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Comparative mapping of higher visual areas in monkeys and humans

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The advent of functional magnetic resonance imaging (fMRI) in non-human primates has facilitated comparison of the neurobiology of cognitive functions in humans and macaque monkeys, the most intensively studied animal model for higher brain functions. Most of these comparative studies have been performed in the visual system. The early visual areas V1, V2 and V3, as well as the motion area MT are conserved in humans. Beyond these areas, differences between human and monkey functional organization are increasingly evident. At the regional level, the monkey inferotemporal and intraparietal complexes appear to be conserved in humans, but there are profound functional differences in the intraparietal cortex suggesting that not all its constituent areas are homologous. In the long term, fMRI offers opportunities to compare the functional anatomy of a variety of cognitive functions in the two species.

The advent of functional imaging, initially PET and now mainly fMRI has greatly enhanced our ability to explore the neurobiological basis of cognitive function in humans [1]. However, fMRI only indirectly reflects neuronal activity and has limited spatial and temporal resolution. Hence, the interpretation of human fMRI data frequently draws on the vast knowledge obtained over recent decades by invasive brain studies in non-human primates, especially the macaque. The study of the visual system serves as a model in this respect, for a combination of reasons. Extensive psychophysical studies have shown that many aspects of visual perception are remarkably similar in the two species. The visual cortex is heavily developed in primates: approximately 50% of cerebral cortex in macaque and 20–30% in humans is devoted to vision, compared with about 3% for audition in monkeys and 8% in humans [2]. The visual cortex of macaque monkeys has been investigated intensively, more than any other cerebral system. This has generated a plethora of functional parcellations of macaque visual cortex: 30 or more anatomically and/or functionally distinct areas have been described (for a review see [2]). Finally, vision is frequently used to study cognitive processes such as discrimination [3], attention [4], working memory [5] and decision processes [6].

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Complications in relating human fMRI to monkey studies

Even in this favorable case of the visual system, establishing the relationship between non-invasive functional imaging in humans and invasive single-cell, lesion or anatomical studies in monkeys is far from straightforward. Making comparisons across species and techniques raises several challenges (see Box 1). Humans and macaques diverged from a small-brained common ancestor ~30 million years ago [7]. Because the ensuing expansion of cerebral cortex was far greater in the human lineage, the cortex is ten-fold greater in surface area and also far more convoluted in humans compared with macaques. The differences are not simply a matter of scale, but instead are likely to involve divergences in the number of visual areas and in how they are functionally specialized.

In single-cell studies, inferences about the function(s) of a visual area are often based on tuning curves or, more generally, selectivity for various stimulus dimensions. There can be considerable diversity in the types and degree of selectivity encountered in the neuronal

Box 1. How close can one get in comparing human and monkey using fMRI?

Even when using fMRI in awake subjects, the experimental procedures for the two species differ in several respects. Typically, monkeys sit in a sphinx position viewing a projection screen directly [15], whereas humans lie on their back viewing the screen through a mirror. There are also differences in head immobilization and reward. The coils used to measure the MR signals are different, as are the signals themselves. The use of a contrast agent (MION) in the monkey enhances sensitivity and signal localization [15,77] compared with the blood oxygen-level dependent effect (BOLD) used in humans. To compensate for these latter differences, one can estimate a scale factor for the sensitivity by comparing MR signals in a landmark region such as V1 [21].

The number of subjects is usually higher in human studies, but the number of functional volumes sampled in each subject is smaller. The standard spatial resolution of the fMRI measure is lower in humans than in monkeys, but with high-field scanners humans can be scanned with the same resolution ($2 \times 2 \times 2$ mm) as monkeys [20]. There are important differences in how functional data are registered to the anatomical MRI, in the details of the statistical analysis, and how data are registered across individuals. Monkeys might pay relatively less attention to the stimuli than humans because only the fixation point controls their behavior. Therefore some experiments have been repeated with monkey and human subjects performing at the same level in a very demanding high acuity task [14,20].

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population within a given area [8]. Functional MRI provides an indirect measure of spike plus synaptic activity [9] of very large numbers of neurons (millions of neurons if the resolution is ~3 mm voxel size). It remains an open question how the MR signals reflect neuronal selectivities within the sampled population. Adaptation of the MR signal might reflect neuronal selectivity [10], but this has not as yet been convincingly demonstrated by correlation with single-cell analyses. Therefore we refer to *sensitivity* for stimulus dimensions rather than selectivity when reporting fMRI results.

Monkey fMRI fills a missing link

Monkey fMRI [11], particularly in the awake monkey, should accelerate progress on many of these questions [12]. It allows comparison of fMRI signals with single-cell properties such as selectivity or adaptation in the same individual. Furthermore, fMRI-based functional neuroanatomy (localization of functional properties in the brain) can be compared directly in humans and monkey [13,14]. The main focus of this review is on the latter question as applied to the visual system. A growing number of studies have addressed this issue in alert monkeys [14–22] and in anesthetized monkeys [23–26]. These comparisons reveal important insights about the nature of interspecies commonalities (particularly for the early areas) plus divergences in functional organization (more pronounced in higher areas).

How relevant is the functional neuroanatomy of vision for understanding cognitive abilities unique to humans? Taking language as an example, there is evidence that linguistic abilities are rooted in preexisting capabilities present in the common ancestors of monkeys and humans [27,28]. In the long term, fMRI offers excellent opportunities to compare the functional anatomy of a variety of cognitive systems that have evolved differently in the two species. The comparison of the visual cortex in humans and monkeys can provide an invaluable testbed for such analyses. Here we review recent progress in charting visual areas in humans and monkeys, illustrate new approaches to interspecies comparison, and evaluate several candidate homologies for both early and higher-order visual areas.

