

A Human Extrastriate Area Functionally Homologous to Macaque V4

Case Study

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Summary

Extrastriate area V4 is crucial for intermediate form vision and visual attention in nonhuman primates. Human neuroimaging suggests that an area in the lingual sulcus/fusiform gyrus may correspond to ventral V4 (V4v). We studied a human neurological patient, AR, with a putative V4v lesion. The lesion does not affect early visual processing (luminance, orientation, and motion perception). However, it does impair hue perception, intermediate form vision, and visual attention in the upper contralateral visual field. Form deficits occur during discrimination of illusory borders, Glass patterns, curvature, and non-Cartesian patterns. Attention deficits occur during discrimination of the relative positions of object parts, detection of low-salience targets, and orientation discrimination in the presence of distractors. This pattern of deficits is consistent with the known properties of area V4 in nonhuman primates, indicating that AR's lesion affects a cortical region functionally homologous to macaque V4.

Introduction

Much of our current understanding about the function of human visual cortex comes from studies of visual cortex in the macaque monkey. The human and macaque visual systems appear to share a similar anatomical organization (Sereni et al., 1995). In addition, the early visual systems of the two species (i.e., retina, visual thalamus, and primary visual cortex) appear to be functionally homologous (DeValois et al., 1974). Beyond area V1, however, functional homology between human and macaque visual cortices is unclear.

In this report, we examine functional homology between extrastriate visual area V4 in humans and macaques by behavioral assessment of visual function in a human achromatopsic patient. The patient, AR, has a small unilateral lesion at the temporal–occipital junction, in the lingual sulcus/fusiform gyrus. This region corresponds to an area identified in functional imaging studies as the ventral portion of human V4, called V4v (Sereni et al., 1995; DeYoe et al., 1996; Hadjikhani et al., 1998; Beauchamp et al., 1999). Many previous studies of human V4 have focused on color vision and have not produced definitive evidence of homology (Heywood et al., 1991; Zeki et al., 1991; Rizzo et al., 1993; McKeefry and Zeki, 1997; Beauchamp et al., 1999; Zeki et al., 1999). Here, we address the question of homology from

a different perspective by focusing on form processing and visual attention.

Area V4 is one of the largest visual areas in the macaque, occupying about 10% of visual cortex and 5% of neocortex as a whole (Felleman and Van Essen, 1991). Anatomically, V4 lies on the prelunate gyrus, immediately anterior to area V2 and dorsal to area V3 (Zeki, 1975; Gattass et al., 1988). V4 receives most of its visual input from area V2, and it projects primarily to area TEO (Felleman and Van Essen, 1991). (There is some disagreement about the extent of TEO; here, we refer to the retinotopic area immediately anterior to V4, which is roughly coextensive with PIT in the nomenclature of Felleman and Van Essen [1991].) Based on anatomical connections alone, V4 appears to be an intermediate processing stage in the ventral visual processing stream (Ungerleider and Mishkin, 1982).

Neurophysiological studies have shown that macaque area V4 contains a high proportion of cells selective for color (Schein and Desimone, 1990; Zeki, 1975, 1983). Color selectivity in V4 is more complex than that observed in earlier areas such as V1 and V2, and V4 has been postulated to play an important role in color constancy (Zeki, 1980; Zeki et al., 1999). Early neurophysiological evidence of color processing in primate V4 has served to focus subsequent experimental attention on color processing in human V4, as discussed below.

Several neurophysiological studies in nonhuman primates have also demonstrated that V4 neurons are sensitive to specific aspects of stimulus shape (Desimone and Schein, 1987; Gallant et al., 1993; Kobatake and Tanaka, 1994). For example, V4 neurons are selective for non-Cartesian grating patterns (Gallant et al., 1993, 1996; Kobatake and Tanaka, 1994) and contour curvature (Pasupathy and Connor, 1999), two aspects of stimulus structure not explicitly represented in earlier visual areas. Neurophysiological studies have shown that cells in area V2 are sensitive to second-order visual stimuli such as illusory contours (Peterhans and von der Heydt, 1987; von der Heydt and Peterhans, 1987) and amplitude-modulated (AM) sinusoidal gratings (Zhou and Baker, 1994, 1996; Mareschal and Baker, 1998). To date, no single-unit studies have examined this issue in V4. However, because V2 projects directly to V4, second-order contours are also likely to be represented in V4. Lesion studies in nonhuman primates have confirmed these physiological results. V4 lesions in macaques affect intermediate aspects of stimulus form while sparing stimulus properties explicitly represented in V1 (Schiller and Lee, 1991; Schiller, 1995; Merigan and Phan, 1998). For example, V4 lesions reduce the ability to discriminate the orientation of illusory contours (De Weerd et al., 1996) and to identify borders defined by texture discontinuities (Merigan, 1996).

