

Laminar and Columnar Distribution of Geniculo-cortical Fibers in the Macaque Monkey

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ABSTRACT Single cell recordings in monkey striate cortex have shown differences in response properties from one cell layer to the next and have also shown that the IVth layer, which receives most of its input from the geniculate, is subdivided into a mosaic of regions, some connected to the left eye, others to the right. In the present study small lesions were made in single layers or pairs of layers in the lateral geniculate body, and the striate cortex was later examined with a Fink-Heimer modification of the Nauta method. We hoped to correlate the laminar distribution of axon terminals in the cortex with functional differences between layers, and to demonstrate the IVth-layer mosaic anatomically.

After lesions in either of the two most dorsal (parvocellular) layers, terminal degeneration was found mainly in layer IVc, with a second minor input to a narrow band in the upper part of IVa. A very few degenerating fibers ascended to layer I. In contrast, lesions in either of the two ventral (magnocellular) layers were followed by terminal degeneration confined, apparently, to IVb, or at times extending for a short distance into the upper part of IVc; no degeneration was seen in layer IVa or in layer I.

After a lesion confined to a single geniculate layer, a section through the corresponding region of striate cortex showed discrete areas or bands of degeneration in layer IV, usually 0.5–1.0 mm long, separated by interbands of about the same extent in which there was no terminal degeneration. When serial sections were reconstructed to obtain a face-on view of the layer-IV mosaic, it appeared as a series of regular, parallel, alternating degeneration-rich and degeneration-poor stripes. When a geniculate lesion involved both layer VI (the most dorsal, with input from the contralateral eye) and the part of layer V directly below (ipsilateral eye), the cortical degeneration, as expected, occupied a virtually continuous strip in layer IVc and the reconstructed face-on view of this layer showed a large confluent region of degeneration.

In some of the reconstructions the cortical stripes seemed highly regular; in others there was a variable amount of cross connection between stripes. The stripes varied in width from 0.25 to 0.50 mm, and width did not seem to correlate with region of retinal representation.

It is concluded that the long narrow stripes of alternating left-eye and right-eye input to layer IV are an anatomical counterpart of the physiologically observed ocular-dominance columns. Because of this segregation of inputs, cells of layer IV are almost invariably influenced by one eye only. A cell above or below layer IV will be dominated by the eye supplying the nearest IVth layer stripe, but will generally, though not always, receive a subsidiary input from the other eye, presumably by diagonal connections from the nearest stripes supplied by that eye.

A glance at a section through the cerebral cortex shows that it is subdivided into alternately cell sparse and cell rich horizontal layers. This subdivision is especially striking in the primary visual, or striate,

cortex (area 17) of the monkey. By recording from single cells in this area it has been possible to demonstrate clear differences in responses to visual stimuli from the different layers. Not surprisingly, cells

of layer IV, which is the site of termination of afferents from the lateral geniculate body, have the simplest properties and show the least intermingling of inputs from the two eyes. The more complex cell-types, for the most part binocularly driven, are found in layers above and below. In its structure layer IV is itself non-uniform, consisting of several distinct subdivisions; up to the time of the present study the exact distribution of the afferent endings within this layer was not known, though this is of obvious importance for an interpretation of the physiology.

Physiological studies have shown that the cortex is also parcelled by vertical partitions into at least two independent but overlapping systems of columns (Hubel and Wiesel, '68). In the first of these, cells with similar orientation preference are grouped together. In the second system, cells are grouped according to eye dominance, the cells of one column mostly favoring the left eye, those of the next the right. Layer IV, whose cells are strictly monocular, is thus divided into a mosaic of left-eye and right-eye patches. While it has long been known that cells deep to a given point on the cortical surface are richly interconnected, there has been no hint from the anatomy that the interconnected cells occur in discrete groupings.

The primary object of the present work was to demonstrate the ocular-dominance columns anatomically. We were anxious to have the satisfaction of actually seeing the mosaic whose existence the physiology suggested, and wanted especially to learn if it had the form of a checkerboard, or of islands of one type embedded in a matrix of the other type, or of alternating left-eye and right-eye stripes.

The following method of demonstrating the ocular-dominance columns occurred to us. A lesion in the lateral geniculate body leads to degeneration of thalamocortical axons and axon terminals that can then be selectively stained by silver-impregnation methods. The geniculate consists of six cell layers, each of which receives input from one eye only. If a lesion could be confined to a single geniculate layer there might be some hope of seeing the predicted patchy distribution of degenerating axon terminals entering the cortex. By

using extracellular microelectrodes it should be possible to ascertain the position of the electrode tip by single-cell recording and then to make small lesions by passing current. Among silver-degeneration methods, the Fink-Heimer modification of the Nauta method seemed especially suitable, since it stains not only degenerating axons, but also what are almost certainly degenerating presynaptic terminals.

Such an experimental approach promised not only to outline the ocular-dominance columns, but also to show the exact distribution of the afferent terminals within layer IV of the cortex. It also opened the possibility of comparing the terminations of axons from the four dorsal geniculate layers with those from the two ventral layers, a matter of some interest because the two sets of layers differ both in their morphological appearance and their physiological properties (Wiesel and Hubel, '66). A preliminary account of some of this work has already been published (Hubel and Wiesel, '69).

METHODS

Eighteen monkeys were used, but not all lesions were suitably placed and for unknown reasons the staining was unsatisfactory in some animals. In all, 12 successful lesions were made, and complete reconstructions of the resulting intracortical fiber degeneration were made for eight of these. Survival times were 4–6 days.

