Eccentricity Bias as an Organizing Principle for Human High-Order Object Areas

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Summary

We have recently proposed a center-periphery organization based on resolution needs, in which objects engaging in recognition processes requiring central-vision (e.g., face-related) are associated with center-biased representations, while objects requiring large-scale feature integration (e.g., buildings) are associated with periphery-biased representations. Here we tested this hypothesis by comparing the center-periphery organization with activations to five object categories: faces, buildings, tools, letter strings, and words. We found that faces, letter strings, and words were mapped preferentially within the center-biased representation. Faces showed a hemispheric lateralization opposite to that of letter strings and words. In contrast, buildings were mapped mainly to the periphery-biased representation, while tools activated both central and peripheral representations. The results are compatible with the notion that center-periphery organization allows the optimal allocation of cortical magnification to the specific requirements of various recognition processes.

Introduction

A substantial number of neuroimaging studies have suggested that cortical activation associated with specific object categories is segregated within the occipito-temporal cortex. Such segregated activation was reported for faces (Halgren et al., 1999; Hasson et al., 2001; Haxby et al., 2000; Kanwisher et al., 1996; Tong et al., 2000)

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and buildings (Aguirre et al., 1998; Epstein and Kanwisher, 1998) as well as for other object categories (Ishai et al., 1999; Downing et al., 2001). However, the organizing principles underlying this putative category-related organization remain a matter of considerable, ongoing controversy.

Various perspectives have been proposed to account for the differential activation. At the one pole of the debate, one can identify accounts which argue for specialized modules dedicated to the processing of specific object categories such as faces, buildings, and, more recently, human body parts (Downing et al., 2001). At the other extreme, there are accounts that argue for widely distributed representations of all object categories, in which various objects are coded through the unique patterns of neuronal activity within the entire representation (Haxby et al., 2001; Edelman, 1998). One shortcoming of both of these classes of theories is that they do not provide any explanation for the fact that the differential activation is anatomically consistent across subjects. For example, it has been demonstrated that within the posterior fusiform region, preferential activation to buildings is situated consistently medial to that of faces (e.g., Epstein and Kanwisher, 1998; Ishai et al., 1999)— but neither of these views provides an underlying principle that might explain this relationship.

Recently, we have found that an orderly map of eccentricity, i.e., anatomical segregation of central versus peripheral visual field bias, which has been previously demonstrated for early retinotopic areas (DeYoe et al., 1996; Sereno et al., 1995; Tootell et al., 1997), actually extends into ventral high-order object areas (Levy et al., 2001). Recently we have termed this eccentricity organization the ventral occipito-temporal cortex (VOT) (Malach et al., 2002). In fact, eccentricity bias maps encompass essentially the entire extent of human visual cortex (see also Tootell and Hadjikhani, 2001). When the location of face-related and building-related regions was projected onto such eccentricity maps, a clear association was found between faces and central-field bias on the one hand, and buildings and peripheral-field bias on the other. Control experiments, using larger faces and smaller buildings, showed that this association was not due to the physical distribution of low-level features, but was related to the shape-identity of the images (Levy et al., 2001).

Given these findings, we hypothesized that processes that depend on central vision, such as face recognition, will be naturally associated with a center-biased cortical representation (Makela et al., 2001; Melmoth et al., 2000). A clear test of this prediction is that this association should be evident in other object categories whose recognition necessitates central vision. Optimal candidates fulfilling this requirement are letters and words, which involve the highly foveal task of reading (Nazir et al., 1992; Rayner, 1998). Extensive neuroimaging literature has identified two left-lateralized regions in extrastriate and occipito-temporal cortex involved in reading and character recognition (for review, see Fiez and Petersen, 1998). The functional selectivity of these two

regions is somewhat varied across studies. While some studies report that both regions are activated to a certain degree by unpronounceable letter strings and real words (Tagamets et al., 2000; Uchida et al., 1999), others claim that the occipito-temporal region is activated solely by real word stimuli (Beauregard et al., 1997; Bookheimer et al., 1995; Price et al., 1996).

Although the letters-related regions are located in the heart of the ventral visual-processing stream, few functional imaging studies tested the relation of those regions to other object-related foci in the occipito-temporal cortex (Bookheimer et al., 1995; Gauthier et al., 2000b; Puce et al., 1996), and no attempt was made to relate those areas to retinotopic and eccentricity maps. In the present study, we did both: first, we examined the relationship between the center/periphery organization of human object areas and the activation to unpronounceable letter strings and real words. Second, to test whether the pattern of activation to faces, letter strings, and words was unique, we compared it to the activation pattern obtained with other stimulus classes: buildings and tools. Importantly, the tool images occupied the same visual field extent as words. Our results reveal a strong association between faces, letter strings, words, and center bias regions, while buildings were mapped to peripheral bias regions. Tool images were mapped to both central and peripheral representations. These results are compatible with the notion that resolution needs and their association with visual eccentricity are part of the driving forces that organize shape representations in high-order object areas.

Results

The Relationship between Letter Strings and Other Object Categories

In the first experiment, we sought to locate the cortical activation associated with letter strings relative to the eccentricity map and relative to the well-known face and building-related activation. The different conditions used in the experiment are shown in Figure 1. We employed an interleaved short-block design (Figure 1B), presenting images of strings of unpronounceable alphanumeric Hebrew characters, faces, and buildings. To map eccentricity, the images were presented either in a central circle (c-letters, c-faces, and c-buildings), or in a peripheral ring (p-letters, p-faces, and p-buildings). By using unpronounceable alphanumeric Hebrew characters, we tried to minimize the involvement of phonological and semantic processes, while concentrating on the perceptual aspects of letter recognition.

To reveal the location of letters-related activation, we conducted a statistical search for voxels that were preferentially activated by letter strings compared to faces and buildings (c-letters > c-faces and c-buildings). The results of this test averaged across 11 right-handed subjects are shown on a Talairach normalized, inflated, and unfolded brain in Figure 2. Regions activated preferentially by letter strings are indicated in purple, while regions activated by faces are indicated in yellow-red. The same results obtained relative to the borders of early retinotopic areas, in one representative subject, are shown in Figure 3.

