The evolution of visual cortex: where is V2?

Marcello G.P. Rosa and Leah A. Krubitzer

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Viewpoint

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cats and simian primates, can have as many as 20 or 30 different cortical visual areas. 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). 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)5,6), the presence of a single and systematic visuotopic map, a well-defined pattern of subcortical afferents, 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)7–11, 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 groups1–3. 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. As discussed in detail elsewhere4,5, 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). From this
The relationships between mammalian species in which extrastriate cortex has been studied in detail are 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, every major branch of the mammalian tree has developed additional visual areas (not shown). Scale bars, 5 mm.

**The comparative evidence**

The major radiation of mammalian orders occurred quite early in eutherian evolution \(^1\) (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 \(^1,2,4,5\). The data so far suggest that this is indeed the case, as, even in animals such as the rat, the area which is homologous to V2 (see Refs 17,21) and presumably forms an 'extra-striate' area found in rodents. For example, in the one of the multiple areas that surround V1 (the lateral geniculate area, LG) has been identified as the ancestral form of area V2 (Refs 17,23), and presumably further studies of other rodent areas would eventually identify additional homologues.\(^2\)

The comparative evidence

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\(^2,13-19\), 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.\(^22\)

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 lateral geniculate area, LG) has been identified as the ancestral form of area V2 (Refs 17,23), and presumably further studies of other rodent areas would eventually identify additional homologues.\(^22\)

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extrastriate cortex in a marsupial, the quoll, 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. 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, and recently confirmed by detailed microelectrode maps 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 Sciuridae to be a conservative rodent group, which most closely reflects the ancestral rodents. Recent physiological studies 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 adjourn V1. Nonetheless, LM is still similar to area V2 both topographically and connectionally. In another rodent, the degu, receptive-field mapping (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 (Fig. 4D) and, according to some studies, the hamster. 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 has proposed the existence of four areas that surround V1 laterally. However, the same data can be interpreted much more parsimoniously as indicating the existence of a large V2-like area, much like that described by Tsao and Blakemore. 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, 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. Finally, the visuotopic map in area V2 (LM) of the rat appears to have no field discontinuities (similar to area V2 in the rabbit), but strongly emphasizes the upper-quadrant representation. Although these variations have been correlated with behavioural specializations in species with developed vision, 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
caused partially by technical factors. In addition, the appearance of modular systems in area V2 that are created by invasion of new afferent systems appears to have occurred independently in different lineages, which creates variability in the local precision of visuotopic maps, such as repetitive mapping. 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, primates, tree shrews or flying foxes. 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, would have more visual 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 encloses one or two cortical areas. 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 lateralization of the injection site.15,16 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 lower quadrant) would label the rostral rings. Thus, the widespread connectivity observed in many 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 vertical visual field, but whose modulatory peripheries extend to the opposite hemifield.46 Corticocortical connections are also typically 'patchy'.17,60 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.46 Similar patterns of patchy connections in area V2 have been reported for squirrels and mice.47,48 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.46 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 is not supported by electrophysiological mapping (Fig. 5). Thus, even if there is a correlation between visuotopic areas and callosal rings in the rat,45 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 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. Notwithstanding the data, one may believe that further physiological study of the cortex in modern 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.

Selected references

12 Roche-Miranda, C.J. et al. (1976) Brain Res. 104, 197–219
15 Rosa, M.G.P. J. Comp. Neurol. (in press)

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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) in the huntingtin gene results in the formation of an expanded CAG repeat genetic disorders, particularly those caused by expansion of CAG trinucleotide repeats. The number of diseases identified to be caused by CAG-repeat expansion continues to grow and a comprehensive list of diseases includes Huntington’s disease (HD), dentatorubral pallidoluysian atrophy (DRPLA), spinobulbar muscular atrophy (SBMA), and spinocerebellar ataxia types 1, 2, 3, 6 and 7 (SCA1, SCA2, SCA3, MJD, SCA6 and SCA7 or CAGNCA).

27 Espíndola, S.G. and Thomas, H.C. (1983) Brain Res. 272, 137–144
43 Kaas, J.H. et al. (1972) Brain Res. 42, 491–496