The animal was anesthetized with thiopental and prepared for recording in the usual way (Hubel and Wiesel, '68), except that no neuromuscular blocking agent was used and intubation and artificial respiration were therefore not necessary. Tungsten microelectrodes with a shaft diameter of 125 μ were tapered to a tip of less than 1 μ over a distance of about 1 cm, and had an uninsulated tip length of 35 μ . The electrode was inserted into the lateral geniculate body either vertically, through the folds of cortex and white matter directly above, or in the coronal plane at an angle of 45° to the vertical. It was usually possible to tell where the electrode tip was in relation to the layers by observing successive changes in the eye from which cells could be driven. On passing from the third to the second layer there was of course no

change in the eye from which responses were evoked, but one could recognize the point of transition by the changes in response properties and receptive-field characteristics of single cells (Wiesel and Hubel, '66). By lowering and raising the electrode, the depths corresponding to the point of entering or leaving a given layer were determined. A large lesion or a series of lesions was then made between these points. When several lesions were made along a track they were spaced closely enough to produce a single long cigar-shaped lesion. This was an especially useful method when the electrode entered the lateral geniculate obliquely and advanced for some distance parallel to a single layer (fig. 8a).

Before the lesions were made the position of geniculate-cell receptive fields was noted on the projection screen, relative to the center of gaze. Because of eye movements it was usually possible to do this only to within a degree or so. From the receptive-field positions the site of the lesion in the geniculate could be estimated, and one could predict the region of striate cortex in which degenerating fibers would be found.

After perfusion-fixation with 10% formal-saline the cortex was cut in parasagittal serial frozen sections at 30 μ , and stained by a variant of the Nauta method (Nauta and Gyax, '54; Fink and Heimer, '67; Wiitanen, '69). The lateral geniculate body was sectioned in the coronal plane and alternate sections stained for Nissl substance or for degenerating fibers.

Degenerating fibers appeared, as in any Nauta preparation, as chains of black dots or black elongated particles about 2–4 μ in diameter that could usually be followed as long as the fiber remained in the plane of section. What we assumed were degenerating synaptic endings appeared as round dark-staining particles, also about 1–2 μ in diameter, peppered at random throughout sharply demarcated regions (see below) rather than in orderly chains. These dots could possibly be confused with background dust that is often found in these stains, but the dust, when it occurred, was much finer in consistency and was widely distributed throughout each section. The great majority of sections were for-

tunately almost totally free of this dust. It should be emphasized, however, that the main weakness of this method is the impossibility of knowing for certain whether any particular dot is a degenerating terminal: the recognition of endings must depend mainly on their grouping. In the present material the endings in layers IVa and IVc were so strikingly dense as to leave little doubt to their identification. On the other hand, it is not possible to say that there were no degenerated endings in the other layers. The proof that the large particles are presynaptic terminals will depend ultimately on electron microscopy. Similar particles in other material have in fact been so identified (Heimer and Peters, '68). While in the descriptions given below we shall refer to the particles as boutons, omitting quotation marks or qualifications, the absence of a rigorous identification should be borne in mind. An important feature of this modified Nauta stain is the ease with which (at least in the system in which we were working) the boutons were sharply distinguishable from degenerating fibers. The very feasibility of the present study depends on this distinction.

Fibers of passage

A lesion in any but the most ventral geniculate layer will not only destroy cells, but also, presumably, geniculo-cortical fibers passing through the lesion site from the layers below. There was a risk that destruction of these fibers of passage might hopelessly contaminate the degeneration arising from destruction of cell bodies. As the geniculate axons leave a given layer, however, they tend to fan out, crossing the more dorsal layers not radially, along corresponding points in the successive retinotopic maps (lines of projection), but along the most direct route upwards and posteriorly. A lesion in a given layer might therefore be expected to lead to a dense and focal cortical projection due to cell-body destruction, and a more diffuse projection due to interruption of fibers of passage. The observed thalamo-cortical projections in fact took this form, with a main focus of dense degeneration occupying a restricted region a few millimeters in diameter, and a region of much lighter degeneration usually extending for many

millimeters along the cortex, generally only on one side of the main focus and resembling the tail of a comet. In reconstructing lesions or determining the cortical laminar distribution of afferents, this sparse projection was ignored. As would be expected, lesions of the most ventral layer showed only the dense focus, with no comet tail.

Reconstructions

Once the region of cortical degeneration was found it was necessary to make a detailed reconstruction. Negative enlargements ($\times 33$) were made directly from each slide, and the regions showing terminal degeneration, as seen by microscopic examination, were indicated on the print in ink. Small blood vessels and other features that appeared on the enlargement were used as a guide in positioning these marks (see fig. 9). The regions of layer IVb or IVc showing degenerating terminals were then traced onto 1 mm lined tracing paper, using a new line for each successive section. Blood vessels were used in bringing successive sections into register. (Where the cortex was curved it was obviously necessary to straighten, in effect, layer IV; this was done by dividing it into a number of segments). The result was a face-on view of layer IV magnified 33 times. No attempt was made to correct for shrinkage, but comparisons of cortical thickness suggested that it did not differ grossly from one brain to the next. To assess the sites of termination of afferent

fibers relative to the cortical layering, occasional slides were counterstained with cresyl-violet.

RESULTS

Of the 12 lesions, seven were in the dorsal (parvocellular) part of the geniculate, and five were in the ventral (magnocellular) part. No lesions were made in dorsal layers 3 and 4 and, while it seems highly likely that these layers project in the same way as the upper two parvocellular layers, studies are now under way to verify this. The lesions were scattered widely through the geniculate, two being within a degree or two of the foveal representation, eight in the midperiphery, and two in areas representing the far periphery, $50-80^\circ$ from the fovea. The position of each of the lesions is given in table 1.

The occipital cortex, and cortex associated with the lunate and superior temporal sulci were examined. No degeneration was seen outside the striate cortex.

For the present paper we have adopted Brodmann's layering system for the striate cortex. A superficial inspection of the Nissl-stained Macaque area 17 (fig. 1) shows it to be composed of three cell-sparse

Fig. 1 Nissl- (cresyl-violet) (A) and myelin- (Loyez) (B) stained sections through striate cortex (area 17) of Macaque monkey to show the layering system used in this paper. The Nissl stain shows three cell-sparse regions, layers I, IVb and V, and three cell-dense regions, layers II, III and IVa collectively, layer IVc, and layer VI. The line of Gennari is roughly located in layer IVb.

