Cortical Connections of Inferior Temporal Area TEO in Macaque Monkeys

C. Distler, D. Boussaoud, R. Desimone, and L.G. Ungerleider
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ABSTRACT

In macaque monkeys, lesions involving the posterior portion of the inferior temporal cortex, cytoarchitectonic area TEO, produce a severe impairment in visual pattern discrimination. Recently, this area has been shown to contain a complete, though coarse, representation of the contralateral visual field (Boussaoud, Desimone, and Ungerleider: J. Comp. Neurol. 306:554–575, ’91). Because the inputs and outputs of area TEO have not yet been fully described, we injected a variety of retrograde and anterograde tracers into 11 physiologically identified sites within TEO of seven rhesus monkeys and analyzed the areal and laminar distribution of its cortical connections.

Our results show that TEO receives feedforward, topographically organized inputs from prestriate areas V2, V3, and V4. Additional sparser feedforward inputs arise from areas V3A, V4t, and MT. Each of these inputs is reciprocated by a feedback projection from TEO. TEO was also found to have reciprocal intermediate-type connections with the fundus of the superior temporal area (area FST), cortex in the most posteromedial portion of the superior temporal sulcus (the posterior parietal sulcal zone [area PP]), cortex in the intraparietal sulcus (including the lateral intraparietal area [area LIP]), the frontal eye field, and area TF on the parahippocampal gyrus. The connections with V3A, V4t, and PP were found only after injections in the peripheral field representations of TEO. Finally, TEO was found to project in a feedforward pattern to area TE and to areas anterior to FST on the lateral bank and floor of the superior temporal sulcus (areas TEM, TEa, and IPa, Seltzer and Pandya: Brain Res. 149:1–24, ’78), all of which send feedback projections to TEO. Feedback projections also arise from parahippocampal area TH, and areas TG, 36, and possibly 35. These are complemented by only sparse feedforward projections to TG from central field representations in TEO and to TH from peripheral field representations.

The results thus indicate that TEO forms an important link in the occipitotemporal pathway for object recognition, sending visual information forward from V1 and prestriate relays in V2–V4 to anterior inferior temporal area TE.

Key words: inferior temporal cortex, extrastriate cortex, visual system, pattern vision

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the inferior temporal gyrus, and the representation of the peripheral field is located on the ventral surface of the cortex, within and medial to the occipitotemporal sulcus. The representation of the upper visual field is located adjacent to that same representation in ventral V4, and the representation of the lower field lies between TEO’s upper field representation and the posterior border of area TE. The retinotopic organization of TEO is less precise than that found in area V4 (Gattass et al., 1988), but clearly different from that described for area TE where no retinotopy at all can be found (Desimone and Gross, 1979). Area TEO corresponds roughly to the regions termed PITv and VOT by Felleman and Van Essen (1991) and Van Essen et al. (1991).

Although the region corresponding to TEO has been studied in owl monkeys (Weller and Kaas, 1987) and squirrel monkeys (Weller and Steele, 1992), little is known about the full areal extent, laminar distribution, and topographic arrangement of the cortical connections of area TEO in macaque monkeys. In the four previous anatomical studies of this area in macaques, tracer injections were confined to the dorsal part of TEO where the central visual field is represented (Fenstemaker et al., 1984; Shiwa, 1987; Morel and Bullier, 1990; Webster et al., 1991). In the present study, by contrast, we injected small amounts of tracers into several physiologically identified visual field representations throughout virtually the entire extent of TEO. This enabled us to compare the connections of central versus peripheral visual field representations, and also to determine the topographic arrangement, if any, of their connections.

MATERIALS AND METHODS

Seven male rhesus monkeys (Macaca mulatta) weighing 3–6 kg were used. Many of these had previously served as normal controls in behavioral studies. Each received small retrograde and/or anterograde tracer injections into physiologically identified sites in TEO. In one of these animals, one of the injection sites was inadvertently placed too deep within the inferior temporal gyrus and consequently involved area PITd rather than area TEO; we analyzed the data from this case for comparison. For retrograde tracers we used the fluorescent dyes fast blue (FB), diaminido yellow (DY), rhodamine coupled to dextrane (RD), as well as wheat germ agglutinin conjugated to horseradish peroxidase (WGA). For anterograde tracers we used WGA and tritiated amino acids (AA).

Injection of tracers

Each animal underwent two recording sessions. The first session established the sites for the FB, DY, and AA injections, and the second, five days later, established the site for the WGA injection. At least 4 days prior to the first recording session, a stainless steel recording chamber and a post for holding the animal in a stereotaxic apparatus were implanted under aseptic conditions. For this surgery, the animal was initially tranquilized with ketamine hydrochloride (10 mg/kg intramuscularly [i.m.]), and then anesthetized with pentobarbital (20 mg/kg intravenously) and treated with atropine sulfate (0.04 mg/kg i.m.). During surgery, anesthesia was maintained by supplementary doses of pentobarbital. Acetaminophen was used as a postoperative analgesic. In one monkey (case 1-RD), the tracer RD (1.0 µl of 5% RD) was injected into the dorsal portion of TEO (its central field representation) during this initial surgery. The visual field representation at this injection site was verified later, during the first recording session.

For each of the two recording sessions, the monkey was again tranquillized with ketamine hydrochloride, then deeply anesthetized with 2.5% halothane in a mixture of 70% nitrous oxide and 30% oxygen, intubated with an endotracheal tube coated with xylcaine gel (2%), and placed comfortably on a cushion and heating pad. The head was held in the stereotaxic apparatus by the previously implanted post, and access to the brain was gained by removing the lid of the recording chamber. The monkey was then paralyzed with pancuronium bromide (Pavulona®). Anesthesia was maintained by artificial respiration with 70% nitrous oxide and 30% oxygen supplemented with 2.5 µg/kg/hr sufentanil citrate (Sufenta®). No surgical or other

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**Abbreviations**

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>amt</td>
<td>anterior middle temporal sulcus</td>
</tr>
<tr>
<td>ar</td>
<td>arcuate sulcus</td>
</tr>
<tr>
<td>cs</td>
<td>calcarine sulcus</td>
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<tr>
<td>ce</td>
<td>central sulcus</td>
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<td>occipitotemporal sulcus</td>
</tr>
<tr>
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<td>posterior middle temporal sulcus</td>
</tr>
<tr>
<td>pp</td>
<td>parieto-occipital sulcus</td>
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<td>pomm</td>
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<tr>
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<tr>
<td>sp</td>
<td>subparietal sulcus</td>
</tr>
<tr>
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<tr>
<td>DMZ</td>
<td>densely myelinated zone of MST</td>
</tr>
<tr>
<td>DP</td>
<td>dorsal prelunate area</td>
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<td>FEF</td>
<td>frontal eye field</td>
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<td>FST</td>
<td>fundus of superior temporal area</td>
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<td>LIPd</td>
<td>lateral intraparietal area, dorsal part</td>
</tr>
<tr>
<td>LIPv</td>
<td>lateral intraparietal area, ventral part</td>
</tr>
<tr>
<td>MST</td>
<td>medial superior temporal area</td>
</tr>
<tr>
<td>MSTc</td>
<td>medial superior temporal area, central visual field representation</td>
</tr>
<tr>
<td>MStp</td>
<td>medial superior temporal area, peripheral visual field representation</td>
</tr>
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<td>MT</td>
<td>middle temporal area</td>
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<tr>
<td>PITd</td>
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<tr>
<td>PITv</td>
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</tr>
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</tr>
<tr>
<td>V4</td>
<td>visual area 4</td>
</tr>
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<td>ventral intraparietal area</td>
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<td>VOT</td>
<td>ventral occipitotemporal area</td>
</tr>
<tr>
<td>VP</td>
<td>ventral posterior area</td>
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</table>
potentially painful procedures were carried out during the recording sessions. Body temperature and end-tidal CO$_2$
were continuously monitored and kept within the normal physiological ranges. The heart rate was continuously monitored for any sign of inadequate anesthesia.

