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Synaptic Organization of Cortico-Cortical Connections From the Primary Visual Cortex to the Posteromedial Lateral Suprasylvian Visual Area in the Cat

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ABSTRACT

The synaptic organization of the projection from the cat striate visual cortex to the posteromedial lateral suprasylvian cortical area (PMLS) was examined. The anterograde tracer *Phaseolus vulgaris* leucoagglutinin (PHA-L) was iontophoretically delivered into area 17, and anterogradely labeled fibers were revealed in PMLS by means of an immunocytochemical detection method. Most axons and presumptive terminal swellings were found in layers III and IV. The neuronal elements (n = 190) that were postsynaptic to anterogradely labeled boutons were quantitatively analyzed. All anterogradely labeled cortico-cortical boutons (n = 182) established type 1 synapses. The results show that 83% of the postsynaptic targets were dendritic spines, probably belonging to pyramidal cells. Dendritic shafts constituted 17% of the targets. The dendritic shafts postsynaptic to cortico-cortical boutons were studied for the presence of gamma-aminobutyric acid (GABA) with a postembedding immunogold method. Most dendritic shafts (85%) that were tested were found to be GABA-positive, demonstrating that they originate from local inhibitory neurons. Taking into account that most postsynaptic targets were spines and extending the results of the immunocytochemical testing to the total population of postsynaptic dendrites, it was calculated that at least 14% of targets originated from GABA-positive cells.

Thus cortico-cortical axons establish direct monosynaptic connections mainly with pyramidal and to a lesser extent with GABAergic nonpyramidal neurons in area PMLS, providing both feedforward excitation and feedforward inhibition to a visual associational area known to be involved in the processing of motion information. The results are consistent with previously demonstrated deficits in physiological properties of neurons in PMLS following removal of cortico-cortical afferents.

Key words: visual system, immunocytochemistry, GABA inhibition, dendritic spines, pyramidal neuron, synapse

The visual system of the cat has often been divided into two components: a geniculo-striate and an extrageniculo-striate visual system. Much of the visual function in cats is preserved after ablation of the geniculo-striate-cortical system (see Creutzfeldt, '88; Spear, '88). One area responsible for the residual vision is the visual cortex around the suprasylvian sulcus, which receives a substantial visual input through the superior colliculus and the pretectum. Neurons in this area respond to visual stimuli even in the absence of striate cortex, preserving some of their specific functional properties (Spear and Baumann, '79). The best-studied area in this region of the cat extrastriate cortex is known as the posteromedial lateral suprasylvian cortical area, or PMLS. This area, located around the posterior portion of the medial bank of the suprasylvian sulcus, was discovered early in the study of visual cortical areas (Marshall et al., '43, Clare and Bishop, '54). It is the target of different parallel visual pathways and therefore ideally situated to integrate different types of visual information. In addition to several subcortical visual inputs, PMLS receives input from areas 17, 18, 19, 20a, 21a, and b, the anteromedial lateral suprasylyian, and ventral lateral suprasylvian areas of the visual cortex (Heath and Jones, '71; Hutchins and Updyke, '88; Sherk, '86a,b; Sherk and Om-

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brellaro, '89; Spear, '88; Sugiyama, '79; Symonds and Rosenquist, '84a; Tong et al., '82; Updyke, '81).

Neurons in area PMLS have large receptive fields and poor spatial resolution. They are direction and orientation selective and highly responsive to moving stimuli. A higher proportion of cells in PMLS is direction selective than in any other cortical or subcortical visual structure. Several investigators have demonstrated that neurons in area PMLS preferentially respond to stimuli moving on the axis connecting the centre of their receptive fields with the centre of the visual field (Blakemore and Zumbroich, '87; Palmer et al., '78; Rauschecker, '88; b; Rauschecker et al., '87a,b; Sherk, '89, Spear and Baumann, '75, Zumbroich and Blakemore, '87). The receptive field characteristics and the particular axis of movement to which PMLS neurons respond preferentially, together with findings that lesions of the suprasylvian cortex produce deficits in speed discrimination (Pasternak et al., '89), have led to the suggestion that this area may be concerned with the detection of flow patterns resulting from self-motion (Blakemore and Zumbroich, '87; Rauschecker, '88; Rauschecker et al., '87a,b).

To determine how physiological response properties in PMLS are generated, the effects of lesions to primary visual cortex and superior colliculus, areas known to provide direct and indirect innervation to PMLS, have been studied (Smith and Spear, '79; Spear and Baumann, '79). Experiments in which areas 17 and 18 were removed indicated: (1) a decrease in the proportion of cells showing direction selectivity, (2) an increase in the proportion of cells that responded as well or better to stationary flashing stimuli as to moving stimuli, and (3) a decrease in cells driven by the ipsilateral eye and an increase in cells being driven by the contralateral eye. It is likely that removal of both excitatory and inhibitory mechanisms were involved in these changes: the loss of response from the ipsilateral eye representing a loss of excitatory inputs, the increased response to stationary flashing stimuli a loss of inhibitory inputs. The loss of direction selectivity could be due either to removal of inhibitory influences to the null directions of movement, or to the loss of excitatory drive to the preferred direction of movement.

Very little is known about the synaptic organization of cortico-cortical connections. Previous studies showed that cortico-cortical terminals form asymmetric synapses with dendritic shafts and spines (Fisken et al., '75; Jones and Powell, '70; Porter and Sakamoto, '88; Sloper and Powell, '79). However, the proportions of the two major cortical cell classes, the spiny excitatory and the GABAergic inhibitory neurons, among the recipient cells have not been established. In order to determine the relative weights of the excitatory or inhibitory components in cortico-cortical connections, we examined the synaptic organization of this projection. We particularly sought to determine whether cortico-cortical afferents provide both excitatory and inhibitory inputs to PMLS, as suggested by the physiological literature (Smith and Spear, '79; Spear, '88; Spear and Baumann, '79). Preliminary reports of this work have been presented as an abstract (Lowenstein and Somogyi, '89).

MATERIALS AND METHODS

Two cats were used. Anaesthesia was induced with nitrous oxide and halothane and maintained with an intravenous mixture of steroid anaesthetics (Saffan, Glaxovet). The lectin *Phaseolus vulgaris* leucoagglutinin (PHA-L, Vector; 2.5% dissolved in 10 mM phosphate-buffered saline, pH 7.4 (Gerfen and Sawchenko, '84) was iontophoretically delivered into the middle layers of the medial portion of the lateral gyrus through glass micropipettes (internal diameter 20–60 μm). The capillary was positioned visually near to the border region of areas 17 and 18 in the posterior pole of the occipital lobe. PHA-L was delivered by positive constant current of 5 μA, the current being delivered in a cycle of 7 seconds on and 7 seconds off over a period of 15–20 minutes per site (Gerfen and Sawchenko, '84). A total of 6–9 injections were made unilaterally in each cat, some of them placed in the same penetration at different depth. After a survival of 6–8 days, the animals were deeply anaesthetized with chloral hydrate (40 mg/100 g initially and supplemented until all reflexes were abolished) and perfused transcardially first with oxygenated Tyrode solution for 1–2 minutes and then with fixative containing 2% paraformaldehyde, 1% glutaraldehyde, 0.2% picric acid in 0.1 M phosphate buffer (PB), pH 7.4. Each animal was perfused with approximately 1.5 l of fixative for 30 minutes.

After perfusion, the brain was immediately removed and the visual cortex was cut into small blocks of tissue. These were cryoprotected in 10 and 20% sucrose in PB, frozen in liquid nitrogen, and immediately thawed. Vibratome sections (50–70 μm thick) were cut and collected into PB. The sections were exhaustively washed in PB (6 × 30 min) before starting the immunohistochemical detection of the lectin. The sections were first incubated in 20% blocking serum (normal goat serum) for 40 minutes, briefly washed in the incubating buffer, Tris-buffered saline (TBS) 50 mM, pH 7.4, and then transfered to a solution of biotinylated rabbit anti-PHA-L (Vector, 1:200), for 2–3 days at 4°C in TBS containing 1% normal goat serum. Alternate sections were incubated in the presence or absence of 0.5% Triton X-100. Triton-treated sections were used for light microscopy. After washing the sections in TBS, they were incubated for 4 hours in avidin-biotin complex (ABC, Vector) diluted 1:100 in TBS. The sections were washed and reacted to reveal peroxidase activity by incubating in the dark in 3–3′-diaminobenzidine tetrahydrochloride (0.05%, DAB, Sigma) solution dissolved in Tris 50 mM at pH 7.6, and then H_2O_2 was added to each vial to a final concentration of 0.01%. The reaction was stopped after 1–5 minutes by removing the DAB/H_2O_2 solution and washing the sections extensively in Tris buffer. Some sections were reacted in the presence of nickel ammonium sulphate as an intensifier. After the immunoreaction, sections for light microscopy were mounted onto glass slides, dried, dehydrated in ascending series of alcohols, and mounted under coverslips. Sections for electron microscopy were extensively washed in PB to remove any remaining DAB, and they were treated with OsO_4 (1% in 0.1 M PB) for 60 minutes. Afterward the sections were dehydrated and embedded flat onto glass slides, using an epoxy resin, Durcupan ACM (Fluka). The resin was cured in an oven at 56°C for 48 hours.

The pattern of fibre distribution in PMLS was assessed in both sets of sections by light microscopy. Selected areas of PMLS were reembedded for electron microscopical study. Series of ultrathin sections were cut from these blocks, and the postsynaptic targets of anterogradely labeled cortico-cortical boutons were examined. Sections were picked up on single slot, formvar-coated nickel grids. Every second grid was stained with lead citrate and examined under the EM. When dendritic shafts were encountered as postsynaptic elements to PHA-L labeled terminals, they were examined

for the presence of GABA by postembedding immunogold reaction in order to determine their cellular origin. The following grid, which had not been lead stained, was reacted with an antiserum (Hodgson et al., '85) against the inhibitory neurotransmitter GABA, followed by a second antibody labeled with 15 nm gold particles (Janssen Pharmaceuticals). The immunocytochemical method has been described earlier (Somogyi, '88; Somogyi and Hodgson, '85). Briefly, after etching the sections and removing the osmium with sodium periodate, the sections were incubated in rabbit antiserum to GABA (code 9; 1:3,000) for 90 minutes. After washing, the sections were incubated with the second antibody for 2 hours. Any unbound second antibody was removed by washing and the sections were stained with saturated uranyl acetate in water followed by lead citrate.

