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Organization of the Thalamo-Cortical Connexions to the Frontal Lobe in the Rhesus Monkey

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Summary. In 25 rhesus monkeys horseradish peroxidase was injected in different parts of the frontal cortex. The retrogradely labelled thalamic neurons formed longitudinal bands, some of which crossed the internal medullary lamina, and extended from one thalamic nucleus into another. On the basis of these findings the frontal cortex was subdivided into seven transverse cortical strips which receive afferents from seven longitudinal bands of thalamic neurons. The most rostral transverse strip receives afferents from the most medial thalamic band which is oriented vertically and extends through the most medial part of the MD into the medial pulvinar. Progressively more caudally located transverse strips receive afferents from progressively more laterally located thalamic bands which in part are situated in the VL and show an increasing tilt towards the horizontal. Moreover, those parts of the various bands which are situated along the dorsal and lateral margin of the thalamus project to the medial portions of the transverse cortical strips, i.e. along the medial margin of the frontal lobe, while the other parts situated ventromedially in the thalamus project to the lateral portions of these strips, i.e. along the lateral margin of the frontal lobe.

These data provide an alternative view of the organization of the thalamus and suggest that this structure contains a matrix of longitudinal cell columns which in some cases extend across specific nuclear borders and may represent the basic thalamic building blocks in respect to the thalamo-cortical connexions.

Key words: Thalamus – Frontal cortex – Cortical HRP injections – Thalamo-frontal connexions – Rhesus monkey – Thalamic organization

Introduction

The organization of thalamo-cortical connexions has been studied repeatedly since the pioneering efforts of Le Gros Clark (1935) and Walker (1938a). These studies generally used the retrograde cell degeneration technique in order to

establish from which thalamic cell group a certain cortical area receives its afferents. However, this technique has the drawback that the retrograde cell changes after ablation of different cortical areas may vary depending on the type of connexions (Rose and Woolsey, 1958), the age of the animals (Brodal, 1940) and the survival period (Walker, 1938a). Moreover, a considerable amount of cortical tissue must be removed in order to obtain pronounced retrograde changes in a circumscribed portion of the thalamus (Walker, 1938a). These drawbacks can be overcome by utilizing the retrograde axonal transport of horseradish peroxidase (HRP) (Kristensson and Olsson, 1971; LaVail and LaVail, 1972; Kuypers et al., 1974). Therefore, in a series of rhesus monkeys HRP was injected in different frontal cortical areas and the distribution of the retrogradely labelled thalamic neurons was studied.

This study forms a part of a larger endeavour aimed at clarifying the organization of the cerebello-thalamo-cortical connexions. The data obtained in the present study are expected to make it possible to determine the ultimate cortical destination of the projections from the various cerebellar nuclei to the different parts of the thalamus.

Materials and Methods

In 23 rhesus monkeys 6–25 closely spaced injections of 0.6 µl, of 10–30% horseradish peroxidase (HRP, Sigma VI) dissolved in distilled water, were made in circumscribed parts of the frontal cortex by means of a Hamilton syringe with a 22 gauge needle, which was introduced to a depth of $\pm 2^1/_2$ mm. In each penetration a total of 0.6 µl HRP was deposited over a period of 6 min. In 13 of the animals the injections were made in one hemisphere. Since in these cases labelled thalamic neurons were present only ipsilaterally, in the remaining 10 animals injections were made in both hemispheres and the labelled neurons in the thalamus on either side were regarded to reflect only the injections in the ipsilateral hemisphere.

After 3 days the animals were deeply anaesthetized with nembutal and perfused with 6% dextran and 0.1% sodium nitrite in 0.9% saline at 38° C followed by a mixture of 2.5% glutaraldehyde and 0.5% paraformaldehyde in 0.1 M cacodylate buffer pH 7.2 at 20° C. Subsequently the brains were removed from the skull and cut in three transverse blocks parallel to the stereotaxic plane. These blocks were kept in a solution of 30% sucrose in 0.1% cacodylate buffer (pH 7.2) at 4° C for 1–3 days. They were then cut in 40 µ transverse sections on a freezing microtome. The sections were incubated according to Graham and Karnovsky (1966), mounted, dehydrated and covered. Some sections were lightly counterstained with cresyl violet. The material was studied microscopically in darkfield and brightfield illumination (Kuypers et al., 1974). The location of the retrogradely labelled HRP-positive thalamic neurons was charted with the aid of an X–Y plotter linked by means of transducers to the microscope state.

Results

In the areas surrounding the cortical needle penetrations HRP-reaction products were abundant both in the cortex and in the immediately underlying white matter. Moreover, HRP-positive granules were present within cortical neurons and some neurons were stained evenly brown. From the injected cortex and the immediately underlying white matter evenly brown stained fibers proceeded towards the internal capsule. The cortical area, around the needle tracks, which was densely packed with HRP-reaction products will be referred

to as the HRP-positive cortical area and its maximum extent is indicated in solid black in Figures 1, 2 and 3. These areas were surrounded by a lighter brown staining zone which gradually faded into the surrounding tissue.

In all cases groups of thalamic neurons contained HRP-positive granules. The cortical areas from where the enzyme had been transported retrogradely by these neurons were, however, difficult to delineate precisely. Yet a comparison of the distributions of the labelled neurons in the different cases strongly suggests that the enzyme was transported mainly from the HRP-positive cortical areas surrounding the needle penetrations (Bunt et al., 1974, 1975; Jones, 1975) and probably also from damaged axons in the immediately underlying white matter (Kristensson and Olsson, 1974; Kuypers and Maisky, 1975). In the cases with injections in the lower one-third of the precentral and postcentral gyri (cf. cases B7, C4, D1) the underlying white matter contains not only thalamic fibres to the surface cortex but also fibres to the opercular cortex. The population of labelled neurons in these cases has therefore been regarded to comprise neurons obtaining the enzyme through the former type of fibres as well as neurons obtaining it through the latter.

The experiments may be subdivided into four groups: A. cases with injections in the orbitofrontal cortex and the cortex of the most rostral portion of the frontal convexity; B. cases with injections in the periarcuate cortex, i.e. above, below and within the concavity of the arcuate sulcus; C. cases with injections in the precentral gyrus; and D. cases with injections in the postcentral and parietal areas.

It had been assumed that after HRP injections in the different frontal areas, different specific thalamic nuclei would be labelled. Instead, longitudinal columns or bands of labelled neurons occurred which ran roughly parallel to the midline. In several cases these bands and columns crossed the intermedullary lamina along their rostro-caudal trajectory and extended from one nucleus into another. After injections in the rostral parts of the frontal lobe the bands and columns were located medially in the thalamus, while after progressively more caudal injections they were located progressively more laterally.

Three-Dimensional Configuration of the Thalamic Nuclei

In order to facilitate the description of the thalamic distribution of the columns and bands of labelled neurons, the three-dimensional configuration of the major thalamic nuclei in the rhesus monkey as described by Olszewski (1952) will be briefly outlined.

The thalamus is wedge-shaped and tapers rostrally (Fig. 4). It is subdivided in a mediodorsal and a lateroventral compartment by the internal medullary lamina which in horizontal sections runs parallel to the lateral side of the thalamic wedge rather than parallel to the midline (Fig. 4). Ventrally the internal medullary lamina bends medially and becomes continuous across the midline with its counterpart on the other side. The medullary lamina reaches caudally only as far as the habenular nuclei (H) and in its caudal part is joined ventrally by the centre median-parafascicular complex (CM-Pf).

The mammillo-thalamic tract (TMT) passes through the rostral part of the internal medullary lamina. Caudal to this level the medullary lamina contains the intralaminar nuclei, i.e. rostrally the paracentral nucleus (PCN) and caudally the central lateral nucleus (CL). The mediodorsal nucleus (MD) which is located medial to the internal medullary lamina, is replaced rostrally by the anterior midline nuclei (Ce), i.e. the central densocellular nucleus (Cdc) as well as the central latocellular (Clc) nucleus, which dorsally adjoins the reuniens nucleus (RE). The elongated MD has its largest cross sectional dimension at midthalamic levels. Caudally, it tapers down to a small cell group which laterally adjoins the habenular complex (H) and meets caudally the anterior part of the medial pulvinar (Pm).