The pupil of the eye contralateral to the recorded hemisphere was dilated with cyclopentolate hydrochloride, and the cornea was covered with a contact lens that focused the eye on a screen 57 cm in front of the animal. Varnish-coated tungsten microelectrodes were introduced through a guide tube, and multiunit activity was recorded. After TEO and adjacent portions of areas V4 and TE were mapped, we selected several visual field representations within TEO as sites for injection. The guide tube was lowered to within 2 mm of the target site, the microelectrode was withdrawn from the guide tube and replaced by a 1 µl Hamilton syringe, and the syringe was lowered to the appropriate depth. Tracers were injected at a rate of 0.01 µl/minute (FB, WGA, AA) or 0.1 µl/minute (DY). To prevent leakage of the tracer along the penetration track, the syringe was left in place for 30 minutes after the injection, then raised 1 mm, and, after an additional 10 minutes, withdrawn into the guide tube. Finally, the guide tube itself was withdrawn from the brain.

As indicated above, injections of FB, DY, and AA were made during the first recording session, and, five days later, an additional injection of WGA was made in the second session. Not all tracers were injected in all animals. The injection volumes were 0.1–0.15 µl of 2% FB, approximately 0.2 µl of 4% DY, 0.1–0.15 µl of 2.5% WGA (Sigma), and 0.15 µl of AA. The activity of the AA was 100 µCi/µl of an equal parts mixture of tritiated prolne [New England Nuclear L-(2,3,4,5$^3$H), specific activity 100–140 Ci/mmol] and tritiated leucine [New England Nuclear L-(3,4,5$^3$H[N]), specific activity 100–140 Ci/mmol]. Following the final injection of each recording session, the infusion of the paralyzing agent was terminated, and the animal was returned to its cage after it recovered from the anesthesia.

Histological processing
Following a survival time of 14 days after the RD injection, 7 days after the FB, DY, and AA injections, and 2 days after the WGA injection, the monkeys were killed with an overdose of pentobarbital and perfused through the heart with 0.9% saline followed by 3% paraformaldehyde in 0.1 M phosphate buffer (pH 7.4), and then by 5% glycerol in 0.1 M phosphate buffer. The brains were blocked stereotaxically, removed from the skull, photographed, stored overnight in 10% glycerol in 0.1 M phosphate buffer, and then placed for 4–5 days in 20% glycerol in 0.1 M phosphate buffer at 4°C on a shaker. After this period, the brains were stored in 2-methyl-butane (95%) at −70°C until they were cut (Rosene et al., '86).

Frozen sections, 50 µm thick, were cut in the coronal plane in case 1 and in the parasagittal plane in cases 2–7. One series of sections, 250 µm apart, was mounted from 0.45% saline as the brain was cut, dried at 37°C, and stored uncovered in light tight boxes at 4°C for the subsequent analysis of fluorescent label. Two adjacent series of sections were processed for autoradiography. These sections were stored in 5% formalin, subsequently mounted, dehydrated, and dipped in Kodak NTB2 emulsion, and, after an exposure time of 20 weeks at 4°C, developed in Kodak D19, fixed, and counterstained with thionin (Cowan et al., '72). A fourth series of sections, also 250 µm apart, was stored in 30% ethylene glycol in 0.1 M phosphate buffer at −30°C and then processed for horseradish peroxidase histochemistry using tetramethylbenzidine as the chromogen (Mesulam, '78; as modified by Gibson et al., '84). These sections were dehydrated, coverslipped, and stored at −30°C. Finally, another series of sections, spaced 1 mm apart, was stained for myelin (Gallyas, '79; as modified by Hess and Merker, '83), and an additional series, also spaced 1 mm apart, was stained with thionin.

Data analysis and nomenclature
The location and laminar distribution of FB, DY, RD, and WGA labeled cells and of WGA and AA labeled terminals were charted onto enlarged photographs of the thionin-stained sections. For each animal, a two-dimensional reconstruction ("map") of the cortex was made by bending wires along layer IV of these photographically enlarged sections at 2 mm intervals; landmarks such as the lips and fundi of sulci were marked on these wires (Gattass and Gross, '81; Ungerleider and Desimone, '86b). Then the wires were soldered together at appropriate intervals, forming a three-dimensional wire model. This model was subsequently unfolded to form a two-dimensional map of the cortex. Anatomical data, myeloarchitectural borders, as well as reconstructed electrode penetration tracks were then transferred onto these maps. In addition, the anatomical data and the location of the injection sites were charted on surface reconstructions of lateral and ventral views of the injected hemispheres.

The data were analyzed with respect to 26 visual cortical areas, which, except for the frontal eye field (FEF), are illustrated schematically in Figure 1C. The criteria we used to identify these areas are described in detail elsewhere (Boussaoud et al., '90). Briefly, areas V2, V4t, MT, FST, the densely myelinated zone of MST (DMZ), as well as V3d (V3 of Burkhalter et al., '86), V3v (VP of Burkhalter et al., '86) and V3A were identified, where possible, on the basis of their distinctive myeloarchitecture (Allman and Kass, '71; Ungerleider and Mishkin, '79; Gattass and Gross, '81; Gattass et al., '81, '88; Van Essen et al., '81, '86; Desimone and Ungerleider, '86; Ungerleider and Desimone, '86a, b; Fiorani et al., '89). We were also able to identify a heavily myelinated zone in the depth of the lateral bank of the intraparietal sulcus, a zone we previously labeled VIP* and included as part of VIP on the basis of its connections with area MT (Ungerleider and Desimone, '86b; Boussaoud et al., '91). However, Colby and Duhamel ('91) have shown that the neurons in the heavily myelinated zone have physiological properties resembling those in LIP (Andersen et al., '87, '90) more than those in the remainder of VIP. Consequently, and in keeping with Blatt et al. ('90), we have termed this heavily myelinated zone "LIPv" and have termed the remainder of LIP "LIPd," which acknowledges the similarity in neuronal properties in the two portions of LIP as well as the differences in their myeloarchitectural appearance and connections with MT.

For the remainder of the visual cortical areas, it was often difficult to determine their borders unequivocally; thus, their boundaries could not be marked on the two-dimensional maps. For a number of these areas, such as V4, PO, VIP, 7a, DP, PItd, STP, TEM, TEa, IPa, and PEF, their locations were inferred from previous anatomical and physiological studies (e.g., Seltzer and Pandya, '78; Van Essen and Zeki, '78; Desimone and Gross, '79; Boussaoud et al., '80; Zeki, '80; Maguire and Baizer, '84; Andersen et al., '85.
Fig. 1. Location of visual areas identified in occipital, parietal, and temporal lobes of macaque monkeys. Areas are shown on a two-dimensional unfolded cortical map at the right (C; adapted from Ungerleider and Desimone, '86b). Striate cortex is not included. Thick lines represent the boundaries of sulci; thin lines at the perimeter of the map indicate where the map was “cut” from the rest of the cortex. The part of the cortex shown on the map is illustrated on the lateral view (shaded areas) at the upper left (A). Sulci (shaded areas) and sulcal labels are indicated on the small map at the center left (B). The topographic organization in TEO is represented on the small map at bottom (D; adapted from Boussaoud et al., '91). In D, plus sign indicates the upper visual field representation, minus sign the lower field representation, star the foveal representation, VM the vertical meridian of the visual field (shown in circles), and HM the horizontal meridian (shown in squares). For other abbreviations in this and following figures, see Abbreviations list.
CORTICAL CONNECTIONS OF AREA TEO

'87, '90; Bruce et al., '85; Burkhalter et al., '86; Desimone and Ungerleider, '86; May and Andersen, '86; Newsome et al., '86; Baylis et al., '87; Huerta et al., '87; Colby et al., '88; Gattass et al., '88; Hikosaka et al., '88; Stanton et al., '89; Blatt et al., '90; Boussaoud et al., '91). TEm and TEa are rostrocaudally oriented bands located anterior to PITd on the lateral bank of the superior temporal sulcus (Seltzer and Pandya, '78). Because we were unable to reliably distinguish these areas from each other on the basis of architectonic criteria, we have used the term TEm/TEa to refer to this portion of the superior temporal sulcus.

