Borders of Multiple Visual Areas in Humans Revealed by Functional Magnetic Resonance Imaging


The borders of human visual areas V1, V2, VP, V3, and V4 were precisely and noninvasively determined. Functional magnetic resonance images were recorded during phase-encoded retinal stimulation. This volume data set was then sampled with a cortical surface reconstruction, making it possible to calculate the local visual field sign (mirror image versus non–mirror image representation). This method automatically and objectively outlines area borders because adjacent areas often have the opposite field sign. Cortical magnification factor curves for striate and extrastriate cortical areas were determined, which showed that human visual areas have a greater emphasis on the center-of-gaze than their counterparts in monkeys. Retinotopically organized visual areas in humans extend anteriorly to overlap several areas previously shown to be activated by written words.

Over half of the neocortex in nonhuman primates is occupied by visual areas. At least 25 visual areas beyond the primary visual cortex (V1) have been identified with a combination of microelectrode mapping, tracer injections, histological stains, and functional studies (1). The analysis of this data has been greatly aided by the use of flattened representations of the cortical surface made from conventional sections with graphical techniques (2) and flattened wire models (3), or more directly from sections of physically flat-mounted cortex (4).

A large portion of the neocortex in humans is likely to be occupied by visual areas too. It has been difficult, however, to outline unambiguously any human cortical area with noninvasive techniques. Previous studies have mapped only a few locations in the visual field or have relied on stimulus features to activate different areas (5), and the tortuous convolutions of the human neocortex have defied previous attempts to see activity across all of its surface area at once.

Many of the cortical visual areas in nonhuman primates are retinotopically organized to some degree (3, 6). These areas are irregularly shaped and somewhat variable in location; consequently, recordings from many locations (400 to 600) in single animals have been required to define areal borders with confidence (7). Here we demonstrate a technique for generating retinotopic maps of visual cortex in humans with a precision similar to that obtained in the most detailed invasive animal studies. Responses to phase-encoded retinal stimulation (8) were recorded with echo-planar functional magnetic resonance imaging (MRI) (9) and analyzed with a Fourier-based method. The resulting volume data sets were sampled with a cortical surface reconstruction made from high-resolution structural MRI images collected separately for each participant (10). The cortical surface containing the data was then unfolded and analyzed with the visual field sign method to distinguish mirror image from non–mirror image representations (7). By combining these four techniques (multislice functional MRI, stimulus phase-encoding and Fourier analysis, cortical surface reconstruction, and visual field sign calculations), it was possible to reconstruct the retinotopic organization of visual areas V1, V2, VP, V3, and V4 in humans in two dimensions and to accurately trace the borders between these areas in the living human brain.

To map polar angle (angle from the center-of-gaze), we obtained 128 asymmetric spin echo MRI images (11) of 8 to 16 oblique sections perpendicul ar to the calcarine sulcus (1042 to 2048 total) in a 512-s session (~8.5 min) while participants (n = 7) viewed a slowly rotating (clockwise or counterclockwise), semicircular checkerboard stimulus. Eccentricity (distance from the center-of-gaze) was mapped with a thick ring (dilating or contracting) instead of a semicircle. These four kinds of stimuli elicit periodic excitation at the rotation or dilation-contraction frequency at each point in a cortical retinotopic map (8, 12). The

expression in Escherichia coli as described by X. Liao, K. R. Clemens, J. Cavanagh, L. Tennant, and P. E. Wright (Biomed. NMR, 4.33 (1994)). We performed the NMR experiments at 300 K at a 1H frequency of 500 MHz. Typical body water spectra were acquired with a 0.5-s multiplication of T2-1-J-in-0.30 mN phosphate buffer (pH 6.5) in a mixture of 90% H2O and 10% D2O containing 30 mM NaCl, 5 mM deuterated dithiothreitol, and 50 μM ZnCl2.

7. Analysis of the data accounting for both dipolar relaxation of the 1H spin mediated by its directly attached proton and relaxation caused by chemical shielding anisotropy, was based on the classical expressions (9)

\[
T'_1 = \sum_i a_i J_{i\alpha}
\]

\[
T'_2 = \sum_i b_i J_{i\alpha}
\]

\[
\eta = 1 + \sum_i a_i b_i J_{i\alpha}
\]

with constant coefficients \(a_i\), \(b_i\), and \(c_i\). The power spectral density \(J_{i\alpha}\) reflects molecular dynamics processes (intramolecular dynamics as well as overall rotational tumbling) and is sampled at frequencies \(\omega_{\alpha}\), which are combinations of the 1H and 19F Larmor frequencies \(\omega_{\alpha}\) and \(\omega_{\alpha}\).


