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Color Architecture in Alert Macaque Cortex Revealed by fMRI

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Abstract

The contribution that different brain areas make to primate color vision, especially in the macaque, is debated. Here we used functional magnetic resonance imaging in the alert macaque, giving a whole brain perspective of color processing in the healthy brain. We identified color-biased and luminance-biased activity and colorafterimage activity. Color-biased activity was found in V1, V2, and parts of V4 and not in V3a, MT, or other dorsal stream areas, in which a luminance bias predominated. Color-biased activity and color-afterimage activity were also found in a region on the posterior bank of the superior temporal sulcus. We review anatomical and physiological studies that describe this region, PITd, and postulate that it is distinct from areas V4 and TEO. When taken together with single-unit studies and lesion studies, our results suggest that color depends on a connected ventral-stream pathway involving at least V1, V2, V4, and PITd.

Introduction

Color vision begins in the retina with 3 classes of cones. Specialized cone-opponent cells in the retinal ganglion layer (Dacey 1996), the lateral geniculate nucleus (De Valois and others 1966; Wiesel and Hubel 1966; Chatterjee and Callaway 2003), and the primary visual cortex (Michael 1978; Livingstone and Hubel 1984; Conway 2001; Johnson and others 2001; Wachtler and others 2001; Horwitz and others 2005) are good candidates for the building blocks of color vision. These specialized cells, particularly the double-opponent cells in V1, are sufficient to account for color opponency and local color contrast (Conway and others 2002; Hurlbert and Wolf 2004) but do not seem sufficient to account for other aspects of color vision—for example, color categorization and color constancy across a visual scene. Presumably other, subsequent steps in color processing are necessary to bring about a rich and complete color percept. It is unclear which extrastriate areas are involved in this, particularly in the macaque monkey (Zeki 1996; Tootell and others 2004), a model for human vision. One question centers on whether or not there is an extrastriate area uniquely specialized for color processing.

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Two extreme possibilities are these: 1) that specialized cells within the primary and secondary visual cortex partially process color information and then send these signals to a specialized extrastriate area that is ultimately responsible for the experience of color (Zeki 1978b) and 2) that all visual areas carry out all visual information processing (see Schiller 1997; Gegenfurtner 2003, for a review). Most current views are polarized toward, though not at, these extremes. A strong piece of evidence favoring an extrastriate “color area” is the observation that stroke patients with particular circumscribed lesions acquire achromatopsia (a deficit of color vision) yet retain motion and depth perception (Meadows 1974; Damasio and others 1980; Vaina 1994). Imaging studies of healthy human brains show localization of extrastriate color responses to a region on the ventral surface of the brain (Lueck and others 1989; Zeki and others 1991; Hadjikhani and others 1998; Wade and others 2002).

In macaques, a model for human color vision, the popular color area candidate is area V4. But despite early single-cell recordings suggesting that area V4 is specialized for color (Zeki 1973), subsequent studies found that V4 neurons were often sensitive to other stimulus dimensions and were not necessarily more color selective than neurons in other visual areas (Schein and others 1982; Desimone and others 1985; Tanaka and others 1986), although most neurons in V4 show some wavelength sensitivity (Schein and Desimone 1990). Macaques with V4 lesions do not show profound or specific losses in color vision (Heywood and others 1992; Schiller 1993; Walsh and others 1993). This has been taken to support a distributed model of color processing (Schiller 1997; Gegenfurtner 2003), although the relationship between macaque V4 and the human color center is unclear (Zeki 1996; Tootell and Hadjikhani 1998).

Alternatively, some have proposed that macaque areas anterior to V4, on the inferior convexity of the temporal lobe (IT cortex), are critical for color processing (Komatsu and others 1992; Takechi and others 1997; Hadjikhani and others 1998; Tootell and others 2004) and may be macaque homologs of the human color center. But there is no consensus on the number, function, or boundaries of areas within the IT cortex. Here we use the anatomical names adopted by Distler and others (1993), in which the IT cortex includes areas TEO, TE, and PITd (see Fig. 6). The boundaries of these areas are provisional because knowledge about the function of this part of the brain is incomplete.

Some have argued that areas TE/TEO, which are anterior to V4, are the macaque color areas, based on anatomical homologies between human and macaque brains (Hadjikhani and others 1998) and 2-deoxyglucose experiments (Tootell and others 2004). Lesion studies suggest that these areas are predominantly concerned with object recognition (Ungerleider and Mishkin 1982) and are concerned with color if color is employed in learning paradigms (Gross 1973). Single-unit studies do not indicate a unique specialization for color in this swath of cortex (Gross and others 1972; Fuster and Jervey 1982; Desimone and others 1984), and discrete lesions of TE and TEO fall short of producing behavioral achromatopsia (Cowey and others 2001) or produce only a transient deficit of color (Dean 1979, but see Buckley and others 1997). Other studies, including single-unit measurements (Fuster and Jervey 1982; Komatsu and others 1992) and PET imaging (Takechi and others 1997) suggest that the IT cortex anterior to V4 but posterior to TE/TEO, centered on PITd, is involved in color.

Thus, there is a discrepancy between lesion studies in macaques, which suggest a distributed model of color vision, and stroke studies in humans, which suggest a more localized model. Similarly, single-unit studies in macaques, which sample only a small fraction of neurons in the brain, are often interpreted as support for a distributed model of color vision, whereas imaging studies in humans, which give coarser resolution of the entire brain, support a more localized model of color vision. Here we attempted to address these gaps by using functional magnetic resonance imaging (fMRI) in the alert macaque (Stefanacci and others 1998; Tsao and others 2003), employing the same technique used to image the human color area (Hadjikhani and others 1998; Bartels and Zeki 2000; Wade and others 2002). Our results suggest that there is an anatomical specialization for color that involves a connected network of ventral-stream areas, best represented by a blend of the 2 extreme models.

Materials and Methods

Male rhesus macaques (2--3 kg) were trained to fixate a spot in the center of a computer display and were scanned in a 3-T Allegra (Siemens, New York, NY) scanner using procedures outlined in Tsao and others (2003). Eye movements were monitored with a video-based eye-tracking equipment (ISCAN, Burlington, MA). Data acquired when the macaques were not fixating were not analyzed. Ultem (General Electric Plastics) was used to make head posts which were implanted on the macaques' skulls; the animals were then trained to sit in a sphinx position, with their heads fixed, inside a custom-built cylindrical plastic chair that fit into the bore of the scanner, facing a plastic (Daplex) screen. Two macaques were used in the first experiment (Figs 1 and 2, Supplementary Figure 1), and 3 were used in the second experiment (Figs 3 and 4, Supplementary Figure 2). All procedures conformed to local and National Institutes of Health guidelines. Surgical details and the other experimental procedures are described elsewhere (Tsao and others 2003).

