Feature Review

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Topographic organization in the brain: searching for general principles

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The neurons comprising many cortical areas have long been known to be arranged topographically such that nearby neurons have receptive fields at nearby locations in the world. Although this type of organization may be universal in primary sensory and motor cortex, in this review we demonstrate that associative cortical areas may not represent the external world in a complete and continuous fashion. After reviewing evidence for novel principles of topographic organization in macaque lateral intraparietal area (LIP) – one of the most-studied associative areas in the parietal cortex – we explore the implications of these new principles for brain function.

Introduction

In many parts of the mammalian brain, spatially adjacent stimuli on sensory receptor surfaces are represented in adjacent positions in the cortex, a pattern known as topographic organization. Topographic organization provides invaluable information about brain function and structure. For example, some of the earliest functional characterizations of human primary visual cortex (V1) were based on correlations between visual field deficits and focal lesions in V1 [1–3]. Although crude by today's standards, these early clinical observations nevertheless helped to confirm some basic facts about V1. First, V1 organization reproduces the spatial organization of the retina (known as retinotopic organization) and, by extension, the visual field (known as visuotopic organization). Second, this part of the cortex is clearly involved in visual processing. More recently, the presence of topographic organization has been used to delineate boundaries between cortical areas, with V1 again providing a paradigmatic example. V1 was originally defined by the prominent stripe of myelin in its layer IV, known as the stria of Gennari, which marks the massive input from the lateral geniculate nucleus (LGN) [4,5]. Subsequent neurophysiological studies revealed that this prominent anatomical feature matches the spatial extent of the retinotopic map, reinforcing the use of retinotopy to delineate cortical areas [6]. This matching of retinotopic maps and anatomical boundaries extends to other visual areas [7–9] and the association of the boundaries of topographic maps with those derived from anatomy has also been noted in other sensory and motor areas [10–12].

These observations have helped to establish two fundamental principles about the relationships between topographic organization, anatomical structure, and function in the brain. The first principle is that topographic maps represent their relevant sensory or motor dimensions continuously and completely. The second principle is that topographic and anatomical boundaries align with one another. These principles together form what we term, for simplicity, the standard model of topographic organization (see also [9,13]).

Topography in associative cortex?

Although usually not stated explicitly, these basic principles operate as powerful heuristics for understanding brain organization and function. Recently, these principles have guided investigations in both human and nonhuman primates into the organization of higher-order cortical areas in frontoparietal cortex [14–18]. For convenience, we use the term 'associative cortex' for these areas, although they are likely to be involved in a much broader range of functional capacities than mere 'association', including transforming sensory information into motor plans [19,20]. Closer scrutiny reveals that these principles may not hold in these areas. In this review, we explore the extent to which these organizational principles generalize (or fail to generalize) beyond sensory and motor cortex to other associative areas of the brain, including the parietal cortex, by examining the topographic organization of macaque LIP, a well-established associative 'hub' in the visual processing network that has been extensively studied using anatomical, electrophysiological, and neuroimaging methods [21] (for a related discussion, see [22]). We discuss the implications of findings in LIP for understanding the organization and function of other associative cortical areas.

The standard model of topographic organization

The principles outlined

The first principle of the standard model – that topographic maps are largely continuous and complete – can be seen throughout the early visual sensory areas (Figure 1). For example, the cells in V1, which have individual receptive

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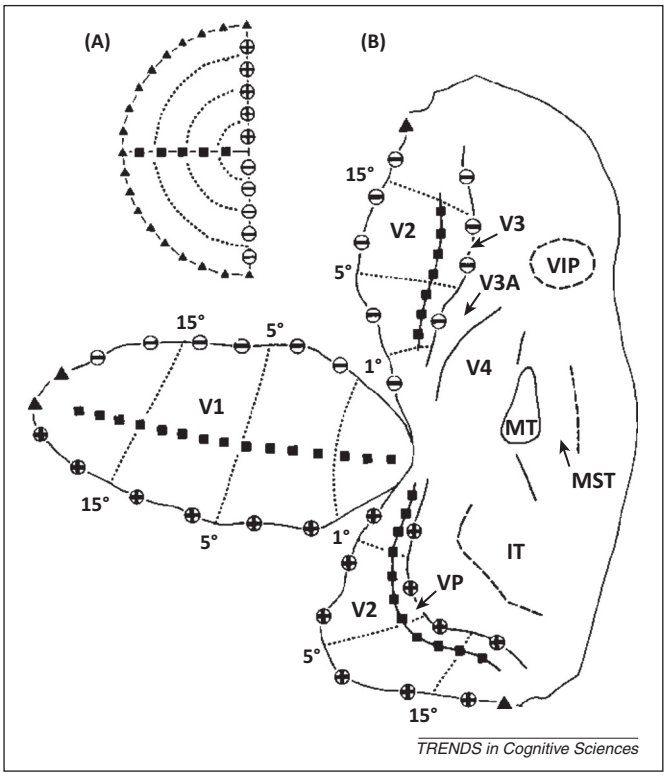

Figure 1. Retinotopic organization of macaque visual cortex. **(A)** The legend demonstrates the organization of the visual field in polar coordinates. The dotted lines delineate eccentricity contours, with the dark triangles marking the visual periphery. The polar-angle coordinates are bounded by meridians that are represented by dark squares (horizontal meridian), + symbols (upper field vertical meridian), and – symbols (lower field vertical meridian). The eccentricity coordinates are bounded by triangles and smaller eccentricities are represented by dashed lines. **(B)** Flattened schematic representation of visual cortical areas, with simulated coordinates from (A) mapped onto each visual area. Note that the represented visual field covers the entirety of each of the visual areas and that all portions of each visual hemifield are represented in each visual area, even if the area (such as the secondary visual cortex (V2) is separated into discontinuous parts. Reproduced from [54].

fields each of which covers a relatively small portion of the visual field, are arranged such that cells with adjacent receptive fields occupy adjacent positions along the cortical sheet, thus representing the visual field in a continuous fashion [23]. This locally continuous representation may be interrupted, for example, when only the contralateral half or upper/lower portion of the visual field is mapped (common in early visual and somatotopic areas). A complete representation of visual space emerges only when these partial maps are combined across hemispheres or different sensory areas.

The second principle of the standard model is that one map completely fills each cortical area, so that topographic map boundaries coincide with areal boundaries. This principle is based on repeated observations in multiple sensory and motor cortical areas that topographic boundaries closely correspond to boundaries defined by anatomical criteria (including cytoarchitecture, myeloarchitecture, and connectivity patterns) and functional criteria such as tuning properties [13,21,24,25]. A logical consequence of this principle is that any individual anatomically or functionally defined area will contain no more than a single representation of each point in the visual field or other sensory or motor parameter and, by extension, no more than one distinct topographic map of the same portion of the relevant parameter space. This correspondence principle plays an especially important role in human brain-mapping studies, where it is difficult to assess the boundaries between cortical areas in humans using anatomical methods due to their invasive nature. Consequently, establishing topography in the intact human brain using blood oxygen level-dependent functional MRI (BOLD-fMRI) and other neuroimaging approaches has become the dominant means by which areal boundaries are identified in humans and often serves as a proxy for these invasive methods [9,14,26–37].