Strategies for comparing human and monkey visual cortical systems

Defining cortical areas

Cortical visual areas have been identified using one or more among four major criteria: (1) cyto- and myeloarchitecture, (2) connectivity, (3) retinotopic organization and (4) function, as revealed by single-cell, lesion and neuroimaging analyses. Each of these criteria has significant limitations and does not apply equally well to all regions or across species. For example, some areas lack clear retinotopy, and cytoarchitectonic subdivisions are often very subtle. Connectivity studies are problematic in humans (although diffusion tensor imaging provides some hope [29]). Consequently, consensus partitioning schemes have yet to emerge for higher-level areas in either macaque or human visual cortex [2].

Figure 1a shows an fMRI-based charting of early visual areas (V1, V2, V3) and several mid-level visual areas (V4, MT and V3A) of the monkey, defined by their retinotopic organization and displayed on a flatmap of the right hemisphere of an individual macaque [18]. This illustrates the power of functional mapping, in which signals can be measured over the entire visual cortex (indeed over the whole brain), whereas single-unit retinotopic studies typically explore only a limited region in any individual monkey. Figure 1b shows the middle and higher-order cortical areas (beyond V3), according to a recent architectonic scheme of Lewis and Van Essen [30], displayed on an atlas surface and viewed in fiducial (original 3D shape), inflated and flat-map configurations.

Retinotopic and functional characteristics revealed using fMRI provide a major basis for delineating visual areas in humans. Figure 1c shows a mosaic of areas defined by retinotopy and/or functional specializations, as mapped onto different configurations of a human surface-based atlas [2]. In general, early and mid-level visual areas are located more medially and posterior than their correspondingly named macaque counterparts. For example human V1 lies almost entirely in the calcarine sulcus on the medial surface of the hemisphere, whereas macaque V1 occupies a substantial portion of the operculum on the lateral surface. The middle temporal (MT)/V5 motion area is located in the superior temporal sulcus (STS) in the macaque and in the inferior temporal sulcus (ITS) in humans (Figure 1a,c)

Criteria for inferring homology

Despite species differences in geographic location, the case for homology of V1 in monkeys, humans and all other primates studied was compelling long before the advent of neuroimaging, based on a constellation of anatomical as well as retinotopic similarities [7]. PET and fMRI subsequently revealed human V2, adjacent to V1, and a more distant motion-sensitive region that was originally identified as human MT or V5 [31–33]. However, the latter region is now commonly called hMT+ [34] to reflect the likelihood that it contains multiple areas, some corresponding to the neighboring MST/FST satellite areas in the macaque (see below). Nonetheless there is widespread consensus that its more posterior portion is a homologue of macaque MT [35]. Thus a major basis for inferring homology from fMRI studies is to show that regions have similar functional and/or retinotopic characteristics in humans and monkeys. This functional equivalence can in some favorable cases complement existing anatomical evidence, as for V1, but in most cases needs further support (see Box 2).

Surface-based approaches to homology evaluation

The case for homology between monkey and human V2 derives in part from the fact that both directly adjoin area V1. More generally, the neighborhood relationships with areas whose homologies are more firmly established provides an important basis for evaluating homologies throughout the cortical sheet. This issue can best be addressed using surface-based warping techniques [36] to explore mappings that reflect species-specific non-uniformities in