TABLE 1

Monkey number	Layer of LGB lesion	Receptive-field positions relative to foveal projection			Period of stripes	Figure number
		Vertical ¹	Horizontal	Total distance		
8	Dorsal (6)	-2.5°	4.5°	5°	1.2	14
9	Dorsal (6)	8.5°	11°	13.5°		
11	Ventral (2)	4°	10°	10°		
12	Dorsal (6)	-9°	10°	14°	0.7	
14	Dorsal (5, 6)	-8°	12°	14.5°	0.6	2, 3, 7-10 5, 11-13
15	Dorsal (5)	0°	0°	0°	0.8	
16	Dorsal (6)	-10°	20°	22.5°	0.7	15
19	Ventral (1, 2)	-30°	40°	50°		
33	Dorsal (3), Ventral (2)	2°	10°	10°		
36	Ventral (1)	6°	13°	14.5°	0.5	
37	Ventral (1, 2)			$40-90^\circ$		16
41	Ventral (1)	-1°	2.5°	3°	0.5	

¹ Negative numbers indicate field positions below the foveal projection.

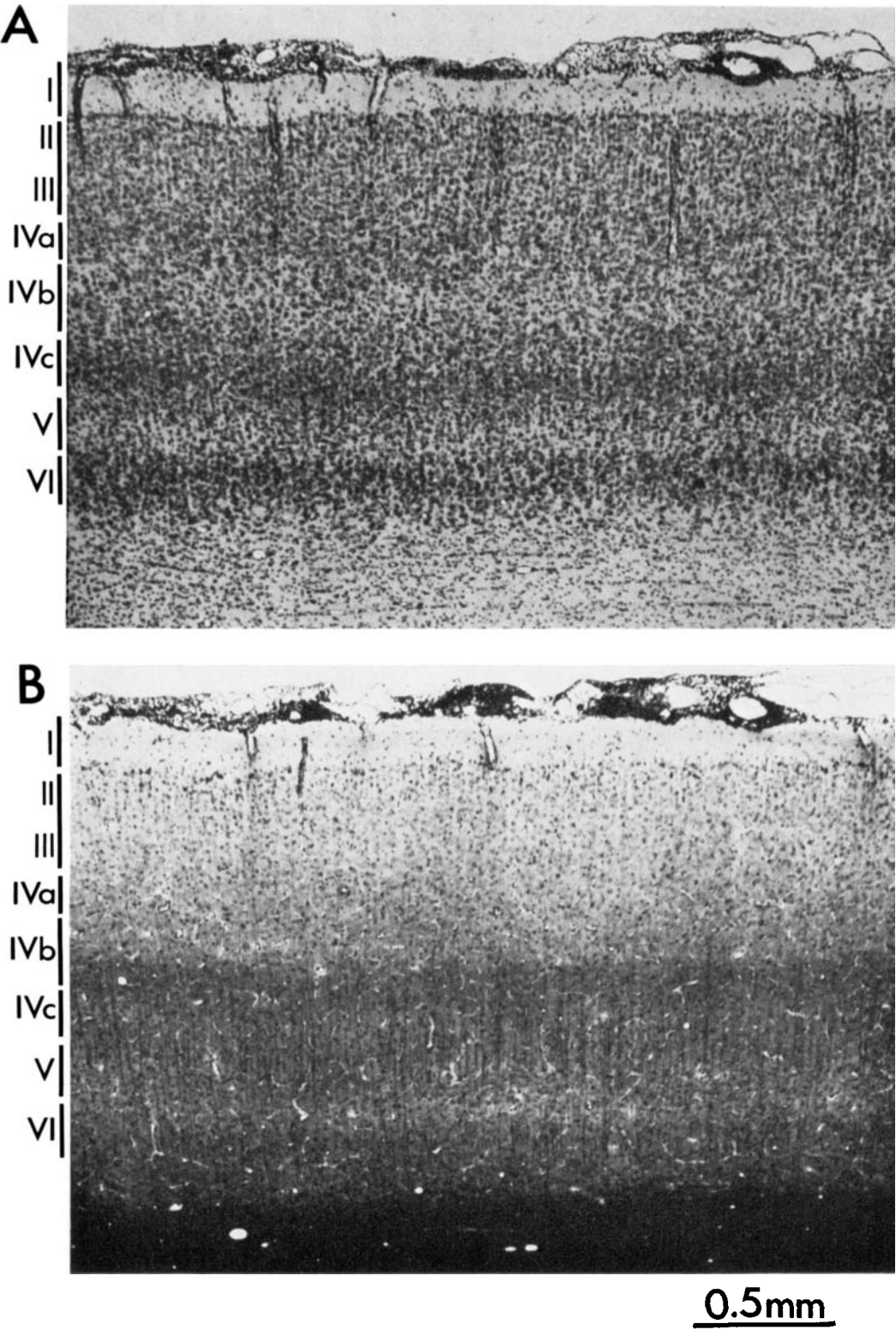


Figure 1

layers alternating with three cell-dense layers. In Brodmann's system the cell sparse layers are I, IVb and V; the cell dense layers are II, III and IVa (which appear as a single layer in the Macaque), IVc, and VI. In previous papers (Hubel and

Wiesel, '68, '69) we saw no justification for separating layers III and IVa, since we did not realize that geniculate afferents reach the lower part of the uppermost cell-dense region (II, III, IVa). We therefore adopted von Bonin's layering system,

