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The position and topography of the human colour centre as revealed by functional magnetic resonance imaging

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Summary

We used a colour Mondrian—an abstract scene with no recognizable objects—and its achromatic version to image the change in blood oxygenation in the brains of 12 human subjects, with the aim of learning more about the position and variability of the colour centre in the human brain. The results showed a consistent association of colour stimulation with activation of an area that is distinct from the primary visual areas, and lies in the ventral occipitotemporal cortex; we refer to it as human V4. The position of human V4, as defined on functional grounds, varies between individuals in absolute terms but is invariably found on the lateral aspect of the collateral sulcus on the fusiform gyrus. There was no indication of lingual gyral activation. In further studies designed to reveal the topographic map within V4, we stimulated the superior and inferior visual fields separately, using the same stimuli. We found that human V4 contains a representation of both the superior and inferior visual fields. In addition, there appears to be retinotopic organization of V4 with the superior visual field being represented more medially on the fusiform gyrus and the inferior field more laterally, the two areas abutting on one another. We find no evidence that suggests the existence of a separate representation of the inferior hemifield for colour in more dorsolateral regions of the occipital lobe.

Keywords: functional magnetic resonance imaging; area V4; human colour vision

Abbreviations: BOLD = blood oxygenation level dependent; EPI = echo planar imaging; fMRI = functional magnetic resonance imaging; SPM = statistical parametric mapping; TE = time to echo; TR = time to repeat

Introduction

The notion of a specialization for colour was first derived from clinical studies, in particular those of patients with an acquired colour vision defect (acquired achromatopsia) following cerebral lesions. The first conjectures (Eperon, 1884; Wilbrand, 1884) supposed that there is a specialization for colour in one of the layers of the then ill-defined primary visual cortex, which Henschen and his colleagues had equated with the striate cortex and which von Monakow and his colleagues had supposed to be a good deal more extensive than that. Whatever the extent, both thought that all visual attributes must be represented in this same area (for a review, *see* Zeki, 1990). In one of the first studies that included a pathological examination of the site of the lesion in an achromatopsic patient, Verrey (1888) found the lesion to be confined to the lingual and fusiform gyri, which he therefore considered to be the 'centre for the chromatic sense'. Even though Verrey's findings were confirmed by Mackay and Dunlop (1899), and the centre for the chromatic sense was further restricted to the fusiform gyrus, the demonstration of Verrey had an unfortunate consequence. It led him and others to suppose that not only was the primary visual cortex itself larger than the striate cortex but that there were regional specializations within it. In refuting this doctrine, neurologists also refuted the evidence for a colour centre, even one lying outside the striate cortex (for a review,

see Zeki, 1990). The consequence was that the notion of a specialization for colour was effectively lost sight of for well over 70 years. It was only after the direct physiological demonstration of a specialization for colour in an area outside the striate cortex, area V4 (Zeki, 1973), that interest in the topic was revived. Since then, the number of cases of achromatopsia in the published literature has increased. But, more interestingly, the advent of imaging techniques has allowed the determination of the position of the human colour centre in normal brains, uncontaminated by lesions.

The first imaging studies that we performed (Lueck *et al.*, 1989) located the colour centre in the lingual and fusiform gyri, much as Verrey had. In a subsequent, more detailed study (Zeki *et al.*, 1991), this general picture was confirmed, but the emphasis was shifted to the fusiform gyrus, where the largest increase in blood flow was found. Since that time, a number of studies have confirmed the activation of this locus with colour stimuli (Corbetta *et al.*, 1991; Allison *et al.*, 1993; Reppas *et al.*, 1995; Sakai *et al.*, 1995). But more recent studies (e.g. Sereno *et al.*, 1995), using functional magnetic resonance imaging (fMRI) and non-functional paradigms to study the topography of visual areas rather than their specializations, have implicated another area, which they call dorsal V4 separate from ventral V4. In fact, a laterally situated area was activated in addition to the region in the fusiform gyrus in a colour study that emphasized attention (Corbetta *et al.*, 1991). If there are, indeed, two subdivisions of V4 in the human that are well separated from one another, the organization of V4 in the human would be different from that in the monkey, where the parts of V4 representing upper and lower visual fields abut each other; this in turn would lend some, though not conclusive, support to the notion that the colour centre in the human and monkey V4 are not homologous (Merigan, 1993; Heywood *et al.*, 1995). One way of resolving the problem was to use an activation study in which the upper and lower fields are separately activated with colour stimuli, and note the distribution of activity in the human brain, using fMRI. By combining this with a full field stimulation of the same subjects, we also hoped to have a better idea of the precise location and extent, as well as the variability, of the colour centre in the human brain. More specifically, we wanted to delineate, for each subject, the position of the colour centre in stereotactic space in order to gain some insight into its positional variability between individuals and also to assess whether there is any consistent relationship between colour function and individual cortical topography. With appropriate visual stimulation, the experiments were performed employing the technique of fMRI, which provides an index of neural activity in the cortex via the measurement of blood oxygenation level dependent (BOLD) changes in magnetization. Our study had the long-term aim of defining and characterizing the visual areas lying within the fusiform gyrus.

Methods

Subjects

Twelve volunteers, with no colour vision deficiencies, were used during the course of this experiment, nine of whom were male and three female (mean age 29.16 years). All subjects gave informed written consent and studies were given approval by the National Hospital for Neurology and Neurosurgery Ethics Committee.

Data acquisition

All experiments were performed on a Siemens Vision scanner operating at 2 T with a head radio-frequency resonator and a gradient strength of 25 mT/m. With the subject lying supine in the scanner, the experimental session began with the acquisition of an anatomically detailed structural MRI image of the subject's brain. This T_1-weighted image was obtained using a MPRAGE (multi-planar rapidly acquired gradient echo) sequence with time to repeat (TR) = 9.7 ms, time to echo (TE) = 4 ms and inversion time of 600 ms. Images were acquired in transverse orientation giving 108 slices with voxel size $1\times1\times1.5$ mm. A gradient echo planar imaging (EPI) sequence was used to acquire the functional, relatively T_2-weighted images (TR = 6.084 s, TE = 40 ms). This EPI sequence was selected to reduce inflow effects and maximize BOLD contrast. The images consisted of 64 transverse slices with each slice being 64×64 pixels (voxel size $3\times3\times3$ mm).

Visual stimulation

Visual stimuli were generated on an Apple 7500/100 computer, the output of which was fed to a liquid crystal display projection system. The stimuli were projected onto a translucent screen and the subjects viewed the image via a 45° angled mirror.

Full field stimulation

In the first experiment the size of the visual field subtended $33°\times23°$ with a mean luminance of 5 cd/m^2 (measured with a Photo Research PR650). Three types of visual stimulus were presented to the subjects during an experimental session.

