The Organization of Connections between Areas V5 and V2 in Macaque Monkey Visual Cortex

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Abstract

Area V2 of the cerebral cortex of higher primates has a complex cytochrome oxidase architecture whose most characteristic element is a set of stripes running orthogonal to its long axis. These stripes can be related to the segregation between the various pathways in which V2 participates. In the macaque monkey the more metabolically active stripes are alternately thick and thin and only one set, the thick stripes, is found to possess clusters of labelled cells following injections of horseradish peroxidase – wheatgerm agglutinin into area V5. Some of these clusters, but not all, coincide with substructures inside the thick stripes. V2 of the owl monkey has a similar organization except that the diversification into thick and thin stripes is less prominent, both in terms of their appearance and in that more than every alternate stripe is connected to area MT, the likely homologue of V5.

The return projection from V5 to V2 is more widespread than the origin of the forward projection. It extends not only between the clusters of V5-efferent cells within the thick stripes but also across the intervening thin stripes and less active interstripes. Because the latter subserve functions different from those of the thick stripes it would seem that their receipt of a back projection from an area to which they do not project, V5, may be relevant to the process of integration of signals relating to different attributes of vision.

Introduction

The territory adjoining the primary visual cortex (V1) of higher primates was divided, historically, into just two concentric regions, areas 18 and 19 (Brodmann, 1905). The sharp architectonic discontinuity between V1 (area 17) and these areas led Brodmann to believe that the latter were non-visual in function (Brodmann, 1909, in von Bonin, 1960). But evidence to the contrary (e.g. Campbell, 1905) promoted the subsequent growth of hierarchical ideas of visual function in the cortex. Only relatively recently has the complementary parallel element in cortical information processing gained a wider acceptance. This is due, in a large part, to the demonstration that Brodmann’s areas 18 and 19 are in fact composed of a much larger number of areas, most of which receive independent inputs from V1 and show some form of functional specialization (Zeki, 1975, 1978a; Baker et al., 1981). Thus V1, as the gateway to the cortex, distributes a number of different signals for further analysis.

The first of the receiving areas, V2, however, shares a number of characteristics with V1. V2 was initially identified on the basis of the topographically organized projections that it receives from V1 (Cragg, 1969; Zeki, 1969) and was later shown to project to all the same specialized areas as V1, including areas V3, V3A, V4 and V5 (Zeki, 1971, 1978b; Rockland and Pandya, 1979). Furthermore it possesses an equally heterogeneous population of functional cell types, including cells selective for wavelength, orientation, retinal disparity, or direction of movement (Baizer et al., 1977; Poggio and Fischer, 1977; Zeki, 1978d; Burkhalter and Van Essen, 1986). And thirdly it has a modular substructure made evident by staining it for the metabolic enzyme cytochrome oxidase (Livingstone and Hubel, 1982; Tootell et al., 1983). As with V1 groupings of cells with common preferences are found to coincide with the cytochrome oxidase architecture (Shipp and Zeki, 1985; Hubel and Livingstone, 1985, 1987; DeYoe and Van Essen, 1985). In V2 this takes the form of alternate thick and thin dark stripes separated by paler staining interstripes. The functional segregation in both V1 and V2 is also reflected in the specific pattern of connections between them, the thin stripes of V2 receiving from the blobs of V1, the interstripes from the interblobs and the thick stripes from layer 4B (Livingstone and Hubel, 1984, 1987a).

In the companion paper (Shipp and Zeki, 1989) we show that V5 makes connections with punctate patches of layer 4B whose disposition strongly resembles that of the blobs. But despite this superficial similarity the two systems bear no fixed relationship to each other. For V2, however, the connections made with V5 are related to the cytochrome oxidase pattern and are found to be concentrated in one set of stripes, the thick stripes; similarly the connections between V2 and V4 are concentrated within the thin stripes and interstripes (Shipp and Zeki, 1985; DeYoe and Van Essen, 1985). Here we present in greater detail the anatomy of the connections of the thick stripes with
V5 and examine the variability of the patterns of connection and of the cytochrome oxidase stripes themselves. In addition we have studied the connections of owl monkey area MT with V2 and show that, on an anatomical basis at least, alternation of character of the darkly staining stripes in owl monkey V2 is a much less regular feature than it is in the macaque.

Thus the segregation between the pathways ascending through V2 to diverge to different destinations suggests that V2, like V1, plays a role in the early distributive functions of the cortical visual system. But the segregation between the return projections to V2, like that from V5 which we describe here, does not appear to be as strict. Though concentrated in the thick stripes the return projection from V5 also invades the thin stripes and interstripes, hence departing from a strictly reciprocal arrangement. And, in forming a link between differently specialized pathways, one of the functions of this reciprocal asymmetry may be integrative in character—one of a wider set of systems for assembling signals relating to different attributes (Zeki and Shipp, 1988).

Materials and Methods

This report is based on the same set of injections of horseradish peroxidase — wheatgerm agglutinin (HRP-WGA) into area V5 of the macaque and area MT of the owl monkey described in the preceding paper (Shipp and Zeki, 1989) and involves similar techniques. In brief, the brains were sectioned in the horizontal plane and at least 1 in 6 sections were stained for HRP by the method of Mesulam (1982) or for cytochrome oxidase by the method of Wong-Riley (1979). In two
macaques the occipital operculum was removed prior to cutting the rest of the brain. It was then flattened and sectioned in the tangential plane (see Fig. 1). Of the three owl monkey brains, one was sectioned horizontally and one in a plane intermediate between horizontal and coronal (roughly parallel to the line of the sylvian sulcus). The occipital and temporal cortex of the third brain was flatmounted and sectioned tangentially. Some owl monkey sections were also stained for myelin by the method of Gallyas (1979). The relationship between the patterns of cytochrome oxidase activity and HRP labelling was studied by making superimposed diagrams of adjacent sections. Normally the outline and blood vessels of the cytochrome oxidase section were drawn first (from the image provided by a conventional slide projector) and labelled cells and terminals superimposed via the drawing tube of the microscope, numerous small adjustments in the relative alignment being made so as to obtain the best fit between the blood vessels in each vicinity (the 'method of local adjustment'). Diagrams of horizontal sections were further used to obtain an impression of the patterns of distribution in the tangential plane by means of computer-aided reconstructions.

Results

Connections between V5 and V2 in the macaque

The cytochrome oxidase architecture of V2. The pattern revealed by staining for cytochrome oxidase in V2 consists essentially of a series of stripes which run in a direction orthogonal to the V1/V2 border. The striped pattern can vary substantially from animal to animal but normally the cytochrome oxidase dense stripes are alternately thick and thin and separated by paler zones, interstripes, of more regular width (Tootell et al., 1983, 1985; Livingstone and Hubel, 1982, 1984; Horton, 1984). Previous detailed descriptions of the stripes have concentrated on the New World owl and squirrel monkeys. In the macaque the pattern is qualitatively similar but the widths of the stripes, and consequently the overall periodicity, are both greater. The flat-mounted operculum preparation (Fig. 1) proved especially suitable for studying the stripes in more detail, giving, as it does, sections which pass tangentially through the cortex of V2 buried within the posterior banks of both the lunate sulcus (LS) and inferior occipital sulcus (IOS). Figure 2 shows a number of examples of the classic pattern and

FIG 3. The radial organization of labelled cells and terminals in macaque area V2, following an injection of HRP-WGA into area V5, in relation to the cytoarchitecture and cytochrome oxidase architecture of V2.
(A) Cross-polarized photomicrograph illustrating a typical cluster of labelled cells and a typical column of labelled axonal terminals.
(B) Bright-field photomicrograph of a column of label similar to A taken from a section counterstained for Nissl substance. Note that the majority of labelled cells occur in layer 3, just above the granular layer.
(C) Photomicrograph of the section adjacent to B stained for cytochrome oxidase and counterstained for Nissl substance. Note that the region staining most densely for cytochrome oxidase (part of a thick stripe) is mainly in layer 3 but just invades layer 4, the granular layer. The scale bar is 200 μm.
variations which involve branching or other irregularities.