13. Structures were calculated from 1284 NOE distance constraints and 45 dihedral angle constraints by variable target function distance geometry and restrained molecular dynamics (X. Liao and P. E. Wright, unpublished data).


17. Contributions from aggregation can be excluded as a result of the excellent agreement found between the effective rotational correlation time obtained by tryptophan fluorescence depolarization measurements at a 2F-1 concentration of 50 μM and that derived from NMR relaxation measurements of more than 10-fold higher concentration (X. Liao, R. Brüschweiler, D. Millar, P. E. Wright, unpublished data).


20. It is not possible to specify uniquely the relative orientations of the diffusion tensors as a consequence of the transformation properties of the responsible spin interactions. The relaxation data cannot distinguish between orientations that relate individual domains by an orthorhombic symmetry transformation of the diffusion tensor ellipsoids. This means that a 180° rotation of any of the domains about the x, y, or z axes of their diffusion frames leaves the relaxation parameters unchanged.


23. We thank T. Macke for making Fig. 1 (with graphics program AVS) and D. Millar and J. Gottleder for helpful discussions. X.L. is a recipient of the Cancer Research Institute-Miriam and Benedict Wolf Fellowship. This work was supported by grant GM 58543 from the National Institutes of Health.

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phase of the periodic response at the rotation or dilation-contraction frequency, measured with the (complex-valued) Fourier transform of the response profile over time at each voxel, is closely related to the polar angle or eccentricity represented at that cortical location (13). This technique results in high signal-to-noise ratios (because at any one point in time, approximately one-half of each visual field map will be activated) yet provides fine spatial resolution. Common (for example, retinal) and between-area phase delays can be removed and examined by considering clockwise-counterclockwise rotation and expansion-contraction pairs (14, 15).

Figure 1A shows a color plot of the response to a dilating ring on a medial view of the cortical surface of the brain of this participant (A.M.D.) (16). The hue of the color at each cortical surface point indicates the response phase, which is here proportional to the eccentricity of the local visual field representation. In Fig. 1B the cortical surface was unfolded. This process is similar to inflating a crumpled balloon except that the surface has not been stretched. In Fig. 1C, the occipital lobe region containing the activated area has been cut off and the resulting approximately conical surface cut again along the fundus of the calcarine sulcus to allow it to be flattened completely (17).

There is a systematic increase in eccentricity (red to blue to green to yellow to red) moving anteriorly along the medial wall of the occipital cortex. Lines of isoeccentricity run approximately in the coronal plane, cutting across several areas, as shown below. Ventrally, the region showing substantial retinotopy extends almost to the anterior-posterior midpoint of the unfolded ventral temporal lobe.

A parallel treatment of data from the rotating hemifield stimulus collected a few minutes later is shown in Fig. 1, D and E. The color again indicates the phase of the periodic response, which is now proportional to the polar angle of the local visual field representation. The picture of polar angle is more complex, alternating between vertical and horizontal meridians both dorsally and ventrally. The upper field vertical meridian is red, the horizontal meridian is blue, and the lower field vertical meridian is green. Several alternations between red and blue stripes are visible ventrally, whereas several alternations between green and blue stripes are visible dorsally. Mapping experiments in monkeys suggest that several additional re-representations of the lower visual field adjoin V1 dorsally, including V2 (second visual area) and V3 (third visual area), whereas several re-representations of the upper visual field adjoin V1 ventrally, including V2, VP (ventroposterior area), and V4v (V4 ventral) (18). In particular, we would expect vertical meridian representations at the dorsal and ventral V1-V2 border, the ventral VP-V4v border, and the dorsal V3-V4 border, and horizontal meridian representations near the fundus of the calcarine sulcus in V1, at the dorsal V2-V3 border, at the ventral V2-VP border, and at the anterior border of ventral V4v (4, 6, 7). Candidates for all of the borders are visible in

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**Fig. 1.** Isoeccentricity and isopolar angle maps of human visual areas. The top row shows isoeccentricity coded by color [red (fovea) → blue → green (paraventral) → yellow → red (periphery)] displayed on the original cortical surface (A), the unfolded cortical surface (B), and the cut and flattened cortical surface (C). The bottom row shows polar angle [red (lower vertical meridian) → blue (horizontal meridian) → green (upper vertical meridian)] plotted on the same three surfaces (D), (E), and (F), respectively. Local eccentricity and polar angle were determined by considering the phase of the response to a slowly dilating ring or a slowly rotating hemifield at the dilation or rotation frequency. The unfolded representations in (B) and (E) were made by relaxing the curvature while approximately preserving local area and local angles (the sulcal cortex is dark gray and the gyral cortex light gray). The flattened representations in (C) and (F) were made with the same algorithm after the occipital lobe was cut off and an additional cut in the fundus of the calcarine sulcus was made.