For the areas within the temporal lobe (TEO, TE, TF, TH, and TG), borders were not marked, but rather, estimated using mainly the criteria of Bonin and Bailey ('47). Although injections were placed into TEO after physiological recordings, we made no attempt to completely map the area and thereby establish its borders. Based on the cytoarchitectonic descriptions of Amaral et al. ('87) and Insausti et al. ('87), the ventromedial part of Bonin and Bailey's ('47) area TE was considered perirhinal cortex and subdivided into areas 35 and 36. However, for the temporal pole, we have not adopted their term 36p (Insausti et al., '87), but have instead retained the original term, area TG (Bonin and Bailey, '47). Finally, the cortex anteromedial to TH (i.e., the entorhinal cortex) was assigned to area 28, based on the descriptions of Amaral et al. ('87) and Insausti et al. ('87).

RESULTS

The anatomical connections of area TEO were determined from the results of 11 tracer injections made into physiologically identified sites of 7 monkeys. Of these injections, 2 were placed into the foveal representation of TEO, 5 were centered in the upper field representation at eccentricities ranging from 10 to 22⁰, 2 were centered in the lower field representation at eccentricities of 17⁰ and 26⁰, 1 was centered on the horizontal meridian at 4⁰, and 1 was centered in the lower peripheral visual field at 23⁰ but probably extended into the upper field representation as well. One additional injection was placed in PITd (case 2-FB; see Materials and Methods). In the results that follow, each injection is referred to as a case, with the animal's number followed by the abbreviation of the tracer.

Furthermore, for the WGA injections, anterograde and retrograde data are treated as separate cases, and are described as WGaa and WGAr, respectively. Thus, there were a total of 15 TEO cases in the study, 7 anterograde and 8 retrograde, and 1 PITd case, which was retrograde. The connections of TEO and PITd with other cortical areas revealed by these 16 cases are summarized in Table 1. The laminar distribution of labeled cells and terminals within these areas is given in Table 2. Note that in none of the cases was a connection found between TEO and V1.

We first describe the connections of the foveal representation in TEO, since this is the portion that has been included in previous anatomical studies (Shiwa, '87; Morel and Bullier, '90; Webster et al., '91). We next compare the connections of the foveal representation with those of the peripheral field, first for a case involving both the upper and lower visual fields and then for cases with injections confined to either the upper or lower field. We then compare the connections of TEO with those from the case with an injection of PITd to determine whether the physiological distinction between the two areas is paralleled by differences in their anatomical connections. Finally, we describe the connections of TEO with the frontal lobe and with areas in the contralateral hemisphere. For simplicity, the laminar distribution of anterograde label only is described in the text. The laminar distribution of retrograde label is summarized in Table 2.

Connections of foveal TEO

There were three cases with injections in the foveal representation of TEO, two retrograde (cases 1-WGAr and 1-RD) and one anterograde (case 1-WGAa), all of which are illustrated (Figs. 2–5).

Case 1-WGAr. In this case, a large injection was placed in the foveal representation of TEO at less than 1⁰ eccentricity. Figure 2 shows the location and size of the injection and the distribution and density of retrogradely labeled cells, both on lateral and ventral views of the brain and on representative cross sections. These data are illustrated on a flattened map of the posterior part of the cortex in Figure 3.

In the posterior prestriate cortex, a dense accumulation of labeled cells was located in the foveal representation of V2, extending out to about 5⁰ in both the upper and lower fields (Gattass et al., '81), which is consistent with the extent of the receptive field recorded at the TEO injection site (see Fig. 2). Dorsally, the labeled region extended anteriorly to occupy a small portion of V3d. Ventrally, the comparable portion of V3v was densely labeled. Within V4, just posterior to the injection site, there was widespread dense labeling of its foveal representation, also extending out to about 5⁰ in both the upper and lower fields (Gattass et al., '88). Neither area V3A, PO, nor DP contained labeled cells.

Because the injection site in case 1-WGAr was placed very posteriorly in TEO, it was possible that the labeled cells in V2 and V3 resulted from spread of tracer into V4, which is connected with both areas (Burkhalter and Van Essen, '83; Fellemman and Van Essen, '83, '84; Ungerleider et al., '83, '86; DeYoe and Van Essen, '83; Shipp and Zeki, '85; Weller and Kaas, '85; Zeki and Shipp, '89; Steele et al., '91). However, if the tracer had spread into V4, then it would have involved the foveal representation in this area. In that event, labeled cells should have been found in V1, since we and others have demonstrated a direct projection from the foveal representation of V1 to that of V4 (Zeki, '78; Yukie and Iwai, '85; Perkel et al., '86; Nakamura et al., '93). But there was no evidence of V1 labeling in this case. Also, in case 1-RD, the injection was placed more anteriorly in TEO, and labeled cells were still found in areas V2 and V3 (Fig. 4), indicating that the presence of label in V2 and V3 in case 1-WGAr was not likely a result of the involvement of area V4. Finally, in the 13 other TEO cases, 11 showed label in V2 and 10 showed label in V3.

In caudal STS, case 1-WGAr showed a moderate accumulation of labeled cells in MT and FST. In MT, the cells were located in the rostral portion of the area, where central vision is represented (Gattass and Gross, '81; Van Essen et al., '81; Desimone and Ungerleider, '86; Albright and Desimone, '87). In FST, the cells were scattered throughout the area, which is consistent with the fact that receptive fields of FST neurons typically include the fovea (Desimone...
### Table 1
**Distribution and Density of Label in Cortical Areas Following Injections Into Area TEO**

<table>
<thead>
<tr>
<th>Area</th>
<th>TEO Case</th>
<th>Posterior Prestriate Areas</th>
<th>Caudal STs Areas</th>
<th>Rostral STs Areas</th>
<th>Temporal Areas</th>
<th>Parietal Areas</th>
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<tbody>
<tr>
<td>Foveal</td>
<td>1-RD</td>
<td>V2, V3d, V3v, V3a</td>
<td>V4, MT, FST, MST, PP</td>
<td>V6, MT</td>
<td>TE, TF, TH</td>
<td>LIPd, LIPv, VIP, 7a</td>
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<td></td>
<td>1-WGAa</td>
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<td>++</td>
<td>++</td>
<td>+</td>
<td>+</td>
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<tr>
<td></td>
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<td>V4, MT, FST, MST, PP</td>
<td>V6, MT</td>
<td>TE, TF, TH</td>
<td>LIPd, LIPv, VIP, 7a</td>
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<td>2-WGAa</td>
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<td>V4, MT, FST, MST, PP</td>
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<td>TE, TF, TH</td>
<td>LIPd, LIPv, VIP, 7a</td>
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<td></td>
<td>1-WGAa</td>
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<td>+</td>
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<tr>
<td></td>
<td>2-WGAa</td>
<td>++</td>
<td>++</td>
<td>++</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

The number of pluses (+) indicates the density of label. The dashes (-) indicate indeterminate results due to missing medial temporal lobe tissue. An asterisk (*) indicates an indeterminate result because of an infarct within the white matter underlying the cortex. Ecc. indicates the eccentricity of the receptive field recorded at the injection site.