One cycle of stripes consists of a thick stripe, a thin stripe and two interstripes. The alternation of thick and thin proved sufficiently regular to extend uninterrupted for at least three cycles and sometimes up to five (e.g. Fig. 2B) within both the LS and IOS of most cases examined. Elements of the striped pattern not readily identifiable in one section were often easier to identify in the adjacent section or one nearby. To estimate the mean length of a cycle (the perpendicular distance from one thin stripe to the next, or one thick stripe to the next) we measured 47 cycles from 15 hemispheres in the LS and 30 cycles from 12 hemispheres in the IOS. Cycles were measured in groups of 2 to 4 in regions where the pattern of alternation was clear and regular and all the stripes near parallel to each other. All the animals weighed between 3 and 4 kg. The result obtained was a cycle length of 4.0 mm (s.d. = 0.3 mm) in the LS and 3.8 mm (s.d. = 0.5) in the IOS. Assuming a shrinkage of 16% during perfusion and histological treatment, the mean cycle length in the brain in vivo is about 4.7 mm. The relative widths of the stripes also vary somewhat and are not simple to determine because the exact placement of their borders is a little arbitrary. An approximate mean ratio for the widths of the stripes is 2:1:1:5 (thick:thin:inter). The identification of thick and thin stripes becomes questionable where they assume a more uniform width, though a provisional identification, based on the principle that thick and thin stripes alternate, is often possible provided that there are at least some stripes present which can be identified with confidence.

Irregularities in the striped pattern more severe than variation in stripe width are relatively common. The medial end of the LS is especially prone to disruption: all four examples in Figure 2 (E-H), for instance, show some form of irregularity. Irregularities are most commonly due to stripes of the same or different type bifurcating, or coalescing diffusely, though more than one interpretation is often possible. The least ambiguous examples of branching we have observed are illustrated in Figure 2C and D where, in both cases, the most laterally located thin stripe within the IOS bifurcates in passing from the fundus to the lip of the sulcus. A similar pattern may be present in Figure 2G; but in this case it looks as if a thick stripe is generated in between the fork of the thin stripe, thus restoring the regular pattern of alternation. Less frequently, two adjacent stripes are of the same type and run parallel to each other without joining, the remainder of the pattern on either side showing the normal regular sequence of alternation: the two clearest examples we have observed both involved a pair of thin stripes in the IOS. Also notable is the variability in the substructure of the stripes. Some are relatively uniform in their staining density (e.g. Fig. 2B and D) whereas in others heavily staining regions alternate with regions where the staining density is no greater than that of the interstripe—which itself is not always uniform (e.g. Fig. 2F, G and H). Finally, in the most irregular cases, the whole striped organization can break down, leaving an array of densely staining blotches several mm wide which do not align in any notable fashion.

Correlation of the V5-efferent zones with cytochrome oxidase architecture. (6) Radial organization. Following injections of HRP-WGA into V5, transported label in V2 appears in isolated dense columns, normally spaced 3–4 mm apart but occasionally in pairs within several

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**Fig. 4.** The disposition of regions of V2 connected to V5, in relation to the cytochrome oxidase architecture of V2, as seen at low power in horizontal sections passing through the medial part of the IOS. (A) Dark-field photomicrograph of a section processed for HRP. There are five major groups of labelled cells and terminals, three of which clearly possess subclusters. (B) The adjacent section stained for cytochrome oxidase. Striate cortex, on the external surface, is distinguished by the densely staining layer 4C and the remainder of the section that is shown is all V2. The plane of section is near radial, which is not advantageous for revealing a regular set of stripes of alternating thickness as smaller scale fluctuations in staining density tend to become more prominent. (C) 'Adjusted' superimposition of A and B. The heavy continuous and heavy dashed lines are respectively the outlines of the pial surface and the base of layer 6 from the cytochrome oxidase section. Lighter outlines indicate regions whose contrast with respect to the background was only very slight. Coarse and fine stipple represent labelled cells and terminals respectively. A few of the blood vessels by which the two sections were aligned (as usual with adjustment from region to region to achieve optimal registration) are also included; those with continuous outline are from the cytochrome oxidase section and those with dotted outline are from the HRP section. The scale bar is 1 mm.
Cortical connections between V5 and V2

FIG. 5 (part 1). (A) Posterior view of a right cerebral hemisphere from which the occipital operculum has been removed. The dashed line follows the course of the lip of the lunate sulcus. The rectangular outline indicates the approximate limits of the region reconstructed within the anterior bank of the IOS; this region was inverted to form the top half of the reconstruction.

(B) The interior surface of an occipital operculum from a right hemisphere, viewed posteriorly as if the external surface were transparent. The rectangular outline indicates the approximate limits of the reconstructed region within the posterior bank of the IOS, which forms the lower half of the reconstruction.

FIG. 5 (part 2). Reconstruction, from 34 diagrams such as Figure 4C, of the joint distribution of cytochrome oxidase activity and of labelled layer 3 cells in macaque area V2 following an injection of HRP-WGA into area V5 (case LV73). The reconstruction is roughly symmetrical about the fundus of the IOS with the lower part representing the posterior bank and the upper part the anterior bank; a fold through its centre parallel to the straightened sections would allow the two banks to be placed in apposition roughly restoring their arrangement in the intact brain. Cytochrome oxidase is represented by broken lines and labelled cells by rows of dots (with each dot corresponding to many cells). The dots derived from each HRP section have been duplicated on either side of the contour line of the adjacent cytochrome oxidase section for greater clarity of appearance. Where the dots are more closely spaced labelled cells were present in greater numbers; four different density levels are shown but the variation in density was greater than the reconstruction conveys. No attempt has been made to represent more than two levels of cytochrome oxidase activity.

A reasonably coherent pattern of stripes emerges from the somewhat fragmentary distribution of cytochrome oxidase activity seen in the individual sections. Some stripes are obviously thicker than others and over most of the reconstruction a regular sequence of alternation can be discerned. Within this region almost all labelled cells coincide with thick stripes. The striped organization is least clear in the most lateral portion of the reconstruction (rightward on the figure), where the stripes appear to be branching, but there are few labelled cells in this vicinity. The sections are spaced vertically at the same scale as their horizontal magnification; the scale bar is 2 mm.
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hundred microns of each other (Figs. 3A and 4A). In agreement with previous reports (Lund et al., 1981; Maunsell and Van Essen, 1983a; Ungerleider and Desimone, 1986b) labelled cells occur principally in layer 3B, with a few in layers 2, 3A and 5. Most labelled cells, in the upper layers at least, are identifiably pyramidal. Terminal label is heaviest in layers 1 and 6, and diminishes in density towards layer 4 (Maunsell and Van Essen, 1983a; Ungerleider and Desimone, 1986b). Layer 4 itself is normally free from terminal label but not invariably so.

The basic laminar organization of cytochrome oxidase activity is simply stated: layers 2, 3 and the upper part of layer 4 stain moderately densely, and the remainder more lightly. This is evident in Figures 3C and 4B and confirms previous reports (Tootell et al., 1983; Wong-Riley and Carroll, 1984). Added to this basic pattern there is a tendency for all layers within thick or thin stripes to stain more densely. The contrast between stripe and interstripe is most marked in layers 3 and 4 and least, if detectable at all, in layer 1. Thick stripes and thin stripes commonly stain equally heavily, except in some instances where the thin stripes are notably more dense in the upper layers (e.g. Fig. 7C).