It has been shown previously that at least some neurons that have high GABA levels in their terminals also have high GABA levels in their dendrites (Somogyi and Soltesz, '86). However, dendritic GABA levels can be variable and often lower than those in terminals. Therefore quantitative criteria are required to classify dendrites as immunonegative or immunopositive. Accordingly, dendritic GABA immunoreactivity was assessed quantitatively, by measuring gold particle density, and compared to that of synaptic boutons forming type 2 or symmetrical synapses as well as of boutons forming type 1 or asymmetrical synapses (Gray, '59). Previous studies have shown that in the cortex of cat boutons forming type 1 synapses are not immunoreactive for GABA and glutamate decarboxylase (GAD); therefore the gold particle density over them can be considered as a baseline, representing nonspecific background or GABA diffused during fixation. In contrast, almost all boutons forming type 2 synapses have been shown to be immunoreactive for GAD (Ribak, '78) and GABA (Beaulieu and Somogyi '90); therefore the density of gold particles over them probably represents the transmitter pool of GABA in nerve terminals.

Measurements were made for 13 axo-dendritic synaptic contacts established by PHA-L positive boutons. The sectional areas of the following profiles were measured from each micrograph: all dendrites, including the dendrite postsynaptic to PHA-L labeled terminal; at least the 2 (up to 5) boutons nearest to the PHA-L labeled terminal and forming type 2 synaptic junctions and/or containing pleomorphic vesicles; at least 2 (up to 5) nearest boutons (excluding the PHA-L labeled terminal) forming asymmetrical synaptic junctions and/or containing round synaptic vesicles. The area covered by mitochondria in each profile was also measured, because in GABA-immunopositive neurons mitochondria reacts most strongly for GABA. Thus measurements on mitochondria may be the most sensitive indicator whether the dendrite originated from a GABAergic neuron. Gold particles were counted over each area and the unit density of particles was calculated for the whole profile and for mitochondria separately. In most cases density values were obtained from 2–3 different sections of the same profiles on the same grid, and values were averaged. Gold particle density was also averaged between the boutons of the same class.

The immunogold reaction gives variable density of gold particles and variable background between reactions carried out on different days and under different conditions. In the present series of experiments, measurements were accepted only from reactions that produced at least a 9 times (21.3 ± 14.3, mean $\pm$ S.D., $n = 12$, range 8.9–61.4) higher particle density over boutons forming type 2 synapses as compared to boutons forming type 1 synapses. Comparison of dendritic immunoreactivity from different incubations and from different animals was made by a normalization process, dividing dendritic immunogold density by gold density over nerve terminals making either type 1 or type 2 synapses in the same section. The same process was also carried out for all dendritic profiles in the same micrographs.

The same sections were also used to examine the postsynaptic targets of boutons unlabeled by PHA-L and forming asymmetric synapses in PMLS. Long series of photographs were taken and the targets of unlabeled boutons were classified as spines or dendritic shafts with the same criteria that were used to classify the targets of labeled terminals. Their GABA immunoreactivity was assessed qualitatively, by comparing the gold density to that of boutons making type 1 (GABA-negative) or type 2 (GABA-positive) synapses. These data were then compared to previously published data for area 17 of the cat visual cortex (Beaulieu and Colonnier, '85; Bueno-Lopez et al., '89; Gabbott et al., '87; Kisvarday et al., '86; McGuire et al., '84).

RESULTS

Injections and light microscopic observations

Injections were centred in area 17. Figure 1 shows the largest injection site in cat 1. Labeled cells are present in all layers, including layers II to VI, but predominantly in layers II–III, which send forward projections to PMLS. Injection sites did not involve the white matter. Up to 9 closely spaced sites were injected in each animal, but not all of them could be reconstructed separately. The largest injection site probably represents the fusion of 2 deliveries along a single track. Although some retrogradely labeled cells can be seen in area 18, no such cells were found in PMLS. In cat number 2, injection sites were smaller and confined mainly to cells in the supragranular layers. In this case no retrogradely labeled cells were found in area 18 or in area PMLS.

In area PMLS, PHA-L labeled fibers were mainly encountered around the middle layers. Ascending axons, which had small enlargements, could be observed in layers V and VI, and some axons were also seen ascending through layers II and III. The axonal arborization in layers II and upper III were less extensive than in layers IV or lower layer III. The density of fibers and boutons was generally low in all layers (Fig. 2). The course of the axon collaterals and the density of boutons can be observed in photomontages of axons in the middle layers of area PMLS (Fig. 3). Cortico-cortical axons were of fine calibre giving mainly small en passant boutons. Some boutons were also found at the end of short stalks (Fig. 3). Although no thin terminal branches were seen in layers V and VI, the ascending axons showed varicosities. These may represent synaptic boutons or concentrations of mitochondria.

Postsynaptic targets of cortico-cortical afferents in PMLS

Two blocks from cat 1 and one block from cat 2 were sectioned serially for electron microscopy from layers III–IV of area PMLS. The areas were selected under the light microscope for their high density of labeled terminals. Cortico-cortical axons were identified under the electron

Fig. 1. An injection site of PHA-L is shown as revealed immunocytochemically. The section shown was treated with detergent to show maximum labeling. The injection site is mainly located in area 17 but encroaches upon the border of areas 17/18. Labeled neurons were present in all layers, but the injection site did not involve the white matter. Note the axon bundle leaving the cortex and the stream of fibers radiating laterally from layer III. A few retrogradely labeled cells were found in area 18. Scale = 1 mm.

microscope by the high electron density of the peroxidase reaction end product (Figs. 4–6), and they were followed in adjacent sequential sections until bouton-like enlargements were found. Labeled boutons were typically small, usually up to 1 μm in diameter, and all established type 1 synapses (Gray, '59), with pronounced postsynaptic membrane specialization (e.g., Fig. 4). Most boutons were found to make one synapse (Fig. 4A,C,D). Only 7 boutons in cat 1 and one bouton in cat 2 established 2 synapses (Fig. 4B). No bouton established more than 2 synapses. The synapse per bouton ratio was 1.04.

In the visual cortex the postsynaptic targets of type 1 synapses can be dendritic spines, dendritic shafts, or somata (Beaulieu and Colonnier, '85). Dendritic spines are not thought to contain either mitochondria or microtubules, and they frequently display a membranous structure called the spine apparatus (Fig. 4A). Spines are found on the dendritic shafts of pyramidal and spiny stellate cells, and infrequently on other types of nonpyramidal neurons. Since pyramidal and spiny stellate neurons possess the vast majority of spines in the visual cortex and they have been shown to make excitatory efferent connections, we considered all spines as belonging to excitatory neurons. In the cortex, dendritic shafts can be distinguished from dendritic spines on the basis of the presence of mitochondria and/or microtubules. Dendritic shafts can belong to pyramidal, spiny stellate neurons or to neurons with few or no spines on their dendrites; most of the latter are thought to be inhibitory and use GABA as transmitter. Serial reconstruction of dendritic shafts can aid in establishing whether a given dendritic shaft belongs to spiny or smooth dendritic neurons. However, this procedure is time-consuming and can give equivocal results in some cases. Instead, the presence of immunoreactive GABA in the dendrite was used to establish whether a postsynaptic dendrite originated from local circuit inhibitory neurons. Osmium, which provides the high electron density of the anterogradely labeled boutons, is removed from the sections during the immunoreaction for GABA; therefore the boutons are easier to recognise in unreacted sections (e.g., Fig. 5).

The 182 PHA-L labeled cortico-cortical boutons established synapses with 190 postsynaptic elements; 83% of them were dendritic spines (Fig. 4; see also Table 2) considered to belong to pyramidal neurons, whereas 17% were dendritic shafts. Only one spine was found to receive both a type 1 synapse from the PHA-L labeled and a type 2 synapse from an unlabeled terminal (Fig. 4A). However, not all spines were completely serially reconstructed, so the proportion of postsynaptic spines receiving dual innervation is not known. Some boutons (8) established 2 synapses either with a spine and a dendritic shaft (Fig. 4B), or with 2 spines.

Dendritic shafts postsynaptic to 17 out of 32 boutons originating from areas 17/18 were reacted for the presence of GABA. In 3 cases the reaction failed for technical reasons. In one case the dendrite was less than 0.1 μm in diameter and in each of 2 immunoreacted sections, one gold particle was found on it. Because of the small area of the dendrite, it appeared immunopositive by the calculated criteria based on gold particle density presented below. Nonetheless, the dendrite was excluded from the sample since one gold particle can occur anywhere by chance. Two PHA-L labeled boutons made synaptic contacts with the same dendrite; therefore a total of 12 postsynaptic dendrites were quantitatively evaluated for GABA immunoreactivity. In addition, 53 dendrites present in the same micrographs, but not receiving synapses from PHA-L labeled terminals, were also measured (Figs. 7, 8).