Visual Stimuli

Visual stimuli were displayed using a Sharp XG-NV6XU LCD projector (640 3 480 pixels, 60-Hz refresh rate) on a screen that was positioned 53 cm from the macaque. The stimulus covered the entire screen, 28 3 21. All stimuli were presented in block design. For the colored stimuli, we used only the red and blue dichroic filters of the LCD monitor to allow comparison with earlier data, obtained using similar stimuli (Hadjikhani and others 1998; Tootell and others 2004). Vertically oriented sine wave gratings (0.29 cycles/degree; 1 cycle/s) that moved back and forth, switching directions every 4 s, were used to determine the red:blue luminance ratio that elicited a minimum response in area MT (see Fig. 1). The stimulus sequence consisted of 16 s of black--white gratings (99% contrast) followed by 16 s of uniform neutral gray, matched in mean luminance to the achromatic grating, then 16 s of red--blue gratings followed by 16 s of neutral gray, and so on for a total of 8 presentations of black--white and 8 intervening colored gratings. The red--blue gratings were made by superimposing a blue--black grating, sin(x), with a red--black grating, (r/b) 3 [1 – sin(x)], where r = peak luminance of red dichroic filter, b = peak luminance of blue dichroic filter. The amplitude of the blue grating was constant throughout the experiment (peak 44 cd/m2), but the amplitude of the red was systematically increased from a red:blue ratio of 1:1 (peak 44 cd/m2) in the first colored grating of the sequence to a ratio of 3 in the eighth colored

grating. The peak red and blue of the macaque equiluminant stimulus (ratio red:blue of 2.3) had L-cone contrast of 34%, M-cone contrast of 9%, and S-cone contrast of 84%. Cone contrasts were determined by taking the dot product of the spectral emission (measured with a SpectraScan PR650, Photo Research, Chatsworth, CA) and the 2 cone fundamentals (Stockman and Sharpe 2000). For example, Lcone contrast = [(Lr – Lb)/(Lr + Lb)] 3 100%, where Lr is the L-cone activity elicited by the peak red of the equiluminant stimulus and Lb is the L-cone activity elicited by the peak of the blue in the equiluminant stimulus. The achromatic grating had a high luminance contrast (99%), resulting in a much higher cone contrast than the colored gratings. We designed the experiment this way because it made the criteria for a color-biased area stringent (response to equiluminant color > response to black and white). Although chromatic aberration might affect our results (Cottaris 2003), it would only obscure the minimum response in MT to moving equiluminant stimuli (Mullen and others 2003). To measure the afterimage responses (see Figs 3 and 4), the macaques were shown a sequence consisting of 4 frames: first, a static display of equiluminant blue and red squares; second, a static gray during which most people report a vivid color afterimage; third, a flickering color display in which the red of each frame was replaced by blue and the blue was replaced by red (2 Hz); and fourth, another static gray during which people do not report an afterimage. Each frame was 16 s.

Data Processing

In total, we obtained 126,752 functional volumes during 33 scan sessions in the 3 macaques. Each experiment consisted of 20–60 functional scans, each lasting 4 min 32 s (echo planar imaging, repetition time (TR) = 2 s, echo time (TE) = 30 ms, 64 3 64 matrix, 1.25-mm3 voxels, 30 coronal slices). Slices were positioned to cover the occipital and temporal lobes, between AP coordinates –25 to +12. In an additional series of scans of the anesthetized animals, high-resolution anatomy was obtained with 1-mm3 voxels. These anatomical scans were used in conjunction with macaque atlases (Paxinos and others 2000; Ungerleider 2000) to define stereotaxic area borders. Data were analyzed using FS-FAST and Freesurfer (http://surfer.nmr.mgh.harvard.edu/) as well as custom code written in Matlab. Data were motion corrected (Cox and Hyde 1997), quadratically detrended, and smoothed with a Gaussian kernel of 2 mm full width at half maximum. Data from several scan sessions were averaged to improve signal to noise, except that shown in Figure 1A, which is quadratically detrended and smoothed data from a single scan session. To generate significance maps, we calculated the mean and variance of the response in each voxel to each condition across the entire scan session. Then t-tests for appropriate comparisons were performed. Artifacts within the sagittal sinus and outside the cortex were masked and time courses were accommodated for hemodynamic delay. To identify color-biased areas, percent blood oxygen level dependent (BOLD) responses were determined as a ratio of the responses to the uniform gray, for all visually active voxels within each area (see Fig. 2). %BOLD = [(response to stimulus) – (response to gray)]/[mean response throughout scan session]. A voxel was considered visually responsive if it showed activation at $P < 10–2$ to any given stimulus (color or achromatic grating) compared with the activation during a blank gray screen. Bar graphs indicate the responses of visually responsive voxels within a given area. For the afterimage experiments, the responses were averaged across 10 scan sessions in 3 animals. Responses were normalized to remove systematic variations between brain areas

introduced by placement of the coil: [(afterimage following static) – (afterimage following flicker)]/ [(response to static) + (response to flicker)]. Time courses shown in Figure 4 are the average of 492 stimulus repeats (1 stimulus sequence = gray, flicker, gray, static), in 3 animals, 6 hemispheres.

Results

Our goal was to identify brain regions that are involved in color processing in the alert macaque. Using a strategy similar to that used to study color in human subjects (Lueck and others 1989; Hadjikhani and others 1998; Wade and others 2002), we compared the fMRI signals elicited by chromatic stimuli, having high color contrast, with the signals elicited by achromatic stimuli, having high luminance contrast. We first had to identify a pure color stimulus—one that contains color contrast but no luminance contrast. The relative luminance at which 2 colors appear “equiluminant” is different across individuals (Livingstone and Hubel 1987) and species (Dobkins and others 2000). In order to identify equiluminant colors for the animals we used, we made the assumption that area MT, which is specialized to process moving stimuli, responds less strongly to moving colors if the colors are equiluminant (Dobkins and others 2000). We presented macaques with a series of colored gratings using a range of luminance ratios of the 2 colors comprising the grating. We used red--blue gratings (Tootell and others 2004) and examined the fMRI activity in the motion area, MT, for the red:blue luminance ratio that produced minimum activity. A total of 8 colored stimuli, which varied in red:blue luminance ratios from 1 to 3 (Fig. 1), were used.