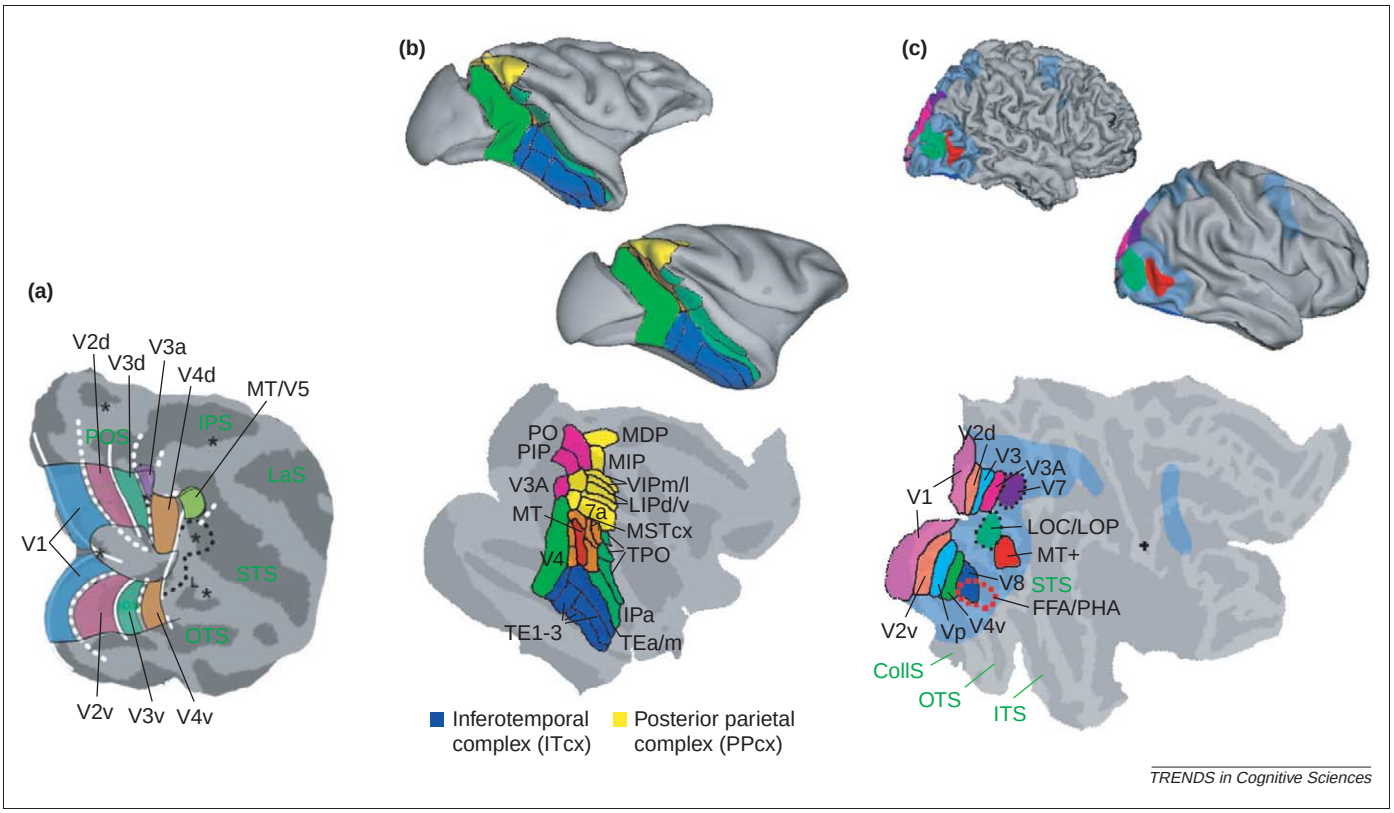

Figure 1. Visual cortical areas in monkey **(a,b)** and human **(c)**. In (a), portions of ventral and dorsal V1, V2, V3, V4 and V3A and MT representing 1–7 degrees eccentricity are color coded (modified from [18]). Full and dashed white lines, and black stars, indicate projections of horizontal and vertical meridians, and central visual field, respectively. IPS: intraparietal sulcus, LaS: lateral sulcus, OTS: occipito-temporal sulcus, POS: parieto-occipital sulcus, STS: superior temporal sulcus. In (b) the middle- and higher-level areas according to the Lewis and Van Essen [30] scheme are shown. In (c) early and middle human visual areas as compiled by Van Essen [2] are shown. Coll S: collateral sulcus, ITS: inferior temporal sulcus. The definition of some areas is only tentative at present (stippled contours). For alternatives to the V4v/V8 scheme see [56,57]. Datasets are accessible in the SumsDB database for online surface visualization (WebCaret) or downloading and offline visualization (Caret) via http://brainmap.wustl.edu:8081/sums/directory.do?dirid=706149.

Box 2. Homology

Cortical areas in humans and macaques are considered homologous if they derive from areas present in a common primate ancestor. For areas that existed in this common ancestor, the challenge is to identify the homologous areas in monkeys and humans despite whatever divergences have occurred in structure, function and geographic location. Given that this common ancestor of humans and macaques had a smaller brain and probably fewer cortical areas, an even more formidable challenge is to evaluate homologies, or lack thereof, in regions where new areas emerged. In evaluating these issues, one should be mindful of two considerations. First, homology cannot be proven, but rather must be inferred with a degree of confidence that depends on the number and distinctiveness of the criteria and the number of species sharing common characteristics (for reviews see [7,73,74]). Second, the evaluations of evolutionary changes will benefit from an improved understanding of the developmental processes underlying cortical parcellation. These include molecular signaling mechanisms (e.g. morphogens that provide positional cues, axonal guidance molecules) and activity-dependent mechanisms that modify thalamo-cortical innervation patterns [73,75]. Possible (but unproven) mechanisms for how new areas can arise during evolution include: (i) duplication of an existing area, analogous to gene duplication [76]; (ii) segregation of what initially were functional modules within a single area; (iii) reorganization driven by altered afferent activity patterns, and (iv) emergence of new neuronal populations in an expanding cortical sheet [73]. Given these diverse developmental possibilities and also the persisting uncertainties regarding the precise partitioning of primate cortical areas, it is useful to note that homologies can be considered at the level of clusters of neighboring areas ('regional' homology) as well as the level of a single area ('areal' homology).

cortical expansion during evolution. The starting point in this approach is to identify a standard set of landmarks whose homology is in little doubt. A set of such landmarks shown on flat maps of macaque (Figure 2a) and human (Figure 2b) include primary areas of the different sensory and motor systems plus MT and the frontal eye field (FEF) [2,37]. Notably, area MT and primary auditory cortex (A1) are much farther apart on the human map than on the macaque map, suggesting a disproportionate expansion of the intervening region in humans. To explore this issue, the landmarks were projected to spherical maps of macaque and human cortex (to circumvent the problems associated with artificial cuts on the flat maps), and the macaque sphere was registered to the human sphere using the projected landmarks as constraints. A Cartesian grid overlaid on a map of identified sulci in the macaque (Figure 2c) appears deformed on the human map (Figure 2d) when registered using the standard landmarks. It suggests large regional differences in which human parietal, temporal and frontal cortex have expanded more than occipital cortex. If the expansion in between the landmarks were in fact relatively uniform, it would suggest that the macaque intraparietal sulcus (IPS; lime green in Figure 2c,d) corresponds not only to human IPS but also to part of the angular gyrus (red arrows in Figure 2d). Also, under this scheme, substantial fractions of human Brodmann areas 20–22 would be