In the present material, boutons forming type 2 synaptic contacts (type 2 bouton) had 21.3 ± 14.3 (mean ± S.D., n = 12, range 8.9–61.4) times higher gold particle density than boutons (type 1 bouton) forming type 1 synapses in the same area (e.g., Fig. 7). Dendrites were considered GABA-positive when the following criteria were met: (1) a particle density ratio of dendrite per type 1 boutons of at least 4 (8.6 ± 5.7, S.D., n = 10, range 4.1–21.1), (2) a particle density ratio of dendrite per type 2 boutons of at least 0.25 (0.42 ± 0.15, n = 10, range 0.26–0.63), (3) a particle density ratio of dendritic mitochondria per mitochondria in type 2 boutons of at least 0.25 (0.55 ± 0.15, n = 9, range 0.26–0.78). Using these criteria, 10 out of 12 dendrites receiving PHA-L labeled synaptic boutons were identified as GABA-immunopositive. This high proportion of GABA-positive dendrites among the successfully tested ones is not due to a generally high level of GABA immunoreactivity in all dendrites, since analysis of the total popula-

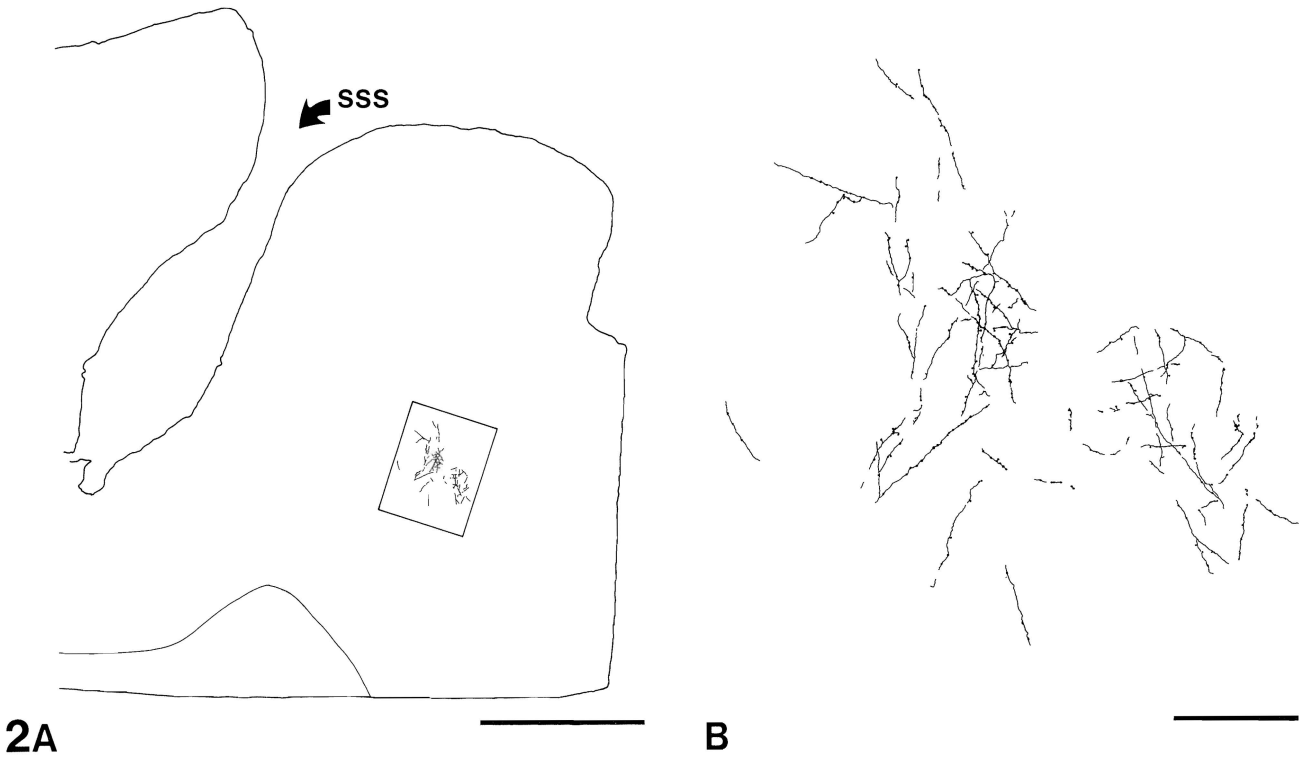

Fig. 2. Drawing of PHA-L labeled axons originating in areas 17/18 and shown in a 70-μm-thick section of area PMLS. The exact location of the fibers and terminals is shown in the inset in **A** (SSS, suprasylvian sulcus), which is reproduced at higher magnification in **B.** This is one of the areas that was subsequently resectioned for electron microscopy. Dorsal is to the top and medial is to the right of the figure. Scales: A = 1 mm; B = 130 μm.

tion of dendrites clearly revealed populations with either low or high GABA immunoreactivity (Fig. 8). The two GABA-negative dendrites and the untested dendrites did not show obvious qualitative features different from the GABA-positive ones that would have allowed their classification without immunoreaction.

It is apparent from the quantitative analysis that even the most strongly immunopositive dendrites show lower particle density than type 2 (GABAergic) boutons in the same section (Fig. 5). The GABA-positive postsynaptic dendrites usually, but not always, had a high volume density of mitochondria (e.g., Fig. 6). The ratio of mitochondrial GABA immunoreactivity was calculated because it was noticed that in GABA-positive dendrites immunogold particle density over mitochondria was 3.1 ± 1.6 (n = 9, range 0.8–5.8) times higher than over the rest of the dendrite (Figs. 5, 6). Only in one dendrite, considered GABA-positive, was particle density lower in mitochondria than in the rest of the dendrite. Although GABA present in nerve terminals is thought to be localized in the synaptic vesicles, the immunolabeling is not restricted to them but is also high over mitochondria (Figs. 5D, 7A). The high immunoreactivity of mitochondria could result from the presence of very high concentration of GABA in situ, or possibly from the coupling of GABA to mitochondrial basic proteins by the fixative. In any case, in a given dendrite all mitochondria were either immunonegative or immunopositive, demonstrating that the latter dendrites originated from local inhibitory neurons. The immunoreactivity ratios obtained on the basis of mitochondria are consistently closer to one than those obtained on the basis of the whole sectional profile, indicating that in most cases immunoreactivity of mitochondria in GABA-positive dendrites and boutons is more similar than other areas of the same structures. Density ratios calculated using mitochondrial particle density in type 1 boutons (GABA-negative) also provided higher ratio both for dendritic and type 2 bouton immunoreactivity. However, in type 1 boutons, mitochondria often had zero gold particle density; therefore the immunoreactivity of GABAergic structures cannot be expressed as multiples of mitochondrial immunoreactivity level.

The data on the postsynaptic elements for each cat are shown in Table 2. Slightly more dendritic shafts were found amongst the postsynaptic elements in cat 1, where the injection in area 17 involved all layers, than in cat 2 where it was limited largely to the supragranular layers. The difference in the distribution of postsynaptic targets may be related to the different types of pyramidal cells giving rise to the projections. No qualitative difference could be identified between the dendritic shafts that were not tested for the presence of GABA and those that were. Nine of the untested ones received other synapses, and they contained between none and 4 mitochondrial profiles. There was no obvious correlation between the number of mitochondrial profiles and the dendritic shaft receiving other synapses.

Quantitative distribution of postsynaptic elements in the middle layers of PMLS

In order to determine any selectivity with regard to targets postsynaptic to cortico-cortical terminals, our data

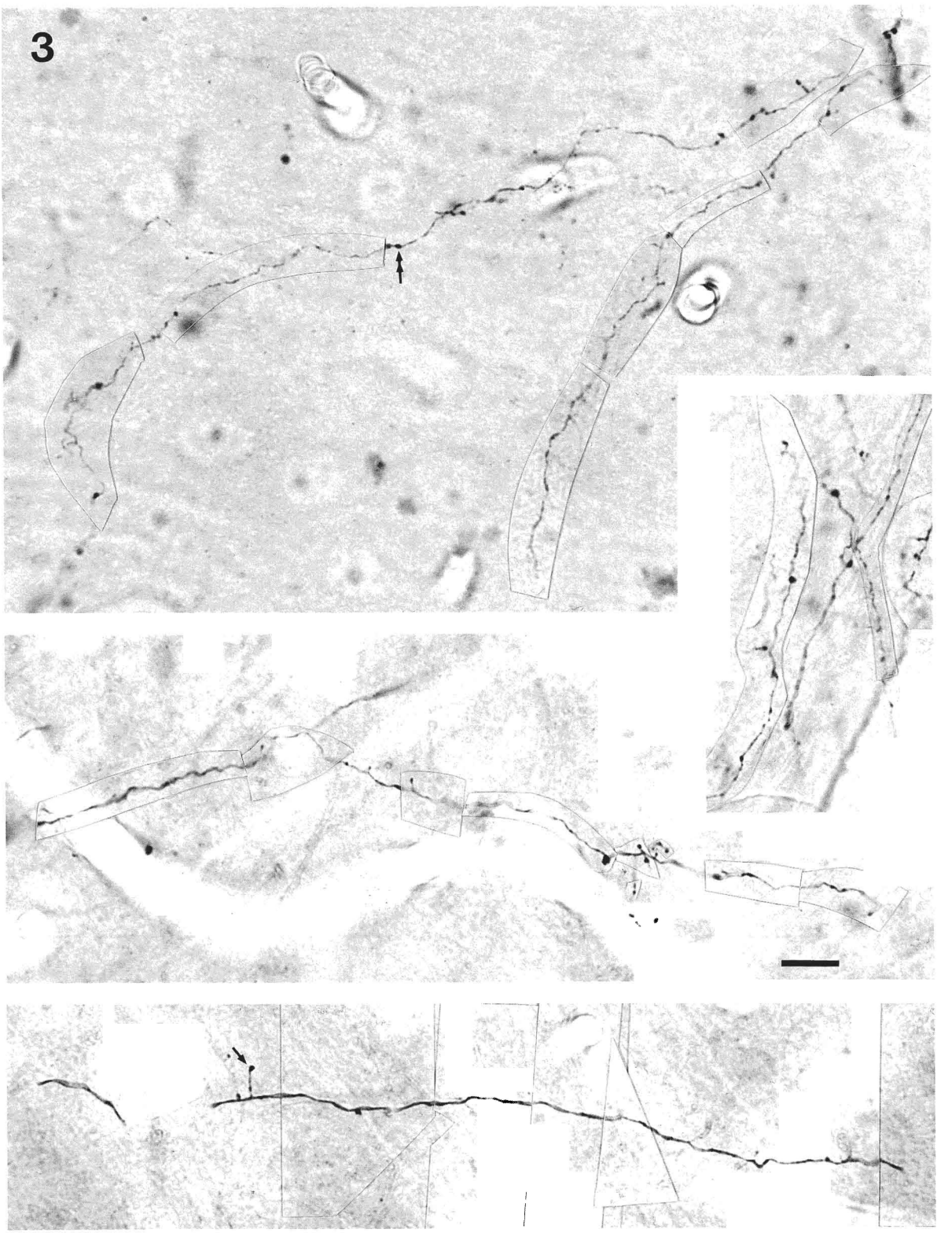

Fig. 3. Light micrograph of anterogradely labeled axons in area PMLS. Notice en passant boutons (e.g., double arrow) and boutons forming clublike endings on thin stalks (e.g., single arrow). Some areas contain clusters of boutons. Scale = 10 μm.

