behaviour of animals, and that use of the term should be avoided'[29]. In view of such difficulties, focusing on the mechanisms that allow animals to find their way might be more rewarding than dealing exclusively with the map–non-map controversy.

Although the contextual cues used to retrieve local vectors, global vectors and landmark memories are not yet clear, the new results from Collett *et al.*[37] and Menzel *et al.*[38] suggest that the association of navigation vectors and landmarks could have an important role in insect navigation. Several flight or walking vectors could be associated with several locations, stored simultaneously, and applied in a novel and adaptive way. Thus, navigational capacities of insects can exceed elementary associations or chains of such associations, although they are not as complex as they should be if a single unifying spatial representation in the form of a cognitive map is assumed.

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VIEWPOINT

The evolution of visual cortex: where is V2?

Marcello G.P. Rosa and Leah A. Krubitzer

A comparative analysis of the area of the cortex that is adjacent to the primary visual area (V1), indicates that the lateral extrastriate cortex of primitive mammals was likely to contain only a single visuotopically organized field, the second visual area (V2). Few, if any, other visual areas existed. The opposing hypothesis, that primitive mammals had a 'string' of small visual areas in the cortex lateral to V1 (as in some rodents), is not supported by studies of the organization of extrastriate cortex in other mammals, nor by the variability in this organization among extant rodents. A critical re-analysis of published evidence on the presence of multiple areas adjacent to V1 in some rodents has led to alternative interpretations of the organization of the areas in these regions.

Trends Neurosci. (1999) 22, 242–248

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THE POSTERIOR NEOCORTEX of all eutherian mammals that have been studied contains multiple interconnected visual areas. Although the exact borders and internal organization of these areas are still the subject of much study and debate, it is clear that their number and layout vary significantly between species[1,2]. Cross-species comparisons demonstrate that, at one extreme, mammals such as insectivores, with simply organized cortices and poorly developed visual systems, have only two or three visually responsive areas and little room for more[3]. At the other extreme, animals with a well-developed visual system, such as

PII: S0166-2236(99)01398-3

cats and simian primates, can have as many as 20 or 30 different cortical visual areas[4]. How did these different types of organization arise in evolution? This article discusses the possibility that a core group of 'primordial' visual areas, which were established early in mammalian evolution, was inherited in all lineages that led to the diverse orders of present-day eutherians. Consequently, these areas are expected to exist in all extant eutherians.

A primary visual area (V1, striate cortex or area 17) has been demonstrated in all species to date (including not only eutherians, but also marsupials and monotremes[1,5,6]). In each of these major branches of mammalian evolution, V1 can be delimited precisely on the basis of architectonic appearance (for example, heavy myelination or the presence of a granular layer 4)[1,2], the presence of a single and systematic visuotopic map[7], a well-defined pattern of subcortical afferents[8], and a distinct constellation of neuronal response properties (for example, small receptive fields in comparison with extrastriate areas and the presence of many orientation-selective cells with 'simple' receptive-field organization[9–12]), all of which are largely conserved in different species. Yet, when one moves beyond area V1, comparisons across species become more difficult. According to different reports, the number of areas that surround V1, their connections, their visuotopic organization and their architectonic appearance can vary in different species. Despite this, some order is beginning to emerge from the large mass of data available. In view of this, the objective of this article is to review the data available on the organization of the cortex that is immediately adjacent to the lateral boundary of area V1, in order to determine if a common area can be identified across species and, if so, whether this area is a likely constituent of the primordial plan of visual-cortex organization in mammals. Two main theories have been proposed to account for the origin and diversity of organization of the peristriate belt areas among contemporary mammals (Fig. 1). We propose that one of these (the 'simple extrastriate cortex' hypothesis) is clearly supported by recent studies, as well as by a critical re-analysis of older data.

The 'simple extrastriate cortex' hypothesis

According to this hypothesis (Fig. 1A) the peristriate cortex of early eutherians had few subdivisions. Most of the isocortex that is lateral and rostrolateral to area V1 was composed of a single area, which was homologous to the second visual area (V2) in present-day mammals. This hypothesis was conceived because of the widespread presence of area V2 in most, if not all, eutherian groups[6,13]. Thus, V2 can be recognized as an elongated area that is smaller and less myelinated than V1, forms a single representation of the visual field, and receives topographically organized projections that originate mainly from the supragranular layers of V1. Area V2 can also be distinguished by the fact that it receives its principal thalamic inputs from the pulvinar (or lateral posterior) complex of the thalamus, although in some species there are also inputs from the lateral geniculate nucleus[8]. As discussed in detail elsewhere[14,15], smaller areas, which are further lateral to V2, might have emerged early in eutherian evolution, including a putative homologue of primate area MT (middle temporal area). The important issue is that these areas, if present in the last common ancestor of all eutherians, did not adjoin V1 at its lateral boundary. In addition to these lateral areas, at least one visual area is likely to have existed in the area of the medial cortex adjacent to the peripheral representation of V1 (which corresponds in location to the splenial visual area in the cat and area 18b in rodents[15–17]). From this