The pulvinar belongs mainly to the lateroventral compartment, which is oriented from caudolateral to rostromedial, somewhat parallel to the lateral side of the thalamic wedge. Thus the rostral part of the lateroventral compartment is situated immediately rostral to the lateral expansion of the MD at midthalamic levels (Fig. 4). Therefore a line drawn from the rostral part of the lateroventral compartment caudally and roughly parallel to the midline passes across the internal medullary lamina into the MD. Some of the longitudinal columns of labelled neurons followed this very same trajectory.

The rostral part of the lateroventral compartment comprises the ventral anterior nucleus (VA) which consists of a medial magnocellular part (VAmc) and a lateral parvocellular part (VApc). The caudal border of the VA is oriented from rostrolateral to caudomedial, roughly perpendicular to the lateral side of the thalamic wedge. In transverse sections the VA therefore appears to be replaced from laterally by the caudally adjoining ventrolateral complex (VL).

The VL complex consists of several subnuclei. The oral part (VLo) is characterized by clusters of medium size darkly staining neurons. However, area X immediately lateral to the internal medullary lamina at this level contains relatively few neurons. The ventromedial part of the VL (VLm) at this level borders medially on the RE. The caudal part of the VL is regarded to comprise the dorsally located subnucleus caudalis (VLc) and the ventrally located oral part of the ventral posterolateral nucleus (VPLo). Both nuclei contain relatively large, uniformly scattered neurons but lack the additional smaller neurons of the caudal part of the VPL (VPLc). In part following Crouch (1934) and Walker (1938a) the ventrally located VPLo will be called the ventral intermediate nucleus (VIM). This nucleus has been grouped with the VLo and the VLc because all three were labelled retrogradely from the precentral gyrus, while the VPLc was labelled from the postcentral gyrus (cf. also Strick, 1976). The dorsally located VLc continues further caudally than the VIM and becomes situated on top of the VPLc where it borders caudally on the lateral posterior nucleus (LP).

The ventral-posteriomedial nucleus (VPM) is located ventral and ventrolateral to the CM-Pf. When proceeding from the level of the Cm-Pf caudally, VPM, VPLc and LP are replaced from medially by the pulvinar (P) such that the VPM is replaced by the oral pulvinar (Po), the LP and the VPLc by the lateral pulvinar (Pl) and the tail end of the MD by the medial pulvinar (Pm).

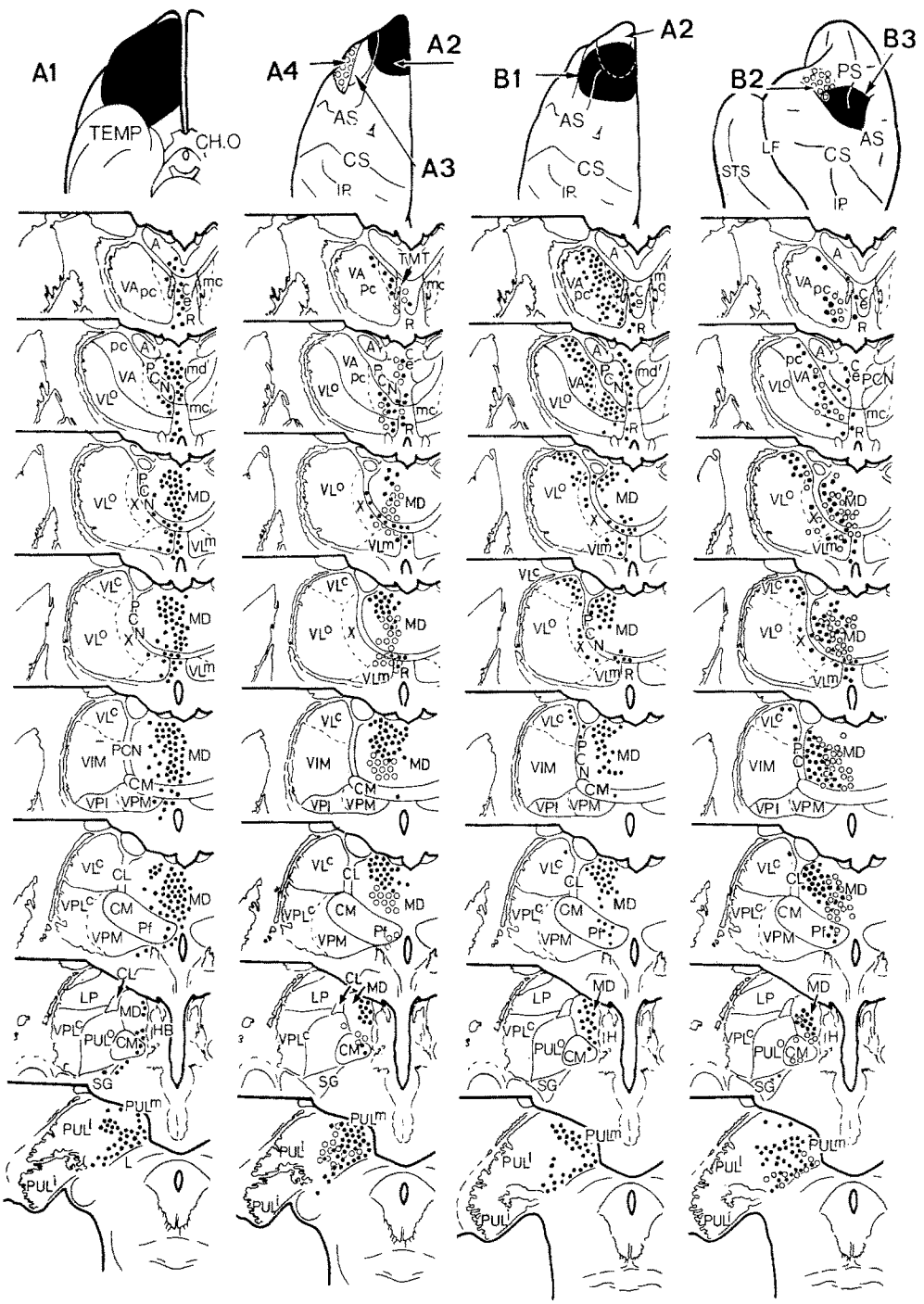

Fig. 1. Semidiagrammatic representation of the HRP-positive cortical areas (solid black and ○○) and the distributions of the retrogradely labelled thalamic neurons (cases A1, A2, B1 and B3 ●● ; A4 and B2 ○○) after injections in different parts of the rostral portion of the frontal lobe

Distribution of Retrogradely Labelled Thalamic Neurons

A. Injections in Orbitofrontal Cortex and Rostral Part of Frontal Convexity

In the four cases of this group the longitudinal bands or columns of labelled neurons were located mainly in the medial part of the thalamus where they extended from the area of the anterior midline nuclei (Ce) and the medial part of the VA through the MD into the anterior part of the Pm (Fig. 1).

In case A1, 25 deposits of HRP were made in the orbitofrontal cortex by means of needle penetrations parallel to the cortical surface. HRP-reaction products were also present in the anterior putamen. Labelled thalamic neurons were present in the medial part of the anterior nucleus, especially the AM and AV as well as in the RE and the Ce, in particular the CDc (Fig. 1). The population of labelled neurons in the Cdc continued caudally as a vertical band throughout the most medial portion of the MD and along the lateral aspect of the habenular complex into the anterior part of the Pm.

In case A2 with 15 injections in the cortex on the convexity of the rostral part of the frontal lobe and in the underlying white matter, the HRP-positive cortical area extended from the injection site into the most anterior parts of the orbitofrontal cortex, and the superior frontal gyrus on the medial surface of the hemisphere. The labelled thalamic neurons in this case also formed a somewhat sagittally oriented column which, however, was situated slightly more laterally than in case A1 and occupied a dorsal position especially in the MD (Fig. 1). Thus, a limited number of labelled neurons was present in the medial part of the VAmc. This population after crossing the internal medullary lamina increased in size and extended, through the dorsal part of the intermediate portion of the MD along the dorsolateral aspect of the habenular complex, into the anterior part of the Pm. In cases A3 and A4 with 12 injections more laterally, above and below the rostral part of the principal sulcus respectively, the longitudinal columns of labelled neurons behaved in roughly the same manner as in case A2 but occupied a relatively more ventral portion in the VA and the MD (Fig. 1). This was especially obvious in case A4 with injections lateral to the principal sulcus.