on anterogradely labeled boutons in area PMLS were compared with the quantitative distribution of postsynaptic target for 893 unidentified boutons forming type 1 synapses in layers III–IV of area PMLS. A similar comparison was also made with 734 boutons making type 1 synapses in layer IV of area 17 (Bueno-Lopez et al., '89). Examples of representative boutons and postsynaptic elements in area PMLS are shown in Figure 7. The data in Table 1 indicate that the synaptic organization of cortico-cortical and unidentified boutons forming type 1 synapses in layers III-IV of area PMLS differs. Unidentified boutons made synapses with dendritic shafts more frequently than did cortico-cortical terminals from area 17 and 18. Furthermore, only 27% of dendritic shafts contacted by unidentified type 1 synapses were GABA-positive; more than two-thirds of dendritic shafts contacted by cortico-cortical boutons were immunoreactive for GABA. These differences indicate a bias in the targets of cortico-cortical boutons in area PMLS.

DISCUSSION

Origin of PHA-L labeling in PMLS

PHA-L was selected as a tracer for labeling cortico-cortical terminals because it labels fibers mainly anterogradely with little retrograde transport (Gerfen and Sawchenko, '84). No retrogradely labeled pyramidal cells were present in PMLS. This enabled us to make the assumption that the presence of PHA-L immunoreactivity in synaptic terminals identified them as originating from area 17 and possibly from area 18. This latter source is largely due to the retrograde labeling of pyramidal cells in area 18 after PHA-L injection in area 17. These cells in area 18 may have collaterals projecting to PMLS.

Another possible interpretation of the observed labeling is that some of the boutons are derived from branched axons originating, e.g., in the C laminae of the LGN, which innervates both area 17, the injection site, and area PMLS (Tong and Spear, '86). However this is unlikely to be the case, because geniculate Y-type axons, the source of the branched projection, differ from known cortico-cortical axons in the pattern of branching, bouton size (Freund et al., '85a; Humphrey '85a,b) and their boutons also make multiple synapses (Freund, '85a; Winfield, '83). Certain characteristics of labeled axons in the present study, such as bouton density, axon thickness, and the clublike endings on short stalks, are similar to cortical axons, which have been shown to originate from pyramidal cells in the cat (Kisvarday et al., '86; Lund et al., '79; McGuire et al., '84; Szentagothai, '73, '78). Furthermore, the labeled boutons in PMLS in most cases made only a single synapse. Thus in all probability the PHA-L labeled terminals in area PMLS originated mainly from area 17 and perhaps to a much lesser extent area 18.

Laminar origin and termination of cortico-cortical axons

The cells that innervate PMLS from area 17 and 18 are located in layers II–III, with a few cells in layer IV–VI (Einstein and Fitzpatrick, '91; Gilbert and Kelly, '75; Henry et al., '78; Sherk, '86a; Symonds and Rosenquist, '84b). The 2 cats used in the present study differed in the location of the PHA-L-labeled cells at the injection site; in cat 1 labeled cells were present in supragranular layers as well as layers V and VI; in cat 2 they were restricted to supragranular layers. The difference in distribution of labeled cells could contribute to the difference in postsynaptic targets between the two animals (see below). Feedforward connections are thought to originate in supragranular layers and terminate mainly in the middle layers of other sensory areas. Feedback connections, in contrast, are thought to originate in infragranular layers and terminate mainly in supra- as well as infragranular layers of primary sensory cortices (Bullier and Kennedy, '87; Henry et al., '78; Symonds and Rosenquist, '84b). The projection from area 17 to PMLS conforms to this categorisation (Kato et al., '86; Kawamura and Naito, '76; Price and Zumbroich, '89; Sherk, '86a,b; Sugiyama, '79; Symonds and Rosenquist, '84a). The main termination zone was also found in the middle layers of PMLS using PHA-L, indicating a predominant feedforward projection. As in previous reports (Kato et al., '86; Sugiyama, '79), some PHA-L labeled terminals were also present in upper layer III and in layer II. Interestingly, thalamo-cortical axons also mainly innervate the middle layers of suprasylvian cortex (Kato et al., '86; Sherk, '86b), providing an opportunity for close interaction with cortico-cortical inputs.

The morphology of individual striate cortical afferent axons to area MT in the macaque monkey brain (Rockland, '89) has been examined using PHA-L. The main layer of termination was in layer IV of area MT, but terminal arbors were also found in layer VI from the same axons. Both area MT and area PMLS contain a very high proportion of direction selective cells and have been implicated in the analysis of motion and suggested to be homologous areas in primates and carnivores (Pasternak et al., '89).

Postsynaptic targets of cortico-cortical terminals

As in previous studies on other cortico-cortical pathways (Elhanany and White, '90; Fisken et al., '75; Gabbott et al., '87; Ichikawa et al., '85; Jones and Powell, '70; Kisvarday et al., '86; Porter and Sakamoto, '88; Sloper and Powell, '79) and on the area 17 to PMLS projection (Sugiyama, '79), dendritic spines constituted the main postsynaptic element to cortico-cortical terminals in PMLS. These spines very likely originate from pyramidal cells since spiny stellate cells have not been described outside primary sensory areas, and other nonpyramidal neurons have been shown to have few if any spines. In the motor cortex, most synapses originating in the somatosensory cortex onto smooth dendritic cells were found to terminate on the shafts, rather than on the occasional spines of identified sparsely spiny cells (Ichikawa et al., '85). Therefore spines of pyramidal cells are the main target of the striate cortex projection to area PMLS.

Several types of pyramidal cells from all layers extend their dendritic arbors within reach of the visual cortico-cortical terminals. For example, terminals of cortico-cortical afferents could establish synapses in the middle layers with the apical dendrites of cells from layers V and VI. Neurons from layers II, III, and V of area PMLS project to other cortical areas, layer V pyramids project to the superior colliculus, and layer VI neurons to the thalamus and other cortical areas (Kato et al., '86; Price and Zumbroich, '89; Symonds and Rosenquist, '84a,b). The afferents from area 17 could make synapses with any or all of these cells. Nevertheless, the predominant terminations in layer III and layer IV suggest that pyramidal cells in these layers are the main targets.