Do these principles apply to associative areas?

It is important to recognize that the standard model is based primarily on data from early sensory areas obtained from nonhuman species such as the macaque. However, topographic organization of associative areas in macaques may be more complex, with evidence of areas that are only partially topographically organized (e.g., an eccentricity but no polar-angle map has been reported in the frontal eye fields [FEF] [38,39]) or with very coarse topography that is inconsistent across studies (e.g., LIP [40,41]). Area LIP is ideal for assessing whether the standard primate model of visual topography can be applied to higher-order areas. Its anatomy and connectivity are well understood (Box 1). The functional role of LIP has also been intensely investigated (Box 2). Notably, the anatomically defined boundaries of LIP do not always appear to be well aligned with boundaries delimited by functional role. For example, numerous single-unit recording studies characterize LIP based on a finding of memory activity during a delayed saccade task (e.g., [19,42–45]). These studies consistently report cells extending 3–6 mm along the lateral bank of the intraparietal sulcus (IPS). Yet anatomical LIP extends for approximately 20 mm along this bank [46]. One might therefore look at topography to clarify the functional organization of LIP and better understand how it relates to the underlying anatomy and connectivity. Two single-unit studies previously reported coarse topography in LIP [40,41] and recently there have been two fMRI and one deoxyglucose study also reporting topographic organization but with different features [47–49]. By looking carefully at the evidence for topography that has emerged from these studies and comparing it with the known anatomy and connectivity of LIP, we now report that the standard model of topographic organization (developed largely based on early sensory areas) stands in important need of revision to apply to higher-order cortical areas.

Topographic organization of LIP

Current evidence from single-unit and neuroimaging studies

The topographic organization of LIP has been explicitly targeted in numerous investigations over the past several decades. Using single-unit recordings, Blatt *et al.* [41] and Ben Hamed *et al.* [40] each found relatively weak evidence for coarse retinotopic maps in LIP. However, the patterns of topography described in the two studies appear to show no correspondence. Moreover, several hundred single-unit recording studies performed in LIP, some involving

Box 1. Anatomy of LIP

Area LIP is located on the lateral bank of the IPS in the parietal cortex. LIP extends from just below the shoulder to the fundus of the IPS and stretches posteriorly/caudally nearly to the intersection of the parietal–occipital sulcus (POS) and anteriorly/rostrally most of the length of the IPS to its border with the anterior intraparietal area (AIP). It can be subdivided into two anatomically distinct areas, LIPv and LIPd, with the border between the two running almost parallel to the IPS [46,83] (Figure IA–C, but see [49,84]). LIPv can be distinguished from LIPd by its increased density of myelination as well as architectonic differences in several of its cortical layers [46,83,85,86] (Figure ID). Connectivity studies indicate that LIP gets much of its input from extrastriate visual areas [including V4 and the middle temporal (MT) area] [63,64,87–89]. It is also reciprocally connected to cortical and subcortical structures involved in the control of eye movements and attention, including FEF and Brodmann area 46, with anterior and posterior LIP being reciprocally connected to FEF ventral/lateral and dorsal/medial, respectively [21,64,87,88], and subcortically to the superior colliculus, the caudate, and the pulvinar nucleus of the thalamus [88,90,91].

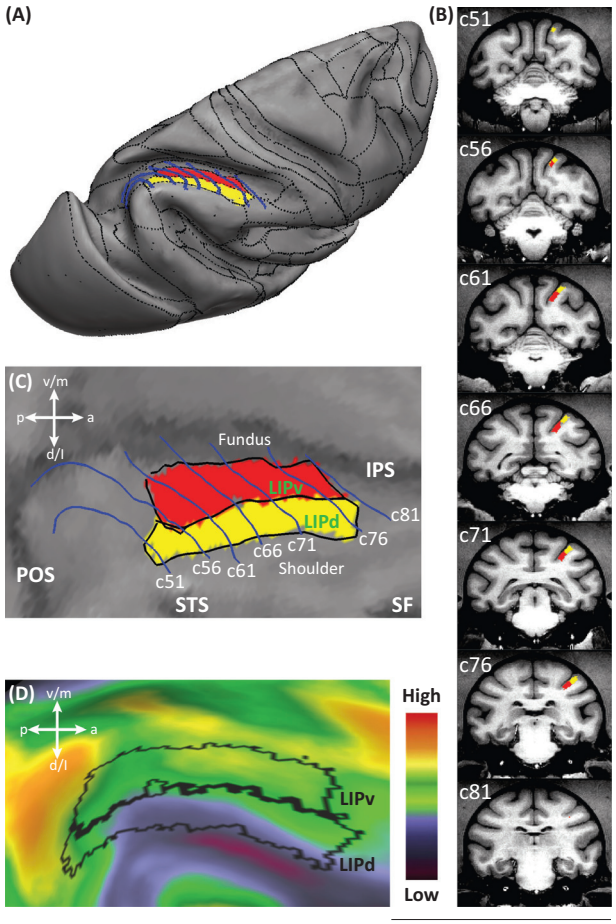

Figure I. Anatomy of the lateral intraparietal area (LIP). **(A)** Dorsal/posterior/lateral view of the inflated right hemisphere. **(B)** Coronal sections through ventral LIP (LIPv) (red) and dorsal LIP (LIPd) (yellow). **(C)** Flattened right hemisphere with tracings (blue) of the lateral bank of the intraparietal sulcus (IPS) from each of the slices in (B). **(D)** LIPv and LIPd (black outlines) can be distinguished by their myelin content. (A–C) Adapted from [92]; LIPv and LIPd reproduced from [46]. (D) Adapted from [86].

hundreds of individual neurons and many focused on their spatial receptive field properties (e.g., [50,51]), have implicitly tested for topography and almost none report even a trend toward global topographic organization (see [52] for

Box 2. Functions of LIP

Early electrophysiological studies of LIP revealed neurons involved in both oculomotor and attentional control [93,94]. The definition of LIP used in most recording studies is a region of neurons on the lateral bank of the IPS with sustained responses to visual stimuli during a remembered saccade task [95]. Functionally defined LIP neurons respond to both visual stimuli and saccadic eye movements and have medium-to-large visual receptive fields (5–30° diameter) mostly distributed in the contralateral visual hemifield [40,50]. However, LIP neurons are not just visually driven. They also demonstrate sustained activity during fixation in an otherwise dark room, provided that subjects are either covertly attending to the receptive field of the neuron or planning an eye movement into the receptive field [93,95]. Lesions to this area produce corresponding deficits in both attention and oculomotor planning [69,96–98]. Controversy persists about the functional role of LIP. Prominent proposals include the idea that it instantiates a 'salience map', according to which LIP neurons represent locations of interest for both attentional control and the planning of eye movements [66]. Others have suggested that LIP subserves oculomotor planning [99], object categorization [100], integrating sensory evidence for making decisions [101], or representing the reward value associated with making a movement decision [102].

