bars, 1 mm. Medial is at the top, and rostral is to the right.

that early mammals had an overlapping sensory–motor amalgam that pulled apart gradually to form separate representations, while Ebbesson[55] suggested that the nervous system increases in complexity by a process of parcellation. The latter theory of brain evolution promotes the idea that early brains were diffuse and basically undifferentiated and, through selective loss of connections, parcellated into multiple, differentiated aggregates or parts. Allman and Kaas[56] suggested that existing cortical fields duplicate as a result of some genetic mutation, and these new fields acquire new connections and functions eventually. In a further elaboration of this theory, Kaas[57] suggested that cortical fields might also evolve from existing fields through a process of gradual differentiation of a single field into two fields. According to Deacon[58], developmental changes in contextual events (for example, axon-target affinities, and timing) bias competitive interactions, and result in loss, addition, or replacement of connections (for a detailed review of theories of cortical-field evolution, see Ref. 58). Most theories of cortical-field evolution have been generated from the premise that early mammalian brains were diffusely organized and


Box 3. Subdividing the neocortex

In most modern approaches, the neocortex is subdivided into various compartments using a number of criteria. A cortical field is defined usually by an architectonic appearance that can be aligned with a complete representation of the sensory epithelium, as well as a unique pattern of connections[a]. A range of histological techniques is now available, including myelin staining, enzymatic reactions and immunohistochemistry. This enables identification of cortical-field boundaries, as well as modules within fields. These histological techniques can be com-

A   Dividing cortex by areas

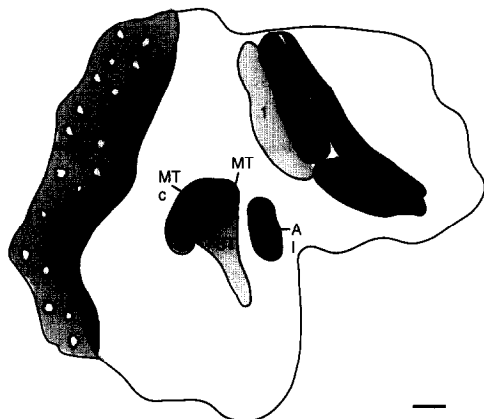### B   Dividing cortex by areas and modules

bined with electrophysiological recordings of multiple or single neurones so that 'maps' of the sensory epithelium can be generated, and characteristics of individual neurones that are tuned to specific features of the stimulus can be ascertained. These techniques can also be combined with anatomical tracing of connections, and a field's intrinsic, intrahemispheric, interhemispheric and subcortical connections determined.

However, any one cortical subdivision does not always fit all the defining criteria. For example, cortical fields are not always homogeneous in appearance (Fig., and see Fig. 5), nor do all neurones within a field possess similar response properties or stimulus preferences[b]. Observed connections of a given field might also differ depending on the presence of modules in some lineages. While the use of multiple criteria to subdivide the cortex helps to overcome this problem, such criteria still encourage us to view the cortex as static and composed of clearly separable parts, rather than as an evolving structure. The true nature of the cortex is dynamic, both within an individual's lifetime, and within a species over time.
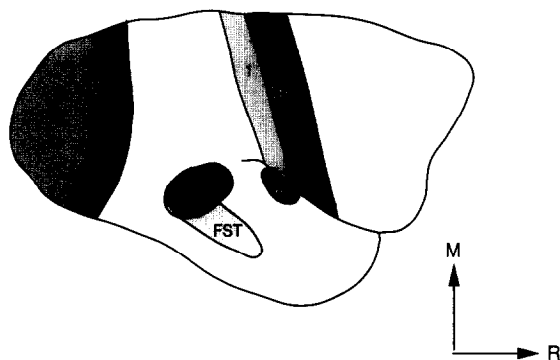
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Fig. Dividing the neocortex by areas and modules. (A) *A dorsolateral view of the neocortex of a marmoset in which the neocortex is divided by area.* (B) *A more complete view of cortical subdivisions, and modules within these subdivisions, in a flattened view of the neocortex. Although fields such as VI do have sharp boundaries, the discovery of modules, defined architectonically, physiologically and connectionally, in a number of visual (shades of green) and somatosensory (shades of pink) areas has led to a reconsideration of cortical-field boundaries, and the criteria that are used to define them. Somatosensory-field boundaries are taken from Ref. c, visual-field boundaries are taken from Ref. d, and auditory-field boundaries are from Ref. e. Scale bar, 2 mm. For abbreviations, see Box 2.*