Three points should be noted regarding these results. First, there were two major foci of preferential letters-related activation, one situated posteriorly, extending toward the occipital pole, and one situated more anteriorly, in the vicinity of the occipito-temporal sulcus. We will term this second, anterior focus, region OT. It is important to emphasize that these foci of activation were located within the range of previously published Talairach coordinates of letters-related activation (Fiez and Petersen, 1998; Mechelli et al., 2000; Moore and Price, 1999; Puce et al., 1996; Rumsey et al., 1997; Tagamets et al., 2000; Uchida et al., 1999). For Talairach coordinates and comparison to other studies, see Table 1.

Second, letter string activation in the anterior occipito-temporal (OT) region was left lateralized; this was established by comparing the number of activated voxels (letters > faces and buildings) in each hemisphere (p < 0.05, one-tail paired t test, n = 10). Activation in the posterior occipital region was less lateralized in extent but also showed a slight left bias (p < 0.05, one-tail paired t test, n = 10; see also Figure 2). On a case-by-case examination, we found that in 2 out of the 11 (all right-handed) subjects, there was bilateral activation in the OT region, and in 6 out of 11, we found bilateral activation in the posterior-occipital region. The opposite trend, i.e., larger activation in the right posterior-occipital region, was observed in 1 out of 11 subjects.

Third, relating the letter foci to the early retinotopic areas defined by meridian mapping (see Experimental Procedures) revealed that the posterior focus was situated within the confines of early retinotopic cortex (red dotted lines in Figure 3). In contrast, the anterior letters-related focus (OT) was situated within the object-related, occipito-temporal cortex.

To determine the relationship of the letters-related regions to face-related regions, we conducted a statistical test aimed at delineating separately the preferential activation to faces (c-faces > c-letters and c-buildings). In agreement with previous reports, the face-related regions were located in two major foci, one in the lateral occipital cortex (LO) and one in the posterior part of the fusiform gyrus (pFs) corresponding to the fusiform face area (FFA) (Kanwisher et al., 1997). See Table 1 for Talairach coordinates. As can be seen in Figure 2, the letters-related region was found in the left occipito-temporal sulcus lateral to the fusiform face-related region. Note that the occasional overlap between the Talairach variance of the face-related and letters-related regions in Table 1 is due to intersubject variability in Talairach coordinates of adjacent regions and was not apparent within individual subjects. Faces showed an opposite trend of hemispheric lateralization, having a relatively larger representation in the right hemisphere. Thus, examining the relative number of activated face-related voxels (faces > letters and buildings) revealed a significant preference to right hemisphere activation in both LO (p < 0.05, one-tail paired t test, n = 9) and pFs (p < 0.05, one-tail paired t test, n = 11).

The Relationship between Letter String Representations and Eccentricity

Having confirmed the location of letter string activation within the ventral visual-processing stream, we then ex-

A

B

| Letters | Buildings | Faces | Buildings | Faces | Letters |
| Periphery | Periphery | Periphery | Center | Periphery | Center |

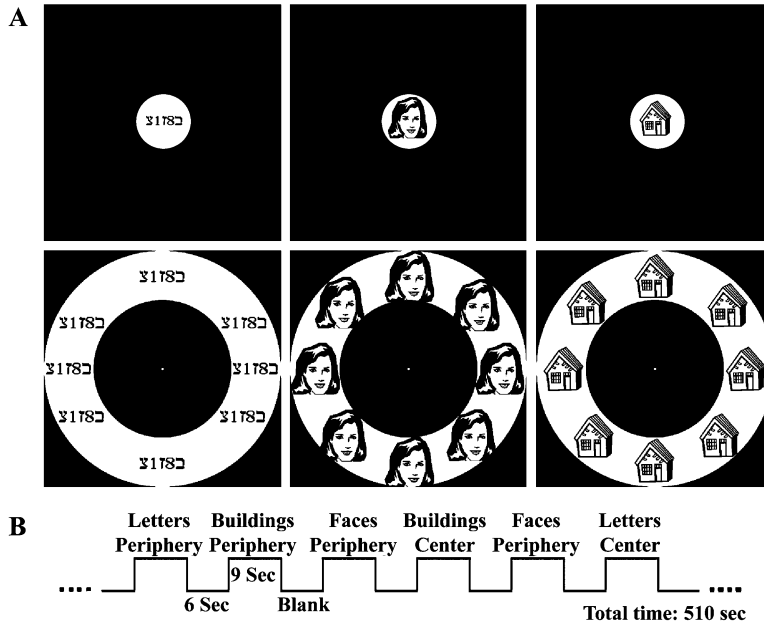9 Sec

6 Sec   Blank

Total time: 510 sec

Figure 1. Concurrent Mapping of Eccentricity and Object Selectivity (Experiment 1)

(A) Examples of stimuli used to map the face, letter string (Hebrew), and building-related areas. These stimuli were presented either singly in a central circle (3° diameter) or in a group of eight within a peripheral ring (between 11.5° and 20° diameters). The center stimulus shown here was enlarged for presentation purposes.

(B) An interleaved short block presentation design was used in the experiment. Each epoch lasted 9 s, followed by a 6 s blank. Nine images of the same type were presented in each epoch, and each image was presented for 200 ms, followed by 800 ms blank. Epochs of peripheral presentation were alternated with those of central presentation.

amined the relationship of the letters-related regions to the eccentricity map. To do so, we delineated the center-periphery organization of visual cortex by contrasting the activation produced by central faces and buildings compared with peripheral faces and buildings (c-faces and c-buildings > p-faces and p-buildings). The statistical map of this comparison for a group of 11 subjects is shown on a Talairach-normalized brain in Figure 4A. Center-biased regions are denoted by blue, while green indicates periphery-biased regions. The center/periphery organization was independent of the specific object type used for creating the eccentricity maps. Mapping eccentricity using only the letter strings' stimuli (c-letters versus p-letters) produced a comparable center/periphery organization (Figure 4B). Similar results were obtained when we used only the face stimuli (c-faces versus p-faces, white lines) or only the building stimuli (c-buildings versus p-buildings, black lines). Thus, map-

ping the activation to a single shape category at center versus peripheral visual field locations is sufficient to reveal the eccentricity organization.

To directly relate these eccentricity maps to the letters-related activation, we superimposed the borders of the letter string regions (purple contours, derived from Figure 2) onto the eccentricity map (Figure 4A). Of particular interest is the consistent overlap of the letters-related regions with central bias regions. In agreement with our previous finding, face-related voxels also overlapped central bias regions (yellow contours) but within this region, showed substantial segregation from the letters-related voxels.