**Fig. 2.** Analysis of the data in Fig. 1 by visual field sign (mirror image versus non-mirror image visual field representation). Mirror image areas (yellow; for example, V1, and non-mirror image areas (blue; for example, V2) are shown in a medial view on the folded (A) and unfolded surface (B) and in a ventral view, folded (C) and unfolded (D). The incision in the fundus of the calcarine is visible in (B). Ventral V1, V2, VP, and V4v (18), comprising four representations of the upper visual field, are visible below the incision, whereas lower visual field V1 and V2 are visible above the incision. The complex folding pattern of the occipital lobe coupled with the weak correlation between sulci and areal boundaries underscores the need for an unfolded representation.
Fig. 1, D and E. Mapping experiments in monkeys have also revealed a number of small visual areas beyond those mentioned so far (including the parietal-occipital area), which may help to explain the presence of several small patches of lower field dorsally as well as upper field ventrally.

Isoeccentricity and isopolar angle maps define two independent coordinates of retinotopy. Areal borders in either one of these maps, however, are often subtle; isoeccentricity lines can extend straight across several areas, whereas polar angle maps often show only a shallow maximum or minimum at the border of an area. For example, the red stripe at the ventral upper field vertical meridian border of V1-V2 actually extends across both V1 and V2. In contrast, the visual field sign technique (7) provides an objective means to draw borders between areas on the basis of an analysis of the local relation between the directions of the fastest rate of change in these two coordinates. Regions of the cortex that contain a retinotopic map, however, distorted, can be divided into two categories when viewed from the cortical surface: those that contain a mirror image representation of the visual field (like V1) and those that contain a non-mirror image representation of the visual field (like V2). This distinction is unlikely to be of any fundamental functional significance, but it provides a convenient way to draw borders between areas because adjoining areas often have the opposite visual field sign. It is a local measure that can be calculated for each small patch of cortex given dense retinotopic mapping data like those obtained here.

A map of visual field sign is shown on the folded and unfolded surface in a medial view (Fig. 2, A and B) and in a ventral view (Fig. 2, C and D) (19). V1 is now clearly outlined as a large mirror image patch (yellow) divided by our incision at the fundus of the calcarine sulcus. V2 forms two non-mirror image patches (blue) dorsally and ventrally. Two more areas are visible ventral and anterior to ventral V2: mirror image VP (yellow) and, finally, non-mirror image V4v (blue).

In Fig. 3, the cortex has been completely flattened, exposing the dorsal and lateral areas of V1-V2 in Fig. 2. Dorsal V2 is adjacent anteriorly by a thin band of mirror image V3 (yellow). Just ventral and anterior to V3 the visual field sign pattern degenerates into noise near the center-of-gaze representations of V1 and V2, likely the result of the difficulty of mapping foveal cortex with this technique (20). Dorsal and anterior to V3 there are additional non-mirror image areas (blue) containing both upper and lower visual field representations that may correspond in part to V3A (V3 accessory) and dorsal V4 (not labeled). Even further anteriorly, areas are less obviously modulated at the stimulus rotation or dilatation-contraction frequency, indicating that they are either foveal (<0.5°), peripheral (>12°), or less well organized retinotopically. Similar results were obtained from six other individuals.

The areas revealed in these experiments show a number of similarities to areas originally discovered in nonhuman primates. A schematic comparison of the human visual areas with macaque monkey visual areas (21) and owl monkey visual areas (7) is shown in Fig. 4. At the top, the three flattened cortices are drawn at the same absolute scale, whereas at the bottom, they are approximately scaled by the area of V1. It has long been known that V1 in humans is shifted medially around the occipital pole when compared with the location of V1 in monkeys. The larger size of some human extrastriate areas relative to human V1 may have partially compensated for this shift.