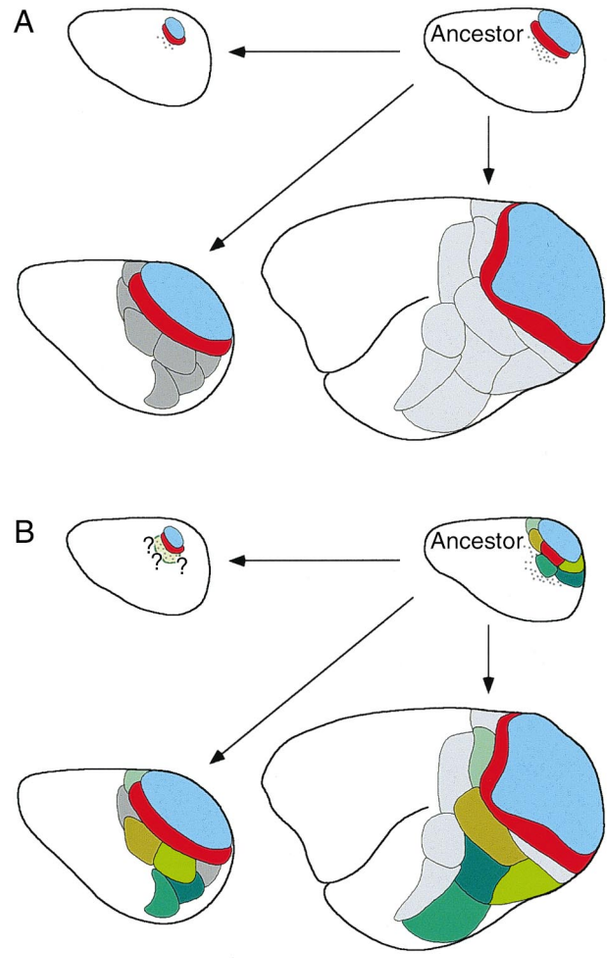

Fig. 1. ***Schematic representations of the simple extrastriate cortex* (A) *and complex extrastriate cortex* (B) *hypotheses.*** *Three hypothetical present-day mammals are derived from an early mammal-like condition (ancestor brain, shown on the top right of each diagram): a small-brained mammal with poorly developed vision (similar to a hedgehog, mole or echolocating bat; top left of each diagram), a small-brained mammal with developed vision (similar to a squirrel, tree shrew or flying fox; bottom left of each diagram) and a large-brained mammal with developed vision (such as a carnivore, prosimian or monkey; bottom right of each diagram). The illustrated brains are schematics and the visual areas are not intended to represent those of any species in particular. In each case, the primary visual area (V1) is indicated in blue and the second visual area (V2) in red. Homologous visuotopically organized areas, according to the complex extrastriate cortex hypothesis, are indicated in different shades of green, and other visuotopic fields, which evolved independently in each lineage (arrows), are shown in grey. The grey dots indicate non-visuotopically organized visual areas that could have existed beyond area V2 in the common ancestor; this cortex could, in theory, originate some of the new visuotopically organized areas in different lineages, through a process of amalgamation and reorganization of afferent populations (see Ref. 1 for details). In* (A) *development of additional visuotopically organized extrastriate areas occurred independently in different lineages, so the areas beyond V2 are not necessarily homologous in distantly related species. In* (B) *many homologous visuotopic areas are retained besides V2, but each lineage also develops additional areas independently. The question marks (top left) indicate that it is unclear what happens to these additional areas in groups of animals with poorly developed visual cortices.*