Single-Condition Mapping of Object Representations

It could be argued that the association of letters with center-biased representation is simply due to the spe-
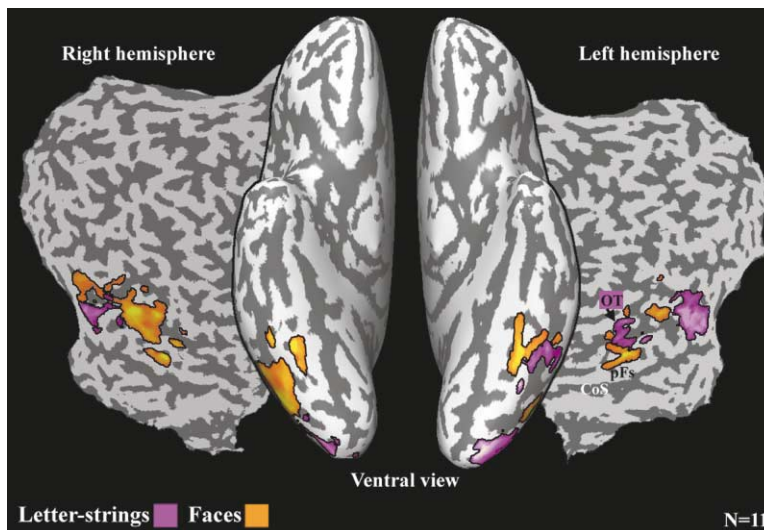

Figure 2. Character-Related Activation in the Visual Cortex

An averaged activation map (11 subjects), showing preferential activation to letter strings (purple) and faces (yellow-red) obtained in experiment 1. The maps are presented on a Talairach-normalized inflated brain (center). The same data are superimposed on flattened right and left hemispheres. Note the two foci of letter string activation and the strong left lateralization of the anterior focus. OT, occipito-temporal sulcus; pFs, posterior fusiform gyrus; CoS, collateral sulcus.
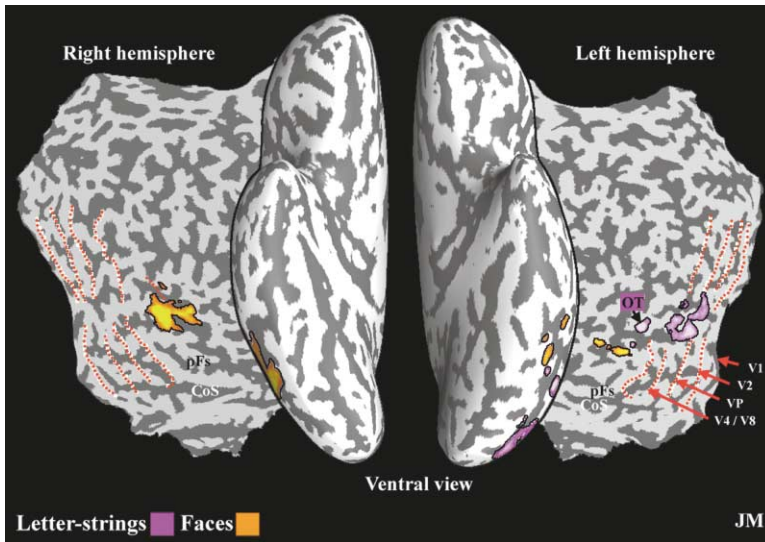
Figure 3. Character-Related Activation and Retinotopic Borders

Preferential activation to letter strings (purple), and faces (yellow-red) obtained in experiment 1, shown on the inflated and unfolded brain of one representative subject (JM). Red dotted lines denote borders of retinotopic visual areas V1, V2, V3, VP, V3A, and V4/V8. Note that the posterior letters-related region encroaches on the foveal representation of early retinotopic areas, while the occipito-temporal region is within the anterior lateral-occipital complex.

cific contrast chosen (letters > faces and buildings), i.e., the contrast with buildings shifts the activation away from the periphery-biased building-related region into the center bias region. To control for this possibility, we examined the activation associated with letters as well as the other categories, when contrasted only with the fixation baseline condition (i.e., letters > blank, faces > blank, and buildings > blank). Figure 5 compares the pattern of activation revealed by such "single-condition" tests in the anterior object-related regions (top). The white dotted line indicates the approximate border between center bias and peripheral bias regions, as defined by our center versus periphery stimuli (right). For comparison, the contrast of each single category against the others is also shown (bottom). Note that even in the single-condition maps, the letter string and face activations were confined to the center-biased visual field. In agreement with our previous finding, the anterior building-related activation overlapped mainly the peripheral bias region. These results show that the

association of the letters-related activation with the central visual field bias is related to the visual characteristics of the letters themselves and is not simply a by-product of the contrast with buildings and faces.

Is the Association with Center-Biased Representation a Consequence of Low-Level Feature Distribution?

The observed association of the letter string activation with center-biased representation may emerge from an unequal center/periphery distribution of low-level visual features between the different categories. Thus, it might be that letter images contain a higher density of local elements in the center of the visual field compared with face and building images and that this led to the central bias of letter activation. To explore this possibility, we searched for voxels showing preferential letters-related activation but only when the images were presented in the periphery of the visual field (p-letters versus p-faces and p-buildings). The results of this analysis are shown

Table 1. Talairach Coordinates of Letter Strings, Words, and Faces

	Left Hemisphere			Right Hemisphere		
	X	Y	Z	X	Y	Z
Letter strings[a]						
Posterior-occipital	-27 ± 8	-85 ± 4	-9 ± 5	20 ± 7	-85 ± 8	-6 ± 7
Occipito-temporal	-40 ± 5	-66 ± 13	-9 ± 5			
Words[b]						
Posterior-occipital	-19 ± 8	-88 ± 6	-12 ± 5	22 ± 10	-89 ± 2	-11 ± 5
Occipito-temporal	-45 ± 2	-50 ± 12	-12 ± 3			
Other studies[c]						
Lateral occipital	-21 ± 11	-79 ± 13	-8 ± 7			
Posterior fusiform	-42 ± 4	-60 ± 26	-11 ± 7			
Faces[d]						
Lateral occipital	-47 ± 5	-69 ± 7	-4 ± 5	41 ± 2	-65 ± 10	-4 ± 8
Posterior fusiform	-38 ± 4	-49 ± 7	-16 ± 2	36 ± 4	-48 ± 2	-12 ± 1

[a] Talairach coordinates of letter string-related regions obtained in experiment 1.

[b] Talairach coordinates of word-related regions obtained in experiment 2.