The gray bars in Figure 1A indicate the response (%BOLD change) during the control stimulus, a moving achromatic grating. The leftmost pink bar is the response to a moving red--blue grating; the red was matched in luminance to the blue, according to human equiluminance criteria (spectrophotometer: PR650 SpectraScan, Photo Research). MT showed a strong response to this colored stimulus and to the achromatic stimulus (Fig. 1A, top panel). The response to the colored gratings got progressively weaker as the ratio of red:blue increased, until a point around ratio 2.3, where further increases in red:blue ratio increased the response. Unlike in MT, the response time course in an extrastriate color-biased area, area PITd (see below), showed stronger activity to the colored gratings (Fig. 1A, bottom panel). There was no significant difference between the 2 macaques tested; a titration curve obtained by pooling responses in MT across 4 scan sessions from both macaques (Fig. 1B) shows that the macaques had an equiluminance ratio of red:blue of ~2.3. This is consistent with the finding that macaques are less sensitive to red or more sensitive to blue than the average human (Dobkins and others 2000; Tootell and others 2004).

We next compared the responses with the equiluminant stimuli with the responses to the achromatic stimuli across different visual areas. Color-biased responses ($P < 10–2$), shown in red--yellow, and luminance-biased responses ($P < 10–2$), shown in blue--green, are projected on coronal functional slices (Fig. 2A); the results from both animals tested were quantified as bar graphs (Fig. 2B). The activity maps in Figure 2A were determined by comparing the responses to equiluminant color with responses to black and white; the quantified maps in Figure 2B show the responses to these different stimuli as separate bar graphs. An atlas of area borders is shown alongside the activity maps. The atlas was

derived from Paxinos and others (2000) and Ungerleider (2000): slices from this atlas were registered to high-resolution anatomical volumes for each macaque. The outlines of the area borders and the highresolution anatomical slices are shown below the functional scans (Fig. 2A). Note that each area's color in the atlas is arbitrary and is independent of the activation scale bar shown in the functional slices.

We used stereotaxic coordinates to define different brain regions because many extrastriate areas, such as TEO, TE, and PITd are not well defined by retinotopic or other (e.g., functional) criteria. Indeed, characterizing the functional activity of this region was one goal of the present paper. Presenting the data on functional coronal slices using stereotaxic coordinates facilitates comparison with electrophysiological results and provides a useful guide for future single-cell recordings.

At a glance, one can see pronounced luminance-biased activity at the base of the superior temporal sulcus, in area MT (the prominent blue--green spot in each hemisphere of slices –8 to –5.5, Fig. 2). On closer examination, one can also see luminance-biased activity in another dorsal area, at the base of the intraparietal sulcus, area VIP (slice –6.75). The color-biased activity, on the other hand, was present throughout the early retinotopic areas V1 and V2 (Fig. 2B) and in 2 discrete patches of V4, a dorsal patch in the anterior bank of the lunate sulcus and a ventral patch in the inferior occipital sulcus (slices –9.25 to –6.75, Fig. 2A; see also Supplementary Figure 1).

A patch of color-biased activity was also found in a region on the posterior bank of the superior temporal sulcus, in sections just anterior to those containing area MT and V4 (large white arrow, Fig. 2A). The color bias of this region is reflected in the time course of the fMRI response (Fig. 1A, bottom panel). This anterior focus of color activity coincides with area PITd (Van Essen and others 1990; Felleman and Van Essen 1991; Distler and others 1993).

Visual aftereffects allow one to measure a perceptual response in the absence of a physical stimulus and have been used to study color responses in the human cortex (Hadjikhani and others 1998). We took advantage of this to explore color processing in macaques by measuring responses that coincide with color afterimages. We used a sequential stimulus consisting of 4 parts—static colored pattern, gray, flickering colored pattern, and then gray again (Fig. 3A). An afterimage is observed during the first gray part but not during the physically identical second gray part. We compared the responses during these 2 gray blocks to determine the response during the afterimage (Fig. 3B).

We consistently obtained color-afterimage responses distributed across extrastriate areas V2, V3, V4, and PITd in a manner consistent with the color-biased regions identified in our first experiment (compare Fig. 3B with Fig. 2B). We quantified this percent BOLD fMRI signal across the 3 animals tested (Fig. 3C). MT and V3a showed no color-induced afterimage response. Interestingly, V1 also did not show a color-afterimage response even though it showed a color bias in our first experiment (Fig. 2B). In contrast, regions within both the upper and lower divisions of extrastriate areas V2, V3, V4, and PITd showed significant afterimage responses (Figs 3C and 4), suggesting that all these areas could be participating

in the experience of color afterimages. TEO also showed a weak color-afterimage response (slices 0.75 and 2, Fig. 3B), although this was not always seen in the other animals tested (Supplementary Figure 2).

Figure 4 shows the time course of the response to 2 repeats of the afterimage stimulus, which were quantified in Figure 3C. V1 showed 4 distinct peaks, each peak separated by a return to a common baseline. V1 and MT showed a stronger response to the flickering color (hatched pink columns) than the static color (solid pink bars), but the responses following the static color (gray columns following the solid pink columns) were no different from the response following the flickering color (gray columns following the hatched pink columns). V3a showed a response to the transition between each block of the stimulus but did not show a difference in activity during the different gray periods. This was not true for the remaining extrastriate areas, V2, V3, V4, PITd, and TEO. In these areas, instead of 4 distinct peaks as in V1, there are 2 broad humps. These result because of the elevated activity during the gray following the static field, which coincides with the perception of color afterimages.

Discussion

Color areas

The history of color vision research is rich in passionate debates, which continue today with the contentious issue of extrastriate color areas—do they exist? And what, in fact, is meant by a color area? There is some consensus that early visual areas—primary visual cortex (Conway 2001; Johnson and others 2001; Wachtler and others 2003; Hurlbert and Wolf 2004; Horwitz and others 2005), V2 (Hubel and Livingstone 1987; Kiper and others 1997; Xiao and others 2003), and perhaps V3 (Burkhalter and Van Essen 1986; Gegenfurtner and others 1997; but see Zeki 1978a)—contribute to color vision. Our fMRI results support this. But the existence of a single cortical area wholly specialized for color that is responsible for integrating the activity of early visual areas is controversial. Pioneering single-cell physiology suggested a “color center” in macaque (Zeki 1973, 1977, 1983b). Zeki (1977) advanced the notion of “a division of labor within the prestriate visual cortex” based on anatomical, connectional, and physiological criteria (Zeki 1978b), declaring V4 a color center primarily because “in every case [the 77 single units] in this area have been color coded, responding vigorously to one wavelength and grudgingly, or not at all, to other wavelengths or to white light at different intensities” (Zeki 1973). But subsequent studies challenged the notion of V4 as a specialized color area for several reasons. First, other areas also contain color-responsive cells, perhaps in the same numbers as are found in V4 (Gegenfurtner and others 1997; Gegenfurtner 2003); second, V4 contains neurons that respond along other stimulus dimensions (Schein and others 1982; Desimone and others 1985; Tanaka and others 1986); and third, lesions of V4 do not result in profound deficits of color vision (Heywood and others 1992; Schiller 1993; Walsh and others 1993; Cowey and others 2001).