Superimposition of sections such as those illustrated in Figure 3A and B shows that the columns of HRP label coincide with regions staining densely for cytochrome oxidase (Fig. 3C). The supragranular labelled cells fall within the most heavily stained laminae, the deepest still slightly superficial to the base of this zone. Labelled terminals by contrast are most prevalent in layers 1, 5 and 6, the very layers where cytochrome oxidase activity is weakest.

(ii) Tangential organization. The conventional horizontal sections illustrated in Figure 4 give only a poor impression of the alternation between thick and thin stripes in the cytochrome oxidase architecture. Indeed it is not always possible to distinguish stripe from interstripe in such sections. In order to establish the two-dimensional relationship between the stripes and the V5-efferent zones we reconstructed their appearance within the tangential plane from a series of superimposed diagrams like that of Figure 4C and sought to confirm the outcome by injecting the central/paracentral visual field representation in V5 with the intention of flatmounting the occipital operculum.

A number of features emerge from the reconstruction (Fig. 5) which are not evident in its component sections. Firstly the labelled cells coincide, on a regular basis, only with every alternate stripe. Secondly, these cells are separated into clusters along the length of the stripe, labelled zones alternating with sparsely labelled or unlabelled zones. Thirdly, on closer inspection, there is an alternating sequence of thick and thin stripes, with the great majority of labelled cells occurring within thick stripes.

These features were confirmed by the two flatmounted cases illustrated in Figures 6 and 7. Figure 6 shows two neighbouring thick stripes in the LS, each of which contains several distinct clusters of labelled cells. Figure 7 shows a series of four bands of label from the IOS of the other case; each of these clearly coincides with a thick stripe, though a number of the more minor details of the cytochrome oxidase pattern in this sulcus are open to interpretation (see legend to Fig. 7).

Several patches of label seem to extend beyond the boundaries of the stripes in the adjacent section, though this may merely reflect the difficulty in determining the stripe boundaries with an accuracy better than a few hundred microns. Indeed it is possible that, functionally, the boundaries of the stripes are as diffuse as they appear to be in the cytochrome oxidase stain. It is perhaps more important to note that we have yet to observe a cluster of V5-efferent cells that is centred on an interstripe. We have, by contrast, observed occasional small clusters of cells situated in thin stripes (e.g. Fig. 5); these were not present in all animals, were infrequent when present, and probably involved far less than 1% of all labelled cells in V2.

An alternative source of the label in the thin stripes would be V4 (Shipp and Zeki, 1985; DeYoe and Van Essen, 1985). But only one V5 injection was situated sufficiently laterally within the STS for involvement of the V4 complex to be at all likely, and it produced no trace of labelled cells in the thin stripes (Fig. 6). One or two of the other injections may have exceeded the limits of V5 more medially (see the accompanying paper, Shipp and Zeki, 1989). But V2 may not be connected with this region of cortex (Ungerleider and Desimone, 1986a) and, if it is, the source of the output must be similar to that leading to V5 itself.

(iii) Clustering within thick stripes. The two neighbouring thick stripes shown in Figure 6 contained patterns of clusters of labelled cells and terminals that were remarkably similar. Superimposition of several sections revealed that one pattern consisted of five elements and the other of four, lacking a corresponding cluster of label in just one location. The clusters were separated by unlabelled or at best sparsely labelled zones both across the width of the stripe as well as along its length. Multiple clusters can also be noted in the reconstructed case (Fig. 5), though nowhere is there such a regular repetition of the same substructure within a stripe. Only one thick stripe, in the posterior bank of the IOS (lower half of the reconstruction as shown in Fig. 5), contains a pair of elements separated across the width of the stripe (the same pair of clusters can be seen in Fig. 4A). One of these is at least 3 mm in length. All the other labelled stripes show signs of clustering along their lengths, the best example being a stripe in the anterior bank (top half of Fig. 5 reconstruction) in which there are four separate clusters. The distance along the stripe from the centre of the first cluster to the fourth is 6 mm, giving a repeat distance of about 2 mm. This is slightly greater than the repeat distance obtainable from Figure 6, which is about 1.5 mm.

Further examples of clustering, at various spacings, can be seen in Figure 8, again from the IOS. In a number of instances (described in more detail in the legends to Figs. 6 and 7) the individual clusters of HRP label coincide with regions within the thick stripes that stain relatively heavily for cytochrome oxidase. We believe that these coincidences are not due to reaction of the HRP with the cytochrome oxidase incubation medium because not all areas with HRP activity stain heavily for cytochrome oxidase. Such areas include patches of label in layer 1 and the injection site itself. Also the outlines of the regions of high HRP and high cytochrome oxidase activity often fail to match each other exactly in regions of close correspondence.

There might thus be a correlation between cytochrome oxidase activity and the pattern of cortico-cortical connectivity at the substripe level. But the variation between individuals or between different parts of V2 in the same hemisphere (e.g. LS vs. IOS), both in the pattern of connections and in cytochrome oxidase architecture, precludes a more definitive statement about the substructure of thick stripes.

Reciprocal and non-reciprocal features of the back projection from V5 to V2. Following all our injections of HRP-WGA into V5 the heaviest deposits of terminal label were consistently found within thick stripes. As with V1, however, the back projection is more diffusely spread than the origins of the forward projection in both topographical and functional terms, a departure from strict reciprocity which we refer to as reciprocal asymmetry (Shipp and Zeki, 1989). Collateral terminal
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label from retrogradely filled cells can potentially intermingle with the direct orthograde terminal label of the back projection, but two considerations can afford some distinction between them. Firstly, intrinsic connections in V2 have a limited range, which has not been demonstrated to exceed 3-4 mm in the macaque (Livingstone and Hubel, 1984; Rockland, 1985), though a range of up to 6 mm has been found in the squirrel monkey (Tigges et al., 1974; Colonnier and Sas, 1978; Cusick and Kaas, 1988). Secondly, the laminar distribution of intrinsic connections is rather diffuse, perhaps heaviest in layers 3 and 5, but involving all layers (Valverde, 1978; Colonnier and Sas, 1978; Lund et al., 1981; Rockland, 1985).

Towards the fringes of the labelled region in V2 we commonly observed patches of terminal label in the upper layers, which were accompanied by relatively few labelled cells or by none at all. A good example is provided by the sequence of five labelled thick stripes illustrated in Figure 7. All of these stripes contained moderately dense patches of terminal label but only the two most medial thick stripes contained large numbers of labelled cells; the remainder displayed little or no cell labelling. Hence, by the arguments above, the majority of this terminal label in the lateral three thick stripes must represent the back projection from V5. The importance of this observation is that in contacting the lateral three thick stripes the back projection from the injected portion of V5 is essentially non-reciprocal, since these three stripes make little or no contribution to the forward projection to this part of V5.

In terms of visual topography the distribution of labelled cells in this case was much as expected given the distribution observed in V1 (see Fig. 1, case SP3, of Shipp and Zeki, 1989)—a region straddling the horizontal meridian representation between eccentricities of approximately 4° and 10°. That is, because of the nature of the split representation of the horizontal meridian in V2 (Cragg, 1969; Zeki, 1969; Allman and Kaas, 1974a; Gattass et al., 1981), labelled cells were found toward the medial ends of both the LS and IOS, but only close to the fundus of the sulci, nearby the horizontal meridian representation forming the border with V3. The back projection from V5, in extending (a) more laterally and (b) further towards the lip of the IOS, succeeds in influencing cortex concerned with visual locations closer to the fovea and closer to the vertical meridian respectively.