The first stimulus was a chromatic Mondrian pattern which comprised eight differently coloured elements, assembled in such a way as to provide an abstract scene with no recognizable objects (*see* Fig. 1). The coloured Mondrian pattern was alternated at a rate of 1 Hz with a blank background of the same mean luminance and mean hue. Prior to scanning the subjects set isoluminance for each of the colours in the stimulus by the technique of heterochromatic flicker photometry (*see* Kaiser, 1991), to ensure that no luminance contrast was contained within the stimulus. Each of the colours in turn was made to alternate

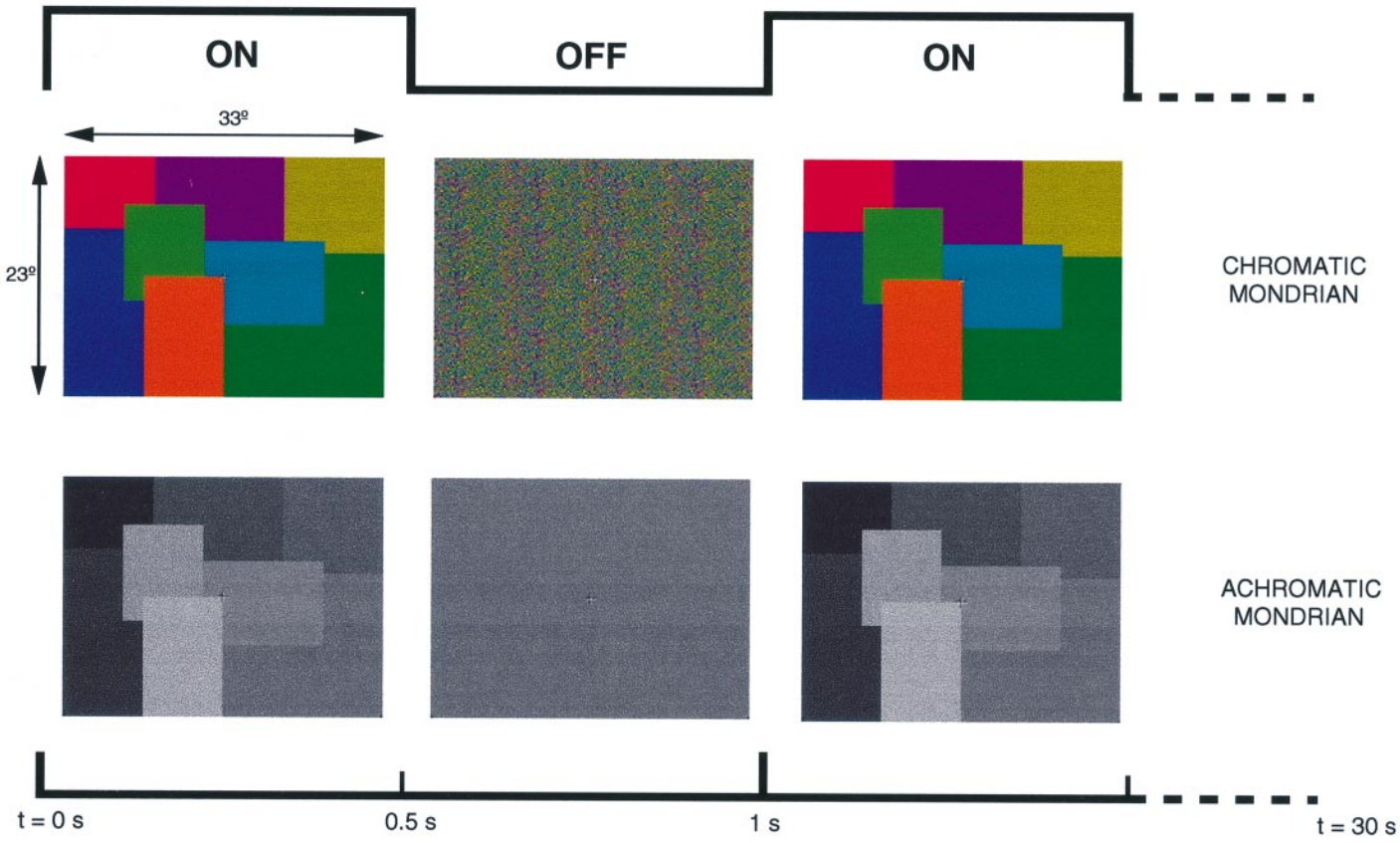

Fig. 1 Stimulus presentation. The chromatic and achromatic Mondrian stimuli (*see* text for full details) were presented in a pattern onset/offset mode with square wave temporal modulation. The pattern remained on for 500 ms, to be replaced for the same period by a blank field of the same mean luminance and mean hue.

at a rate of 15 Hz with a standard mean grey and their luminances were adjusted in a staircase fashion, until minimum flicker was perceived.

The second stimulus was an achromatic Mondrian, identical to the chromatic version except that each of the elements was of a different grey level, rather than a different colour, modulated about a standard mean grey level, i.e. it contained luminance contrast. Like its chromatic counterpart, the achromatic Mondrian was also alternated at a rate of 1 Hz with a uniform grey stimulus of the same mean luminance, i.e. there was no luminance flash between the two conditions. The uniform grey stimulus formed the standard mean grey used to set isoluminance for the chromatic Mondrian.

The third stimulus, the resting condition, consisted of a blank screen. In the centre of this stimulus (as in all of the visual stimuli) a central cross was constantly present, upon which the subjects were instructed to maintain fixation throughout the whole of the session.

In a single experimental session a total of 315 brain volumes were acquired. The fMRI data were obtained in a continuous sequence lasting ~32 min. During this period each of the three stimulus conditions was presented in blocks lasting 30.4 s (five scans) (*see* Fig. 2). Each condition was presented 21 times in all.

Superior and inferior visual field stimulation

In the second experiment we employed similar temporally modulated chromatic and achromatic Mondrian stimuli, except that in this case they were restricted to either the uppermost or lowermost third of the visual field stimulated in the main experiment. The stimulus configuration is schematically shown in Fig. 3. Thus in total there were four conditions: (A) superior field chromatic; (B) superior field achromatic; (C) inferior field chromatic; and (D) inferior field achromatic. The comparisons of A versus B and C versus D would therefore indicate regions of the cortex activated by superior and inferior visual field stimulation, respectively. All scanning acquisition parameters were exactly the same as those used previously except for the fact that 320 volumes were acquired instead of 315. Six of the subjects (all male) used in the main study were scanned again on a separate occasion and were instructed to maintain fixation on a centrally placed cross while viewing A, B, C or D.

Data analysis

Imaging data was analysed using the statistical parametric mapping (SPM) software (Friston and Frackowiak, 1991) as subsequently modified and augmented (Friston *et al.*, 1995*a*,

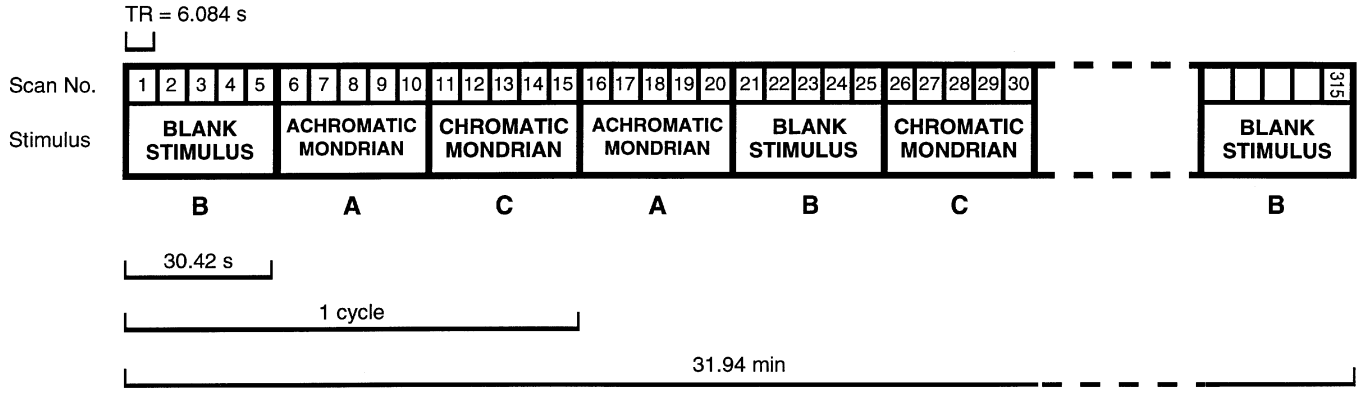

Fig. 2 Sequence of stimulation during the main experiment; the three conditions A, B and C were presented in a pseudo-randomized continuous sequence lasting 31.94 min. A total of 315 whole brain volumes were acquired in a scanning session (TR = 6.084 s).