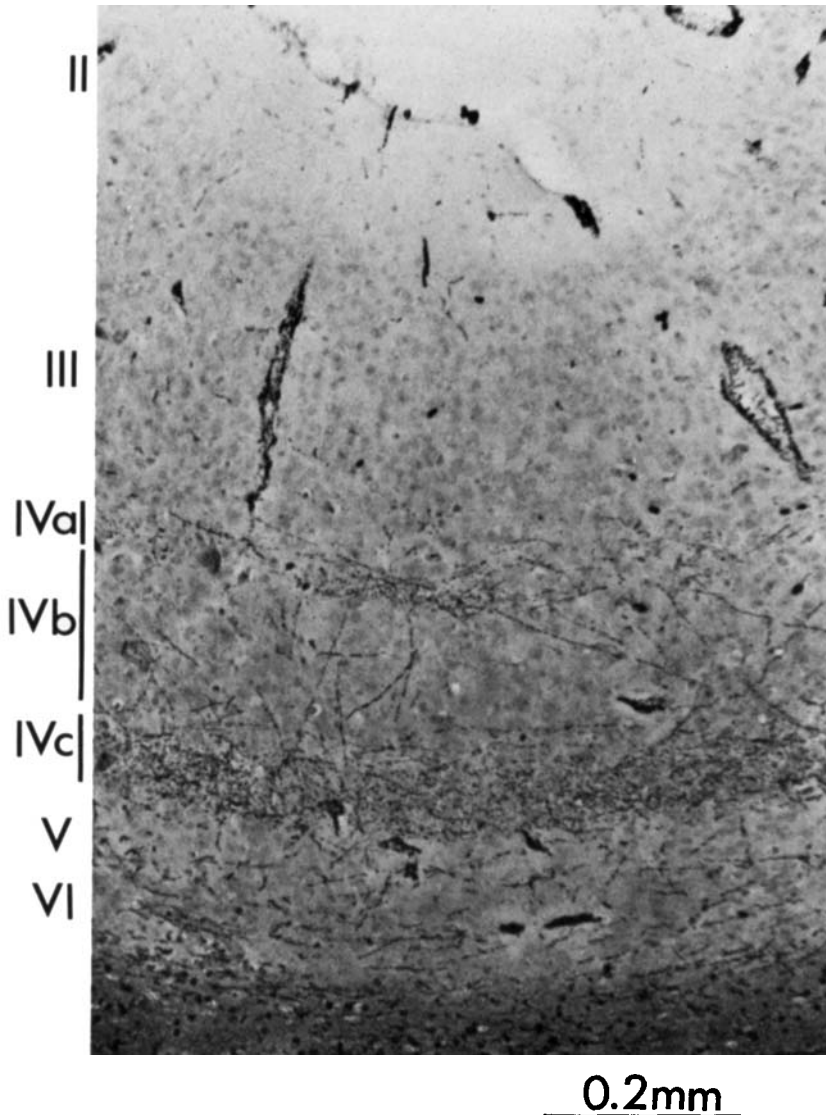


Fig. 2 Low and high power photographs of a Fink-Heimer stained section through the striate cortex of monkey 12 in which a microelectrode lesion had been made in LGB layer 6, four days prior to perfusion (see table 1 and figs. 3, 7-10). Degenerating fibers ascend diagonally through layers VI and V, and presumably branch extensively in IVc, which is densely loaded with boutons. A moderate number of fibers ascend further through layer IVb to IVa, where more boutons are seen.

which makes no distinction between III and IVa. The results of the present work show that some afferents indeed ascend further than was previously realized, ending in the lower portions of the upper cell-dense region. We have therefore reverted to Broadmann's system, calling this region IVa even though it cannot easily be distinguished from layer III in Nissl preparations.

Laminar distribution of afferent fibers

Lesions of dorsal (parvocellular) geniculate layers

The laminar distribution of degenerating afferents following a dorsal-layer geniculate lesion formed a highly consistent pattern in the seven monkeys. Figure 2, from monkey 12, shows the degenerating fibers and terminals in a section that was

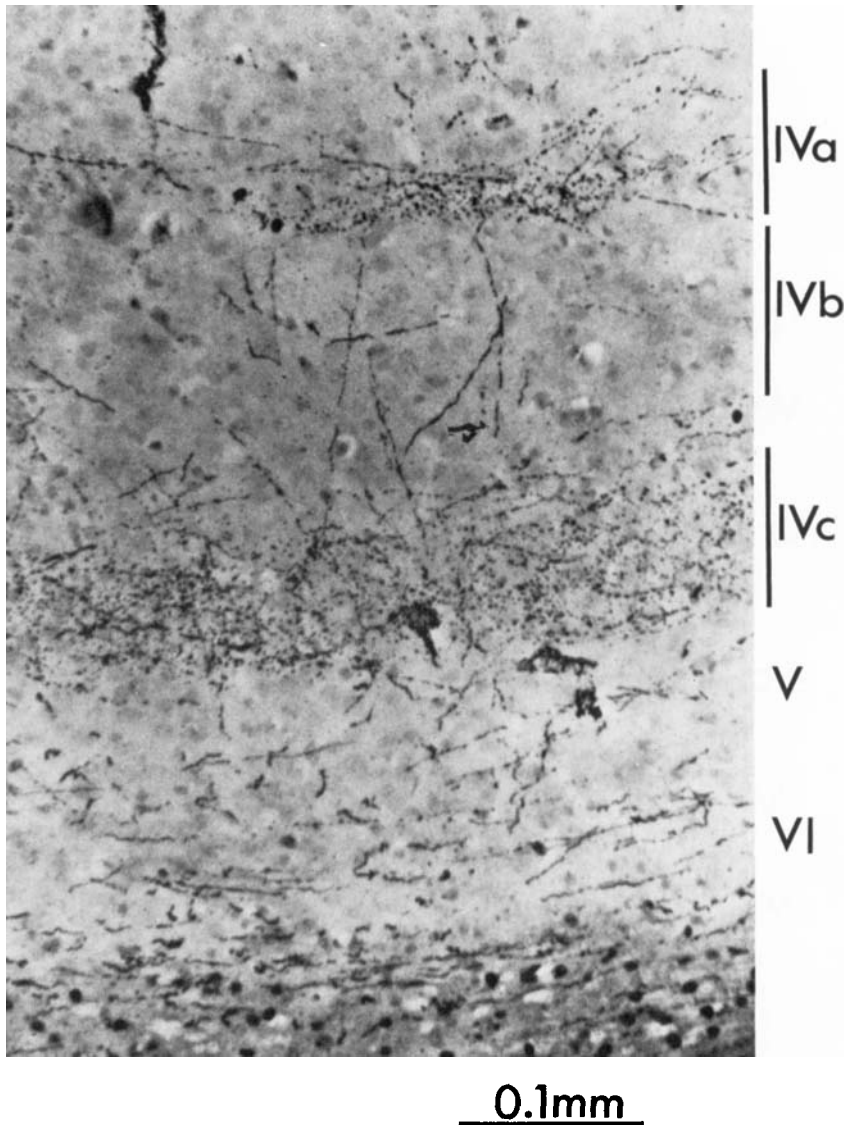


Figure 2B

not counterstained. Degenerating fibers entered from the white matter with uniform density throughout the entire main focus, criss-crossing diagonally in all directions and apparently branching as they ascended through layers VI and V, but giving off no obvious terminal arborizations. In IVc fibers were also abundant, but they were probably slightly thinner at this level. Here, however, there was a sudden very