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undifferentiated. However, recent observations in a variety of mammals whose ancestors branched off early in evolution do not support this contention[1,2,26] (Figs 3C–F, 5B–D and H), because some of the same mammals on whom these theories were founded have now been shown to have multiple, highly differentiated cortical fields.

Based on observations in our laboratory[1,8,9], we propose that cortical fields evolve by a process of initial invasion of new correlated inputs to the cortex (module formation), followed by a process of gradual aggregation of similar types of inputs. This process occurs in both directions so that partially aggregated groups might eventually aggregate further and form a new field, or might disperse or retract, or both, and form a more homogeneous arrangement. This process can stabilize in any lineage, so that the initial invasion might not aggregate or separate. The organization of anterior parietal fields in the grey-headed flying fox (*Pteropus poliocephalus*) represents an aggregation of inputs, as well as a partial segregation. Recently, a rep-

resentation of deep inputs that form separate islands (area 2) within a representation of cutaneous inputs (area 1) has been identified[8,9]. Furthermore, this field, which we call area 1/2, is embedded partially (Fig. 7C) in the primary somatosensory area, 3b and, given the close relationship between primates and flying foxes, we propose that this field is a primitive form of areas 1 and 2 in primates. The second visual area, VII, in some primates (for example, *Cebus apella*) represents a more distinct aggregation stage (Fig. 7D) in that a rerepresentation of the visual hemifield occurs in the different modules (which also differ in architectonic appearance and connections) within the field[59]. While it is tempting to consider these as intermediate stages of the aggregation process (as we have in the past[9]), it would be inaccurate to do so. All extant species represent different frames of the evolutionary process, each containing cortical fields 'frozen' at a particular stage of initial invasion, aggregation or segregation. In any given extant mammal, a field might be at one particular stage, while a homologous field in another

mammal might be at a different stage. The number of invasions, aggregations and segregations that have occurred in the evolution of a particular field within a given lineage is unknown.

Our theory implies that cortex is performing similar computations across its extent, and it is the unique pattern of inputs from the thalamus, and ipsilateral and contralateral cortical fields, that defines a cortical field[1] (Fig. 7). These patterns are capable of changes over many generations, resulting in the evolution of new patterns of activation (modules and fields), and a reweighting of existing afferent and efferent connections of these networks.

The mechanisms that are involved in module formation, cortical-field changes, and cortical-field addition are not well understood, and there is a continuing debate on how cortical fields are specified in development[35,60-64]. It is proposed that the thalamus is the driving force of these changes, and the developing cortex is to a large extent multipotential[60-62]. For example, small changes in the timing of events (heterochrony) in, or the addition of new cells to, the developing thalamus might cause discorrelations between neural groups therein, and result in significant changes in the size, number and internal organization of the cortical fields that are generated by these thalamic inputs. Based on studies of thalamocortical development in rats, a similar hypothesis has been proposed previously by Blakemore and Molnár[65].

