

Cingulate Cortex of the Rhesus Monkey: I. Cytoarchitecture and Thalamic Afferents

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ABSTRACT

The cytoarchitecture and thalamic afferents of cingulate cortex were evaluated in the rhesus monkey (*Macaca mulatta*). Area 24 has three divisions of which area 24a is adjacent to the callosal sulcus and has the least laminar differentiation. Area 24b has more clearly defined layers II, III, and Va, and area 24c, which forms the lower bank of the anterior cingulate sulcus, has a particularly dense layer III. Area 23 also has three divisions, each of which has a distinct layer IV. Area 23a is adjacent to the callosal sulcus and has the thinnest layers II-IV, which have the same cell density as layers V and VI. Area 23b has the largest pyramids in layers IIIc and Va, and area 23c, in the depths of the posterior cingulate sulcus, has the broadest external and thinnest internal pyramidal layers. Finally, areas 29 and 30 are located in the posterior depths of the callosal sulcus. Two divisions of area 29 are apparent: one with a granular layer directly adjacent to layer I (area 29a-c) and another with differentiation of layers III and IV (area 29d). Area 30 has a dysgranular layer IV.

Injections of the retrograde tracer horseradish peroxidase (HRP) were made into subdivisions of cingulate cortex in the monkey. Area 25 received thalamic input mainly from the midline parataenial (Pt), central densocellular (Cdc), and reuniens nuclei as well as from the dorsal parvicellular division of the mediodorsal nucleus (MDpc). A less dense projection also originated in the intralaminar parafascicular (Pf), central superior, and limitans (Li) nuclei as well as the medial division of the anterior nuclei (AM).

Areas 24a and 24b received most thalamic afferents from fusiform and multipolar cells in the Cdc and Pf nuclei with fewer from the ventral anterior (VA) and MDpc and MD densocellular (MDdc) nuclei and only minor input from AM. Most input to premotor cingulate area 24c appeared to originate in VA, MDdc, and Li.

Area 29 received the most dense input from nuclei traditionally associated with limbic cortex including the anteroventral (AV), anterodorsal (AD), and laterodorsal (LD) nuclei. Areas 23a and 23b, in contrast, did not receive AV, AD, or LD input, but the greatest proportion of their thalamic afferents arose in AM. Less-pronounced input also came from the lateroposterior (LP), medial pulvinar, and MDdc nuclei. This latter nucleus projected more to area 23b than to areas 30 or 23a.

Anterior medial nucleus efferents to cingulate cortex were of particular note for two reasons. First, AM projected primarily to posterior cingulate areas with area 23 receiving its principal thalamic input from AM. Second, projections to areas 30, 23a, and 23b were topographically organized with ventral areas 30 and 23a receiving from the central core of AM, while the more dorsally located area 23b received input from peripheral and medial parts of AM.

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In light of the extensive projections of Cdc, Csl, and Pf to anterior cingulate cortex, it is proposed that the midline and intralaminar thalamic nuclei be classified as part of limbic thalamus along with the anterior, LD, and MD nuclei. Furthermore, although AM projects mainly to posterior cingulate cortex, it also has light projections to area 25 and minor input to area 24. As such, AM is the only limbic thalamic nucleus that has such widespread projections to cingulate cortex. Finally, visually evoked activity in area 23 may be the result of projections from the LP and medial pulvinar

Key words: anterior thalamic nuclei, midline thalamic nuclei, intralaminar thalamic nuclei, lateroposterior thalamic nucleus, pulvinar thalamic nucleus, primate

Primate cingulate cortex is involved in attention and memory and mediates somatic and autonomic motor responses, phonation, and responses to painful sensation (Smith, '45; Ward, '48; Kaada, '51; Barris and Schuman, '53; Foltz and White, '62, '68; Dua and MacLean, '64; Talairach et al., '73; Watson et al., '73; Haller et al., '76). Ablation of cingulate cortex or its underlying white matter, the cingulum bundle, has proven to be clinically useful in treating depression, obsessive-compulsive behavior, and chronic pain (LeBeau, '52; Livingston, '53; Tow and Whitty, '53; Foltz and White, '62, '68; Kanaka and Balasubramaniam, '78). The underlying neuronal mechanisms for these broadly characterized functions are not known and the results of clinical intervention are often variable. A more precise understanding of the architecture and connections of cingulate cortex should lead to a mechanistic understanding of cingulate cortex functions. Our working hypothesis is that since cingulate cortex is not a unified or homogeneous cortical region, its functions may be characterized on the basis of discrete subareas. The aim of the present study is to provide a morphological basis for more refined functional studies.

The cytoarchitecture of primate cingulate cortex is more diverse than most experimental studies indicate. Brodmann's ('09) two major subdivisions of cingulate cortex, areas 24 and 23, are not structurally homogeneous. Area 24, for example, has been noted to undergo graded changes from poorly differentiated cortex next to the corpus callosum to well-defined laminae in the depths of the cingulate sulcus (Walker, '40; Smith, '45). Furthermore, Braak ('76) and Muakkassa and Strick ('79) have identified a motor area in the depths of the cingulate sulcus that includes part of area 24. Electrical stimulation studies also suggest heterogeneities in area 24 as vocalization and changes in respiration can be evoked by stimulation of different parts of area 24 (Kaada, '51). Finally, Rose ('27), von Economo ('29), and Sarkissov ('55) each divided both anterior and posterior cingulate cortices into three ventrodorsal parts in their cytoarchitectural analyses.

Definitions of the cingulate region have been based on topographical criteria (e.g., Kappers et al., '67) or on connections with the anterior thalamic nuclei (Clark and Boggon, '33; Rose and Woolsey, '48). These latter studies, however, employed the retrograde cell degeneration method after relatively large lesions in subprimate species that do not have an area 23. In the monkey it is not known if the anterior nuclei project specifically to area 23, since Locke et al. ('64) made lesions in area 23 in the monkey and did

not observe retrograde changes in the anterior thalamic nuclei. Because areas 23, 30, and 29 are usually involved in experimental procedures, for example, those employing retrogradely transported tracers (e.g., Vogt et al., '79; Baleyrier and Mauguiere, '80), the only thalamic projection reported to terminate specifically in area 23 is one that originates in the medial pulvinar (Baleyrier and Mauguiere, '85). Thus, there still remains a great deal of uncertainty regarding precise thalamic projections to different parts of cingulate cortex.

The strategy for this investigation was to make large and then restricted injections of horseradish peroxidase (HRP) into monkey cingulate cortex such that the distribution of thalamic afferents could be characterized in terms of a comprehensive cytoarchitectural analysis. Small injections restricted to areas 23a, 23b, or 30 provide a basis for distinguishing among the connections of these areas and those of area 29.

MATERIALS AND METHODS

Surgical procedures

In all instances in which injections were made into cingulate cortex, the monkey was anesthetized with sodium pentobarbital and mounted in a stereotaxic instrument. A midline craniotomy was made and mannitol (Osmitol, 25%) was injected I.V. Then the dura was opened and retracted to one side; bridging veins between the cortex and falx cerebri were cauterized; the hemispheres were gently retracted; and the corpus callosum was sectioned. A smaller slit was then made in the falx so that a 5- μ l Hamilton syringe with a 32-gauge needle could be positioned in different parts of cingulate cortex.

Nissl preparations

Thalamic and cortical cytoarchitecture was evaluated in monkeys that had been perfused intracardially with 1 liter of 0.9% saline and then 1 liter of 10% formalin. The brains were removed and postfixed in 10% formalin for 2–4 weeks in a refrigerator and then dehydrated and embedded in celloidin. Sections were cut 25–40- μ m-thick and a one-in-six series was stained with cresyl violet.