But these studies do not preclude V4 from playing an important role in color. The high concentrations of color cells that Zeki (1983b) found in V4 were localized to discrete columns in the anterior bank of the lunate sulcus. Most studies of V4 center on the adjacent chunk of cortex, on the surface of the prelunate gyrus. There is consensus that this more

accessible region of V4 contains only ~20% strongly color-specific cells (Zeki 1983b; Tanaka and others 1986). Thus, instead of V4 being entirely color biased, it seems that V4 contains specialized subregions of the color cortex (Fig. 5, from Zeki 1983b), an idea that is supported not only by electrophysiological evidence (Zeki 1977, 1983b) but also by connectional data (Shipp and Zeki 1995; Felleman and others 1997), 2-deoxyglucose studies (Tootell and others 2004), and functional imaging data shown here.

Is PITd a Color-Biased Area, Distinct from V4 and TEO? Is there a distinct area anterior to V4 that is important in processing color? Zeki's single-unit recordings show a second clump of color cells in the posterior bank of the superior temporal sulcus (Fig. 5), a region he described as distinct from V4 (Zeki 1977), but which he grouped with V4 as the V4 complex of areas. Functional imaging confirmed that this region is color biased (large white arrow, Fig. 2A); moreover, electrophysiological studies since Zeki's show that many neurons in this region are tuned to specific hues (Komatsu and others 1992). But whether neurons in this region are exclusively color tuned or tuned to other stimulus dimensions as well will have to await targeted single-unit recordings and adaptation experiments (e.g., Engel 2005). Moreover, establishing a causal role for this region in conscious color perception will have to await studies of macaques in which this area has been functionally identified and then selectively stimulated or removed.

In the meantime, is this region distinct from area V4 and area TEO? Many terms have been used to describe this region, including PITd (Distler and others 1993), V4A (Shipp and Zeki 1995; Zeki 1996), and DLr (Stepniewska and others 2005). The term V4A has also been used to describe the region of V4 on the surface of the prelunate gyrus that is not overwhelmingly sensitive to color (Zeki 1983b, 1996; Pigarev and others 2002). To avoid ambiguity, we use the anatomical term PITd, which is consistently used to describe the region of the cortex on the posterior bank of the superior temporal sulcus (Van Essen and others 1990, 2001; Felleman and Van Essen 1991; Distler and others 1993).

Zeki (1978b) described the region encompassing V4 and PITd as a single complex because he found that both PITd and portions of V4 were sensitive to color. But he intimated that these regions could be distinguished as distinct areas; cumulative evidence suggests this is so: topographic mapping reveals a distinct area coinciding with PITd (Gattass and others 1988; Pigarev and others 2002; Stepniewska and others 2005), containing its own crude representation of the upper and lower visual fields (Boussaoud and others 1991; Fize and others 2003) along with its own callosal projection (Zeki 1977).

PITd also seems distinct from region TEO (Zeki 1996; Stepniewska and others 2005), although the boundaries between these areas are tentative (see Introduction). Ungerleider and Desimone (1986) initially showed TEO as extending into the STS, thus including PITd, but after careful study they parceled the region into 2 areas: a dorsal area, PITd, and a ventral area, which they call TEO (Boussaoud and others 1991; Distler and others 1993). The relationship of PITd to TEO and V4 is shown in Distler and others (1993), reproduced here as Figure 6, and is consistent with PITd in other maps (Van Essen and others 1990). TEO seems to have its own complete visual field representation independent of PITd (Boussaoud and others 1991). PITd and TEO receive distinct segregated inputs

from V4 (Felleman and others 1997; also see Zeki 1977) and have distinct targets: TEO is strongly connected with the subicular-- hippocampal complex, whereas PITd is strongly connected with the amygdalar complex (reviewed in Felleman and Van Essen 1991). We wonder whether the direct amygdalar target of PITd provides a rationale for the emotional salience of color. Regardless, the 2 areas can be functionally dissociated in lesion studies (Buckley and others 1997) and distinguished by fMRI, which shows color-biased activity in PITd but little color-biased activity in areas TEO and TE (Fig. 2B). More detailed imaging and single-unit studies are needed to conclusively distinguish PITd and TEO and resolve the degree to which these areas overlap, if at all.

We may have underestimated the overall amount of color activity in all areas because the criteria for “color bias” was stringent (see Materials and Methods); this might account for the discrepancy between our results showing little color bias in TEO, with other results showing stronger color responses in TEO (Tootell and others 2004). We did find significant afterimage activity in TEO in some animals, although this activity is difficult to interpret in the absence of a significant result in the direct test of a color bias. If the afterimage activity in TEO represents a genuine color response of TEO, it may be the result of reciprocal connections between TEO and PITd (Distler and others 1993), which may also be critical for color-based behavioral tasks that depend on an intact TEO (Gross 1973; Fuster and Jervey 1982). Regardless, the difference in results produced by different imaging studies and the variation in results between the animals studied here suggest that different animals of a given species can have variable cortical organizations (Komatsu and others 1992), which underscores the utility of fMRI in providing a road map for guiding targeted single-unit recordings and lesions within a given animal.

Color Afterimages Receptoral adaptation may be sufficient for afterimages (Barbur and others 1999), although neural adaptation in cortical areas contributes, too (Virsu and Laurinen 1977; Gerling and Spillmann 1987; Takahashi and others 1988). We used fMRI to examine the brain response to afterimages. Some extrastriate areas (V2, V3, V4, and PITd), and not V1, gave BOLD responses during a stimulus in which humans report color afterimages. It is tempting to speculate that this reflects not only the critical role of extrastriate areas in color afterimages but also a specific lack of involvement of V1. The temporal dynamics of coloropponent cells in V1 do not directly reflect the timing of color afterimages (Conway 2002; Conway and others 2002): neural “OFF” discharges of cone-opponent cells in V1 are brief regardless of the duration of the stimulus, unlike afterimages which tend to be longer with longer duration inducing stimuli. But it is unknown whether the temporal dynamics of color cells in extrastriate areas are much different from those in V1. Moreover, there is no direct relationship between the BOLD signal and the response of single units and there is no simple correlation between these measurements and perception, so it would seem impossible to conclude that V1 plays no role in the perception of color afterimages based on the present data.