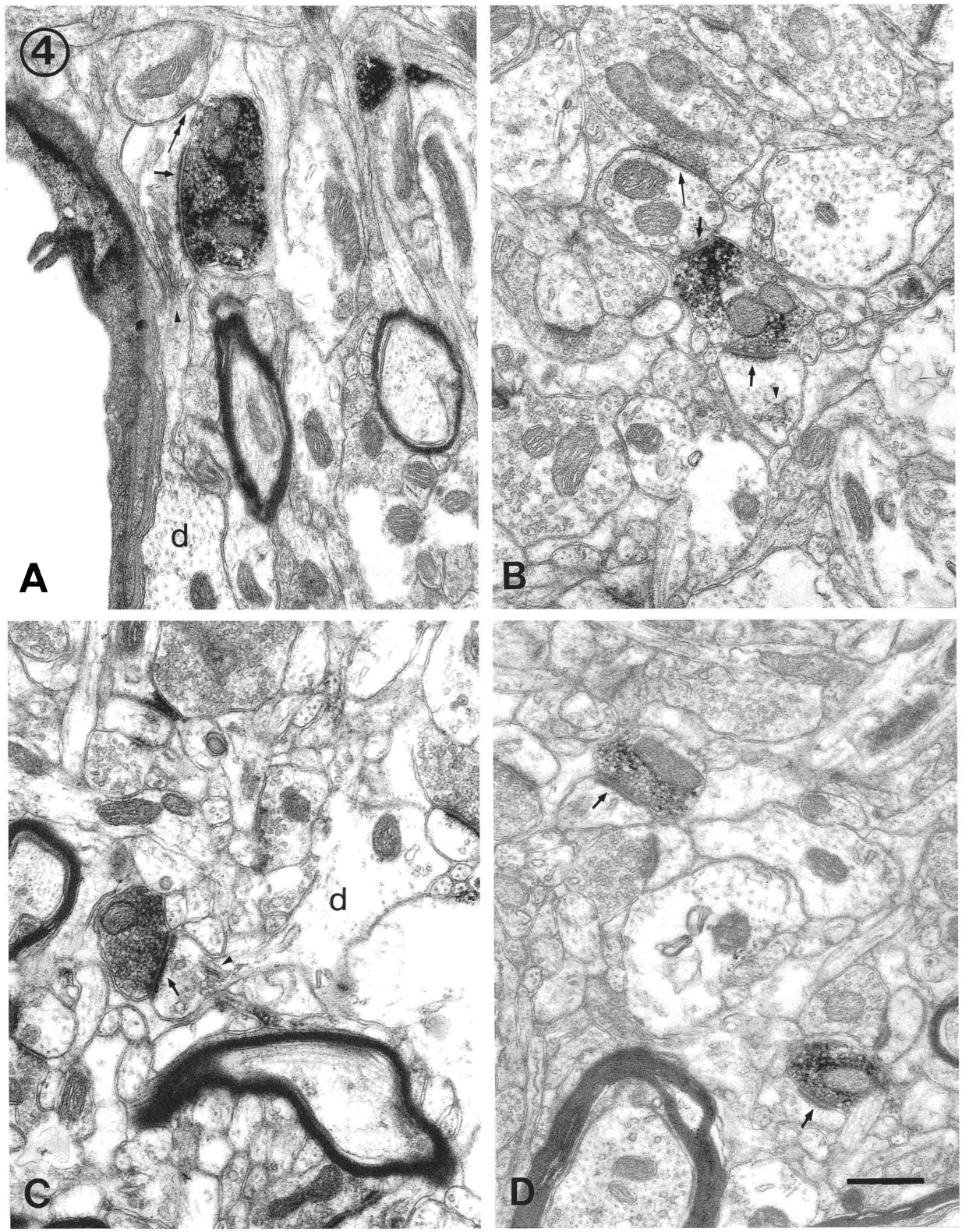

Fig. 4. Electron micrographs of cortico-cortical boutons establishing type 1 synapses mainly with dendritic spines in PMLS. **A, C.** Anterogradely labeled boutons establishing synapses with spine heads. The spine head can be followed through the spine neck back to the parent dendritic shaft (d). Small arrows indicate the postsynaptic densities. Small arrowheads label the spine apparatus. Double arrow in A labels a type 2 synapse established with the same spine receiving direct cortico-cortical input. **B.** A single bouton establishing two asymmetric synapses, one with a dendritic spine and another one with a dendritic shaft (long arrow). The dendritic shaft receives a second asymmetric synapse. Scale = 0.5 μm.

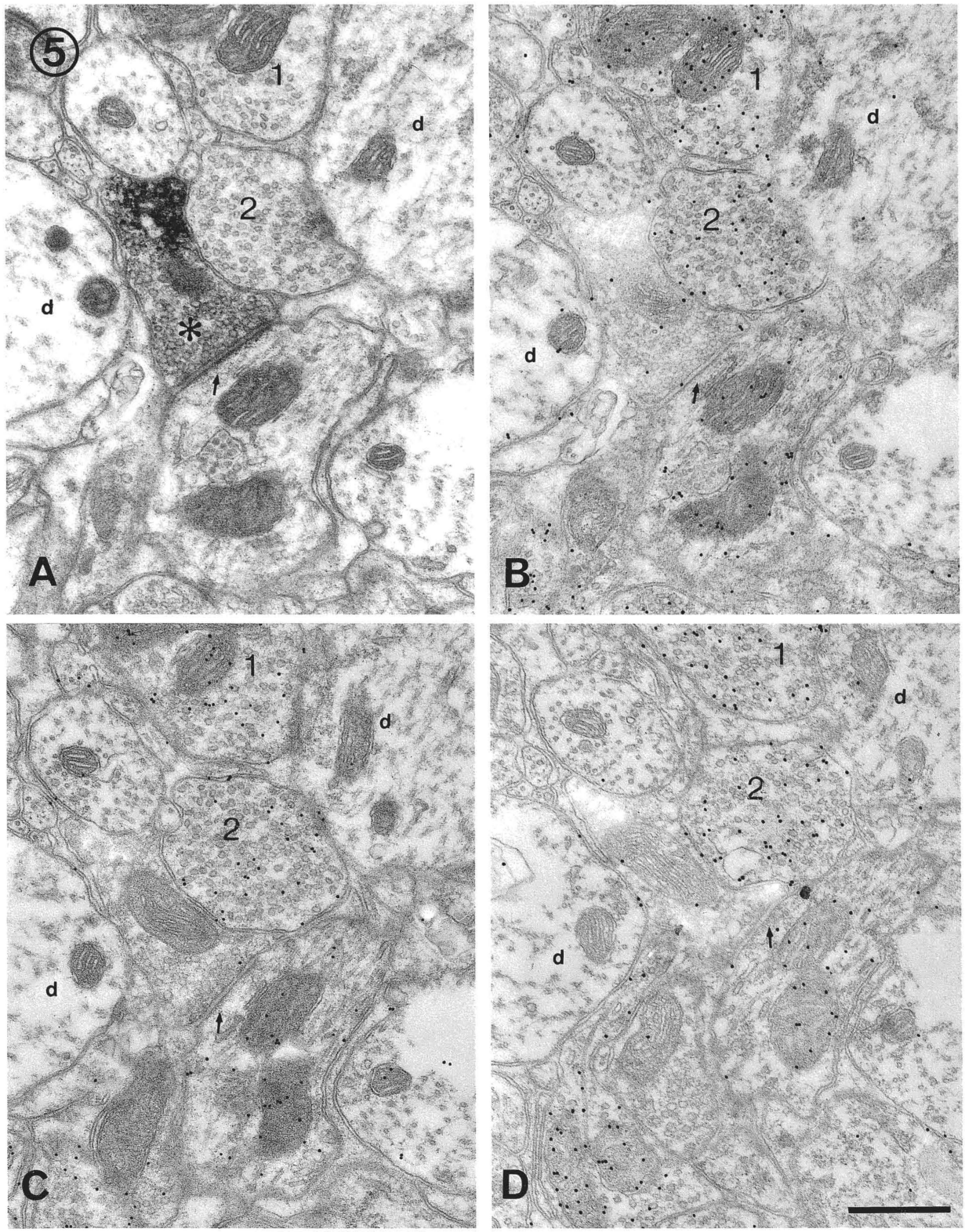

Fig. 5. Monosynaptic cortico-cortical innervation of a GABAergic interneuron in PMLS demonstrated in electron micrographs. **A–D.** Serial sections of an anterogradely labeled bouton (*) forming a synapse (arrow) with a dendritic shaft. **B–D.** Three sections immunoreacted for GABA. The postsynaptic dendrite, and some of the synaptic terminals (e.g., 1 and 2) have a high density of gold particles consistently demonstrating their GABA immunoreactivity. Other large dendrites (d) are unlabeled. Scale = 0.5 μm.

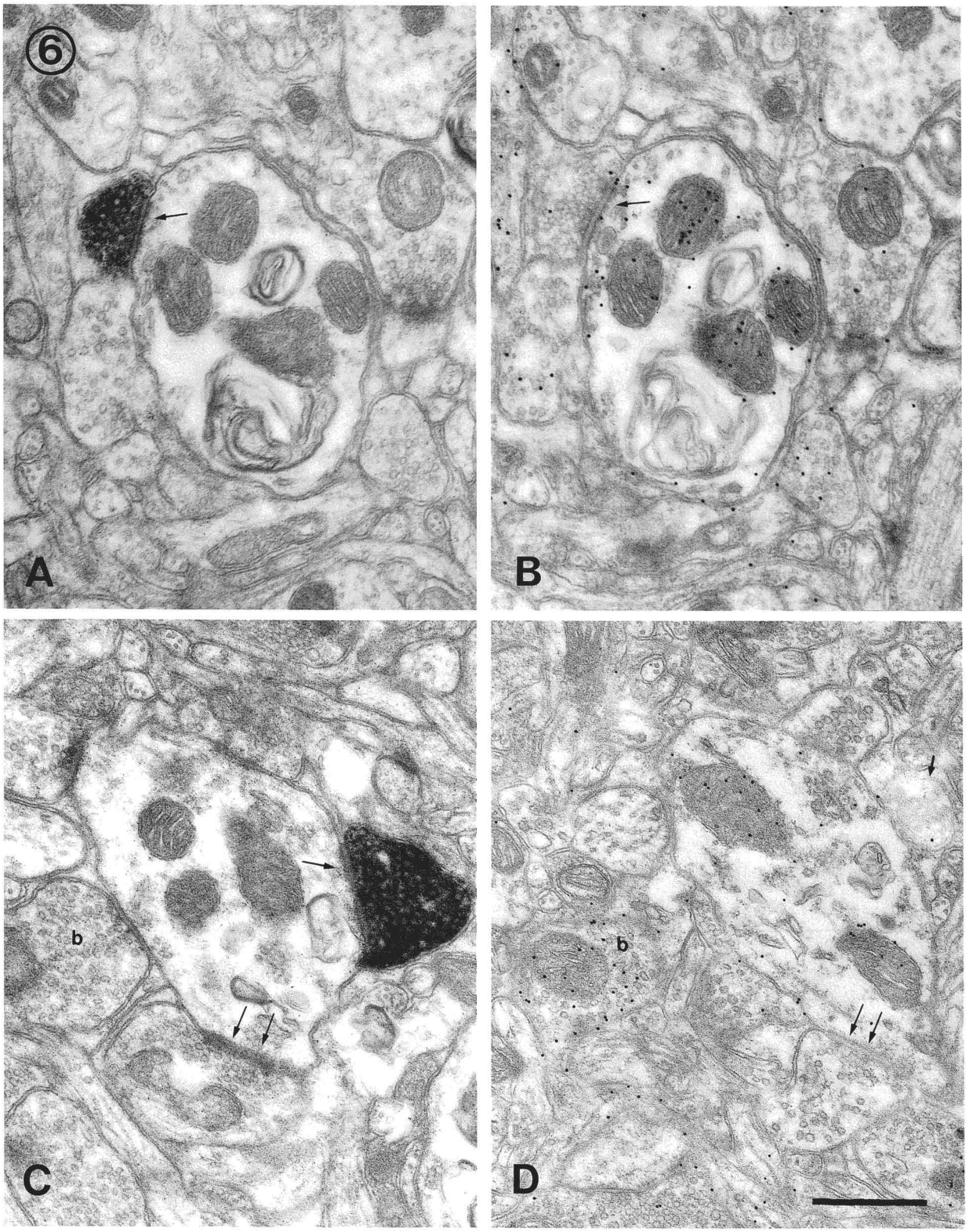

Fig. 6. Electron micrographs of PHA-L labeled boutons originating from areas 17/18 and establishing type 1 synapses (single arrows) with GABA-immunopositive dendrites. **A** and **C.** Two different anterogradely labeled boutons forming synapses (single arrows) with dendritic shafts, conventional sections. **B** and **D.** Serial sections reacted to detect GABA-like immunoreactivity. Both postsynaptic dendrites, and particularly their mitochondria have higher density of gold particles than the surrounding neuropil. The postsynaptic dendrite in C and D receives other synapses from a GABA-positive bouton (b) and from an immunonegative bouton forming a type 1 synapse. The electron density of the PHA-L labeled boutons (e.g., short arrow in D) is reduced during the immunoreaction. Scale = 0.5 μm.