HRP histochemistry

Two series of animals were prepared for retrograde tracer analysis. First, ten animals received large 0.2–0.3- μ l injections of 20% HRP in cingulate cortex and were allowed to survive 2 days. The animals were then anesthetized and killed by perfusion-fixation according to the protocol of Ro-

sene and Mesulam ('78). Thus, they were perfused through the heart with physiological saline followed by 2 liters of quarter-strength Karnovsky fixative (Karnovsky, '65) and finally 1 liter of phosphate buffer containing 10% sucrose. The brains were stored for one night in sucrose phosphate buffer and then frozen and sectioned into 40- μ m-thick sections. An interrupted series of one-in-eight sections was processed by using tetramethyl benzidine, mounted on subbed slides, dried, and then counterstained with neutral red. In a second series of five animals, very limited HRP injections were made with 0.015 μ l of 5% HRP conjugated to wheat germ agglutinin (HRP-WGA, Sigma), and the brains were prepared according to the above protocol. The full rationale behind the use of HRP-WGA in studies of cingulate cortex connections has been presented elsewhere (Vogt and Miller, '83; Miller and Vogt, '84). The locations of HRP-labeled neurons were plotted with an X-Y recorder coupled to the mechanical stage of a microscope by linear potentiometers. In a few cases the sections were drawn with the aid of a drawing tube attachment to the microscope or an Aus Jena Documentor projector onto which labeled neurons were plotted.

RESULTS

Cytoarchitecture

A map of the distribution of areas in monkey cingulate cortex is presented in Figure 1 and photomicrographs of Nissl-stained sections at low and higher magnifications are shown in Figures 2 and 3, respectively. As a general rule the cortex adjacent to the corpus callosum is least differentiated whereas the cortex near and in the depths of the cingulate sulcus contains the most elaborate lamination patterns. The cingulate region includes areas 25, 24, 29, 30, 23, and possibly 31 as outlined by dotted lines in Figure 1 and can be distinguished in the following manner. Area 25 has essentially two cellular layers with the deep layer V-VI that is more cell dense than in any other cingulate area and a superficial layer II-III and no layer IV. Area 24 also does not have a layer IV. Compared to area 23, layer V of area 24 is denser and more homogeneous. Area 23 has a distinct layer IV of small cells, and a layer IIIc of pyramidal cells is more prominent than in area 24. Finally, area 29 has dense and poorly differentiated layer II-IV while adjacent area 30 is dysgranular (i.e., has a poorly developed layer IV).

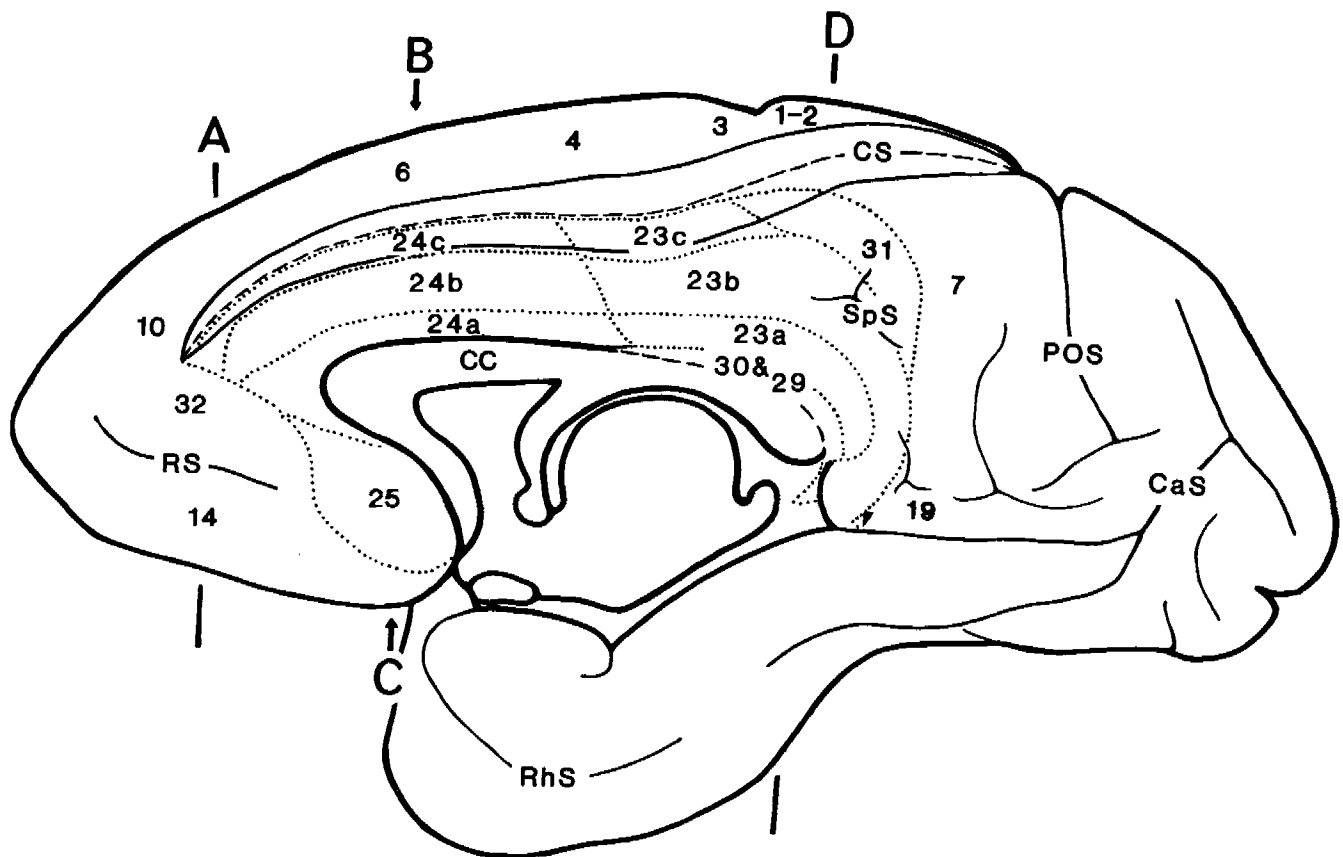


Fig. 1. Distribution of cytoarchitectural areas in monkey cingulate cortex. Coronal sections at levels A-D are presented in Figure 2. CC, corpus callosum; CS, cingulate sulcus; SpS, splenial sulcus; RS, rostral sulcus; RhS, rhinal sulcus; POS, parieto-occipital sulcus; CaS, calcarine sulcus.

Fig. 2. Coronal sections through different levels of the monkey cingulate gyrus. Levels designated in Figure 1. IG, indusium griseum; Sub, subiculum. Cresyl violet. $\times 18$.