Fig. 3. Visual field sign displayed on the completely flattened occipital cortex (brightness indicates significant response). Upper visual field V1, V2, VP, and V4v and lower visual field V1, V2, and V3 are now all visible. There are several robustly responding non-mirror image regions anterior to dorsal V2 and V3 that may correspond in part to V3A and dorsal V4 (not labeled). Regions with dimmer coloration may represent the central fovea (20) or the visual field beyond 12° eccentricity, or they may be less retinotopic.

Fig. 4. Schematic summary of retinotopic visual areas in the owl monkey (7), the macaque monkey (21), and the human (present study) at the same scale (A) and approximately normalized by the area of V1 (B). (Human V1 is twice the area of macaque V1, with larger ocular dominance columns and cytochrome oxidase blobs, but a similar number of cells.) Visual areas in humans show a close resemblance to visual areas originally defined in monkeys. The anterior border of the visual cortex in humans was estimated by using the superior temporal sulcus and intraparietal sulcus as landmarks. In (C), the mapping functions (heavy lines; scale is on the right axis) are shown for the upper field representations of human V1, V2, VP, and V4 (24). The V1 mapping functions for owl monkeys (OM°, dotted) and macaque monkeys (MM°, dashed) shown at the left were scaled up to match the overall size of human V1 (25). An increased emphasis on the center-of-gaze in human V1 is evident. OM°, cortical magnification factor.
 Results of experiments designed to examine cortical responses to more complex and meaningful stimuli such as pictures, words, scenes, and sentences. It is interesting to note that several of the foci identified in previous noninvasive and invasive studies of responses to complex stimuli such as words (28) may overlap retinotopically organized areas already known from nonhuman primates. The techniques used here could be adapted to map toponoty and amplitropy in the auditory cortex and somatotopy in the somatosensory cortex.

REFERENCES AND NOTES


11. Eye-planar images were collected on a 1.5-T scanner (GE Signal) with full-body gradient coils (Advanced NMR) by using an asymmetric spin echo sequence [2.4 ms, TE (echo time) = 70 ms, TR (repeat time) = 3000 to 4000 ms] [G. L. Wismer et al., J. Comp. Assist. Tomogr. 12, 259 (1988); J. R. Baker et al., Proc. Soc. Magn. Reson. Med., 12, 1400 (1993); R. H. Tootell et al., J. Neurosci., in press]. A 5-inch receive-only surface radio frequency (RF) coil or a receive-only wrap RF coil was positioned near the occipital pole. Eight to 16 successive images (frequencies ~2 to 3 mm by 3 mm by 4 mm) were chosen to lie approximately perpendicularly to the calcarine sulcus. Before and after the set of functional scans, a scan was recorded to monitor the T1 values of the eye-planar images [spin echo inversion recovery sequence: TE = 40 ms, TI (inversion time) = 1500 ms, TR = 20,000 ms, NEX = 1, yoked for all images in the same orientation, slice thickness, and field of view as the functional scans. We used the T1 sequence to align the functional scans with the higher resolution structural scan (voxel size: 1 mm by 1 mm by 1 mm) used for surface reconstruction that were collected in a separate session with a head coil.

12. The visual stimuli were generated in real time on a Silicon Graphics Onyx computer with GL graphics library functions. The position of the green blue (RGB) video output signal was subsampled and converted to a composite video signal that was used to drive a Sony 2000 color liquid crystal display (LCD) projector. Informed consent to these experiments was obtained from the participants, several of whom were also authors (M.S., A.M.D., R.B.H.T.). Supine participants looked up into an adjustable angled mirror that allowed them to comfortably view a frosted back-projection screen arranged perpendicular to the bore just below their chin. Residual head movements were controlled through the use of a dental impression bite bar that allowed a participant to support this view. Care was taken to block the participant’s direct view of the screen. Participants were given the opportunity to view the visual field before the scan as a prophylactic against the minor discomforts that typically accompany attempts to remain still for extended periods of time. Images were projected onto the retina via a retinal prosthesis and subtended a maximum visual angle 35° wide and 26° tall. Stimuli consisted of black and white checkerboard patterns that flickered at 4 Hz (the mean frequency for both black and white was 2 Hz). The pattern was scaled with eccentricity. These patterns stimulated a circle in the visual field with a radius of 10° to 13°. The rings and hemifield stimuli were designed to activate approximately half the fovea and the other half of the visual field with a radius of 10° to 13° of the retina at any one point in time.