In all these four cases some less strongly labelled neurons were also present in the intralaminar nuclei, especially in the rostral part of the PCN, while in addition a few labelled neurons occurred in the Pf.

B. Injections in the Periarcuate Area

The labelled neurons in each of the seven cases of this group also formed longitudinal columns, which, however, were located more laterally than in the cases of group A. These columns occupied together a slightly tilted broad longitudinal thalamic band which was oriented somewhat parallel to the midline (cf. cases of group A) and extended from the VA into the caudally adjoining paralaminar part of the VL and across the internal medullary lamina through the paralaminar MD into the anterior part of the Pm (Figs. 1, 2). Thus this band and its constituent columns when traced caudally seem to shift from lateral to medial in the thalamus. However, this shift is more apparent than real because due to

the wedge-shape of the thalamus a longitudinally oriented cell column which extends roughly parallel to the midline inevitably becomes located further and further away from the lateral thalamic border at progressively more caudal levels (Fig. 4).

In five cases (B1–B5) injections were made rostrally in the periarcuate area. In case B1 with 18 injections around the rostral tip of the upper limb of the arcuate sulcus the HRP-positive cortical area overlapped rostrally with that of case A2 and extended from the superior frontal gyrus on the medial surface of the hemisphere into the intermediate portion of the upper bank of the principal sulcus. The longitudinal column of labelled neurons was located dorsally, as in case A2, but relatively more laterally (Fig. 1). Thus in the rostral thalamus many labelled neurons were present in the VAmc and the medial parts of the VApc and some were present in the Ce. The population in the VA continued caudally roughly parallel to the midline into the dorsomedial parts of the VLo and the rostral VLc as well as into the dorsorostral part of area X. Along this trajectory the population gradually moved across the internal medullary lamina and continued through the MD into the Pm. While proceeding through the MD the population seemed to shift medially because due to the caudally increasing lateral expansion of the MD, the population extended from the lateral part of the MD at rostral levels into its intermediate part at more caudal levels (cf. case B1, Fig. 1).

In case B2, 6 injections were made laterally in the periarcuate area, i.e. immediately rostral to the inferior limb of the arcuate sulcus. The column of the labelled neurons was located ventral to one in case B1 and slightly more medially. It extended (Fig. 1) from the ventromedial part of the VApc into the rostroventral part of area X and from there continued, across the internal medullary lamina, through the ventromedial MD into the anterior part of the Pm.

In case B3 with 25 injections in the arcuate gyrus (Fig. 1) the labelled neurons were most numerous at midthalamic levels where they tended to be concentrated in the area between the populations of cases B1 and B2. Thus the longitudinal group of labelled neurons extended from the centrocaudal part of the VApc into the caudally adjoining dorsomedial parts of the VLo and the rostral VLc. Further caudally the population gradually moved across the internal medullary lamina and while increasing in size and density extended into the lateral paralaminar MD, while avoiding the ventral paralaminar MD, especially at caudal levels. Further caudally the population continued from the MD into the anterior part of the Pm (Fig. 1). In two additional cases (B4 and B5) with 12 and 15 injections in the arcuate gyrus above and below the caudal part of the principal sulcus respectively, the longitudinal groups of labelled neurons occupied roughly the same position as in case B3 but the one in case B4 with the injections above the principal sulcus tended to be located slightly more dorsally than the one in case B5 with the injections below the sulcus. Further in these three cases (B3–B5) as well as in the two preceding ones (B1 and B2) some labelled neurons also occurred in the intralaminar PCN and in the Pf.

In two other cases (B6 and B7) 19 injections were made more caudally in the periarcuate area, i.e. in the caudal part of the area above the arcuate sulcus (B6)

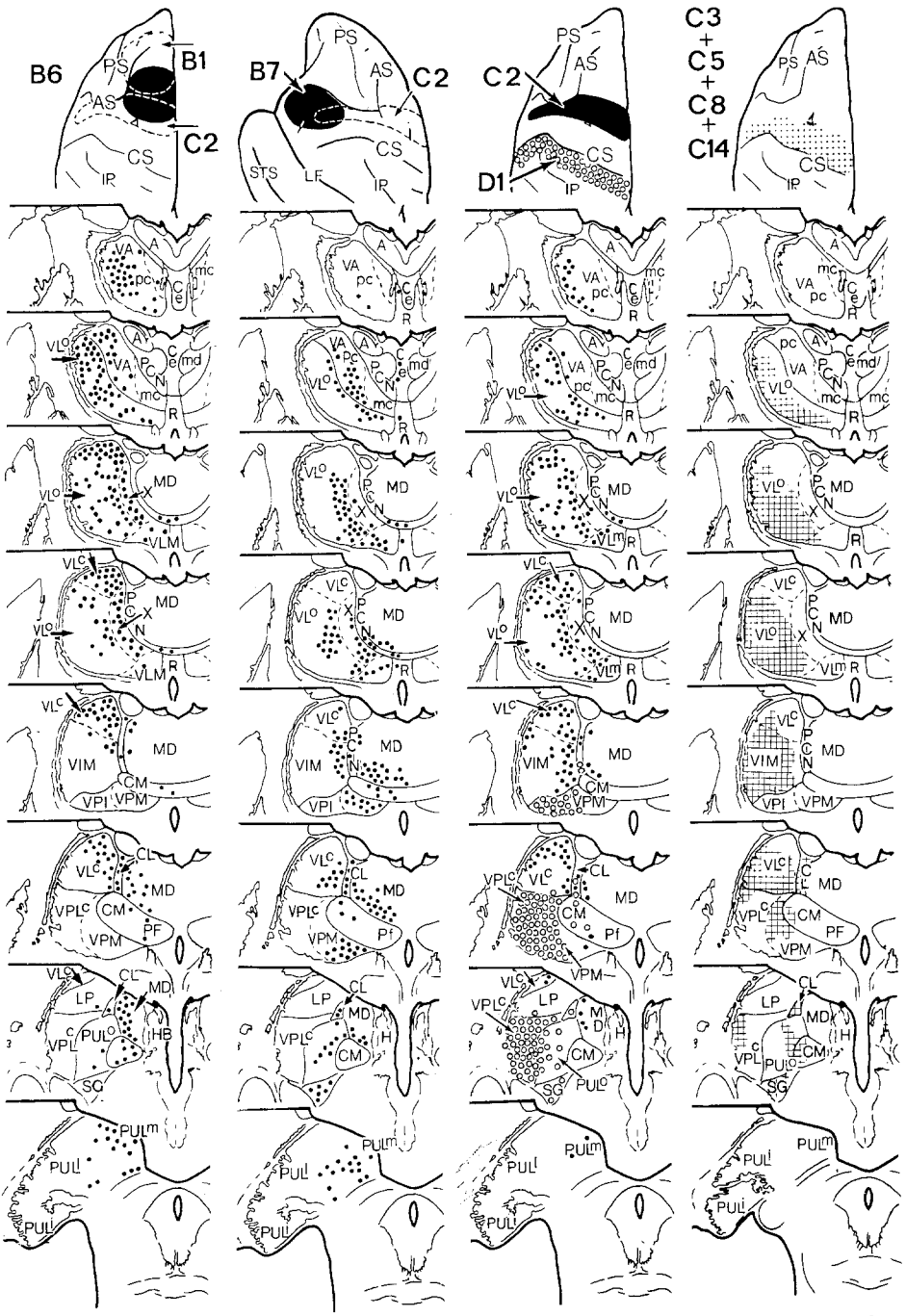

Fig. 2. Semidiagrammatic representation of the HRP-positive cortical areas (solid black and ○○) and the distributions of the retrogradely labelled thalamic neurons (cases B6, B7 and C1 ●● ; case D1 ○○) after injections at the rostral border of the precentral gyrus and in the postcentral gyrus respectively. For comparison, the total thalamic area occupied by the labelled neurons after injections in the caudal parts of the precentral gyrus is shown on the right

and immediately caudal to the inferior limb of this sulcus (B7) respectively (Fig. 2). The longitudinal populations of labelled neurons were located the one (case B6) dorsal to the other (case B7). They were both situated more laterally than those in the previous cases and were located mainly in the lateroventral compartment from where they extended only caudally across the internal medullary lamina. Both populations also showed the apparent medial shift and extended from the lateral half of the VApc through the medial parts of the VLo, VIM and VLc into the caudal paralaminar MD and the anterior part of the Pm.