[c] Talairach coordinates of letter- and word-related regions averaged across six different studies (Fiez and Petersen, 1998; Mechelli et al., 2000; Moore and Price, 1999; Puce et al., 1996; Rumsey et al., 1997; Tagamets et al., 2000; Uchida et al., 1999).

[d] Talairach coordinates of face-related regions obtained in experiment 1.
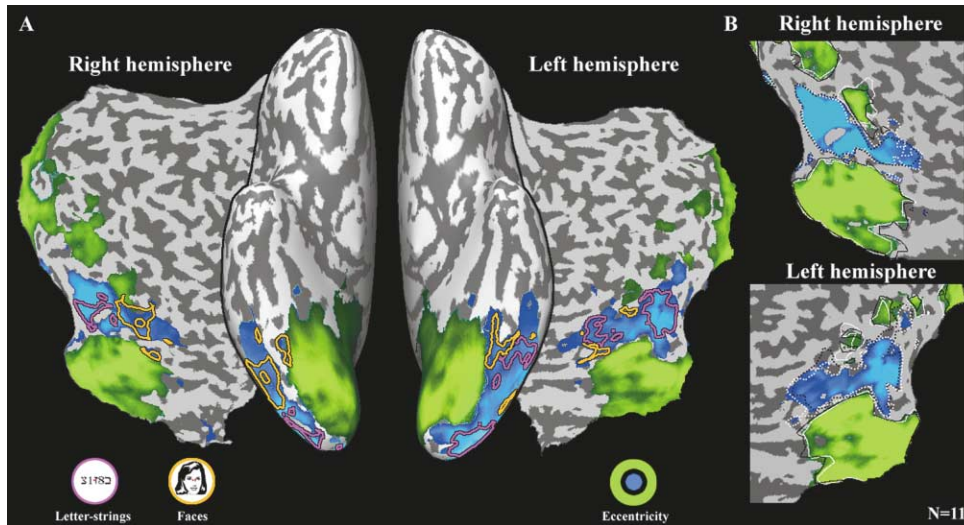
Figure 4. The Relationship between Letter String Activation, Eccentricity, and Object Selectivity

(A) Average activation map of eleven subjects, shown on an inflated and an unfolded brain. Borders of letters-related (purple contours) and face-related (yellow contour) regions (from Figure 2) are superimposed on central (blue) and peripheral (green) visual field representations. The center bias and periphery bias were defined by contrasting the activation produced by central faces and buildings compared with peripheral faces and buildings. Note the strong association of the letters-related regions with the central visual field representation.

(B) Similar center-periphery maps were obtained using only the letter strings' stimuli (c-letters versus p-letters; blue and green, respectively), as well as using only the face stimuli (white dotted line, center; continuous white line, periphery) or only the building stimuli (black dotted line, center; continuous black line, periphery).

in Figure 6, which depicts an averaged subject map (n = 11) presented on unfolded cortical hemispheres. In these maps, voxels were color coded according to the relative contribution of the peripherally presented letter strings versus faces and buildings to their activation. Red-yellow shades indicate preferential activation to letter string stimuli compared with faces and buildings, while green-blue colors indicate the reverse.

As can be seen in posterior retinotopic areas, the peripherally presented letter strings preferentially activated a large bilateral region, which appeared to overlap the peripheral visual field representations of early retinotopic areas. This pattern is due most likely to a higher density of local visual features in the peripheral letter string stimuli. However, the only focus that showed left lateralization was the letters-related occipito-temporal region (filled black arrow). The location of this focus overlapped with the occipito-temporal letters-related region defined using the central letter string stimuli (purple contours from Figure 2 superimposed on this image). In contrast, the posterior occipital region was not activated by the peripheral stimulus (empty red arrow depicting empty purple contours from Figure 2), as expected given its location within highly retinotopic foveal cortex. Thus,
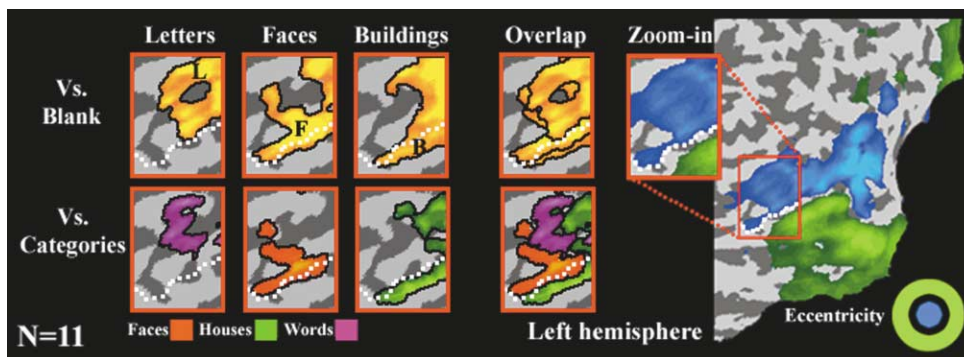

Figure 5. Single-Condition Mapping of Object Representations

Average activation maps (eleven subjects) for each category versus blank (top). For clarification purposes the activation is shown only for the anterior occipito-temporal cortex (zoom-in from the region marked by the red box on the flattened left hemisphere). White dotted line indicates the approximate border between center bias and periphery bias regions, as defined by the contrast between the central and peripheral rings (right map). For comparison, the contrast of each category versus all other categories is also shown (bottom). Note that even in the single-condition maps, the letter string and face activation were confined to the center-biased visual field representation. In addition, the peak of the letter activation (marked by "L") was situated laterally to the peak of the face activation (marked by "F"), while the peak of activation for buildings (marked by "B") was situated medially to the peak of the face activation.
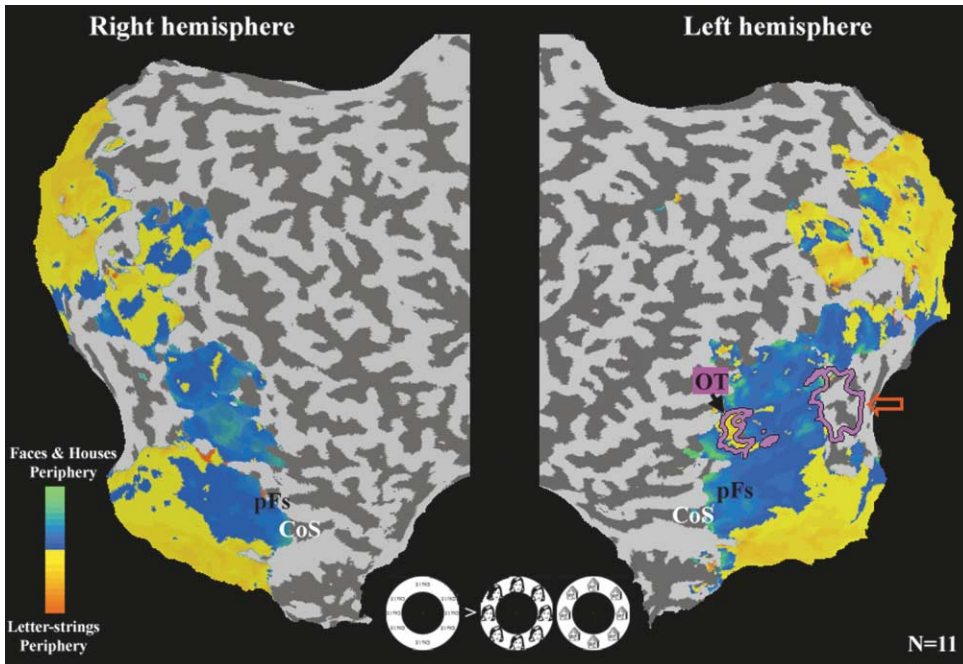
Figure 6. Preferential Letter Activation for Peripherally Presented Stimuli