Both physiological and lesion studies in nonhuman primates suggest that area V4 is important for allocating visual attention. Attentional modulation appears to increase the selectivity of V4 cells by improving spatial selectivity and neuronal tuning (Moran and Desimone, 1985; Haenny et al., 1987; Maunsell et al., 1991; Motter, 1994; McAdams and Maunsell, 1999). Attentional modulation of spatial receptive field profiles in V4 may also

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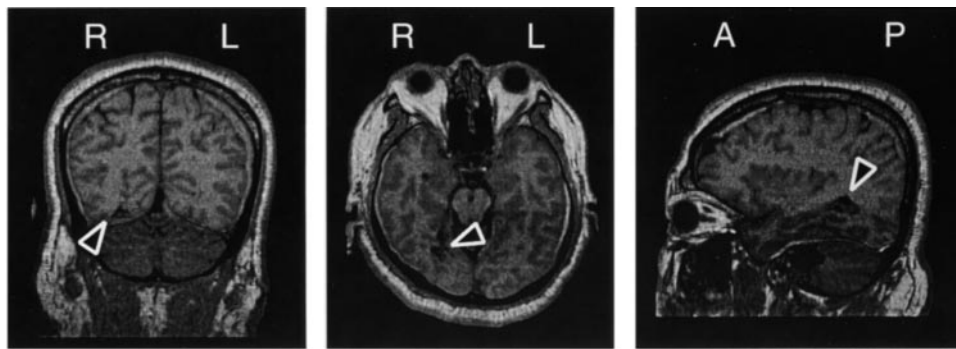


Figure 1. Location of Lesion

AR's lesion is shown in coronal (left), axial (middle), and sagittal (right) sections. Sections were selected to illustrate the maximum extent of the lesion in each plane. The small, right-hemisphere lesion (arrows) is located close to the temporal–occipital junction. The lesion is about 4 mm at its longest extent and runs along the fusiform gyrus and into the lingual sulcus, with little involvement of the underlying white matter. Images were acquired using T1-weighted MR imaging at 1.5 T.

reflect the representation of the relative position of image features within a single object (Connor et al., 1996, 1997). Lesions of area V4 in nonhuman primates disrupt attentionally demanding visual search tasks. V4 lesions bias attentional allocation, making highly salient (e.g., brighter, bigger) stimuli more detectable than stimuli of lower salience (Schiller and Lee, 1991; Schiller, 1995). Similar lesions also impair target selection in the presence of flanking distractors (De Weerd et al., 1999).

Recent functional magnetic resonance imaging (fMRI) studies in humans have revealed the functional topography and organization of several early visual areas in human occipital cortex. One of these areas represents the upper visual field and appears to be homologous to macaque V4v (Serenio et al., 1995; DeYoe et al., 1996). To date, the dorsal subdivision of V4 (V4d) has not been identified in humans.

Whether or not human area V4v is functionally homologous to macaque V4v is still a matter of substantial debate. Many studies have examined patients with temporal–occipital lesions encompassing putative area V4v (Kolmel, 1988; Rizzo et al., 1993; Cowey and Heywood, 1995; Heywood et al., 1995; Heywood and Cowey, 1998; Mendola and Corkin, 1999). Unfortunately, these lesions are typically quite large and often involve both striate and extrastriate areas other than V4, as well as underlying white matter (but see the report of Merigan et al. [1997], which studied a patient with a focal lesion comparable to the one examined here). As noted above, many of these studies have focused on achromatopsia (Zeki, 1990). It is unclear whether achromatopsia is due specifically to V4 damage (Kolmel, 1988; McKeefry and Zeki, 1997); several studies now suggest that this syndrome may in fact be a consequence of collateral damage to visual processing modules that receive input from area V4 (Cowey and Heywood, 1995; Heywood et al., 1995; Hadjikhani et al., 1998; Heywood and Cowey, 1998).

A few studies of putative human V4 lesions have examined intermediate form vision (Rizzo et al., 1993; Merigan et al., 1997). However, these studies did not evaluate the full range of stimuli that, based on studies in nonhuman primates, would be expected to require V4. Human functional imaging studies suggest that V4 might be sensitive to the orientation of illusory contours (Mendola et al., 1999), but these stimuli have not been used in human V4 lesion studies. Other second-order tasks

likely to be affected by V4 lesions, such as detection and discrimination of static Glass patterns (Glass and Switkes, 1976), also remain to be tested. Psychophysical (Wilson et al., 1997), electrophysiological (Allison et al., 1999), and neuroimaging (James et al., 1999, *Invest. Ophthalmol. Vis. Sci.*, abstract) studies in normal humans all suggest that human V4 explicitly represents curvature, although this hypothesis has not been tested in patients with V4 lesions.

Despite extensive neurophysiological evidence from macaques that V4 plays an important role in visual attention, few studies have investigated the effects of V4 lesions on attention in humans. To our knowledge only one human lesion study has specifically assessed attentional allocation using a task similar to those used in animal studies (Mendola and Corkin, 1999). This study reported deficits similar to those reported by Schiller and colleagues (Schiller and Lee, 1991; Schiller, 1995) in macaques. However, the lesion described by Mendola and Corkin was relatively large and encompassed areas beyond V4, making it unclear exactly which area is specifically responsible for the observed behavioral deficits.

Results

In this paper, we describe deficits in color perception, intermediate form vision, and visual attention in a 56-year-old male patient, AR, following a right hemisphere posterior cerebral artery infarct two years prior to this study. Neurological examination following the infarct revealed achromatopsia confined to the left upper visual quadrant, with no other significant visual or cognitive deficits (see Experimental Procedures). Subsequent MR imaging revealed a small (2–4 mm) right hemisphere lesion in the lingual sulcus/fusiform gyrus close to the temporal–occipital junction (see Figure 1). This lesion is coincident with putative human V4v (Kolmel, 1988; Serenio et al., 1995; DeYoe et al., 1996; Hadjikhani et al., 1998) and substantially smaller than most previously reported human V4 lesions (Zeki, 1990; Cowey and Heywood, 1995; Heywood et al., 1995; Heywood and Cowey, 1998; Mendola and Corkin, 1999).