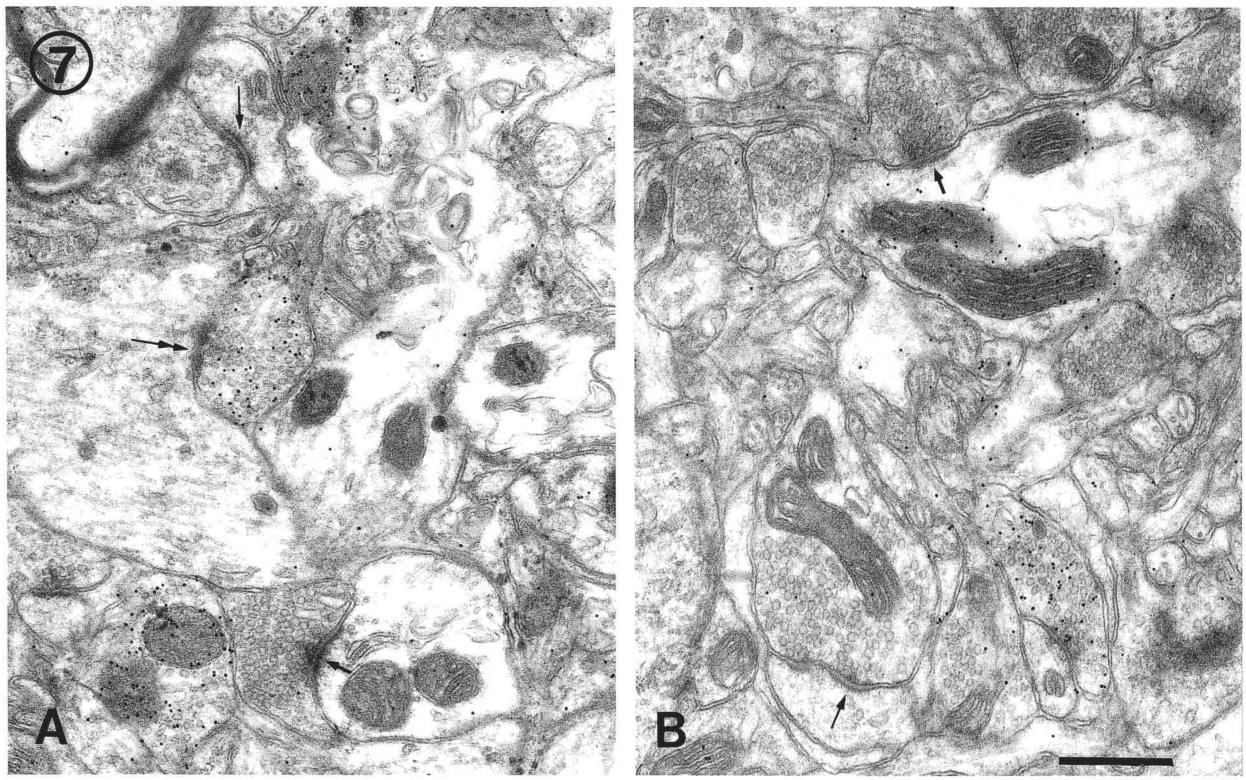

Fig. 7. This figure shows several categories of synaptic elements counted in the quantitative analysis of the middle layers of PMLS. Long arrows indicate type 1 asymmetric synapses with spines; short arrows indicate type 1 asymmetric synapses with dendritic shafts, (GABA-negative in **A;** GABA-positive in **B**). The double arrow in A indicates the presence of a GABA-immunopositive bouton establishing a synapse onto a GABA-negative dendritic shaft. Scale = 0.5 μm.

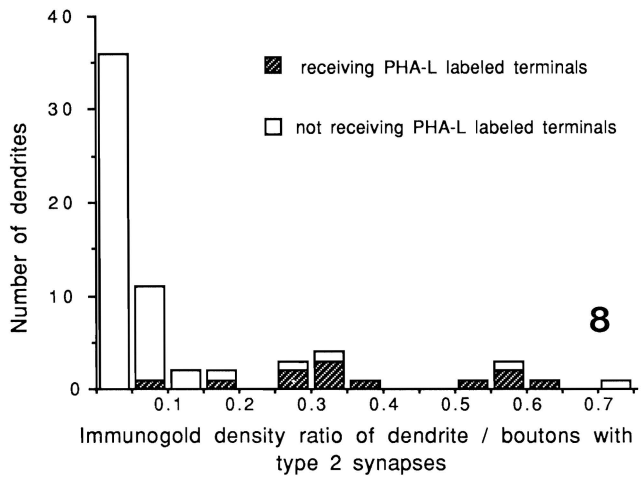

Fig. 8. Distribution of relative dendritic GABA immunoreactivity in area PMLS. Ratio of immunoreactivity was calculated relative to boutons containing pleomorphic vesicles and establishing type 2 synapses (GABAergic boutons) because the absolute density of gold particles depends on reaction conditions. Dendrites were considered to originate from GABAergic neurons if the ratio was higher than 0.25. Note that all but 2 of the dendrites receiving synapses from areas 17/18 were GABA-positive.

TABLE 1. Postsynaptic Targets of Type 1 Synapses in the Visual Cortex of the Cat[1]

	Spines	D. shafts	GABA-positive shafts/tested	Totals
Terminals in PMLS (middle layers) originating in area 17	158 (83%)	32 (17%)	11 out of 13 (85%)	190
Terminals forming asymmetric synapses in middle layers of PMLS (unknown origin)	634 (71%)	258 (29%)	71 out of 258 (27%)	893
Layer III pyramidal neurones in area 17 (terminals in layer III and V, area 17; Kisvarday et al., '86)	165 (86%)	25 (13%)	4 out of 12 (30%)	191
Terminals forming asymmetric synapses in area 17 (unknown origin, layer IV; Bueno-Lopez et al., '89)	421 (53%)	365 (46%)	75 out of 368 (20%)	794
Layer V pyramidal neurones in area 17 (terminals in layers IV, V, and VI, area 17; Gabbott et al., '87)	213 (80%)	53 (20%)	—	266
Layer VI pyramidal neurones in area 17 (terminals in layer IV, area 17; McGuire et al., '84)	43 (28%)	108 (72%)	—	151

[1]Quantitative distribution of electron microscopically identified targets of pyramidal cells in area 17 and area PMLS, and comparison with the overall population of type 1 synapses of unknown origin. The data on the targets of cortico-cortical boutons and unidentified boutons in PMLS were obtained in this study.

The postsynaptic targets in the two cats differed slightly in the proportion of dendritic shafts. This may be accounted for by the difference in the location of the injection sites, since in cat 1 they included layers V and VI, whereas in cat 2 they were restricted to the supragranular layers. It is possible that the postsynaptic targets differ for afferents originating from supragranular and infragranular neurons. It is interesting to note that the proportion of postsynaptic targets to supragranular pyramidal cells (cat 2) is almost identical to the proportion of postsynaptic targets of local

TABLE 2. Postsynaptic Targets of Cortico-Cortical Terminals in PMLS[1]

	Spines	Dendritic shafts	GABA-positive shafts	GABA-negative shafts	Unknown shafts	Totals
Cat 1	82 (79%)	22 (21%)	8	1	13	104
Cat 2	76 (88%)	10 (12%)	3	1	6	86
Total	158 (83%)	32 (17%)	11	2	19	190

[1]Quantitative distribution of postsynaptic structures in area PMLS receiving synapses from cortico-cortical terminals originating in area 17(18).

collaterals of intracellularly HRP-filled pyramidal cells in layer III of area 17 (Kisvarday et al., '86). These neurons project to distant targets, including area PMLS, and it seems that the proportion of postsynaptic targets locally and at the distant target area are similar. The postsynaptic targets of intracellularly filled layer V pyramidal cells has also been studied in area 17 (Gabbott et al., '87). In this case, the proportion of dendritic shafts was 20%, higher than for layer III cells. This proportion is very similar to the one found in PMLS for the injection sites encroaching onto both supra and infragranular layers in area 17 (Table 1). Moreover, cells of layer VI in area 17 provide local collaterals, which establish synapses with up to 70% of dendritic shafts in layer IV (McGuire et al., '84). Other long-range cortico-cortical cells in the deeper layers may also make synapses with a high proportion of dendritic shafts. It is therefore possible that the difference among the proportion of postsynaptic targets in the 2 animals is due to the location of the labeled cells. We also suggest that the proportion of postsynaptic targets of infra- and supragranular layers in area PMLS are different.

The presence of GABA immunoreactivity in dendrites postsynaptic to visual cortical afferents demonstrates that local inhibitory neurons in PMLS are directly contacted. This has been suggested previously on the basis of ultrastructural criteria (Sugiyama, '79), but in the absence of a marker for nonpyramidal cells, the relative importance of this termination could not be established. Surprisingly, 85% of the dendrites that were tested proved to be GABA-positive. If it is assumed that the rest of the dendrites contained similar proportions of GABA-negative and GABA-positive targets, it can be calculated that 14% of the total targets derived from inhibitory neurons. It should, however, be pointed out that this is a minimum value because some of the dendrites originating from GABAergic neurons may not have a sufficiently high level of this amino acid for detection with the immunogold method.