13. The time series of activation (across the 128 images of each slice) was examined on a pixel-by-pixel basis. The linear trend and baseline offset for each pixel time series was first removed by subtracting off a line fitted through the data by least squares. The discrete Fourier transform of the time series for each pixel was then computed to give 128 complex values. In retinotopically organized areas, the amplitude spectrum showed a sharp peak at the stimulus rotation or dilation-contraction frequency (~0.015 Hz) to 50 times as large as the peaks at other frequencies. The phase angle of this frequency was measured by subtracting off the known order in which the slices were collected (1, 3, 5, 2, 4, 6, ...). Finally, the phase angles were mapped to different hues whose intensity was proportional to the amplitude at the stimulus frequency and the average amplitude of all other frequencies (this ratio can reach 25 to 30 in V1). Our basic procedure is closely related to correlation of the signal with a sinusoid [compare P. A. Bandettini et al., Magn. Reson. Med. 25, 390 (1992); P. A. Bandettini, A. Jesmanowicz, E. C. Wong, J. W. Hyde, ibid., 30, 161 (1993)].

14. In general, the phase of the periodic response will be delayed because of a finite vascular response time. The basic stimulus frequency was low enough so that there was no whole-cycle phase ambiguity. Retinal delay was to be determined by subtracting off the temporal average of the phase angles obtained for opposite directions of stimulus motion (contraction versus expansion, clockwise versus counterclockwise) at each voxel after the phase angles for the opposite stimulus direction were corrected around 0°.

15. We rejected scans in which substantial movement (~2 mm) had occurred. This was easily recognized by viewing the anatomical scans for each slice. Nevertheless, even in the presence of such movements, a sharp peak at the basic stimulus frequency (~0.015 Hz) was usually larger than the lower frequency peak (less than 0.005 Hz) for movement. Note that we have deinterleaved sampled a continuous function: the integral of a given voxel over time. Because that signal has not been explicitly limited in bandwidth.
before sampling, there is also the danger that frequencies higher than the Nyquist critical frequency $(f_c = 1/2 \Delta f = 0.12 - 0.25 \text{ Hz for } 7\mu = 2000$ to 4000 m/s) could alias back into the spectrum we intended to measure. Changes in the signal due to blood oxygenation are unlikely to be fast enough to cause such a problem. Artificial signals due to brain motion caused by rapid head motion were controlled through the use of a bar. Brain movement artifacts induced by cardiac pulsation are potentially more problematic; however, there is enough variation in frequency and phase of the cardiac signal to avoid the generation of large aliased peaks in the Fourier amplitude spectrum given the number of stimulus cycles used in the present study.

16. To paint the functional data onto the cortical surface, blink comparison in three orthogonal planes was first used to align the echo-planar inversion recovery images (3 mm by 3 mm by 4 mm, taken in the plane of the functional images) with the high-resolution data set (1 mm by 1 mm by 1 mm) used to reconstruct the cortical surface (17). The functional data set was then sampled with the cortical surface. By using a surface nearer to the gray-white matter border than to the pial surface, we were able to accurately assign activations to the gray matter, even in a sulcus despite the fact that the individual functional voxels were comparable in size to the thickness of the cortex. Our success in this endeavor is demonstrated by the lack of ambiguity in recovering the closely apposed upper and lower visual field representations situated on opposite sides of the calcaneus sulcus. The lower resolution activation data (one sample = 3 mm by 3 mm) was smoothly interpolated onto the high-resolution surface reconstruction (one polygon = 1 mm by 1 mm).

17. The folded, unfolded, and flattened surfaces were made from high-resolution T1-weighted images (1 mm by 1 mm by 1 mm) optimized for gray-white matter contrast with techniques similar to those presented in (10) [compare E. L. Schwartz, in Computational Neuroscience, E. L. Schwartz, Ed. (Wiley, New York, 1990), pp. 295–315; and G. J. Carman, thesis, Columbia Institute of Technology (1990)]. The skull was first automatically stripped off by “shrink-wrapping” a stiff deformable template onto the brain. The gray-white matter boundary for each hemisphere was then estimated with a region-growing method. The result was tessellated to generate a surface (~150,000 vertices) that was refined against the MRI data by using a deformable template algorithm, inspected for topological defects (for example, “handles”), and remade if necessary. It was unfolded by area-preserving curvature reduction. A completely flattened cortical surface was obtained by cutting off the occipital lobe and inscribing the fundus of the internal occipital fissure. The resulting surface fragment was then pushed onto a coronal plane in one step and unfurled on the plane. The vertex update rule was modified from that in (10) to include both local area-preserving and shear-minimizing terms. Beautiful images of the cortical surface can be generated by rendering stacked slices [H. Damasio and R. Frank, Arch. Neurol. 49, 137 (1992)]. Such images, however, lack explicit information about the cortical surface orientation and connectivity required for cortical unfolding. It is possible to trace the cortical ribbon in individual slices and manually connect them into a surface [M. L. Juan-"{a}pez et al., J. Comp. Neurol. 1, 88 (1989)], but these techniques are difficult to implement in regions where sulci run nearly parallel to slices, as they do in any slice plane through the occipital lobe.