The back projection is not only more widespread than the origin of the forward projection in visuotopic terms but also in functional terms: though concentrated within the thick stripes it also contacts stripes of other types lying in between. In our more sensitively stained HRP material we observed, in the upper layers, occasional faint patches of labelled terminals in the thin stripes but not in the interstripes (Fig. 7D). These patches were too faint to be visible in a low power darkfield micrograph. In layers 5 and 6, and sometimes layer 1, labelled terminals were more diffusely distributed, encompassing both thin stripes and interstripes such that parts of these layers were continuously labelled throughout a cycle of stripes. An example is shown in Figure 8, a reconstruction of the distribution of labelled cells in layer 3 superimposed upon the distribution of terminals in layer 6, taken from a series of conventional horizontal sections through the posterior bank of the IOS. The reconstruction involves six (presumed) thick stripes; between three of these there are two relatively fainter concentrations of terminal label which might coincide with thin stripes. We are uncertain because the adjacent cytochrome oxidase stained sections were not easily plotted for the purpose of reconstruction. Figure 9 shows part of one of the sections from which the reconstruction is derived.

Examination of sections from an animal with an injection of 3H proline and 3H leucine into V5 provided a rather different picture, illustrated in Figure 10. Terminal label in V2 is much more diffuse in comparison with the HRP material, being continuously distributed in all layers except layer 4 where it is more or less absent. Heavier patches of label, doubtless corresponding to thick stripes, are evident but the difference between thick stripes and the others is less marked. Although the autoradiographic example involved the posterior bank of the parieto-occipital sulcus (POS), a different region of V2 to that illustrated in Figures 8 and 9, we doubt that the difference in labelling reflects correspondingly different patterns of connectivity of V2 in the IOS and POS. This is because all of our HRP material has yielded qualitatively similar distributions of terminal label, including one case which also involved V2 in the POS. Since the autoradiographic label in layer 4B of V1 is also more diffuse than that produced by HRP-WGA (Shipp and Zeki, 1989) we suspect that certain technical factors yet to be resolved, are more likely to be responsible for the dissimilarity. Hence the autoradiographic case serves to emphasize a non-reciprocal characteristic that is apparent, if less obvious, in the HRP material too: that the back projection from an area specifically sensitive to motion (V5) can influence subregions of a second area (V2) which are differently specialized from the first and which do not provide it with an input.

Connections of area MT with extrastriate cortex in the owl monkey

We carried out a parallel investigation of the connections of MT in the owl monkey. Two animals were given single injections of HRP-WGA into MT and sectioned conventionally and in a third, MT received multiple injections, following which the occipital cortex was dissected for flatmounting. Though many features of the organization of the connections with V2 were similar to those observed in the macaque, we were unable to arrive at an equally succinct conclusion concerning the relationship of MT-efferent regions to the cytochrome oxidase architecture of V2, principally because the latter is frequently irregular. Due to the largely lissencephalic nature of the cerebral cortex of the owl monkey, the reconstructions and flatmounts presented to show the distribution of label in V2 also extend further to reveal connections

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FIG. 6. The distribution of cytochrome oxidase activity and of HRP label following an injection into V5, in macaque area V2 as visualized in tangential sections through the flatmounted occipital operculum (case L.V97).

(A) Section through the entire occiput to show the location of the enlarged region, the central and medial portions of the LS.

(B) Dark-field photomicrograph of a section processed for HRP.

(C) The adjacent section stained for cytochrome oxidase.

(D) Adjusted superimposition of B and C. N signifies a thin stripe and K a thick stripe; other conventions are as for Figure 4C. All the clusters of labelled cells and terminals clearly fall within thick stripes and, in this case, there is no discernible label in the intervening thin stripes or interstripes. There is a further degree of correspondence between these clusters and the more densely staining elements within the thick stripes. This is notable for all the clusters within the more medial of the two heavily labelled thick stripes (the leftward of the pair in the figure) and for at least two clusters in the more lateral thick stripe, though the activity of cytochrome oxidase in this stripe is more uniformly dense. In further sections two more thick stripes, lying on either side, were also found to contain patches of labelled cells and terminals. A faint patch of terminals corresponding to one of the latter is just visible to the right in B, once more coinciding with a relatively dense constituent of the stripe. The scale bar is 2 mm.
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made by MT with a number of extrastriate areas beyond V2. In general we found that the areas involved, and the topographic and laminar distribution of label between them, conformed to the description previously given by Weller et al. (1984). Most of these connections were also patchily organized, and in all instances the patchiness was more evident in the upper layers than in the lower layers. However a detailed description of the tangential and laminar organization of the connections outside V2 is beyond the scope of this paper.

Cytochrome oxidase architecture. The cytochrome oxidase architecture of owl monkey V2 has previously been described by Horton (1984) and Tootell et al. (1985). From these examples it is clear that the striped structure of V2 is considerably less regular than that observed in the macaque or even in the more closely related squirrel monkey (Tootell et al., 1983; Livingstone and Hubel, 1984). Individual stripes are less distinct and tend to fuse with a neighbour more frequently such that the intervening interstripe is vestigial in its appearance. This can be seen in the tangentially sectioned preparation in Figure 11 (from an animal which did not receive an injection of HRP-WGA). But in this example there is a more obvious sequence of alternation of thickness of the stripes than has previously been described in the owl monkey. The alternation of thick and thin stripes is here most evident in ventral V2, but disappears centrally only to re-emerge in dorsal V2, though not with equal clarity. The length of one cycle of stripes is 2.4 mm in ventral V2 and 2.8 mm in dorsal V2, agreeing with the figure of 1–1.5 mm for the spacing between individual stripes reported by Tootell et al. (1985). Correcting for shrinkage, the mean length of a cycle of stripes in the brain in vivo is thus about 3 mm.

The connections of MT with V2. Following injections of HRP-WGA into area MT labelled cells are distributed in V2 in much the same way as they are in V2 of the macaque following a V5 injection. Dense clusters are found at intervals in layer 3, with a few cells located more superficially in layer 2 and fewer still in layer 5 (Weller et al., 1984). Relative to the macaque, however, the clusters are more closely spaced and a little broader, such that a greater overall proportion of V2 is occupied by labelled cells. Labelled terminals were heaviest in layer 1, diminished in density toward layer 4, and were moderately dense in layers 5 and 6. The terminal label was densest immediately above and below the clusters of cells in layer 3, but the gaps between these columns were spanned by lighter concentrations of label. This was most obvious in layers 5 and 6 but could also be observed superficially, especially in layer 1.

On reconstruction, the clusters of labelled cells were found to be aligned into bands running near perpendicular to the V1/V2 border. The example illustrated in Figure 12 shows five bands within V2 on the dorsal surface and medial convexity of the hemisphere. The density of cell labelling along each band was not entirely uniform, but longitudinal clustering was not as evident as in the similar reconstruction carried out on the macaque (cf. Fig. 5). Some degree of clustering across the width of the band was also seen in a few instances. More ventrally in V2 there were further sporadic groupings of cells which were too sparse or isolated to give any impression of a band-like structure.

Sections from a 1 in 12 set stained for cytochrome oxidase were superimposed with those treated for HRP, as before. This revealed that every cluster of label coincided with a cytochrome oxidase density though, at this frequency, the reconstruction of entire stripes was a little incomplete. Somewhat surprisingly, however, there was little indication that only every alternate dense stripe is connected to MT: the two most dorsal bands of cells in Figure 12 appeared to be separated by an unlabelled stripe, but not the others. There was also no reliable sign that the stripes alternated in thickness.