dense aggregation of degenerating boutons, so dense that at first glance it tended to obscure the fibers. The position of these endings relative to the layering is shown in a Nissl-counterstained section in figure 3. The boutons appeared abruptly at the base of IVc (which in Nissl sections is sharply demarcated from layer V), and showed a uniform density over its lower two-thirds, becoming gradually less dense

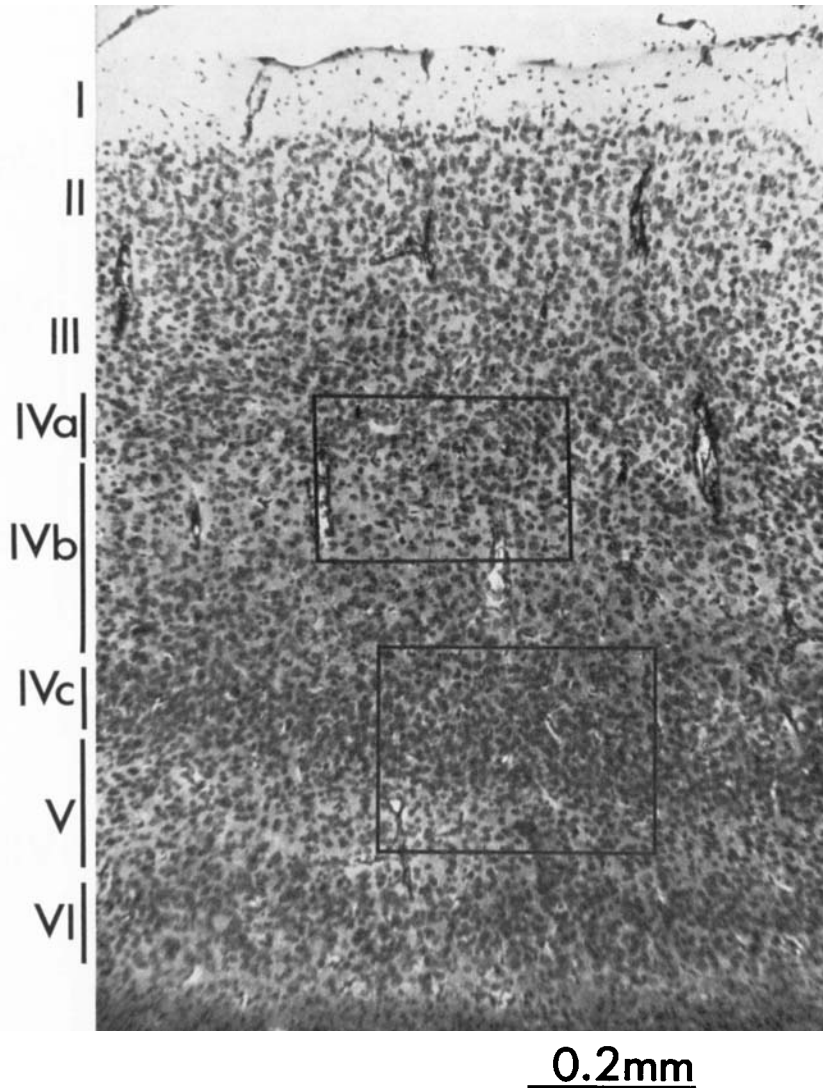


Fig. 3 Counterstained Fink-Heimer section showing relationship between distribution of degenerated boutons and the cytoarchitecture. A, low power, B and C, high power of enclosed areas. Same monkey as in figure 2.