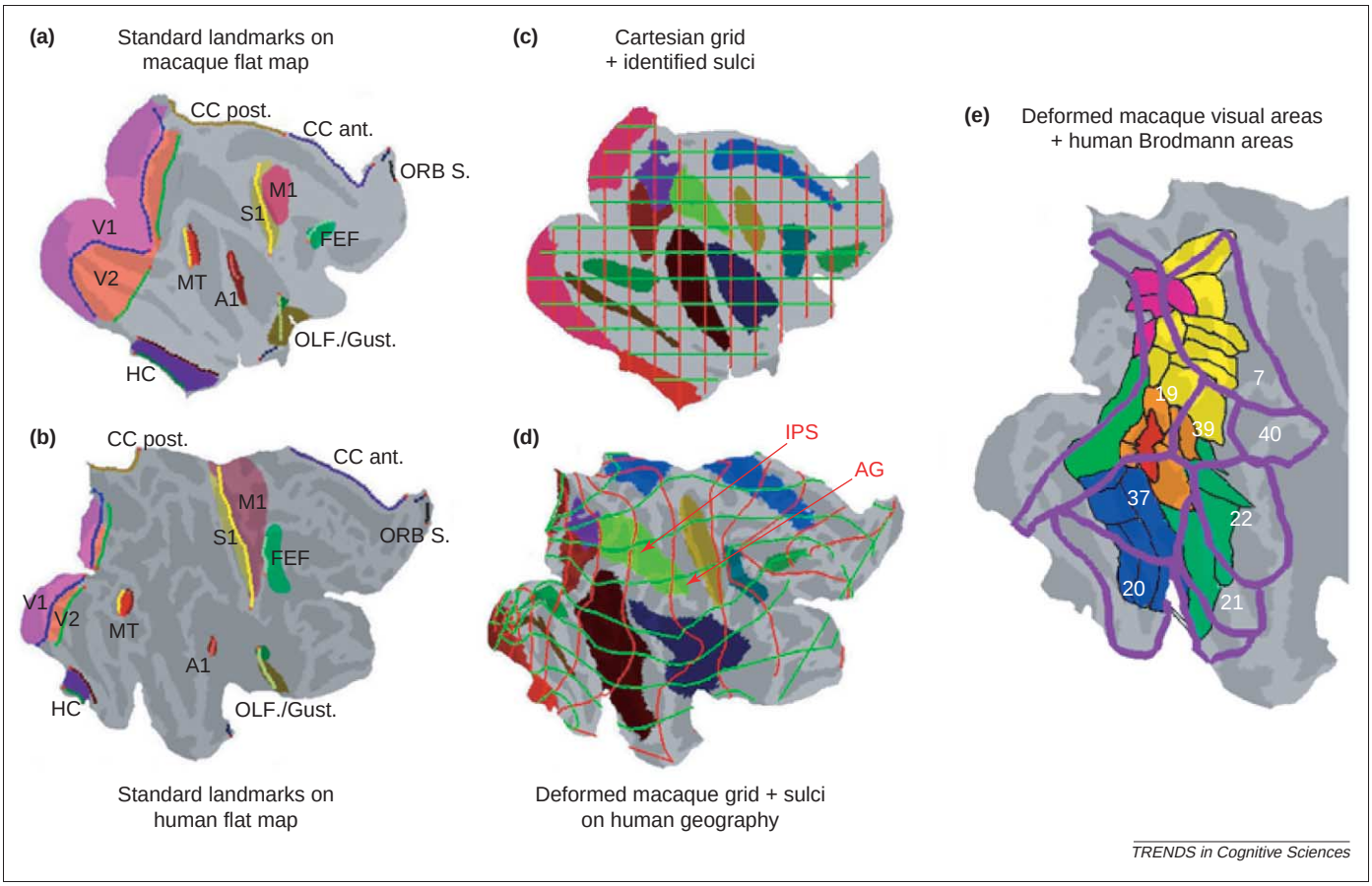

Figure 2. Standard landmarks used for surface-based registration between monkey and human cortex. **(a,b)** Delineation of landmark regions and contours in monkey (a) and human (b). CC: corpus callosum, FEF: frontal eye fields, HC: hippocampus, ORB S, orbital sulcus, OLF/Gust., olfactory/gustatory cortex. **(c,d)** Visualization of deformation: Cartesian grid and identified sulci on monkey flat map (c) and deformed grid and sulcal pattern (standard warping) projected onto human flat map (d). **(e)** Deformed monkey areas (from Figure 1b) from the standard warping projected onto human cortex with human Brodmann areas outlined in purple (modified from [2,20]). In (d) red arrows point to intraparietal sulcuc (IPS) and angular gyrus (AG). Datasets are accessible in the SumsDB database for online surface visualization (WebCaret) or downloading and offline visualization (Caret) via http://brainmap.wustl.edu:8081/sums/directory.do?dirid=706149.

potentially homologous to the inferotemporal complex and adjoining parts of the macaque STS (Figure 2e).

One valuable approach for evaluating the plausibility of this warping is to compare fMRI-based functional maps generated using equivalent stimulation paradigms in the two species. For example, Figure 3 shows maps of 2D-shape sensitivity in monkey (3a) and human (3b) cortex based on the paradigm of Kourtzi and Kanwisher [38], in which intact object images were compared with scrambled stimuli. The deformed monkey activation (green) was not well-matched to the actual human activation (red) in temporal and parietal cortex (arrows in Figure 4c). One interpretation is that the monkey and human activation did not arise from homologous regions, which would signify a major divergence in functional organization of these regions. Alternatively, the parietal and temporal activations might indeed arise from homologous clusters of areas, coupled with highly differential expansion of neighboring cortical regions. To explore the latter hypothesis, four landmarks based on the fMRI activation patterns (white and yellow pairs in Figure 4a,b) were added to the standard set. The results of this modified warping are shown in Figure 4d: in this case, the deformed monkey activation and actual human activation are substantially better matched as evidenced by the increase in overlap (yellow). A corollary of this hypothesis is that the potential homologue of the monkey IT complex is contained mainly within Brodmann's area 37, plus small parts of areas 19 and 20 (Figure 4e). Also the anterior part of macaque STS would correspond to the anterior fusiform cortex (arrow in Figure 4e) rather than inferior temporal gyrus (Figure 2e). The deformed macaque parietal visual areas (yellow) involve disproportionate expansion of area 7a and nearby regions relative to more medial intraparietal areas (Figure 4e), in qualitative agreement with the suggestion made by Simon *et al.* [39]. The fMRI-constrained warping suggests a larger expansion than previously appreciated of parietal visual cortex and a relatively smaller expansion of ventral visual cortex (compare the extent of yellow and blue regions in Figure 4e and Figure 2e). This suggests that the human dorsal stream areas [40] of the visual system, which are related to the representation of space to guide action, might have undergone greater expansion than ventral stream areas, which are related to representation of objects for recognition and categorization. This hypothesis can be further explored using fMRI paradigms that reveal the full extent of each stream in each species.