To assess the tangential organization of MT-efferent regions more directly we prepared an animal with three injections of HRP-WGA into roughly the central portion of MT and flattened its occipital cortex. The flatmount preparation was carried out by a relatively simple method. Briefly the occipital and temporal lobes were dissected away from the remainder of the cortex and then divided transversely, one part containing cortex on the lateral surface, the other including cortex of the medial and ventral surfaces and all the cortex buried within the calcartine sulcus. Both were flattened and sectioned tangentially, alternate sections being stained for HRP, cytochrome oxidase, and myelin.

Figure 13 summarizes the overall distribution of label that we obtained in this case. Perhaps the most prominent feature was the presence of at least seven irregularly shaped but distinct bands of labelled cells and terminals within V2, arranged over the medial, lateral, and ventral surfaces. Further clusters of label situated ventrally on the
FIG. 8. Reconstruction from serial horizontal sections of the distribution of labelled cells in layer 3 and of labelled terminals in layer 6 of macaque area V2 in the posterior bank of the IOS following an injection of HRP-WGA into area V5 (case SP19). Labelled cells are represented by large dots (each dot corresponding to a number of cells) and labelled terminals by fine stipple. Both are shown at four levels of density. The reconstruction is based on a 1 in 3 series of sections which run horizontally across the reconstruction; they are spaced vertically at the same scale as their horizontal magnification. The scale bar is 2 mm. The label derived from each section is expanded vertically so as to fill in the space corresponding to the 2 out of 3 sections omitted from the reconstruction. Medial is to the left, lateral to the right.

lateral surface were also probably within V2 but some doubt must remain because the location of the anterior border of V2 could not be ascertained exactly. The appearance of the posterior parts of the lateral and ventro-medial surfaces under darkfield illumination (mainly reflecting the distribution of terminal label) is illustrated in Figure 14. Figure 15A shows the distribution of labelled cells in the same section as Figure 14A and Figure 15B a section 150 μm more superficial, in which the distribution of cells amongst two of the bands was a little more widespread. Part of the irregularity in the shape of the bands derives from the way they appear to deform around the outlines of more evenly shaped non-labelled zones, leading to the formation of occasional cross-links. The distribution of labelled cells within the bands

FIG. 9. Dark-field photomicrographs of one of the sections reconstructed in Figure 8.
(A) Shows three separate columns of label which correspond to the three bands lying to the left of Figure 8; the central column also appears in Figure 3A.
(B) Is an enlargement of the rectangular region outlined in A. Although lying outside the thick stripes it still contains terminal label at upper- and lowermost layers. This distribution conforms to the pattern of a reciprocal projection from V5 but is unlike the pattern of intrinsic collateral label, which should also involve layers 2 to 5. The scale bar is 200 μm.
Cortical connections between V5 and V2

is relatively uniform; some signs of clustering can be detected, but again the phenomenon is much less prominent than in the macaque (cf. Fig. 6B).

The large size of the injection in this animal made it possible that the crescent-shaped area surrounding MT, area DL (Allman and Kaas, 1974b), was also involved to some extent. Though we were unable to identify a reliable boundary for area MT from the myelin stains, the presence of weak labelling in inferotemporal cortex (see Fig. 13), known to be connected to DL (Weller and Kaas, 1985), also indicated that this was likely. A small fraction of the label in V2 may thus also have derived from DL (Kaas and Lin, 1977; Weller and Kaas, 1984). But, as demonstrated by the extent of labelling in V1, the involvement of MT was massive by comparison and the label derived from DL could not have significantly influenced the overall distribution in V2. Similar considerations apply to the previous case, which also has a small amount of label in inferotemporal cortex (not shown in Fig. 12).

The pattern of cytochrome oxidase staining in dorsal V2 of the flatmounted case was very irregular and ‘blotchy’ in appearance, in that the contrast in staining density between light and dark patches varied substantially from region to region. This was partly because the large cortical exposure made during injection impaired the perfusion of the cortex in its vicinity. Yet the pattern of staining on the ventral surface was also irregular, so we assumed that the smaller scale fluctuations of cytochrome oxidase activity revealed in the stain were of natural origin. Figure 16 affords a direct comparison between the patterns of HRP labelling and cytochrome staining on both the lateral and ventral surfaces. Though neither has a pattern of cytochrome oxidase activity immediately suggestive of a set of stripes, on closer inspection it is possible to discern a periodic variation in staining density along the axis parallel to the border with V1. Each of the four HRP bands on the lateral surface and the two bands on the ventral surface seem to coincide, roughly, with zones staining relatively densely for cytochrome oxidase. Hence there is some likelihood that these zones do indeed correspond to the striped architecture that is normally more evident in cytochrome oxidase stained material. But it is less clear whether some of the smaller dense patches which lie between the bands of HRP label (indicated by arrowheads in Fig. 16) should also be regarded as separate stripes, or perhaps as rogue, densely staining elements within interstripes.

We had difficulty in identifying densities in the cytochrome oxidase stain corresponding to clusters of labelled cells in the third animal, but these bands of cells occurred in the monocular representation of far peripheral visual field within the calcarine sulcus where cytochrome oxidase stripes may not be present (Tootell et al., 1983, 1985). This was also true of one macaque where the involvement of V2 was very peripheral. The presence of bands of labelled cells in both cases would nonetheless suggest that some kind of segregation of function remains even in the absence of stripes.

To summarize, our evidence shows that the regions of V2 connected with MT are distributed in a band-like fashion that correlates with the

FIG. 10. The continuous distribution of labelled axonal terminals in V2, following an injection of tritiated proline and leucine into V5, as visualized in a coronal section through the parieto-occipital sulcus (see Acknowledgements). No direct comparison with cytochrome oxidase stained tissue was available, but the two heavier concentrations of terminals very probably coincide with thick stripes, and the terminals distributed continuously around them must therefore involve both thin stripes and interstripes. Neighbouring sections showed a similar pattern over a range of several mm ruling out the unlikely possibility that all the label in this section corresponds to a single thick stripe running parallel to the plane of section. The scale bar is 1 mm.
Cortical connections between V5 and V2
cytochrome oxidase architecture of V2. Stripes with relatively high cytochrome oxidase activity are the major source of output to MT, but we cannot be certain whether this involves every dense stripe or every alternate dense stripe. By comparison with the macaque we would have expected the latter, but our evidence for the presence of alternate unlabelled dense stripes was weak. Isolated cytochrome oxidase dense patches which lacked label were observed in a number of instances, but in none of the animals was the overall pattern of cytochrome oxidase activity sufficiently resolved to allow positive identification of these patches as separate stripes in their own right. An alternative and more indirect line of reasoning is to consider the various periodicities we have observed. The four adjacent bands of MT-efferent cells in dorsal V2 of Figure 12 had a periodicity (mean centre-to-centre interband interval) of 1.5 mm and those of dorsal V2 in Figure 14A 1.7 mm. (Based on measurements in adjacent cytochrome oxidase stained sections, since the HRP sections undergo substantially greater shrinkage.) In dorsal V2 of a third animal (Fig. 11) the cytochrome oxidase stripes had a periodicity of 1.4 mm and alteration of thickness was also evident, such that one cycle of stripes occupied 2.8 mm. In the absence of more detailed knowledge of the variation associated with stripe-like periodicity in V2 of the owl monkey we note that, faced with a strict choice between the 'every stripe' and 'every alternate stripe' hypotheses, these figures would favour the former.