In case B6 the HRP-positive cortical area extended from the superior frontal gyrus on the medial surface of the hemisphere into the upper bank of the arcuate sulcus. The dorsally situated longitudinal population of labelled neurons of this case was located lateral to the B1 population and extended (Fig. 2) from the dorsolateral part of the VApc into the dorsal and medial portions of the VLo and into area X. Caudal to area X the medial part of the population extended across the internal medullary lamina through the lateral paralaminar MD into the Pm, while the lateral part continued lateral to the internal medullary lamina into the dorsal and medial parts of the VLc (Fig. 2).

In case B7 in which the HRP-positive cortical area extended from the caudal bank of the arcuate sulcus into the area of the inferior precentral dimple, the opercular white matter also contained an abundance of HRP-reaction products up to the upper border of the insula. The ventrally located longitudinal population of labelled neurons of this case was situated lateral to the B2 population (Fig. 2) and extended from the ventrolateral caudal part of the VApc into the medial part of the VLo, lateral to area X. Further caudally the population increased in size and density and extended also into the ventral portion of area X and into the VLm. Caudal to this level the medial part of the population continued across the internal medullary lamina through the ventral paralaminar MD into the Pm. The lateral part, however, remained lateral to the internal medullary lamina and continued dorsal to the CM-Pf into the medial parts of the VIM and the VLc, and ventral to the CM-Pf mainly into the medial part of the VPM including the parvocellular VPMpc. In both cases (B6 and B7) some lightly labelled neurons were also present in the caudal part of the PCN and in the CL as well as in the Pf.

C. Injections in the Precentral Gyrus

In the first two cases (C1 and C2) of this group injections were made in the rostral part of the precentral gyrus but in the other cases in the caudal parts. In all the cases of this group the columns of labelled neurons were almost entirely restricted to the lateroventral compartment, but in the first two cases they were situated in its medial and dorsal parts, while in the other cases they were situated in its ventral and lateral parts.

In the first two cases (C1 and C2) linear rows of seven to eight injections were made rostrally in the precentral gyrus, parallel to the central sulcus. The HRP-positive cortical areas overlapped rostrally with that of case B6. The longitudinal populations of labelled neurons correspondingly overlapped with

the lateral portion of the B6 population and showed the same apparent medial shift. Thus in the rostral thalamus a limited group of labelled neurons was present (Fig. 2) in the outer shell of the VApc and continued through the caudally adjoining medial and intermediate parts of the VLo and the laterocaudal part of area X into the medial to intermediate parts of the VIM and the adjoining dorsomedial and dorsal parts of the VLc (Fig. 2). However, labelled neurons were lacking in the medial part of area X and in a thin paralaminar strip along the dorsal and medial margin of the VIM and VLc. In case C2 in which the row of injections continued into the lower one-third of the precentral gyrus, the longitudinal population of labelled neurons extended ventromedially (Fig. 2) into the ventral part of the VApc, the ventrocaudal part of area X and the VLm. A few sporadic labelled neurons also occurred caudally in the ventral paralaminar MD and in the anterior part of the Pm (cf. case B7). In both cases some lightly labelled neurons were present in the CL and a very few occurred medially in the CM.

In the other cases of this group, with injections in different mediolateral parts of the caudal portion of the precentral gyrus, tall vertically oriented longitudinal groups of labelled neurons occurred which after progressively more lateral injections in the precentral gyrus were located progressively more medially in VL. These groups together constituted a thick longitudinal band (Fig. 2) which was strongly tilted towards the horizontal and occupied the ventral and lateral parts of the VLo, the lateral three-fourths of the VIM and the adjoining ventral and lateral parts of the VLc.

In one case (C3) 18 injections were made in the lower one-third of the precentral gyrus next to the central sulcus and the HRP-positive cortical area extended into its rostral bank. The vertically oriented group of labelled neurons (Fig. 3), which constituted the most medial part of the thick tilted band (see above) extended from the medial part of the VLo, lateral to area X, into the medial part of the VIM and ventral to the CM into the dorsolateral part of the VPM.

In three cases (C5, C6 and C7) with 6, 6 and 14 injections respectively, in the precentral gyrus immediately above the knee of the central sulcus the vertically oriented longitudinal group of labelled neurons extended through the intermediate segments of the VLo, the VIM and the ventral part of the VLc (case C5, Fig. 3). In three other cases (C8, C9 and C10) with 6, 8 and 11 injections respectively at the level of the superior precentral dimple, the

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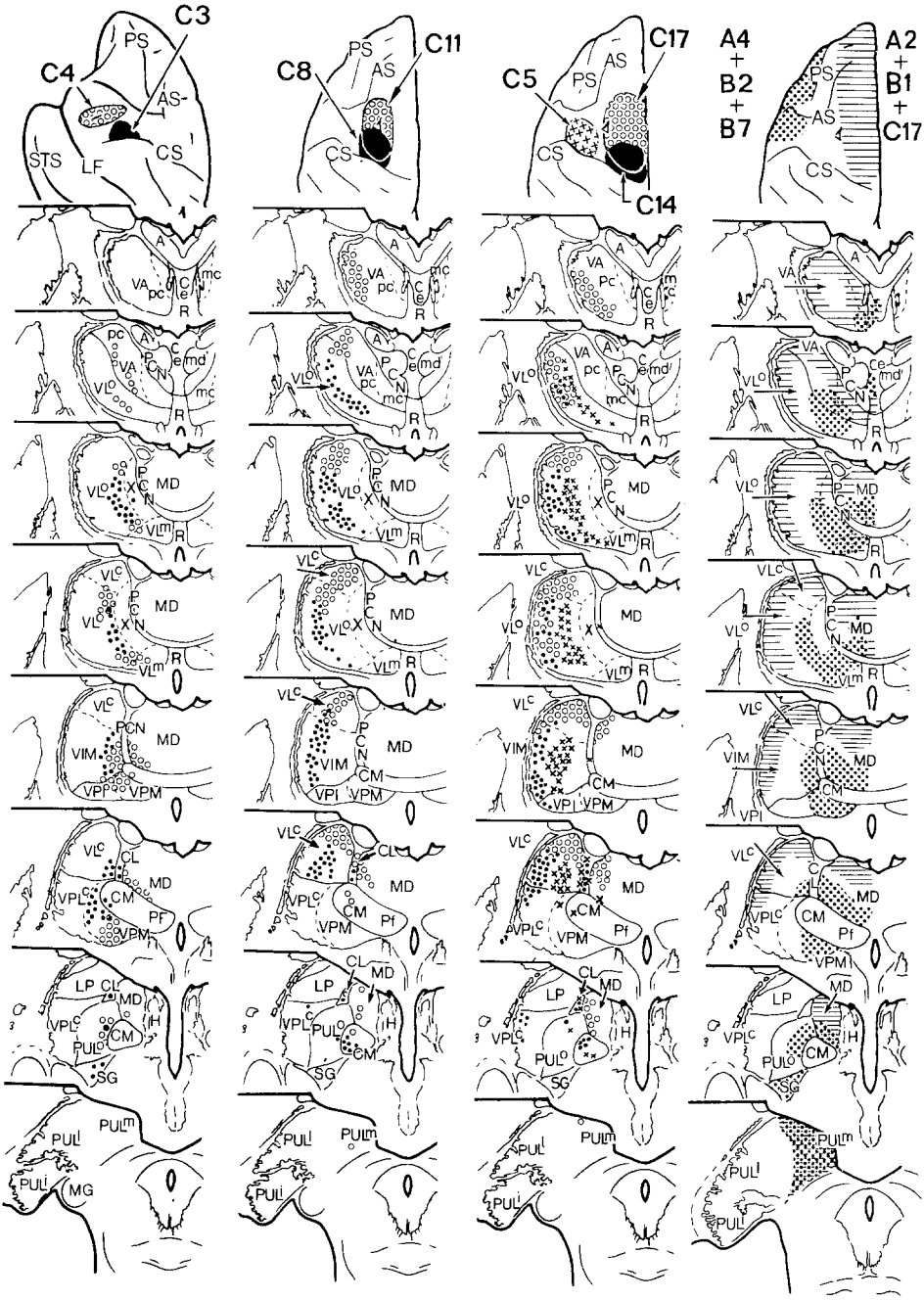
Fig. 3. Semidiagrammatic representation of the HRP-positive cortical areas (solid black, ++ , ○○) and the distributions of the retrogradely labelled thalamic neurons (●● , ++ , ○○) after injections in the caudal part of the precentral gyrus. First column on left shows the relatively more dorsal, ventral and rostral distribution of the labelled neurons in case C4 (○○) as compared to case C3 (●●). However, the C4 neurons (○○) occupied a different part of the VPM than the C3 neurons (●●). Second and third columns from left show the relatively more rostral and dorsal distributions of the labelled neurons in cases C11 and C17 (○○) as compared to cases C8 and C14 (●●). Column on right shows combined distributions of the labelled neurons in the central and peripheral parts of the thalamus in cases with injections along medial (⋰) and lateral (≡) margin of the frontal lobe respectively


