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SPECIAL COLLECTION

Controversial Issues in Visual Cortex Mapping

INTRODUCTION

Controversial issues in visual cortex mapping: Extrastriate cortex between areas V2 and MT in human and nonhuman primates

The visual cerebral cortex of primates includes a mosaic of anatomically and functionally distinct areas processing visual information. While there is universal agreement about the location, boundaries, and topographic organization of the areas at the earliest stages of visual processing in many primate species, i.e., the primary (V1), secondary (V2), and middle temporal (MT) visual areas, there is still ongoing debate regarding the exact parcellation of cortex located between areas V2 and MT. Several parcellation schemes have been proposed for extrastriate cortex even within the same species. With the exception of V1, V2, and MT, these schemes differ in areal borders, areal location, neighboring relations, number of areas, and nomenclature. As a result, most anatomical and physiological studies of these areas have been carried out following one or another scheme, in the absence of any general agreement. This situation is inevitably hampering our understanding of the function and evolution of these visual areas. The goal of this special issue is to provide a critical review and evaluation of the literature on the most controversial issues regarding the parcellation of extrastriate cortex, to identify the main reasons for the controversy, and to suggest critical future experimental approaches that could lead to a consensus about the anatomical and functional identity of these areas.

Visual cortical areas have traditionally been defined on the basis of multiple converging criteria, including visuotopic organization, architectonics, pattern of corticocortical connections, and receptive field properties. One major reason for the lack of consensus on the parcellation of extrastriate cortex is that for most areas these converging criteria have been obtained from different animals and even different primate species. This is because limitations inherent to the experimental approaches have made it impossible to characterize all of these aspects of cortical organization within the same animals. Moreover, due to technical limitations and time constraints, it has also been difficult to obtain extensive electrophysiological or anatomical mapping data from the same animal, especially in species with gyrencephalic brains, where most of these areas are located within difficult-to-access sulci. Therefore, the different cortical parcellation schemes that have been proposed over the years represent best attempts to summarize the sparse mapping data obtained from different animals, using a variety of different techniques, and often from different species. It is important to emphasize that most of the published data are consistent with several alternative parcellation schemes, albeit they have typically been presented as supportive of one or other scheme. The articles in this special issue attempt to highlight the problems with past studies, and propose new ways to overcome these problems.

The problem of the third visual complex

The first section of this special issue deals with the controversy regarding the parcellation of the third visual complex, i.e., the strip of cortex located immediately rostral to area V2. There has been a long-standing debate as to whether this cortical region comprises a single area V3, or multiple smaller areas. The history of this debate in the nonhuman primate is reviewed in the articles by Angelucci & Rosa, Kaas et al., Gattass et al., Arcaro & Kastner, and Gamberini et al. [the latter limited to the medial portion of the parieto-occipital (PO) cortex]. Angelucci & Rosa argue for the need of a more rigorous model-testing approach in the experimental design of future studies than has been used in past studies. By systematically comparing specific predictions of each proposed scheme of cortical parcellation with the available data (primarily from New World primates), they conclude that only three of these models can accommodate the breadth of the experimental evidence. This does not necessarily imply that these models are fully correct as currently formulated, rather that there are no published data that are inconsistent with these models. What is common to these three models is that none of them views the third visual complex as comprising only a single, elongated, and continuous area V3. The authors argue that distinguishing between these three models, as well as refining them, will require more extensive physiological and connectional mapping data of the full mediolateral extent of the third tier cortex in the same animal, and data from a larger number of animals than currently available (especially in macaques and humans).