Summary

Despite pronounced differences in interpretation, the results of many color studies are consistent (Gegenfurtner 2003) and are best characterized by a hybrid of the 2 extreme

possibilities outlined in the Introduction. Color vision consists of several steps: wavelength discrimination, color opponency, local color contrast, hue, global color constancy, and the experience of color. These different stages are probably accomplished at different stages of the visual system (Zeki and Marini 1998; Conway 2003). Wavelength discrimination begins with the 3 classes of cones; cone opponency with specialized retinal ganglion cells, relayed to parvocellular and koniocellular neurons of the lateral geniculate nucleus (De Valois and others 1958; Wiesel and Hubel 1966; Martin and others 1997); local color contrast with the double-opponent cells (Conway 2001; Conway and others 2002) in the blobs of primary visual cortex (Livingstone and Hubel 1984; Tootell and others 1988; Landisman and Ts'o 2002; but see Lennie and others 1990; Leventhal and others 1995); hue with the thin stripes in V2 (DeYoe and Van Essen 1985; Hubel and Livingstone 1985; Tootell and Hamilton 1989; Roe and Ts'o 1999; Moutoussis and Zeki 2002; Xiao and others 2003; but see Levitt and others 1994; Kiper and others 1997); and global color constancy with V4 (Zeki 1983a; Walsh and others 1993). Could PITd be responsible for integrating all these signals, serving a similar function in macaques as the human color center does in humans? PITd is the most anterior brain area that shows a strong color bias. This, together with the fact that more anterior visual areas tend to represent more advanced stages of visual processing and that very large lesions encompassing PITd (Cowey and Heywood 1995) result in impaired color vision whereas large lesions of IT cortex that do not include PITd fall short of achromatopsia (Cowey and others 2001), leads us to suggest that PITd is the most likely candidate for the macaque color center, if one exists.

In summary, cumulative evidence suggests that color is processed by a ventral-stream pathway, through a connected network involving V1, V2 (perhaps V3), V4, and PITd, a pattern that is remarkably similar to the one found in humans (Wade and others 2002). The specific contribution of these extrastriate areas, particularly PITd, will have to await further studies, including targeted single-unit recordings, perhaps guided by fMRI.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Notes

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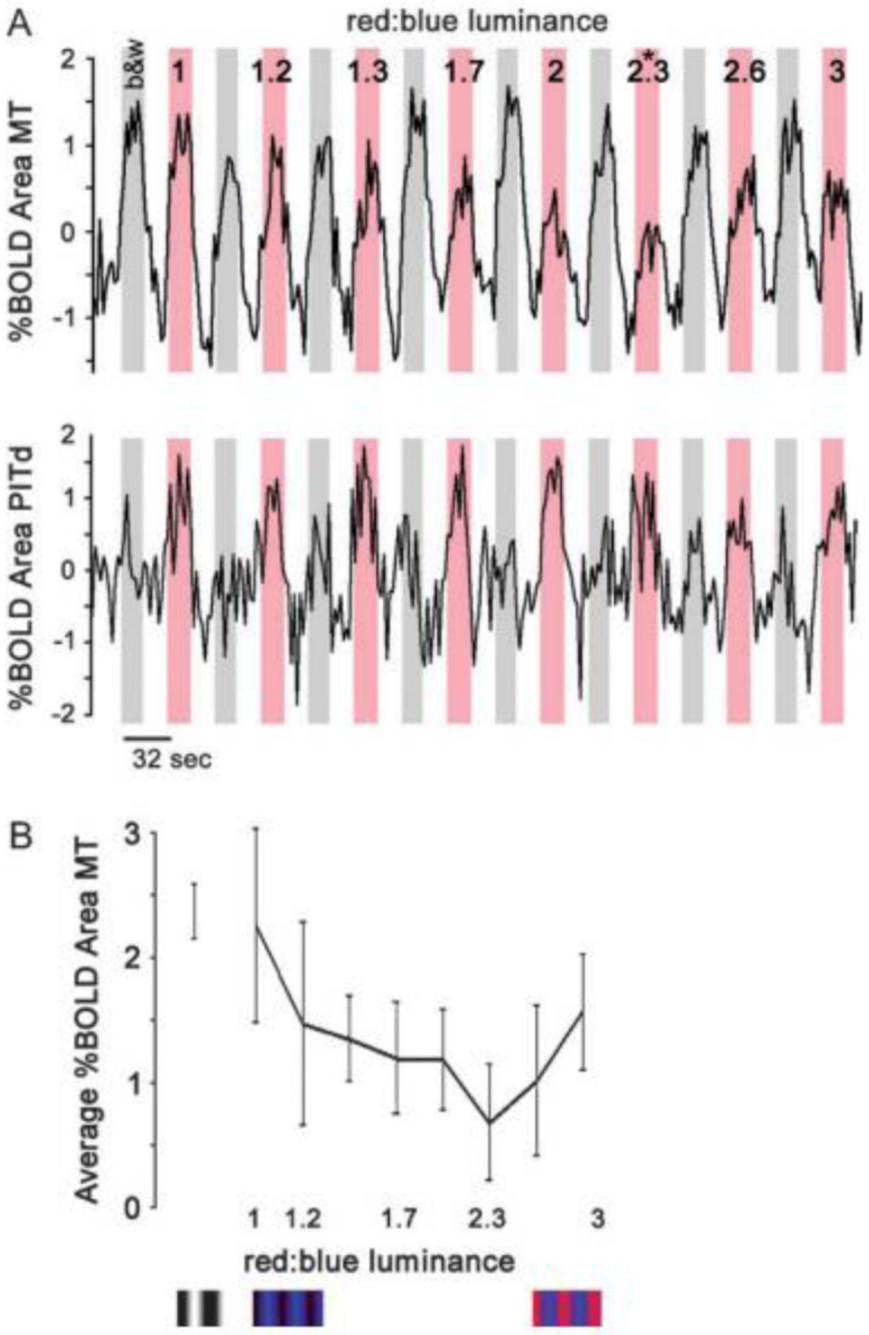

Figure 1.