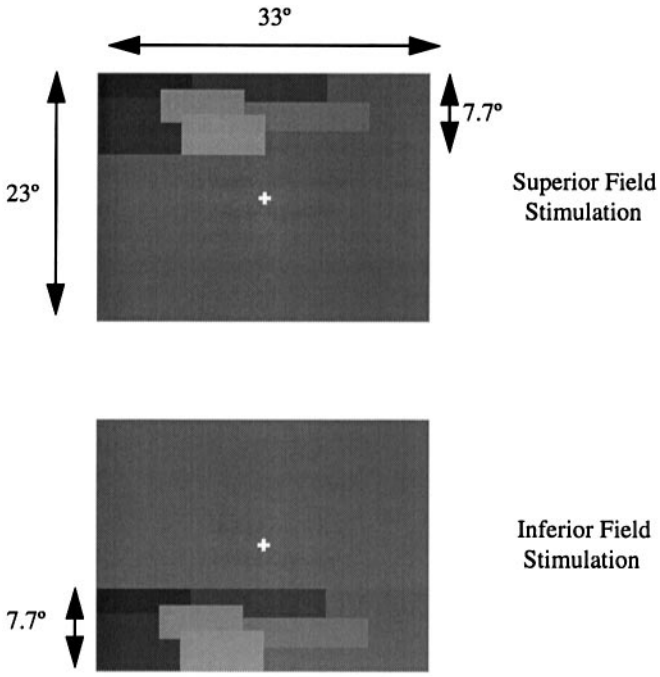

Fig. 3 Stimulus configurations employed for the separate stimulation of superior and inferior portions of the visual field. The chromatic and achromatic Mondrian stimuli were restricted to either the upper or lower third of the visual field stimulated in the main experiment. Both the colour and black and white stimuli were presented in onset/offset mode at a rate of 1 Hz.

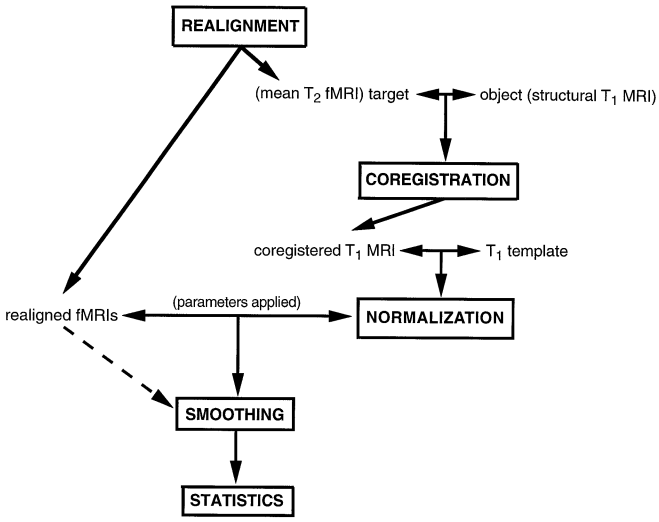

Fig. 4 Schematic representation of the pre-processing stages performed on the images prior to statistical processing. Realignment generates a mean fMRI image in addition to all of the realigned fMRIs. This mean image acts as the target image on to which a structural, T_1-weighted, MRI is coregistered. Following this, the coregistered T_1 image is normalized to a standard T_1 template image. The parameters that bring about this normalization are then applied to each of the fMRI images in turn (note that for the non-stereotactic analysis this normalization step was omitted). The final stage in processing prior to statistical analysis involves smoothing the image with a Gaussian filter (8-mm and 4-mm full widths at half maximum for normalized and non-normalized analysis, respectively).

b) for data analysis (SPM96, Wellcome Department of Cognitive Neurology, London, UK) which runs within PRO MATLAB (MathWorks Inc., Natick, Mass., USA). Additional analysis was performed using ANALYZE version 7.5.4 image display software (BRU, Mayo Foundation, Rochester, Minn., USA). The different stages of analysis are shown schematically in Fig. 4. The first stage of analysis of the fMRI data involves realignment of the 315 brain volumes acquired, thus removing the movement related artifacts in the time series. The procedure utilizes a least squares approach and a six parameter (rigid body) spatial transformation with the first scan in the series acting as the reference.

In addition to removing movement related variance components, the realignment procedure also generates a mean fMRI image. This mean image is used as a target image with which the anatomically detailed structural T_1-weighted MRI can be co-registered. The first stage of the co-registration involves an affine normalization of the mean functional T_2 image with a T_2 template, and the T_1 (object) image with a T_1 template. This produces a rough co-registration of the images. The next stage involves the segmentation of the target and object images into grey matter, white matter and CSF. This procedure is based upon a cluster analysis with a

modified mixture model and *a priori* information about the likelihood of each voxel being in one of the different tissue types. The segments are then co-registered using the results of the rough co-registration as a starting estimate. The structural (T_1-weighted) MRI is also re-sliced so that the resultant co-registered T_1 image has the same voxel dimensions as the T_2 fMRIs ($3 \times 3 \times 3$ mm).

In order that the analysis of the activation foci could be standardized across the 12 subjects, the images were transformed into the anatomical space of Talairach and Tournoux (1988) which enabled comparable coordinates to be given for foci in each subject. This normalization process relies upon the stereotactic fitting of the MRI images to a template defined by the ICBM/NIH 10 project, which corresponds to the space described by Talairach and Tournoux (1988). The normalization algorithms work by minimizing the sum of squares difference between the MRI images and the template. Firstly, a 12-parameter affine normalization stage estimates various parameters of the image. An elastic deformation is then computed which will match the image to the template. Normalization is actually performed upon the co-registered and re-sliced T_1-weighted structural MRI, which is matched to a template of the same modality. The parameters which achieve this match are then applied to all of the T_2 images. This stage was excluded from the preprocessing sequence when we examined the relationship between the activation foci and the structural anatomy of the cortex of the individual subjects.

The final stage of image processing prior to statistical analysis involves smoothing the fMRI images, i.e. convolving the images with an isotropic Gaussian kernel. For the analysis within the stereotactic space of Talairach and Tournoux (1988) (i.e. which included normalization of the images) a kernel with an 8-mm full width at half maximum was employed. For the non-stereotactically normalized analysis a 4-mm full width at half maximum was used. Smoothing of the images has the combined effect of increasing signal to noise and minimizing the effects of differences between individuals in functional and gyral anatomy.

After specifying the appropriate design matrix, changes in the haemodynamic response produced by the different experimental conditions were assessed at each voxel using the general linear model and theory of Gaussian fields (Friston *et al.*, 1995*a*) which constitutes SPM. In order to maximize signal variance, smoothing of the data in time is implemented. This temporal smoothing approximates the haemodynamic response function and in this case is modelled as a box-car reference waveform with a delay of 6 s; low frequency variations in the BOLD signal were modelled as covariates of no interest. Waveforms are specified for each epoch of scans that constitute a particular condition and as such can be used to test specific hypotheses by considering a *t*-value at each and every voxel. These *t*-values constitute the $SPM_{\{t\}}$ which is transformed to the unit normal distribution to give an $SPM_{\{Z\}}$. The $SPM_{\{Z\}}$ is then subject to thresholding on the basis of height (Z) and the number of voxels contained within its clusters (k).