Detection and discrimination thresholds were estimated using a nonparametric staircase procedure (Levitt, 1970). For each task, behavioral thresholds were obtained concurrently in each quadrant of the visual

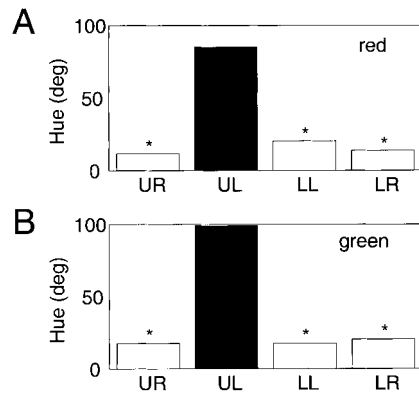


Figure 2. Hue Discrimination Thresholds in the Lesioned Upper Left Quadrant Are Significantly Higher than Those Observed in the Three Remaining Quadrants

(A) Hue discrimination thresholds for a red reference patch. The ordinate gives thresholds obtained in the upper right (UR), upper left (UL), lower left (LL), and lower right (LR) quadrants, respectively. The lesion affects the upper left quadrant, and the corresponding threshold is shown in black. Asterisks indicate significant ($p < 0.01$) differences between the lesioned quadrant and each normal quadrant.

(B) Hue discrimination thresholds for a green reference.

field using four independent interleaved staircases. All stimuli were flashed briefly in the relevant quadrant while AR fixated a spot at the center of the display (see Experimental Procedures for details).

Color Perception

A hue-matching task was used to assess both the spatial extent and degree of achromatopsia. Each trial consisted of a brief reference patch that appeared at fixation, followed by a brief test patch that could appear in any visual quadrant (stimuli not shown). Red and green reference hues were tested in separate sessions. The test stimulus could either have the same hue as the reference or a different hue as determined by the staircase. AR had to indicate whether or not the test hue was the same as the reference hue. The results revealed that AR has a significant deficit in color perception that is confined to the upper left quadrant (see Figure 2).

The remainder of our experiments can be divided into two broad categories: early and intermediate vision tasks. Early vision tasks are those that macaques can perform accurately following lesions of area V4 (Schiller, 1995; Schiller and Lee, 1991; Merigan, 1996; Merigan and Phan, 1998). Intermediate vision tasks are those affected by V4 lesions in macaques (Schiller and Lee, 1991; Schiller, 1995; Merigan, 1996; Merigan and Phan, 1998; De Weerd et al., 1999) and those selected based on published physiological properties of macaque V4 neurons (Gallant et al., 1993, 1996; Connor et al., 1997). Intermediate vision tasks include both form vision and visual attention tasks.

Early Vision Tasks

We examined early vision using three different tasks: luminance detection, orientation discrimination, and motion direction discrimination (see Figures 3A–3C). In all three tasks, a single test stimulus appeared briefly in one of the four visual quadrants, and AR had to indicate whether it matched a reference stimulus specified by

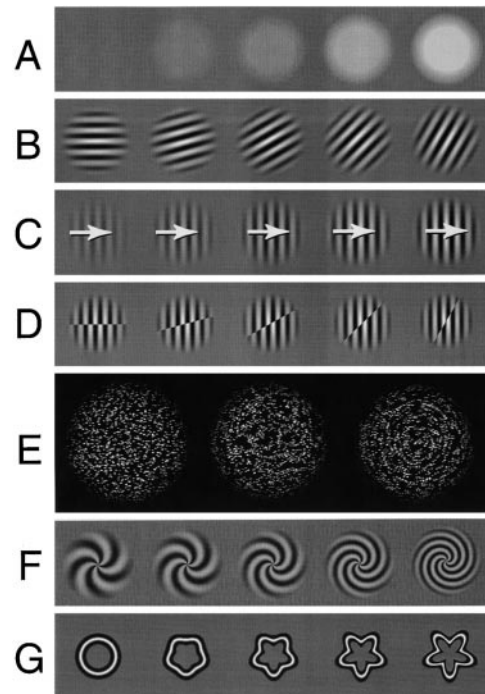


Figure 3. Stimuli Used in the Various Tasks Discussed in This Report
The stimuli are shown for illustration purposes and do not necessarily reflect the range of thresholds.

(A) Circular luminance patches.

(B) Oriented sinusoidal gratings.

(C) Drifting sinusoidal gratings (motion shown schematically).

(D) Sinusoidal gratings containing a second-order oriented border.

(E) Concentric Glass patterns differing in signal-to-noise ratio. To preserve visibility, only three large patterns are shown in this panel.

(F) Non-Cartesian spiral sinusoidal gratings.

(G) Radial-frequency-modulated circles. See Experimental Procedures and text for details of psychophysical procedures.

verbal instructions. For luminance, AR had to indicate whether the brightness of the test patch was different from the background. In the orientation task, he had to indicate whether the test grating was horizontal or oblique. In the motion task, he had to indicate whether the test grating drifted to the left or right.

In contrast to AR's clear color perception deficit, he showed no significant impairment on any of the early form vision tasks (see Figures 4A–4C). This is generally consistent with previous results obtained in both human achromatopsic patients (Kolmel, 1988; Rizzo et al., 1993; Merigan et al., 1997) and nonhuman primates with V4 lesions (Schiller and Lee, 1991; Schiller, 1995; Merigan, 1996; Merigan and Phan, 1998). Note, however, that the patient examined by Merigan et al. (1997) showed impaired contrast sensitivity, while AR appears to have normal contrast sensitivity. This may reflect subtle differences in experimental procedures or differences in the extent of the lesion or involvement of the underlying white matter in the two cases.

