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# From monkeys to humans: what do we now know about brain homologies?

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Different primate species, including humans, have evolved by a repeated branching of lineages, some of which have become extinct. The problem of determining the relationships among cortical areas within the brains of the surviving branches (e.g. humans, macaque monkeys, owl monkeys) is difficult for several reasons. First, evolutionary intermediates are missing, second, measurement techniques are different in different primate species, third, species differ in body size, and fourth, brain areas can duplicate, fuse, or reorganize between and within lineages.

## Addresses

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## Introduction

The detailed homology of brain regions among monkeys, apes and humans is intrinsically interesting to evolutionary biologists. But as humans, we also have a particular interest in brain regions that are similar enough among these groups that studies of their non-human counterparts might be directly relevant to human cognition. Brain regions in humans that have changed substantially from those in other primates are also intriguing. Here, we begin by reviewing methodological issues and then consider current ideas about the homologies of cortical areas in primates with a focus on vision.

## Why a comparative approach remains important

Invasive anatomical and physiological experiments can be carried out routinely only in a small number of species of non-human, non-ape primates. In practice, these experiments have been limited to one loris (*Galago*), several New World monkeys (*Cebus*, *Aotus*, *Saimiri*, *Callithrix*) and one Old World monkey (*Macaca*). Apart from lesser apes and great apes, macaque monkeys come from the group

most closely related to humans; thus, they are the natural model system for humans. However, the last common ancestor of humans and macaques dates back to more than 30 million years ago [1]. Since that time, New and Old World monkey brains have evolved independently from the brains of apes and humans, resulting in a complex mix of shared and unique features of the brain in each group [2].

Evolutionary biologists are often interested in shared derived characters — i.e. specializations that have diverged from a basal condition that are peculiar to a species or grouping of species. Such divergent features are important for classification (e.g. a brain area that is unique to macaque-like monkeys, but not found in any other primate group). Evolutionary biologists also distinguish similarities caused by inheritance (homology), from similarities caused by parallel or convergent evolution (homoplasy — a similar feature that evolved in parallel in two lineages, but that was not present in their last common ancestor). An example of homoplasy comes from layer 4A of primary visual cortex, which stains densely for cytochrome oxidase in virtually all New and Old World monkeys, indicating that the common ancestor of this group probably had this feature. Layer 4A in apes and humans, by contrast, stains lightly for cytochrome oxidase. But one New World monkey, the owl monkey, also has a lightly stained layer 4A. Given the distribution of this feature, it is likely that owl monkeys evolved this feature in parallel with apes and humans [3].

By contrast with taxonomists, neuroscientists are usually interested in trying to determine which features are conserved across species (whether by inheritance or parallel evolution), indicating that those features might have a basic functional and/or developmental role. The only way to obtain either of these kinds of information is to examine data from multiple species.

The power of the comparative approach was re-emphasized in the study of ocular dominance columns in area V1. Originally thought to be related to stereo vision, such columns were visualized and experimentally manipulated in macaque monkeys by monocular deprivation, and were shown to be absent in 'lower' mammals such as the rat. Then it was revealed that some New World monkeys (e.g. squirrel monkeys) have poorly organized ocular dominance columns. This initially made sense because of an implicit 'Great Chain of Being' assumption: macaques are the next 'level up' from squirrel monkeys, and should, therefore, be less well organized, in similar way to 'lower'

mammals. However, squirrel monkeys appear to have good stereo vision [4]. Recent studies have shown that V1 exhibits either well-defined ocular dominance columns or well-defined angioscotomas (cortical images of the retinal blood vessel pattern unique to each eye), but not both, even within a species [5<sup>•</sup>]. It is thus possible that rather than being involved in stereo vision, the presence or absence of ocular dominance columns reflects two different possible stable outcomes — both equally useful — of the competitive growth of two sets of activity-dependent axon terminals (contralateral and ipsilateral) in the context of both of them having to maintain a high resolution retinotopic map [6]. There might even be an advantage to not having well-defined ocular dominance columns, because their absence reduces the lateral displacement on the V1 retinotopic map of the two copies of information from the left and right eyes [7]. Consistent with this idea, the visuotopic map in squirrel monkey 4C was found to be so precise that retinal blood vessel patterns generating shadows only 3 cones wide were resolved [5<sup>•</sup>].

The fact that some primate species do not have a homolog to macaque ocular columns has cautionary implications for broader assumptions about visual area homologies: it is quite possible that some areas in macaque monkeys will turn out to have no homolog in humans, and vice versa.