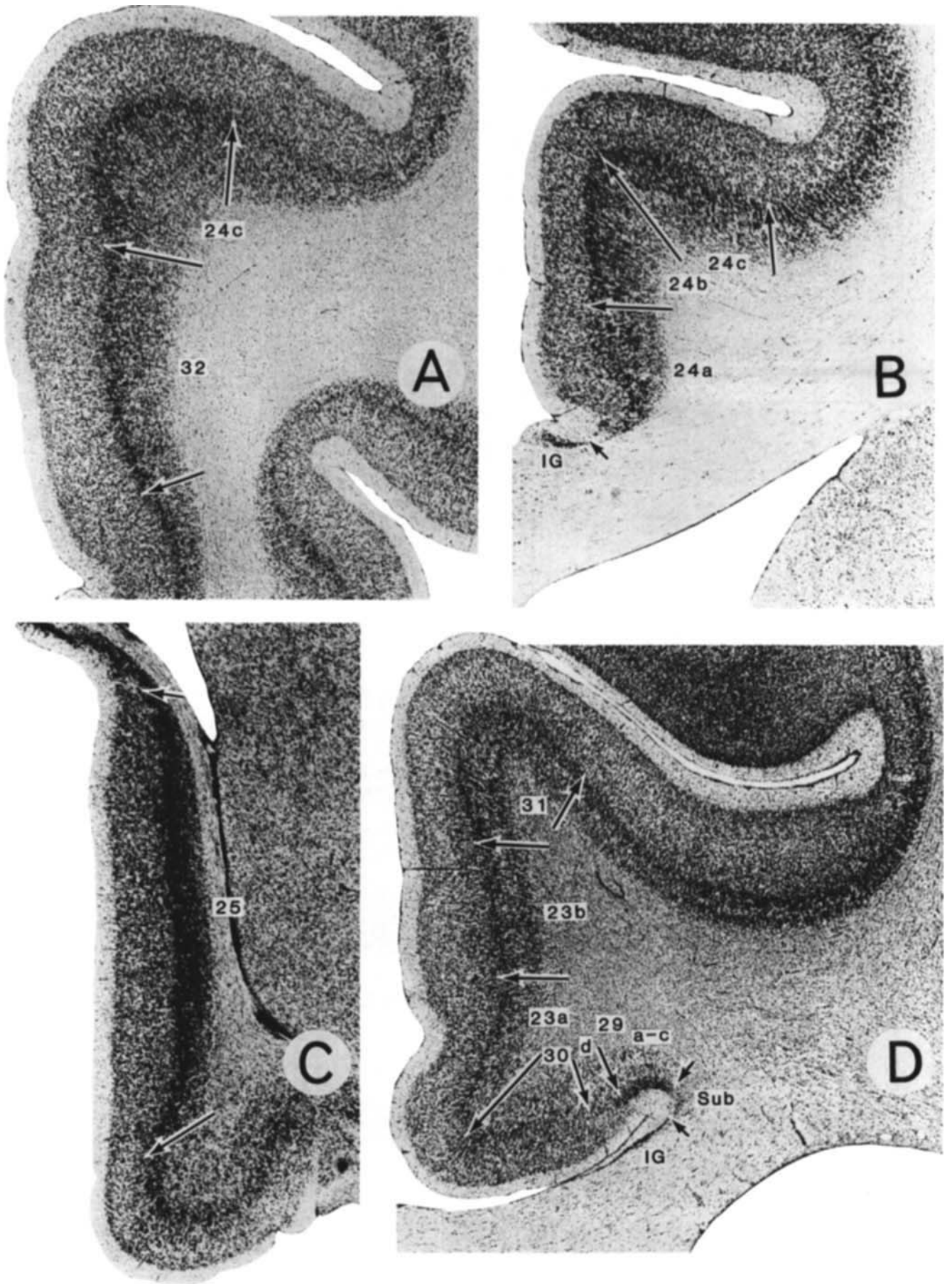


Figure 2

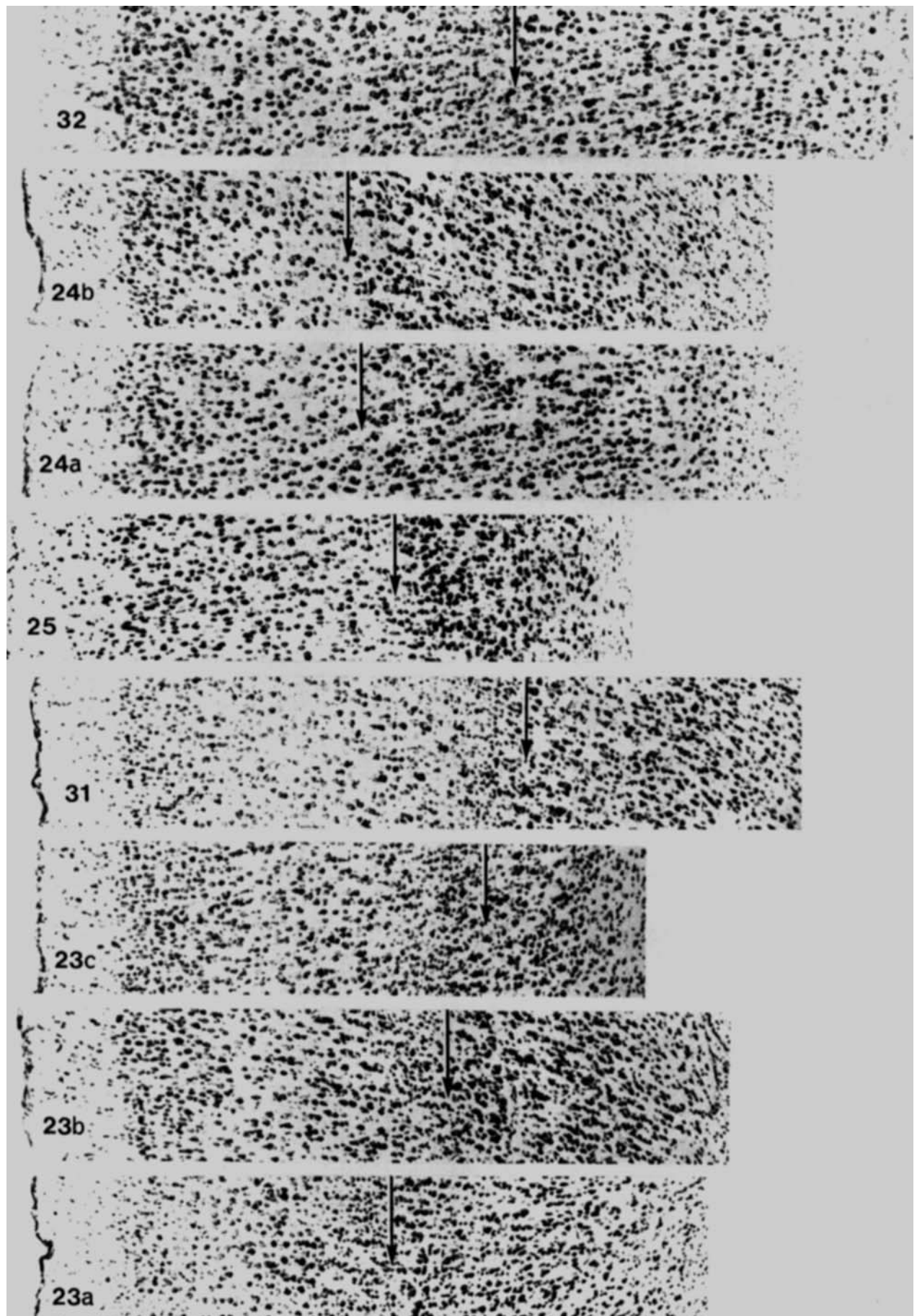


Figure 3

Area 24. This area can be divided into three subregions. Area 24a lies adjacent to the corpus callosum and is a relatively uniform cortex; i.e., layers II and III are virtually indistinguishable and in the deeper layers Va and Vb are difficult to differentiate. In contrast to area 25, layer VI is distinct from layer V in area 24a.

Area 24b has a layer III that is less dense than layers II and Va, so a clear distinction can be made among layers II, III, and Va. Also, cells in layer Va are more dense than in the outer part of layer V in area 24a.

Area 24c forms the lower bank of the rostral half of the cingulate sulcus. It has a dense layer III that contains large pyramids, and the deep layers are somewhat less dense than in area 24b. Finally, the layer I-II border is very straight.

Area 32 lies rostral and ventral to area 24. Its cytoarchitecture is similar to area 24a in the homogeneity of layers II-III and Vb-VI; however, layer Va forms a distinct band and the outer layers (II-IV) are much thicker than in area 24b.

Area 29. Area 29 does not appear to be extensively differentiated in the monkey as it is in rodents and lagomorphs. There are essentially two components to this area (Fig. 2D), a lateral area 29a-c that abuts the supracallosal subiculum (previously termed RSg1, Vogt, '76) and a medial area 29d (previously termed RSg2, Vogt, '76). These designations are employed to maintain consistency with previous work in other species and to draw attention to possible structural equivalencies among species (Vogt and Peters, '81; Vogt, '85; Vogt et al., '86).

Area 29a-c has a broad layer I and essentially homogeneous and densely packed granular layer II-IV. Layer V is divided into a Va part with large pyramids and a cell-sparse Vb, whereas there is a poorly developed (i.e., thin and cell sparse) layer VI. Because of the lack of differentiation of layer II-IV and the location of area 29a-c next to the subiculum, this area is a periallocortex. The adjoining area 29d has a sparse layer III of medium-sized pyramids that abuts layer I and a very slender and irregular layer IV, and the composition of layers V and VI is similar to that of area 29a-c. In the latter instance, however, these layers are thicker and more cell dense. Both areas 29a-c and 29d extend along the caudal depths of the callosal sulcus and into the calcarine sulcus.

Area 30. This area lies medial to area 29d and is classically considered retrosplenial agranular or dysgranular cortex. Layer IIIc has large pyramids; there is a thin, irregular, and cell-sparse layer IV and a layer Va with very large pyramidal neurons. These features, particularly those of layer IV, characterize this region as proisocortex, as is the case for areas 29d and 23a.