Average activation of eleven subjects, shown on unfolded right and left hemispheres. The statistical map shows preferential activation to *peripherally* presented letter strings (yellow-red) versus *peripherally* presented faces and buildings (blue-green). Borders of regions activated by letter strings presented centrally (purple-contours from Figure 2) are superimposed on this map. Note that the only left-lateralized activation for peripherally presented letter strings (yellow) was obtained in the occipito-temporal region (filled black arrow), which overlaps the occipito-temporal letters-related region (purple contours). In contrast, the more posterior occipital region was not activated by the peripheral stimulus (empty red arrow).

activation of the anterior OT region within the central-field-biased cortex is not a simple consequence of activation by centrally positioned low-level features, but reflects an interaction between letter-shapes and central visual field bias.

Generalizing the Results to Words and Another Object Category

The results so far show clearly that letter strings are associated with central visual field bias. This result is compatible with the notion that object categories involved in foveal vision are associated with central bias of higher order visual maps. To further explore this relationship, we conducted a second experiment (see Figure 7A) that was aimed at exploring three additional issues. First, we wished to examine whether the same center bias association was not a unique property of unpronounceable letter strings but that it extended to meaningful words. Second, we wanted to rule out the possibility that the association with central bias regions was a general property of all object categories, with the exception of buildings. To address this latter issue, we added a second category: tools. To control for field eccentricity confounds, only horizontally elongated tool images were chosen so that the images closely paralleled the eccentricity distribution of the words (illustrated by the red boxes in Figure 7A). Third, in order to ensure that the letters-related activation was not a result of a specific task performed by the subjects, subjects participating in the second experiment were instructed to perform a one-back memory task. Note that in the first experiment, subjects were instructed to passively view the stimuli while fixating on the fixation point (see Experimental Procedures for details).

First, we contrasted the activation to words and tools stimuli with the fixation baseline using the single-condition method, as above (words > blank; tools > blank). The results of these tests, averaged across six subjects, are shown on a ventral view of an inflated brain in Figure 7B. The red dotted line indicates the approximate border between central bias and peripheral bias regions, as defined by our center versus periphery stimuli. The single-condition activations for words and tools are shown on the left and mid panels, respectively. Similar to letter strings, activation for words (Figure 7B, left inset) exhibited strong lateralization and was confined to the center-biased regions. This finding confirms our prediction that the activation to words will be associated with center-biased representation and shows that orthographic stimuli, irrespective of their lexical status, activate center-biased regions. In contrast, activation for tools was not confined to the center-biased representation, despite the fact that their eccentricity distribution mirrored that of words; instead, the tool-related activation showed a more complex representation, activating intermixed regions within the center, mid, and periphery representations.

We further analyzed these data by localizing those voxels that were preferentially activated for each category relative to the tool stimuli (i.e., words > tools,
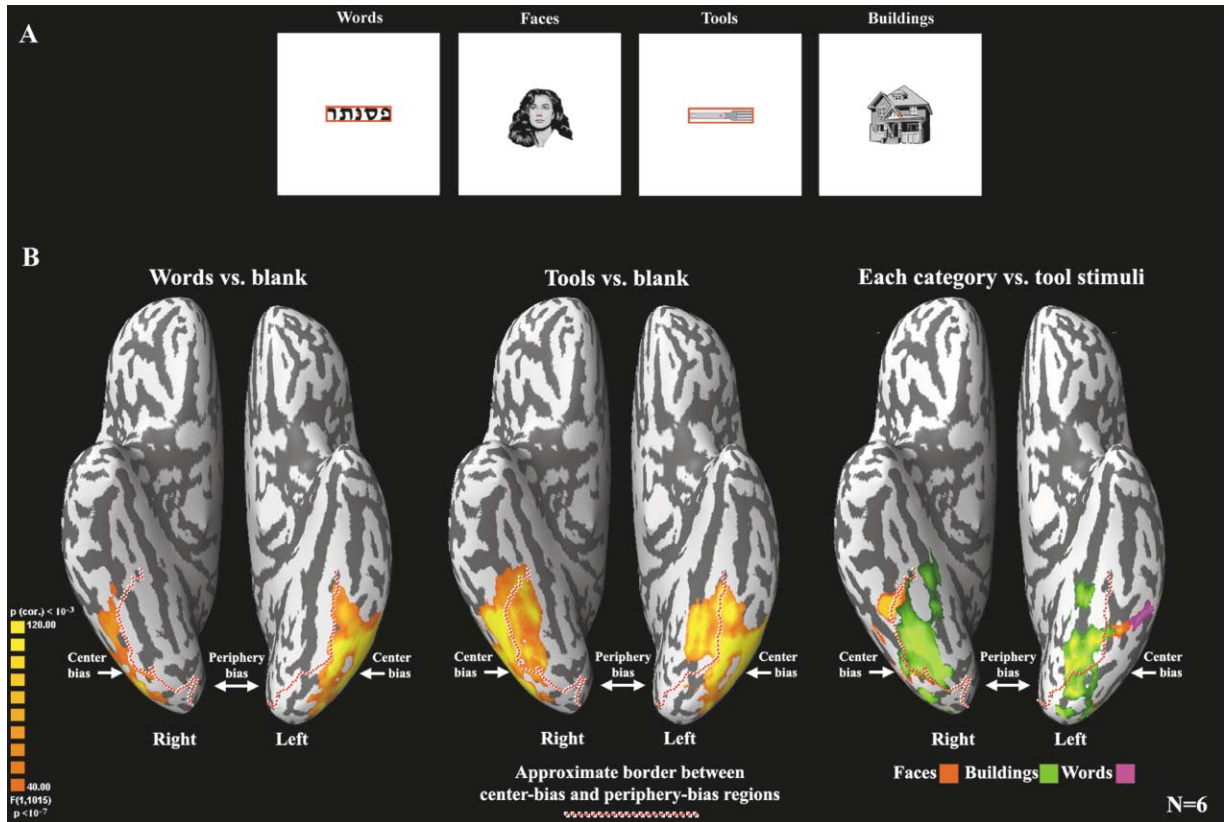
Figure 7. Mapping Activations to Words, Tools, Faces, and Buildings (Experiment 2)