18. Area VP has sometimes been labeled V4 (ventral V3), and area V4V has sometimes been labeled VA (ventral occipital area). More definitive statements of homology await future studies of the functional properties of these retinotopically defined regions in humans.

19. The gradients in retinal eccentricity and polar angle with respect to cortical x and y, $\nabla_x$ and $\nabla_y$, are vector quantities whose norms have units of de- grous per millimeter (the reciprocal of the magnification factor). They were computed by fitting a plane to the r (or $\theta$) values of the current vertex and its immediate neighbors with least squares. The clockwise angle, $\alpha$, between $\nabla_x$ and $\nabla_y$ was then measured to determine whether the local representation of the visual field at that vertex was non- mirror image (a near r2) or mirror image (a near $\pi$). Finally, the intensity of the field sign coloring at a point reflected the significance of the eccentricity and polar angle data sets.

20. The limited resolution of the video projector made it difficult to present checkerboard patterns scaled with eccentricity near the center-of-gaze while still covering a reasonable amount of visual angle peripherally. Small imperfections in fixation also have a much more deleterious effect at the center-of-gaze than they do in the periphery. In order not to occlude the fixation cross, the central 0.5° of the ring and semicircle stimu- large were omitted. These considerations lead us to expect the periodic signal to fall off in the foveal parts of the visual field. The region of the visual field we hoped to be represented was expected to be represented across several square centimeters of cortex just anterior to the occipital pole on the lateral surface of the brain. Mapping this region would require high resolution and additional averaging to overcome fixation jitter.


24. The falloff in the linear cortical magnification factor, M (millerimeters of cortex per degree of visual angle), with increasing eccentricity has often been described with the equation $M(r) = A + B/r$ (23), where $r$ is the eccentricity and A, B, and C are constants (with C sometimes constrained to be 1). To estimate M(r), first we marked activated regions (ver- tices) of the flattened visual field map by visual area and by whether they contained upper or lower field representations, omitting regions of ambiguous visual field sign. The average direction of the cortical eccentricity gradient (the vector sum of r across every vertex assigned to an area) was estimated independently for each upper and lower visual field representation. The mapping function, $D(r) = f(M(r), r)$, where $D$ is the distance in millimeters from the cortex in the center-of-gaze, was determined for each area by measuring distances from the most central response zone (representing approximately 0.75 mm) to higher resolution data. The average eccentricity gradient for each labeled vertex. The measurements were combined into 30 eccentricity bins. The resulting points were then fit with the equation for the mapping function

$$D(r) = M(r) + A(r) + B/r - C$$

by adjusting the parameters A, B, and C. The resulting cortical magnification factor equations for human

25. The magnification factor at a particular eccentricity will be proportional to the size of VI (or horizontal magnification factor) and vertical magnification factor. The results for cortical magnification factor were $M_r(r) = 19.35* (r + 2.5)^{-1}$ and $M_\theta(r) = 19.51* (r + 0.94)^{-1}$. The cortical magnification factor equations are some-

26. The magnification factor at a particular eccentricity will be proportional to the size of VI (or horizontal magnification factor) and vertical magnification factor. The results for cortical magnification factor were $M_r(r) = 19.35* (r + 2.5)^{-1}$ and $M_\theta(r) = 19.51* (r + 0.94)^{-1}$. The cortical magnification factor equations are some-

27. It is possible that differences at the level of the human retina (or lateral geniculate nucleus) may partly account for the differences in the cortical magnification factor we observed. For example, human OFF midget retinal ganglion cells have dendritic fields with diameters 70% those of their ON counterparts, a contrast not seen in the macaque monkey retina [D. M. Dacey, J. Neurosci. 13, 5334 (1993); and the fibers of Herle are espe- cially long in the human retina IC. A. Curcio and K. A. Allen, J. Comp. Neurol. 300, 5 (1990)]. These observations are consistent with the increase in the foveal density of human midget ganglion cells with respect to macaque monkeys, which could explain our result.