The cortex of the cat contains many types of nonpyramidal cells (Lund et al., '79; Meyer, '83), several of which have been shown to contain GABA (Somogyi, '89). Since these neurons differ in their termination pattern, it would be important to identify the particular type that receives cortico-cortical afferents in order to predict their action. The immunogold method does not give direct information about the neuronal type, but the morphological features of the postsynaptic dendrites, namely, the high volume density of mitochondria, suggests that the dendrites belong to basket cells. Similar dendritic features have been demonstrated for basket cells identified with intracellular injection of HRP in the primary visual cortex (Somogyi et al., '83), two of which have been shown to receive monosynaptic callosal cortico-cortical input (Martin et al, '83). How can so few synapses effectively activate the postsynaptic GABAergic cells? One possible explanation is that the terminals are not distributed randomly over all GABAergic cells, but the particular cells involved in the cortico-cortical connections receive highly convergent input. In the motor cortex it seems that individual nonpyramidal cells receive from the somatosensory cortex a higher proportion of cortico-cortical synapses than pyramidal cells (Ichikawa et al., '85).

Do cortico-cortical terminals establish synapses with postsynaptic elements randomly?

The targets of the overall population of type 1 synapses involve more dendritic shafts (29%) than that of the identified cortico-cortical terminals (17%). This demonstrates that different subpopulations of terminals making type 1 synapses have a particular selection of targets in PMLS. The relative enrichment of postsynaptic spines in the visual cortical input predicts that some other inputs show preference for dendritic shafts above the mean value for the overall population of type 1 synapses. One likely source of such input is from the recurrent collaterals of cortico-thalamic cells in layer VI. These neurons have been shown in another cortical area to form synapses preferentially with dendritic shafts in layer IV (McGuire et al., '84).

Another difference between the general population of type 1 synapses and those made by cortico-cortical terminals is in the proportion of GABA-positive dendritic shafts amongst the postsynaptic dendritic shafts; 85% for cortico-cortical synapses vs. 27% for the overall population of type 1 synapses. The results indicate that some other pathways form type 1 synapses preferentially with GABA-negative dendritic shafts, whereas the cortico-cortical population establishes synapses preferentially with GABA-positive shafts. It seems that pathways with different cells of origin and converging on the same layer have particular target populations in PMLS.

There appear to be differences in the proportion of the different postsynaptic targets of type 1 synapses in PMLS as compared to area 17. In the latter area, type 1 synapses contact as many dendritic shafts as spines, and most of the dendrites are GABA-negative (Bueno-Lopez et al., '89). This is not completely unexpected considering the different cytoarchitectonic composition and afferents of the 2 areas. In particular, spiny stellate cells dominate in layer IV of area 17 and they may contribute as well as receive a substantial density of axo-dendritic type 1 synapses (Lund, '84). Thalamo-cortical axon terminals in area 17 establish synapses with few dendritic shafts (Freund et al., '85a,b). A possible source for the observed difference between area 17 and PMLS is the local recurrent collaterals of cortico-thalamic pyramidal cells, which preferentially terminate on dendritic shafts in layer IV (McGuire et al., '84). They may not be as well represented in area PMLS as in area 17. Whatever the source of boutons establishing type 1 synapses, the results demonstrate that different cortical areas should be compared before generalizations can be applied to the basic cortical circuitry.

Functional implications for the organization of PMLS

The results demonstrate that area 17 innervates mainly putative excitatory neurons and to a lesser but significant extent inhibitory interneurons in PMLS, providing both feedforward excitatory and inhibitory input. This is in line with the results of physiological experiments, which demonstrated changes in receptive field properties following lesions (Smith and Spear, '79; Spear and Baumann, '79).

Ablation of areas 17 and 18 reduced the proportion of direction selective cells in PMLS from 80 to 7.5%. In contrast, neurons in PMLS responded much more readily to stationary light flashes (5% in normal cats, 44% in lesioned animals), and there was a reduction in the proportion of cells driven by the ipsilateral eye accompanied by an increase in the proportion of cells driven by the contralateral eye (from 33% in normals to 86% in lesioned animals). The loss of both excitatory and inhibitory influences originating in the ipsilateral primary visual cortex could be responsible for these effects. The loss of ipsilaterally responding neurons could occur primarily due to a loss of an excitatory projection; the increase in response to stationary stimuli due to a loss of an inhbitory connection. The loss of direction selectivity could be due to a combination of removal of inputs that inhibit the response to null directions of movements or to removal of excitatory inputs that produce a response to preferred directions of movement (Spear and Baumann, '75). Based on studies of receptive field properties of neurons in the thalamic latero-posterior (LP) complex and lateral suprasylvian cortex, Rauschecker (1988) postulated that receptive field properties in PMLS are generated through an interaction of cortico-cortical and thalamo-cortical afferents. Sherk ('86b) also demonstrated that retinotopically matched areas of the LGN and area 17 project to overlapping areas in layer IV of area PMLS, which also receives input from the LP-complex (Kato et al. '86). It remains to be established whether these different types of afferents to the middle layers of PMLS converge onto the same cells, or whether each projection has its own separate subpopulation of targets, which combine the information through local connections.

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LITERATURE CITED

Beaulieu, C., and M. Colonnier (1985) A laminar analysis of round-asymmetrical and flat-symmetrical synapses on spines, dendritic trunks, and cell bodies in area 17 of the cat. J. Comp. Neurol. *231:*180–189.

Beaulieu, C., and P. Somogyi (1990) Targets and quantitative distribution of GABAergic synapses in the visual cortex of the cat. Europ. J. Neurosci. *2:*296–303.

Blakemore, C., and T.J. Zumbroich (1987) Stimulus selectivity and functional organization in the lateral suprasylvian visual cortex of the cat. J. Physiol. *389:*569–603.

Bueno-Lopez, J.L., C. Beaulieu, and P. Somogyi (1989) Proportions of GABA-immunopositive and GABA-negative synaptic elements in layer 4 of cat's striate cortex. Europ. J. Neurosci. Suppl. *2:*106.

Bullier, J., and H. Kennedy (1987) Axonal bifurcation in the visual system. Trends Neurosci. *10:*205–210.

Clare, M.H., and G.H. Bishop (1954) Responses from an association area secondarily activated from optic cortex. J. Neurophysiol. *17:*271–277.

Creutzfeldt, O.D. (1988) Extrageniculo-striate visual mechanisms: Compartmentalization of visual functions. In: T.P. Hicks and G. Benedek (eds): Progress in Brain Research, Vol. 75, Vision Within Extrageniculo-Striate Systems, Amsterdam: Elsevier Science, pp. 307–320.

Einstein, G., and D. Fitzpatrick (1991) Distribution and morphology of area 17 neurons that project to the cat's extrastriate cortex. J. Comp. Neurol. *303:*132–149.

Elhanany, E., and E.L. White (1990) Intrinsic circuitry: Synapses involving the local axon collaterals of corticocortical projection neurons in the mouse primary somatosensory cortex. J. Comp. Neurol. *291:*43–54.

Fisken, R.A., L.J. Garey, and T.P.S. Powell (1975) The intrinsic, association and commisural connections of area 17 of the visual cortex. Philos. Trans. R. Soc. Lond. Biol. *272:*487–536.

Freund, T.F., K.A.C. Martin and D. Whitteridge (1985a) Innervation of cat visual areas 17 and 18 by physiologically identified X- and Y- type thalamic afferents. I. Arborization patterns and quantitative distribution of postsynaptic elements. J. Comp. Neurol. *242:*263–274.

Freund, T.F., K.A.C. Martin, P. Somogyi, and D. Whitteridge (1985b) Innervation of cat visual areas 17 and 18 by physiologically identified X- and Y- type thalamic afferents. II. Identification of postsynaptic targets by GABA immunocytochemistry and Golgi impregnation. J. Comp. Neurol. *242:*275–291.

Gabbott, P.L.A., K.A.C. Martin, and D. Whitteridge (1987) Connections between pyramidal neurons in layer 5 of cat visual cortex (area 17). J. Comp. Neurol. *259:*364–381.

Gerfen, C.R., and P.E. Sawchenko (1984) An anterograde neuroanatomical tracing method that shows the detailed morphology of neurons, their axons and terminals: immunohistochemical localization of an axonally transported plant lectin, Phaseolus vulgaris Leucoagglutinin (PHA-L). Brain Res. *290:*219–238.

Gilbert, C.D., and J.P. Kelly (1975) The projections of cells in different layers of the cat's visual cortex. J. Comp. Neurol. *163:*81–106.

Gray, E.G. (1959) Axo-somatic and axo-dendritic synapses of the cerebral cortex. J. Anat. *93:*420–433.

Heath, C.J., and E.G. Jones (1971) The anatomical organization of the suprasylvian gyrus in the cat. Adv. Anat. Embryol. Cell. Biol. *45:*6–61.

Henry, G.H., J.S. Lund, and A.R. Harvey (1978) Cells of the striate cortex projecting to the Clare-Bishop area of the cat. Brain Res. *151:*154–158.

Hodgson, A.J., B. Penke, A. Erdei, I.W. Chubb, and P. Somogyi (1985) Antisera to γ-aminobutyric acid. I. Production and characterization using a new model system. J. Histochem. Cytochem. *33:*229–239.

Humphrey, A.L., M. Sur, D.J. Uhlrich, and S.M. Sherman (1985a) Projection patterns of individual x- and y-cell axons from the lateral geniculate nucleus to cortical area 17 in the cat. J. Comp. Neurol. *233:*159–189.

Humphrey, A.L., M. Sur, D.J. Uhlrich, and S.M. Sherman (1985b) Termination patterns of individual x- and y-cell axons in the visual cortex of the cat: Projections to area 18, to the 17/18 border region, and to both areas 17 and 18. J. Comp. Neurol. *233:*190–212.