Given the uncertainty surrounding LIP function, one interesting yet neglected possibility is that these different functional hypotheses are not mutually exclusive. The above-listed studies implicating LIP in numerous functions often record from neurons with oculomotor delay activity, implying that many of these functions are colocalized in the same neurons [100,101,103]. However, several recent studies provide evidence that different populations of LIP neurons may be involved in the control of attention and eye movements [68,69,104]. A major challenge in assessing these different possibilities arises from the fact that recording locations across these single-unit studies have not been plotted into a common frame. Consequently, it remains difficult to know whether different functions involved the same set of neurons, intermingled but differing neurons, or neurons clustered by function.

one possible exception). From these results, the consensus view among neurophysiologists has been that macaque LIP does not show anything similar to the topography found in primary visual cortex or other extrastriate visual areas (M.E. Goldberg, W.T. Newsome, J.D. Crawford, and L.H. Snyder, personal communications).

Recently, however, neuroimaging studies have reported evidence for topography [47–49]. Interestingly, this more recent evidence does not strictly follow the standard model of topographic organization that has been observed in sensory and motor areas. We compare results across five recent studies and review these deviations from the standard model below.

Aligning data for cross-study comparison

As outlined above, the first principle of topographic organization holds that topographically organized brain areas contain largely continuous maps of the relevant sensory modality. Based on this principle, we might therefore expect LIP to contain an orderly and continuous map of the contralateral hemifield with eccentricity and polar angle represented along orthogonal axes. To explore this possibility, we first projected data from all of the studies into a common reference frame (Figure 2). To accomplish this we projected the data directly to the F99 atlas or approximated its projection based on anatomical features such as the IPS fundus and shoulder (see Figure 2 legend for more details). As a result, the accuracy of the matches varies from extremely precise to approximate. Figure 2

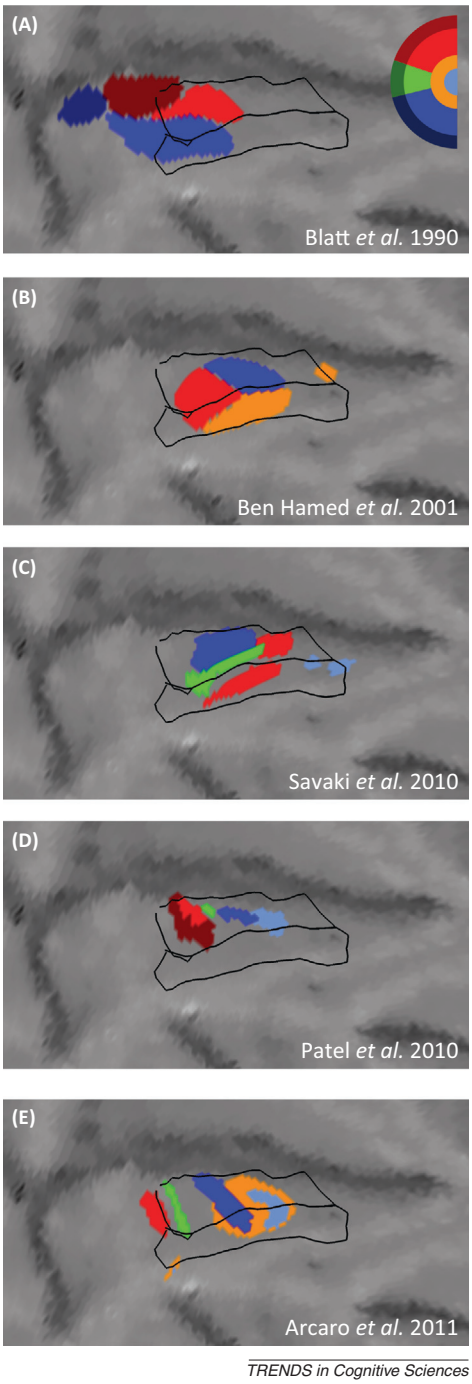

Figure 2. Topographic organization of the lateral intraparietal area (LIP) from five studies. Data transferred to flattened segments of the F99 macaque atlas. For Patel *et al.* the data were directly projected from the F6 atlas used in the study to the F99 surface. In the two other imaging studies **(C–E)**, the data alignment was approximated by matching anatomical markers such as the fundus of the intraparietal sulcus (IPS) with the F99 surface. In the single-unit recording studies **(A,B)**, alignment was achieved by matching the illustrated coronal sections to the coronal sections of the F99 macaque atlas and these aligned slices were used to anchor the projections to the F99 surface. Because of potential scale differences between the two species (and between fixed versus *in vivo* brains), we relied more heavily on anatomical features than stereotaxic coordinates. Primary colors represent stimulation in the upper (red) or lower (blue) visual fields or at the horizontal meridian (green). Light blue represents stimulation at fixation or at the fovea, orange represents parafovea (<7° eccentricity), lighter polar-angle colors 7–15° eccentricity, and darker colors >15° eccentricity. Ventral LIP (LIPv) and dorsal LIP (LIPd) borders reproduced from [46].

already reveals several surprising aspects of the topographic organization of LIP.

Polar-angle maps

All five topographic mapping studies report the presence of a polar-angle map in posterior ventral LIP (LIPv). In particular, stimuli presented in the contralateral upper visual field and lower visual field and along the horizontal meridian elicit the strongest responses in spatially segregated but adjacent populations of LIP neurons. The approximate layout of the polar angle map is congruent across three of the five studies [40,47,48]. In these three studies, the upper and lower contralateral peripheral visual fields are represented at the posterior end and middle of LIPv, respectively, so that the upper to lower field axis runs posterior to anterior (Figure 2B,D,E). The other two studies [41,49] also support a map of polar angle topography, but the polarity of the map is reversed compared to the other three studies (Figure 2A,C).

Foveal representation

In striking contrast to the clear evidence for a continuous map of polar angle, the evidence for a continuous map of eccentricity is poor. Three of the five studies – Ben Hamed *et al.*, Arcaro *et al.*, and Blatt *et al.* – argue for an eccentricity axis running dorsal–ventral, perpendicular to the polar-angle axis, with the fovea represented dorsally [40,41,48]. If correct, LIP would then contain a full retinotopic map of the contralateral hemifield, following the standard model of topographic organization. However, neither Blatt *et al.* [41] nor Ben Hamed *et al.* [40,53] found a systematic ordering of neurons with respect to the eccentricity of their receptive fields, as has been described in single-unit studies of visual cortex [54], and Arcaro *et al.* [48] found that the location and size of the dorsal foveal representation varied across animals and even across hemispheres within a single animal. Moreover, Patel *et al.* [47] found no evidence of an eccentricity axis and Savaki *et al.* [49] reported evidence of an axis with the opposite orientation to those described above.