C3
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B1
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MG

Fig. 3

longitudinal groups of labelled neurons were distributed in roughly the same way as in the preceding three cases (case C8, Fig. 3) but occupied a slightly more lateral position.

In three cases (C14, C15 and C16) with 18, 16 and 5 injections respectively in the upper portion of the caudal part of the precentral gyrus and the immediately underlying white matter the longitudinal group of labelled neurons was located very laterally in the thalamus and extended from the lateral parts of the VLo into the lateral parts of the VIM and the ventrolateral portion of the VLc. However, in cases C14 and C16 with injections in the cortex immediately adjoining the upper portion of the central sulcus, the group of labelled neurons continued caudally into the most lateral part of the VPLc (case C14, Fig. 3), while in case C15 without injections in this area no labelled neurons were present in the VPLc. In addition, in all cases with injections in the caudal part of the precentral gyrus many lightly labelled neurons were present in the caudal parts of the CL and some in the CM.

In four other cases linear rows of injections were made which extended from the central sulcus rostrally. In cases C11–C13 these rows of 16 injections extended through the area of the superior precentral dimple towards the area above the caudal part of the arcuate sulcus, while in case C17 a longer linear row of injections was placed along the medial margin of the hemisphere, extending from the upper part of the precentral gyrus into the area above the upper limb of the arcuate sulcus (cases C11 and C17, Fig. 3). In these cases longitudinal groups of labelled neurons were present in the intermediate and lateral parts of the VLo, the VIM and the ventral portion of the VLc, in the same way as in cases C8–C10 and in cases C14–C16 respectively. However, in the present cases the groups of labelled neurons extended further rostrally into the lateral part of the VApc and further dorsally into the dorsal parts of the VLo and VLc (cases C11 and C17, Fig. 3). Moreover, especially in case C17 the population of labelled neurons extended from the dorsal parts of the VLo and the VLc across the internal medullary lamina into the dorsolateral paralaminar MD.

In case C4, 8 injections were made around the inferior precentral dimple, i.e. more rostrally than in case C3, and an abundance of HRP-reaction products was present in the immediately underlying white matter. The distribution of the labelled neurons in this case (Fig. 3) resembled those in the above four cases such that in comparison to case C3 the group of labelled neurons in case C4 extended more rostrally into the laterocaudal part of the VApc, more dorsally into the dorsal part of the VLo and more medially trough the most medial part of the VIM into the ventral paralaminar MD (Fig. 3).

D. Postcentral and Parietal Injections

In case D1, 10 injections were made in the rostral part of the postcentral gyrus. HRP-reaction products were also present in the caudal bank of the central sulcus along its entire length and in the opercular white matter. The vast majority of labelled neurons was situated more caudally than in the preceding cases and occurred in the VPI, the VPLc and in the lateral part of the VPM (case

D1, Fig. 2), while virtually none were present either in the most dorsolateral part of the rostral VPLc (cf. cases C14 and C16) or in the VL complex including the VIM. Some labelled neurons also occurred in the Po as well as in the suprageniculate nucleus and a very few were present in the PCN and the CL as well as in the CM-Pf.

In case D2, 18 injections were made in the superior and the inferior parietal lobules. The area containing HRP-reaction products extended rostrally into the caudal part of the upper one-third of the postcentral gyrus, laterally into the banks of the posterior part of the intraparietal sulcus as well as the rostral bank of the upper part of the luneate sulcus and medially into the banks of the caudal part of the cingulate sulcus. Surprisingly enough, retrogradely labelled neurons were present not only in the caudal part of the thalamus but also in its rostral part. Caudally the bulk of the labelled neurons was distributed throughout the LP and the lateral part of the lateral pulvinar and some occurred also in the dorsal part of the VPLc and in the most caudal part of the VLc. Rostrally many labelled neurons were present in the rostral part of the PCN as well as in the adjoining VAmc. This latter population extended caudally into the ventral part of the MD and the adjoining medial part of the PCN and continued caudally in decreasing density up to level of the CM-Pf.