### Table 2
**Laminar Distribution of Label in Cortical Areas Following Injections into Area TEO**

<table>
<thead>
<tr>
<th>Area</th>
<th>TEO Case</th>
<th>Posterior Prestriate Areas</th>
<th>Caudal STs Areas</th>
<th>Rostral STs Areas</th>
<th>Temporal Areas</th>
<th>Parietal Areas</th>
</tr>
</thead>
<tbody>
<tr>
<td>Foveal</td>
<td>1-RD</td>
<td>V2, V3d, V3v, V3a</td>
<td>V4, MT, FST, MST, PP</td>
<td>V6, MT</td>
<td>TE, TF, TH</td>
<td>LIPd, LIPv, VIP, 7a</td>
</tr>
<tr>
<td></td>
<td>1-WGAa</td>
<td>++</td>
<td>++</td>
<td>++</td>
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<td>+</td>
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<td>2-WGAa</td>
<td>++</td>
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<td>+</td>
<td>+</td>
</tr>
<tr>
<td>UVf-LvL</td>
<td>1-RD</td>
<td>V2, V3d, V3v, V3a</td>
<td>V4, MT, FST, MST, PP</td>
<td>V6, MT</td>
<td>TE, TF, TH</td>
<td>LIPd, LIPv, VIP, 7a</td>
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<tr>
<td></td>
<td>1-WGAa</td>
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<tr>
<td>UVf</td>
<td>1-RD</td>
<td>V2, V3d, V3v, V3a</td>
<td>V4, MT, FST, MST, PP</td>
<td>V6, MT</td>
<td>TE, TF, TH</td>
<td>LIPd, LIPv, VIP, 7a</td>
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<td></td>
<td>1-WGAa</td>
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<tr>
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<td>V2, V3d, V3v, V3a</td>
<td>V4, MT, FST, MST, PP</td>
<td>V6, MT</td>
<td>TE, TF, TH</td>
<td>LIPd, LIPv, VIP, 7a</td>
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<tr>
<td></td>
<td>1-WGAa</td>
<td>++</td>
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<td>2-WGAa</td>
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</table>

Symbols: B, labeled terminals avoid layer IV; F, labeled terminals heavier or only in layer IV; I, labeled terminals homogeneously distributed in all layers including IV; L, labeled cells predominantly in infragranular layers; S, labeled cells predominantly or exclusively in supragranular layers; =, labeled cells equally distributed in supragranular and infragranular layers; asterisk (*) and dashes (-), see Table 1.
Fig. 2. Case 1-WGAr: Distribution of retrogradely labeled cells after wheat germ agglutinin (WGA) injection into the foveal representation of TEO. The receptive field recorded at the injection site is shown at the right. Injection site (black), diffusion halo (hatched), and labeled cells (dots) are shown on the lateral (upper left) and ventral views (lower right), as well as on representative coronal sections (#1-5). The position of these sections in the brain is indicated by the vertical lines on the surface views. The density of the dots corresponds qualitatively to the density of labeled cells. Arrows on the sections and dashed lines on the surface views indicate myeloarchitectonic boundaries of visual areas.

and Ungerleider, '86). No cells were found in V4t or PP, but a few were seen in the DMZ portion of MST. By contrast, there was very dense labeling in PITd.

In rostral STS, there were two separate patches of labeled cells in the region occupied by TEM and TEd on the lateral bank of the sulcus (Seltzer and Pandya, '78; Baylis et al.,
Case 1-WGAr

Fig. 3. Case 1-WGAr: Distribution of retrogradely labeled cells after WGA injection into the foveal representation of TEO, shown on an unfolded map of the posterior part of the cortex. Heavy dashed lines on the map indicate myeloarchitectonic borders. Thin lines (#1–5) are the layer IV contour lines of the same sections shown in Figure 2. The sulcal pattern in this case was unusual in that io and pmt merged to form a single sulcus. Note that the width of V2 seems greater dorsomedially and ventromedially than laterally. This reflects a distortion in the flattened map that is typically most pronounced in extreme lateral cortex. All conventions are as in Figures 1 and 2.

'87). The posterior patch extended medially into the floor of the sulcus, where area IPa is located (Seltzer and Pandya, '78). No labeled cells were seen on the medial bank of the sulcus in area STP.

In the temporal cortex, the labeled region extended anteriorly from the injection site into area TE, which contained moderate accumulations of labeled cells. Moderate accumulations were also seen in parahippocampal areas...
Case 1-RD

Fig. 4. Case 1-RD: Distribution of retrogradely labeled cells after a dextrane (RD) injection into the foveal representation of TEO, shown on the lateral and ventral views (left) and an unfolded cortical map (right). All conventions are as in Figures 1–3.

TF and TH, in TG at the temporal pole, and in perirhinal area 36. A few labeled neurons were also located in area 35 within the rhinal sulcus. Entorhinal area 28 was devoid of labeling.

In the parietal cortex, there were a few labeled cells in both the dorsal and ventral subdivisions of area LIP (LIPd and LIPv, respectively), but none in area VIP or 7a.

Case 1-WGAA. This case demonstrates the anterograde labeling for the same WGA injection as the previous case. In posterior prestriate cortex, all areas that contained labeled cells also showed labeled terminals (Fig. 5). Terminal label in these areas either avoided layer IV or was less dense in this layer than in the other layers (Fig. 6A–C).

In caudal STS also, all areas that contained labeled cells showed labeled terminals, except for MST where no terminals were found (Fig. 5). The laminar distribution of terminal labeling in the other caudal STS areas was variable. In MT, labeled terminals were present in all layers, but in some patches they avoided layer IV. In FST, labeled terminals appeared either to avoid layer IV or to be less dense in this layer. In PITd, labeled terminals included all layers, and they were not heavier in layer IV.

In rostral STS again, the same areas that contained labeled cells contained labeled terminals. In both TEM/TEa and IPA, labeled terminals occupied all layers and in some places were heavier in layer IV.

In temporal cortex, of the areas with labeled cells (TE, TG, TF, TH, 36 and 35), only areas TE and TG contained labeled terminals, and these were concentrated in layer IV (see Fig. 6D).

In parietal cortex, areas LIPd and LIPv showed an overlapping distribution of labeled cells and terminals. In LIPd, labeled terminals were heaviest in layer IV, whereas in LIPv they seemed to avoid layer IV.

Connections of peripheral TEO

There were 12 cases with injections outside the foveal representation of TEO, six retrograde cases and six antero-
Case 1-WGAA

Fig. 5. Case 1-WGAA: Location of anterogradely labeled terminals after the same foveal WGA injection shown in Figures 2 and 3. Projections avoiding layer IV are represented by light shading, while projections occupying all layers or heavier in layer IV are represented by dark shading. All other conventions are as in Figures 1-3.

grade cases (see Tables 1 and 2). Of these, five cases have been selected for illustration.

Case 2-WGAr. In this case, an injection was placed into TEO's peripheral field representation (Fig. 7). Although the receptive field recorded at the injection site was centered at an eccentricity of 23° in the lower field, the labeling in ventral as well as dorsal posterior prestriate areas suggested that the tracer had spread into more posterior portions of TEO where the upper field is represented (Boussaoud et al., '91). Alternatively, the presence of label in ventral prestriate cortex could reflect heterotopical connections, although we think this unlikely, given that mainly homotopical connections with prestriate areas were seen in the other cases. Like case 1-WGAr, which had an injection in the foveal representation, case 2-WGAr also showed labeled cells in prestriate areas V2–V4. However, in case 2-WGAr, the labeled cells were found in the peripheral but not the central field representations of these areas (Gattass et al., '81, '88). Unlike case 1-WGAr, case 2-WGAr showed additional label in areas V3A and DP.

In caudal STS, labeled cells were seen in the same areas that contained labeled cells in case 1-WGAr. In addition, cells were found in areas V4t and PP, both of which were devoid of label in case 1-WGAr.

In rostral STS, both TEm/TEa and IPa contained labeled cells. In addition, a small patch of labeled cells was found in area STP.

In the temporal lobe, only areas TE, TF, and TG could be examined, since the most medial part of the temporal lobe was lost in cutting. As in case 1-WGAr, all three areas contained labeled cells, although the cells within TG were all contained in the most posterior part of the area.