Conserved early visual areas

As noted above, the retinotopic organization of early visual areas V1, V2 and V3 is similar in monkeys and humans [18,25,31,34]. fMRI has revealed important functional

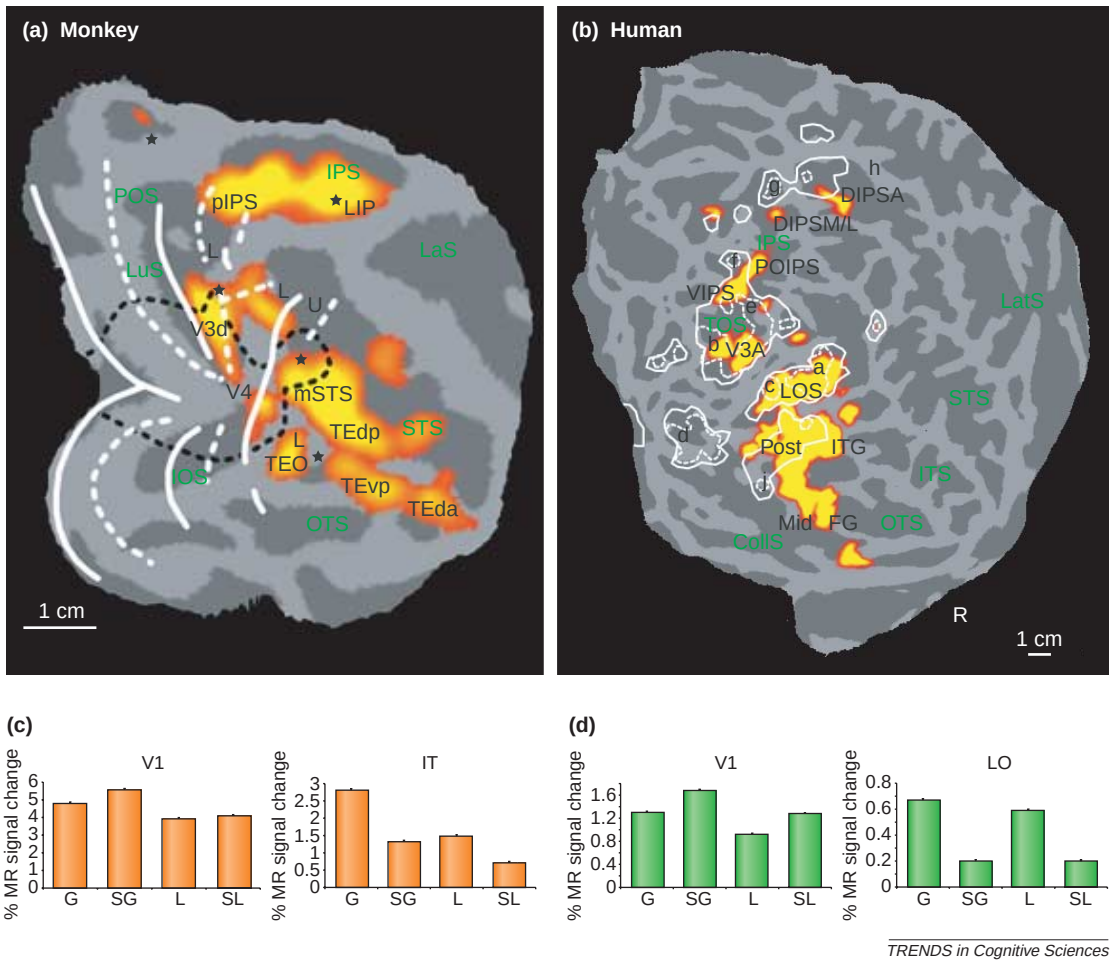

Figure 3. Object-related activation in human and monkey (group data, modified from [20]). **(a,b)** Flatmaps showing the statistical parametric maps (SPMs) indicating the voxels with significantly ($p < 0.05$ corrected for multiple comparisons) larger activity for viewing intact images of objects compared with viewing scrambled images. Same data as in Figure 4a,b, but shown on flattened (Freesurfer) maps of posterior cortex to reveal the relationship with retinotopic borders in the monkey (a) and with motion sensitive regions (white outlines) in humans (b). **(c,d)** Activity profiles plotting percentage MR signal change compared with fixation baseline in intact greyscale (G) and scrambled greyscale (SG) images and intact (L) and scrambled (SL) drawings of objects (stimuli used in [38]) in V1 and inferotemporal cortex (IT) of the monkey (c) and V1 and lateral occipital complex (LOC) of humans (d). These profiles are the averages of MR signal changes obtained in four and five local maxima in V1 and temporal cortex, respectively. In (a) abbreviations m, d, v, p, a indicate: middle, dorsal, ventral, posterior, anterior, respectively; in (b) letters a to j indicate local maxima of motion sensitive regions [19]; LuS: lunate sulcus, IOS: inferior occipital sulcus, CollS: collateral sulcus, TOS: transverse occipital sulcus; ITG: inferior temporal gyrus, FG: fusiform gyrus. Other conventions as in Figure 1.

similarities in these early areas. These include similarities in local integration of line elements in V1 and V2 [26], in the effect of scrambling in V1 [20] (Figure 3c,d), and in the involvement of V2 and V3 in the extraction of 3D-structure from motion (SFM) [14] (Figure 5a,b).

Other studies have revealed modest species differences in function and structure. V1 shows species differences in its laminar architecture [41] indicating a greater differentiation of the magnocellular signals reaching V1 in humans and hinting that motion processing might be more important in humans than in monkeys. In monkeys, V3 is more motion sensitive than V3A [15], whereas in humans the opposite is true [42]. Monkey V3d is more shape sensitive than human V3 [20].

One intriguing question concerns possible dorso/ventral asymmetries in the early visual areas. This can shed light on the likelihood of finding what Zeki refers to as 'improbable areas' [43]: areas that represent only a quadrant of the visual field rather than a complete hemifield. Two such asymmetries have been documented with fMRI recently, adding to previous physiological and anatomical evidence for asymmetries [2]. In monkey, V3d is more engaged in 2D-shape processing than V3v [20]. In humans, ventral parts of V1–V3 are more active in color discrimination, compared with a dimming control task, than their dorsal counterparts [44]. Interestingly, activity in the upper and lower field representation of the human color responsive region was equal. Discrimination performance was also comparable in upper versus lower fields and is thus better correlated with higher-level activation than the early visual activation.