### The pervasive effects of body size

Another difficulty in comparing humans with monkeys is that humans have much larger bodies than monkeys. By comparing animals with different body sizes, it is apparent that the most important factor explaining brain size is body size, followed only very distantly by encephalization (i.e. brain size increase beyond that expected because of body size) [8]. In every mammalian group, larger-bodied species have larger, more fissured brains, and many times more neurons. For example, large rodents such as beavers (40 pounds) and capybaras (150 pounds) have many more sulci than smaller rodents such as rats and mice — but also more fissures than small monkeys. The same pattern holds true within primate groups. Larger members of the macaque-like monkey family such as baboons have more fissures than rhesus macaques (Figure 1; see <http://brainmuseum.org/Specimens/primates/> [macaque monkey and hamadryas baboon]). These include a deep postcentral sulcus, several additional frontal sulci surrounding and extending from the arcuate and principal sulci, and the beginnings of a frontal operculum, all of which give the brain a more human-like appearance.

Figure 2 shows a comparison between folded and inflated reconstructions of a macaque monkey, a common chimpanzee, and a human. Because there is no living 200 pound monkey from the macaque family, it is impossible to directly factor out the effects of body size from encephalization in this comparison. Nevertheless, it is clear

that the amount of non-primary cortex has increased in apes and especially humans. V1 occupies only 3% of the total volume of cortex in humans, compared with 6% of the total cortex in chimpanzees, and 11–12% in macaques. Many theories have been built around why humans acquired this ‘extra’ non-primary cortex and what they do with it. However, by inspecting many different primates ranging from humans to the tiny mouse lemur (with a cortex 1/1000 the size of a human cortex, in which V1 is 19% of its cortex), it becomes apparent that as primate body size (and, correspondingly, brain size) increases, the non-primary cortex beyond V1 systematically grows faster than V1 does in every primate [9<sup>•</sup>]. For example, within macaque-like monkeys, the larger-bodied hamadryas baboon illustrated in Figure 1 has more non-primary cortex than a macaque; V1 is about 9.5% of the baboon cortex versus 11–12% of macaque cortex. A hypothetical 200 pound macaque (4–5 times the weight of a hamadryas baboon) would probably be even more human-looking in this respect. Thus, part of the explanation for why apes and humans have so much non-primary cortex compared with monkeys is simply that they are larger-bodied primates. A similar analysis across all primate groups shows that frontal cortex also hyperscales as body size increases (visible in Figure 2). This regular and systematic relationship with size is not due to a series of grade shifts in the line leading to humans [10]; in fact, frontal cortex hyperscaling is actually greater in lemurs and lorises (strepsirrhines) than that in the primate line leading to humans (haplorhines).

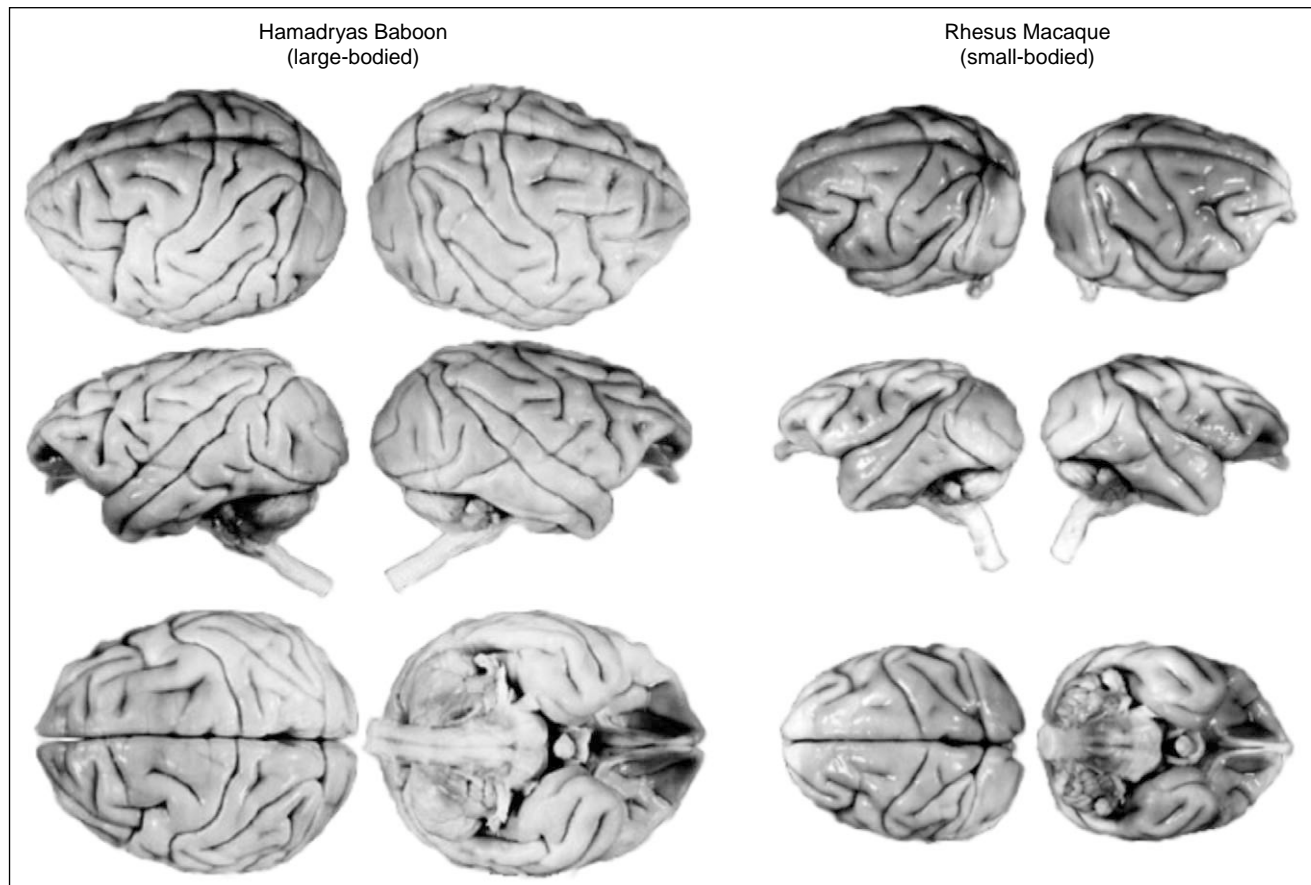
To accommodate this extra non-primary cortex, additional sulci appear (e.g. between the superior temporal sulcus and the occipital pole in chimpanzees and humans [Figure 2]). In occipital cortex, another difference is the orientation of the lunate sulcus, more commonly known in humans as the transverse occipital sulcus. Its inferior end — which is near the V1/V2 border, possibly a preferred folding margin — seems to have been dragged posteriorly as the foveal representation of a relatively smaller V1 has been drawn closer and closer to the occipital pole.