Intermediate Form Vision Tasks

We investigated the effects of AR's lesion on intermediate vision by measuring detection and discrimination thresholds in several different tasks. First, we measured AR's ability to discriminate the orientation of illusory contours formed by the addition of an oriented phase

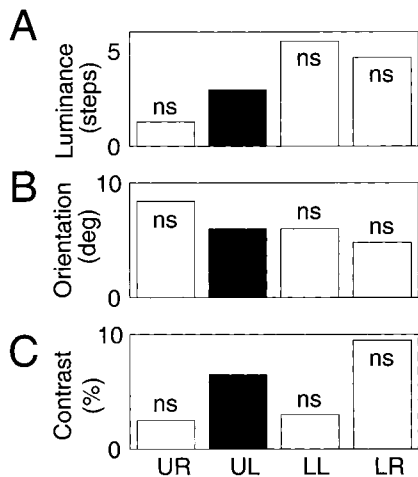


Figure 4. Early Form Vision Thresholds for the Lesioned Quadrant Are Not Significantly Different from the Three Normal Quadrants

(A) Luminance detection thresholds. ns, not significant.
(B) Orientation discrimination thresholds.
(C) Motion direction discrimination thresholds.

shift to a sinusoidal grating (see Figure 3D). On each trial, a single illusory contour stimulus appeared briefly in one of the four visual quadrants, and AR had to indicate whether the illusory contour was horizontal or oblique. His thresholds were significantly higher when stimuli appeared in the upper left quadrant; thresholds in the other three quadrants were comparable to those obtained with conventional gratings (see Figure 5A).

Next, we examined AR's ability to distinguish radial and concentric static Glass patterns from random noise patterns (Glass and Switkes, 1976; Wilson et al., 1997; Wilson and Wilkinson, 1998; also see Figure 3E). On each trial, a single Glass pattern composed of Gaussian

dots appeared briefly in one of the four visual quadrants. The staircase controlled the ratio of signal to noise dots. AR had to indicate whether the dots formed a Glass pattern or were distributed randomly. Radial and concentric patterns were tested in different sessions.

Pilot studies with normal observers in our laboratory indicate that Glass pattern discrimination at peripheral locations is a demanding psychophysical task. Consistent with this, AR's overall performance was poor in all quadrants, and absolute threshold values varied substantially across testing sessions. However, within each session his performance was consistently and significantly worse in the lesioned upper left quadrant than in the other three quadrants (see Figure 5B).

Finally, we evaluated AR's perception of curvature using two different tasks. The first task employed spiral gratings modulated in non-Cartesian polar coordinates (Gallant et al., 1993, 1996; also see Figure 3F). On each trial a spiral reference grating appeared briefly at the fixation point, followed by a spiral test grating that could appear in any visual quadrant. AR had to indicate whether the concentric frequency of the test grating was the same or higher than the reference (i.e., whether it had higher spiral curvature). He had a significant behavioral deficit in the upper left visual quadrant (see Figure 5C).

The second curvature task used radial-frequency-modulated circles as test patterns (Wilkinson et al., 1998; also see Figure 3G). One of two stimuli could appear on any trial: a single circle or a radially deformed circle containing five lobes. AR had to indicate whether a circle or deformed circle had appeared. Once again, he showed a significant deficit in circle discrimination restricted to the upper left quadrant (see Figure 5D).

Attention Tasks

We examined the effects of the lesion on visual attention using three different tasks. First, we designed a task to assess the effect of AR's lesion on his ability to discriminate the relative positions of object parts (Logan, 1994). For this task, stimuli were bipartite circular disks, half white and half black, divided horizontally. On some trials the white half was above the black, while on others the black half was above the white. A single disk appeared in one quadrant on each trial; AR had to indicate whether the white half was above or below the black half. In this experiment, the staircase determined the display duration rather than stimulus structure. In all three unlesioned quadrants, AR was able to perform this task in a single video frame (14 ms). In contrast, the patterns had to be displayed for over 100 ms to achieve equivalent performance in the lesioned quadrant (see Figure 6A).

To verify that AR was able to detect the presence of the contrast border, we used similar bipartite stimuli in two control tasks. In the first, the border could be oriented either horizontally or vertically, and AR indicated the border orientation on each trial. In the second, AR had to discriminate between bipartite and solid (white or black) disks. AR could easily perform each of these tasks equally well in the lesioned and unlesioned quadrants (data not shown). These results confirm that the lesion impairs judgment of the relative position of the parts of an object but not detection of the component parts.

We also investigated whether the lesion affected AR's

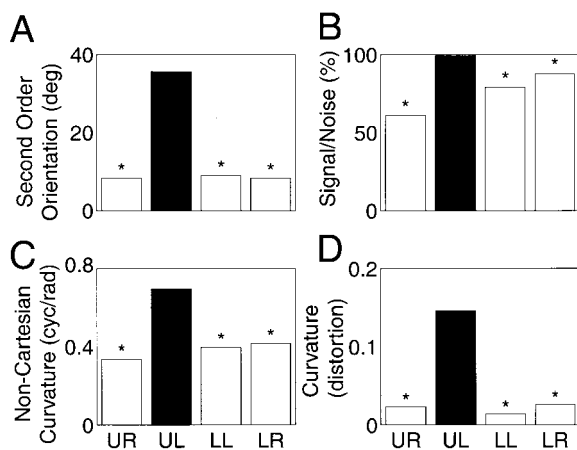


Figure 5. Intermediate Form Vision Thresholds Are Significantly Elevated in the Lesioned Quadrant

(A) Second-order border orientation discrimination thresholds.
(B) Concentric Glass pattern discrimination thresholds. Similar results are obtained with radial Glass patterns.
(C) Spiral non-Cartesian grating discrimination thresholds.
(D) Radial-frequency-modulated circle discrimination thresholds. The abscissa represents arbitrary units of curvature; see Experimental Procedures for details.