(A) Examples of the four object categories used in the experiment: meaningful Hebrew words, faces, man-made tools, and buildings. Note that the tool stimuli were chosen to be close in eccentricity extent to that of the word stimuli (as illustrated by the red rectangle bordering the stimuli).

(B) Averaged map (six subjects) for words versus blank (left) and tools versus blank (mid), is shown on a ventral view of an inflated brain. Note that similar to the letters-related activation (Figure 5), the word-related activation in this single-condition test was confined to center bias regions, while tools activated additional mid and peripherally biased regions. On the right, averaged map for each category versus tool stimuli. Preferential activation for words, faces, and buildings are marked by purple, red, and green, respectively. Approximate border between center bias and periphery bias regions is indicated by the red dotted line.

buildings > tools, and faces > tools). The results, averaged across six subjects, are shown in Figure 7B (right inset). Similar to the result obtained for letter strings in the first experiment, the activation to words (purple) was confined to the left occipito-temporal sulcus, lateral to the fusiform face-selective region (red). For Talairach coordinates of the word-related regions and comparison to the letters-related regions observed in experiment 1, see Table 1. Importantly, preferential face and word activations were largely separate and were inversely lateralized, again replicating our findings from experiment 1. Additionally, the most selective building-related activation (green) was confined to the peripherally biased region in the vicinity of the collateral sulcus.

Discussion

Eccentricity Maps and Object Recognition

The motivation for the present study stems from our previous finding that high-order, human object-related cortex contains an organized visual field map based on eccentricity biases. Furthermore, certain object images are differentially localized relative to this map. Taking

note of the tight association between eccentricity and cortical magnification (which translates to density of retinal sampling), we hypothesized that this object-related localization might reflect differences in the resolution needs of different recognition processes. Previous work demonstrated the association between the cortical representation of faces and the center-biased cortex (Levy et al., 2001). A clear prediction of this finding is that another class of objects, which has a similar demand for high resolution (high-retinal sampling), would also be associated with a center bias representation.

To address this issue, the current study examined three additional stimulus classes, two of which, alphanumeric characters and written words, would be predicted to adhere to this same organization principle. Indeed, letters and words are probably the paradigmatic class of objects whose recognition involves foveation (Nazir et al., 1992; Rayner, 1998). The third class of objects (tools) was chosen as a control since its eccentricity distribution could be matched quite well to that of letter strings and words, but the expectation is that this class does not have preferential high-resolution demand.

The major finding of this study was that both the let-

ters-related and the word-related foci in human occipito-temporal cortex are consistently associated with center-biased representations (Figures 4, 5, and 7). Importantly then, these findings reveal the same reliance on center bias as was demonstrated for faces. In contrast, the activation pattern associated with tools did not show this clear reliance on center-bias, notwithstanding the fact that eccentricity was shared with the orthographic stimuli. Taken together, these data are fully compatible with our hypothesis and support the claim that resolution needs is one of the driving factors in the organization of object representations.

The Representation of Tool Images

Unlike the other object categories, tool images, which shared the same visual eccentricity distribution, were not confined to the center bias representation and showed a complex pattern of activation which included highly active zones within center, mid, and peripheral representations. This result argues against the possibility that, with the exception of building images (which may be considered a special case [Epstein and Kanwisher, 1998]), the association to center bias is a property of all object categories. Unlike words and letter strings, whose association with foveal vision is clear cut, the situation with tools appears more complex, and one can envision tapping both high and low resolution in tool recognition and manipulation. Thus, the involvement of tool images with central, mid, and peripheral visual field biases is not surprising.

Center Bias and High Resolution

We have argued that the topography of the object-related regions is related to the demand for resolution. There are, however, additional issues that should be considered. There has been a longstanding debate in the literature as to whether face recognition requires coarse or fine-resolution vision. Some have suggested that face processing depends predominantly on low-resolution information (Oliva and Schyns, 1997; Schyns and Oliva, 1999). Others have suggested that face images engage a wide and diverse set of recognition processes, which depend on drastically different scales of resolution (Costen et al., 1994, 1996; Gold et al., 1999; Hayes et al., 1986).

Close inspection of our findings provides support for this multiprocess approach. We have suggested that some face-related visual processes such as identifying expressions and gaze direction crucially depend on central viewing. Evidence to support this is also obtained from behavioral studies which reveal that face recognition deteriorates rapidly with peripheral viewing, even when corrected for magnification changes (Makela et al., 2001). It is also the case, however, that other face-related visual processes may not depend to such an extent on central viewing: for example, performing a judgment of whether a stimulus is upright or inverted. Consistent with this multiplicity of processes, our results show that even within the letter-related representation, there is a significant contribution from letters in the visual periphery (Figure 6; see also Levy et al. [2001] for a similar effect in face-related regions).

In light of this, our hypothesis is that the center/periph-

ery organization might provide a powerful mechanism that allocates cortical magnification resources to recognition processes that crucially depend on detailed analysis. The preferential bias of some object images to specific eccentricities is because these images engage an unequal "mix" of recognition processes that depend to a larger degree on specific range of resolution needs.