Regardless of proposed mechanisms that underlie cortical-field evolution, most observations indicate that new fields evolve from existing ones. Thus, theories that regard the development of the neocortex should take into account that the developing nervous system is also an evolving nervous system. New fields are being interspersed between retained fields, and retained fields are undergoing modifications in size, configuration, location, and patterns of connections. Thus, the study of cortical-field evolution is the study of the evolution of development, and development is a series of events upon which selection acts both within the developing organism[58] (epigenetic), and later upon the postnatal animal it generates. Comparative studies suggest that some events in development must be restricted, since common features of
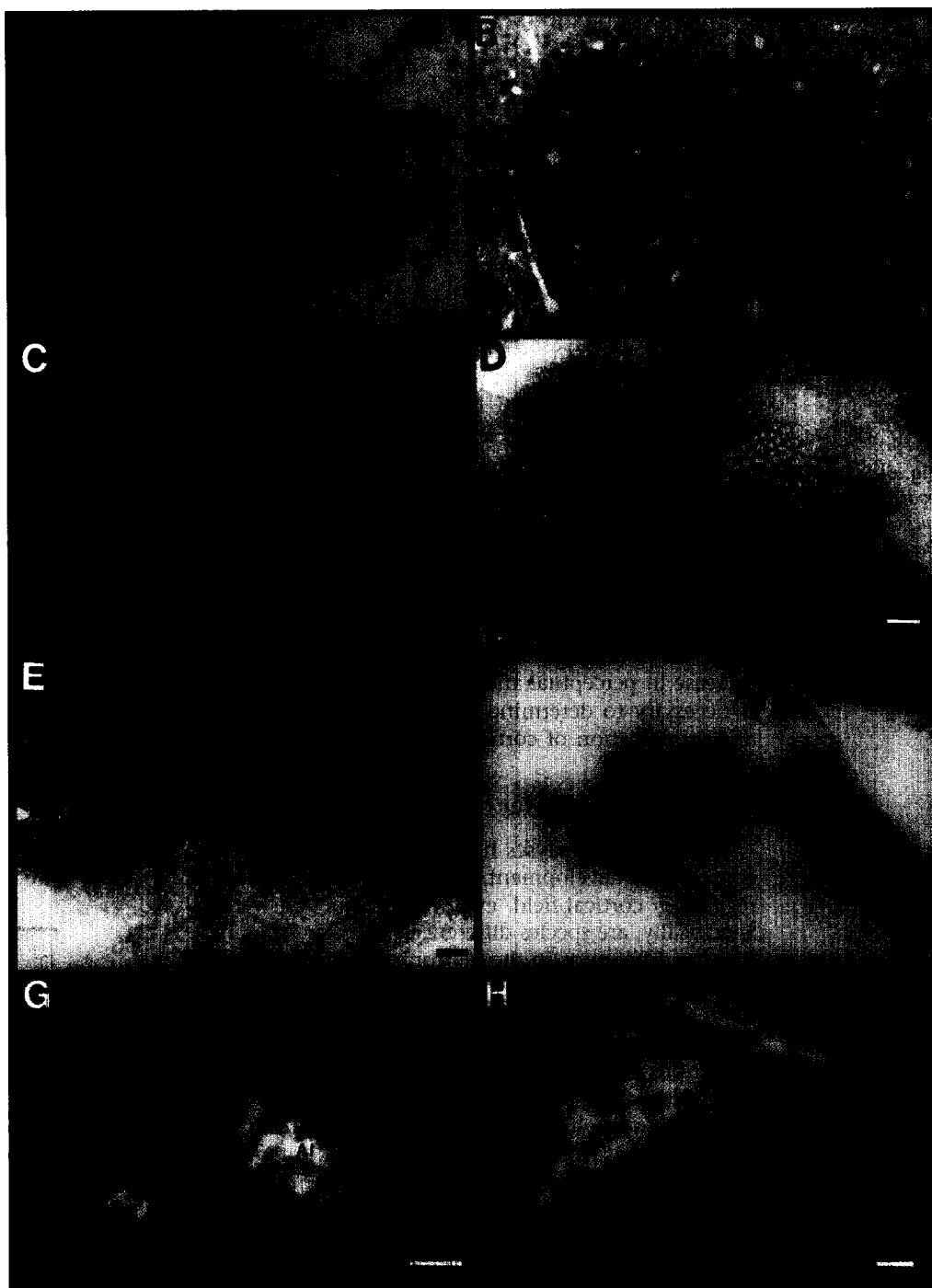
Fig. 5. *Architectonically and anatomically defined modules in the neocortex in different sensory systems and different species. Brightfield (A–F) and darkfield (G and H) photomicrographs of cortex that has been flattened and cut parallel to the cortical surface, illustrating the discontinuities within cortical fields. (A) cortex, including SI, has been processed for succinic dehydrogenase[49], and an array of darkly staining cortical barrels is observed for the vibrissae representation, as well as for representations of the forepaw and hindpaw. (B) Separate cytochrome oxidase (CO) dense representations of individual appendages (1–11) of the nose of the star-nosed mole are depicted[50]. (C) The CO light and dense organization of the bill representation of SI in the platypus related to electrosensory + mechanosensory and mechanosensory inputs, respectively. (D) Myelin light- and dark-staining regions can be identified in the vibrissae representation in field SI of the brush-tailed possum. In primates such as the squirrel monkey, (E) myelin light- and dark-staining bands can be identified in VII, and are related to differential patterns of connections, as well as to different neuronal properties and, in field VI, the lattice-like appearance of dense myelin staining in superficial layers is related to feedback connections from extrastriate visual areas[12]. (F) In marmosets, myelin light- and dark-staining regions in MT are related to patterns of ipsilateral and contralateral cortical connections[12]. (G) A darkfield photomicrograph that shows the patchy nature of callosal connections of A1 of the tamarin[14]. (H) Patchy interhemispheric connections via the anterior commissure are also observed for opossums (L. Krubitzer, unpublished observations). Scale bars, 1 mm.*