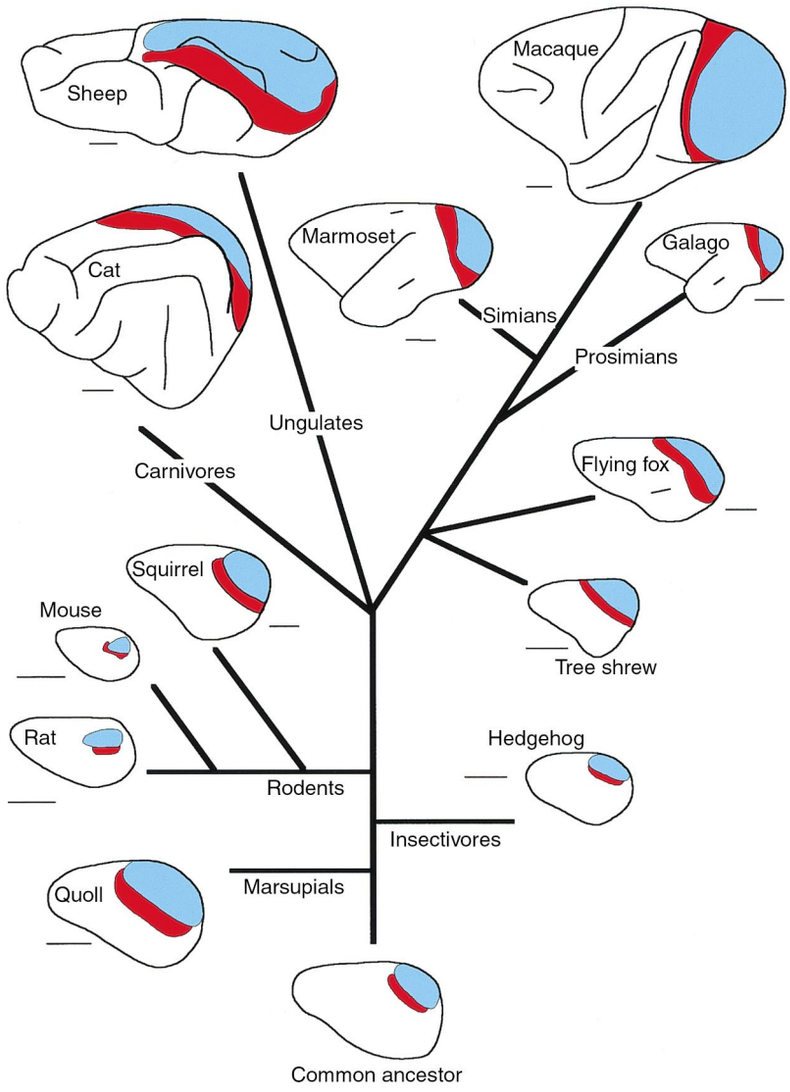

Fig. 2. ***The relationships between mammalian species in which extrastriate cortex has been studied in detail illustrated as a phylogenetic tree.*** *A schematic of the neocortex of each species is shown at the end point of each branch, with the primary and second visual areas (V1 and V2) indicated in blue and in red, respectively. Despite variation in size and shape, V1 and V2 can be recognized in each species, independently of its ecological niche. A hypothetical common ancestor (according to the simple extrastriate cortex hypothesis) is shown at the base of the tree. With the possible exception of marsupials, insectivores and monotremes[5,6], every major branch of the mammalian tree has developed additional visual areas (not shown). Scale bars, 5 mm.*

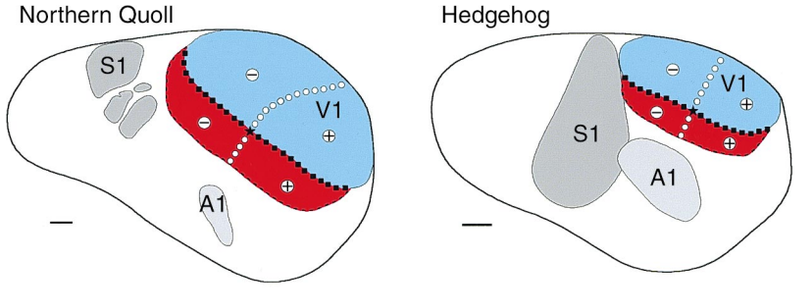

Fig. 3. ***Location and visuotopic organization of the primary visual area (V1; blue) and the second visual area (V2; red) in two conservative mammalian groups.*** *Dorsolateral views of the left cortical hemispheres of a marsupial* (left) *and an insectivore* (right). *Only the neocortices are illustrated. The left-hand diagram was created on the basis of information from Ref. 6 and the right-hand diagram was created on the basis of details in Ref. 3 (visual cortex) and from L.A. Krubitzer, unpublished observations (somatosensory and auditory areas, S1 and A1). In V1 and V2, the representation of the vertical meridian is indicated by the black squares, the representation of the horizontal meridian is indicated by open circles, the representation of the area centralis is indicated by the black star, the representation of the upper quadrant is indicated by '+' and the representation of the lower quadrant is indicated by '−'. Scale bars, 1 mm.*

initial situation, further expansion and subdivision of the isocortex rostral and lateral to V2 (the 'classical' extrastriate cortex) has occurred more or less independently, according to the specific selective pressures faced in the different lineages of mammals.