Area 23. Area 23 occupies most of the posterior half of cingulate cortex and can be divided into three parts. Rostrally it merges with area 24, dorsally with area 31, and caudally it extends to areas 7 and 19. Of the three divisions

of area 23, area 23a has the thinnest external pyramidal layers II-IV (Fig. 3). Both internal and external pyramidal layers are relatively homogeneous and of approximately equal cell density. Area 23 is most differentiated in area 23b, which has the largest neurons in layers IIIc, V, and VI. The ventral part of area 23b forms most of what has been termed the caudomedial lobule (Goldman-Rakic et al., '84). A small extension of area 23b also continues into the most rostral part of the calcarine sulcus, as does area 29. Area 23c, in the depths of the posterior cingulate sulcus, has the broadest layers II-IV but layers V and VI are not well developed. Whereas area 23a has features of a proisocortex, the thick layer IV and large layer IIIc pyramids in areas 23b and 23c characterize them as isocortical (i.e., neocortical) structures.

Area 31 forms the dorsal and posterior rim of the cingulate region in the monkey and is cytoarchitecturally intermediate between area 23c and the medial parietal area 7 or PGM (Pandya and Seltzer, '82). It has the broadest layers I-IV and the largest layer IIIc pyramids. Layers Va, Vb, and VI are distinct and the cells in these layers are not arranged radially as in medial area 7.

Thalamus. Olszewski ('52) described in detail the cytoarchitecture of monkey thalamus. In light of thalamic projections from both the anterior and midline nuclei to cingulate cortex, it is necessary to clarify structural distinctions between them. Figure 4 is a micrograph from a level just caudal to where the anteromedial (AM) nucleus crosses the midline. At this level the centrodensocellular nucleus (Cdc) arches over and just beneath AM. Although cells in Cdc can be as large as those in AM, there are also many smaller fusiform and multipolar cells in Cdc and so the overall packing density is much higher.

Thalamic afferents

Anterior cingulate cortex. Figure 5 presents a case in which a large HRP injection involved areas 24a-c. In this case most labeled neurons in the thalamus were in the ventral, midline, intralaminar, and mediodorsal nuclei. Although labeled neurons were also present in the anterior nuclei, the number of these cells was limited in comparison to that in other regions.

Labeled neurons in the ventral nucleus were entirely in the rostral part of the anterior (VA) division. Labeled cells in the midline were predominantly in Cdc while fewer were also in the paraventricular (Pa), parataenial (Pt), central latocellular (Clc), central inferior (Cif), and reuniens (Re) nuclei. Of the intralaminar nuclei, the central superior lateral (Csl), central lateral (Cl), parafascicular (Pf), and limitans (Li) nuclei contained most labeled neurons. In the mediodorsal nucleus neurons were labeled in the periphery of the parvicellular division (MDpc) and at the most caudal levels of the densocellular division (MDdc). Fewest labeled neurons occurred in a dorsal part of the medial pulvinar.

Examples of HRP-labeled fusiform and multipolar neurons in Cdc following the area 24 injection are shown in Figure 6. The fusiform neurons were in the most medial part of Cdc (i.e., approximately at the level of the middle arrow in Fig. 4), while the multipolar cells were in the dorsal limb of Cdc (i.e., at the level of the top arrow in Fig. 4). For comparative purposes HRP-labeled neurons in AM following an area 30-23a injection are presented in Figure 10 that are at the same magnification as those in Figure 6. The AM labeled neurons in both cases were larger and the

Fig. 3. Photographs through representative sections of some cingulate areas. Arrows are placed at the border between layers III or IV and Va. Cresyl violet. $\times 93$.

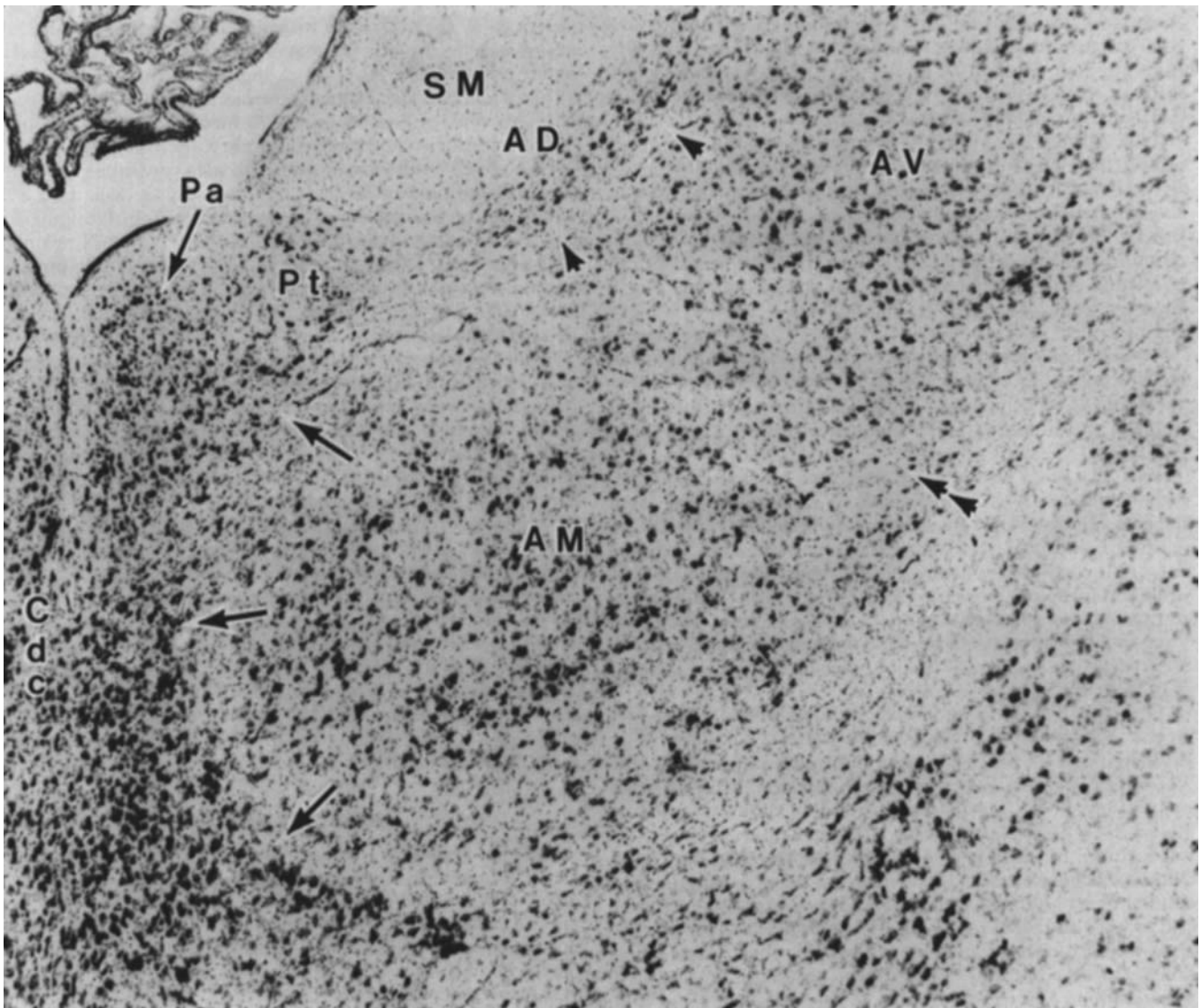


Fig. 4. Anterior and midline thalamic nuclei at a level just caudal to the midline crossing of AM. The following borders are indicated: AM/Cdc, arrows; AD/AV, arrowheads; AM/AV, double arrowhead. Cresyl violet. A, anterior; M, medial; D, dorsal; V, ventral. $\times 68$.

overall cell packing density much reduced when compared to those in Cdc following the area 24 injection.

In a smaller, anterior-placed area 24a,b injection (Fig. 7C-F) HRP-labeled neurons were in most of the same thalamic nuclei as in the previously described area 24 case, however, the density of labeled cells in VA, MDdc, and Li was greatly reduced, possibly because these nuclei project strongly to area 24c. In an area 32 case (Fig. 7A,B), labeled neurons were only in MDpc, MDdc, Li nuclei and a few were in the Pa nucleus. No cells were labeled in VA, Cdc, or AM in this case.

An HRP injection that involved mainly area 25 (not shown) produced labeling of cells in Cdc, Pt, and throughout the full length of the dorsal part of MDpc. Lighter labeling also occurred in AM, Re, Csl, Pf, and Li.