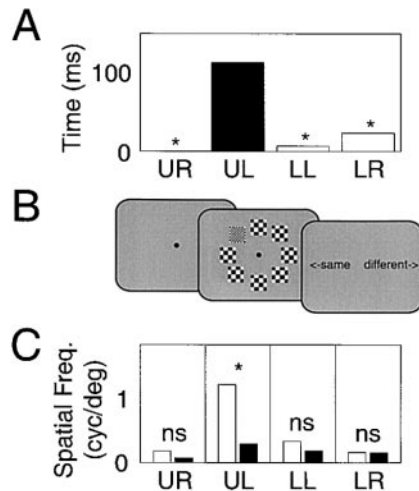


Figure 6. Spatial Position Discrimination and Visual Search Thresholds Are Higher in the Lesioned Quadrant than in the Normal Quadrants

(A) Relative position discrimination thresholds.
(B) Visual search for an odd item. Each trial consisted of eight identical items (not shown) or seven identical items and one odd item, as illustrated here.
(C) Visual search thresholds. White bars show thresholds obtained when the spatial frequency of the target pattern was higher (i.e., less salient) than that of the distractors. Black bars show thresholds observed when the frequency of the target pattern was lower (i.e., more salient) than that of the distractors. Search asymmetry is significantly greater in the lesioned than in the unlesioned quadrants. Similar results were obtained with circular outlines of different sizes.

ability to distinguish between stimuli differing in perceptual salience (Schiller and Lee, 1991; Schiller, 1995; Mendola and Corkin, 1999). For these experiments, we used a conventional visual search procedure (see Figure 6B). Each search display was composed of eight items arranged in a circle around the fixation point. A given trial contained either eight identical items or seven identical items and one odd item that could appear at any of the eight locations. Two different stimulus classes were tested in different sessions: high contrast, white circular outlines and high contrast checkerboard patterns with random luminance polarity phase. High-salience and low-salience target items were tested in separate sessions on the same day. The high-salience circles were larger than the distractors, and the high-salience checks had lower spatial frequency than the distractors; the low-salience circles were smaller than the distractors, and the low-salience checks had higher spatial frequency than the distractors. Distractor salience was held constant throughout a session, while the staircase controlled the salience of the odd items. In all cases AR simply had to indicate whether or not the search display contained an odd item.

Previous psychophysical studies have demonstrated a small performance asymmetry for stimuli differing in perceptual salience; detection and discrimination of more salient items is better than that for less salient items (Treisman and Gormican, 1988). Consistent with this, AR's performance was generally better when the targets were more salient than the distractors. However, the asymmetry was significantly larger in the lesioned quadrant than in the unlesioned quadrants (see Figure

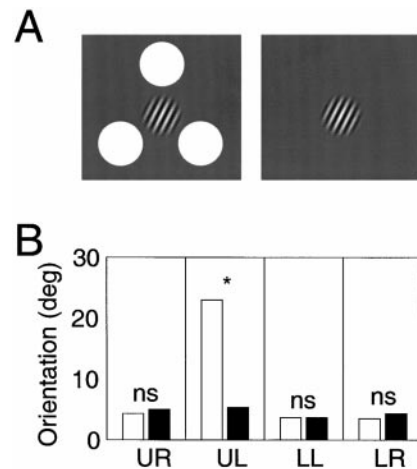


Figure 7. Distractors Elevate Orientation Discrimination Thresholds in the Lesioned Quadrant

(A) Orientation discrimination in the presence of distractors. Each trial included one oriented sinusoidal grating that could appear alone or flanked by three white or black distractors.
(B) Thresholds for orientation discrimination in the presence of distractors. Black bars show thresholds observed when no distractors were present. White bars show the thresholds obtained with white distractors. Similar results were obtained with black distractors. Distractors impaired orientation discrimination performance in the lesioned quadrant but had no effect in the unlesioned quadrants.

6C). These results are consistent with studies of both animals (Schiller and Lee, 1991; Schiller, 1995) and humans (Mendola and Corkin, 1999).

Finally, we examined the allocation of spatial visual attention in the presence of distractors (De Weerd et al., 1999). On each trial a single sinusoidal grating appeared at the center of one visual quadrant. On half of the trials, the grating appeared alone, while on the other half it was surrounded by three circular distractors (see Figure 7A). Trials with and without distractors were randomly interleaved within each session. White and black distractors were tested in different sessions. The staircase controlled the orientation of the grating. In all cases AR had to determine whether the grating was vertical or oblique. AR showed a significant performance deficit restricted to the lesioned quadrant in the distractor-present condition, relative to the distractor-absent condition (see Figure 7B). The deficit was independent of distractor polarity. This finding is consistent with the results of an earlier lesion study in macaques (De Weerd et al., 1999).

Discussion

AR shows no deficit on early vision tasks such as luminance detection and orientation and motion discrimination. In contrast, he shows profound deficits on color, intermediate form, and visual attention tasks. Moreover, these deficits are confined to the lesioned visual quadrant. The fact that both visual acuity and early form and motion discrimination are unaffected by the lesion suggests that information explicitly represented in primary visual cortex can bypass the lesioned area, possibly via the dorsal visual processing stream (Ungerleider and Mishkin, 1982). Unimpaired performance in the early

vision tasks also suggests that the observed deficits are not simply due to a general attentional deficit.