The 'complex extrastriate cortex' hypothesis

Another proposal is that the extrastriate cortex was already rather elaborate in the earliest eutherian mammals, with perhaps as many as 6–8 core fields that were subsequently inherited by other mammals (Fig. 1B). According to this view, there were many different visuotopically organized areas of the cortex immediately adjoining the lateral aspect of V1, rather than a single area (V2). The rationale for this hypothesis comes mainly from studies in some rodents[17–19], which reported a multiplicity of independent representations of the visual field where V2 was expected to exist. Because rodents form one of the earliest[20] and most-diverse branches of the mammalian tree (about half of all mammalian species are rodents!), and because this organization is believed to exist in many rodent species, irrespective of size and ecological niche, it has been proposed that the organization of extrastriate cortex in rodents represents a mammalian prototype[17]. According to this view, the more elaborate organizations found in large-brained mammals (for example, primates) would include homologues of the primordial extrastriate areas found in rodents. For example, one of the multiple areas that surround V1 (the lateromedial area, LM) has been identified as the ancestral form of area V2 (Refs 17,21), and presumably further studies of other rodent areas would eventually identify additional homologues[22].

The comparative evidence

The major radiation of mammalian orders occurred quite early in eutherian evolution[23] (Fig. 2), with the visual cortex of the last common ancestor of all eutherian mammals unlikely to have developed much beyond the 'primordial' stage. While it is obvious that new neural circuits and areas have appeared during the evolution of different groups of mammals, these probably added to, rather than replaced, old circuits. Thus, one corollary of the simple visual cortex hypothesis is that V2 should be present in all mammals, albeit modified in some cases[13,24,25]. The data so far suggest that this is indeed the case, as, even in animals such as the rat, where a markedly different organization of lateral extrastriate cortex has been reported, an area V2 homologue has been identified[21]. Given that V2 seems to be universally accepted as one of the primordial visual areas, the real differences between proposals can be reduced to two points: (1) the number of areas that existed in addition to V2, and (2) whether or not these areas were laid out as a series of small fields along the border of area V1, in lateral extrastriate cortex.

Support for the proposal that primitive mammals, which include the ancestor of rodents, possessed a single V2 that bordered the lateral aspect of V1 comes from studies of mammalian groups whose ancestors branched off early in mammalian evolution, much earlier than the ancestor of extant rodents. These mammalian groups include metatherians (marsupials), as well as primitive eutherians such as insectivores. In this context, an early study of the hedgehog[3] and the recent physiological exploration of the lateral

extrastriate cortex in a marsupial, the quoll[6], have been particularly informative As shown in Fig. 3, in both cases, a single area (which is similar to V2 in terms of shape, extent and visuotopic organization) was found in the cortex that is laterally adjacent to V1. This strongly indicates that our earliest ancestors had at least a V1 and a V2. Although it is not clear if early mammals had only areas V1 and V2, the comparative evidence indicates that a rat-like string of small areas in the cortex lateral to area V1 is unlikely.

The argument in favour of the complex extrastriate cortex hypothesis relies heavily on the idea that there is a rodent prototype of visual-cortical organization, which includes a large number of areas, and that this prototype is common to all rodents, as well as to lagomorphs[17,19]. In contrast, according to the simple extrastriate cortex hypothesis, the organization of lateral extrastriate cortex in the rat would be interpreted as being derived from animals with a 'typical' area V2. Assuming this is true, one would expect some rodents (including representatives of basal, less differentiated groups) to have only area V2 adjacent to V1 in lateral extrastriate cortex, and to have fewer areas than those reported in the rat. Consequently, most of the areas reported in the rat would have no homologue in other mammalian orders.

The physiological evidence

Figure 4A,B compares the organization of extrastriate cortex in two rodent species, the squirrel and the rat. As first reported over a quarter of a century ago[29], and recently confirmed by detailed microelectrode maps[26] and the patterns of connectivity with V1 (Ref. 30), squirrels have a typical mammalian area V2 that borders the entire representation of the vertical meridian in V1 and encompasses a single representation of the visual field that roughly mirrors that in V1. Confirmation of the organization of area V2 in squirrels is particularly important because most scholars consider the superfamily *Sciuroidea* to be a conservative rodent group, which most closely reflects the ancestral rodents[31]. Recent physiological studies[26,32] have reported the existence of a number of other areas, which are lateral to V2 (Fig. 4A); however, their total number still falls short of that proposed for the rat.

In some rodents, like the rat (Fig. 4B), area LM (which we interpret as being V2) appears to be reduced in size, which allows other representations of the visual field to adjoin V1. Nonetheless, LM is still similar to area V2 both topographically[27] and connectionally[33]. In another rodent, the degu, receptive-field mapping[28] (Fig. 4C) has revealed an area LM that, as in the squirrel, is much larger than any other extrastriate area and forms the entire lateral border of V1. Thus, in this species, LM is typical of area V2 in mammals in everything but name. A very similar V2 organization has been proposed for the mouse[16] (Fig. 4D) and, according to some studies, the hamster[34]. In fact, the hamster seems to be particularly important for the present argument, as studies in this species demonstrate that erroneous interpretation of the data might have been a major contributing factor to the current disagreements in the literature. As shown in Fig. 5, a recent study that included high-density mapping of extrastriate cortex in this species[19] has proposed the existence of four areas that surround V1 laterally. However, the same data can be interpreted much more parsimoniously as