A more consistent finding is the existence of a foveal representation in anterior LIP. In Figure 2, four of the five studies find foveal/fixation (light blue) and parafoveal (orange) representations that lie anterior to the peripheral representation, either entirely within LIPv or straddling the border between LIPv and dorsal LIP (LIPd). The fifth study probably did not find this representation because they did not record far enough anteriorly [41]. This representation is almost certainly not one end of an eccentricity axis; if it were, the polar-angle and eccentricity axes would lie nearly parallel to one another. A more likely explanation is that this anterior foveal representation is separate from the posterior polar-angle map, with no continuous map connecting the two. Indeed, Arcaro *et al.* show that when eccentricities from the fovea out to the periphery are sequentially stimulated, the foveal representation does not appear to be continuous with the more posterior peripheral field map [48] (Figure 2E). Consequently, the current weight of evidence suggests that LIP contains a separate foveal representation that is anterior to and discontinuous

from a posterior polar-angle map. As for a dorsal–ventral eccentricity axis, the evidence for this remains weak. An eccentricity axis may be present but variable from hemisphere to hemisphere [48] or the posterior map may, like the topographic map reported in FEF, reflect only a single dimension [38,39].

LIP versus V1

In summary, to the extent that it exists, the topographic organization of macaque LIP does not match the clear organization found in early visual areas such as V1. In V1, polar angle and eccentricity are mapped out along perpendicular axes [7,9]. In LIP, however, the evidence for an eccentricity axis perpendicular to the polar-angle axis is weak, whereas evidence of a discontinuous foveal representation is much stronger. LIP therefore appears to violate the first principle of the standard model of topography because it fails to have the requisite continuous topographic organization.

LIP also appears to violate the second principle of the standard model, according to which each cortical area contains one and only one map and this map completely fills that area such that map and areal boundaries coincide. The edges of the topographic map in LIP do not appear to align with any areal boundaries, but instead enclose only a portion of LIPv and may even cross over into the territory of LIPd. The lower edge of the map does consistently align with the border between LIPv and the ventral intraparietal area (VIP) across the studies surveyed above. Yet critically, the upper edge aligns with LIPv/LIPd border in at most three of the five studies and in no case do the anterior and posterior edges of the map align with anterior and posterior LIP borders. Furthermore, although three of the five studies find a polar-angle map with a similar orientation, the other two studies find a polar-angle map with nearly the opposite orientation, raising the possibility of multiple polar angle maps within LIP. The implications of these findings are discussed below.

Finally, it is worth emphasizing that the absence of a topographic map in no way implies an absence of a complete representation of visual space. Representations do not need to be topographically mapped. Individual cells can have spatially selective responses without being topographically organized across the cortical surface.

Discussion: interpreting findings about LIP topography

Single-unit studies

The literature before the publication of the imaging studies indicates that LIP topography is weak. Ben Hamed *et al.* state that 'LIP does not appear to contain a continuous and orderly retinotopic organization' (p. 142, [40]) and instead emphasize a patchy clustering of cells with similar properties. This evidence for topography is weakened further by the fact that the coarse topographies that the two electrophysiological studies describe are exactly opposite in polarity and therefore contradictory. Due to the language in the Blatt *et al.* abstract, this point of discordance was not widely appreciated {Blatt *et al.* report that the 'upper field representation was concentrated in the rostral [anterior] two-thirds of LIP, while [the] lower field representation was restricted to the caudal [posterior] two-thirds of LIP' (p. 430, [41]); however, their abstract describes the reverse polarity}.

Neuroimaging studies

Against this default negative view about LIP topography, the three recent primate neuroimaging studies using different methods all demonstrate clear topographic mapping in LIP [47–49]. Savaki *et al.* [49] imaged the accumulation of tritiated deoxyglucose in post-mortem brain slices from animals who performed multiple back-and-forth saccades. Patel *et al.* [47] used BOLD-fMRI to image responses while animals performed a difficult peripheral attention task. Arcaro *et al.* [48] also used BOLD-fMRI, but employed a markedly different task in which a pie-shaped flashing checkerboard was swept in a circle while animals fixated central crosshairs. Despite the difference in methods and discrepancies in the eccentricity axis detailed above, there were clear similarities across all three studies. In each study, the deep and posterior portion of LIP (roughly corresponding to the posterior portion of LIPv) mapped the periphery, whereas a point midway to anterior LIP (close to LIPv/LIPd border) mapped stimuli placed at or near fixation.

At first glance, it appears that the single-unit and imaging studies are inconsistent within and between modalities; however, we believe that these discrepancies can be explained. Below we briefly highlight the three major discrepancies regarding topographic organization in LIP that stand in need of resolution and sketch potential explanations. First, LIP topographic map appears to be less coarse with neuroimaging compared with single-unit studies. Second, the emerging picture of discontinuous topographic organization in LIP differs in important ways from the standard model. Third, two of the studies report results that are almost exactly the opposite of the results in the remaining three studies, raising the possibility that LIP may contain more than one map. All of these issues present difficulties that the field must somehow reconcile.

Single-unit recording versus neuroimaging

The natural conclusion to draw from the conflicting literature is that LIP is only weakly topographically organized. However, although a few neuroimaging studies have been inconclusive about topographic organization [55,56], most report clear evidence for topography. What might explain this discrepancy?

A simple explanation is that imaging essentially 'low passes' spatial information and so may be sensitive to coarse topography that is difficult to see with higher spatial resolution methods such as single-unit recording. As an intuitive example, consider how an image in a pointillist painting comprising many small dots is indecipherable when viewed up close (high spatial resolution) but obvious when viewed from a distance (low spatial resolution). LIP may similarly show no spatial organization at a fine scale ('up close') such that receptive fields of sampled single units exhibit no discernible regularity. Nevertheless, when viewed at a lower spatial resolution, relatively subtle biases in receptive field distributions may sum to produce clear topography. For example, consider two adjacent square millimeters of cortex, one containing 45% upper

Box 3. Differences in the neural signals measured by single-unit recording and neuroimaging methods

Single-unit recording techniques (used by Blatt *et al.* and Ben Hamed *et al.*) measure action potentials originating in the axons of neurons [40,41]. It is likely that single-unit recording mainly picks up action potentials coming from large cell bodies (e.g., those of pyramidal cells) or from their proximal axons. By contrast, the BOLD response is not known to be markedly differentially sensitive to large neurons. Although the neural basis of the BOLD signal remains subject to intense debate, the consensus view is that BOLD-fMRI (used by Arcaro *et al.* and Patel *et al.*) is primarily sensitive to dendritic currents and not axonal potentials [47,48,105]. The evidence for this view is based on the idea that local field potentials (LFPs) are likely to be driven by spatially aligned and temporally synchronized dendritic currents rather than by action potentials [106] and that the correlation between BOLD and FP remains even when action potentials are abolished [107–109]. A parallel argument applies to the 2-deoxyglucose imaging method of Savaki *et al.*, which measures energy consumption and so would, like BOLD-fMRI, be more sensitive to synaptic and dendritic events than single-unit recording techniques [49,109,110].

and 55% lower receptive fields and the other containing the reverse proportions. At high resolution, such a bias would require sampling of over 200 cells from each region to discern a statistically significant difference (chi-squared test). At low resolution, however, a significant difference would be easily discernible. There are on the order of 100 000 cells in one cubic millimeter of tissue, so an imaging method with a resolution as small as 150 μm would be sufficient to register significant topography in this scenario. Therefore, one explanation for the apparent ease of finding topography using imaging compared with single-unit recording is that imaging is better suited to detecting coarse patterns.