Posterior cingulate cortex. A large HRP injection in posterior cingulate cortex involved areas 23a-c, 30, and 29, and the greatest density of labeled neurons was in the anterior nuclei and along the dorsal thalamus (Fig. 8). Most cells were in AD, AV, LD, LP, MDdc, and medial pulvinar. Fewer HRP-labeled neurons were in AM, Csl, and MDpc, and the fewest were in Cdc and Li. Although the projection zones of these nuclei were often associated with posterior cingulate cortex, six cytoarchitectural areas have been involved in the injection site. Injections restricted to area 30 and/or parts of area 23 indicated that there were selective preferences in the distribution of thalamic inputs to each cytoarchitectural subdivision.

Three of eight restricted posterior cingulate cortex HRP injections are presented in Figure 9. In the first of these

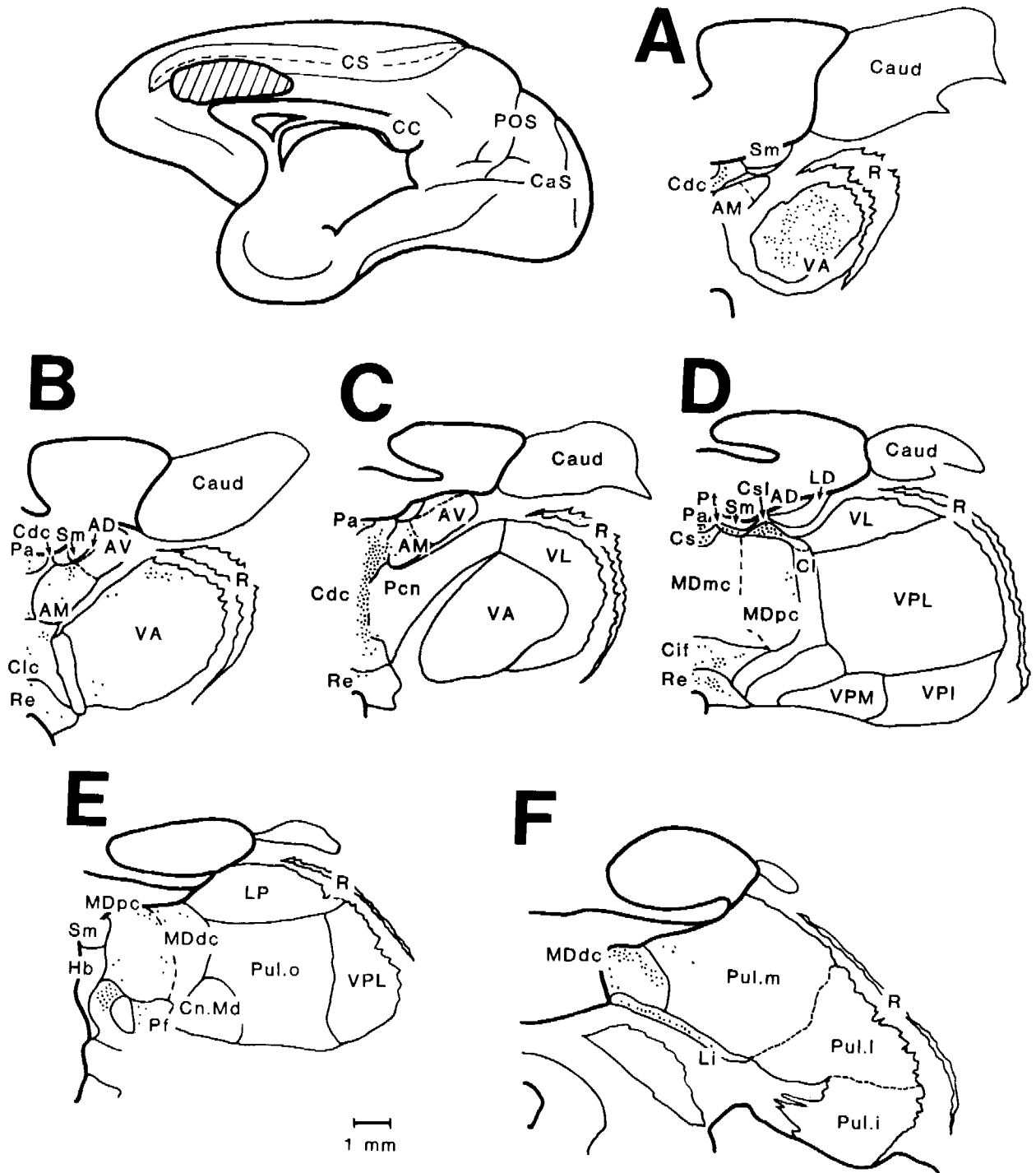


Fig. 5. Distribution of HRP-labeled neurons (dots) in the thalamus following a large injection into area 24 (hatched). Levels A-F represent progressively caudal sections through the thalamus. Sm, stria medularis; Caud,

caudate; R, reticular; VL, ventrolateral; Pcn, paracentral; VPL, I, M, ventroposterior lateral, inferior and medial, respectively; Hb, habenula; Cn.Md, centromedianum; Pul. o, l, i, pulvinar oral, lateral, and inferior, respectively.

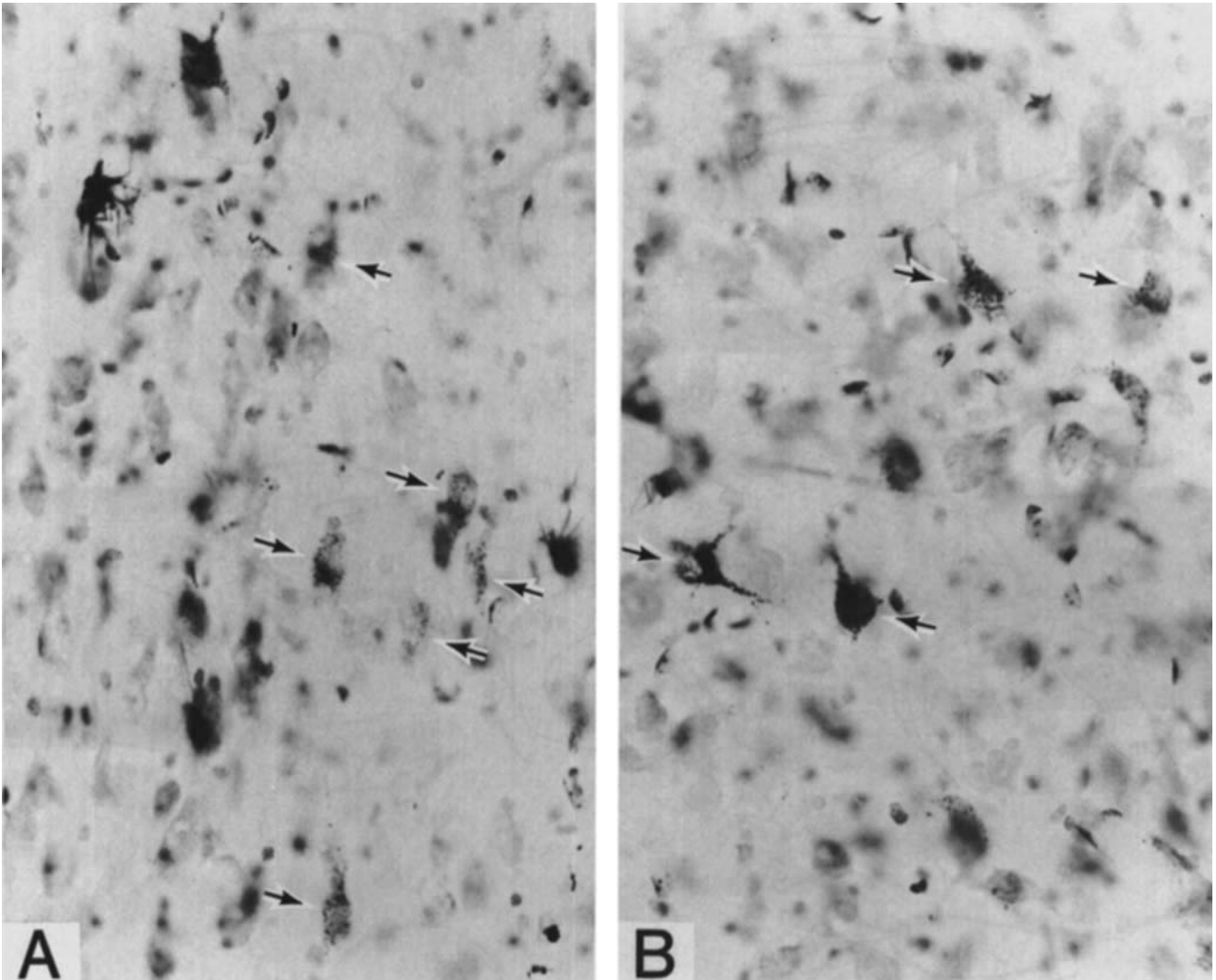


Fig. 6. HRP-labeled neurons in Cdc following an area 24 injection (see also Fig. 4). **A:** Fusiform neurons from the medial part of Cdc; some are

emphasized with arrows. **B:** Multipolar neurons from dorsal limb of Cdc; some are emphasized with arrows. $\times 553$.