Discussion

Our chief finding is that the V5-efferent cells of V2 are mostly restricted to just one set of stripes, the thick stripes, whereas the back projection to V2 from V5 is more widely distributed and thus has the potential to influence not only the V5-efferent cells but also cells projecting elsewhere. We interpret these observations in the light of two contrasting ideas: the segregation and reintegration of information within the visual system. The former, which might equally be referred to as functional specialization (Zeki, 1978a), is a well attested phenomenon for which much evidence — anatomical, physiological, psychophysical, and clinical — has been amassed and whose value can be understood in terms of concepts such as efficiency of engineering. The concepts underlying the latter are less well founded. But the impetus for discussing interregation is a strong one deriving from everyday experience — that our visual perceptions bear little or no trace of the internal subdivisions of function from which they are derived. Hence some mechanism must ensure that the various attributes of a visual scene, such as its forms, colours, and motions, are correctly referred to each other in order to give a coherent and unified percept. Here it is our aim simply to present the idea that asymmetrically organized reciprocal connections, such as those we have observed between V5 and V2, might be a part of this mechanism. We begin, however, with a discussion of the more firmly rooted evidence supporting the ideas of segregation and specialization.

Tangential segregation in V2

Like V1, V2 is involved with several visual attributes, but unlike V1 the pathways subserving different attributes do not involve separate layers. Layer 3B of V2, for instance, in which most V5-efferent cells reside, is much like layer 4B of V1 in that it lies just above the granular layer and possesses a plexus of horizontally running fibres (Lund et al., 1981). But layer 3B is not restricted to the 'motion' submodality since it also houses cells projecting to V4 and V3 and perhaps elsewhere (Rockland and Pandya, 1979, 1981; Lund et al., 1981; Fries and Zeki, 1983). Rather, groups of cells with different prestriate targets are segregated tangentially from each other and in a way which coincides with the striped cytochrome oxidase architecture of V2 (Shipp and Zeki, 1985; De Yoe and Van Essen, 1985). According to our past and present observations the great majority of V5-efferent cells are located within the thick stripes, whereas V4-efferent cells mostly avoid the thick stripes and occur in bands or clusters centred on thin stripes or interstripes. Our evidence so far also points to the thick stripes as being the major source of the output to V3, but we are as yet uncertain about the origin of the projection of V2 to a fourth prestriate area, V3A (Zeki, 1978b).

Most instances where a departure from this scheme seems possible involve cases of irregularity in the pattern of cytochrome oxidase stripes making identification of a particular stripe unique. We have occasionally observed small clusters of V5-efferent cells situated within thin stripes and examples of bands of V4-efferent cells stretching across thick stripes, but in general, using HRP—WGA as a tracer of neural connectivity, V2 appears to maintain a high degree of segregation between its output to V4 and to V5. De Yoe and Van Essen (1985), while essentially in agreement with our results, report rather larger numbers of V5-efferent cells between the thick stripes. Some, at least, of this variance may be due to the different technical characteristics of the fluorescent dyes they employed as neuronal tracers.

The three types of stripe defined by the cytochrome oxidase architecture of V2 show distinct differences in their physiological response selectivities, most of which correlate with what is known of the physiology of their immediate targets in prestriate cortex, areas V3, V4 and V5. We have found directionally selective cells only within the thick stripes and units with frank colour-opponent properties, all of which lacked orientation selectivity, only within thin stripes (Shipp et al., 1983). Rather, groups of cells with different prestriate targets are segregated tangentially from each other and in a way which coincides with the striped cytochrome oxidase architecture of V2 (Shipp and Zeki, 1985; De Yoe and Van Essen, 1985). According to our past and present observations the great majority of V5-efferent cells are located within the thick stripes, whereas V4-efferent cells mostly avoid the thick stripes and occur in bands or clusters centred on thin stripes or interstripes. Our evidence so far also points to the thick stripes as being the major source of the output to V3, but we are as yet uncertain about the origin of the projection of V2 to a fourth prestriate area, V3A (Zeki, 1978b).

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and Zeki, 1985). The frequencies of these responses in the two types of stripe were approximately 20% and 50% respectively. Correspondingly, directional selectivity is very frequent, perhaps universal, in V5 (Zeki, 1974; Maunsell and Van Essen, 1983b; Albright, 1984) and substantial (40%) in V3 (Zeki, 1978c; Felleman and Van Essen, 1987), areas to which the thick stripes project, whereas only about 10% of V4 cells are directionally selective (Zeki, 1978d; Desimone and Schein, 1987). Similarly V4, the target of the thin stripes, contains a much higher proportion of wavelength or colour selective units than either V3 or V5 (Zeki, 1978d; Desimone et al., 1985). We refer here only to V3 in the dorsal part of the hemisphere: lower V3 has been reported to differ significantly from upper V3 in its properties (Burkhalter and Van Essen, 1986) and we do not know the source of its input from V2.

The results of Hubel and Livingstone (1985, 1987) are in accord with ours concerning the coincidence of wavelength selective cells, and cells lacking orientation selectivity, within the thin stripes. The study of DeYoe and Van Essen (1985) reported selectivity for wavelength and non-selectivity for orientation to be near equally prevalent in both thin stripes and interstripes; note, however, that they employed different criteria for assessing selectivity. The distribution of directionally selective units was not reported by Hubel and Livingstone, but DeYoe and Van Essen found them more frequently in thick stripes than thin stripes and most frequently amongst clusters of V5-efferent cells, again largely in accord with our own findings.

The three types of stripe in V2 also appear to be distinguished by features in addition to those related to the detection of motion and colour. Both the reports of Hubel and Livingstone and of DeYoe and Van Essen agree, for instance, that cells selective for binocular disparity (a feature we ourselves did not examine) are relatively concentrated within the thick stripes. Furthermore Hubel and Livingstone report that the interstripes are characterized by an abundance of end-stopped
FIG. 13. Diagrams to illustrate the distribution of HRP label observed in flatmounts of the visual cortex from owl monkey FP6, following multiple injections into area MT. The upper diagram shows a tangential view of cortex on the lateral surface, and the middle diagram a tangential view of cortex on the medial and ventral surfaces; the lower diagram is a section through the inner part of the medial flatmount which passes semi-tangentially through both banks of the calcarine sulcus (CS). WM is white matter. Cortex lying within the temporal sulcus (ts) and sylvian sulcus (ss) is indicated by a dashed outline; the V1/V2 border is marked by dashed lines, determined from adjacent sections stained for myelin or cytochrome oxidase; and the three injection sites and the limit of diffusion of HRP-WGA are shown by dark rings surrounded by a continuous border. Arrowheads indicate the approximate location of the anterior border of V2, assuming that V2 is about 4 mm wide (Allman and Kaas, 1974a). The distribution of both retrograde and orthograde label is depicted by stipple of variable density, and represents a combination of the patterns observed in all sections passing through the supragranular layers. The label in V1 was distributed continuously between the dorsal and ventro-medial surfaces but did not extend quite up to the posterior margins of the sections owing to some residual curvature of the cortical laminae in this vicinity. It also extended into the upper bank of calcarine sulcus. The label in V2 occurred in seven bands, four on the lateral surface, one on the medial surface and two on the ventral surface. On the lateral surface these bands extended up to the anterior border of V2 and were continuous with the patchily distributed label occupying the areas beyond, DM and DI and possibly DL. On the ventral surface the bands probably extend out of V2 into area VP. No architectural features could be found to reliably identify the borders of these areas, even within the myelin stained sections. Further patches of label were found between MT and the sylvian sulcus, nearby and inside the caudal end of the temporal sulcus, and more anteriorly on the ventral surface.
cells. But neither of these characteristics has been examined sufficiently extensively in V3, V4 and V5 to permit an effective comparison with these areas.