One major issue in the debate over the organization of the third visual complex has been whether its dorsal aspect contains a representation of the upper visual quadrant, a finding that would be inconsistent with the proposal of a single and continuous dorsal V3 bordering dorsal V2. Major proponents of this idea have most recently been Lyon and Kaas (2001, 2002*a*,*b*,*c*). In this issue, Kaas et al. re-evaluate the experimental evidence for an upper visual field representation bordering dorsal V2, and find it to be, to some extent, valid, at least in New World primates. They, thus, put forward a new proposal, according to which the dorsal half of area V3 has a gap in the middle, containing a representation of the upper visual quadrant belonging to a different visual area. This new scheme strongly resembles the model previously

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proposed by Gattass et al. (1988) for the macaque, and one of the models proposed by Rosa et al. (2005) for the marmoset monkey; this is also similar to one of three models identified in the article by Angelucci & Rosa as still viable (see above). Gattass et al. in this special issue continue to argue in favor of such a model, or slight variants of it, in gyrencephalic monkeys (macaques and capuchin). These authors identify as possible causes for the controversy regarding the parcellation of the third tier cortex the variability among individuals of the same species as well as interspecies differences. Not all macaques show a continuous representation of the vertical meridian at the border of dorsal V3, and V3 can be broken into multiple islands in some, but not other macaques. Moreover, these authors argue that gyrencephalic monkeys differ in cortical organization from lissencephalic monkeys, and hypothesize that the transition to lissencephaly in evolution may have triggered a reorganization of the third visual complex in the small New World primates. A similar argument is presented in the article by Angelucci & Rosa, who hypothesize that there exists a homologous, but not identical, configuration of the third visual complex in New World and Old World primates and humans; these authors suggest that differences in configuration could be understood in a developmental/evolutionary context, whereby later-developing areas become relatively larger in species with larger brains.

The original research article by Sereno et al. represents one of the first attempts to retinotopically map within the same animal large expanses of dorsal extrastriate cortex between V2 and MT, combined with an analysis of cortical architectonics, in a New World primate. Using dense electrophysiological retinotopic mapping, and map analysis using the visual field sign technique developed by Sereno et al. (1994), these authors demonstrate the existence of multiple small areas in the dorsal aspect of the third visual complex, including a representation of the upper visual quadrant directly bordering dorsal V2. These authors also suggest a clever experimental approach that may help resolve the controversy on the organization of the third visual complex in New World primates.

The original research article by Jeffs et al. tests the model proposed by Kaas et al. in this special issue [and previously by Rosa et al. (2005); see above], i.e., that dorsal V3 has a gap in the middle, representing the upper visual quadrant. A quantitative analysis of the inter-areal projections to the cortical territory immediately surrounding this "gap", in a New World primate, suggests that dorsal V3 only occupies the territory lateral to the gap, and that a different visual area (the dorsomedial area–DM) occupies the gap and the territory just medial to it. These results are consistent with the model favored by Rosa and colleagues in New World primates, according to which the dorsal aspect of the third visual complex consists of at least two areas, V3 and DM.

Rosa and colleagues have suggested that area DM is the homologue of macaque and human area V6/PO. There has been debate regarding the identity and extent of this area in macaque and humans. The history of this debate is reviewed in the articles by Gamberini et al, Gattass et al. and Pitzalis et al. Gamberini et al. identify as major reasons for the debate the difficult-to-access location of this cortical territory (within deep sulci near the midline of the hemispheres), and inter-individual variability in its configuration. Based on an evaluation of the literature, encompassing architectural, connectional, and functional data, these authors propose that area V6 in macaque is a visual motion area emphasizing the visual periphery, which occupies the fundus of the parieto-occipital sulcus and the ventralmost part of its anterior wall; the rest of the anterior wall is instead occupied by two distinct visuomotor areas, V6Av and V6Ad. These authors propose that V6 and V6Av together encompass the territory previously described as area PO (Colby et al., 1988), but, while PO only represents visual field eccentricities greater than 20–30 deg, V6 extends over a larger territory, which includes a representation of the central 20 deg of the visual field (albeit still over-representing the visual field periphery). These authors further identify outstanding issues regarding the visuotopic organization of V6 and its relationship with neighboring areas that will need to be addressed by future studies.