A mixed bag: the mid-level visual areas

Likely homology: area V3A

Human V3A has a retinotopic organization similar to that of monkey V3A: a complete representation of the visual field split by a horizontal meridian, which also adjoins V3d [18,25,42]. This constitutes strong evidence for homology even in the face of evidence for significant divergence in function. V3A is stereo sensitive in both species [16,45].

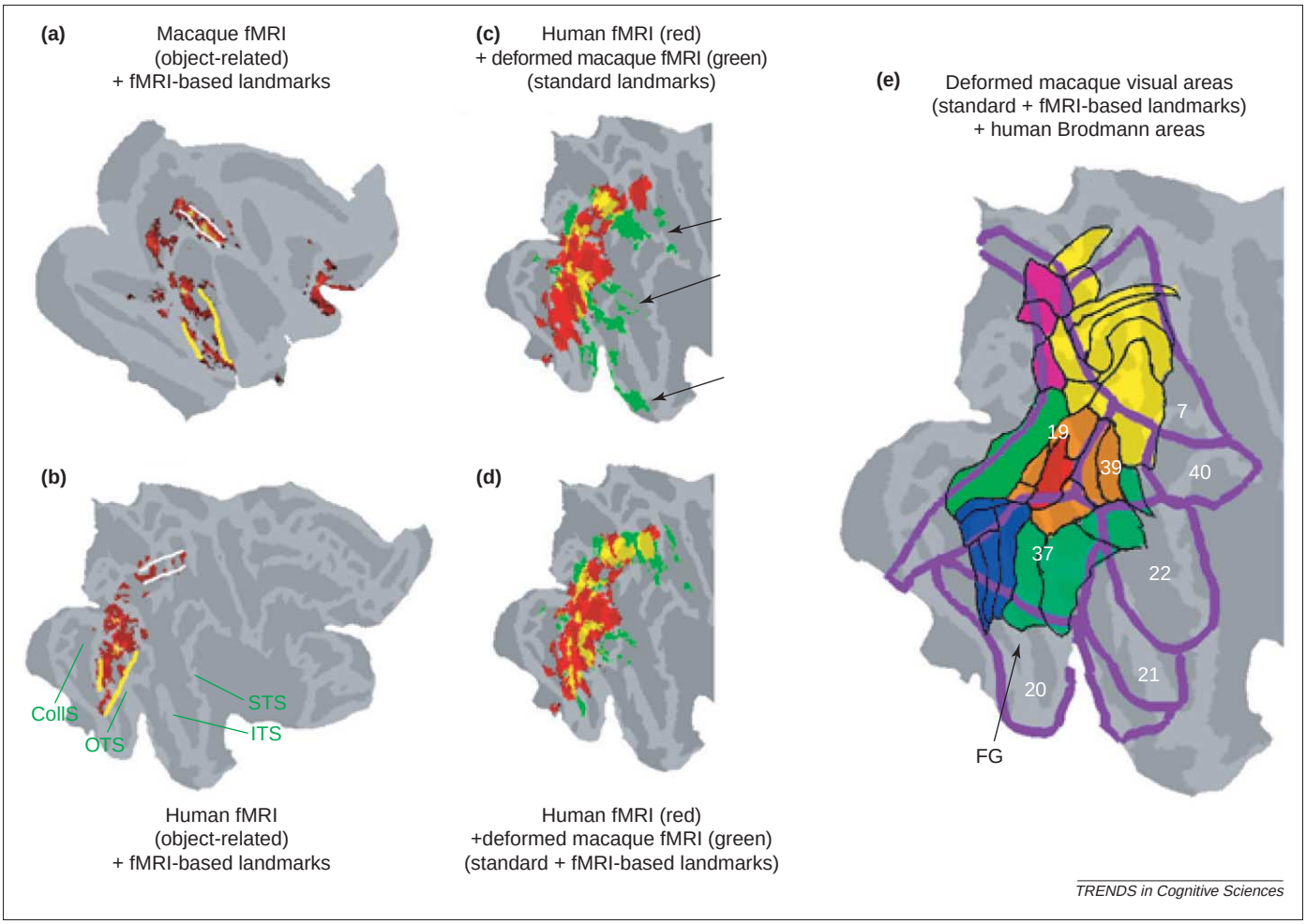

Figure 4. Additional fMRI-based landmarks and evaluation of the warpings (modified from [20]). Monkey **(a)** and human **(b)** object-related activation (SPM, $p < 0.05$ corrected for multiple comparisons; same data as in Figure 3 registered to atlas maps) with the landmark lines (white and yellow pairs) fitted. **(c,d)** Comparison of deformed monkey activation (green) and actual human activation (red) for standard landmarks (c) and standard plus functional landmarks (d). In (c) arrows point to deformed monkey activation that is located anterior to human activation. The larger extent of the red regions in (c,d) compared with the fMRI pattern in (b) reflects the inclusion of a 3 mm spatial uncertainty in mapping data to the surface (see [20], Fig. 4). **(e)** Deformed monkey areas (Figure 1b) from the fMRI-constrained warping projected onto human cortex with human Brodmann areas outlined in purple. FG: fusiform gyrus (located between collateral and occipito-temporal sulci). Other conventions as in Figure 1,2. Datasets are accessible in the SumsDB database for online surface visualization (WebCaret) or downloading and offline visualization (Caret) via http://brainmap.wustl.edu:8081/sums/directory.do?dirid=706149.

