Multiple processing streams in occipitotemporal visual cortex

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The earliest stages of cortical visual processing in areas V1 and V2 of the macaque monkey contain internal subdivisions (‘blobs’ and ‘interblobs’ in layer 4B in V1; thin, thick and interstripes in V2) that are selectively interconnected and contain neurons with distinctive visual response properties. Here we use anatomical pathway tracing to demonstrate that higher visual areas, V4 and the ventral posterior inferotemporal cortex, each contain anatomical subdivisions that have distinct input and output projections. These findings, in conjunction with others, suggest that modularity and multistream processing within individual cortical areas are widespread features of neocortical organization.

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We injected two retrograde tracers (three tracers in one case) into nearby sites in V4 of five hemispheres from three macaque monkeys. For three pairs of injections, strongly segregated clusters of cells labelled by each tracer were found within extrastriate visual areas V2, V3/V3A, V4/V5/VP and PITv (see legend to Table 1 for abbreviations). Figure 1 illustrates results from one such case (case 1 in Table 1) in which bsinzenimide and nuclear yellow were injected at sites 4.3 mm apart in V4 (Fig. 1a). Each injection labelled several bands of cells throughout a 14-mm swath of dorsal V2 (Fig. 1b), demonstrating that the two injections involved similar parts of the perifoveal visual field representation. The bsinzenimide was concentrated in the pale-staining interstripes revealed by cytochrome oxidase histochemistry, whereas the nuclear yellow was centred along a subset of the dark cytochrome-oxidase-staining stripes (red outlines in Fig. 1b). We infer that the nuclear yellow was primarily in the thin-stripe compartments (even in regions where the pattern was somewhat irregular), because it has been shown elsewhere that (1) the thick stripes do not have a substantial projection to V4 (refs 1, 3, 1, 14, and 14) and (2) anatomical segregation is maintained even within regions of irregular stripe geometry.13,14

The pattern of retrograde labelling in the remainder of extrastriate cortex is shown as a three-dimensional reconstruction of occipitotemporal cortex in Fig. 1a, as a single section through the prelunate gyrus in Fig. 1c, and as a two-dimensional map of 'unfolded' cortex in Fig. 1d. Throughout occipitotemporal cortex, labelled cells were found in clusters of variable shape and size ranging from ~4 mm² to >70 mm².
FIG. 1. Segregated, retrograde labelling of extrastriate visual areas following dual tracer injections in V4: a, Three-dimensional computer reconstruction of tracer labelling in occipitotemporal cortex visible from the exposed lateral surface of the brain. A Silicon Graphics IRIS workstation with custom software was used for data acquisition and visualization. Crosshatch ovals: approximate core of tracer injection sites. All dense core injection sites in this and other experiments were restricted to cortical grey matter and were within the boundaries of the desired target area as described in ref. 16. Yellow site, 100 nl 3% nuclear yellow (Sigma) in distilled water; blue site, 100 nl 10% bisbenzimide (Sigma) in distilled water. Yellow and blue dots, cells labelled with the respective tracer (occasional white dots are photographic artefacts due to yellow and blue superposition). Thin white and red contours (A, B, C) outline horizontally sliced histological sections (minimum
FIG. 2 Clustering of retrograde and anterograde labelling in V4 following tracer injection in posterior inferotemporal cortex (PIT). a, Approximate location of tracer injection sites in PIT and range of sections shown in c (dashed lines). Blue dot, 250 nl injection of Fast blue (FB); white dot, 250 nl diaminido yellow (DY) placed 5 mm more dorsal at the crown of the STS encroaching on area PITd. b, Computer reconstruction of labelling in three superimposed horizontal brain sections through V4 near dorsal tip of inferior occipital sulcus. c, Computer reconstruction of retrogradely labelled cells in 80 horizontal brain sections spanning 20 mm dorsoventrally across V4. The three-dimensional stack of sections is shown in a lateral view with the lunate, superior temporal and inferior occipital sulci outlined for reference. Major contours (red lines) are drawn at 1-mm intervals (straight horizontal gaps are due to missing sections). d, Anterograde labelling in a different case in which 25 μCi (200 nl) [3H]-proline was injected in PITv just above the posterior middle temporal sulcus (red dot on inset view). Clusters of anterogradely labelled terminals in V4 and V3A are marked by multiple red patches on an unfolded, two-dimensional cortical map. Also shown is the distribution of HRP-labelled, callosal-projecting cells (diagonal hatch) used to help identify areal boundaries. Results for all V4 injections are shown in Table 1 (see legend for details of index calculation). Bold-face entries indicate regions that had segregation indices above 0.60 and that also were judged prior to quantitative analysis to have strongly segregated labelling.