The form and attention deficits observed here are consistent with those reported in lesion studies of non-human primates. V4 lesions in macaques impair perception of second-order stimuli such as texture-defined borders (Merigan, 1996). Likewise, AR has difficulty discriminating second-order stimuli (illusory contours) in the lesioned quadrant. V4 lesions in macaques also impair performance in attentionally demanding tasks such as visual search; the lesions appear to make it difficult for the animals to exclude irrelevant or more salient distractors (Schiller and Lee, 1991; Schiller, 1995; De Weerd et al., 1999). In similar search tasks, AR shows deficits that are restricted to the lesioned quadrant.

Our findings are also consistent with single-unit studies of macaque V4. Several neurophysiological experiments have demonstrated that macaque V4 neurons preferentially represent curvature (Pasupathy and Connor, 1999) and non-Cartesian patterns (Kobatake and Tanaka, 1994; Gallant et al., 1996) not explicitly represented in area V1. Although AR can normally judge the orientation of simple gratings, he is severely impaired at discriminating non-Cartesian patterns presented in the lesioned quadrant. This novel result confirms recent neurophysiological evidence suggesting that non-Cartesian patterns are processed preferentially in human extrastriate cortex (Allison et al., 1999). Neurophysiological studies also suggest that single neurons in macaque V4 may encode the position of object parts relative to the current focus of attention (Connor et al., 1996, 1997). AR's lesion impairs his ability to identify the relative position of parts of objects, though he has no difficulty detecting their presence. This is direct evidence suggesting that human V4 might be involved in encoding the relative positions of object parts.

Location of Lesion

The data presented here demonstrate that AR's focal lesion encompasses a human extrastriate visual area functionally homologous to macaque area V4. Previous functional neuroimaging studies suggest that human V4v lies along the lingual sulcus and fusiform gyrus (Serenio et al., 1995; DeYoe et al., 1996; Hadjikhani et al., 1998; Beauchamp et al., 1999), and anatomical MRI confirms that AR's lesion is also located at this site. It is possible that the lesion may also affect adjacent anterior extrastriate areas. However, because AR's deficits are confined to a single visual quadrant, collateral damage must be both confined to retinotopic areas and limited in scope. Only area TEO (Boussaoud et al., 1991) and the recently reported V8 (Hadjikhani et al., 1998) meet these requirements.

Ideally, we could resolve this issue by testing AR using a task that would unambiguously distinguish between V4 and TEO/V8. Unfortunately, at this time we don't know enough about the role of these anterior areas in form vision and attention to devise appropriate psychophysical tasks. Shape selectivity in TEO is similar to V4, although TEO neurons have more complex tuning (Kobatake and Tanaka, 1994) and larger receptive fields (Boussaoud et al., 1991). In macaques both V4 and TEO lesions produce small form vision deficits on simple tasks but large deficits on tasks that engage attention (De Weerd et al., 1999). TEO lesions have also been reported to produce more profound color perception

deficits than those resulting from V4 lesions (Heywood and Cowey, 1987; Heywood et al., 1995).

In summary, there are currently insufficient data to allow us to unequivocally determine whether AR's lesion is restricted only to area V4v. However, the pattern of deficits indicates that any damage beyond area V4v is most likely confined to a limited region of TEO/V8.

Color Vision

In addition to form and attention deficits, AR exhibits a profound color discrimination deficit in the lesioned quadrant. The functional implications of this deficit are unclear. Zeki and colleagues have argued that V4 lesions are the underlying cause of achromatopsia (Zeki, 1990; Zeki et al., 1999). However, similar lesions in nonhuman primates have been consistently reported to produce only mild color deficits (Cowey and Heywood, 1995; Merigan et al., 1997).

There are three possible explanations for this apparent species difference. First, it could reflect differences between human and macaque experimental methods. Animal experiments tend to involve significantly more training than similar experiments on human neurological patients. This additional training might enable animals to compensate for some of the perceptual deficits accompanying V4 lesions. Second, the difference could reflect a real and important functional difference in color processing between the two species; area V4 could be important for color perception in humans but not in macaques. Third, AR's achromatopsia might reflect focal damage to TEO/V8, anterior to area V4v. In this case there would be no discrepancy to resolve, because lesions anterior to V4 appear to affect color perception in both species (Heywood et al., 1995).

Conclusion

We tested the hypothesis that human V4 is functionally homologous to V4 in the macaque by testing a neurological patient, AR, with a putative V4v lesion. In every form vision and visual attention task we examined, AR's performance was consistent with the predicted effects of a V4 lesion based on anatomical, lesion, and neurophysiological data from the macaque. The only inconsistency involves color vision; AR showed clear color vision deficits in the lesioned quadrant, but the role of V4 in macaque color vision is currently unclear. Taken together, these data provide strong evidence that a retinotopic region in the human lingual sulcus/fusiform gyrus is functionally homologous to area V4v in the macaque. Moreover, our data indicate that this region is crucial for normal intermediate visual form processing and attention in humans. This leads us to conclude that, with respect to form vision and visual attention, the human and macaque visual systems are functionally homologous up to the level of V4.

Experimental Procedures

Patient

AR is a 56-year-old male diabetic with chronic hypertension. At age 52, 2 years prior to the beginning of this study, AR suffered a right hemisphere lesion near the temporal-occipital junction following a posterior cerebral artery infarct. Immediately after the infarct, AR reported a transient blindness that resolved without treatment within 12 hr. A subsequent neurological exam and visual field map revealed persistent achromatopsia confined to the upper left quadrant and a small perifoveal scotoma (about 0.5° diameter at 2° eccentricity).