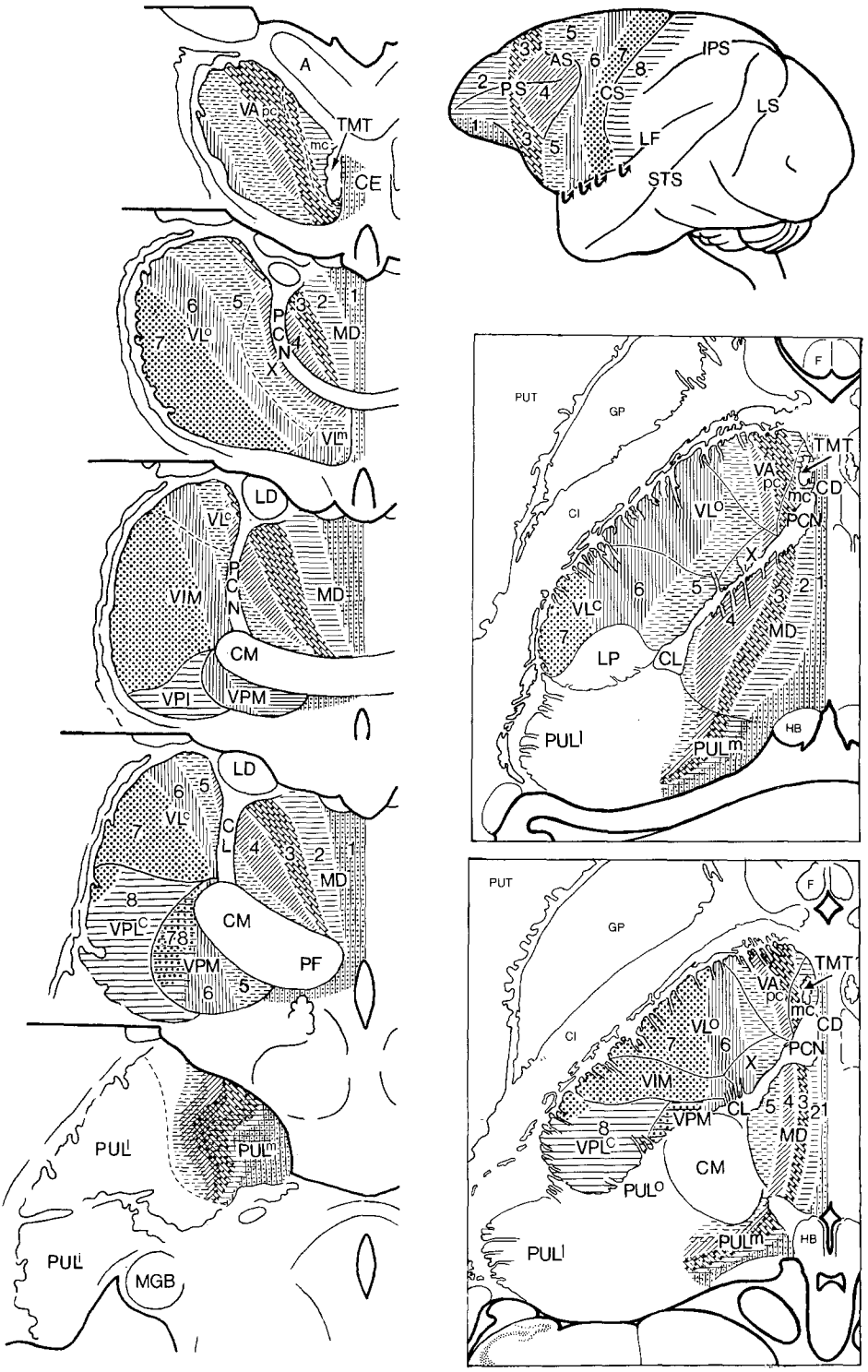
Discussion

The present findings demonstrate that HRP-injections in different frontal cortical areas result in the labelling of longitudinal columns of thalamic neurons. A comparison of the findings in cases A2 and A4; B1 and B6; C1, C5 and C8 indicates that the vast majority of the labelled neurons of these columns must have transported the enzyme from the HRP-positive cortical areas and the immediately underlying white matter and therefore will be regarded to distribute fibres to these cortical areas.

Cortical Strips and Thalamic Bands

The various injection sites were chosen such that the resulting HRP-positive cortical areas could be combined into transverse cortical strips resembling the anatomical and functional subdivisions of the frontal lobe (von Bonin and Bailey, 1947; Woolsey et al., 1950; Kuypers and Lawrence, 1967). In doing so the longitudinal columns of labelled neurons aggregate into rostrocaudally oriented bands which occupy the VA, VL, MD and the anterior Pm. Due to the wedge-shape of the thalamus as seen in horizontal sections, many of these longitudinal bands display along their rostrocaudal trajectory an apparent medial shift away from the lateral thalamic border and in several cases cross the obliquely oriented internal medullary lamina.

The most rostral transverse strip appears to receive afferents from the most medial thalamic band, while the progressively more caudal strips receive afferents from progressively more lateral bands which display an increasing tilt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4
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8
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PF
PUL l
PUL m
MGB
IPS
AS
PS
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STS
PUT
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Fig. 4

towards the horizontal. Thus the bands are distributed through a thalamic cross section as the ribs of a fan radiating from the area at the lower margin of the massa intermedia (Fig. 4). The central parts of these bands, i.e. those parts located ventromedially in the thalamus, appear to project to the lateral parts of the transverse cortical strips adjoining the lateral fissure, while the peripheral parts located dorsally, dorsolaterally and laterally in the thalamus appear to project to the medial parts of these strips adjoining the medial margin of the hemisphere (cf. combined distributions in cases A4, B2, B7 and in cases A2, B1, C17; Fig. 2). The cortical areas supplied by the more medial bands also appear to receive projections from the interlaminar PCN and from the Pf, while those supplied by the more lateral bands receive projections from the CL and from the CM.

The bands and columns in the different groups of cases show some mediolateral overlap which seems to reflect the rostrocaudal overlap between the HRP-positive cortical areas. When taking this into account, the present findings make it possible to distinguish seven transverse frontal cortical strips and longitudinal thalamic bands, the approximate positions of which are shown diagrammatically in Fig. 4.

Strip 1 comprises the orbitofrontal cortex (case A1) and receives afferents mainly from the most medial band, passing through the paramedian part of the MD into the anterior Pm. Strip 2 comprises the cortex of the most rostral part of the frontal convexity (cases A2 to A4) and receives afferents from band 2, which extends from the medial part of VAmc, across the internal medullary lamina, through the medial to intermediate portion of the MD into the anterior part of the Pm. Strips 3, 4 and 5 (cases B1 to B7) comprise the periarcuate area and should be regarded to include the rostral precentral operculum (see case B7). This periarcuate area appears to receive afferents from a slightly tilted broad thalamic band which extends from the medial three-fourths of the VApc through the dorsal and medial parts of the rostral VLo, area X, as well as the VLm, across the medullary lamina into the paralaminar MD and the anterior part of the Pm. A portion of this broad band continues, however, lateral to the internal medullary lamina into the extreme dorsomedial part of the VLc and the medial part of the VPM. The findings in cases B1 and B2 versus those in B6 and B7 indicate that the rostral and the caudal parts of the periarcuate area, i.e. strip 3 and strip 5, receive afferents from the medial and lateral parts of this broad thalamic band, i.e. from bands 3 and 5 respectively. The arcuate gyrus (cortical substrip 4) in the centre of this periarcuate area (cases B3 to B5) appears to receive afferents from a neuronal column (band 4) which is sandwiched between bands 3 and 5 and extends from the VApc, while increasing in size, mainly through

Fig. 4. Diagrammatic approximation of the position of eight transverse cortical strips (see text) and the corresponding eight thalamic afferent bands. Note in cross sections (left) that progressively more caudal strips receive afferents from progressively more lateral bands which display an increasing tilt towards the horizontal. Note in horizontal sections (right) that the bands are oriented rostrocaudally and in some cases extend across the internal medullary lamina from one nucleus into another

the lateral paralaminar MD into the anterior part of the Pm. Strip 6 comprises the rostral part of the precentral gyrus (cf. cases B6, B7 and cases C1, C2, C4) as well as the adjoining opercular cortex (see case C4). This strip appears to receive afferents from the tilted band 6 which is located lateral to band 5 and extends from the caudolateral border of the VApc through the medial to intermediate parts of the VLo, probably including the caudal part of area X, into the medial to intermediate parts of the combined VIM and VLc and VPM. Strip 7 (cases C3, C5, C6 to C10, C14 to C16) comprises the caudal part of the precentral gyrus and appears to receive afferents from a strongly tilted thick band (7) which occupies the ventral and lateral parts of the VLo, the VIM and the VLc as well as the dorsolateral part of the VPM. The upper part of this strip appears to receive afferents also from the lateral part of the VPLc (cases C14 and C16). The postcentral strip 8, including the postcentral opercular cortex, appears to receive afferents from the VPLc, the VPI and the lateral part of the VPM.

Earlier studies have defined the organization of the thalamo-cortical projections by outlining the cortical distribution area of the various specific thalamic nuclei. From this vantage point the present findings confirm and extend earlier observations. However, the present data also suggest that the population of thalamic neurons which project from a specific nucleus to a certain cortical area form part of a band or column of neurons which may extend from one nucleus into another. Both points will be dealt with in the following discussion.

Labelling of Specific Thalamic Nuclei

The distribution of labelled MD neurons after the various injections supports earlier conclusions (Walker, 1938a; Nauta, 1962; Akert, 1964; Tobias, 1975) concerning the organization of the MD projections to the frontal lobe. The VA, because the strong labelling of its neurons as compared to the CL (Jones and Leavitt, 1974) will be regarded as a specific thalamic nucleus. According to degeneration studies this nucleus projects to the areas rostral to the precentral gyrus (Le Gros Clark and Boggon, 1935; Chow and Pribram, 1956; Kruger and Porter, 1958; Carmel, 1972) and possibly also to areas further rostrally (Le Gros Clark and Boggon, 1935; Carmel, 1972) in agreement with the present findings (e.g. case A2). The labelling of VA neurons from the parietal cortex (case D2) may correspond with findings in the cat (Mizuno et al., 1975). Earlier evidence for projections from area X and probably also from the VLc to the area immediately rostral to the precentral gyrus (Le Gros Clark and Boggon, 1935; Roberts and Akert, 1963; Strick, 1976) is supported by the present observations and the existence of such projections is reflected in the tilted position of band 5 which extends from the ventromedial to the dorsolateral parts of the VL.