cases, areas 30 and 23a were involved in the injection (see also Fig. 10 inset). In this case most labeled neurons were in the core of AM (Fig. 9) with fewer in LP. Some neurons were also in the pc and dc divisions of MD and the medial pulvinar with only occasional cells in the Li/Pf complex. In this case as in all of the restricted cases that did not involve area 29 there were no labeled neurons in AV or AD and only a few were labeled in LD. Therefore, the primary termination zone of AD, AV, and LD is in area 29.

In a case where HRP was restricted to areas 23a and b (Fig. 9, middle case) there was a shift in the location of labeled neurons such that most were in LP, less in AM and the medial pulvinar, and fewest were in the MD and intralaminar nuclei (Pf, Pc, and Csl). In all instances the restricted injections showed only limited labeling in the

intralaminar nuclei. In the case that involved area 23b (Fig. 9, third case), the distribution of labeled neurons was similar to the previous case; however, more cells were in Li and there were more labeled neurons in ventral parts of AM.

There was a topographical organization of AM projections to areas 30 and 23 (Fig. 9). In the most ventral case (areas 30 and 23a) labeled cells were concentrated in the core of AM while in area 23a and 23b cases these neurons were more dispersed in AM. In the area 23b case labeled cells were most concentrated in the periphery of AM. Also, the main projections to subdivisions of area 23 were from AM, LP, and medial pulvinar, with small and variable contributions from the midline, intralaminar, and mediodorsal nuclei.

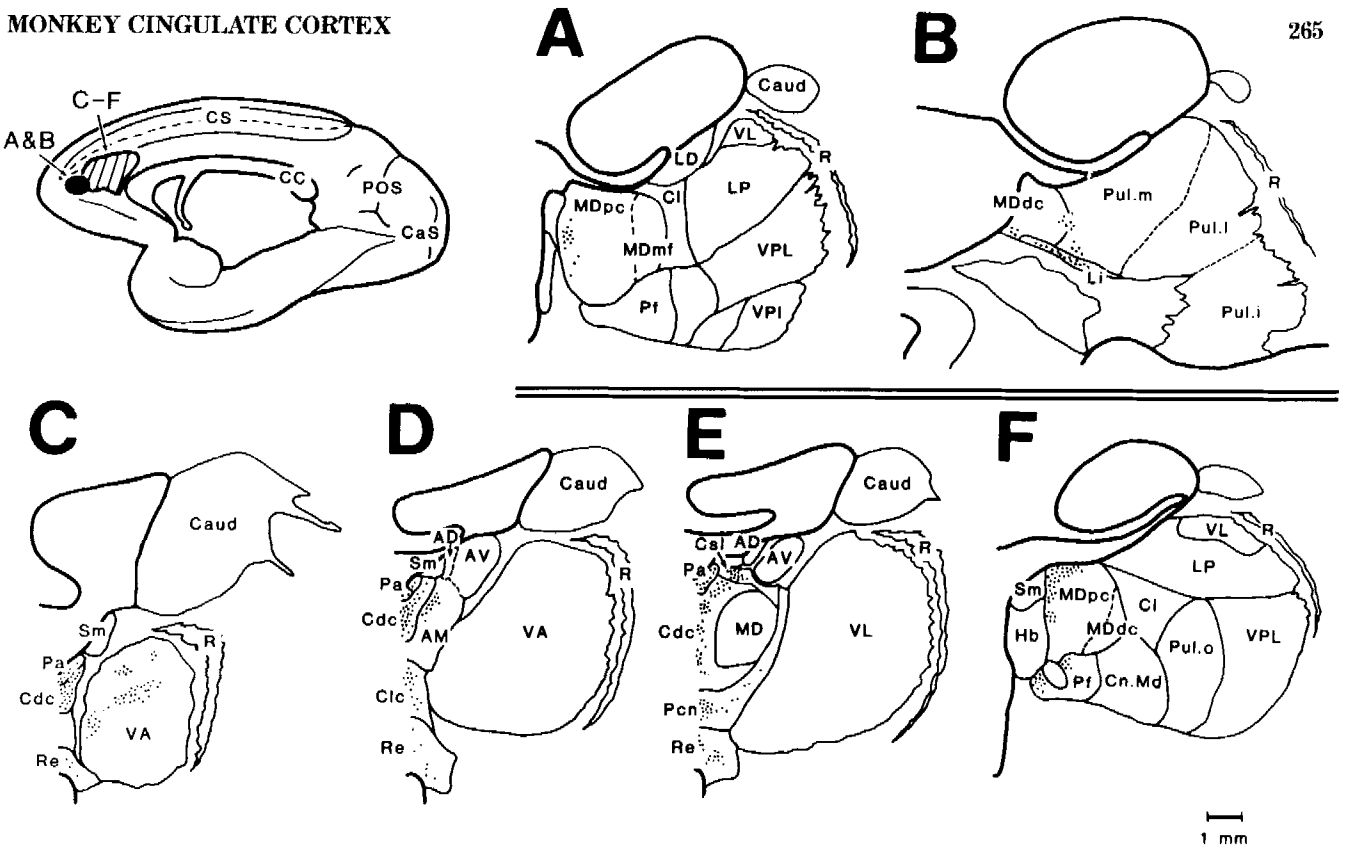


Fig. 7. Location of HRP-labeled neurons in the thalamus following injections into area 32 (filled, levels A and B) and areas 24a and b (hatched, levels C-F).