Identification of macaque equiluminant colors. (A) fMRI responses in the motion area (MT) and a color-biased area (PITd) to black--white gratings (gray bars) and a sequence of red--blue gratings of different luminance ratios of red to blue. The time course is averaged over 11 presentations of the complete stimulus during a single scan session, quadratically detrended and smoothed (see Materials and Methods). (B) Quantification of the percent BOLD response in area MT (2 animals, both hemispheres, all scan sessions, all voxels in

each area). Area MT shows a dip in the response to the colored gratings at red:blue ratio ~2.3. Standard errors are shown.

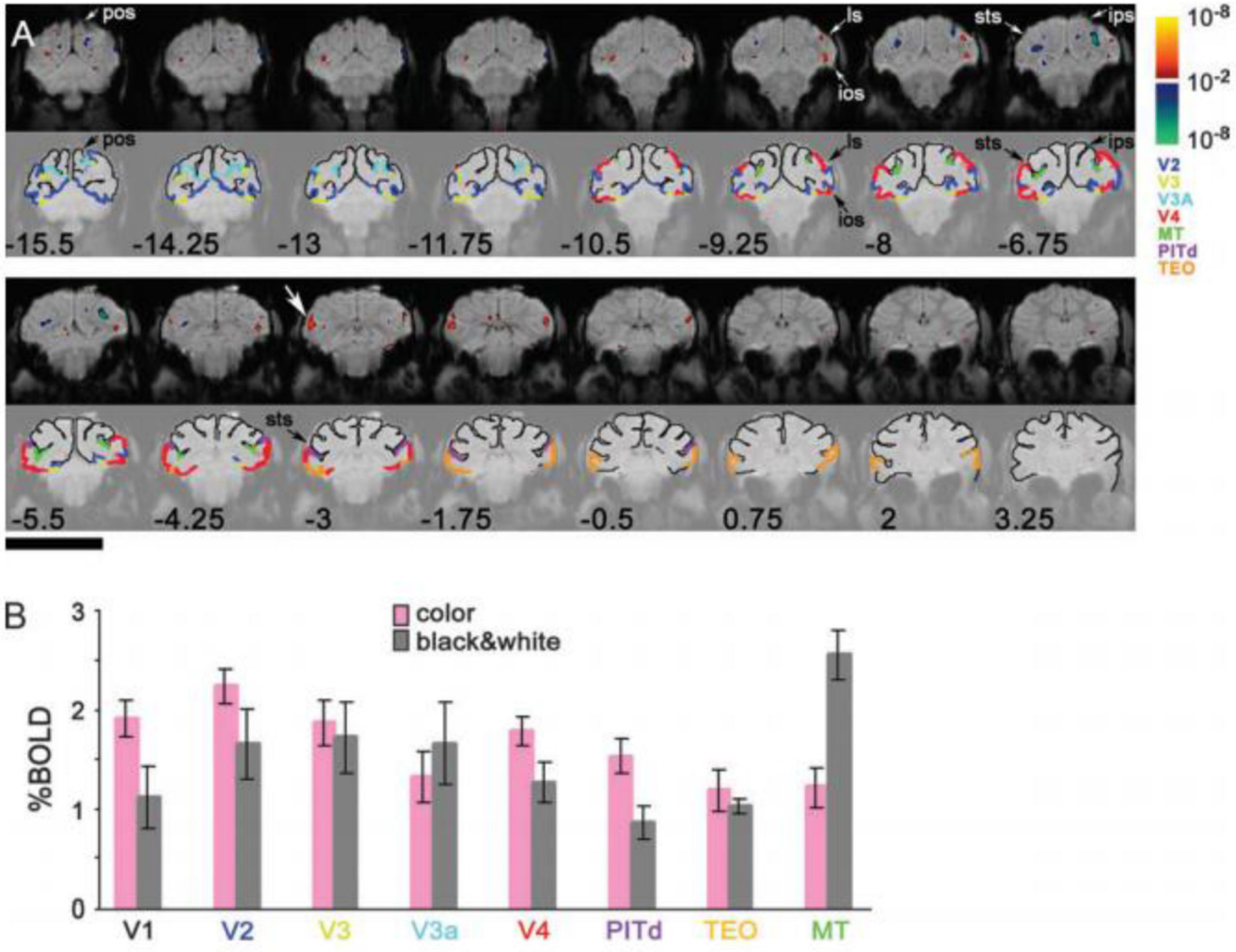

Figure 2.

Color-biased and luminance-biased responses in macaque visual cortex. Responses to saturated equiluminant color stimuli (see Fig. 1) were compared with responses to 99% luminance contrast stimuli. (A) The sections on a black background are functional coronal slices for all scans of 1 macaque (30 scans). Regions in yellow indicate a color bias (1 in 108 by chance); regions in green show a luminance bias. Area boundaries and anterior--posterior coordinates are shown below each functional slice: V2, blue; V3, lime; V3a, cyan; V4, red; MT, green; PITd, purple; TEO, orange. Large white arrow indicates the focus of color-biased activity in PITd. ios, inferior occipital sulcus; ips, intraparietal sulcus; ls, lunate sulcus; pos, posterio-occipital sulcus; sts, superior temporal sulcus. Scale = 5 cm. (B) Quantification of color-biased and luminance-biased responses (2 animals, 4 hemispheres). Standard errors of means are shown.