The VLo, VIM (VPLo). VLc and VPM projections to the precentral gyrus as demonstrated in the present material have been reported earlier (Walker, 1938a, 1938b; Chow and Pribram, 1956; Kruger and Porter, 1958; Roberts and Akert, 1963; Dekker et al., 1975; Strick, 1976). These projections parallel the reciprocal precentral projections to several of these nuclei (Sakai, 1967; Petras,

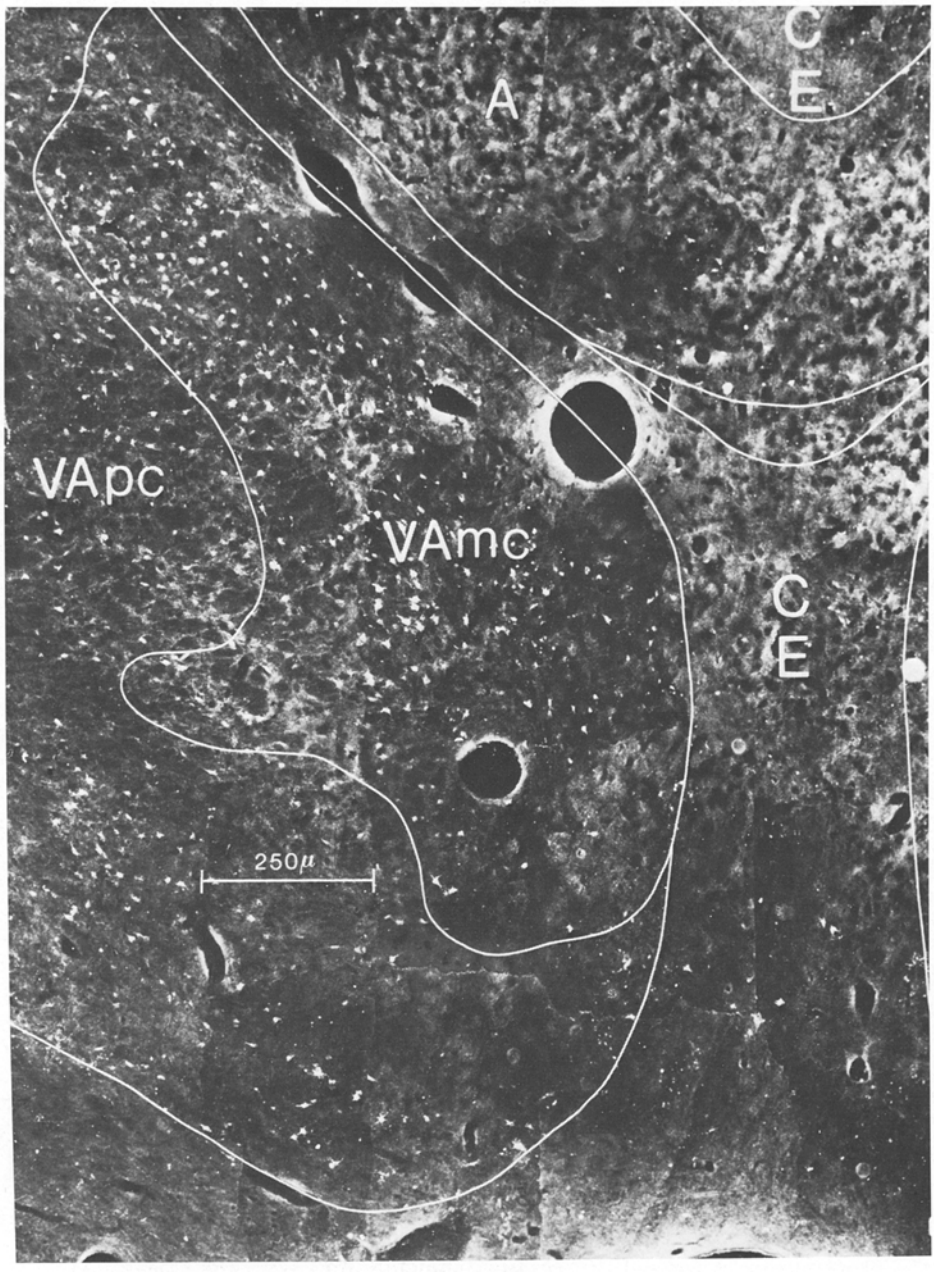

Fig. 5. Composite darkfield photomicrograph of the VA in case B1 (cf. Fig. 1) with injections around the rostral end of the upper limb of the arcuate sulcus. Note presence of labelled neurons in VAmc and in VApc

1969; Künzle, 1976). The almost exclusive labelling of VPLc and VPM and VPI after postcentral injections is in keeping with earlier findings (Strick, 1976) and supports the contention that the VB complex, and apparently especially its caudal part (VPLc), projects mainly to areas 3, 1 and 2 (Jones and Powell, 1970; Burton and Jones, 1976). This is also in keeping with the fact that the reciprocal postcentral fibres are distributed to these same nuclei; VPLc, VPM and VPI (Sakai, 1967; Jones and Powell, 1970; DeVito and Simmons, 1976). Labelling of neurons laterally in VPLc after injections in the rostral bank of the upper end of the central sulcus (cases C14 and C16) probably reflects the presence of area 3a in the deep part of the rostral bank at this level (Powell and Mountcastle, 1959).

The existence of VPM projections to the postcentral gyrus, the lower one-third of the precentral gyrus (area 3) and the precentral operculum (Walker, 1938a; Roberts and Akert, 1963; Burton and Jones, 1976) is compatible with the labelling of the VPM after precentral and postcentral injections (cases C3 and D1) and is in keeping with the existence of projections from the lower one-third of the precentral and the postcentral gyrus to the VPM (Sakai, 1967; Künzle, 1976). The labelling of VPMpc neurons in case B7 probably resulted from the deposition of enzyme in the white matter close to the insular border (cf. Burton and Jones, 1976). The present findings also confirm the existence of Pm projections to the rostral frontal cortex (Trojanowski and Jacobson, 1974; Bos and Benevento, 1975).

The projections from the central and peripheral parts of the thalamic bands to the lateral and medial parts of the frontal lobe respectively (Fig. 3) provide a framework for the earlier conclusions that the neurons projecting to the frontal operculum and the insula are located around the CM-Pf (Roberts and Akert, 1963) while the neurons dorsally in the MD project to the medial parts of the frontal lobe (Walker, 1938a; Akert, 1964). The labelling of neurons in the lateral paralaminar MD after arcuate gyrus injections, i.e. in the middle one-third of the mediolateral extent of the periarcuate area (cases B3, B4, B5) also conforms to this principle because the lateral paralaminar MD is located in the intermediate one-third of the broad periarcuate thalamic band (bands 3, 4 and 5). The pronounced tilt of band 7 (Fig. 4) converts its central-peripheral subdivision into a medial-lateral one, which explains the earlier findings that the medial, intermediate and lateral segments of the VL, including the VPLo, project to the precentral face, arm and leg areas respectively (Le Gros and Boggon, 1935; Walker, 1938a; Strick, 1976)

The findings of a limited CM and Pf projection to the precentral gyrus and the more rostral, frontal areas respectively support earlier observations (Bowsher, 1966; Dekker et al., 1975; Strick, 1976). These projections parallel the pronounced reciprocal projections from these areas to the CM-Pf (Petras, 1964; Kuypers, 1966; Kuypers and Lawrence, 1967; DeVito, 1969). The findings of PCN and CL projections to the rostral and caudal parts of the frontal lobe respectively resemble earlier degeneration findings in cat (Murray, 1966; Macchi et al., 1970) and HRP findings in the monkey (Dekker et al., 1975; Strick, 1976). However, the PCN was found to project also to the parietal cortex (case D2).