In the parietal lobe, LIPd and LIPv contained labeled cells. In addition, the labeled region in the intraparietal
Fig. 6. Darkfield photomicrographs show the pattern of retrograde and anterograde label after foveal TEO injection with WGA (case 1-WGA). A, B: Labeling in V2. A is taken from the focus of the labeled region, whereas B is taken from a less densely labeled region. C: Labeling in V4. D: Labeling in TE. The cortical layers (I-VI) and white matter (WM) are indicated. In V2-V4, retrogradely labeled cells occur mainly in the supragranular layers and labeled terminals are lightest in layer IV. In TE, retrogradely labeled cells occur mainly in the infragranular layers and labeled terminals are heaviest in layer IV. Scale bars = 250 µm.

The sulcus extended posteriorly from LIPv into still unidentified cortex adjacent to V3A. Similarly, extensive labeling of cortex in the intraparietal sulcus was seen previously after injections of peripheral but not central field representations of V4 (Ungerleider et al., '86).

Case 2-WGAa. With the exception of MST and IPA, all areas that contained labeled cells also contained labeled terminals. Furthermore, the laminar distribution of terminals was very similar to that observed in case 1-WGAa (see Table 2) but included additional areas. Of the latter, the
Case 2-WGAr

Fig. 7. Case 2-WGAr: Location of retrogradely labeled cells after a WGA injection into the periphery of TEO, including both lower and upper visual fields (see text). Arrow on the lateral view of the brain (upper left) points to the location of the injection site buried in the sulcus. Note that MT and V4t appear closer to the lip of st than one might expect (see also Fig. 13). The explanation is that, in this case, the layer IV contour lines of the parasagittal sections that ran through the extreme lateral portion of st had to be compressed in order to flatten the map. Thus, this portion of the sulcus underwent some distortion. All conventions are as in Figures 1–3.

Upper visual field
Case 3-DY. In this case, a small injection was placed in the representation of the upper peripheral field of TEO at an eccentricity of 22°. Figures 8 and 9 show the location and size of the injection and the distribution and density of labeled cells on surface views of the injected hemisphere, selected sections through the brain, and a flattened map. Consistent with the receptive field recorded at the injection site, labeled cells were found in ventral but not dorsal parts of V2 and V3 (Gattass et al., '81, '88). A large accumulation of labeled cells was also found in ventral V4 and, unexpectedly, a few cells were also seen dorsally on the prelunate gyrus. We have assigned these cells to V4, though they may be located beyond V4 in area DP. The central field representation of V4 contained no labeled cells (Gattass et al., '88). As in the previously described peripheral field case (case 2-WGAr), V3A also contained labeled cells.

Within caudal STS, as in case 2-WGAr, labeled cells were found in areas V4t, MT, FST, and PP. Within MT, the cells were mainly in the postero medial part of the area, which contains the representation of the upper peripheral visual field (Gattass and Gross, '81; Van Essen et al., '81; Desimone and Ungerleider, '86; Albright and Desimone, '87). No cells were found in either MST or PITd. Within V4t, the labeled cells were also located posteriorly. Although V4t has been reported to contain a representation of the lower
Case 3-DY

Fig. 8. Case 3-DY: Distribution of retrogradely labeled cells after a diamidino yellow (DY) injection centered in the upper peripheral field representation of TEO. Data are shown on the lateral (upper left) and ventral (lower right) views of the injected hemisphere as well as on representative parasagittal sections (#1–3). Arrows on parasagittal sections mark myeloarchitectonic boundaries of visual areas. Arrow on the ventral view of the brain points to the location of the injection site buried in the sulcus. All conventions are as in Figure 2.

visual field only (Desimone and Ungerleider, '86), the presence of label in the posterior portion of V4t in this case and others with TEO injections involving the upper peripheral visual field (see Table 1) suggests that in the periphery of V4t, the receptive fields may be very large and extend from the lower visual field across the horizontal meridian to include parts of the upper visual field.

In rostral STS, areas TEm/TEa and IPa were devoid of labeled cells, although both of these areas were labeled in at least one of the other two retrograde upper field cases (see Table 1).

In the parietal cortex, labeled cells were found in areas TE, TF, and TH, but not in TG, 36, or 35.

In the parietal cortex, LIPd but not LIPv was labeled, and, as in case 2-WGAr, additional labeling was again found in the cortex of the intraparietal sulcus posterior to LIPv. A large patch of labeled cells was also found in area 7a on the inferior parietal gyrus.
Fig. 9. Case 3-DY: Distribution of retrogradely labeled cells after a DY injection centered in the peripheral upper field representation of TEO, shown on an unfolded map of the posterior part of the cortex. Conventions are as in Figure 3.

Case 4-AA. In case 4-AA, a large injection was placed in the representation of the upper peripheral field of TEO at an eccentricity of 10°, and the resulting distribution of anterograde label is shown in Figure 10. This was one of the two TEO cases where no labeled terminals were seen in V2. Otherwise, the labeled areas in posterior prestriate cortex corresponded to those just described for case 3-DY, with a laminar distribution of terminals similar to that of case 2-WGAA. It should be noted that the receptive field recorded at the injection site in case 4-AA included the vertical meridian, and, correspondingly, the labeled region spanned the V3A/V4 border dorsally and the V3v/V4 border ventrally, both of which represent the vertical meridian (Gattass et al., '88).

In caudal STS, there were only two patches of labeled terminals, a large patch located in area PP and another
small patch close to the lip of the medial bank of the sulcus, probably outside area MST. In both patches, the labeled terminals were evenly distributed across all layers. Of the three other anterograde upper field cases, all contained labeled terminals in areas V4t and MT, and two contained such terminals in FST (see Table 1). In all areas, the laminar distribution of the terminals either avoided layer IV or included all layers but was not heavier in layer IV, resembling the distribution described for case 2-WGAa (Table 2).

In rostral STS, labeled terminals were located in areas TEM/TEa and IPa, predominantly in layer IV.

In the temporal cortex, labeled terminals were found in TE and TF; in TE and in one patch in TF, the labeled terminals were heaviest in layer IV, while in another patch in TF they avoided layer IV. In the three other anterograde upper field cases, no consistent laminar pattern of terminal labeling was seen (see Table 2). Although labeling within TH in either this case or case 7-WGAa could not be determined due to missing tissue, both of the other anterograde upper field cases contained labeled terminals in area TH. In case 6-AA, they were either evenly distributed across all layers or heaviest in layer IV, while in case 5-WGAa they showed the former laminar pattern.

In the parietal cortex, LIPd but not LIPv was labeled, although other anterograde cases did show LIPv labeling. Whereas the label in LIPd was heaviest in layer IV in case 4-AA, the laminar distribution among the other anterograde cases did not follow a common pattern. Among the cases with LIPv labeling, the terminals either avoided layer IV or were evenly distributed across the layers. As in case 3-DY, there was a labeled region posterior to LIPv in the intraparietal sulcus. Within this region, the labeled terminals avoided layer IV.

Lower visual field
Case 1-DY. In case 1-DY, a small injection was placed in the representation of the lower peripheral field of TEO at an eccentricity of 26°, and the resulting distribution of retrogradely labeled cells is shown in Figure 11. In contrast to case 3-DY, which had an upper peripheral field injection site, the labeled cells in this lower field case were found mostly in the dorsal portions of posterior prestriate areas V2, V3, and V4, concordant with their lower visual field representations (Gattass et al., '81, '88). There were,
Case 1-DY

Fig. 11. Case 1-DY: Distribution of retrogradely labeled cells after a DY injection into the peripheral lower field representation of TEO. Arrow (upper left) points to the location of the injection site buried in the sulcus. Conventions are as in Figures 1-3.

However, a few scattered cells in the ventral portions of V2-V4, indicating that the injected region may have also encroached on tissue representing the upper visual field. Surprisingly, the label in V2-V4 was located in regions of cortex representing eccentricities from 2 to 10°, even though the receptive field at the injection site seemed to extend from about 8 to 26° along the vertical meridian. Like case 2-WGAr, a few labeled cells were also located beyond V4 in area DP.

In caudal STS, only areas FST and PITd contained labeled cells. In rostral STS, labeled cells were found in TEm/TEa, and a handful was also seen in IPa.