Results

Stereotactically normalized analysis

Individuals

In all 12 subjects, well-circumscribed activation foci were found (bilaterally in 10 out of 12 subjects) in the ventral occipitotemporal cortex with colour stimulation. The $SPM_{\{Z\}}$s shown in Fig. 5 are examples of the three main patterns of activation elicited by the comparison of chromatic versus achromatic stimulation in the 12 subjects scanned. There are three main trends in the pattern of activation; the most common (Fig. 5A), exhibited by eight of the 12 subjects, shows activation of the area surrounding the posterior calcarine fissure, the primary visual cortex (area V1), in addition to two discrete foci bilaterally placed in the ventral occipitotemporal cortex (left and right area V4). The V1 activation almost certainly involved V2 but we cannot be sure of this because of the difficulty of seeing borders between the two areas in our scans. The second pattern (Fig. 5B) exhibited by two subjects, shows bilateral activation in the ventral occipitotemporal cortex but without any apparent activation of V1. The third pattern (Fig. 5C), exhibited by two subjects, shows a unilateral activation in ventral occipitotemporal cortex of the left hemisphere in conjunction with activation of the primary visual cortex.

In an attempt to quantify the variability in the position of human V4 we have listed the most significantly activated voxels lying in the ventral cortex with their Talairach coordinates (*see* Table 1). The largest variation in the position of V4 lies in the anteroposterior (y) axis where it can vary by as much as 34 mm in the left hemisphere and 30 mm in the right. In the mediolateral (x) axis the positions of V4 span a range of 12 mm in the left hemisphere and 16 mm in the left, and in the dorsoventral (z) axis 14 mm in the left and 16 mm in the right.

Group

Figure 6 shows the pattern of cortical activation for the group averaged data, with Table 2 listing the positions of the maximally activated pixels in these regions. Also indicated in Table 2 is the maximum extent of both right and left V4 activations in the mediolateral, superoinferior and anteroposterior axes. The analysis shows that there is bilateral and approximately symmetrical activation of a well-localized region in the ventral occipitotemporal cortex. As in the single subject analysis, these activation sites are distinct from the large area of activation located in the occipital pole which presumably incorporates areas V1 and V2.

Superior and inferior field stimulation

A noteworthy aspect of the group result is the fact that, outside the primary visual cortex, the activation by colour

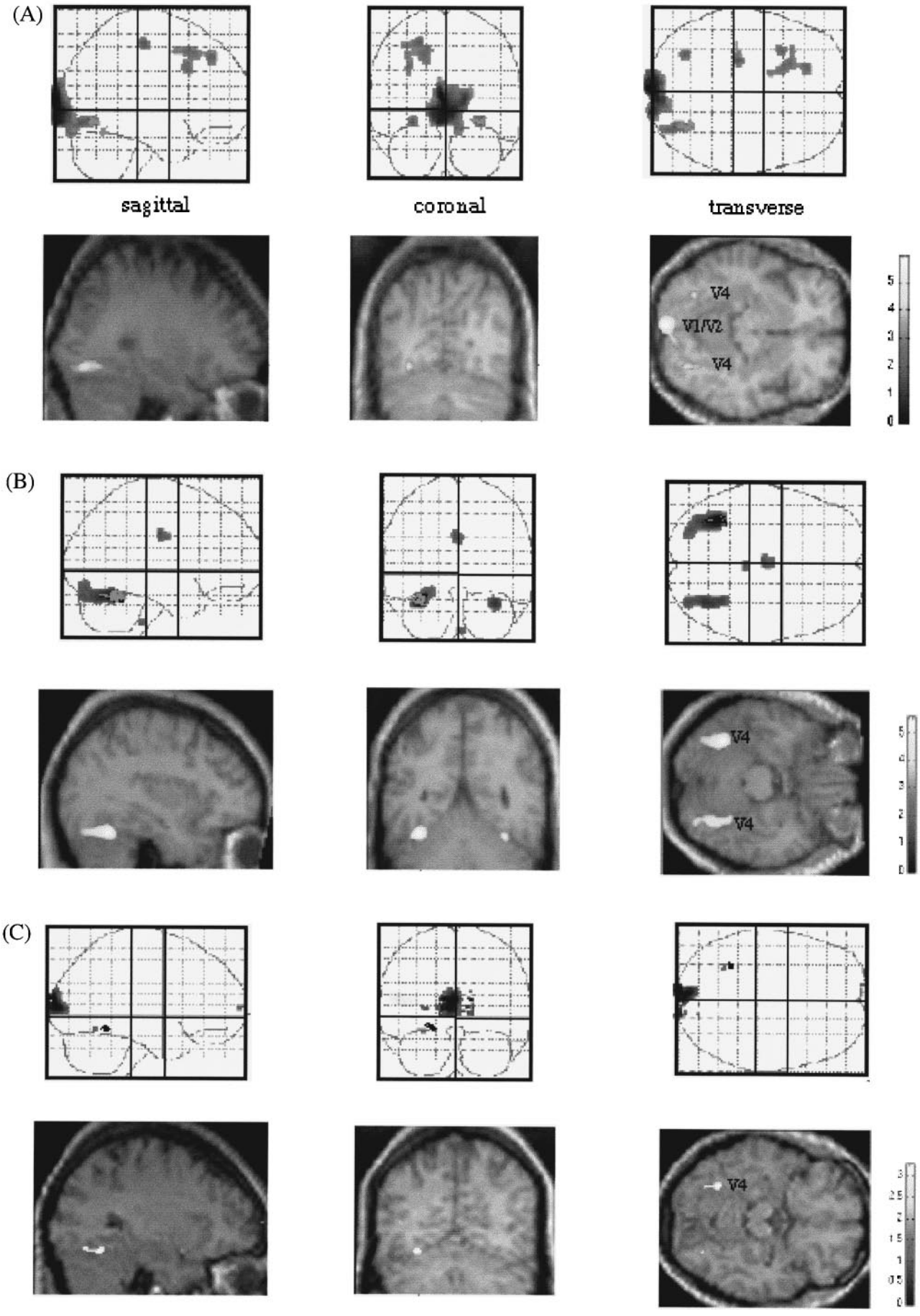
(A)
sagittal
coronal
transverse
V4
V1/V2
V4
5
4
3
2
1
0
(B)
V4
V4
(C)
V4

Table 1 *Talairach coordinates and Z-scores of the maximally activated pixels in area V4 associated with the comparison of chromatic versus achromatic stimulation*

Subject (sex)	Left hemisphere				Right hemisphere			
	Coordinates			Z-score	Coordinates			Z-score
	x	*y*	*z*		*x*	*y*	*z*	
1. PM (M)	–30	–70	–10	4.49	30	–78	–10	4.48
2. RE (M)	–24	–66	–12	5.56	30	–78	–20	8.01
3. PP (M)	–28	–80	–14	3.59	26	–82	–26	2.96
4. Dff (M)	–26	–70	–12	6.41	30	–76	–14	4.44
5. DM (M)	–36	–56	–24	5.55	34	–66	–24	4.52
6. SS (M)	–28	–84	–16	8.29	36	–78	–20	5.23
7. RV (M)	–26	–50	–18	3.18	30	–52	–20	3.12
8. LM (F)	–32	–58	–16	6.16	22	–80	–16	4.81
9. AMD (F)	–30	–58	–14	3.28				
10.AM (M)	–34	–76	–12	3.72	30	–80	–16	4.55
11. AB (M)	–26	–78	–12	5.07				
12. ME (F)	–28	–72	–10	4.36	32	–78	–20	4.34
Mean	–29	–68	–14		30	–75	–19	
SD	3.56	10.7	3.95		3.88	9.10	4.71	
SEM	1.02	3.08	1.14		1.22	2.87	1.48	
95% confidence limits								
Upper	–30.99	–74.19	–16.39		32.39	–80.42	–21.5	
Lower	–27.00	–62.12	–11.93		27.61	–69.17	–15.7	

is completely restricted to the ventral cortex. There is no evidence of any separate activation foci in more dorsal regions of the occipital lobe. This finding implies that human V4, as defined functionally in this study, contains a representation of both the superior and inferior contralateral hemifields. There appears to be no split of visual field representation for colour analysis in V4 between dorsal and ventral regions. In our second experiment, separate stimulation of the superior and inferior visual field was performed in order to confirm this finding and Fig. 7 shows the results from a single subject.