In many instances, multiple patches could be assigned to individual visual areas using the pattern of interhemispheric connections (grey bands in Fig. 1d) as an independent guide to areal boundaries. For example, in inferotemporal cortex there were three large, alternating yellow and blue clusters (numbered 1-3 in Fig. 1d) which could be assigned to area PITv by virtue of their proximity to a band of callosal-projecting cells that runs along its posterior boundary.4 Further anterior in the temporal lobe (to the right in Fig. 1d), area CTV also contained multiple clusters. Similarly, the anterior bank of the lunate sulcus including parts of visual areas V3, V3A and V44 contained at least 10 distinct, alternating yellow and blue clusters (Fig. 1c, d). In contrast, labelled clusters within the superior temporal sulcus, especially anteriorly, were more intermixed, as indicated by the green zones of overlap in Fig. 1d.

To quantify the degree of segregation, we computed a segregation index designed to yield values near zero in regions of extensive intermixing and values approaching (or occasionally exceeding) unity in regions where segregation was pronounced.
## Table 1: Segregation indices for extrastriate visual areas following paired tracer injections in V4

<table>
<thead>
<tr>
<th>Case</th>
<th>Sep.</th>
<th>V2</th>
<th>V3A/V3</th>
<th>V4/VOT</th>
<th>PITv</th>
<th>CITv</th>
<th>STS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4.3</td>
<td>0.90</td>
<td>0.87</td>
<td>0.86</td>
<td>0.89</td>
<td>0.66</td>
<td>0.44</td>
</tr>
<tr>
<td>2</td>
<td>4.5</td>
<td>0.92</td>
<td>C</td>
<td>0.86</td>
<td>0.75</td>
<td>0.38</td>
<td>0.55</td>
</tr>
<tr>
<td>3</td>
<td>4.0</td>
<td>0.93</td>
<td>0.86</td>
<td>0.61</td>
<td>0.84</td>
<td>0.37</td>
<td>0.52</td>
</tr>
<tr>
<td>4</td>
<td>4.4</td>
<td>0.28</td>
<td>0.35</td>
<td>0.56</td>
<td>0.33</td>
<td>0.12</td>
<td>0.30</td>
</tr>
<tr>
<td>5A</td>
<td>2.0</td>
<td>0.46</td>
<td>—</td>
<td>C</td>
<td>0.07</td>
<td>0.57</td>
<td>—</td>
</tr>
<tr>
<td>5B</td>
<td>4.0</td>
<td>0.67</td>
<td>—</td>
<td>C</td>
<td>0.28</td>
<td>—</td>
<td>0.47</td>
</tr>
</tbody>
</table>

The segregation index for each region was calculated in several steps. First, clusters were identified on computerized reconstructions of individual histological sections (Fig. 1c for example) by initially displaying only one tracer label. Each group of cells that was clearly separated from other groups was circumscribed by a rectangular, radially aligned counting window. Groups that were not clearly separated were included in the same counting window. Next, the second tracer labeling was displayed with the first. Any cells that did not fall within the previously established counting windows were circumscribed by additional non-overlapping windows until virtually all cells were included. For each window, cells labelled by the two tracers (denoted as A and B) were then counted and a distribution index was calculated as $D_{AB} = (A_{AB} - B_{AB})/(A_{AB} + B_{AB})$. This index equals zero when all labelled cells in the area were uniformly mixed, and it takes into account the different numbers of labelled cells by each tracer. Departures from $D_{AB}$ indicate distributions that were more segregated than expected. Consequently, the index of segregation for each counting window ($S$) was computed as the deviation from $D_{AB} = S = (D - D_{AB})$. Although values of $S$ can exceed 1.0 if $D_{AB}$ is negative, they correctly reflect deviations from the uniformly mixed distribution. Final entries in the table are mean of all segregation indices (one for each counting window) calculated for each region. Bold type indicates regions with mean segregation index $>0.6$ that were to be strongly segregated by visual inspection before quantitative analysis. C. clustered labelling, but only one tracer present. Sep. injection site separation (mm): V3A/V3, anterior bank of floculate sulcus containing area V3A and part of V3; V4/VOT, ventral V4 plus ventral occipital temporal area and ventral posterior area if labelled; PITv, ventral division of inferior frontal cortex; CITv, ventral division of central inferotemporal cortex, also including areas TF and TH when labelled; STS, superior temporal sulcus including areas MT, MST, FST and PITd. Labelling in CITd and AITd was weak but intermixed in case 1 and was too weak for classification in other cases. Case identification: 1: 91AL; 2: 90LR; 3: 85SL; 4: 91AR; 5: 90LL; 5B: 90LL. * Case 5B in V2 reflects retinotopically based segregation (see text). The tracer bisbenzimide (Sigma) was paired with nuclear yellow (Sigma) in cases 1, 3, 4 and 5B; or with rhodamine-labelled dextrans (Molecular Probes) in cases 2 and 5A.

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