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**BRAIN MAPPING**

**Researchers Get a Sharper Image of the Human Brain**

To the neuroscientist, the human brain is anything but crystal clear. Although neuroscientists are anxious to see it in action, they can't use the invasive methods that are available for other species. As a result, although researchers have been able to produce detailed maps of brain areas that perform particular functions in primates such as the macaque monkey, they haven't been able to duplicate that knowledge for the human brain.

Now, aided by a set of new brain imaging techniques, Martin Sereno and Anders Dale of the University of California, San Diego, with Roger Tootell's group at the Massachusetts General Hospital Nuclear Magnetic Resonance Center in Charlestown have, for the first time, mapped with a precision similar to that achieved in monkeys the areas of the human brain that process visual images (see p. 889). "I consider this to be a very important study," says neuroscientist David Van Essen of Washington University in St. Louis, a leader in mapping the monkey's visual cortex. "It gives us significant new information about the organization of visual areas in the human cortex."

That new information supports what some researchers have suspected for a while—that the human visual areas identified so far seem to follow the same basic organization as those of monkeys, although they differ in size and position. By clearly defining the borders of these areas, this study has opened the way for researchers to ask whether those areas whose lineages can be traced back to monkeys have, during the course of evolution, taken on new and distinctly human functions, such as those necessary for language, or whether such functions are instead handled in areas unique to human brains. The techniques, which so far have been applied only to the visual cortex, are also likely to prove useful for identifying and mapping brain areas that process other types of sensory information, such as hearing or touch.

Until now, most human brain-mapping work has used a noninvasive technique called positron emission tomography (PET), which detects the changes in blood flow that accompany increased activity in specific brain regions. By making PET images of a person's brain while that person performs a mental task, PET can locate the brain areas involved in the task. PET has helped researchers identify visual areas that respond to color or motion and those that participate in recognizing written words.

Those revelations constituted a major advance, but they were a far cry from the detailed visual maps available for animal brains. A PET study that localizes a certain visual function, such as word recognition, to a particular fold in the cerebral cortex is a bit like a spy-satellite photo that reveals a missile base on a hill. Without a detailed map that shows that hill's location relative to national borders, you still don't know who owns the missile base.

Neuroscientists needed better maps that precisely locate the borders of the human visual areas. Such maps had been made of monkey brains by painstaking experiments in which researchers inserted electrodes into the monkeys' brains and recorded the activity of neurons at many locations while images were flashed before the monkeys' eyes. This, along with studies of brain structure and neural connections, enabled researchers to find more than 30 visual areas in the monkey brain; each of which analyzes information corresponding to particular features, such as shape, color, or movement, then passes the information to other areas. In many areas, each neuron responds to signals coming only from a specific part of the retina, resulting in a "retinotopic map," in which each position in the visual area represents a position in the visual world. With the detail provided by retinotopic maps, researchers were able to define the borders of the visual areas.

Sereno and his colleagues set out to make comparable maps of the human brain, but they realized that several technical hurdles had to be overcome. The first was finding a way to take snapshots of brain activity detailed enough to construct a retinotopic map. For that task they turned to a brain imaging method developed in the early 1990s, called functional magnetic resonance imaging (fMRI), that not only has better spatial resolution than PET, but is also much faster, enabling researchers to take thousands of images in less than 10 minutes.

That speed, coupled with a clever trick called "phase encoding," developed by Stephen Engel, a postdoc with neuroscientist Brian Wandell at Stanford University, enabled the Sereno team to get enough data to map a person's visual areas in a matter of minutes. Phase encoding involves sweeping an image across the subject's field of view, in cycles lasting a minute, and tracking the response with fMRI images of the subject's brain. Areas with retinotopic maps stand out, Sereno says, because "at each spot you see activities that are going up and down every minute. The phase of that oscillating activity then tells you what visual field location is represented at that spot."

But getting the images was only half the challenge. The team next faced a complicated version of the old mapmaker's problem: how to accurately project a map of a rounded object—such as Earth or a brain—onto a flat surface. Without a way to flatten the cortex, says Washington University's Van Essen, "we would be hopelessly tangled trying to wind our way through [the data]." But flattening a convoluted brain surface is a very difficult problem. Van Essen and other monkey researchers developed manual methods that Van Essen calls "tedious and not terribly accurate" and too cumbersome to apply to the much more convoluted human brain. In the past few years, however, several groups have devised computer algorithms that can flatten human as well as monkey brains. Sereno's group used one developed by Sereno and Dale, who is now at the University of Oslo in Norway.