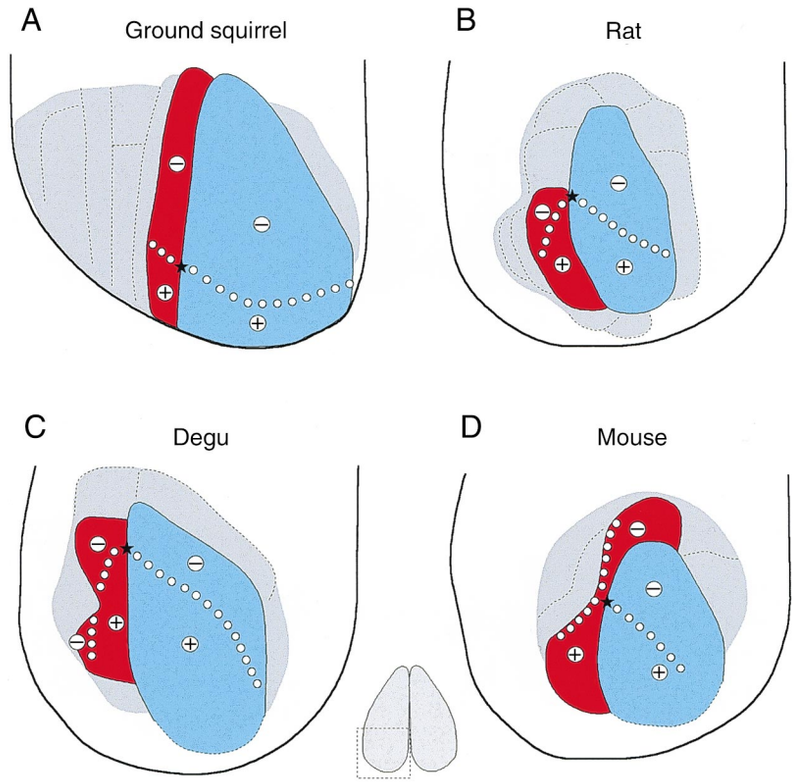

Fig. 4. ***Comparison of the organization of the visual cortex in four rodent species*** **(A)** ***to*** **(D).** *Each diagram is a dorsal view of the caudal half of the brain (see insert for location), with the location and organization of primary and second visual areas (V1 and V2) shown: the representation of the horizontal meridian is indicated by open circles, the representation of the area centralis is indicated by the black star, the representation of the upper quadrant is indicated by '+' and the representation of the lower quadrant is indicated by '−'. The probable extent of the visual cortex and the borders of other extrastriate areas that have been mapped, are indicated by the grey fill and broken lines.* (A) was created using data from Ref. 26; (B) was drawn using data from Ref. 27 (areas V1 and LM) and Ref. 17 (borders of other areas); and (C) and (D) were produced using data from Refs 28 and 16, respectively.

indicating the existence of a large V2-like area, much like that described by Tiao and Blakemore[34]. Studies in the rat also appear to be open to different interpretations, as physiological recordings suggest the existence of a V2 (LM) that is elongated and covers much of the lateral border of V1 (Ref. 27), whereas anatomical tracing reveals a much smaller LM (Refs 17,33).

As reviewed elsewhere[13,25], details of the topographic organization of area V2, such as the exact placement of the field discontinuity in the representation that usually forms the rostral border of V2, can vary even between closely related species. This is reflected in the maps of the different rodents illustrated in Figs 4 and 5: the visuotopic maps of area V2 in the hamster and the degu appear to be similar to those described in flying foxes and galagos (with a split representation of the lower contralateral quadrant), while the map in V2 of the mouse appears to be similar to that of monkeys, with a field discontinuity about the horizontal meridian[35,36]. Finally, the visuotopic map in area V2 (LM) of the rat appears to have no field discontinuities (similar to area V2 in the rabbit[37]), but strongly emphasizes the upper-quadrant representation. Although these variations have been correlated with behavioural specializations in species with developed vision[13,38], where the exact position of the horizontal meridian is easy to determine, the small eyes of rodents can cause additional problems for the experimenter, and it is possible that the variation evident in Fig. 4 is also