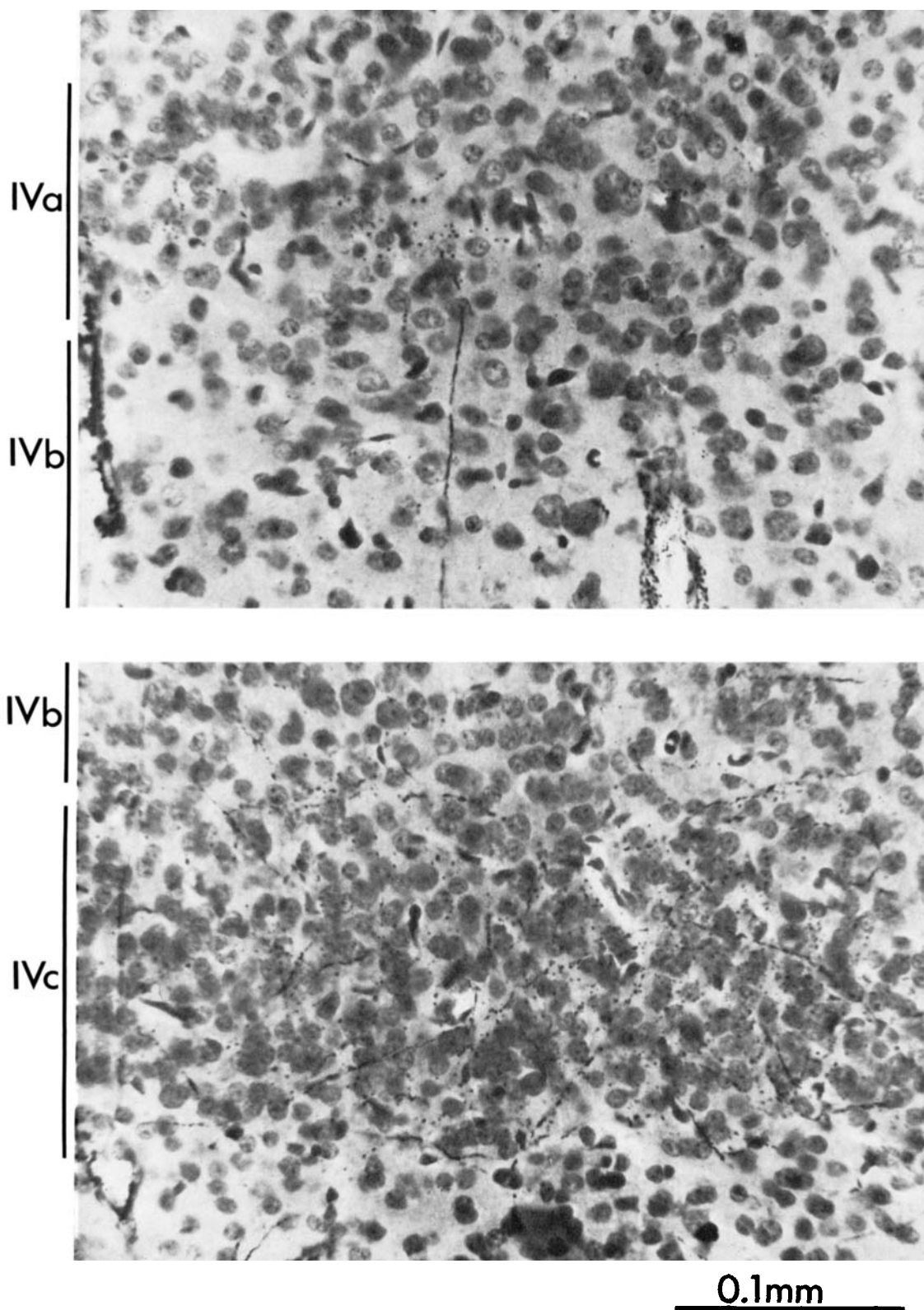


Figure 3B-C

in the upper third, paralleling, more or less, the decline in cell density. There were very few boutons within the uppermost part of IVc, and none in IVb. Layers IVb and IVc showed considerable numbers of degenerating fibers, perhaps one-third the number that were seen in the deeper layers.

In layer IVa there was another horizontal band of degenerating boutons, thinner than the band in IVc (roughly $1/4$ the thickness, or about $30\ \mu$), and less dense (fig. 2). Counterstained sections (fig. 3B) showed that this upper tier of degeneration was not situated immediately above layer IVb, i.e., not right at the base of the cell-

dense II-III-IVa complex, but somewhat above this level.

Although Nissl and myelin stains showed no hint of a separate layering correlated with this upper tier of degeneration, the Fink-Heimer material often showed a faint but clear line precisely at this level, that appeared as a white band in the negative prints (figs. 9, 12, arrows). The line was seen both within the focus of degeneration and well outside it, in the normal cortex, and so could not have been produced by degenerating fibers or endings. We do not know what is being stained to produce it.

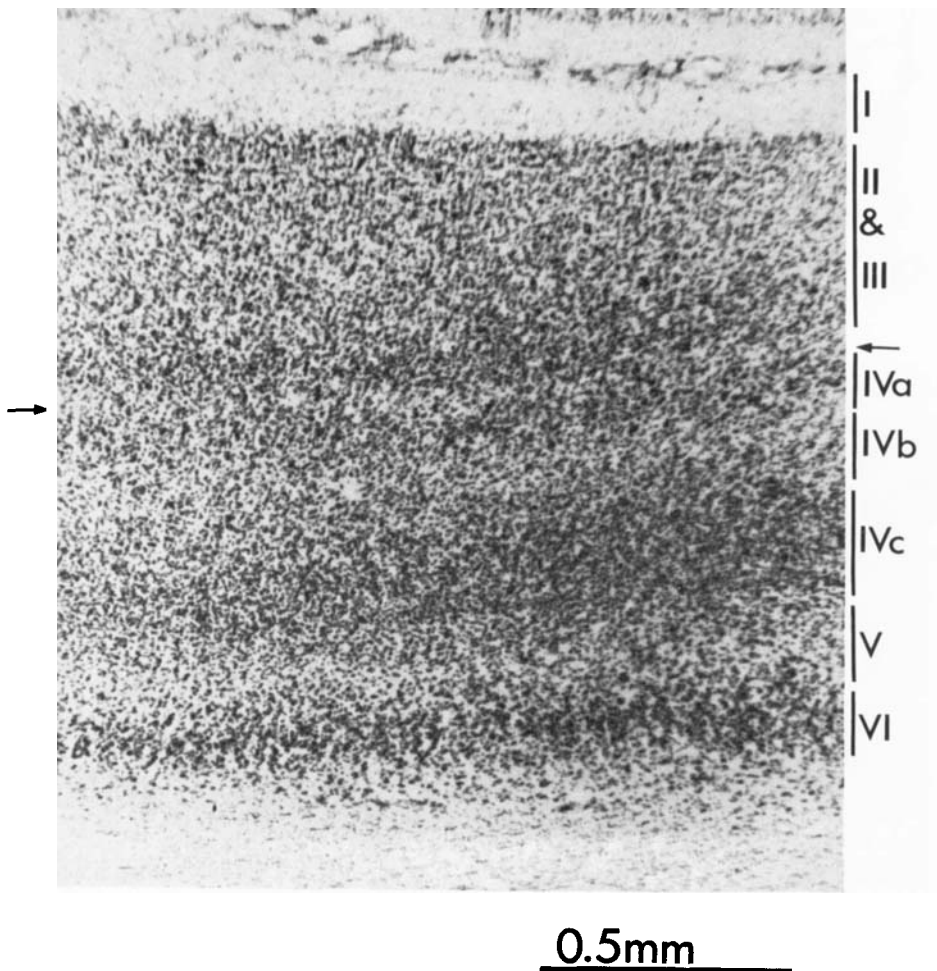


Fig. 4 Nissl-stained section through area 17 in spider monkey (*Ateles*), showing an additional narrow cell-sparse layer in what is tentatively assumed to be layer IVa (arrows), and which may be the site of an upper tier of terminations in this species.