An anatomical MRI scan taken 2 years after the injury revealed a small right hemisphere lesion of the lingual sulcus close to the temporal–occipital junction. The lesion extends ~4 mm along its longest axis from the lingual sulcus into the fusiform gyrus with little involvement of the underlying white matter. This unilateral lesion encompasses the putative human area V4v (Kolmel, 1988; Zeki, 1990; Sereno et al., 1995; DeYoe et al., 1996; Hadjikhani et al., 1998).

A neurological examination conducted at the beginning of these experiments confirmed the persistence of AR's achromatopsia but revealed no additional visual deficits. AR reports no difficulties in form vision other than occasional problems resolving written text in the left periphery, consistent with his small scotoma. AR continues to work and drive normally.

Stimulus Presentation

AR sat 50 cm from a high-quality computer display (Sony Trinitron, 72 Hz, 40° horizontal, 1280 × 1024 pixels). During testing, his head was stabilized at a constant distance from the monitor using a chin rest. With one exception (orientation discrimination in the presence of distractors, see below), test stimuli were 6° in diameter, appeared at 12° eccentricity, and were blended smoothly into a neutral gray background to eliminate potential edge artifacts. These parameters were chosen to ensure that stimuli were confined to a single quadrant while avoiding the vertical and horizontal meridians (except for the perceptual saliency task, as noted below), the visual blindspot, and AR's perifoveal scotoma.

Psychophysical Methods

Detection and discrimination thresholds were estimated using a standard nonparametric staircase procedure (Levitt, 1970). Thresholds were obtained simultaneously in each visual field quadrant using four independent, interleaved staircases. The discriminability of stimuli in each quadrant was decreased after three correct trials in a row in that quadrant and increased after one error in that quadrant. This 3-down/1-up procedure converges on a stimulus level that corresponds to 80% correct responses regardless of the underlying psychometric function. Data from pilot studies in normal subjects and AR were used to set the stimulus parameters for each task so that targets were initially highly discriminable. The first four steps of the staircase were relatively large to facilitate rapid convergence. Trials continued in all four quadrants of the visual field until at least 12 reversals occurred in each quadrant. Threshold values were computed separately for each quadrant by averaging stimulus values at the last six reversal points.

Significance was assessed using nonparametric randomization (or permutation) tests (Manly, 1991). For all experiments, the mean stimulus level of the last six staircase reversals obtained in the lesioned quadrant was compared to the mean stimulus level of the last six reversals in each of the unlesioned quadrants. Statistical significance was estimated by comparing the measured mean difference to the distribution of 100 random permutations of the same data obtained in lesioned and unlesioned quadrants. For all experiments reported here, significance was set at $p < 0.01$.

Except where noted below, all experiments followed the same trial structure. A fixation target appeared at the center of the screen. AR was instructed to fixate and then press a key. After a 600 ms delay, the test stimulus appeared for 200 ms accompanied by a brief tone. After another 300 ms, the fixation spot was extinguished and a response screen appeared, indicating two possible responses. AR then responded by pressing a left or right key. Stimulus location was varied randomly to eliminate any anticipation effects. Responses were not timed and AR was allowed to take short breaks as required.

AR received substantial practice (2–5 hr) on each task before data reported here were collected. Pilot experiments and early practice sessions were conducted without feedback, while later sessions and all of the data reported here were conducted with feedback. Eye position was not monitored, but brief presentations were used to minimize the effects of voluntary eye movements. AR's lesion affects only one quadrant. If he attempted to improve performance by shifting fixation toward the lesioned quadrant, it would improve his performance in the lesioned quadrant while reducing performance in the opposite quadrant. The magnitude of the deficits we

report here are conservative in the sense that any uncontrolled eye movements will tend to minimize the apparent effect of the lesion.

Color (Hue) Discrimination

To estimate color discrimination thresholds, we presented a reference stimulus (6°) at the fovea for 250 ms following fixation. Two hundred and fifty milliseconds after the reference stimulus was extinguished, the test stimulus appeared in one quadrant, chosen at random. Colors were specified using hue, saturation, and brightness (HSB) coordinates. A slice through HSB space in which brightness is held constant can be visualized as a circle, where hue is given by the angular component around the circumference of the circular slice, and saturation is given by the radial component. By convention red is located at 0°, green at 120°, and blue at 240°. For the current experiments, saturation and brightness were both held constant (at 80% of the maximum screen saturation and 40% of the maximum screen brightness) while hue angle was varied systematically to estimate color discrimination thresholds. We tested red and green reference hues in different sessions. On trials in which the test stimulus did not match the reference stimulus, hue could vary in either direction from the reference hue (i.e., with a red reference hue, the test hues could vary either toward yellow–green or toward magenta–blue; with a green reference hue the test hues could vary either toward yellow–red or toward cyan–blue). In all cases AR had to indicate if the reference and test stimuli were the same or different.

Luminance Detection

Luminance detection thresholds were measured by varying the luminance of circular patches relative to the background (~10–15 cd/m², though monitor luminance and ambient brightness could not be controlled perfectly in the clinical setting). Each trial contained either a circular patch that was brighter or darker than the background, or no circular patch (i.e., a patch that was the same brightness as the background). The circular patch could appear in any quadrant. AR had to indicate whether the trial contained a patch the same as or different from the background.

Conventional Orientation Discrimination

Thresholds were measured by varying the orientation of sinusoidal gratings (1.33 cycles/°, 50% contrast) around the horizontal. On each trial a single horizontal or oblique grating appeared in one quadrant. Oblique gratings could be tilted either clockwise or counterclockwise from the horizontal. AR had to indicate whether the grating was horizontal or oblique.