In the temporal cortex, areas TE, TF, TH, and 36 all contained labeled cells. A few cells were also found in the caudal portions of area TG (rostral to the anterior middle temporal sulcus) and area 35 (in the depth of the rhinal sulcus).

In the parietal cortex, there were a few cells in area 7a, as well as three discrete small patches of cells in the cortex posterior to LIPv within the intraparietal sulcus.

Case 1-AA. In this case, a large injection was placed in the representation of the lower peripheral field of TEO at an eccentricity of 17°, and the resulting distribution of anterograde label is shown in Figure 12. In posterior prestriate cortex, terminal labeling was present in V2, V3d, V3A, and V4, but not in DP. Consistent with the receptive field recorded at the injection site, the label was found only in the dorsal portions of these areas, i.e., their lower field representations. However, as in case 1-DY, the label was located in more central parts of the visual field representation than would have been predicted from the receptive field recording. The labeled terminals in all posterior prestriate areas avoided layer IV.

In caudal STS, there was heavy terminal labeling in PITd and light label in FST, both of which showed labeled cells in case 1-DY. Additional areas labeled in case 1-AA included V4t and MT. Whereas the terminals in V4t avoided layer IV, they were evenly distributed across all layers in MT, FST, and PITd.
In rostral STS, terminal labeling was present in TEm/TEa and IPa. In TEm/TEa the terminals were heaviest in layer IV, while in IPa they were evenly distributed across the layers.

In the temporal lobe, in contrast to the findings in case 1-DY, only area TE was labeled. The labeled terminals were heaviest in layer IV.

In the parietal cortex, labeled terminals were found in LIPd and LIPv as well as in more anterior parts of the intraparietal sulcus. Within LIPd and LIPv, the terminals showed an evenly distributed laminar pattern, while the pattern of labeling in the more anterior cortex was variable.

Connections of PITd

As stated in Materials and Methods, one of the injection sites (case 2-FB) was inadvertently placed too deep within the inferior temporal gyrus and consequently involved area PITd on the lower bank of the STS rather than TEO on the surface of the cortex. Because PITd was excluded from TEO on the basis of physiological mapping results (Boussaoud et al., '91), we investigated whether the physiological differences between TEO and PITd would be mirrored by connectional differences. The PITd injection in case 2-FB was small, but larger than the TEO injection in case 1-RD. In both cases, the injections resulted in limited labeling, but in general the same areas were labeled, with one exception (cf Figs. 13 and 4). In case 1-RD, but not in case 2-FB, V2 and V3 were labeled. The absence of label in V2 and V3 in case 2-FB is probably not due to the small size of the injection, since the injection in case 1-RD was even smaller. It is also probably not due to limited transport of the tracer, since distantly located areas in both the temporal and parietal cortex contained labeled cells.
CASE 2-FB

Fig. 13. Case 2-FB: Distribution of retrogradely labeled cells after an FB injection into PITd. Arrow (top) points to the location of the injection site buried in the sulcus. Conventions are as in Figures 1–3.

Connections of TEO with the prefrontal cortex

In most cases, label was found in the anterior bank of the inferior limb of the arcuate sulcus, but in two cases (cases 2-WGAr and 2-WGAa), it was also seen on the immediately adjacent portion of the prearcuate gyrus. In all instances but one, the labeled cells and terminals were located within the region corresponding to the frontal eye field (FEF), which has been defined physiologically as the area in and around the arcuate sulcus from which low-threshold saccadic eye movements can be evoked (Bruce et al., '85; Huerta et al., '87) and which is distinguishable from surrounding cortex on the basis of its high concentration of large layer V pyramidal cells (Stanton et al., '89). The single exception was a small patch of terminals in case 2-WGAa that was located on the prearcuate gyrus just beyond the FEF border, suggesting either that the projection from TEO extends beyond the FEF border or that the large layer V pyramidal cells are not a precise marker for this border.

Figure 14 illustrates the FEF labeling in two TEO cases, one with an injection in the foveal representation of TEO (case 1-WGAr) and another with an injection in the peripheral representation (case 2-WGAa). There was no evidence that the part of the FEF labeled was retinotopically related to the part of TEO injected. In addition, there did not seem to be any consistent laminar pattern of either labeled cells or terminals in the FEF (Table 2).

Contralateral connections of TEO

The densest retrograde and anterograde label in the contralateral hemisphere was always seen in approximately the same location as the site injected. In most cases, strong contralateral label was also found in V4 and TE. In about half of the cases, contralateral label was also present in V3, and in about a third of the cases very sparse label was present in V2. Finally, in most cases, some contralateral label was also found in rostral STS. Labeled cells were always located in the supragranular layers, whereas the laminar pattern of labeled terminals seemed to follow the pattern of the corresponding ipsilateral connection.
CORTICAL CONNECTIONS OF AREA TEO

Fig. 14. Location of retrogradely labeled cells in the frontal lobe after foveal (case 1-WGAr) and peripheral (case 2-WGAr) TEO injections. The positions of the sections shown on the bottom are indicated on the lateral (case 1-WGAr) and on the dorsal views of the brain (case 2-WGAr), respectively. Arrows (top) point to the regions within the arcuate sulcus where labeled cells were found. Conventions are as in Figure 2.

connection in each case, as indicated by the number of plus signs in Table 1. Table 1 indicates that there is a certain amount of variability not only in the strength but also in the existence of specific anatomical connections across cases. We have discussed in detail this problem of variability in our previous study of the connections of areas MST and FST (Boussaoud et al., '90). In that study, we considered a connection to be reliable if it was present in at least 40% of the cases. Though 40% is an arbitrary criterion, it does provide an explicit quantitative threshold for rejecting connections that may have resulted from inadvertent spread of tracer beyond TEO or from uptake of tracer by fibers of passage. We have therefore adopted the same criterion in the present study.

Connections with posterior prestriate areas. Connections between TEO and areas V2, V3, and V4 were found to be topographically organized, such that the central, peripheral, upper, and lower visual field representations in TEO are connected with the corresponding representations in these posterior prestriate areas (Gattass et al., '81, '88; Boussaoud et al., '91). Although TEO connections with V2 and V3 were not described in some earlier studies (Burkhal-ter and Van Essen, '83; Ungerleider et al., '83; Felleman and Van Essen, '84), projections from both areas have been found in more recent investigations (Fenstermaker et al., '84; Shiwa, '87; Morel and Bullier, '90; Baizer et al., '91; Nakamura et al., '93), possibly due to more sensitive tracing techniques. Our results confirm these projections and also demonstrate that they are reciprocal; furthermore, they include visual field representations extending out to at least about 25° eccentricity. Recently, it has been shown that the cells in V2 that project to TEO occupy the same compartments as those that project to V4, namely, the thin cytochrome oxidase rich stripes and the interstripes (Nakamura et al., '93). Reciprocal projections between V4 and TEO have also been described in earlier studies (Felleman and Van Essen, '83; Fenstermaker et al., '84; Ungerleider et al., '86; Shiwa, '87; Morel and Bullier, '90; DeYoe and Sisola, '91; Felleman and McClendon, '91), but there was only limited evidence that such connections are topographically organized (Van Essen et al., '91; see also Weller and Steele, '92). It is clear from our data that all of the connections of TEO with posterior prestriate cortex the one with V4 is the strongest.
In addition to the connections with V2-V4, we found a connection between TEO and V3A, but only for visual field representations greater than 4° eccentricity. This connection has not been consistently reported in the literature (Fenstemaker et al., '84; Baizer et al., '91; but see Shiwa, '87; Morel and Bullier, '90), probably due to variable involvement of the peripheral field representation in the TEO injection sites. Several previous studies have indicated that V3A also receives peripheral but not central visual field connections from other visual areas (for review, see Desimone and Ungerleider, '89). For example, Zeki ('80) reported peripheral but not central field inputs to V3A from V1; Ungerleider and Desimone ('86b) found peripheral but not central field inputs to V3A from MT, and Ungerleider et al. ('86) reported peripheral but not central field inputs to V3A from V4.