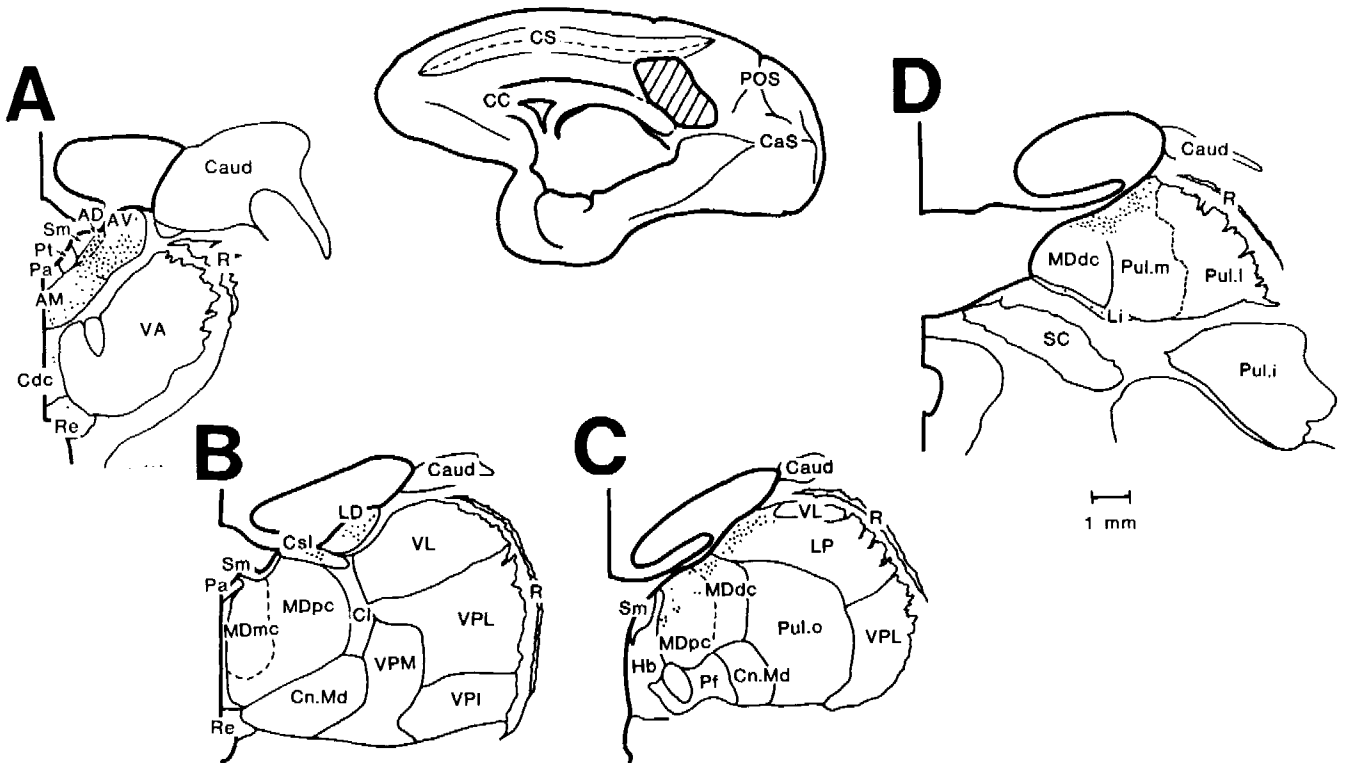


Fig. 8. Distribution of labeled neurons at four levels of the thalamus following a large HRP injection into posterior cingulate cortex.

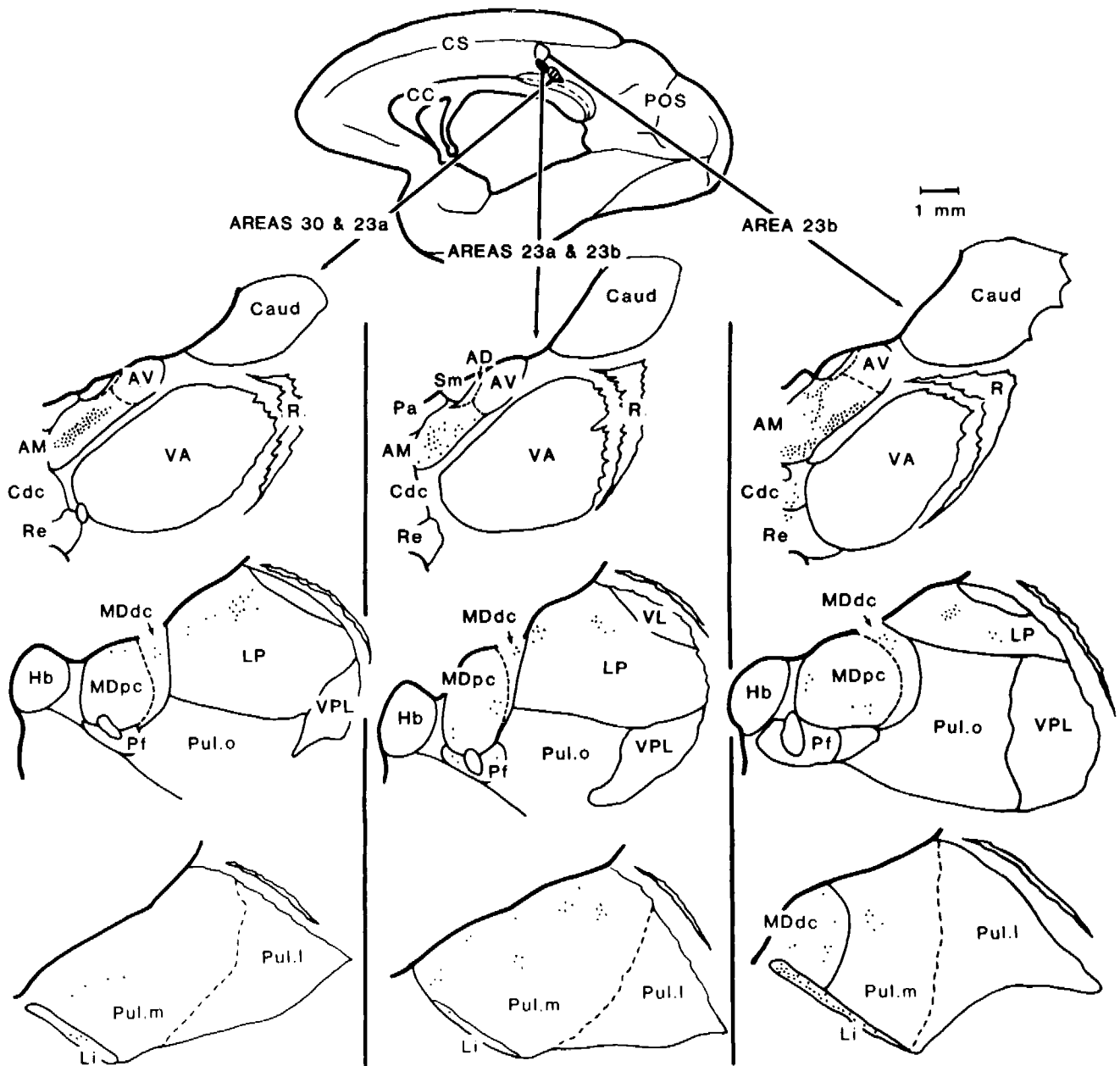


Fig. 9. Three small injections into posterior cingulate cortex and the positions of labeled neurons in the thalamus.

DISCUSSION

In anterior cingulate cortex, area 25 receives mainly Cdc, Pt, Re, and MDpc input with only limited afferents arriving from the AM and Pf nuclei. Areas 24a and 24b receive mainly Cdc and intralaminar (i.e., Csl, Pf, and Li) inputs, while less arises from VA and MDpc and least from AM. Area 24c receives mainly VA, MDdc, and Li afferents. In posterior cingulate cortex area 29 receives AV, AD, and LD input, while areas 30 and 23 get mainly AM, LP, and medial pulvinar afferents and less from MD, Pf, and Li.

Limbic thalamus

The present study demonstrates that the midline Cdc and intralaminar Pf and Cl nuclei are the principal sources of thalamic input to area 24. Though a minor projection from AM is present, this is not the main source of thalamic afferents, as is true for rodents and marsupials (Beckstead, '76; Benjamin and Golden, '85). Yakovlev et al. ('60) showed in the monkey that, in addition to the anterior nuclei, the midline nuclei are connected with this region, and many subsequent studies in the cat and monkey have demon-