This new bag of tricks has so far enabled the Sereno group to map five visual areas in the human brain that process information that has been received and passed along by the primary visual cortex. Based on the positions and other characteristics of these areas, the team concluded that they are counterparts of visual areas found in monkeys. Others who have seen the data agree. "It looks just like the monkey brain," says Leslie Ungerleider, who does brain mapping in monkeys and humans at the National Institute of Mental Health. Ungerleider says that is what she expected, but that "it was done in such a convincing and elegant way that ... it just blows you away."

In unpublished work, a team led by Edgar DeYoe of the Medical College of Wisconsin...
Keeping the Kilo From Gaining Weight

The French are known for their finesse in many areas of life, and British physicists are finding that the reputation holds in the arcane realm of weights and measures as well. For years, a specialist named Georges Girard labored unrecognized at the heart of the international metric system at the Bureau International des Poids et Mesures (BIPM) near Paris, keeping the standard kilogram from picking up contaminations—and hence weight. His tools: nothing more than a chamois cloth, a bottle of cleaning fluid, and that old je ne sais quoi. Now Girard has retired, and Martin Seah and Peter Cumpson at the U.K.’s National Physical Laboratory in Teddington near London are hoping that a regimen of ozone and ultraviolet light can match his deftness in keeping the standard kilogram, well—standard.

The curators of the kilogram, a platinum-iridium cylinder kept at the BIPM, say they are eager to test the British scheme. For the moment, they are still trying to keep the kilogram clean by hand-polishing it. But as the keepers of the only standard of measurement still based on an object rather than on a fundamental physical quantity—time, for example—is set by a specific frequency of radiation—they are eager to find ways to maintain the standard that rely more on science and less on one man’s skillful fingers.

Thought to have been made in the early 1880s by a Paris instrument-maker, the 4-centimeter-high, 4-centimeter-wide cylinder is the prototype for reference kilograms in national laboratories throughout the world. These standard kilograms—exact copies of the French original—ultimately tie all mass-measuring systems back to the BIPM standard. But over the last decade or so, improved balances have shown that the reference kilogram and its duplicates vary in weight. “We have been measuring the differences between these apparently similar artifacts, and we see they are drifting apart,” says Terry Quinn, director of the BIPM. The weight of a freshly minted copy of the standard mass, says Cumpson, “increases by tens of micrograms in the first few weeks after manufacture.”

The explanation for this unwanted weight gain, say Seah and Cumpson, is contaminants accumulating on the metal surface. Through spectroscopic analysis of the surface of replica kilograms, they have found that the platinum-iridium alloy picks up hydrocarbons from air pollution and other sources, along with mercury vapor from laboratory instruments. Every so often, explains Cumpson, an instrument breaks, releasing “a very subtle presence of mercury—well below health and safety levels—but enough to adsorb onto the surface of the reference kilogram.”

Girard was able to keep the hydrocarbon buildup in check by rubbing the surface with a chamois cloth dipped in a mixture of ultrapure ethanol and ether; a hand-directed steam jet then removed any residue. The cleaned mass “returned to [within] a few micrograms of where it was originally,” says Cumpson. “He used just the right degree of abrasion to remove the carbonaceous contamination without removing metal.”

Cumpson believes that Girard’s technique probably didn’t remove the mercury, which worked its way into the grain structure of the metal. Still, it was better than any other standards laboratory could manage, even though a videotape of Girard at work polishing the kilogram was circulated among them. Scientists from the U.S. National Institute of Standards and Technology and the Physikalisch-Technische Bundesanstalt, the German standards institute, even flew to Paris to watch him up close and personal, but to no avail. “It’s almost impossible to get the right degree of pressure,” says Cumpson.

Now, with Girard’s retirement 2 years ago, the BIPM faces the same dilemma. But Cumpson and Seah think they’ve come up with an answer: Expose the kilogram to ozone and ultraviolet light to oxidize the hydrocarbon contaminants, freeing them to diffuse away into thin air. “The technique looks very promising,” says Cumpson. “There’s no contact with the mass at all, and the concentrations we use are low,” so there’s little risk of oxidizing and damaging the kilogram itself.

BIPM Director Quinn is intrigued. “We shall be working with them to assess what they’ve found,” he says. He also hopes to try out the cleaning technique on some of the laboratory’s own platinum-iridium test objects. But the laboratory isn’t rushing into anything. “We may not know exactly how the old process works,” he says, “but we don’t want to change until we know how to do it better.”

—Sally Croft

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