Longitudinal Columns of Labelled Neurons

One of the unexpected findings of the present study was the fact that some of the longitudinal groups of labelled neurons extended from one nucleus into another. For example, after rostral frontal injections these groups of neurons extended from the medial part of the VA, across the internal medullary lamina, through the MD into the Pm (cf. cases A2 and B1; Fig. 1). Moreover, after injections in the caudal part of the area above the arcuate sulcus (case B6, Fig. 2) the group of neurons extended from the lateral part of the VA through the paralaminar VL and the caudal paralaminar MD into the Pm. These findings obtain some support from earlier data which may be interpreted to suggest overlap in the VA, MD and Pm projections to the rostral part of the frontal lobe (Le Gros Clark and Boggon, 1935; Carmel, 1972; Tanaka, 1973; Trojanowski and Jacobson, 1974; Bos and Benevento, 1975) and overlap in the VA, area X and VLc projections to the cortex above the arcuate sulcus (Le Gros Clark and Boggon, 1935; Chow and Pribram, 1956; Roberts and Akert, 1963; Akert, 1964; Carmel, 1972). The findings are also reminiscent of the fact that in monkey, chimpanzee and man, after frontal lesions retrograde degeneration may occur in the rostrolateral MD in combination with the medial part of the VA (Walker, 1938b; Freeman and Watts, 1947) and in the VL in combination with the lateral part of the VA (Walker, 1938b; Freeman and Watts, 1947; Meyer et al., 1947).

In view of the present findings the thalamus seems to contain a hidden matrix of longitudinal cell columns which may represent the basic thalamic building blocks in respect to the specific thalamo-cortical connexions. Some of these columns would extend across the internal medullary lamina and traverse specific nuclear borders (Fig. 4). Such a matrix would imply that afferents to two different nuclei located in different parts of the thalamus may ultimately converge on the same cortical area.

The existence of such a matrix is supported by the fact that several fibre systems seem to follow its pattern. For example the intrathalamic trajectories of the thalamo-cortical and the cortico-thalamic fibres to and from the rostral part of the frontal lobe display a similar rostrocaudal orientation as the longitudinal columns projecting to these cortical areas (Scheibel and Scheibel, 1966, 1967) and these trajectories apparently involve the MD together with the VA (Showers, 1958; DeVito and Smith, 1964; Astruc, 1971; Tobias, 1975; Tanaka, 1976). The trajectories of the descending intrathalamic fibres (Carmel, 1972) from the VA across the internal medullary lamina into the MD and of the ascending CM fibres through the internal medullary lamina and the VA to the putamen (Mehler, 1966) also seem to conform to the matrix.

The same seems to apply to the distribution areas of the cerebellar and fastigial fibres. The former area which occupies most laterally the VLc and the caudolateral part of the MD tapers down rostrally to the lateral part of the VA, while the latter area which occupies most caudally the ventral part of the VLc tapers down rostrally through the VIM and the caudal part of area X to the lateral part of the VLo (Kievit and Kuypers, 1972).

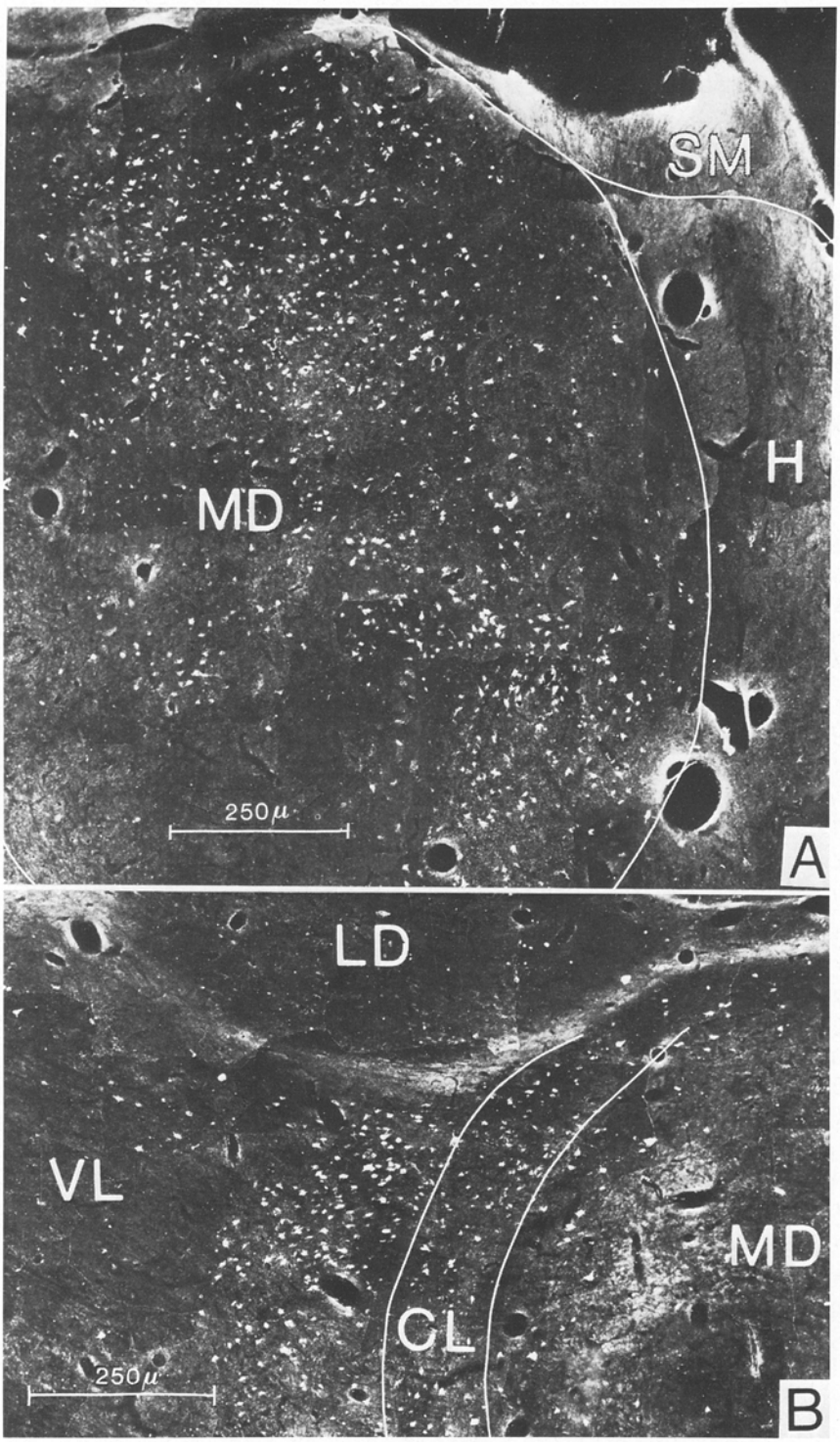

Fig. 6

Assuming the existence of such a thalamic matrix it is, however, surprising that only few studies (Le Gros Clark and Boggon, 1935; Tanaka, 1973) reported columns of retrograde degeneration extending across nuclear borders after frontal lesions. This may be due to the fact that the thalamus has generally been studied in transverse sections and strong emphasis has been placed on midthalamic levels (Akert, 1964). It may also be due to the fact that only the MD segment of the prefrontal thalamic band shows severe degeneration since the retrograde changes in the VA generally are less pronounced than in the MD (Walker, 1938a; Powell, 1952) and those in the anterior part of the Pm apparently only occur after combining frontal lesions with rostral temporal lesions (Chow, 1950). However, it may also be argued that the longitudinal distribution of labelled neurons across nuclear borders does not represent a thalamic organization but reflects the rather large size of the HRP-positive areas comprising parts of the presumably distinct projection areas of the different specific nuclei. Yet, the fact that columns of labelled neurons extending through several nuclei also occurred after restricted injections (cases B2, C4) and that such columns show a systematic shift through the nuclei after injections in adjacent cortical areas (cf. cases A2, B1, B6, C2, C14 and A4, B2, C4, C3) strongly favour the existence of a columnar arrangement.

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Fig. 6. Composite darkfield photomicrograph (A) shows the labelled neurons in caudal part of MD in case B1 (cf. Fig. 1) with injections around the rostral end of the upper limb of arcuate sulcus and (B) shows the labelled neurons in the lateral part of MD, in CL, and in the medial part of VL in case B6 (cf. Fig. 2) with injections in caudal part of the area above arcuate sulcus

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