Another possible explanation for the greater ease in identifying topography using imaging compared with single-unit recording could arise due to differences in what the different methods are measuring (Box 3). These potential differences have important implications for comparing and interpreting studies of topographic organization collected with different methods. For example, if topography is present in the inputs to LIP, or even in both the inputs and in small local interneurons that are not easily recorded using extracellular electrodes, the neuroimaging methods used by Patel *et al.*, Arcaro *et al.*, and Savaki *et al.* would reveal the topographic organization whereas single-unit recording studies would be less sensitive [47–49]. By considering the different sensitivities of different techniques, one can see how apparent conflicts about topographic organization can be rendered consistent. Below we explore in more detail the possibility that different elements of a neural circuit may reflect different topographic organizations.

Distorted and discontinuous topographic organization in LIP

In early visual areas, there is a single, continuous map of the visual field and, within this map, representations of polar-angle and eccentricity axes lie orthogonal to one another. The results of all five studies discussed above show that this is not the case in LIP. Instead, there are spatially separate representations of the periphery and fovea (Figure 2). The foveal representation cannot be

Box 4. Theoretical arguments for the existence of topographic organization

There are at least two nonexclusive reasons that topographic organization may exist. First, it may reflect a developmental accident. The mechanisms that guide axons from one structure to another structure during development may incidentally preserve the relative positions of those axons with respect to one another, thus preserving topographic organization [111,112]. This cannot be the full story, however, because there are instances of topography that this cannot explain. For example, consider axons from the dorsal root ganglia that carry fine touch information from the periphery to the brainstem. When these axons enter the dorsal columns, they do so dermatome by dermatome. Because dermatomes overlap, the representation of the body surface is not one to one. However, within the dorsal column they re-sort themselves back into a single continuous topographic representation [113]. This cannot be explained, for example, as a mere side-effect of guidance factor concentration gradients that maintain a microscale organization as they direct the axons to enter and form synapses in the dorsal column nuclei.

A second reason for the existence of topography is that it may provide substantial functional benefits. Brain volume is driven largely by the volume of axons. Because travel down the birth canal limits skull size, reducing axon length provides space for more neurons [114,115]. In addition, shorter connections conserve metabolic resources and reduce processing time [116]. The correct type of topography can provide these benefits. Total axon length is minimized when computational units (neurons) that share dense connectivity with one another are clustered together [58,116–118]. For example, one way to compute changes in intensity values in an image (large changes are often associated with object edges or boundaries) involves local comparisons of the intensity values of several nearby pixels. Critically, because this algorithm requires information about neighboring pixels only, total wire length can be minimized by mapping neighboring parts of the image or input space onto neighboring computational units. Early visual processing similarly involves the computation of local features (e.g., orientation, visual motion, speed). Thus, placing neurons with adjacent or overlapping receptive fields as closely together as possible will minimize total axon length and thereby save space, metabolic resources, and time [58,118].

construed as comprising one end of the eccentricity axis, because within the representation of the periphery the eccentricity axis is either weakly organized or altogether absent. We suggest that these departures from the standard model are related to the fact that LIP is involved in directing gaze and attention. For this purpose, the processing requirements for the fovea and the periphery are different and, consequently, it is computationally efficient to segregate these two representations (see Box 4 for additional discussion of topography and efficiency constraints).

Topographic distortions and computational efficiency

How might a distorted topographic map result in more efficient computation? First, continuity-preserving distortions such as the cortical magnification for the fovea in V1 [57], which are presumed to reflect differences in the number of neurons devoted to representing each portion of the sensory dimension, are consistent with the nearest-neighbor rule for computational efficiency. However, the topographic map in LIP does not preserve continuity and so violates this rule. According to the effective wire-length argument, discontinuous topographic maps in LIP and elsewhere in the brain must therefore reflect situations

in which proximity along the represented dimension (e.g., sensory receptor or bodily surface) is no longer the primary determinant of computational traffic (see Box 5 for an additional discussion of discontinuous topographic maps in somatosensory cortex).

More generally, a neural population arranged across the cortical sheet that minimizes effective connection length could be described as efficiently representing, without distortion, the information or parameter space relevant to that particular computation [58]. As we move from early areas subserving basic sensory processing into higher-order areas involved in sensorimotor transformations and more complex cognitive functions, we should therefore expect to leave behind simple organizational schemes (e.g., retinotopy, somatotopy) in favor of more complex topographic representations whose apparent distortions and discontinuities reflect, in scrutable or inscrutable ways, the computations being performed in those areas (for a related discussion, see [59]).

Topographic separation of foveal and peripheral representations

In early visual areas, the only prominent distortion in retinotopy is cortical magnification, the relative expansion

Box 5. Topographic map discontinuities in somatosensory cortex

The hand representations in primary somatosensory cortex (SI) provide a clear example of topographic map discontinuity because adjacent body surfaces are represented in nonadjacent cortical loci [119,120]. A minimally distorted topographic representation would map each finger with something like adjacent and concentric rings representing progressively more proximal portions of the finger, incorporating both ventral and dorsal surfaces, especially the fingertip (Figure IA). Yet the hand representation in SI is organized so that the ventral surfaces of each finger are side-by-side (Figure IB,C). This is likely to reflect the fact that local computations across the ventral surfaces of adjacent fingers are at least as common as computations between the ventral and dorsal surfaces of each individual finger (see [121]). More dramatic map discontinuities in SI include the representation of the posterior and anterior portions of the hind leg, which is interrupted by the representation of the foot [119,122], and the representation of the hands in cortical tissue adjacent to the representation of the face [123]. Although the latter reflects in part the separation between spinal and cranial pathways, one might speculate that such discontinuity is also shaped by the functional advantages this organization confers by minimizing the effective wire length between these two representations. Organisms use their forelimbs to bring food to their mouth and therefore computations involving the fingers and the face are quite frequent. Over millions of years of evolution, this could explain why the two representations have ended up side-by-side in the cortex.