A final example demonstrating that absolute brain size cannot be considered independently of body size comes from the new dwarf hominin species, *Homo floresiensis*, just discovered on Flores Island in Indonesia [11<sup>•</sup>]. It had an extremely small body (barely 3 feet tall), and a brain that was actually slightly smaller than that of a chimpanzee — yet it was associated with a stone tool kit similar to that found alongside *Homo erectus* [12]. Taken together, this suggests that it had similar cognitive power to *H. erectus*, but with a brain half as large.

### The difficult cross-species morphing problem

Recently, computational methods for reconstructing, unfolding, flattening, sphereing and aligning the 2-D

Figure 1



The brains of two closely related Old World primates, the large-bodied hamadryas baboon (left), and the small-bodied rhesus macaque (right), are shown at the same scale in dorsolateral (top row), lateral (middle row), and dorsal and ventral (bottom row) views. The major sulci in the two animals are arranged similarly. Additional smaller sulci appear in the baboon to accommodate the larger amount of non-primary cortex in this animal (see text). Because of this, the folding pattern of the baboon appears more human-like than that of the macaque (see Figure 2). This seems to be largely due to the fact that it has a larger body than the macaque (though still only about 1/4 the size of the human body) (images from <http://brainmuseum.org/>).

cortical sheet across individual human subjects have become more widely accepted [13<sup>•</sup>,14]. There has also been a renewed interest in physical flatmounting methods applied to non-human primates [15,16<sup>•</sup>,17].