The article by Pitzalis et al. extends this line of studies to humans. Similarly to macaque, there are two architectonically distinct areas in the human dorsomedial occipital cortex, V6, which processes wide-field visual motion, and V6A, which combines visual and somatomotor information during visually-guided reaching. This article discusses the complexities of cross-species mapping. Because of the growth of the laterally located angular gyrus in humans, many human visual areas have been displaced toward the medial surface, inferiorly (MT), posteriorly (V1), or superiorly (lateral intraparietal area, LIP). But human V6 almost reaches the superior midline convexity in humans, in contrast to its more inferior position in macaques (because of V1 overflowing the banks of the calcarine as it moved medially). This study subdivides, in humans (as in macaques), V6A into a visually responsive V6Av and a reach-related V6Ad, and combines information from nonhuman neurophysiology and human functional magnetic resonance imaging (fMRI) and lesion studies.

In contrast, Gattass et al. argue against the existence of an extended area V6 encompassing the original area PO, in the macaque, but favor the original proposal that PO is a distinct visual area representing exclusively the far visual periphery, noting that some receptive fields in this area are, however, large enough to encompass the foveal representation. These authors' point of view is largely based on anatomical observations demonstrating connections from areas V2 and V4 to the PO territory, which arise exclusively from the peripheral representation of the visual field in these areas.

The problem of area V4

The second part of this special issue deals with the controversy regarding the parcellation of the cortical region usually referred to as V4 in humans. Winawer & Witthoft summarize the controversies surrounding the definition of V4 in the human. Although V4 was initially identified in the macaque monkey by Zeki based on response to wavelength selectivity (see Roe et al., 2012, for a review), attempts to define V4 in human cortex have given rise to different views. These views include: (1) a V4v representing only the dorsal visual field bordered by a color area termed V8, (2) human area V4, termed hV4, containing a full representation of the contralateral hemifield, bordered by ventral occipital areas VO1 and VO2 anterior to hV4, (3) a V4 similar to that in the macaque, split into V4v and V4d, and (4) another model which places the lateral occipital areas 1 (LO1) and 2 (LO2) between dorsal V3 and human MT, in conflict with the V4d proposal. Thus there are fundamental differences in views regarding whether V4 represents only a quadrant or a hemifield, what defines the boundaries of V4, what areas lie adjacent to V4, and the criteria used to define V4 (such as the spatial, temporal, and spectral response). The authors point out possible factors that may have contributed to the controversy, such as low signal reliability in these extrastriate regions, inter-individual differences, and the presence of the transverse sinus near V4. Thus, despite the best imaging methodologies and the best minds, controversy remains.

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The problem of area V4t/MTc

The article by Tootell et al. discusses evidence in humans for the existence of a distinctive area in primates that directly surrounds MT. This region, or more precisely part of it, was originally named area DL in owl monkey, and later renamed DLa, then V4t, and then MTc. Given that its expected width is comparable to a single standard fMRI voxel, it has been difficult to definitively identify these areas in humans by retinotopy. Tootell et al. instead provide a clever argument, based on overlap of functional localizers, which is itself based on the expected physiological properties of DLa/V4t/MTc.

Further thoughts and new perspectives

The special issue concludes with two articles proposing a new perspective, and a provocative article by Olman on how fMRI can best help understanding cortical organization.

Arcaro & Kastner, propose a new way to look at the problem of V3 and V4. These authors argue that in both macaque and humans, large-scale fMRI studies have demonstrated the existence of a larger supra-areal visuotopic organization encompassing areas V1, V2, V3, and V4, and that this idea is also consistent with the connectivity patterns across these areas. The authors, therefore, propose that rather than viewing areas V3 and V4 as distinct visual areas, one may view these areas as part of a larger supra-areal cluster working in concert toward a common computational function, namely that of partitioning information it receives from the visual periphery into parallel channels, and distributing this information to higher-order cortex.