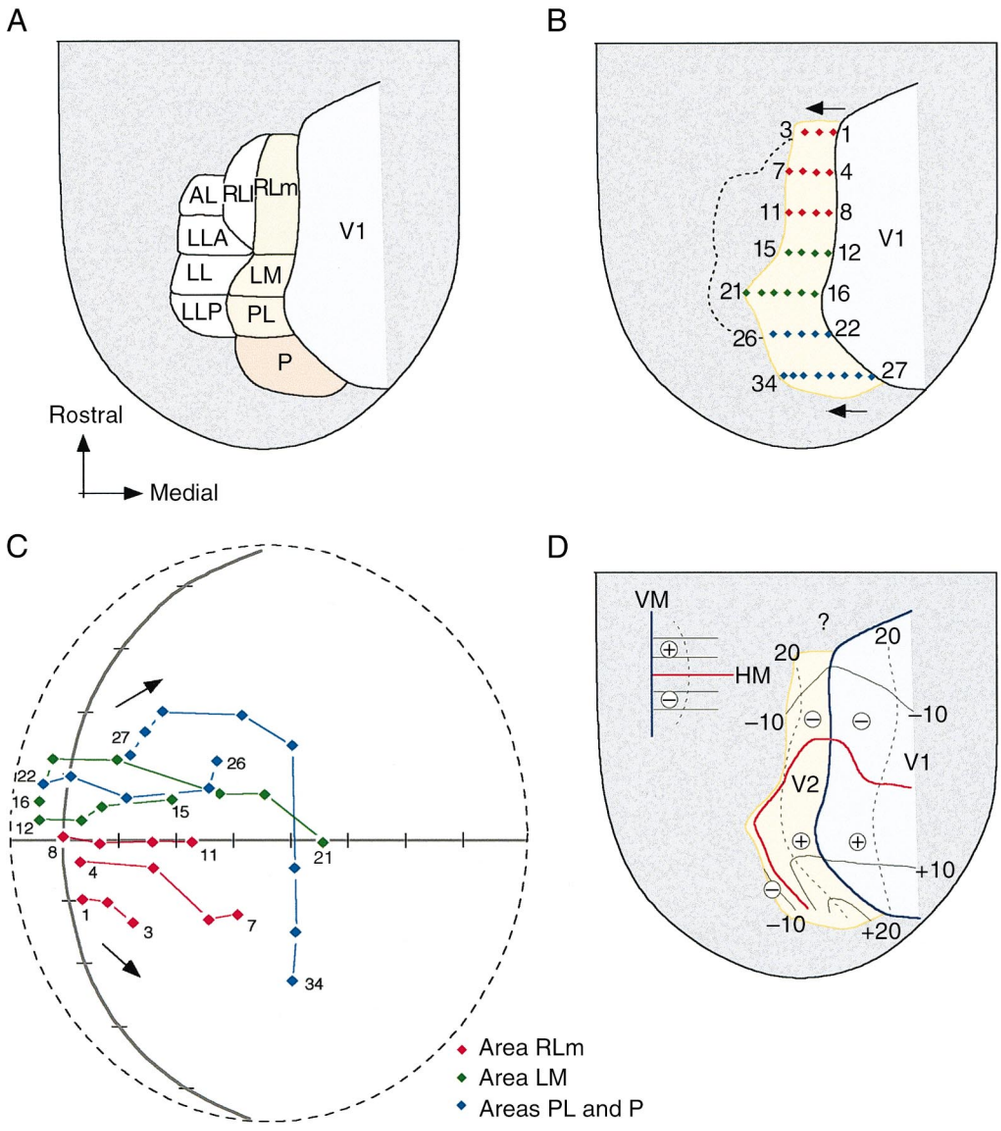

Fig. 5. ***A re-interpretation of physiological data on the organization of hamster lateral extrastriate cortex.*** *The dorsal view of the hamster brain is shown* **(A)**, *which indicates the subdivision of the visual cortex into areas*[19]. *This subdivision was based on receptive fields (◆) recorded at the sites shown in* **(B)**. *To re-analyse the same data, we have joined the recording sites in seven medial–lateral sequences (for example, 1–3, 4–7, etc.). The corresponding centres of the receptive fields, which are redrawn from the same study, are shown in* **(C)**, *which is a schematic view of the hamster's visual field (horizontal and vertical meridians are shown using thick grey lines with minor subdivisions that correspond to 10° of elevation or azimuth). This analysis demonstrates that the visuotopic gradient, seen as one moves from rostral regions (1–3) to caudal regions (27–34) in the prestriate belt, is consistent with the existence of a single second visual area (V2), that encompasses four of the areas detailed in Ref. 19 (RLm, LM, PL and P). The scatter in the representation (that is, the 'criss-crossing' of sequences 16–21 and 22–26) is typical of that observed in high-density maps of area V2; the invasion of the lower visual-field periphery by receptive fields recorded in rostrolateral V2 is also typical of many mammals (see, for example, Ref. 13). On the basis of these data, a re-interpretation of the organization of the cortex lateral to the primary visual area (V1) is shown in* **(D)**. *Arrows in* (B) *and* (C) *indicate the medio–lateral sequences of recording sites and the corresponding direction of change in receptive-field position. Abbreviations: AL, anterolateral field; LL, laterolateral fields; LLA, laterolateral anterior field; LLP, laterolateral posterior field; LM, lateromedial field; P, posterior field; PL, posterolateral field; RLI, rostrolateral–lateral field; RLm, rostrolateral–medial field.*

caused partially by technical factors[27,39]. In addition, the appearance of modular systems in area V2 that are created by invasion of new afferent systems[1] appears to have occurred independently in different lineages[40–42], which creates variability in the local precision of visuotopic maps, such as repetitive mapping[36].