Activation of the calcarine cortex is a prominent feature of both superior and inferior field stimulation. In the former case (Fig. 7A) the activation focus (Talairach coordinates: $x = 2$, $y = -76$, $z = 2$, Z-score = 7.08) is located in position inferior to the calcarine fissure and in the latter case (Fig. 7B) the focus (Talairach coordinates: $x = -8$, $y = -98$, $z = 12$, Z-score = 5.86) is superior to the calcarine fissure. Such an inversion, with respect to the calcarine, is highly consistent with the representations of the superior and inferior visual fields in the striate cortex (e.g. Holmes, 1945; Horton and Hoyt, 1991).

Figure 8 shows that for the group analysis there are separate activations of V4 by the superior field (Talairach coordinates: right hemisphere $x = 28$, $y = -72$, $z = -12$, Z score = 4.59, left hemisphere $x = -24$, $y = -76$, $z = -14$, Z score = 4.61) and inferior fields (Talairach coordinates: right hemisphere $x = 38$, $y = -74$, $z = -20$, Z score = 4.71, left hemisphere $x = -32$, $y = -76$, $z = -12$, Z score = 4.71) stimuli, respectively. This shows that human area V4 contains a complete representation of the visual field that is contained wholly within the ventral cortex. Furthermore, there is some evidence of retinotopy in this area as the inferior field is mapped more laterally on the ventral surface than the superior field which is mapped more medially.

Non-stereotactic coregistration

The co-registration of the non-stereotactically normalized fMRI $SPM_{\{Z\}}$ images (filter at 4-mm full width at half

Fig. 5 Three subjects who are typical of the three major activation patterns revealed by the comparison of chromatic versus achromatic stimulation. The $SPM_{\{Z\}}$ data are shown on sagittal, coronal and transverse 'glass brain' views. The data are also represented on the subjects' coregistered (normalized) T_1 structural images; in each case the sagittal, coronal and transverse planes are coincident with the *x*, *y* and *z* planes, respectively of the most significantly activated pixel in area V4. (**A**) The most frequently encountered pattern, exhibited by eight of 12 subjects, reveals prominent activation of the occipital pole surrounding the calcarine fissure (V1/V2), in addition to which are separate, bilaterally placed foci in the ventral occipital cortex (V4). (**B**) The pattern of activation exhibited by two subjects. In this case, bilateral foci can be seen in the ventral cortex but there is no activation of the primary visual cortex at the occipital pole. (**C**) The final pattern observed (also in two subjects) revealed activation of the calcarine cortex at the occipital pole in addition to a unilateral focus in the ventral cortex.

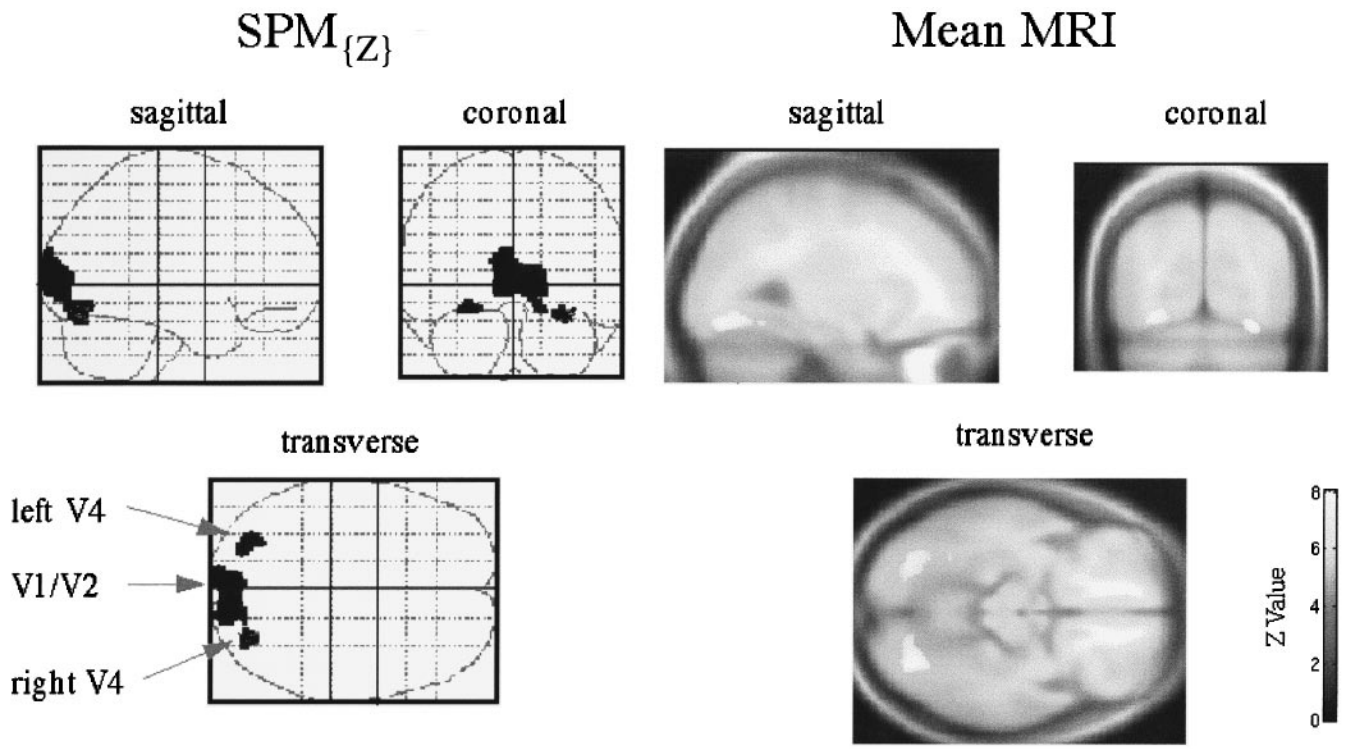

Fig. 6 Group result ($n = 12$) for the comparison of chromatic versus achromatic Mondrian stimulation thresholded at corrected $P < 1 \times 10^{-3}$ display conventions are similar to those used in Fig. 5).