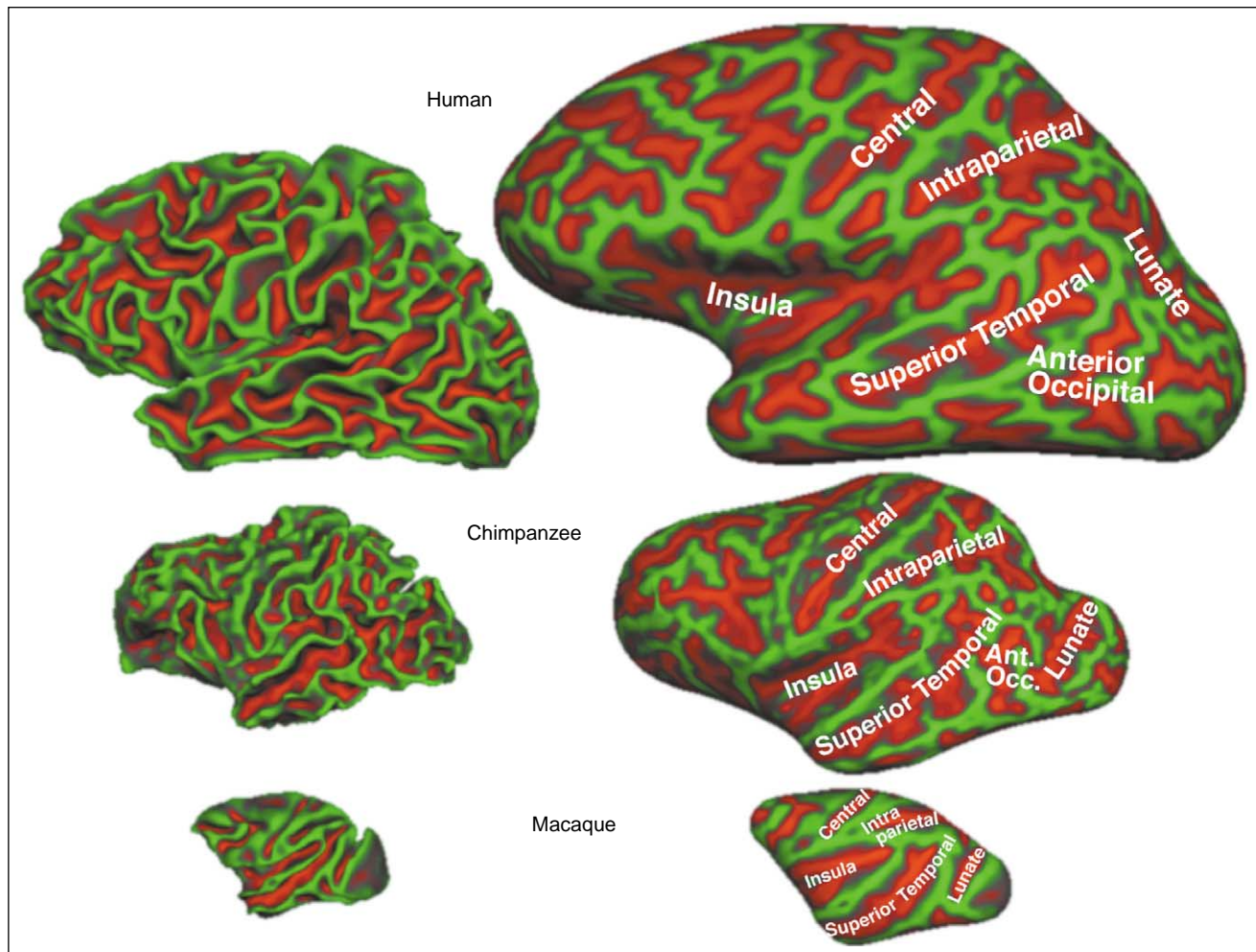
As cortical surface reconstructions have become more commonplace for non-human primates in addition to for humans, there have been several attempts to solve the more difficult problem of computationally registering the flattened or sphered cortical surfaces of a non-human primate with that of humans. The simplest approach is to stretch one brain into alignment with a target by minimizing the error in a vertex-by-vertex sulcus-likeness measure across the entire cortex [18]. However, this approach typically fails because sulci multiply rather than just expand. As the cortex enlarges, sulci such as the superior temporal sulcus do not expand nearly enough in width to accommodate the increased amount of non-primary cortex. As noted above, the extra surface area

is instead accommodated by the formation of additional intervening sulci (e.g. the anterior occipital sulcus situated in between the posterior superior temporal sulcus and the occipital pole in humans).

To overcome this problem, knowledge-based strategies have been added. Particular sulci or functionally defined landmarks (e.g. MT+, the middle temporal complex) are pinned to their human target positions and then the intervening surface points are allowed to space themselves out in between these tethers [19]. Given that it is challenging to align visual areas even across different human individuals because of their small size and somewhat variable position and orientation, it seems likely that direct macaque–human registrations are currently more suggestive than definitive. This problem will probably be ameliorated as our knowledge of cortical areas increases. Another problem is that a given set of areas might have become duplicated in one species in comparison with



Figure 2



Folded (left column) and unfolded (right column) reconstructions of the left cerebral cortex of a human, common chimpanzee, and macaque monkey are shown at the same scale. The cortical surface was reconstructed from T1-weighted MRI images and unfolded using FreeSurfer. The surface is colored according to its original local curvature (green = convex, red = concave) in both folded and unfolded views. As with the baboon compared with the macaque, additional sulci appear (e.g. the anterior occipital sulcus) in order to accommodate the larger amount of non-primary cortex that accompanies larger body size. In humans, the lunate sulcus rotates so that its ventral end is tilted posteriorly, in contrast to the posterior tilt seen in chimpanzees and macaques.

another (see below); this would make it impossible to construct a topological 1:1 map between such brains.