Melcher & Morrone highlight the question of how a steady view of the world is established despite the constant barrage of changing conditions, such as eye movements, self motion, changes in attention, changes in behavioral goals, and external contextual changes in the environment. The authors refer to this as 'nonretinotopic visual processing' or 'spatiotopic processing', a computation that (somehow) produces a visual map that is spatially and situationally invariant. Beginning with compelling examples of common spatiotopic experience (e.g., after an eye movement objects are perceived in the same spatial-world coordinates despite new retinotopic coordinates), this article underscores the surprising nonretinotopic nature of visual receptive fields. Drawing from both nonhuman primate and human neuroimaging studies, they describe 'gain fields' in which neuronal response is modulated by eye position, the remarkable remapping of receptive fields to 'future' locations to which eye movements are made, as well as dramatic changes in visual maps depending on conditions such as passive fixation or attention. Thus, in contrast to traditional retinotopic concepts, this article emphasizes the importance and ubiquity of nonretinotopic, dynamic visual maps. How such nonretinotopic maps are created and dynamically maintained, without losing access to detailed spatially localized information, remains a mystery.

The perspective article by Olman explores combining data from the techniques of single unit recording in nonhuman primates and fMRI primarily in humans, which probe (two different!) functioning brains at different levels of organization. In particular, she argues that if a signal modulation shows up in fMRI, it is hard to determine whether the basis for it was computed locally or somewhere else. She notes, however, that single unit studies can have a similar problem in determining whether activity was modulated by local computation or top-down synaptic influences. Her firm conclusion, however, is that higher resolution, bottom-up information, and models constructed from it at the level of individual neural responses are absolutely critical for interpreting fMRI results. It is worth pointing out that this strategy also relies on finding homologous areas, and furthermore, on the assumption that their functional specialization has not evolved differently.

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References

Colby, C.L., Gattass, R., Olson, C.R. & Gross, C.G. (1988). Topographical organization of cortical afferents to extrastriate visual area PO in the macaque: A dual tracer study. *The Journal of Comparative Neurology* **269**, 392–413.

Gattass, R., Sousa, A.P. & Gross, C.G. (1988). Visuotopic organization and extent of V3 and V4 of the macaque. *The Journal of Neuroscience* **8**, 1831–1845.

Lyon, D.C. & Kaas, J.H. (2001). Connectional and architectonic evidence for dorsal and ventral V3, and dorsomedial area in marmoset monkeys. *The Journal of Neuroscience* **21**, 249–261.

Lyon, D.C. & Kaas, J.H. (2002a). Connectional evidence for dorsal and ventral V3, and other extrastriate areas in the prosimian primate, *Galago garnetti*. *Brain, Behavior and Evolution* **59**, 114–129.

Lyon, D.C. & Kaas, J.H. (2002b). Evidence for a modified V3 with dorsal and ventral halves in macaque monkeys. *Neuron* **33**, 453–461.

Lyon, D.C. & Kaas, J.H. (2002c). Evidence from V1 connections for both dorsal and ventral subdivisions of V3 in three species of New World monkeys. *The Journal of Comparative Neurology* **449**, 281–297.

Roe, A.W., Chelazzi, L., Connor, C.E., Conway, B.R., Fujita, I., Gallant, J.L., Lu, H. & Vanduffel, W. (2012). Toward a unified theory of visual area V4. *Neuron* **74**, 12–29.

Rosa, M.G., Palmer, S.M., Gamberini, M., Tweedale, R., Pinon, M.C. & Bourne, J.A. (2005). Resolving the organization of the new world monkey third visual complex: The dorsal extrastriate cortex of the marmoset (*Callithrix jacchus*). *The Journal of Comparative Neurology* **483**, 164–191.

Sereno, M.I., McDonald, C.T. & Allman, J.M. (1994). Analysis of retinotopic maps in extrastriate cortex. *Cerebral Cortex* **4**, 601–620.

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