A related question of interest is whether the association of certain object categories with eccentricity is dynamic, changing from moment to moment depending on the task, or whether it is established via long-term visual experience. In the present study, we have used two different visual tasks: passive viewing and one-back memory task (see Experimental Procedures). In both tasks, the overall topography did not change (compare Figures 4 and 7). Thus, it is more likely that the association with eccentricity maps is rather constant, possibly established via long-term training and expertise (Tarr and Gauthier, 2000). It is also the case, however, that top-down attentional effects can affect the activity of ventral object areas, so a dynamic modulation of eccentricity might also be observed over and above the activation of the bottom-up ventral representations (O'Craven et al., 1999).

Role of Low-Level Features in the Letters-Related Activation

The association between the more anterior occipito-temporal, letter related region and the central bias representation cannot be explained as a simple consequence of a center/periphery imbalance in the statistical distribution of low-level visual features (e.g., corners and terminations) present in the letters and face images. The preferential letter activation of the left occipito-temporal region was maintained even when the letter strings were confined to the peripheral ring. As expected, no peripheral letter activation was found in the posterior-occipital region, which lay in the foveal representation of early retinotopic areas.

The Relationship between the Letters/Word and Face-Related Regions

The activation for letter strings, words, and faces was confined to center bias regions. When the activation pattern for each category was compared to the no stimulus (blank) condition, it appeared that the activation pattern was distributed across large and overlapping parts of the center bias representation. Nevertheless, when searching for foci most activated by each category *relative* to all other categories, letter strings and words occupied a separate territory from faces and were inversely lateralized to faces (see Figure 2 for letters and faces, and Figure 7B for words and faces), with the fusiform face-related region always appearing somewhat medially to the occipito-temporal region. The anatomical relationship between the letter/word-related focus and the face-related focus within the ventral occipito-temporal cortex (VOT) was quite consistent, and was also preserved across different contrasts (i.e., words and faces relative to a third category—tools). This anatomical relationship is also apparent in the single condition comparison in Figure 5 (the peak of activation for letters is lateral to the peak of activation for faces).

Thus, our results show an uneven but consistent distribution of activation within the center bias region, where the peak of the letter/word related activation is always found laterally to the face-related-region. It is tempting to speculate that this points to a fine-grained topographic shift within the center bias region along the eccentricity axis. Thus, it may be that letters and words are the extreme case of stimuli, which rely on fine-grain foveal discrimination and are associated with a more foveal representation (more lateral) relative to faces. Faces are a less extreme case and occupy a region with slightly more intermediate eccentricity and, thus, are associated with a less foveal-biased region (more medial). However, on the basis of this study, we cannot rule out the possibility that the further subdivision within the center bias region is a result of other principles, such as shape-related factors. This issue awaits further clarification and testing.

Is There a Specialized Module for Character Recognition?

Does the preferential activation for letter strings and words described above argue for the existence of a specialized module for character recognition? If we take a strict view of modularity—whereby a cortical area should respond exclusively to one object category— then clearly we did not find such a "letter/word" area, since even in the most word-selective regions there was significant activation to other object categories (e.g., activation to tools in Figure 7). Furthermore, the association of letters to center-biased regions could be established even when the eccentricity map was defined by non-words as the eccentricity stimuli (see Figure 4). However, even in the cases of faces, which are considered perhaps the prime example of a reported modular organization (Kanwisher et al., 1997), the selectivity is never absolute. More studies, e.g., of the performance of individuals with highly localized lesions, will be needed to clarify the level of modularity of letters/words representations within the center-biased maps.

Possible Sources for the Lateralization of Letter Stimuli

In addition to the segregation between the letter/word-related and face-related regions, faces and words were inversely lateralized. The hemispheric lateralization effects reported here are compatible with several lines of evidence stressing hemispheric asymmetries, where reading is associated with the left hemisphere while face recognition is associated with a right hemisphere bias (for a detailed review, see Springer and Deutsch, 1997).

What is the source of this lateralization effect? The ability to recognize letters is a relatively recent skill, both phylogenetically (approximately 5000 years) and ontogenetically (around the age of six). Therefore, if the letters-related lateralization is associated with reading processes per se, as suggested by the location of lesions in patients with a selective deficit in reading (Behrmann et al., 1998; Leff et al., 2001), then the sources for this letters-related lateralization are likely to be tied to postnatal developmental processes. The idea that the selectivity of higher visual areas can be modified by experience and training is intriguing and fits well with a substantial number of studies. In monkey IT, training was shown to modify the properties of neuronal responses in IT cortex (Kobatake et al., 1998; Logothetis et al., 1995; Rolls et al., 1989). More recently, neuroimaging studies by Gauthier et al. (2000a) have shown that expertise training can modify high-order object representations while Grill-Spector et al. (2000) have demonstrated such effects for backward masking tasks.

However, at this point, we cannot rule out the alternative possibility that the letters-related lateralization may be triggered by subtle, ipsilateral feedback from high-order language areas. In that case, the left-lateralized, letters-related activation may be the consequence of the evolutionary, older left-lateralized language-centers and thus would not necessitate postnatal specializations. Studying brain-damaged patients having reduced activation in high-order language areas might resolve the role of such putative feedback effects. Another possibility is that the letter/word lateralization is secondary to the strong lateralization observed for faces so that the right hemispheric bias for faces "pushes" the activation to letter strings into the left hemisphere (for examples of how specialization might emerge from differential pressure between cognitive subsystems, see Jacobs, 1999; Karnath et al., 2001).

In contrast to the more anterior occipito-temporal focus, the posterior focus was much less lateralized (see Figures 2 and 3). The source of the weak left lateralization in this posterior region is not clear at present. It might again be related to lateralization of low-level features, such as spatial frequency (Ivry and Robertson, 1998). Alternatively, it may reflect hemispheric-specific feedback effects from the left-lateralized anterior occipito-temporal regions. We are currently exploring this potential relationship.

Two Foci of Activity

We have consistently found two foci of activation associated with letters and words in the left hemisphere: a posterior region within the posterior-occipital cortex and a more anterior occipito-temporal region (OT). The posterior-anterior axis might hint at a hierarchical organization in which the posterior region is specialized for character identification, and the more anterior region is specialized for whole word recognition (Tagamets et al., 2000). A hint for this conjecture is seen when comparing the activation for letter strings and words across the two experiments, where the activation for letters is stronger in the posterior region (brighter colors in Figure 2), and the activation for words is stronger in the anterior region (Figure 7).