### Defining visual areas by retinotopic mapping

Visual cortical areas are typically small, irregularly shaped, and somewhat variable in size and location (although neighborhood relationships are usually preserved between individuals). Visual areas are most convincingly defined when multiple measures (including connections, anatomical features, retinotopy and functional preferences) can be shown to agree on borders. The first two methods are not yet practical in humans. Scan-time and head-stabilization constraints make it difficult to detect the boundaries of even architectonically distinct visual areas such as V1 across their entire extent. And although

tract-tracing methods based on measuring diffusion in a large number of directions (beyond the diffusion tensor) show promise, they have not yet passed a crucial test — tracing fibers from a retinotopically mapped point in V1 to the corresponding retinotopically mapped points in multiple target areas such as V2, V3, and MT/V5. This remains a distant (perhaps unreachable) goal given the ‘freeway ramp’ problem (tracts joining and branching off of fiber bundle ‘freeways’, but indistinguishable when running within them). Thus, retinotopy remains the technique best suited to defining areal borders in humans.

Retinotopy is a complex-valued function with respect to cortical location. At each point on the cortex, two orthogonal coordinates are needed to identify the location in

the visual field that is represented at that point – eccentricity (distance from the center of gaze) and polar angle (angle relative to the center of gaze). This poses a problem for visualization. A common way to determine the borders of areas is to measure one of these coordinates — for example the polar angle — using phase-encoded stimuli and Fourier-based analysis, and then to look for maxima or minima in this measure across cortical space. Typically, the goal is to find a maximum near the upper field vertical meridian or the horizontal meridian, or a minimum near the horizontal meridian or the lower field vertical meridian. These four kinds of inflection points are then, by convention, defined as areal borders. This method works well in the case of the canonical V1/V2 and V2/V3 borders.

Unfortunately, this approach does not work for every border. For instance, an area might adjoin the peripheral representation of another area such that the boundary is defined by maxima in eccentricity, with little change in polar angle across the border. A border of this kind is found at the peripheral representation of the horizontal meridian in MT/V5 [20].

Another complexity is that an inflection point might occur at a polar angle that is not on a vertical or horizontal meridian, if an area has a secondary discontinuity of the kind originally described between area 18 and area 19 in cats [21], and more recently discussed with respect to primate visual areas [22,23\*]. To get an idea of how this works, first imagine two areas joined at a border similar to the V1/V2 border; then make a small cut perpendicular to the border that extends into each area; now stretch the two areas (thought of as a rubber sheet) in a direction parallel to their shared border until the cut edges within the interior of each area are extended into straight lines that touch their counterparts from the other area.

Analysis of visual field sign [20,24] can recover borders in all these cases. However, using functional magnetic resonance imaging (fMRI), this approach requires a second set of scans taken at a different time using different stimuli, which can introduce systematic errors. Also, because it is based on a derivative measure, it is noise-sensitive (calculating the two gradients requires measuring changes in polar angle or eccentricity as a function of small movements in  $x$  or  $y$  along the cortical surface). Finally, it is possible that one might want to allow a single visual area to combine visual field representations with opposite visual field sign if other information strongly suggests that the composite map is actually unitary [23\*].

There is another problem with studying retinotopy in higher-tier areas. It has been shown that fMRI signals there are more strongly affected by attention than they are in early areas such as V1 (although attention effects are found in V1 too). Many of these higher areas are poorly

activated by unattended, passively viewed stimuli that strongly activate V1. This does not mean that higher areas are not retinotopically organized, but it does put an especially high premium on the subject's mental performance. Subjects must maintain a slowly and consistently moving focus of spatial attention over many minutes to avoid weakening the phase-encoded signal by introducing dropouts due to attentional lapses or worse, by introducing artifactual periodic variations in attention that can be mistaken for retinotopy. One way to help maintain attention is to use more complex stimuli within retinotopic stimulus apertures [25,26].

### Delays and inhibition

With phase-encoded methods, variations in hemodynamic response functions can perturb the estimate of response phase, leading to an error in the estimate of polar angle or eccentricity for a voxel. This can be corrected by taking measurements with the stimulus moving in opposite directions (e.g. clockwise and then counterclockwise) in order to generate a phase advance and a phase delay. By combining the two data sets, variable phase delays can then be cancelled. A subtler problem arises from neural inhibition. There is some physiological evidence suggesting that negative blood oxygenation level-dependent (BOLD) signals correspond to a reduction in neural activity below baseline [27]. Given physiological data on non-classical surround inhibition, it is likely that a moving, retinally localized stimulus, such as a rotating wedge, will generate a traveling wave of surround inhibition ahead and behind the traveling wave of excitation. If the background activity recovers to baseline when the wedge is 180 degrees away, then a second harmonic of the base rotation frequency will be generated in the voxel time course. This is often seen, and easy to remove. A more insidious problem arises when a wedge stimulus does not extend to the limiting periphery of the visual field (the usual situation). In this case, the traveling wave of surround inhibition beyond the cortical representation of the end of the wedge will have the same frequency as the base signal; but it will be 180 degrees out of phase. This could make a peripheral upper vertical meridian representation appear to be a lower vertical meridian representation, or make a contralateral horizontal meridian representation appear to be an ipsilateral response.