However, as mentioned earlier, human V3A is motion sensitive [42], 2D-shape sensitive [46], and involved in the extraction of 3D SFM [14,47] whereas monkey V3A is not [14,15,20].

hMT+, a complex in need of subdivision

Although there is general agreement that the posterior part of the hMT+ motion complex corresponds to macaque middle temporal area, MT, the homologues of the more anterior portions remain to be elucidated. In macaque, the satellites of MT include FST (floor of the superior temporal visual areas) and several MST (medial superior temporal) subdivisions (Figure 1b). Although most investigators are aware of the inclusion of the MST homologues in the hMT complex (e.g. [35]), the FST homologue is usually neglected. Yet FST is the main responsive element of the macaque complex, other than MT, when tested with simple translational motion [15]. Further complications could arise because additional regions in the macaque STS outside the MT complex are motion sensitive [2] and in humans a satellite of hMT+ responsive to optic flow has been described that might have no counterpart in monkeys [48].

In search of the human homologue of macaque V4

The human homologue of macaque V4 is unclear at present. Early retinotopic studies in humans [31,34] proposed that human cortex includes a ventral V4 very similar to monkey V4v [18,49], but no studies have yet revealed a retinotopic equivalent of V4d. The monkey fMRI retinotopic study [18] indicates that in macaque the retinotopic organization of ventral and dorsal V4 differ, contrary to findings regarding new world monkeys [50]. Thus there is some evidence to suggest that ventral and dorsal parts of V4 have evolved differently among primates. The region in the expected location of dorsal V4 (based on deformed macaque V4 in Figure 4e) has been assigned a variety of labels (lateral occipital complex or LOC/LOP as in Figure 1c, V3B, V4D topo), reflecting differing interpretations of an elusive retinotopy [51–53]. Denys, Orban and colleagues [20,47] refer to it as LOS, given its proximity to

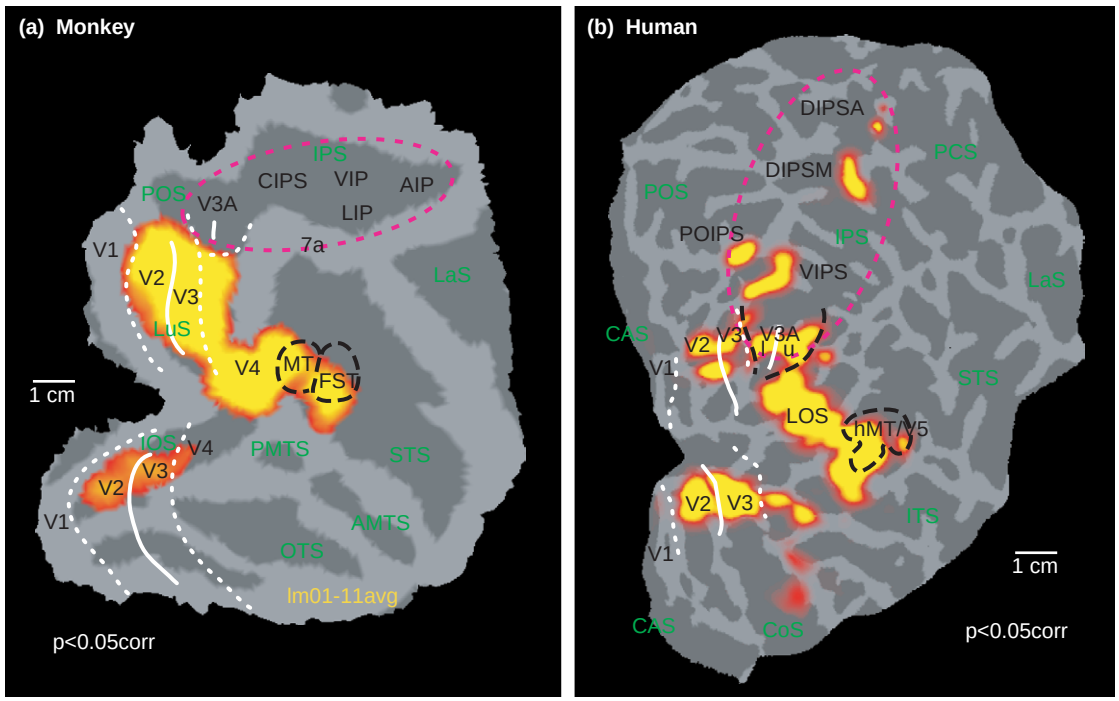

Figure 5. SPM for the subtraction of viewing 3D rotating lines minus viewing 2D translating lines ($p < 0.05$ corrected) of a single monkey **(a)** and human **(b)** subject projected on the posterior part of the flattened right hemisphere (modified from [14]). White stippled and full lines: vertical and horizontal meridian projections (from separate retinotopic mapping experiments); black stippled lines: motion-responsive regions from separate motion localizing tests; purple stippled lines: region of interspecies difference encompassing V3A and intraparietal sulcus. AMTS anterior middle temporal sulcus, CAS: calcarine sulcus, CoS: collateral sulcus, PCS: post central sulcus, PMTS: posterior middle temporal sulcus. Other conventions as in Figures 1, 3.

the lateral occipital sulcus and its 2D-shape sensitivity. It is part of the original LO described by Malach *et al.* [54], but is not included in recent descriptions of the LO complex (see [55] for review), which has two components: LO (located in posterior inferior temporal gyrus; ITG) and LOa (located in middle fusiform region). Several alternatives to the V4v plus LOS scheme have been proposed [32,56,57].

Several observations suggest that the LOS region is functionally heterogeneous. The LOS region is motion sensitive [19,58,59], but the motion-sensitive and shape-sensitive parts are not co-extensive [20]. The kinetic occipital (KO) region, which is specialized for the processing of moving boundaries [52,60,61] and is contained in the LOS region, might represent another functional subdivision. In contrast to other motion-sensitive regions [62], KO is involved in extracting 2D shape from motion, especially under active conditions [63], but also, more generally, in shape processing based on different cues [60,61,64], as has been observed in monkey fMRI experiments [65].