The division into two foci, one anterior and one posterior, appears to be a common theme in the organization of human object areas and may reflect a global hierarchical sequence of processing. In eccentricity mapping, it is often found that two separate foveal representations are located in ventral stream human areas, one associated with early retinotopic areas, and the other with higher order occipito-temporal regions (Tootell and Hadjikhani, 2001). Similarly, face-related regions appear both in the lateral occipital cortex as well as more anteriorly, in the region termed the fusiform face area (Halgren et al., 1999; Haxby et al., 2000; Kanwisher et al., 1997; Lerner et al., 2001).

In conclusion, we have provided empirical evidence and a proposed framework for the topographic organization of object classes and eccentricity maps in higher visual areas. We have documented the generality of our findings across different tasks and shown that faces and words, both of which have high-resolution demands, are associated with center bias, whereas tools do not exhibit this pattern. Although many functional imaging studies have shown the differential activation associated with different stimulus classes, we have proposed an underlying principle for the systematic neuroanatomical organization of these patterns of activation.

Experimental Procedures

Subjects
Thirteen healthy, right-handed, Hebrew native speakers (seven females and six males, ages 25–50) participated in one experiment or both. Four subjects participated in both the first and second experiments. All subjects provided written informed consent. The Tel-Aviv Sourasky Medical Center Ethic Committee approved the protocol. All subjects filled out a conventional handedness test to ensure their right-handed preference.

Visual Stimuli and Experimental Design
An interleaved short block design was used in both experiments. Each scan started with 24 s and ended with 12 s of a blank (fixation only) screen. Each epoch lasted 9 s, followed by a 6 s blank screen. Nine images of the same type were presented in each epoch; each image was presented for 200 m and was followed by 800 ms blank screen. A central red fixation point was present throughout all experiments. The stimuli were generated on a PC and projected via a LCD projector onto a tangent screen located in the scanner.

The first experiment (Figure 1; 11 subjects) used unpronounceable Hebrew letter strings intermixed with digits as well as images of faces and buildings (see Figure 1). Each type of stimulus was presented either in a central circle (3° of visual field diameter) or in a peripheral ring containing eight enlarged images of the central stimulus (between 11.5° and 20° diameters). The experiment lasted 510 s. The two letter strings' conditions (central-letter, peripheral-letter) were repeated eight times each; the other conditions were repeated four times each. In order to minimize the tendency for eye movements to the peripheral stimuli during the first experiment, subjects were specifically instructed to maintain fixation on the central dot, while passively viewing the images.

The second experiment (Figure 7; six subjects) included meaningful Hebrew words as well as line drawings of faces, buildings, and tools. The stimuli were presented only centrally (5° × 5°). In addition, the tool images were confined to 5° in width and between 1.8° and 2° in height to match the visual eccentricity of the word stimuli. The experiment started with a 9 s epoch of pattern stimuli, which was excluded from all the statistical analyses. The experiment lasted 525 s. Each experimental condition was repeated eight times. In order to make sure that the letters-related activation was not a result of a specific task performed by the subjects, subjects participating in the second experiment were instructed to perform a one-back memory task. During the experiment, one or two consecutive repetitions of the same image occurred in each epoch. The subject's task was to report whether the presented stimulus was identical to the previous stimulus or not.

MRI Setup
Subjects were scanned in a 1.5T Signa Horizon LX 8.25 GE scanner equipped with a custom quadrature surface coil (Nova Medical Inc., Wakefield, MA), to provide a high signal-to-noise ratio in occipito-temporal brain regions. Blood oxygenation level dependent (BOLD) contrast was obtained with gradient-echo echo-planar imaging (EPI) sequence (TR = 3000, TE = 55, flip angle = 90°, field of view 24 × 24 cm^2, matrix size 80 × 80). The scanned volume included 17 nearly axial slices of 4 mm thickness and 1 mm gap. T1-weighted high-resolution (1 × 1 × 1 mm) anatomical images and 3D-spoiled gradi-ent echo sequence were acquired on each subject to allow accurate cortical segmentation, reconstruction, and volume-based statistical analysis.

Data Analysis
fMRI data were analyzed with the "Brain Voyager" software package (Brain Innovation, Maastricht, Netherlands). First, data from each subject from each scan were analyzed separately. The first three images of each functional scan were discarded and a lag of 3 s was assumed. The cortical surface was reconstructed from the 3D-spoiled gradient echo scan. The procedure included segmentation of the white matter using a grow-region function, the smooth covering of a sphere around the segmented region, and the expansion of the reconstructed white matter into the gray matter. The sulci were smoothed using a cortical "inflation" procedure. The surface was cut along the Calcarine sulcus and unfolded into the flattened format. The obtained activation maps were superimposed on the unfolded cortex, and the Talairach coordinates (Talairach and Tournoux, 1988) were determined for the center of each ROI (region of interest). Preprocessing of functional scans included 3D motion correction and filtering out of low frequencies up to five cycles per experiment (slow drift). No spatial smoothing algorithm was applied to the data.

Statistical analysis was based on the general linear model. The GLM analysis was performed independently for the time course of each individual voxel. In all experiments described in this paper, each experimental condition was defined as a separate predictor. Percent signal change for each subject in each experiment was calculated as the percent activation from a blank baseline. Only voxels at the significant level of $p < 10^{-5}$ (uncorrected) were included in the statistical map. Clusters of six or more contiguous voxels were considered significant.

After completing the subject-by-subject analysis, we also analyzed the data in a multisubject approach. To obtain the multisubject maps, the time courses of subjects were converted into Talairach space, z normalized, and concatenated. The statistical tests were performed on the concatenated time course. The multisubject functional map is projected on the inflated and flattened brain of one subject.

Mapping Borders of Visual Areas
The representations of vertical and horizontal visual field meridians were mapped in a separate scan for all subjects in order to delineate the borders of the retinotopic areas (DeYoe et al., 1996; Engel et al., 1994; Grill-Spector et al., 1998b, 2000; Sereno et al., 1995). Visual stimulation was presented in epochs of 18 s. The stimuli consisted of triangular wedges that compensated for the expanded foveal representation. The wedges were presented either vertically (upper or lower vertical meridians) or horizontally (left or right horizontal meridians). The wedges consisted of either gray-level natural images or black and white objects-from-texture pictures (Grill-Spector et al., 1998a). Each image was presented for 250 ms. Subjects were requested to fixate on a small central red dot. Visual epochs alternated with 6 s blanks. Four cycles of the stimuli were shown. This exact method of retinotopic delineation has been successfully used in many of our studies to date (Grill-Spector et al., 1998a; Levy et al., 2001).

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