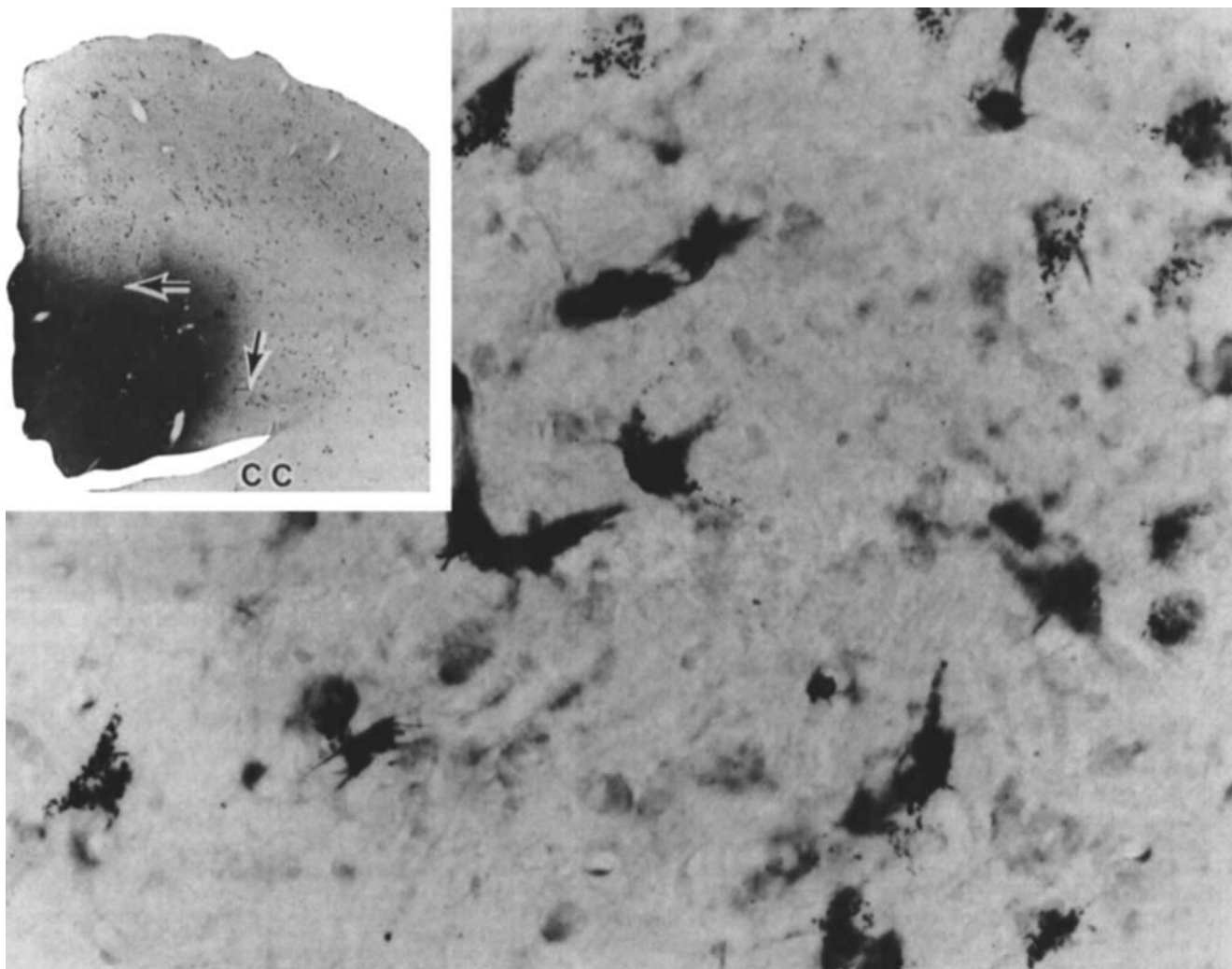


Fig. 10. HRP-labeled neurons in AM following an area 30/23a injection. $\times 533$. Inset: HRP injection site between arrows; see also the first case in Figure 9. $\times 14$.

strated AM, VA, midline, and intralaminar connections with area 24 (Siegel et al., '73; Jones and Leavitt, '74; Müller-Preuss and Jürgens, '76; Macchi et al., '77; Niimi et al., '78; Vogt et al., '79; Baleyrier and Maugiere, '80; Robertson and Kaitz, '81; Royce, '83; Royce and Mourey, '85). In none of these latter studies is there evidence that AM is the predominant thalamic input to area 24. In light of their strong connections with cingulate cortex, it is proposed that the midline and intralaminar nuclei be classified as part of limbic thalamus.

Yakovlev et al. ('60) included LD in limbic thalamus of monkey because it has projections to the cingulate and parahippocampal cortices (see also Locke et al., '64; Locke and Kerr, '73). Tracer studies in the rat (Robertson et al., '80), cat (Niimi et al., '78; Robertson and Kaitz, '81; Kaitz and Robertson, '81), and monkey (Vogt et al., '79; Baleyrier and Maugiere, '80) show that the projection to the cingulate cortex is mainly to posterior areas and that it is reciprocal.

In the present study it was shown that LD projections were quite limited. Thus, LD neurons failed to label following HRP injections that did not involve area 29, suggesting that areas 30 and 23 do not receive LD input. The cat, however, differs from the monkey in this regard, since a larger area of the posterior cingulate cortex receives LD input (Robertson and Kaitz, '81). Although the role of LD in cingulate cortex function is unknown, it is interesting that LD receives pretectal input (Robertson, '83; Robertson et al., '83) and so could provide a source of visual input to posterior cingulate cortex.

Projections of AM

Definitions of the extent of cingulate cortex should include AM connections as one characteristic feature of this region. Although the projection of AM to area 24 is light, AM connections form a connective link for all cingulate cortical areas, as observed in the monkey in this study and

in cat (Niimi et al., '78; Robertson and Kaitz, '81). Furthermore, areas 23 and 30 in the monkey receive relatively more input from AM than any other nucleus, and that includes only minor input from the midline and intralaminar nuclei. When an injection also involves area 29, however, at least equal numbers of neurons are labeled in AV as in AM.

Anteromedial projections are not limited to cingulate cortex, however, since light AM projections have also been observed to terminate in prefrontal cortex (Goldman-Rakic and Porrino, '85). Thus, anterior thalamic inputs are characteristic of but not unique to the cingulate cortex. Conversely, MD projections are not limited to prefrontal cortex as area 23b of posterior cingulate cortex has both MDdc and MDpc inputs. In light of these shared AM and MD as well as medial pulvinar thalamic inputs and extensive connections between area 46 of the prefrontal cortex and cingulate cortex (Nauta, '64; Pandya et al., '71, '81; Künzle, '78; Vogt et al., '79; Baleyrier and Maugiere, '80; Goldman-Rakic et al., '84; Barbas and Mesulam, '85), it is likely that these two cortical regions are involved in similar functions such as delayed response performance (Niki and Watanabe, '79).

Comparative organization of posterior cingulate cortex

Connections with the AD and AV thalamic nuclei are generally considered to be a distinguishing trait of posterior cingulate cortex in the rat (Domesick, '72), rabbit (Rose and Woolsey, '48), and monkey (Vogt et al., '79; Baleyrier and Maugiere, '80). However, this generalization requires reconsideration because posterior cingulate cortex is neither cytoarchitecturally nor connectionally the same in rodents/marsupials and primates. The major structural difference is the presence of area 23 in monkey. It has been demonstrated in the monkey in this study that area 23 lies dorsal to areas 29 and 30 and that it has a well-developed layer IV and differentiated layers II and III. It also receives input mainly from the AM, LP, and medial pulvinar thalamic nuclei but does not appear to receive input from AD or AV.

The posterior cingulate cortex in the rat has four divisions of area 29 (Vogt and Peters, '81); none of them meets cytoarchitectural criteria for an area 23, and the most dorsal division, area 29d, might receive light AD and AV input (Vogt, '85), as do the granular cingulate areas (Domesick, '72). In the rabbit brain there are five divisions of area 29 in posterior cortex (Vogt et al., '86), and a dorsolateral part of area 29d does have a granular layer IV similar to that of area 23. However, this part of area 29d receives AD and AV input (Rose and Woolsey, '48; Vogt and Sikes, unpublished observations) and so may not be viewed as equivalent to area 23.

A principal difference, therefore, between primate and nonprimate (i.e., rat and rabbit) brains is the presence of area 23 in primate posterior cingulate cortex. The main differences in thalamocortical connections among these species can be accounted for by the presence of area 23 connections in primates.

Sensorimotor connections

Cuénod et al. ('65) and MacLean et al. ('68) reported flash-evoked unit responses in posterior and ventral parts of area 23 on the caudomedial lobule. Although area 23 does not receive direct afferents from the lateral geniculate nucleus,

there are two other possible thalamic sources for this activity including the LP and medial pulvinar thalamic nuclei. It is known that the visual cortex projects to both of these nuclei (Graham et al., '79; Raczkowski and Diamond, '80; Updyke, '83) and that the medial pulvinar receives retinal input (Mizuno et al., '82; Nakagawa and Tanaka, '84). The pulvinar also receives pretectal input (Robertson et al., '83), there is a retinotopic organization of neurons in the LP-pulvinar complex (Raczkowski and Rosenquist, '81) and some of these neurons respond to auditory and somatic stimuli as well as visual ones (Kreindler et al., '68). In light of the extensive connections of LP and the medial pulvinar with the visual system, it is likely that visual-evoked activity in area 23 can be partially accounted for on the basis of activity in these two thalamic nuclei.

Although much of cingulate cortex projects to parts of the motor system such as the caudate and pontine nuclei, area 24c, in the depths of the cingulate sulcus, appears to contain a premotor region with unique motor projections. This region has been defined with pigment architecture in the human brain (Braak, '76) and in the monkey projects to the primary motor cortex (Muakkassa and Strick, '79) and the spinal cord (Biber et al., '78). Data in the present study indicate that VA and MDdc projections are greatest to area 24c and less to areas 24a and 24b. Therefore, VA and MDdc are probably inputs to the cingulate premotor area.

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