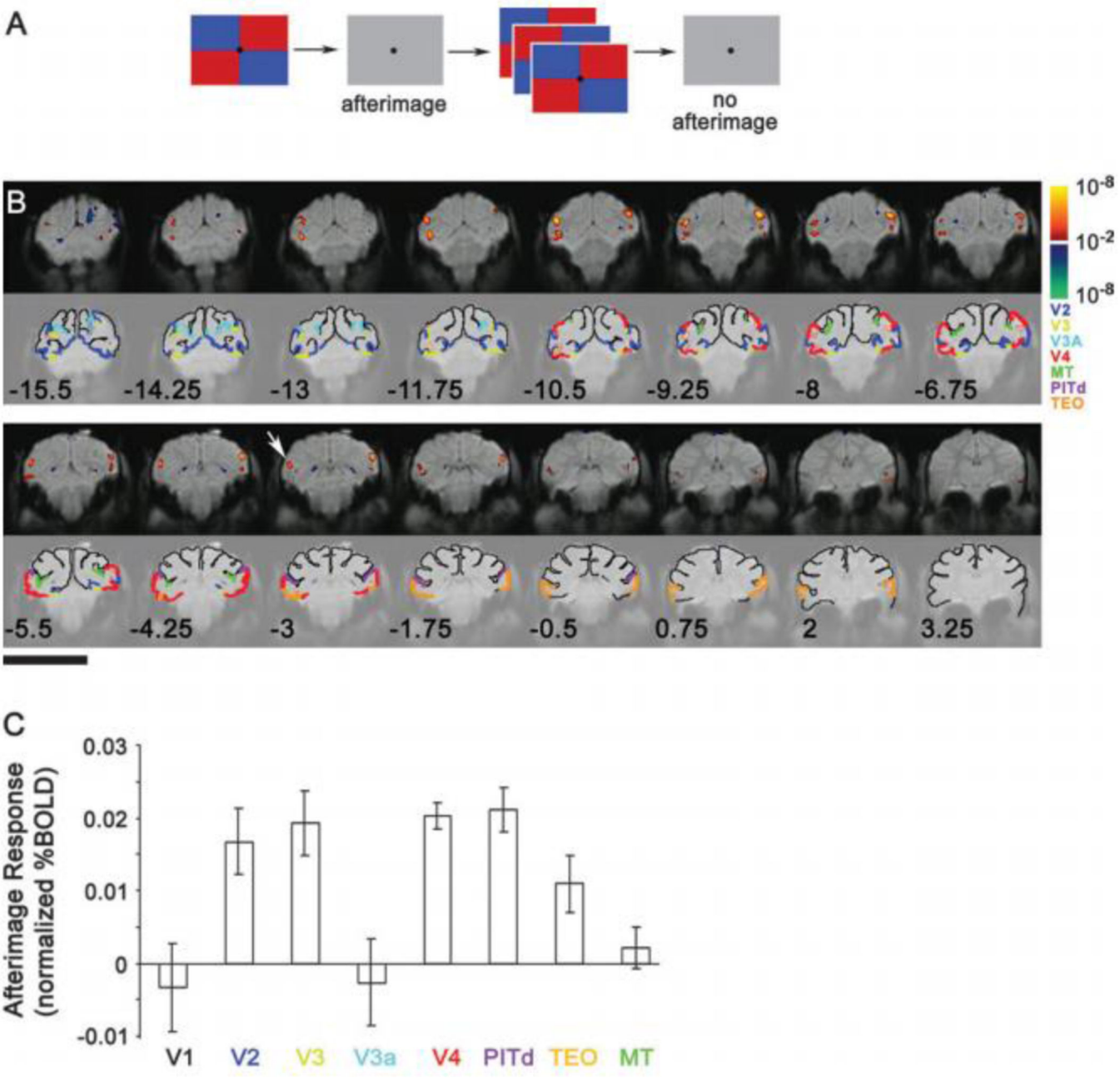

Figure 3.

Color-afterimage responses in macaque visual cortex. (A) Stimulus used (see Materials and Methods). (B) Responses that were larger to the first gray block of the stimulus, during which human observers report a vivid color afterimage, are shown in red--yellow; responses that were larger to the second gray (no afterimage) are shown in blue-- green. Responses are for the same macaque as shown in Figure 2A. Scale = 5 cm. (C) Quantification of the afterimage responses. Responses above the baseline are colorafterimage responses; responses below the baseline are flicker-afterimage responses. Standard errors of means are shown

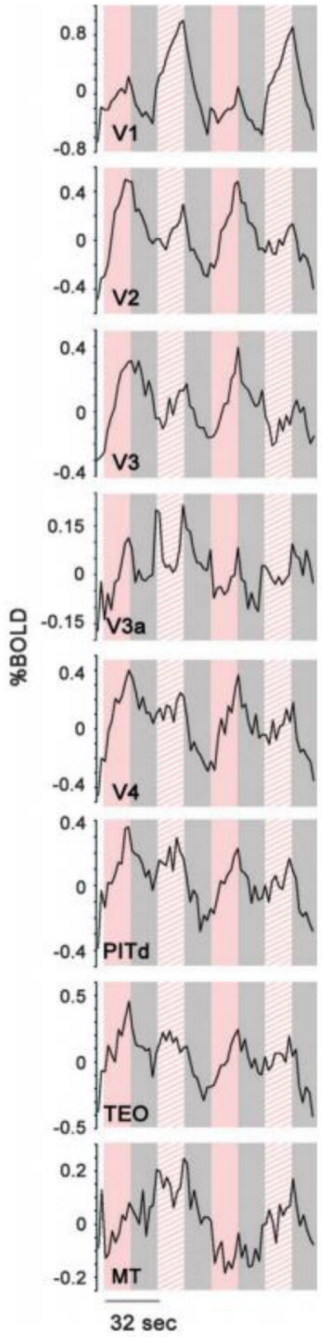

Figure 4.

Time courses of color-afterimage responses in macaque visual cortex to 2 repeats of the 4-part stimulus diagramed in Figure 3A. Responses to the static color display are shown superimposed on pink columns and to the flickering color on hatched columns. An elevated response to the gray following the static stimulus as compared with the gray following the flickering stimulus corresponds to the perceptual experience of an afterimage (3 animals, 6 hemispheres, all visually active voxels analyzed).