Table 2 Group averaged results for the chromatic versus achromatic comparison

Region	Talairach coordinates			*Z*-score
	x	*y*	*z*	
Right V4				
Maximum activation	30	–78	–18	8.05
Extent of activation	24 to 36	–70 to –82	–12 to –24	
Left V4				
Maximum activation	–26	–80	–14	7.99
Extent of activation	–20 to –36	–66 to –84	–8 to –18	
V1/V2				
Maximum activation	10	–90	0	8.48

Talairach coordinates: x = medial–lateral (RHS positive); y = anterior–posterior; z = superior–inferior.

maximum) with the T_1-weighted structural MRIs for each subject enables the assessment of any relationship that may exist between functional specialization and cortical topography. Consistent with more recent brain imaging studies of colour perception (Sakai *et al.*, 1995), this study localizes colour related activation predominantly in the fusiform gyrus (*see* also Zeki *et al.*, 1991). In order to assess the generality of this relationship between structure and function in our group of subjects more closely, we marked the position of the collateral sulcus in each of the brains prior to co-registration with the $SPM_{\{Z\}}$ images. This gave us a structural landmark with which we could compare the relative location of the human colour centre (*see* Fig. 9). The collateral sulcus was chosen because it is one of the most prominent anatomical features in the ventral brain, although its precise pattern and course may vary from one individual to the next (*see* Ono *et al.*, 1990). In addition, the collateral sulcus conveniently separates the lingual gyrus, which forms its medial border, from the more laterally placed fusiform gyrus as it runs anteroposteriorly along the ventral surface of the cortex. In the coregistered images shown in Fig. 10 the collateral sulcus has been identified (as defined by Ono *et al.*, 1990) in three subjects and marked. As can be observed, the colour activation foci are always located in close proximity to the collateral sulcus, typically found on its lateral aspect, i.e. the fusiform gyrus. There appears to be little evidence, in any of the subjects, of encroachment into the more medially located lingual gyrus.

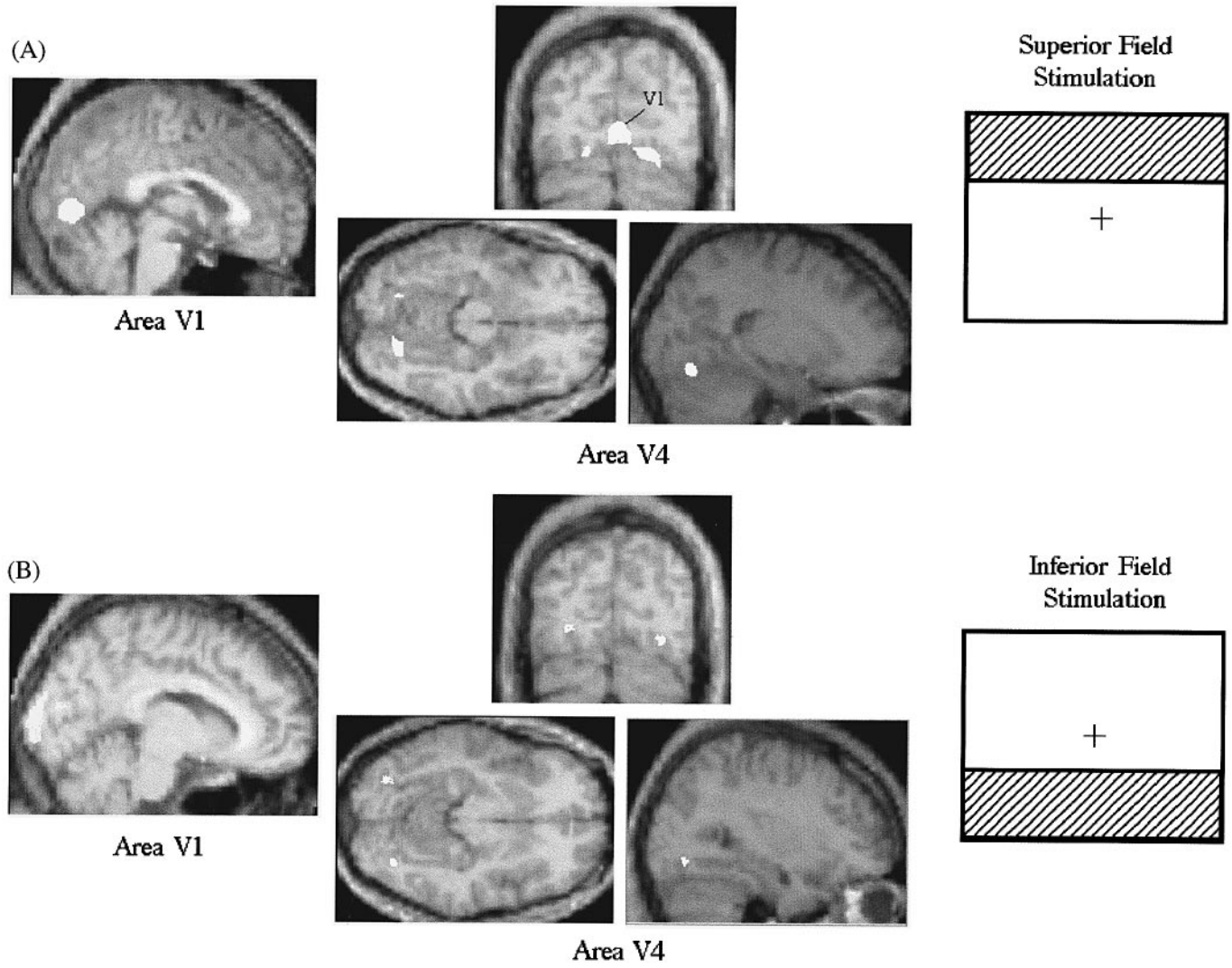

Fig. 7 Activations generated in a single subject in areas V1 and V4 by stimulation of (**A**) the superior visual field and (**B**) the inferior visual field.

Discussion

In this study, we have tried to chart the part of the human visual brain that is critical for the perception of colours more precisely and learn something about the nature of the visual field map in it. We have shown that, when individuals view a temporally modulated chromatic pattern, as opposed to an achromatic pattern, there is a consistent activation of a region in the ventral occipitotemporal cortex, the region already demonstrated in our previous studies to be specifically activated by colour (Zeki *et al.*, 1991) and that in which lesions are known to result in the syndrome of cerebral achromatopsia or dyschromatopsia; the critical feature of these syndromes is an imperception of colours or a severe disturbance in colour perception (for reviews, *see* Meadows, 1974; Zeki, 1990). The region thus delineated is separate from the primary visual cortex (V1). As in our previous studies of another specialized prestriate area, V5 (Watson *et al.*, 1993), we found that, even though located in the vicinity of the collateral sulcus on the fusiform gyrus, the precise location of the colour centre in humans varies from one individual to another. The earliest localization of the colour centre had supposed that it included both the lingual and fusiform gyri (Verrey, 1888). Soon thereafter, MacKay and Dunlop (1899) refined the localization to the fusiform gyrus, although both studies were soon dismissed in a general opinion—championed by Henschen, Holmes and von Monakow—that was hostile to the notion of specialization for different attributes of vision (for a review, *see* Zeki, 1990). This study shows more convincingly that the colour centre can be localized to the fusiform gyrus in individual brains, a localization that is consistent with previous imaging experiments (e.g. Corbetta *et al.*, 1991; Zeki *et al.*, 1991; Allison *et al.*, 1993; Sakai *et al.*, 1995).