Motion Discrimination

Thresholds were measured by varying the Michelson contrast (0%–100%) of vertical sinusoidal gratings (1.33 cycles/°) drifting to the left or right (0.6 cycles/s). The staircase controlled the contrast of the grating. Each trial contained a single moving grating in one quadrant, and AR had to determine whether the grating drifted to the left or the right.

Second-Order Orientation Discrimination

The methods for this experiment were identical to those used to measure conventional orientation discrimination thresholds, except that the stimuli contained a second-order illusory contour. The second-order contour was created by introducing an oriented phase shift along a diameter of a vertical sinusoidal grating. Although the carrier grating was always vertical, the magnitude and orientation of the second-order contour varied across trials. AR was instructed to indicate whether the illusory contour was horizontal or oblique. Discrimination thresholds were measured by varying the orientation of the second-order contour according to the staircase procedure.

Glass Pattern Discrimination

Static Glass patterns were generated by uniformly distributing Gaussian dots (3 pixel diameter) on a rectangular grid. Dot coordinates were rotated or translated relative to the center of the grid and redrawn to form concentric or radial Glass patterns, respectively. For concentric Glass patterns, dots were rotated such that each dot translated the same distance in rectangular coordinates (as opposed to a constant angle in polar coordinates). This procedure

produces a Glass pattern with no density cues near the center that might be used for detection. For presentation all patterns were presented on a black background and were masked with a circular aperture. During testing, each Glass pattern was combined with a random noise signal (uniformly distributed Gaussian dots). On each trial, AR indicated if the test pattern was a Glass pattern or a noise pattern. Detection thresholds were measured by using the staircase to vary the ratio of signal to noise dots, keeping overall dot density constant. Concentric and radial Glass patterns were tested in separate sessions.

Non-Cartesian Spiral Frequency Discrimination

Spiral sinusoidal gratings were constructed using the method of Gallant et al. (1996). Each sinusoidal luminance grating was modulated in polar coordinates to produce a spiral pattern. For these experiments the radial frequency component was fixed at 5 cycles/360°. Thresholds were measured by increasing the concentric frequency component beyond its baseline value of 8 cycles/stimulus. On each trial a test grating appeared at fixation, and after it was extinguished a single spiral grating appeared in any one quadrant. AR had to indicate whether or not the test grating matched the reference.

Radial-Frequency-Modulated Circle Discrimination

Radial-frequency-modulated circles were constructed according to the method of Wilkinson et al. (1998). The cross-sectional luminance profile was defined by the radial fourth derivative of a Gaussian. The circles were radially deformed by a circular sinusoid with 5 cycles/360°. As the radial amplitude modulation increases in these patterns, stimuli become increasingly distorted and total curvature increases. During testing, the staircase controlled the radial amplitude, and AR was asked to indicate whether each stimulus was circular or noncircular.

Relative Position Discrimination

Stimuli were high-contrast, bipartite black and white circular disks. For the relative position task, the contrast-defined border was always horizontal, and AR had to indicate whether the white portion was above or below the black portion. Presentation time was varied in 14.4 ms steps (1 video frame) according to the staircase procedure to measure the minimum time required to determine disk polarity with 80% accuracy. In one control task, disks could appear with either horizontal or vertical borders. AR was instructed to ignore disk polarity and simply indicate if the contrast-defined border was horizontal or vertical. In a second control task, half of the disks were bipartite and the other half were solid (all black or all white). AR had to indicate whether he had seen a bipartite or solid disk.

Perceptual Salience

On each trial a circular array of eight stimuli appeared around the fixation point. The array consisted of either eight identical items (*same* trials) or seven identical items and one odd item (*odd* trials). To maintain a constant attentive load, odd stimuli could appear on the horizontal and vertical meridians, but those trials were not used to drive a staircase nor to compute behavioral thresholds. AR had to indicate whether an odd item was present in the display.

Two different stimulus sets were tested in different sessions. In the first, stimuli were high-contrast, white circular outlines (6° diameter). The odd target was either larger or smaller than the surrounding distractors and could appear in any visual quadrant. In the second stimulus set, targets were high-contrast checkerboard patterns (6°, variable number of checks) with random phase. In this case the spatial frequency of the odd target was either higher or lower than the frequency of the distractors. High- and low-salience stimuli were tested in separate sessions.

Independent staircases were used to vary target size or frequency concurrently in each visual quadrant. Thresholds were calculated only for the four locations at the center of each quadrant of the visual field. Significance was assessed by comparing the performance difference between high- and low-salience stimuli obtained in the lesioned quadrant with that obtained in each of the normal quadrants.

Orientation Discrimination in the Presence of Distractors

On each trial a single sinusoidal grating (4° diameter, 1.33 cycle/deg, 50% contrast) appeared at one of four locations at the center of each visual quadrant (9° eccentricity). AR had to indicate whether the grating was vertical or oblique. On half of the trials the grating appeared alone, and on half it was surrounded by three circular distractors arranged in a triangle centered on the grating (3.8° diameter, centered 4° from center of grating). Trials with and without distractors were interleaved within each session, and thresholds were estimated simultaneously and independently in each quadrant. White and black distractors were tested in separate sessions.

Acknowledgments

We gratefully acknowledge and thank Dr. Robert Knight for his neurological acumen in identifying AR and bringing him to our attention. We also thank Donatella Scabini for patient scheduling and Nina Dronkers for helping us obtain the structural MRI. This study was partially funded by Whitehall and Sloan Foundation grants to J. L. G. R. E. S. was supported by a National Institutes of Health grant to Dr. Robert Rafal.

Received March 3, 2000; revised July 11, 2000.

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