One recently applied method for mapping that avoids some of these problems is presents a different series of pseudo-randomized impulses at each retinal location, and then analyzes the data by deconvolution [28\*]. This approach is analogous to the linear reverse correlation method widely used to characterize the receptive fields of simple cells in V1. This method assumes linear spatial and temporal summation. In V1 at least, direct tests of spatial and temporal summation with retinotopic sector stimuli suggest that this assumption is justified for positive-going

BOLD responses, but not for negative BOLD responses [28\*].

One problem with a randomized design is that the next locus of attention is (by definition) unpredictable. This requires that the subject be ready to change their attention to any location, which then reduces the resources that can be allocated to the current focus of attention (e.g. there is fMRI evidence that the focus of attention can be split [29]). By contrast, phase-encoded designs are (mind-numbingly!) predictable. This might be an advantage for experiments in which the signal-to-noise ratio is at a premium, because there is absolutely no uncertainty as to where the focus of attention should be at each successive time point.

### Visual maps with non-retinotopic coordinates

It is possible that some multimodal maps contain visual representations that are head-centered, body-centered, or hand-centered. For example, single-unit studies have reported head-centered visual receptive fields in some neurons within macaque area VIP ventral intraparietal — that is, visual receptive fields of neurons that are approximately fixed with respect to a position on the face independent of eye position [30]. Head-centered visual maps can be distinguished from retinotopic maps only by independently varying eye position and retinotopic position. If eye position is also varied, however, it can be difficult to keep the stimulation of the retinotopic periphery constant so that retinotopic maps can be clearly distinguished from head-centered ones.

Mapping hand-centered [31] and body-centered visual representations is more difficult because even tiny head movements disrupt the signal, and limb or body motions *per se* can affect the flatness of the static B0 field, introducing task-dependent image distortions that can be mistaken for activations. The difficulty of keeping retinotopic stimulation constant (while hand position is varied) presents itself here, too.

### Somatotopy and tonotopy

The phase-encoding method described above can also be used to define somatosensory maps in unimodal somatosensory areas, or in visual areas with somatosensory inputs. One important difference between visual maps and somatosensory maps is that the somatosensory maps contain many more discontinuities with respect to the receptor surface. There are many boundaries within single somatosensory cortex body maps where nearby cortical locations across the boundary represent disparate points on the sensory surface that have non-overlapping receptive fields (e.g. receptive fields suddenly jump from the face to the arm, from one finger to another, or from one whisker to another) and anatomical discontinuities are visible at these boundaries [32]. In visual cortex, it is rare to find a true discontinuity of this kind (where a small

movement along the cortex results in a completely non-overlapping receptive field). Moreover, the barrel-like structures associated with these map discontinuities — which occur in somatosensory cortex for individual pads on a digit and for individual whiskers — are not apparent in visual cortex. This visual–somatosensory contrast probably reflects the reduced tendency for locally correlated stimulation of a complexly shaped skin receptor surface in the somatosensory system, when compared with the stimulation of the retina in the visual system.

Phase-encoded mapping methods have been successfully applied to the human auditory system also, revealing a series of six tonotopic areas similar to those originally mapped with microelectrodes in owl monkeys and macaque monkeys by Merzenich, Brugge, Imig, Morel and Kaas [33,34\*].

### Development and evolution

Soon after the discovery of MT/V5, another retinotopic area (DL, dorsolateral area) was described that appeared to surround most of MT/V5 [35]. The combination of MT and DL resembled a miniature, mirror-image version of V1 and V2. Allman and Kaas [35] speculated that visual areas, or perhaps small clusters of visual areas, might duplicate during evolution (by analogy with known instances of gene and body part duplication in evolution); then, the copy would be free to differentiate new functions. Although the details of the retinotopy of DL have since been revised — the lower field part of DL is now thought to be subdivided into at least three areas (DLp/DLc, DLi/DLr, and DLa/MTc/V4t [17,20,36,37]) — the idea of a mirror-image duplication of an area or areas remains a very influential idea. Such mirror-image duplications have even been found even in the hand representation in the somatosensory cortex of the gray squirrel [38].