Subdivision of function within stripes. There are a number of indications that different functions are segregated within stripes as well as between them. Firstly the pattern of cytochrome oxidase activity within all three types of stripe is itself frequently 'blob-like' or patchy, though it is also sufficiently irregular from individual to individual to discourage any attempt to generalize about the size or periodicities of the blobs-within-stripes (see Fig. 2). Secondly the cells efferent to V3, V4 and V5 all tend to fall into clusters along the lengths of their respective stripes and we have observed that at least some of the V5-efferent clusters coincide with periodic densities within the thick stripes. Also in the case of the thick stripes there is the possibility that zones connected to V3 might be segregated from zones connected to V5, a question to be resolved by a double label experiment.

A third indication of functional heterogeneity derives from experiments utilizing 2-deoxyglucose. Tootell et al. (1983) demonstrated that low and high spatial frequency gratings (1 and 7 cycles per degree, respectively) presented at all orientations, gave rise to distinctly different patterns of activity. In particular the high frequency stimulus produced multiple isolated spots of activity, in between more elongated strip-like regions of activity whose periodicity suggested that they coincided either with thick stripes alone or thin stripes alone (Fig. 3B of Tootell et al., 1983). The spots must therefore have coincided with the interstripes and perhaps with the other set of dark stripes, suggesting the presence in them of clusters of cells selective for high spatial frequencies.

Segregation of function in owl monkey V2. The definition of stripes in the cytochrome oxidase architecture of V2 in the owl monkey is distinctly poorer than in other primates and the example we illustrate in Figure 11 is exceptional in the clarity with which alternate thick and thin stripes can be discerned. Like the macaque, MT-efferent cells in the owl monkey reside within the darkly staining stripes, but we
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FIG 15. Diagrams illustrating the distribution of individual labelled cells in tangential sections through occipital cortex on the lateral surface following multiple injections of HRP-WGA into area MT of the owl monkey (case FP6). The diagram on the left is of the same section that is shown in Figure 14A; the section illustrated to the right was located 150 μm more superficially (the two sections intervening were not treated for HRP). Arrowheads indicate the approximate location of the anterior border of V2, assuming a width of about 4 mm (Allman and Kaas, 1974a). The scale is adjusted to the level of shrinkage in the accompanying cytochrome oxidase stained section.

have no evidence that these are alternate thicker ones. Instead it seemed that most dark stripes within the labelled region of V2 contained labelled cells, perhaps with an occasional unlabelled stripe breaking the sequence. Hence segregation of different functions may be a less prominent feature in owl monkey V2, with alternate dark stripes possessing little or no diversification. Or, possibly, diversification takes place to differing extents in different individuals, perhaps even to different extents at different locations within V2 of a single individual. Owl monkeys possess rather poor colour vision (Jacobs, 1977) and perhaps the loss, effectively, of one of the specialist functions that in the macaque helps to differentiate between the stripes diminishes the developmental forces responsible for diversification. Yet the cytochrome oxidase blobs of V1 are prominent and well defined in the owl monkey and if not involved with colour, the blob-to-stripe pathway may retain an involvement in greyness (lightness) constancy and possibly other tasks too (Allman, 1988). It would thus be useful to know whether the patterns of connection (a) between blobs and stripes and (b) between V2 and area DL, the likely homologue of V4 in the macaque (Weller and Kaas, 1985), also differ from those of the macaque. It may be noted that bands of labelled cells have been observed in V2 following an injection into the caudal part of area D1 (Weller and Kaas, 1985). No comparison with cytochrome oxidase stained tissue was available but, judging from their Figure 17, the bands of cells had a periodicity of just over 1 mm at the level of the V1/V2 border. This corresponds to the presence of at least two bands of labelled cells per cycle of stripes, implying that the bands could thus have coincided with every dark stripe or with every interstripe. Alternatively the rearrangement of the connections of V2 may not be consequent upon the loss of colour vision or unique to the owl monkey. Recent reports suggest that in the squirrel monkey, too, area MT receives input from every dark stripe (Krubitzer and Kaas, 1987) and area DL mainly from the interstripes (Cusick and Kaas, 1988).
FIG 16. The distribution of cytochrome oxidase activity and of HRP label following multiple injections into area MT, in owl monkey area V2 as visualized in tangential sections through flatmounted occipital cortex (case FP6).

(A) Darkfield view of a section through layer 3 of dorsal V2 on the lateral surface. The border with V1, marked by a linear, narrow concentration of label, is evident to the right. There is a clear series of 4 bands of label in V2, though anteriorly and especially within the lower half of the frame, the pattern becomes less regular. The exact location of the anterior border of V2 is not readily determinable.

(B) The identical part of an adjacent section stained for cytochrome oxidase. An outline of the major concentrations of HRP label seen in A has been superimposed, but note that fainter traces of labelling are also present beyond this outline. The pattern of cytochrome oxidase activity in this case is very irregular, but a periodic variation in staining density along the axis parallel to the V1/V2 border, roughly matching the periodicity of the HRP bands, is still apparent. Arrowheads point to smaller cytochrome oxidase densities lying between the HRP bands whose status is more equivocal. The scale bar in A, applicable to both A and B, is 2mm.

(C) Dark-field view of an HRP section through V2 on the ventral surface. The plane of section is not perfectly tangential, as seen by the presence of white matter (WM) towards the top of the section.

(D) The corresponding part of an adjacent section stained for cytochrome oxidase. The border between V1 and V2 is clearest where it passes through layer 4C of V1, indicated by an arrow. The dotted outlines again indicate the location of the HRP label visible in C. The arrowhead points to an unlabelled cytochrome density lying between the two HRP bands. The scale bar in C, applicable to both C and D, is 2 mm.

This is more surprising, since colour vision is better developed in this species (Jacobs, 1983) and a clear diversification of function between thick and thin stripes has been demonstrated physiologically (Hubel and Livingstone, 1985, 1987). Overall there is the possibility that the segregation of pathways through V2 of New World monkeys shows some significant differences from that found in the Old World macaque.

Integration

Viewed within the context of the visual system as a whole the segregated connections of V2 we discuss above have been regarded (a) as extensions of the magnocellular (M) and parvocellular (P) divisions of the retino-geniculo-cortical pathway and (b) as the antecedents of two distinct 'streams' of cortical areas leading respectively to the parietal and temporal lobes where the visual functions of motion/spatial awareness and object recognition respectively are emphasized (Mishkin et al., 1983; Van Essen and Manussell, 1983; Desimone et al., 1985; Livingstone and Hubel, 1987a,b). The essential tenet of this view is that these two pathways, though each themselves possessing elements...
of a parallel organization, are two largely independent subdivisions of the visual system, segregated physically from each other from the lateral geniculate nucleus (LGN) onwards and specialized to provide different attributes of visual perception.

However, in tracing the connections more centrally and in greater detail, one uncovers a substantial anatomical potential for interactions at all levels both within and between the broad M and P systems. Rather than interpret these cross-connections in a negative fashion as evidence for a blurring of specialization, it is preferable to consider 'specialization' as first and foremost a property of an individual area (or other structure). The cross-connections can then be considered to be playing a significant integrative role, in one or both of the following respects: (a) in bringing together information of diverse types to be used for a common purpose and thus making, in fact, a useful contribution to specialization; (b) as providing the intercommunication necessary for a unified and coherent percept to arise out of the activities of separate specialized areas (Zeki and Shipp, 1988).