organization (the retained plan of organization) are identified in most mammals investigated, as well as common modifications to the retained network. The set of mechanisms that is responsible for such modification must, in turn, constrain the development of the
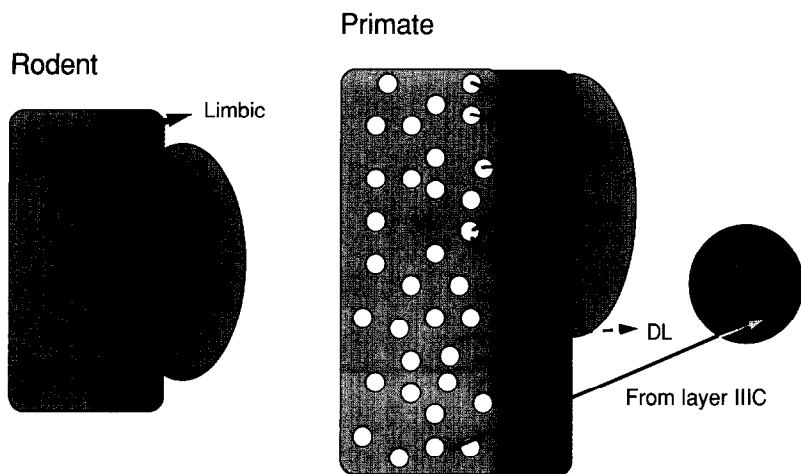
Rodent

Primate

Fig. 6. *Schematized and generalized connections of the primary visual area, field VI, in rodent and primate neocortex. With the addition of cortical fields, and the generation of modules within fields, connection patterns have changed, often dramatically, in some lineages. Because of these changes, homologous fields might not be analogous (see Box 1).*

neocortex and, therefore, its evolution[58]. To understand how cortical fields evolve, and how organisms increase in perceptual and behavioural complexity, it is necessary to determine what triggers the addition and modification of cortical fields under rather rigid constraints.

Concluding remarks

Comparative analyses help generate hypotheses of cortical-field development, and enable some questions regarding cortical-field evolution to be answered. Specifically, are species differences really so different? Because differences in the neocortex consistently take the form of module formation, changes in cortical-field size, internal organization and number, and changes in connection patterns, it is likely that such alterations are generated from similar mechanisms. These mechanisms were probably present very early in mammalian evolution, and it is hypothesized that future changes will be shaped by similar mechanisms. Indeed, while the product in a given lineage of several million years of further evolution cannot be predicted exactly, which features are likely to be retained, the types of modification that are likely to occur, and what will not happen can be predicted with some certainty. By contrast, the amount of phenotypic variation that simple modifications confer is remarkable, especially since these changes might occur with little change to the genome[32]. Thus, the restricted patterns of organization that have evolved in extant species, with minor, consistent, and often predictable modifications, can generate exceedingly variable behavioural, perceptual and cognitive abilities in mammals.