Although Nissl stains of Macaque area 17 showed nothing that would correlate with this upper tier, favorable sections of *Ateles* striate cortex show a cell-sparse lamina in roughly the same region (fig. 4). A similar lamination was noted by von Bonin in *Cercocebus* and *Cebus* monkeys ('42, figs. 7, 8). It would be interesting to make geniculate lesions in the New-World monkeys in order to see how the upper tier, if there is one, correlates with the more elaborate layering pattern.

Above the upper tier of degeneration an occasional degenerating fiber was seen running vertically. In lesions that produced the densest degeneration (such as that in monkey 14) an occasional fiber ran all the way to layer I, and then turned, or divided in the form of a T, the branches running horizontally precisely in the middle of the first layer (fig. 5). On an occasional section, two or three such horizontal fibers could be seen running closely spaced at this level for at least 0.5 mm before leaving the plane of section. At least one or two such fibers were seen on each section in monkey 14, undoubtedly because the lesion in this animal was relatively large. Very rarely, a vertical fiber on its way to layer I could be seen emitting a horizontal branch in layers II or III.

In summary, there appears to be a three-fold distribution of endings from the dorsal (parvocellular) layers of the lateral geniculate to area 17: a dense thicket of terminals in IVc, a second much smaller but still substantial outcropping in IVa, and a third very sparse set of fibers running in the midthickness of layer I, whose terminals were not seen. One cannot, of course, rule out a scanty distribution of endings, or the presence of very fine endings, in layers II, III, V, or VI.

Lesions of ventral (magnocellular) geniculate layers

A different distribution of degenerating endings was seen following lesions of the ventral layers. Figure 6 shows the results of a lesion in the most ventral layer (cf. fig. 17, monkey 41). As before, obliquely running fibers threaded their way up through layer VI and V but instead of producing a dense mass of boutons in IVc, they bypassed this layer in its lower portions.

There was a dense layer of terminal particles in the deeper half of IVb, extending into IVc for a distance that varied from brain to brain. The very cell-dense part of IVc was either spared entirely or was occupied only in its upper one-third or one-half. Precise estimates of the regions involved are made difficult by the lack of sharpness in the boundaries between these layers. What was clear, however, was that following every ventral-layer lesion the region occupied by the degenerating terminals was at a higher level than the degeneration following dorsal-layer lesions. Results from the two ventral-layer experiments in which the staining was of best quality suggest that in some monkeys the two sites of termination may not overlap at all (compare figs. 3C, 6B).

Layers above IVb and IVc showed no degenerating fibers and no hint of terminals; there was thus no obvious upper tier of degeneration following ventral-layer lesions. The ventral layers of the geniculate are much thinner than the dorsal ones, and presumably as a consequence of this the cortical degeneration was considerably less dense than that following lesions in the dorsal layers. Since in the dorsal-layer lesions the upper tier of degeneration was always more scanty than that observed in the lower tier, it is possible that an upper tier following ventral layer lesions was missed, being that much more sparse. The same problem exists, to an even greater degree, with respect to the possibility of degeneration in layer I. Subject to these reservations, however, one can say that terminals from ventral layers are probably confined to one major level.

Ocular-dominance columns

After geniculate lesions involving either the two most dorsal geniculate layers, as in monkey 14, or the two ventral layers, as in monkey 37, degenerating terminals occupied a continuous band or bands in the fourth layer, interrupted only at the end (see fig. 12). A marked difference was seen in animals in which the lesion involved one layer only. Here the bands of degenerating terminals were interrupted at regular intervals by segments of equal extent that were, as far as one could tell, completely free of terminals. We call these