Relation to human anatomy

The results from this study are also consistent with human anatomical studies. Clarke and Miklossy (1990), for example,

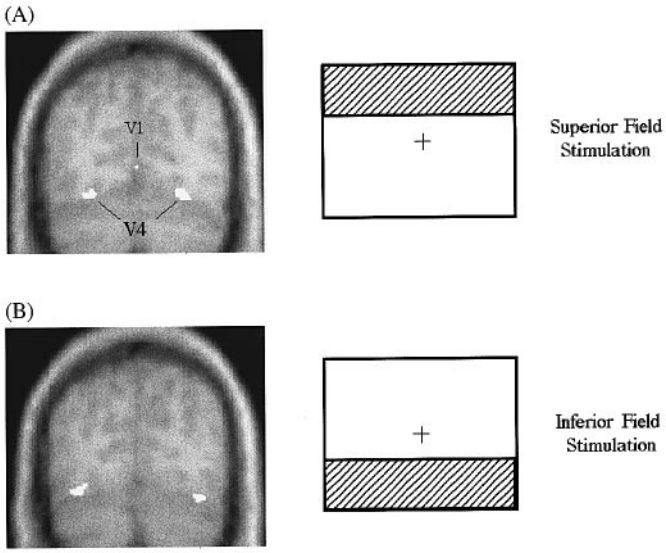

Fig. 8 Group result for the activations produced in area V4 by the stimulation of (**A**) the superior visual field and (**B**) the inferior visual field.

have examined patterns of degeneration in callosal afferent fibres in the brains of humans who had suffered unilateral occipital infarctions. In doing so they were able to identify the boundaries between visual areas which contained a representation of the vertical meridian, in a similar way to that already used in the monkey brain (e.g. Zeki and Sandeman, 1976; Zeki, 1977, 1978). A callosal boundary was identified on the ventral occipitotemporal cortex, usually in close proximity to the collateral sulcus. In the absence of any direct functional evidence, Clarke and Miklossy (1990) tentatively identified this pattern of callosal afferents as forming the V4–ventral V3 border, a conclusion that is justified in the light of the close association between the collateral sulcus and the activation foci elicited by chromatic stimulation shown in this study (*see* Fig. 7). Thus, evidence from both anatomical and functional imaging studies converge in placing human area V4 firmly on the ventral surface of the brain, in close proximity, but lateral, to the collateral sulcus, one of the major anatomical features of the occipitotemporal cortex.

The retinotopic organization of the human colour centre

In the macaque monkey, the cells of area V4 have much larger receptive fields than their counterparts in areas V1–V3 but, in spite of this enlargement of field sizes, a topography is definitely maintained within V4. The most striking feature of this topography is the separate representation of the upper and lower visual fields within V4, the lower fields being represented superiorly and the upper fields inferiorly (Gattass *et al.*, 1988). But the two parts of V4 are continuous. In the human, no direct studies of V4 combining colour stimulation with discrete visual field stimulation have been done, until now. Nevertheless, Sereno *et al.* (1995) have interpreted their results to mean that there are two separate parts of V4, one located ventrally and corresponding to the area that we have demarcated here and elsewhere and the other located more dorsally, which was not activated in our present or previous studies, and was not specifically activated by colour in the study of Sereno *et al.* (1995). The present study, the first to map visual field representation functionally, has shown that the human V4 located in the fusiform gyrus has a representation of both superior and inferior fields. Moreover, the superior field occupies a more medial position than the inferior field. If V4 in the monkey were to be displaced ventrally and medially to the same extent that V5 is displaced ventrally in human, relative to the monkey, it would occupy roughly the same position and have the same topographic organization as in the human. The evidence that the entire visual field is mapped in the colour centre located in the fusiform gyrus is further supported by clinical evidence, which shows that a lesion here can lead to an achromatopsia that includes the entire contralateral hemifield. Consistent with what is demonstrated here, there is no evidence from the clinical literature of achromatopsic subjects with field defects restricted to the inferior hemifield (Meadows, 1974; Plant, 1991).

Because of the results given here, we suggest that the dorsolaterally activated region in the study of Sereno *et al.* (1995) is not part of V4. Indeed, there is no example of selective damage to the dorsal occipital cortex leading to achromatopsia. We are aware of the fact that the study of Corbetta *et al*. (1991) did result in a ventrolateral activation, in addition to an activation within the zone of the fusiform gyrus. But the position of the former area is not identical with the dorsolateral area identified in the Sereno study, and was in any case activated by stimuli in which attention to colour was critical (*see* below). Thus the relationship of this lateral area to the colour centre, as defined here, remains ambiguous.

A segregated pathway for colour in the human brain

Activation of area V1 and (probably) V2, which are difficult to distinguish from each other in these scans, was a consistent feature in a majority of the subjects scanned during this experiment, and was also noted in other brain imaging studies involving colour vision (e.g. Corbetta *et al.*, 1991). The involvement of these two areas is to be expected, given what is known about the anatomy of the colour pathway in the monkey. What is perhaps more interesting, in showing that there are specialized colour pathways in the human visual brain, is the absence of any activation in most other parts of the occipital lobe, including well-demarcated areas such as V3 or V5, for example. Collectively, the positive evidence, together with the negative evidence, gives strong support to the notion of specialized pathways dealing with colour in the

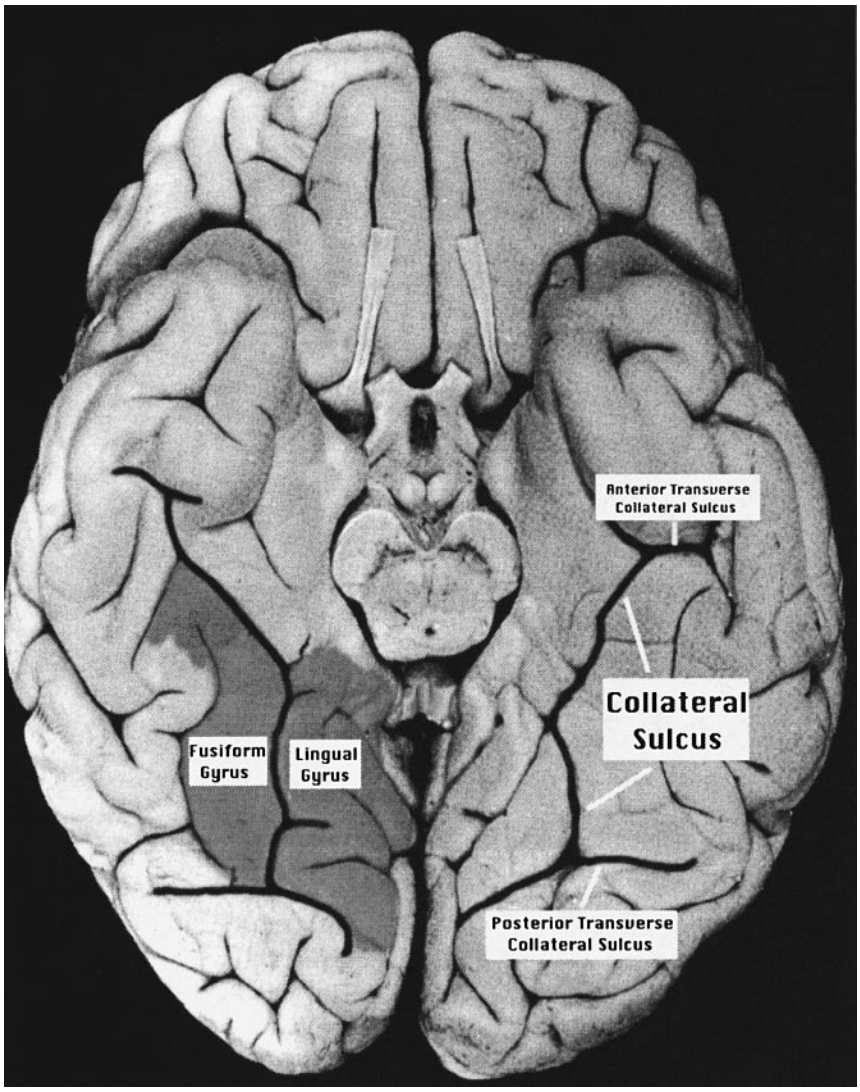

Fig. 9 The ventral surface of the human brain. The shaded regions medial and lateral to the collateral sulcus (in the right hemisphere only) indicate the posterior regions of the lingual and fusiform gyri, respectively.

human brain. We do not suppose that the centre in the fusiform gyrus is necessarily the endpoint of this pathway, because the stimuli that we used were relatively simple. The use of other, more meaningful colour stimuli or colour tasks that involve higher cognitive aspects may activate further areas. The study of Corbetta *et al*. (1991) is one such example, where attention to colour generated activation of areas that are not coincident with the regions shown to be active in this study. More recent studies (e.g. Martin *et al.*, 1995) also suggest that there may be a parcellation of function for different aspects of colour perception in the human ventral occipitotemporal cortex.