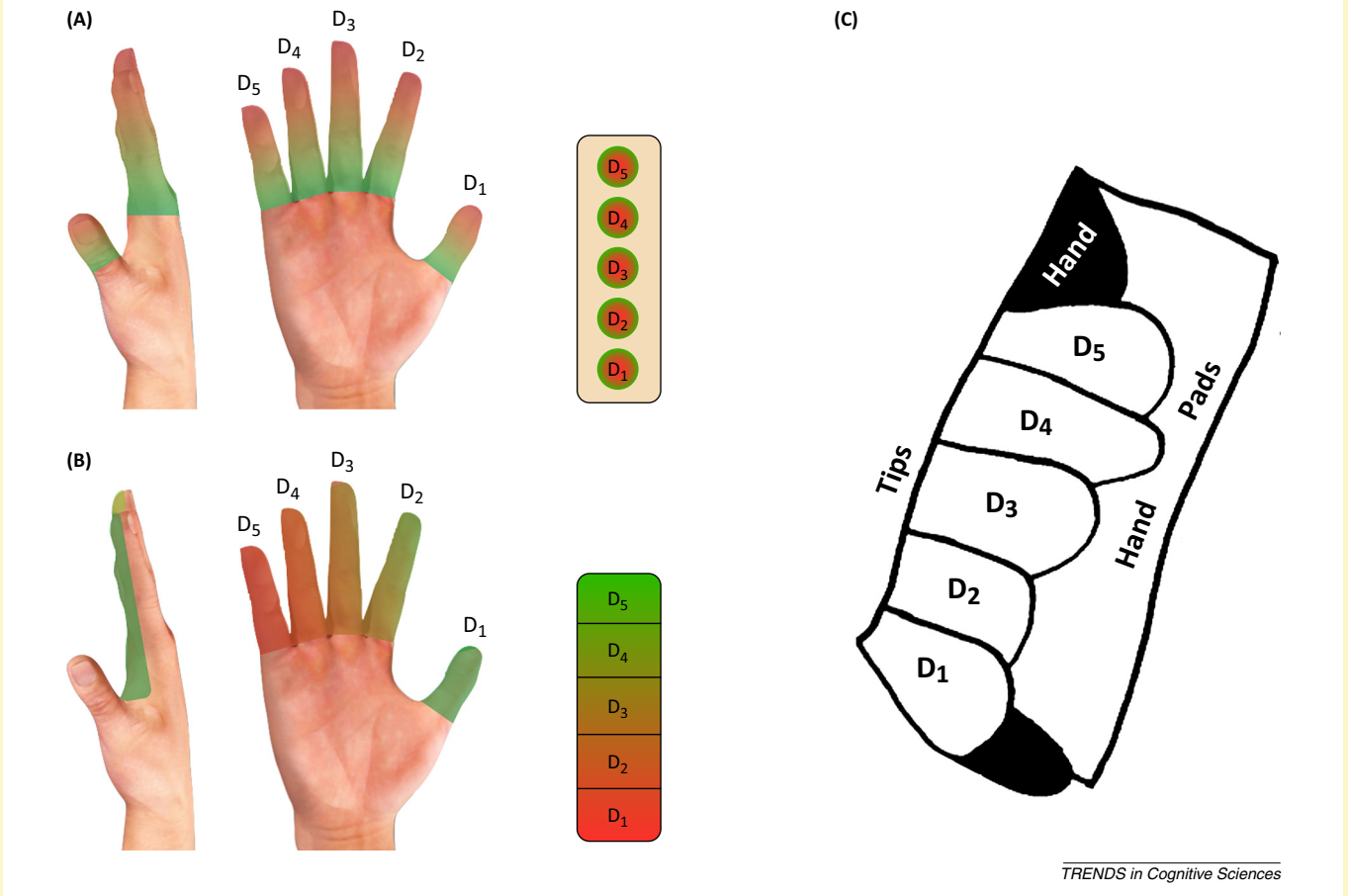

Figure I. Possible topographically organized hand representations. **(A)** Schematic of minimally distorted, topologically intact hand representation. Color gradient indicates dorsal/ventral surface locations on digits (D_1–D_5) from distal (red) to proximal (green). **(B)** Schematic of actual topographically discontinuous hand representation found in the somatosensory cortex. Color gradient indicates locations on ventral digit surfaces from D_5 (red) to D_1 (green). **(C)** Hand representation in somatosensory areas 3b and 1 of the owl monkey. White and black indicate the ventral and dorsal surfaces, respectively. Adapted from [119].

of areas close to the fovea as if the visual field were being viewed through a fisheye lens. Based on the computational considerations outlined above, what distortions might we expect as we move away from the sensory periphery to neural systems involved in directing gaze and attention? One possibility is that computations involving foveal input might differ from computations that involve peripheral input. In support of this idea, studies suggest that foveal and peripheral distractors can have qualitatively different effects on the control of visual attention [60–62]. Therefore, it is not unreasonable to posit that the machinery for processing foveal versus peripheral visual inputs might become distinct in gaze or attention control areas, leading to separate foveal topographic representations.

The imaging studies we have reviewed all suggest that LIP may contain two representations of the visual field that are discontinuous from one another. The first, at the posterior end of LIP, represents the visual periphery in polar-angle coordinates but without a clear eccentricity axis. The second, at the anterior end of LIP, represents the fovea. LIP–FEF connectivity data provide further support for this idea. Macaque FEF contains a clear and continuous mapping of eccentricity from lateral (foveal) to medial (peripheral). However, the projections from FEF to LIP do not follow the possible superficial-to-deep axis eccentricity axis described by Arcaro *et al.* and others [40,41,48]. Instead, lateral/foveal FEF is more strongly connected with anterior LIP and medial/peripheral FEF is more strongly connected to posterior LIP [63,64]. This is inconsistent with the superficial-to-deep eccentricity axis in LIP first proposed by Blatt *et al.* and instead supports a posterior representation of the periphery and an anterior representation of the fovea [41].

We propose that this discontinuity reflects fundamental processing differences for foveal compared with peripheral stimuli in LIP. Visual features within or very near the fovea might belong to the stimulus currently being fixated or might be a stimulus of interest that can be inspected with only a minimal and perhaps low-cost shift in spatial attention. Alternatively, inspection of a stimulus in the periphery would require the additional computation of targeting a saccade. Given the differences in the computations required to attend to something in the fovea versus the periphery, it may be advantageous to separate the circuitry underlying these two types of attention, resulting in separated foveal and peripheral representations.

In summary, the separation of the foveal representation from the peripheral map in LIP is a marked departure from the distortions observed in early visual areas and is likely to represent a change in the types of computation occurring in LIP. These changes may emphasize interactions between neurons at the fovea or in the periphery but decreased interactions between the fovea and periphery, and this topographic organization may reflect the most efficient configuration of these neurons.