Like Morel and Bullier ('90), we saw a connection between TEO and area DP in some cases, but this connection was not found reliably. Finally, we never found label in area PO after TEO injections, confirming the results of a previous study of PO connections (Colby et al., '88).

Connections with caudal STS areas. TEO was also found to be connected with areas V4t, MT, FST, PP, and PITd in caudal STS. As with V3A, V4t and PP were only labeled after injections into peripheral field representations of TEO. Although Morel and Bullier ('90) also found a connection between TEO and V4t, they did not report one between TEO and PP, i.e., the cortex in the most posterior medial portion of the STS. The connection with FST has also been described previously in two separate studies (Boussaoud et al., '90; Morel and Bullier, '90), but the one with MT has not been found before (Maunsell and Van Essen, '83; Ungerleider and Desimone, '86b; Morel and Bullier, '90; Baizer et al., '91; but see Krubitzer and Kaas, '90 for findings in non-macaque monkeys). However, the connection with MT tended to be very weak and was not found in all cases (see Table 1), suggesting that optimal tracer techniques may be necessary to detect it. The absence of a reliable connection with MST confirms the results of Boussaoud et al. ('90). A direct comparison of our data with those of Shiwa ('87) is difficult, since his results are described in relationship to cortical sulci rather than visual areas. An examination of his Figure 2, however, which shows a case with an injection in TEO, provides no evidence for a connection with MT, FST, or MST, but does indicate a connection with PITd. We too found a connection between TEO and PITd, as did Morel and Bullier ('90). Consistent with Boussaoud et al. ('91), who found receptive fields of cells in PITd to be centered in both the upper and lower visual fields, we could trace the connection with PITd from all field representations in TEO. The connection with PITd, when present, was usually the strongest among the caudal STS areas.

Connections with rostral STS areas. We found TEO to be reciprocally connected with the cortex on the lateral bank and floor of the STS, anterior to PITd and FST, respectively. The cortex on the lateral bank has been termed TEm laterally and TEa medially, while the cortex within the floor has been termed IPa (Seltzer and Pandya, '78). Because we could not reliably distinguish between TEm and TEa on the basis of cytoarchitecture, label within the lateral bank was assigned to “TEm/TEa.” Anterograde degeneration in TEm/TEa after a lesion including but not confined to TEO was first described by Seltzer and Pandya ('78; see their Fig. 6). Similarly, Shiwa ('87; see his Fig. 2) and Morel and Bullier ('90; see their Fig. 6) showed cells in TEm/TEa after retrograde tracer injections in TEO. Moreover, Morel and Bullier also found, as we did, input from IPa to TEO. However, unlike Morel and Bullier ('90), we saw no connection with area PGa, the cortex at the junction of the floor and the medial bank of the STS (Seltzer and Pandya, '78). Finally, we did not see a reliable connection between TEO and STP.

Connections with temporal areas. We found connections between TEO and temporal lobe areas TE, TF, TH, TG, and STP. A reciprocal connection with area TE is well established in the literature (Desimone et al., '80; Fenstemaker et al., '84; Shiwa, '87; Webster et al. '91; see also Weller and Kaas, '87; Weller and Steele, '92), and this connection was moderate to strong in almost all of our cases (see Table 1). Input to TEO from areas TF and TH has already been described by several laboratories (Van Hoesen, '80, '82; Shiwa, '87; Webster et al., '91). However, two studies have reported that TEO does not project back to these parahippocampal areas (Webster et al., '91; Martin-Ellins and Horel, '92). We confirm the results of those studies for the central field representation of TEO, which does not appear to project to either TF or TH. However, we found that the peripheral field representation of TEO does project to these areas.

Although Webster et al. ('91) saw no connection between the central field representation of TEO and TG, we found that they are reciprocally connected. However, the label was very light and concentrated in the most posterior portion of TG. Unexpectedly, only two of the nine cases with injections in peripheral field representations of TEO in which TG could be analyzed showed label in this area, and in both instances the label was retrograde. Thus, we cannot conclude that the projection from TG to the peripheral field representation of TEO is reciprocated. Input from TG to TEO has also been described by Shiwa ('87).

Like Webster et al. ('91), we found that TEO receives input from area 36 but does not project back to this perirhinal area. Webster et al. ('91) also reported a nonreciprocal projection from area 35 to TEO, but the data from the present study are too few to draw a definitive conclusion on this point.

Connections with parietal areas. We found a reciprocal connection between TEO and area LIP, confirming the results of prior studies (Seltzer and Pandya, '80; Shiwa, '87; Andersen et al., '90; Blatt et al., '90). Furthermore, our data indicate that this connection includes both the dorsal and ventral portions of LIP, i.e., LIPd and LIPv, respectively. However, we failed to see a topographic arrangement for this connection, though Blatt et al. ('90) have reported a crude retinotopic organization within LIP. We also observed a connection between TEO and an as yet undefined region of cortex posterior to LIP in the intraparietal sulcus. This connection, unlike the one with LIP, was seen only after peripheral field injections in TEO. Interestingly, the same undefined region of cortex has been shown to be connected with the peripheral but not the central field representation of V4 (Ungerleider et al., '86) as well as with area PO (Coily et al., '88), an area in which the peripheral field representation is greatly emphasized (Coily et al., '92).

Connections with frontal areas. In the frontal lobe, most of our cases showed labeling of cells and terminals in the anterior bank of the arcuate sulcus and, in two cases, on the adjacent prearcuate gyrus, thereby confirming the results of other studies (Barbas and Mesulam, '81; Huerta...
et al., '87; Shiwa, '87; Barbas, '88). Except for a small patch of anterograde label in one case, the label was always within the FEF, defined as the periarcuate region containing large, layer V, pyramidal cells (Stanton et al., '89). We saw no evidence for a topographic organization in the TEO-FEF connection.

Laminar distribution of TEO connections

Numerous anatomical studies of visual cortex have demonstrated that projections directed away from V1 tend to arise from cells in the supragranular layers and terminate mainly in layer IV of the target area, whereas projections directed toward V1 originate mainly from cells in the infragranular layers and terminate both above and below layer IV, thus avoiding layer IV of their target area (Kuypers et al., '65; Spatz and Tiggges, '72; Tiggges et al., '73, '74; Spatz, '77; Wong-Riley, '78; Rockland and Pandya, '79; Wall et al., '82; Maunsell and Van Essen, '83; Weller et al., '84; Kennedy and Bullier, '85; Weller and Kaas, '85; Ungerleider and Desimone, '86b; Boussaoud et al., '90; Felleman and Van Essen, '91). The terms “forward” or “feedforward” have been used for the former pattern of projections, while the terms “backward” or “feedback” have been used for the latter pattern (Rockland and Pandya, '79; Maunsell and Van Essen, '83). According to the hierarchical model of Maunsell and Van Essen ('83), feedforward projections characterize those from lower-order to higher-order visual areas, whereas feedback projections characterize those from higher-order to lower-order visual areas. These authors also described a third type of laminar pattern that is not clearly feedforward or feedback, in that the terminals either vary their laminar pattern from one patch to another or are evenly distributed across all layers including layer IV. They termed this type of connection “intermediate” and suggested that it characterizes connections between areas located at the same hierarchical level. Both we (Boussaoud et al., '90) and Felleman and Van Essen ('91) have concluded that a bilaminar pattern of projecting cells could characterize feedforward, feedback, or intermediate-type connections, and therefore retrograde data in the absence of anterograde data are inconclusive.