The most-important issue here is that, in spite of some variation between species, physiological maps of lateral extrastriate cortex in many rodents demonstrate an organization that is only superficially different from that found, for example, in cats[38], primates[35,36], tree shrews[43] or flying foxes[13] (Fig. 2). Thus, the physiological evidence argues against the suggestion that a string of small areas lateral to V1 is the typical pattern for rodents. Furthermore, re-analysis of data suggests that some of the differences in organization reported might actually be due to differences in interpretation, rather than to any real difference among rodent species.

At best, the above arguments indicate a scenario whereby the complex organization of lateral extrastriate cortex of the rat is derived from a simpler pattern (which includes a large area V2). Although this explanation is parsimonious, it still leaves the question unanswered of why rats, which have low visual acuity and rudimentary vision[44,45], would have more visual areas than squirrels and other animals with highly developed visual systems. It has been suggested that a large number of areas appeared early in evolution in response to a prime need for diversification of cortical visual function[46]. However, this view is inconsistent with the comparative data reviewed above and with the way that, so far, studies indicate that cortical changes accompany behavioural specializations. Mammals that have become independently reliant on vision for much of their behaviour, such as simians and felines, have converged on similar neural solutions, such as an enormous magnification of the representation of central vision in area V1, a large number of cortical areas devoted to processing different features of the visual scene and an overall increase in the proportion of cortex devoted to visual areas[1,15]. In contrast, in animals such as the platypus or hedgehog, which place little reliance on their visual system, few (perhaps only two) visual areas have been described. The rat, which explores the environment mainly by touch and smell (a fact that is reflected in the enormous representation of the snout vibrissae in the primary somatosensory cortex and the large olfactory bulbs), would also be expected to conform to the latter pattern.

The anatomical evidence

Detailed physiological maps of visual topography are available only for a handful of rodent species. In many more species, data from anatomical tracer injections in

area V1, the superior colliculus and the contralateral cortex have been used to promote the idea that multiple small areas are present in the area adjacent to V1, in a pattern that varies little between species[17,18,47]. The anatomical evidence can be summarized as follows:

(1) The tracing of interhemispheric connections in rodents often reveals a pattern of islands that are free of callosal nerve terminals and are embedded in a matrix of callosal-rich 'rings'. Because many studies suggest that callosal connections terminate mainly around the representations of the vertical meridian, this was taken to be evidence of multiple representations of the vertical meridian, such that each callosal ring encompasses one or two cortical areas[46,48].

(2) Connections with area V1, and projections to the superior colliculus, appear to originate from each of the areas identified by the above criterion. Single injections of anatomical tracers into area V1 result in many patches of label, which coincide with each of the proposed areas, with little variation in relation to the location of the injection site[17,47]. If one assumes that area V2 in rodents has a simple and precise visuotopy, as in mammals with developed vision, one would expect that injections in the caudal and ventral parts of area V1 (which represent the upper quadrant) would label predominantly the caudal rings, and that injections in the rostral and medial parts of area V1 (which represent the lower quadrant) would label the rostral rings. Thus, the widespread connectivity observed in most rodents has been deemed to be indicative of complete representations of the visual field within each callosal ring.

These arguments are not persuasive. Sites of interhemispheric connections, when studied with modern neuroanatomical techniques, are often proved to include elongated 'stripes' of cortex that run perpendicularly to the V1–V2 border, even in species such as the cat and monkey, where a single global visuotopic map undoubtedly exists in area V2 (Refs 49–53), which suggests that regions of the visual field that are distant from the vertical meridian are also interconnected across the two hemispheres. Undoubtedly, the large receptive fields in extrastriate areas make the interpretation of data more difficult: for example, these bands of callosal connections might include cells with excitatory receptive fields centred in the peripheral visual field, but whose modulatory peripheries extend to the opposite hemifield[54]. Corticocortical connections are also typically 'patchy'[55–57]. For example, single injections of anatomical tracer into area V1 in the monkey can result in several isolated patches of label in area V2, which are 4 mm or more apart[58]. Similar patterns of patchy connections in area V2 have been reported for squirrels[30] and mice[59]. Thus, in many cases, the observations in rodents are equally compatible with the interpretation that, in these species, area V2 is formed by modules that differ in their pattern of connectivity.