We patronize them for their incompleteness, for their tragic fate of having taken form so far below ourselves. And therein we err, and greatly err. For the animal shall not be measured by man. In a world older and more complete than ours they move finished and complete, gifted with extensions of the senses we have lost or never attained, living by voices we shall never hear. They are not brethren; they are not underlings; they are other nations,
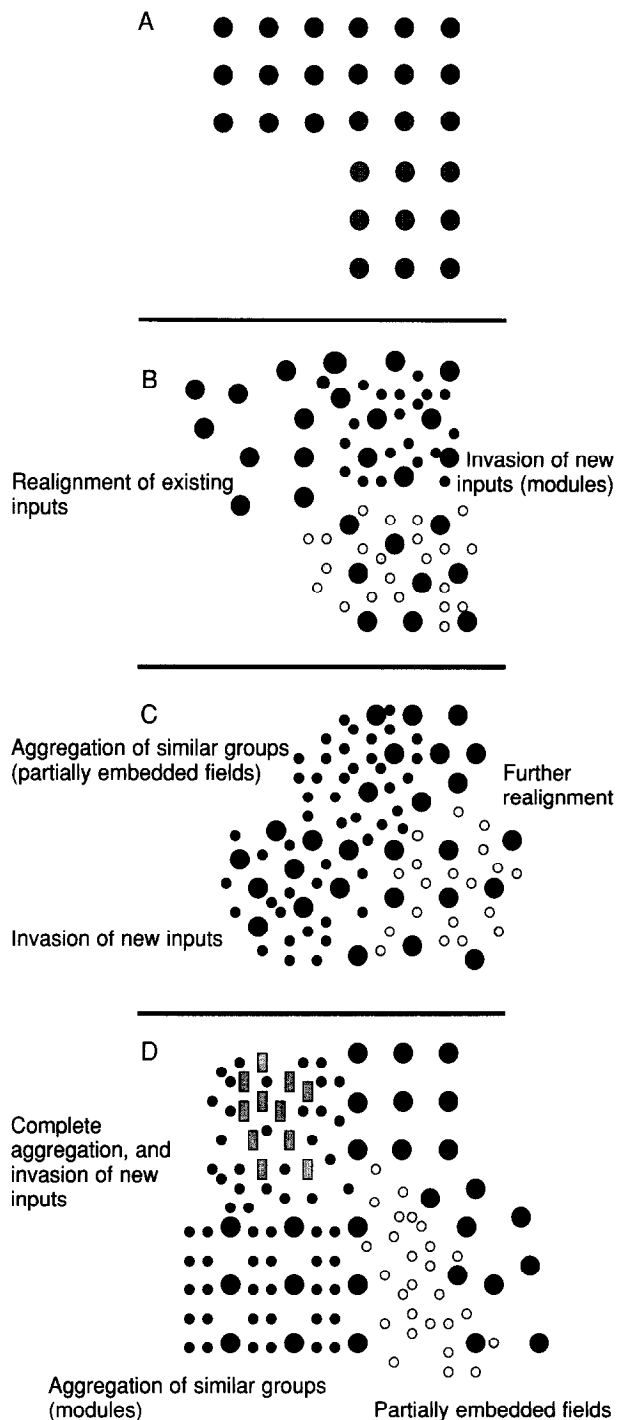

Fig. 7. *Graphic depiction of how cortical fields might be modified or added in evolution.* (A) *A hypothetical stage of cortical-field evolution in which three separate fields, shown as three separate colours, are internally uniform in appearance and afferent patterns.* (B) *An invasion of new, but related (for example, topographically), inputs to a particular region (small circles), and a realignment of existing inputs occurs.* (C) *New inputs might aggregate, and a further realignment of input occurs.* (D) *For some of the fields, a complete separation from the original field occurs with a further realignment and invasion of new inputs (yellow/peach), or a discrete aggregation of new inputs occurs and forms modules within a field (green). Finally, in some fields, new inputs separate from the original field but incompletely so that fields are partially embedded within other fields. This process can occur in either direction (A to D or D to A).*

caught with ourselves in the net of life and time, fellow prisoners of the splendour and travail of the earth.

Beston, 1949 (Ref. 66)

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