**Ascending pathways.** Given that cross-connections can be identified in forward, backward, and lateral connections between cortical areas (Zeki and Shipp, 1988), can functions such as (a) and (b) above be associated with any type of connection in particular? Despite knowing little about the systematic physiological differences between these types of connection, some inference might be drawn from the fact that forward connections normally give rise to larger receptive fields whereas backward connections do not succeed in enlarging the excitatory (or classical) receptive fields of their target cells. Because the cells with larger receptive fields are normally capable of responding to stimulation within any small part of their field it would see that they are capable of being activated by a small proportion of their afferents active in isolation. If the same is true of afferents representing different visual attributes, as opposed to different regions in space, then the cell will be able to detect a feature by any one of a number of alternative means.

To cast the argument in perceptual terms, take the example of the analysis of visual form. Cortical areas involved in this task could make use of information about contours and shapes derived from either luminance, colour or textural changes, retinal disparity, or relative motion. Information about structure in three dimensions is provided not only by disparity but also by velocity gradients and a variety of textural, perspective and shading cues (e.g. Cavanagh, 1987). Undoubtedly varieties of form processing are carried out by both the M and P systems and convergent forward projections, operating both within and between them, could allow an area to use diverse types of information in performing a particular role. Lateral interconnections between areas and intrinsic connections may also bring about this type of integration. But if the same is to be achieved by backward projections, which we infer to be incapable of exciting cells on their own, then the mechanism involved must be more subtle.

**Descending pathways.** We have described here how the back projection from V5 to V2 invades not only the thick stripes but also the thin stripes and interstripes, so forming a continuous distribution. Similarly we have observed that V4 projects back to the thick stripes as well as the thin stripes and interstripes from which it receives its output (Zeki and Shipp, 1989). Both are examples of a descending cross-connection.

Since the functional role of descending connections within a specialized pathway is not particularly clear, it is even less obvious what role is played by the asymmetric component in extending between specialized pathways. One possibility we have considered, however, is that the overlapping projections of V4 and V5 within V2 may be involved with the mechanism whereby sensations of colour and motion are perceived as belonging to each other and to the appropriate object, so as to yield a coherent and unified visual image. We have no concrete evidence to support this proposition, but can offer a number of inferential arguments. Firstly there is the idea, however, simplistic, that attributes such as colour and motion are associated with each other by virtue of occupying identical parts of the visual field. Since topographic organization appears to be progressively eroded in higher visual areas, the projection of a focus of activity in V5 or V4 back to V2 where topographic order is less eroded could constitute a means of re-establishing or maintaining information as to the location in space of the stimuli eliciting that activity. This is a view elaborated by Edelman (1987) and is one of the roles he proposes for re-entrant connections—the preservation of spatio-temporal continuity in the representation of an object across separate maps.

Secondly the overall architecture of V2 may itself be of significance. Note that the segregation afforded between the pathways through the thick, thin and interstripes has already been achieved at the level of V1, in the segregation of blobs and interblobs in layers 2 and 3 and of these from layer 4B. The gross anatomical reorganization in V2 is simply to place all the segregations within the tangential plane and at a larger scale. Since, a priori, we might expect that the functions of the thick stripes could have been embodied in V3 or V5 and those of the thin stripes and interstripes in V4, the suspicion arises that the major utility to the visual system of a second visual area that retains an involvement in all visual attributes, organized so as to remain in close association, is that it facilitates interactions between them. These interactions could be achieved both by intrinsic connections within V2 stretching between the different types of stripe (Rockland, 1983) and by diffuse descending projections of the type we have described. It is interesting to observe in this context that the descending projection from V5 to V1 does not appear to invade layers 2 and 3 and is potentially re-entrant only with respect to the V5- and V3-efferent cells of layer 4B within the M pathway (Shipp and Zeki, 1989). Thus the first cortical site for re-entrant connections between the M and P pathways seems to be V2 rather than V1.

The striped architecture of V2 may also be of significance in determining the size and configuration of the 'focus of attention'—the limited part of the field of view upon which attention is concentrated at any one moment and which may be shifted to a new location independently of eye movements (e.g. Bergen and Julesz, 1983). We introduce this idea here because the feature integration theory of Triesman (Triesman and Gelade, 1980; Triesman and Gormican, 1988) suggests that it is only within the focus of attention that the features of an object within separately coded dimensions such as colour, shape and motion are reliably combined so as to yield an accurate perception. Forcible 'stretching' of the focus of attention over a number of objects appears to generate errors in the recombination process (Triesman and Schmidt, 1982). Similarly, in visual search tasks, a target item defined by a conjunction of two features—such as its colour and shape, or colour and direction of motion—is not immediately detectable (does not 'pop out') and can be found only by a serial scan of focal attention from one item to the next (Triesman and Gelade, 1980; Nakayama and Silverman, 1986). Sagi and Julesz (1985) devised a means of charting the size and configuration of the focus of attention when it was directed outside foveal vision. Surprisingly it was found to be asymmetrical in shape and elongated along an isoeccentricity meridian—extending over an arc of almost 90° at an eccentricity of 4°. This immediately suggests the possibility of an association with V2 since
each stripe describes a similar arc within the visual field, passing from the vertical meridian at the border with V1 to the horizontal meridian at the border with V3 (Zeki, 1969; Cragg, 1969;Gattass et al., 1981). Furthermore the extent of the focus in the radial direction (along a meridian perpendicularly intersecting lines of isoeccentricity) was, at just over 2°, very similar to the meridional shift in receptive field location that we have recorded in passing through one cycle of stripes in V2 at a comparable eccentricity (Shipp and Zeki, in preparation).

Thus, though the mechanisms of attention doubtless involve many separate areas, some of their spatial properties may be determined by the nature of the modular architecture of V2. We note that Anderson and Van Essen (1987) have also made a similar proposal. The assumption is made, of course, that human V2 has a cytochrome oxidase architecture not too dissimilar from that of the macaque, which, so far as we know, has yet to be confirmed.

The above observations constitute, we believe, reasonable grounds for supposing that the descending projections to V2 may be involved in the process of perceptual unification, though many conceptual difficulties remain. A useful experimental approach is to consider situations in which the mechanisms responsible for unification break down. One such demonstration, not dependent on lapses of attention, is described by Ramachandran (1987) and also discussed in relation to V2. It involves the adherence of colour and motion, a pair of attributes whose initial computation is probably performed entirely independently (e.g. Carney et al., 1987). A field of dots drifts uniformly over a stationary red square in a green surround. As long as there is a luminance difference between the red and the green the square appears stable, but at isoluminance it appears to adopt the motion of the dots, oscillating convincingly to and fro as the direction of drift of the dots is reversed. Other demonstrations of ‘motion capture’ (Ramachandran and Inada, 1985; Ramachandran and Cavanagh, 1987) indicate that within a given region of the visual field there is a tendency for a single motion signal to prevail over others which are weaker, so in this instance it might be surmised that at isoluminance the representation of a stationary contour is sufficiently attenuated to allow it to undergo ‘capture’ by the motion of the dots. But the neural mechanisms underlying this effect are far from clear. Is there a specific class of neurons which become active around the point of isoluminance and whose activity is responsible for the change in perception? Or is the illusory motion of the colour contour due to a correlated change in the firing patterns of separate direction and colour neurons which otherwise remain active throughout the variations in luminance? Finally is it possible to account for either of these changes in terms of the modulating influences normally associated with back projections? It goes without saying that answers to these questions would substantially enhance our understanding of the process of perceptual unification.

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Abbreviations

<table>
<thead>
<tr>
<th>Abb.</th>
<th>Description</th>
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<tbody>
<tr>
<td>DL</td>
<td>dorsolateral visual area</td>
</tr>
<tr>
<td>I</td>
<td>interstripe</td>
</tr>
<tr>
<td>I0S</td>
<td>inferior occipital sulcus</td>
</tr>
<tr>
<td>K</td>
<td>thick cytochrome oxidase stripe</td>
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References