Hutchins, B., and B.V. Updyke (1988) The lateral posterior complex of the cat: studies of the functional organization. In T.P. Hicks and G. Benedek (eds): Progress in Brain Research, Vol. 75, Vision Within Extrageniculo-Striate Systems, Amsterdam: Elsevier Science, pp. 75–83.

Ichikawa, M., K. Arissian, and H. Asanuma (1985) Distribution of corticocortical and thalamocortical synapses on identified motor cortical neurons in the cat: Golgi, electron microscopic and degeneration study. Brain Res. *345:*87–101.

Jones, E.G., and T.P.S. Powell (1970) An electron microscopic study of the laminar pattern and mode of termination of afferent fibre pathways in the somatic sensory cortex of the cat. Phil. Trans. Roy. Soc. Lond. B. *257:*45–62.

Kato, N., S. Kawaguchi, and H. Miyata (1986) Postnatal development of afferent projections to the lateral suprasylvian visual area in the cat: An HRP study. J. Comp. Neurol. *252:*543–554.

Kawamura, K., and J. Naito (1976) Corticocortical afferents to the cortex of the middle suprasylvian sulcus area in the cat. Exp. Brain Res. Suppl. *1:*323–328.

Kisvarday, Z.F., K.A.C. Martin, T.F. Freund, Z. Magloczky, D. Whitteridge, and P. Somogyi (1986) Synaptic targets of HRP-filled layer III pyramidal cells in the cat striate cortex. Exp. Br. Res. *64:*541–552.

Lowenstein, P.R., and P. Somogyi (1989) Synaptic organization of cortico-cortical connections in the visual cortex of the cat. Soc. Neurosci. Abstr. *15:*1399.

Lund, J.S. (1984) Spiny stellate neurons. In A. Peters, E.G. Jones (eds): Cerebral Cortex, Vol. 1. New York: Plenum Press, pp. 255–308.

Lund, J.S., G.H. Henry, C.L. MacQueen, and A.R. Harvey (1979) Anatomical organization of the primary visual cortex (area 17) of the cat. A comparison with area 17 of the macaque monkey. J. Comp. Neurol. *184:*599–618.

McGuire, B.A., J.P. Hornung, C.D. Gilbert, and T.N. Wiesel (1984) Patterns of synaptic input to layer 4 of cat striate cortex. J. Neurosci. *4:*3021–3033.

Marshall, W.H., S.A. Talbot, and H.W. Ades (1943) Cortical response of the anesthetized cat to gross photic and electrical afferent stimulation. J. Neurophysiol. *6:*1–15.

Martin, K.A.C., P. Somogyi, and D. Whitteridge (1983) Physiological and morphological properties of identified basket cells in the cat's visual cortex. Exp. Brain Res. *50:*193–200.

Meyer, G. (1983) Axonal patterns and topography of short-axon neurons in visual areas 17, 18, and 19 of the cat. J. Comp. Neurol. *220:*405–438.

Palmer, L.A., A.C. Rosenquist, and R.J. Tusa (1978) The retinotopic organization of lateral suprasylvian visual areas in the cat. J. Comp. Neurol. *177:*237–256.

Pasternak, T., K.M. Horn, and J.H.R. Maunsell (1989) Deficits in speed discrimination following lesions of the lateral suprasylvian cortex in the cat. Visual Neurosci. *3:*365–375.

Porter, L.L., and K. Sakamoto (1988) Organization and synaptic relationships of the projection from the primary sensory to the primary motor cortex in the cat. J. Comp. Neurol. *271:*387–396.

Price, D.J., and T.J. Zumbroich (1989) Postnatal development of corticocortical efferents from area 17 in the cat's visual cortex. J. Neurosci. *9:*600–613.

Rauschecker, J.P. (1988) Visual function of the cat's LP/LS subsystem in global motion processing. In: T.P. Hicks and G. Benedek, Progress in Brain Research, Vol. 75, Vision Within Extrageniculo-Striate Systems, Amsterdam: Elsevier Science, pp. 95–108.

Rauschecker, J.P., M.W. von Grunau, and C. Poulin (1987a) Centrifugal organization of direction preferences in the cat's lateral suprasylvian visual cortex and its relation to flow field processing. J. Neurosci. *7:*943–958.

Rauschecker, J.P., M.W. von Grunau, and C. Poulin (1987b) Thalamocortical connections and their correlation with receptive field properties in the cat's lateral suprasylvian visual cortex. Exp. Br. Res. *67:*100–112.

Ribak, C.E. (1978) Aspinous and sparsely-spinous stellate neurons in the visual cortex of rats contain glutamic acid decarboxylase. J. Neurocytol. *7:*461–478.

Rockland, K.S. (1989) Bistratified distribution of terminal arbors of individual axons projecting from area V1 to middle temporal area (MT) in the macaque monkey. Visual Neurosci. *3:*155–170.

Sherk, H. (1986a) Location and connections of visual cortical areas in the cat's suprasylvian sulcus. J. Comp. Neurol. *247:*1–31.

Sherk, H. (1986b) Coincidence of patchy inputs from the lateral geniculate complex and area 17 to the cat's Clare-Bishop area. J. Comp. Neurol. *253:*105–120.

Sherk, H. (1989) Visual response properties of cortical inputs to an extrastriate cortical area in the cat. J. Comp. Neurol. *3:*249–265.

Sherk, H., and M. Ombrellaro (1988) The retinotopic match between area 17 and its targets in visual suprasylvian cortex. Exp. Brain Res. *72:*225–236.

Sloper, J.J., and T.P.S. Powell (1979) An experimental electron microscopic study of afferent connections to the primate motor and somatic sensory cortices. Phil. Trans. R. Soc. Lond. Biol. *285:*199–226.

Smith, D.C., and P.D. Spear (1979) Effects of superior colliculus removal on receptive-field properties of neurons in lateral suprasylvian visual area of the cat. J. Neurophysiol. *42:*57–75.

Somogyi, P. (1988) Immunocytochemical demonstration of GABA in physiologically characterized, HRP-filled neurons and their postsynaptic targets. In F.W. Van Leeuwen, R.M. Buijs, C.W. Pool, and O. Pach (eds): Molecular Neuroanatomy. Amsterdam: Elsevier Science, pp. 339–359.

Somogyi, P. (1989) Synaptic organization of GABAergic neurons and $GABA_A$ receptors in the lateral geniculate nucleus and visual cortex. In D.K.T. Lam and C.D. Gilbert (eds): Neural Mechanisms of Visual Perception. Houston: Portfolio Pub. Co., pp. 35–62.

Somogyi, P., and A.J. Hodgson (1985) Antiserum to γ-aminobutyric acid. III. Demonstration of GABA in Golgi-impregnated neurons and in conventional electron microscopic sections of cat striate cortex. J. Histochem. Cytochem. *33:*249–257.

Somogyi, P., Z.F. Kisvarday, K.A.C. Martin, and D. Whitteridge (1983) Synaptic connections of morphologically identified and physiologically characterized large basket cells in the striate cortex of cat. Neuroscience *10:*261–294.

Somogyi, P., and I. Soltesz (1986) Immunogold demonstration of GABA in synaptic terminals of intracellularly recorded, horseradish preoxidase-filled basket cells and clutch cells in the cat's visual cortex. Neuroscience *19:*1051–1065.

Spear, P.D. (1988) Influence of area 17, 18, and 19 on receptive-field properties of neurons in the cat's posteromedial lateral suprasylvian visual cortex. In T.P. Hicks and G. Benedek (eds): Progress in Brain Research, Vol 75. Vision Within Extrageniculo-Striate systems, Amsterdam: Elsevier Science, pp. 197–210.

Spear, P.D., and T.P. Baumann (1975) Receptive field characteristics of single neurons in lateral suprasylvian visual area of the cat. J. Neurophysiol. *38:*1403–1420.

Spear, P.D., and T.P. Baumann (1979) Effects of visual cortex removal on receptive-field properties of neurons in lateral suprasylvian visual area of the cat. J. Neurophysiol. *42:*31–56.

Sugiyama, M. (1979) The projection of the visual cortex on the Clare-Bishop area in the cat. A degeneration study with the electron microscope. Exp. Brain Res. *36:*433–443.

Symonds, L.L., and A.C. Rosenquist (1984a) Corticocortical connections among visual areas in the cat. J. Comp. Neurol. *229:*1–38.

Symonds, L.L., and A.C. Rosenquist (1984b) Laminar origins of visual corticocortical connections in the cat. J. Comp. Neurol. *229:*39–47.

Szentagothai, J. (1973) Synaptology of the visual cortex. In R. Jung, H. Autrum, W.R. Loewenstein, D.M. McKay, and H.L. Tenber (eds): Handbook of Sensory Physiology, Vol. VII/3B. Berlin: Springer-Verlag, pp. 269–324.

Szentagothai, J. (1978) The neuron network of the cerebral cortex: A functional interpretation. The Ferrier Lecture, 1977. Proc. R. Soc. Lond. Biol. *201:*219–248.

Tong, L., R.E. Kalil, and P.D. Spear (1982) Thalamic projections to visual areas of the middle suprasylvian sulcus in the cat. J. Comp. Neurol. *212:*103–117.

Tong, L., and P.D. Spear (1986) Single thalamic neurons project to both lateral suprasylvian visual cortex and area 17: A retrograde fluorescent double-labeling study. J. Comp. Neurol. *246:*254–264.

Updyke, B.V. (1981) Projections from visual areas of the middle suprasylvian sulcus onto the lateral posterior complex and adjacent thalamic nuclei in cat. J. Comp. Neurol. *201:*477–506.

Winfield, D.A., and T.P.S. Powell (1983) Laminar cell counts and geniculocortical boutons in area 17 of cat and monkey. Brain Res. *277:*223–229.

Zumbroich, T.J., and C. Blakemore (1987) Spatial and temporal selectivity in the suprasylvian visual cortex of the cat. J. Neurosci. *7:*482–500.