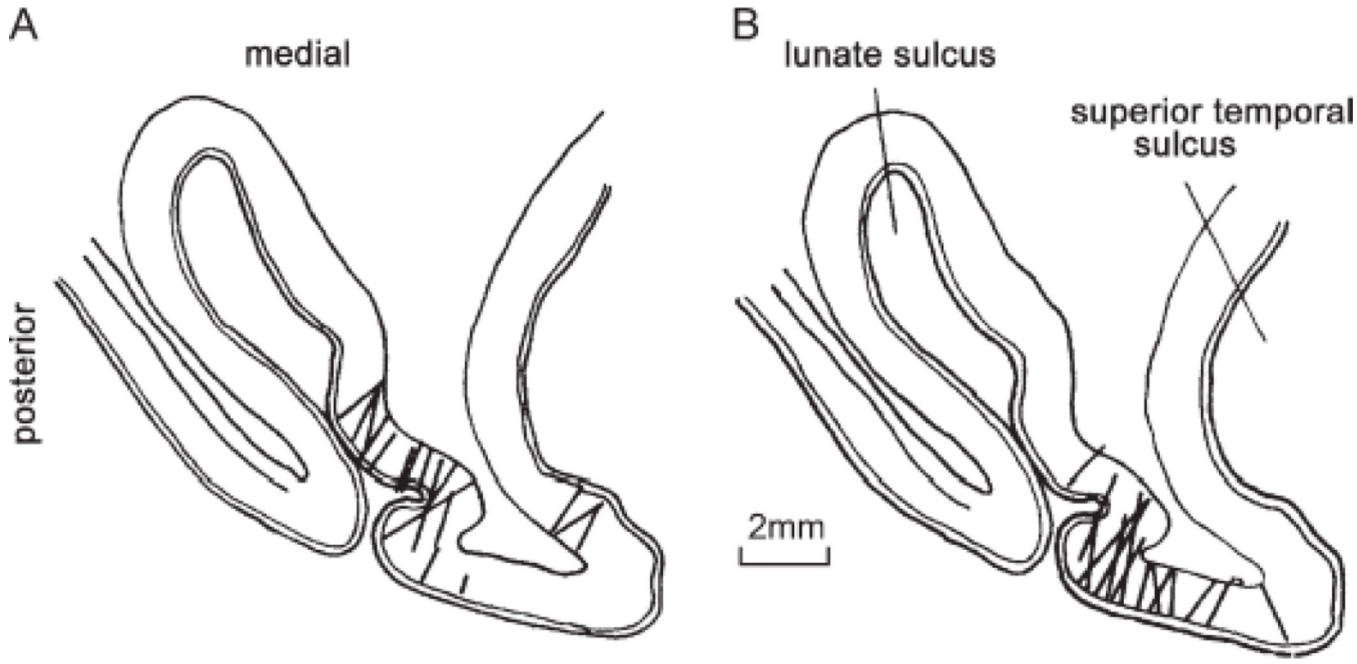

Figure 5.

Area V4 is not homogenous and contains color-rich regions (from figure 8, Zeki 1983b). (A) The positions of electrode penetrations in horizontal sections of macaque brain in which a high percentage (84%) of wavelength-selective cells was found. The posterior cluster is located in the anterior wall of the lunate sulcus, in area V4. The 3 anterior penetrations, in the superior temporal sulcus, are located in the region we refer to as PITd. (B) The penetrations in which a low percentage (19%) of wavelength-selective cells was found. These penetrations are on the prelunate gyrus portion of V4.

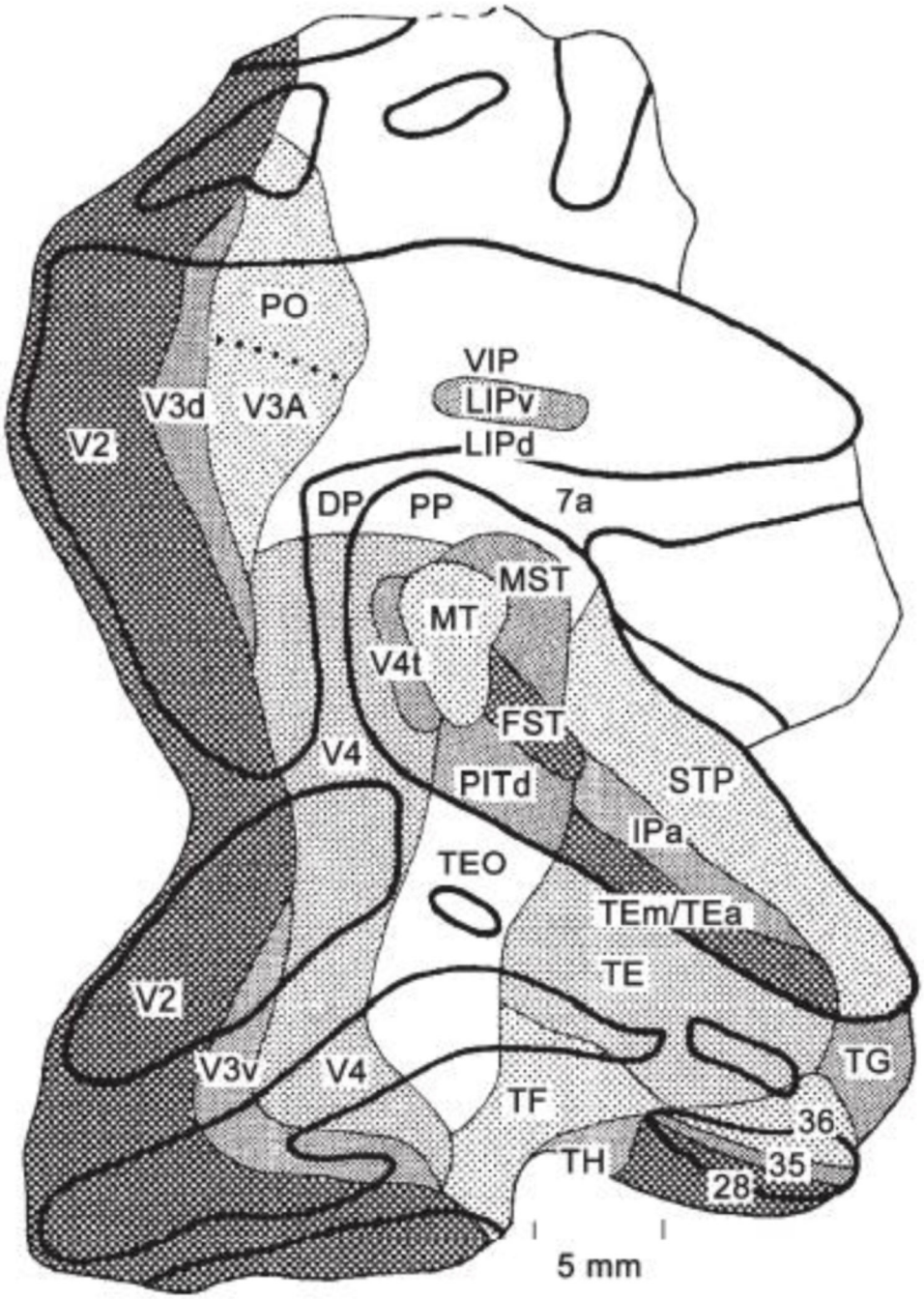

Figure 6.

Location of extrastriate visual areas in macaque shown on a 2-dimensional unfolded cortical map (adapted from Distler and others 1993; see also Van Essen and others 2001). Thick lines represent the boundaries of sulci. Note that PITd is mostly within the superior temporal sulcus. When the cortex is in the skull, folded, PITd is displaced superior and anterior to V4 and superior and posterior to TEO (see Fig. 2).