Extending the hierarchical model to the connections of area TEO, we found feedforward projections to TEO from areas V2, V3d, V3v, V3A, V4, V4t, and MT, and feedback projections to these areas from TEO; that is, labeled cells in these areas were located predominantly in the supragranular layers, while labeled terminals mainly avoided layer IV. We found intermediate-type connections with PP, LIPd and LIPv, FST, PITd, TF, and FEF. Labeled cells in these areas tended to have a bilaminar distribution, while labeled terminals were found in all layers but were not heavier in layer IV. Finally, we found feedforward projections from TEO to areas TE, TEM/TEa, IPA, TG and TH and feedback projections to TEO from these areas; labeled cells in these areas were located mainly in the infragranular layers, while terminals were heavier in layer IV. Additional feedback projections were found to arise in area 38. Figure 15 summarizes these connections on a schematic illustration of the macaque brain (see also Table 2). A comparison of these connections with the ones found for the comparable part of inferior temporal cortex of New World monkeys is summarized in Weller and Steele ('92).

Figure 16 shows the hierarchical scheme for extrastriate cortex from Ungerleider and Desimone ('86b), updated by the results of the present study and those of Boussaoud et al. ('90). The wiring diagram is consistent in general with other recently proposed anatomical schemes (Maunsell and Newsome, '87; Colby et al., '88; Andersen, '89; Felleman and Van Essen, '91). There are only two major differences between our scheme and those of others. First, based on the laminar pattern of connections of MST and FST, we placed all subdivisions of Bonin and Bailey’s (‘47) cytoarchitectonic area PG, including area 7a, at the same hierarchical level (Boussaoud et al., '90), whereas others have placed area 7a at a higher level (Andersen, '89; Felleman and Van Essen, '91; but for a scheme similar to ours, see Maunsell and Newsome, '87). Second, based on the laminar pattern of connections with TEO (especially with TEO’s peripheral field representation), we placed area TF at the same hierarchical level as TEO and areas within PG cortex, whereas others have placed area TF at a higher level (Maunsell and Newsome, '87; Felleman and Van Essen, '91; Webster et al., '91). One further complication is that Webster et al. ('91) found a feedback projection from TF to TE, suggesting that TF stands at an even higher level in the hierarchy than area TE. A possible explanation for the discrepancies regarding TF is that this area is not homogeneous. In an earlier study, we reported evidence for subdivisions in TF (Boussaoud et al., '91). We showed, for example, that neurons in the posterior portion of the area are visually responsive and that this posterior portion contains a crude visual topography (Boussaoud et al., '91). Additional studies are clearly needed to investigate further the properties and functions of area TF, which is at present a poorly understood region of cortex.

Position and role of TEO in cortical pathways

There is now considerable evidence for the existence of two or more visual cortical pathways in primates (for reviews, see Ungerleider and Mishkin, '82; DeYoe and Van Essen, '88; Desimone and Ungerleider, '89). According to the model originally proposed by Ungerleider and Mishkin ('82) on the basis of behavioral studies, the dorsal pathway, which projects from V1 through multiple prestriate areas to the posterior parietal cortex, mediates visual spatial perception and the visual guidance of movements. By contrast, the ventral pathway, which projects from V1 through multiple prestriate areas to the inferior temporal cortex, mediates the visual recognition of objects. Anatomical studies have supported this distinction. The major element of the dorsal pathway appears to involve projections from V1, V2, and V3d via MT to further areas in parietal cortex, whereas the ventral pathway involves projections from V1 and V2 to V4 which in turn projects to TEO and TE in the inferior temporal cortex. Recent work has indicated the possible existence of a third pathway, one which also begins with the projections of V1, V2, V3d to MT, but which continues with the further projections via MST and FST to areas in the rostral part of the superior temporal sulcus (Boussaoud et al., '90). Since neurons in the rostral STS often respond to complex kinds of motion, such as optical flow, rotational movement, or opponent vector motion (Bruce et al., '81; Hikosaka et al., '88), this third pathway may be specialized for the analysis of visual motion. Indeed, some cells in this region have been reported to be selective for particular types of “biological” motion, such as walking (Perrett et al., '85). Alternatively, the pathway into the rostral STS may be involved in more than motion analysis. Cortex in the rostral STS receives strong convergent input from areas in both
Fig. 15. Schematic illustration of the connections of area TEO, shown on a lateral view of the macaque brain. The lunate, intraparietal, superior temporal, and arcuate sulci have been opened up to reveal the location of visual areas within them. Solid arrowheads indicate feedforward connections, i.e., those in which labeled terminals are heaviest in layer IV; open arrowheads indicate feedback connections, i.e., those in which labeled terminals are lightest in layer IV, and reciprocal solid arrowheads indicate intermediate-type connections, i.e., those in which labeled terminals are evenly distributed across all layers.

The anatomical connections of area TEO clearly indicate that it occupies an important position in the ventral processing pathway (see Fig. 16). Of those areas connected with TEO, V4 provides the strongest input and TE receives the strongest output (see Table 1). The results of behavioral studies support the idea that TEO plays a crucial role in processing information needed for object recognition. In monkeys, lesions confined to TEO cause severe deficits in discrimination of two-dimensional patterns (Iwai and Mishkin, '68, '69; Kikuchi and Iwai, '80). By contrast, lesions of TE leave this ability nearly unimpaired but result in marked impairment in object recognition memory (Iwai and Mishkin, '68, '69; Kikuchi and Iwai, '80; Spiegler and Mishkin, '81; Mishkin, '82). Furthermore, lesions of area V4 result in significantly elevated thresholds for color and orientation matching and hue discrimination, while pattern and texture matching and shape discrimination are moderately impaired and achromatic intensity thresholds are not changed at all (Heywood and Cowey, '87; Desimone et al., '90; Schiller and Lee, '91; Walsh et al., '92). Therefore, even though V4, TEO, and TE are part of the same processing pathway, at each level of processing the neural coding of visual objects appears to be based on object features that are increasingly complex. Consistent with this idea, recent studies indicate that the visual properties of cells in TEO are intermediate in complexity between V4, on the one hand, and TE, on the other (Fenstermaker et al., '85; Tanaka et al., '87, '91; Boussaoud et al., '91; Fujita et al., '92).

Our results on the connections of TEO also provide a possible explanation for why monkeys with V4 lesions, though impaired on a variety of color, orientation, and form discriminations, show some sparing of function on these tasks. Until now, it had been assumed that a lesion of V4 would disconnect the inferior temporal cortex from its visual input. However, we have shown that V2 and V3 both project directly to TEO, thereby providing a pathway for visual input to TE that bypasses V4. Moreover, Nakamura et al. (93) have shown that the cells in V2 that project to TEO and those that project to V4 are located in the same subregions of V2, namely, the thin cytochrome oxidase rich stripes and the interstripes. This implies that the same color and form information that is being transmitted to V4 is also being sent to TEO (DeYoe and Van Essen, '85; Zeki and Shipp, '89). Our anatomical results would thus explain why TE neurons are still visually responsive after V4 lesions (Desimone et al., '90).

In addition to its role in the ventral processing pathway, our data indicate that TEO interacts with a number of areas outside this processing pathway. In particular, in
Fig. 16. Summary diagram of the visual cortical hierarchy (adapted and updated from Ungerleider and Desimone, '86b; Boussaoud et al., '90). Solid lines indicate connections originating from both central and peripheral field representations, while dotted lines indicate connections restricted to peripheral field representations. Solid arrowheads indicate feedforward connections, open arrowheads feedback connections, and reciprocal solid arrowheads intermediate-type connections (see figure 15). The diagram demonstrates the crucial anatomical position of TEO within the inferior temporal (object vision) processing stream as well as its potential for communication with the parietal (spatial vision) and superior temporal (motion analysis) processing streams. The shaded regions on the lateral view of the brain represent the extent of visual cortex contributing to the three streams of processing. The shaded areas enclosed by boxes indicate the final stations of these processing streams.
parietal cortex. TEO is interconnected with area LIP, and, among the motion-sensitive areas, TEO is interconnected with MT and FST. It is tempting to speculate that the interaction of TEO with these areas might contribute to networks underlying the perception of objects in space and objects in motion.

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LITERATURE CITED


CORTICAL CONNECTIONS OF AREA TEO