Results from lesion work and single unit physiology in monkeys have suggested different roles for areas V1/V2 and V4 in the analysis of colour, at least in part because the responses of cells in the former are heavily wavelength-based, the cells responding to a patch of any colour provided it reflects a sufficient amount of light of their preferred wavelength; by contrast, the responses of some cells in V4 at least correlate with perceived colour rather than with wavelength composition (Zeki, 1983). As a result of these findings area V4 has been considered to be important in the processes that subserve colour constancy (Zeki, 1980; Wild *et al.*, 1985; Walsh *et al.*, 1993). Areas V1 and V2, on the other hand, are hypothesized as being important in wavelength discrimination (Kulikowski and Walsh, 1993; Kulikowski *et al.*, 1994). V1 and V2 may also be involved in the segregation of the visible spectrum into constituent hues; Vautin and Dow (1985) have shown that four major classes of chromatically responsive neuron exist in the foveal striate cortex, each with sensitivity profiles covering a different part of the spectrum. Similar classes of neuron may constitute the neurological basis for the hue categorizations that have been identified by psychophysical methods in human vision (Boynton and Olson, 1990; Mullen and Kulikowski, 1990). Our hypothesis is that, as in the monkey, rudimentary wavelength detection and discrimination in humans can be subserved by areas antecedent to area V4, namely areas V1

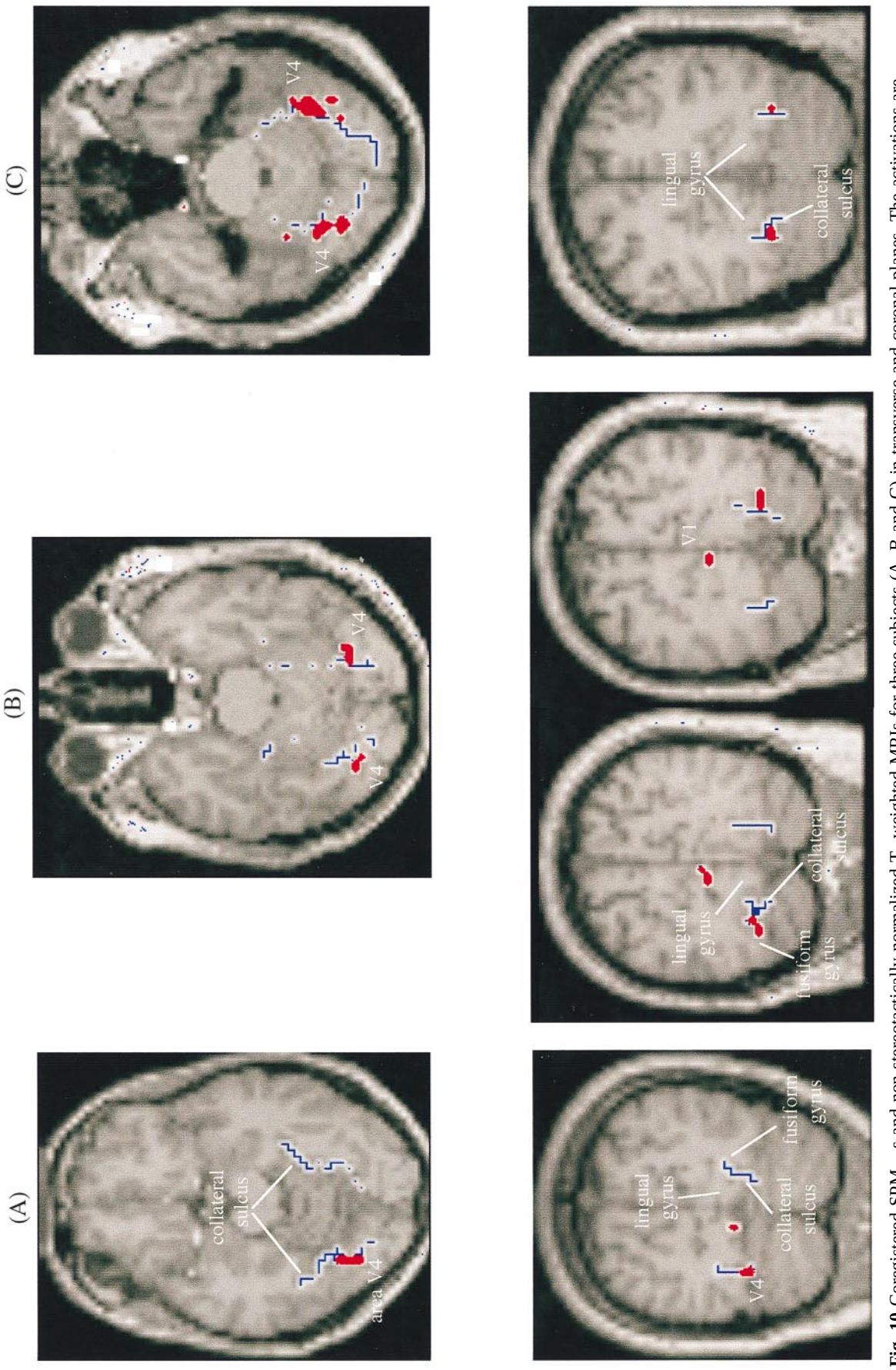

Fig. 10 Coregistered SPM$_{\{Z\}}$s and non-stereotactically normalized T_1-weighted MRIs for three subjects (A, B and C) in transverse and coronal planes. The activations are marked in red and the collateral sulcus in blue.

and V2, whereas V4 itself is more concerned with colour constancy mechanisms. Indeed, the results of Vaina (1994) and unpublished results from this laboratory (W. Fries and S. Zeki) show that achromatopsic subjects discriminate wavelength differences, though with elevated thresholds, in a similar way to monkeys with V4 lesions .

Homology between human and monkey V4

We have throughout this paper used the term human colour centre and human V4 interchangeably, implying a homology between this centre and monkey V4. There are arguments in favour of this supposition (Wild *et al.*, 1985; Kennard *et al.*, 1995) as well as arguments against (Heywood and Cowey, 1987; Heywood *et al.*, 1991, 1992, 1994, 1995; Merigan, 1993; Cowey, 1994; Cowey and Heywood, 1995). We will address this issue in a separate context. Here it is sufficient to point out that our present results, though telling us about the location of the human colour centre and the similarity in the nature of visual field representation between it and monkey V4, do not speak conclusively in favour of a homology between the two structures, but they make such a homology seem less unlikely.

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