Multiple topographic maps in LIP

Functional and topographic subdivisions of LIP

As described above, of the five studies of topography in LIP, the polar-angle axis runs posterior to anterior in three studies but anterior to posterior in the other two (Figure 2). What could account for these discordant results? We suggest that there may be two distinct topographic maps of polar angle in LIP, whose relative levels of activity depend on the particular task being performed. In the three studies that report a posterior-to-anterior polar axis (Figure 2B,D,E), animals were required to maintain fixation and ignore salient peripheral stimuli. In each case, the peripheral stimuli were designed to be exogenously salient and in some cases were task relevant, but in all three of these studies the animals were explicitly trained not to saccade to these stimuli. As a result, these animals were performing an attentional rather than oculomotor task. In contrast, in the other two studies (Figure 2A,C), animals were not trained to fixate and there was no requirement to suppress saccades toward a peripheral stimulus. Savaki *et al.* [49] used a simple oculomotor task in which animals moved their eyes to a peripheral target as soon as it appeared. Blatt *et al.* [41] presented peripheral stimuli to lightly sedated animals whose eyes were mechanically restrained. Although the animals were unable to move their eyes, one might reasonably assume that oculomotor circuitry was nevertheless engaged by the peripheral stimuli, because these animals were never trained to suppress saccades. It is even conceivable that, to the extent that a distinction can be made, the low level of sedation might have interfered more with attentional over saccadic circuits. Therefore, the maps uncovered by Blatt *et al.* [41] and Savaki *et al.* [49] may correspond to a population of neurons within LIP primarily involved in oculomotor planning, whereas the maps uncovered by the other three studies may correspond to neurons primarily involved in orienting spatial attention. This possibility of multiple maps within LIP breaks the second principle of topographic organization that one anatomically defined area contains one topographic map and raises the possibility that LIP and associative areas contain multiple subunits, each representing separate functions.

Adjacent versus overlapping topographic maps

Where are these maps located relative to one another? The three attention maps (Figure 2B,D,E) and one of the two oculomotor maps all appear to be located in posterior LIPv. The Blatt *et al.* [41] map appears to be posterior to the other four and straddling the border between LIP and caudal IPS (cIPS). Averaging the locations of the two oculomotor maps suggests that the oculomotor map lies slightly in front of the attentional map (Figure 3A). A variant of this configuration is that the Blatt *et al.* [41] map may lie posterior to the attention map (corresponding to the 'CIP-2' map described by Arcaro *et al.* [48]) and the Savaki *et al.* [49] map anterior to the attention map. This may explain the differing orientations of the eccentricity axes between the two studies.

A second possibility is that the attention and oculomotor maps overlap one another (Figure 3B). Attention and oculomotor control are intimately connected [65,66] and studies of LIP have found an intermingling of neurons involved in oculomotor control and covert shifts of attention [67,68]. Selective inactivation of LIPv affects both saccades and covert visual search [69]. However, the lesion effects on saccades and attention can be dissociated from one another by varying eye position, suggesting that the circuitries subserving the two functions are at least partially distinct

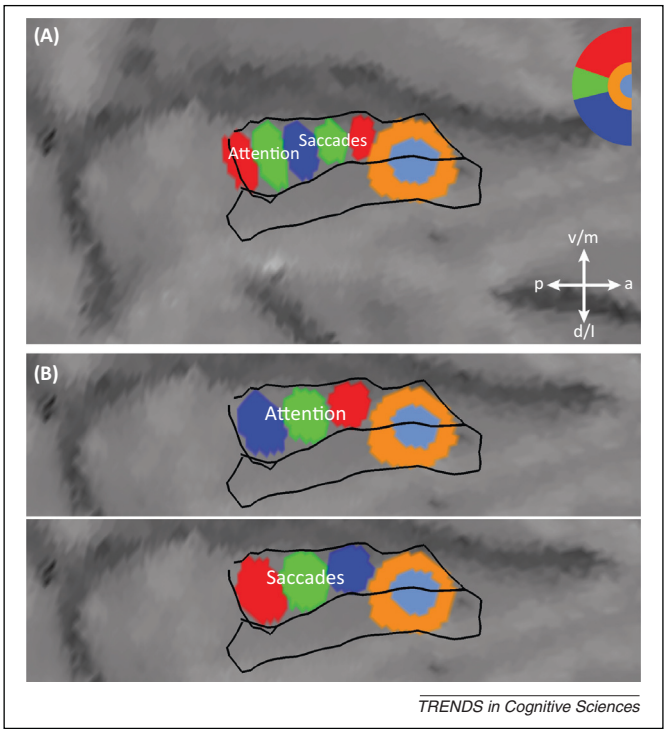

Figure 3. Possibilities for lateral intraparietal area (LIP) topographic organization. **(A)** Separate maps for attention and saccades. **(B)** Overlapping attention and saccade maps.

[69]. If separate circuits coexist in LIPv to subserve these two functions, it is conceivable that the topographic organization of the two overlapping circuits might not be aligned with one another. In this case, one might reasonably speculate that the topography measured *in vivo* in the behaving animal depends on which circuit was being activated during the experiment.

Mechanistic consequences of overlapping topographic maps

A variation on this theme is that the inputs and outputs of even a single neural circuit may not be topographically aligned. For example, a circuit involved in mediating overt shifts of gaze or covert shifts of attention might receive two spatial inputs, one encoding the current attentional locus and the other encoding the desired future locus. This might be useful, for example, in computing head- or body-centered vectors or for transiently remapping activity [70,71]. One can imagine that the two inputs (current and future attentional loci) might each be only coarsely topographically mapped, such that any one neuron (or cluster of neurons) would receive information from a highly distributed region of space. Topography might be evident at low, but not high, resolutions. If the goal is to compute shifts in spatial location, it might be advantageous for the two topographies to be out of register with one another. Different tasks might emphasize either the current or future attentional locus (e.g., perhaps the representation of the future location is more strongly represented in the case of an overt compared with a covert shift). This could lead to different apparent topographies, depending on the particular task at hand. As another example, the same neuronal circuit might be involved in either activating or suppressing saccadic eye movements, depending on the task demands. The function of the circuit might depend on the current task demands, such that the topography of its output might be in alignment with the topography of its input in some states but dissociated from it in others.

What purpose might this decoupling of inputs and outputs serve? Studies of neural plasticity suggest it may reflect the rapid reconfiguration of circuitry needed to support the current task. These rapid reconfigurations may be mediated by selective activation or inhibition of corticocortical connections, because it is much faster to activate or deactivate these connections than it is to phagocytose old connections and grow new ones [72]. Studies of functional organization in temporarily blinded human subjects [73,74] and in macaque area 7a and dorsal prelunate (DP) [75] support this concept because large-scale functional reorganization occurs too rapidly to be mediated by the growth of new cell processes. Thus, the topographic maps found in LIP and other associative areas may use selective activation and deactivation to respond to rapidly changing task demands [72].

In summary, the apparent conflicts between studies on polar-angle map orientation may reflect the fact that different tasks were being performed. The two distinct maps revealed by the five studies may lie side by side or may overlap one another. Overlapping maps might occur if, for example, inputs, outputs, or other circuit elements are partially shared by the circuits in question.