Human LOS and macaque V4d differ in retinotopic organization, and also in motion sensitivity [15,19] and stereo sensitivity [16]. However, they have a similar sensitivity for kinetic patterns [65] and 2D- shape processing [20], as well as for 3D SFM [14]. Thus the evidence for areal homology is roughly split in the middle. Although some functional differences between dorsal and ventral V4 have been reported in monkey fMRI studies [14,16] (Figure 5), a systematic comparison has yet to be performed.

Functional differences in higher-order regions

The IT complex: an example of 'regional' homology

The monkey IT complex and the human LO complex are relatively similar [20]. They are located in similar positions relative to neighboring regions (e.g. MT) in the brain, and they lack a clear retinotopic organization, yet there is some evidence for separate central representations in humans [55] and in monkeys [18,25]. On the one hand, in both species the activation by scrambled patterns decreases along a posterior-to-anterior gradient, object-related responses show adaptation [46,66,67], and both regions include patches specialized for face processing [17]. On the other hand, monkey IT responds less to drawings of objects than to greyscale images of objects [20], whereas the human counterpart responds equally to both types of stimuli [20,38]. Also the monkey face sensitive patches might be more specialized than their human counterparts [17]. The overall evidence favors the view of a 'regional' homology. As the exact parcellation of these complexes is still unresolved, one cannot exclude the possibility that some of the constituent areas of these complexes will turn out not to be homologous (see Box 2).

The IPS region: can the discrepancies be resolved?

As noted above, the intraparietal sulcus is expanded markedly in humans compared with monkeys. Functionally, the IPS appears very different in the two species at the areal level. In humans, Sunaert *et al.* [62] described four motion-sensitive regions along the IPS that were assigned anatomically-based labels, to avoid suggesting homologies

with monkey areas. From its ventral (occipital) end to its dorsal (anterior) end, abutting the postcentral sulcus, they described: ventral intraparietal sulcus (VIPS), parieto-occipital intraparietal sulcus (POIPS), dorsal intraparietal sulcus medial (DIPSM) and anterior (DIPSA). Subsequently, all four regions (Figure 5) were also found to be involved in 3D SFM [14,47]. As shown in Figure 3b, there is a roughly similar activation pattern associated with 2D-shape sensitivity [20]. Corresponding tests in the monkey have revealed motion sensitivity in VIP [15], as expected from single unit studies [68]; no region involved in 3D SFM (Figure 5) [14]; and two 2D-shape sensitive regions, an anterior one that overlaps with LIPd and perhaps extends into AIP plus a posterior one that does not match any of the known parcellations of posterior IPS [20].

However, other studies suggest important similarities between species in the most anterior and posterior portions of IPS. In the anterior IPS a human homologue of monkey AIP has been proposed [69,70]. In the posterior IPS, the region immediately anterior to V3A (CIPS in monkeys, and CPDR or VIPS in humans) shows sensitivity to stereoscopic depth stimuli [17,71]. This supports the notion that the most pronounced species difference is in the middle part of human IPS, as also suggested by Simon *et al.* [39]. A human homologue of macaque LIP has been proposed [37,72], a suggestion supported by a recent comparative functional neuroanatomy study [22]. These findings suggest that one or more new areas have appeared in the vicinity of the homologues of macaque LIP and AIP, but this remains consistent with a homology of IPS at the regional level.

Box 3. Questions for future research

Given the capabilities of fMRI, the number of questions that could be addressed in the future is almost unlimited.

General issues

- What is the full extent of the human visual cortex and the number of visual areas in humans and monkeys?
- At a technical level, how can we improve the criteria available for the delineation of visual areas in humans; for example, using morphological differences (e.g. [78]) or anatomical connections?
- Can we work over a broader range of species, for example other primates [7], to illuminate our quest to compare human and monkey brain? Is it feasible and acceptable to obtain functional data in great apes as well?
- Can we improve techniques for the estimation of functional connectivity between different regions in humans and monkey, to derive an additional characteristic from the fMRI data to assess homology?

Specific issues

- Establishing the homology between the different components of the middle temporal (MT) complex in humans and monkeys should be possible. Until now most of the studies have attempted to separate MT from medial superior temporal (MST), neglecting FST.
- How extensive are the functional asymmetries between upper-field and lower-field representations of the visual field, and what do these signify for partitioning into distinct areas? What are the psychophysical correlates of such functional asymmetries?
- What is V4 in humans: one entity [56], two [52], or more?
- How can we define better the retinotopic regions in humans beyond V3/V3A; not only V4, but V3B, V7, etc.?
- What is the relationship between the functional regions that begin to appear consistently in human intraparietal sulcus (IPS), notably dorsal anterior IPS (DIPSA), dorsal medial IPS (DIPSM), posterior occipital IPS (POIPS) and ventral IPS (VIPS) and the monkey IPS regions (AIP, LIPd, LIPv, CIP/LOP) (see Figure 5)?

Conclusions

The macaque is the primary animal model for neurophysiological and lesion studies of cognitive functions. Monkey fMRI is essential for establishing informed relationships between human fMRI and a diverse portfolio of non-human primate data and can pave the way for enhanced progress in systems and cognitive neuroscience (see also Box 3). Despite several functional differences, many areas are homologous, especially at early levels of the visual hierarchy. In higher-order cortex, 'regional' homology still largely applies, and further functional imaging studies should clarify many homologies at the level of individual areas.

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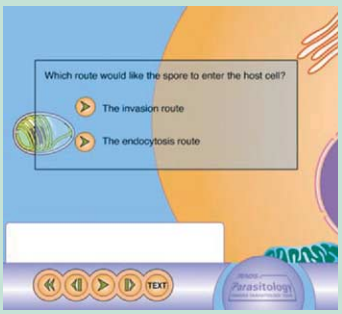

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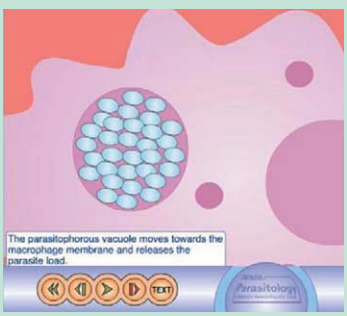

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