Given their small eyes and the low cortical magnification factor in the extrastriate cortex of many rodents, it is likely that each neurone has to deal with a much larger 'slice' of the visual field than a V2 neurone in the cat or monkey. Thus, widespread convergence of projections can be expected from many V1 sites to each V2 cell, which results in a rather coarse anatomical topography. In this context, it should be remembered that rodents with developed vision, such as the squirrel, show considerable order in the V1–V2 anatomical projection[30]. To further complicate matters, there is controversy as to whether or not connections between area V1 and several of the callosal rings are independent of the topographical location of the injection sites in the rat. At least one study has reported a crude caudal–rostral topography in the lateral cortex, which mirrors the upper–lower quadrant segregation in area V1 (Ref. 24).

Concluding remarks

In summary, the anatomical tracing data on rodent areas, when taken in isolation, are at best ambiguous and might be misleading. In some animals, such as the hamster, a complex organization predicted by the anatomical pattern[60] is not supported by electrophysiological mapping (Fig. 5). Thus, even if there is a correlation between visuotopic areas and callosal rings in the rat[48], this cannot be extrapolated to other species without direct confirmation by electrophysiological recordings. Even if further study confirms that some of these rodent species have many areas where V2 is expected to be found, this would still not remove the main weakness of the complex extrastriate cortex hypothesis; namely, that many other rodents, and almost every other mammal, have a 'typical' area V2 that dominates the rostrolateral border of area V1.

Taking the present evidence at face value, it is far more parsimonious to propose that some rodents have added other new areas to the cortex that surrounds V1, than to propose that a large, elongated area V2, which dominates the cortex immediately lateral to V1, arose independently in all species. Nonetheless, we still believe that further physiological study of the cortex in murid rodents is necessary, which perhaps emphasizes the functional differences or similarities, or both, between the proposed areas around V1. The proposal that most rodents have multiple small areas in the cortex lateral to area V1 is based on a generous interpretation of the anatomical and physiological evidence, and it is possible that further studies will bring animals like the rat back to the mainstream of nocturnal mammals, as far as the organization of extrastriate cortex is concerned.

Acknowledgements
The authors thank Jack Pettigrew, Rowan Tweedale and Guy Elston for their helpful comments on the manuscript, and Martin Sereno for allowing them to use the results of electrophysiological recording experiments on the squirrel visual cortex. The authors' research is supported by research grants from the National Health and Medical Research Council of Australia, the National Institutes of Health (USA), Whitehall Foundation and The James S. McDonnell Foundation.

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PERSPECTIVES ON DISEASE

Recent advances in understanding the pathogenesis of Huntington's disease

P. Hemachandra Reddy, Maya Williams and Danilo A. Tagle

Huntington's disease (HD) is an autosomal, dominantly inherited neurodegenerative disorder that is characterized by abnormal involuntary movements (chorea), intellectual impairment and selective neuronal loss. The expansion of a polymorphic trinucleotide repeat (the sequence CAG that codes for glutamine) to a length that exceeds 40 repeat units in exon 1 of the gene, *HD*, correlates with the onset and progression of the disease. The protein encoded by *HD*, huntingtin, is normally localized in the cytoplasm, whereas the mutant protein is also found in the nucleus, suggesting that its translocation to this site is important for the pathogenesis of HD. Although several proteins that interact with huntingtin have been identified *in vitro*, the significance of these interactions with the mutant protein in the pathogenesis of HD has yet to be determined. Recent progress in the development of cellular and animal models for the disease have provided invaluable insights and resources for studying the disease mechanisms underlying HD, and will be useful for screening and evaluating possible therapeutic strategies.

Trends Neurosci. (1999) 22, 248–255

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RECENTLY, great attention has been paid to triple-repeat genetic disorders, particularly those caused by expansion of CAG trinucleotide repeats[1]. The number of diseases identified to be caused by $(CAG)_n$ (in general $n \geqslant 35$ repeats) continues to grow and a common mechanism could underlie these diseases. To date, eight such inherited neurological disorders have been identified to be caused by CAG-repeat expansion in their respective genes: Huntington's disease (*HD*)[2], dentatorubral pallidoluysian atrophy (*DRPLA*)[3], spinobulbar muscular atrophy[4] (*AR*), and spinocerebellar ataxia types 1, 2, 3, 6 and 7 [*SCA1*, *SCA2*, *SCA3* (or *MJD*), *SCA6* and *SCA7* (or *CACNA1A*)][5–9]. Most of the diseases caused by expanded CAG repeats, $(CAG)_n$, share common features, which include neurodegeneration, a dominant pattern of inheritance and genetic anticipation[10–13]. The CAG trinucleotide repeats in all these genes are found in the coding region and are translated

PII: S0166-2236(99)01415-0