Open questions about LIP topography

Several issues concerning the topographic organization of LIP remain unclear. The first issue is whether attention and oculomotor maps are overlapping or adjacent within individual macaques. Another issue is whether an eccentricity axis exists in the posterior topographic map and, if so, to confirm the orientation of this axis. Yet another issue is whether the anatomical subdivision LIPd also contains topographic maps like LIPv. Although LIPd is clearly involved in oculomotor planning [69], no topographic map has been found within this anatomical subdivision of LIP; the presence or absence of topographic maps in certain functional areas may help to reveal the functional utility of topographic organization. Despite these open questions, the differences in topographic mapping across studies should not be dismissed out of hand. Instead, differences in tasks and methodologies should be carefully considered as potential drivers capable of revealing true differences in topography. Associative cortical areas may support more than one function and therefore may contain multiple topographic maps, as many as one for each function. This functional multiplicity may be supported by reweighting across multiple inputs and multiple outputs from individual neural circuits or reweighting the relative activity of different circuits that are interdigitated across the cortical surface. If the topographies of these different elements are not aligned with one another, we may find violations of the standard model of a single topographic map per brain area.

Concluding remarks: revising the principles of topographic organization

We describe five findings in this review that suggest that some of our deep-seated assumptions about topographic

organization in the brain do not generalize beyond early sensory and late motor areas. We show that the fovea and periphery are mapped in entirely separate locations in LIP (Figure 2); a polar-angle map may exist without a clear eccentricity map (Figure 2); the maps we observe may depend on the particular task being performed (Figures 2 and 3); areas may contain more than one topographic map (Figure 3); and, most speculatively, multiple topographic maps may sometimes overlie one another (Figure 3B).

Revised principles of topographic organization

We propose that the first principle of topography, rather than requiring each map to reflect the entirety of a particular sensory or motor dimension, may instead be modified to accommodate continuous mappings of a subset of that dimension, with the extent determined by the precise functional demands of the particular circuit. An important consequence of this is that we should expect a spectrum of types of topographic organization across brain areas with different functional profiles. We suggest that the second principle, which requires that a single map occupy the entirety of a single anatomically defined area, be understood to apply to only early sensory and late motor areas. Topographic maps in parts of the cortex that serve more intermediate functions should encompass all of the neurons performing a single unified function, but this does not necessitate anatomical or even spatial separation of each map.

Examples of the revised principles in other associative areas

These modified principles may also apply to the organization of prefrontal cortical areas. Macaque FEF is one clear example. FEF is functionally defined as an area on the anterior bank of the arcuate sulcus in which electrical stimulation results in both saccades and shifts in attention [38,76,77]. This area has two striking features. First, within FEF there is a clear eccentricity axis of organization, but no clear orthogonal polar-angle map [38,39], fitting the first principle of the modified criteria. Second, although the functionally defined borders correspond to those of the eccentricity map, they do not match any architectonic borders – one recent parcellation scheme splits the functional area across four architectonic divisions [46,78]. This fits with the second modified principle.

Area 46 dorsal to the principal sulcus (area 46d) potentially serves as another example. Area 46d is involved in maintaining spatial working memory in delayed saccade tasks [79,80]. This area is reciprocally connected to retinotopically and non-retinotopically organized areas [80,81]. Although no single-unit study has provided evidence of topographic organization in area 46d, reversible inactivations with muscimol that induce deficits in a memory saccade task reveal a topographic map this area [82]. Muscimol, a gamma-aminobutyric acid type A ($GABA_A$) receptor agonist, will inhibit not just the pyramidal output neurons that would normally be recorded from, but also any topographically arranged inputs projecting to area 46d. Thus, it is possible that single-unit recording studies have not found topographic organization because the outputs may not be arranged topographically even if the inputs are. This area then may serve as an example of the second principle, in which a functionally unified population of neurons is topographically organized and overlapping with other neurons with different (or no) topographic organization, although this clearly needs to be investigated further.

Advantages of the revised principles

One major advantage of the revised organization principles over the current model is that they gracefully accommodate more complex forms of topographic organization of the sort observed in associative areas including parietal cortex (see Box 6 for a discussion of how to define an area in light of these revised principles). Another advantage of the revised principles is that they are more inclusive. In particular, they subsume the more restrictive principles at the core of the standard model derived from sensory and motor areas. Now those original principles can be more appropriately understood as special or limit cases. As brain research continues to shift from its original focus on the sensory and motor periphery (e.g., early visual and late motor areas) to brain areas and networks involved in more complex modes of cognition, it is incumbent on us to consider more flexible models of how neural populations underlying these computations may be distributed across the cortical surface. The revised organizing principles

Box 6. Defining 'area'

The definition of 'area' is fraught with difficulty. Cortical areas are typically defined in terms of architectonics, connectivity, functional characteristics, topography, or some combination of these [21]. In the primary sensory and motor cortex, the task of identifying areas is greatly simplified by the fact that all of these standard approaches can be used more or less interchangeably to deliver comparable answers about areal boundaries. In associative cortical areas like LIP, this neat alignment breaks down. In human neuroscience, the problems associated with defining cortical areas is compounded by the fact that information about architecture and connectivity is largely unavailable because the invasive techniques required to attain this information cannot be deployed. In light of these difficulties, one option is to jettison talk of cortical areas entirely (e.g., [9]). Another option (the one we prefer), which is consistent with much of the field (e.g., [21]), is to retain the term 'area' but also to acknowledge that the construct is more nuanced than is often assumed. According to this view, one may operationally define an 'area' as any cortical territory that can be consistently segregated from a neighboring territory by any combination of architectonics, connectivity analysis, functional characteristics, and topography. This way of defining areas will often result in multiple functionally and topographically defined areas contained within a single architectonically defined area. This is likely to imply that these functionally and topographically defined areas share similar neuronal circuit architecture for performing different functions.

This definition of an area will impact the interpretation of human studies of cortical organization, because topography is often used to partition the cortex into areas [9]. For instance, the multiple topographic maps in the human parietal cortex may each belong to functionally distinct but related areas and, like the multiple topographic maps in LIPv, may share similar architectonic features such as dense myelination. The existence of partial topographic maps may also explain the relative weakness of eccentricity topography the human parietal cortex – only one parietal topographic mapping study has reported an eccentricity axis of organization [124], whereas multiple others have not (see, for instance, [26,125]).

provide a much more suitable framework/foundation for this kind of flexible model.

Having a coherent set of general principles of topographic organization is a pressing objective for contemporary neuroscience. With the emergence of multiunit recording, higher-resolution neuroimaging, and interventional methods such as optogenetics, topographic organization in both nonhuman primates and humans is more easily observed and interrogated than ever before. Consequently, it has never been more important to understand what topographic organization does (and does not) tell us about brain function and structure. We believe that by keeping these principles in mind, the importance and complexity of topographic organization in the brain can be more readily appreciated and understood.

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