Recently, the idea of mirror-image duplication has been given strong support by developmental studies [39\*]. When a second source of fibroblast growth factor 8 (FGF8; a growth factor involved in antero-posterior patterning originally studied in birds) was introduced into the developing cortex, it resulted (after maturation) in a mirror image duplication of the barrel fields just posterior to the ones in the native S-I (primary somatosensory cortex), in some cases directly adjoining it and in other cases separated from the native S-I by additional non-barrel cortex. Interestingly, this new representation was innervated by the thalamus, despite the cortical source of the developmental perturbation. The common occurrence of multiple adjacent mirror-image visual representations in large primate brains might therefore be the result of a series of as-yet-undiscovered positional factors, perhaps with more local spheres of influence. The more limited reach of growth factors in a larger brain might be one reason why larger brains can have more areas than smaller brains.

### Areas surrounding MT/V5

A good illustration of the problems faced in drawing homologies between non-human primates and humans comes from the areas around MT/V5. In owl monkeys, MT was originally defined as a small, densely myelinated oval containing a complete representation of the visual field without any discontinuities that was direction-selective, similar to macaque V5. Later work showed that it was surrounded by several smaller areas, including MST (medial superior temporal area) superiorly (which itself is subdivided into two parts), FST (fundus of the superior temporal sulcus area) anteriorly and ventrally (also subdivided into two parts), a thin crescent posteriorly (DLa/V4t/MTc), and possibly even a small contact with V4v/VA and/or posterior inferotemporal cortex. Some of these areas are very small; for example, the area DLa/V4t/MTc represents the entire lower quadrant in a thin strip less than 1 mm wide in owl monkeys. Retinotopically mapping such an area in humans would be difficult because the entire area is probably contained within a single voxel, even after accounting for its larger than expected size in humans. In light of this, the area identified by a contrast between moving and stationary patterns (MT+) might contain areas beyond MT and MST.

One way to solve the problem of blurred retinotopy in fMRI studies is to use an array of many receive-only surface coils coupled with higher fields to enable the use of smaller voxels. This technology has very recently become available and is just beginning to be exploited. As the field strength increases, however, spatial distortions due to magnetic-field-susceptibility-induced deviations in the flatness of the static ( $B_0$ ) field become more severe. These can be corrected by higher order shimming and by post-hoc image unwarping using additional scans to estimate the deviation from flatness of the  $B_0$  field (e.g. [40<sup>•</sup>]); however, these techniques have not yet been widely applied. Another promising approach is to use contrast agents to improve the signal-to-noise ratio of blood volume measurements.

### Posterior superior occipital cortex

The detailed organization of the region anterior and superior to V3d remains controversial, both in non-human primates and in humans. Early reports in owl monkeys that there were several areas containing both lower and upper visual fields directly bordering V2 [41] have been challenged. A recent examination of owl monkey retinotopy using optical imaging with meridian-mapping and lower-field-only stimuli provided data consistent with a lower-field-only macaque-like V3 adjoining the anterior border of V2 [42]; however, the key test of an upper-field-only stimulus was not performed. High-density microelectrode recording experiments [20] following up on the original description of V2-adjoining upper-field-containing areas DI and DM (dorsointermediate and dorsomedial areas), suggest that upper fields directly adjoin a portion

of lower field V2. This is inconsistent with a continuous, lower-field-only V3. Because the superior direction-selective area in both humans (V3A) and owl monkeys (DM) contains upper and lower fields, it is possible that a lower-field-only direction-selective macaque V3 is a unique feature of macaque-like monkeys. The peculiar function of human V3 — if it has one — remains to be revealed.

A new retinotopic area in humans has been reported on the medial wall, in the posterior part of the parieto-occipital sulcus [43<sup>•</sup>]. This area has an extensive representation of the periphery, and in fact is difficult to activate without a wide field retinotopic stimulus. It might be homologous to macaque V6 [44] (which partially overlaps with the earlier-defined PO), and possibly also to owl monkey area M [45], both of which were reported to emphasize the periphery. However, an alternative scheme divides PO (parieto-occipital area) into two areas, DM and P<sub>Om</sub> (PO medial), and suggests that DM = V6 and P<sub>Om</sub> = M [46].

### Parietal visual areas

The initial report of a retinotopic area in parietal cortex [47] used a 1.5 T magnet and an occipital placement of a surface coil. Recent investigations using higher fields and a larger effective field of view have suggested that there might actually be more than one retinotopic area in the approximate location reported for putative human LIP (lateral intraparietal area) [48<sup>•</sup>]. Moving anteriorly from V3, the progression of areas would then be: V3A, V7, posterior 'LIP', and anterior 'LIP'. Some accounts include an area V3B ventral and anterior to V3A. Multiple areas between V3A and LIP were previously reported in several monkeys [49–51].

### Inferior areas anterior to VP/V3v

In inferior occipital cortex of humans, the region anterior to VP/V3v was originally found to contain an upper field representation that joined VP/V3v on an upper field vertical meridian [24]. This resembled the situation in owl monkeys and macaque monkeys, in which receptive field mapping in combination with callosal termination patterns had revealed two upper field representations (VP and VA in owl monkeys; V3v and V4v in macaque monkeys) joined at the vertical meridian in this position [52–54]. The human area was named V4v by analogy with macaques.

The organization of the region anterior to V4v in non-human primates remained disputed. In macaques, another thin upper-field-only area (VOT) adjoining the anterior horizontal meridian border of V4v/VA has been proposed [49]. In both macaques and owl monkeys [53], there is a second weaker band of callosal terminations, probably indicating another vertical meridian representation, just anterior to the anterior border of V4v and VA, which is consistent with (and partly gave rise to) this idea.



Anterior to the second callosal band in macaques are one (TEO) or two (PITd, PITv; posterior inferotemporal area, dorsal and ventral divisions) areas that were suggested to be roughly retinotopic [49,54]. A connection-based parcellation of two moderately retinotopic posterior inferotemporal areas was also reported in owl monkeys [55]. However, that study did not distinguish VP from VA, nor VP+VA from another thin VOT-like area anterior to them but posterior to inferotemporal cortex proper.

In humans, evidence was presented for a color-selective area, V8, containing a complete hemifield representation anterior to upper-field-only V4v, with its horizontal meridian oriented perpendicular to the V2/VP and VP/V4v borders, its upper field medial and lower field lateral, and its center of gaze anterior [56]. A second proposal is that V8 (as described above: horizontal meridian perpendicular to the V2/VP border) should be called human V4, and that there is no additional V4v-like upper-field-only area in humans between V4 and VP [57]. A third group presents evidence in favor of yet a different scheme for an upper-and-lower field human V4 (hV4): its posterior upper field portion resembles V4v, its horizontal meridian is parallel to the V2/VP and VP/V4 borders, and its center of gaze is near the confluence of the center of gaze of V2 and VP [58<sup>\*</sup>]. Wandell *et al.* also argue for another more medially placed representation of the entire hemifield (VO-1). It should be noted that the contour plots shown in Figure 3 in Hadjikhani *et al.* [56] are consistent with the existence of additional representations superior and anteromedial to V8.

Beyond the upper-field-only VP, these three mapping schemes are all inconsistent with each other (and with the monkey data reviewed above). The experimental conditions were relatively similar except for the fact that the third group used a stimulus that extended to a much smaller maximum eccentricity (~3 deg versus 30 deg). The competing schemes group different sets of upper and lower fields into single areas. Perhaps a higher-resolution study of visual field sign together with functional properties will be able to settle this issue definitively in the future.

### Frontal visuomotor cortex

The human frontal eye fields are located more posteriorly and superiorly than they are in New and Old World monkeys as a result of frontal cortex hyperscaling described above. Several recordings from monkey frontal cortex lateral to the eye fields have shown that neurons are sometimes activated there during observation of the performance of an action. Lateral frontal activity has been recently demonstrated in humans watching point-light motion when compared with that of those watching scrambled point light motion [14]. Also, there is evidence that both the frontal eye fields and the more lateral frontal areas involved in working memory [59<sup>\*</sup>] show a degree of retinotopy in both non-human primates and humans [60,61<sup>\*</sup>].

### Conclusions

After many decades of cortical mapping, it is humbling to see how much work remains to be done. Perhaps only the homologies of V1, V2 and MT/V5 in monkeys and humans are completely without dispute. Our review suggests that considerable uncertainty remains for most of the remaining retinotopically mapped areas. Even areas with the same generally accepted name can have very different functional properties; for example, the sensitivity to motion of human V3A resembles that of macaque V3, not macaque V3A.

A fruitful avenue remains the repeated scanning of small groups of well-trained subjects who are extremely familiar with the milieu of the scanner and who can precisely control their attention and head movements, in the spirit of psychophysical investigations.

It is likely that there will be considerable improvement in signal-to-noise ratios by using many-element phased array coils. Another area for improvement is distortion correction through the use of additional field-mapping or point-spread-function mapping scans. This is particularly crucial to achieve accurate overlays of functional data onto the reconstructed cortical surface at higher fields.

The moderately large number of partly overlapping area names is unavoidable in the early stages of a taxonomy and is likely to persist for some time, especially between species. One can hope the different groups will read each other's papers and prune names when appropriate.

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