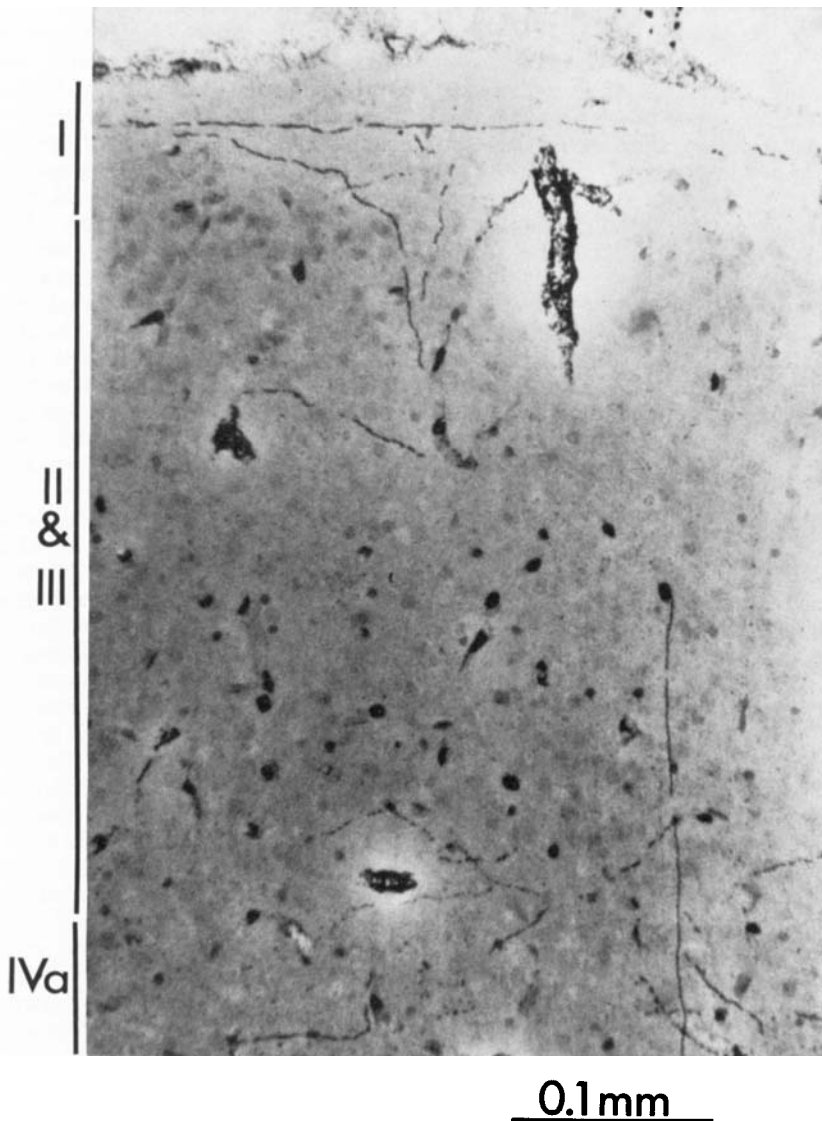


Fig. 5 Two photomicrographs from upper part of cortex in monkey 14 (see also figs. 11-13). One or two fibers ascend vertically through layers III and II, branch a few times in II and I and then run horizontally through the middle of layer I. Fink-Heimer stain.

regions "interbands." The borders of the bands, where the transition took place from a high concentration of terminals to few or none, were usually distinct (fig. 7). We assume that this pattern of bands and interbands is the anatomical counterpart of the ocular-dominance system and represents regions of alternating left-eye and

right-eye inputs to layer IV (Hubel and Wiesel, '68).

In the smallest lesions, such as that made in monkey 8 (fig. 14) a single cortical section showed only one or two patches of degeneration, whereas with longer lesions there were as many as 6-8 sets of bands and interbands (figs. 8-10).

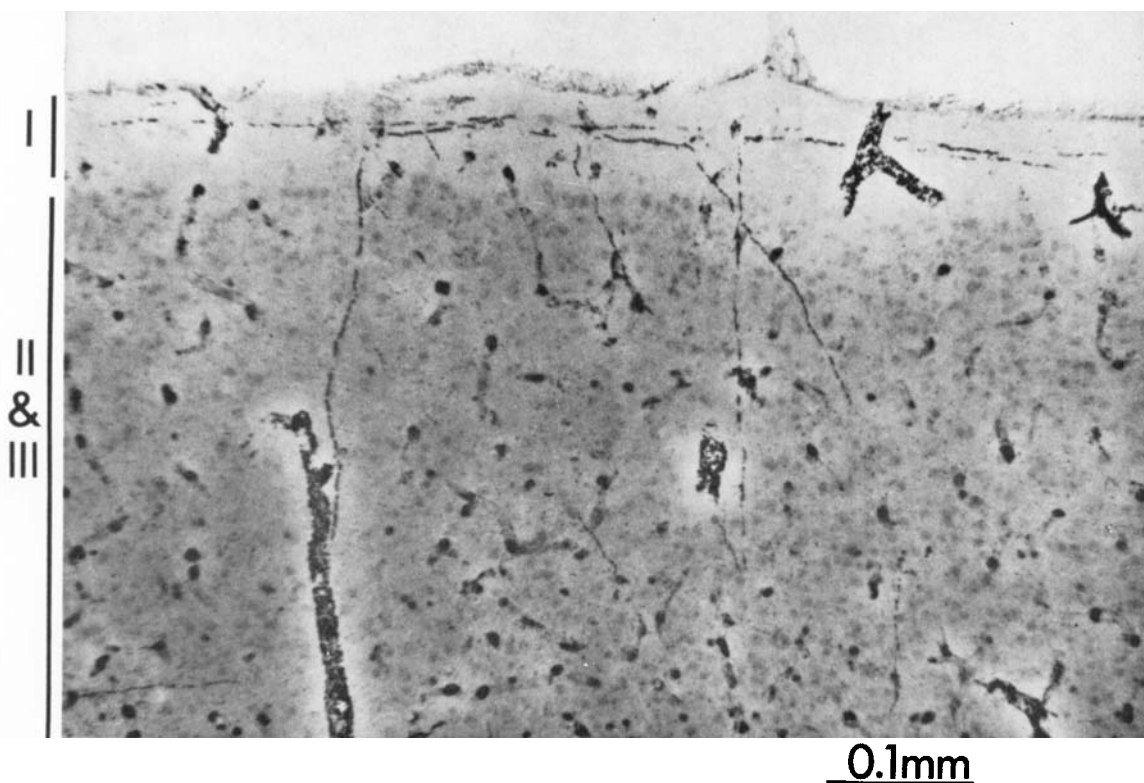


Figure 5B

Following a lesion of a dorsal layer, the band appeared as before in layers IVa and IVc. Here, as a rule, the bands and interbands lay in register one above the other, though this pattern was sometimes distorted when the cortex was markedly curved or was cut in a plane that was not perpendicular to the surface.

The degenerating fibers entering cortex from white matter did so rather uniformly and criss-crossing fibers were present throughout layers VI and V. It was as if a fiber only decided on its destination after entering the cortex, and took a diagonal course in the deeper layers in order to get to an appropriate band or interband in layer IV. In the interbands of layer IV there were many horizontally or diagonally running degenerating geniculate fibers, perhaps as many as in the bands themselves. These seemed frequently to be spanning the gap between one band and its neighbor, supplying branches and terminals in

the bands but none at all in the interbands. Layer IVb, though having few or no terminals, nevertheless showed numbers of degenerating fibers, running mostly vertically or obliquely, in about the same numbers over the bands as over the interbands. It is perhaps worth emphasizing that degenerating fibers in a given layer were fairly uniform in their horizontal distribution, so that the conventional Nauta method, staining fibers but not terminals, would not necessarily have demonstrated the columnar organization.

*Horizontal distribution of degeneration:
Reconstruction of columns from
serial sections*

The most extensive lesion confined to a single layer was seen in monkey 12 (figs. 8, 9). Here the electrode entered layer 6 of the left lateral geniculate at its medial aspect, and lesions were made over a distance of 1 mm. The initial receptive fields

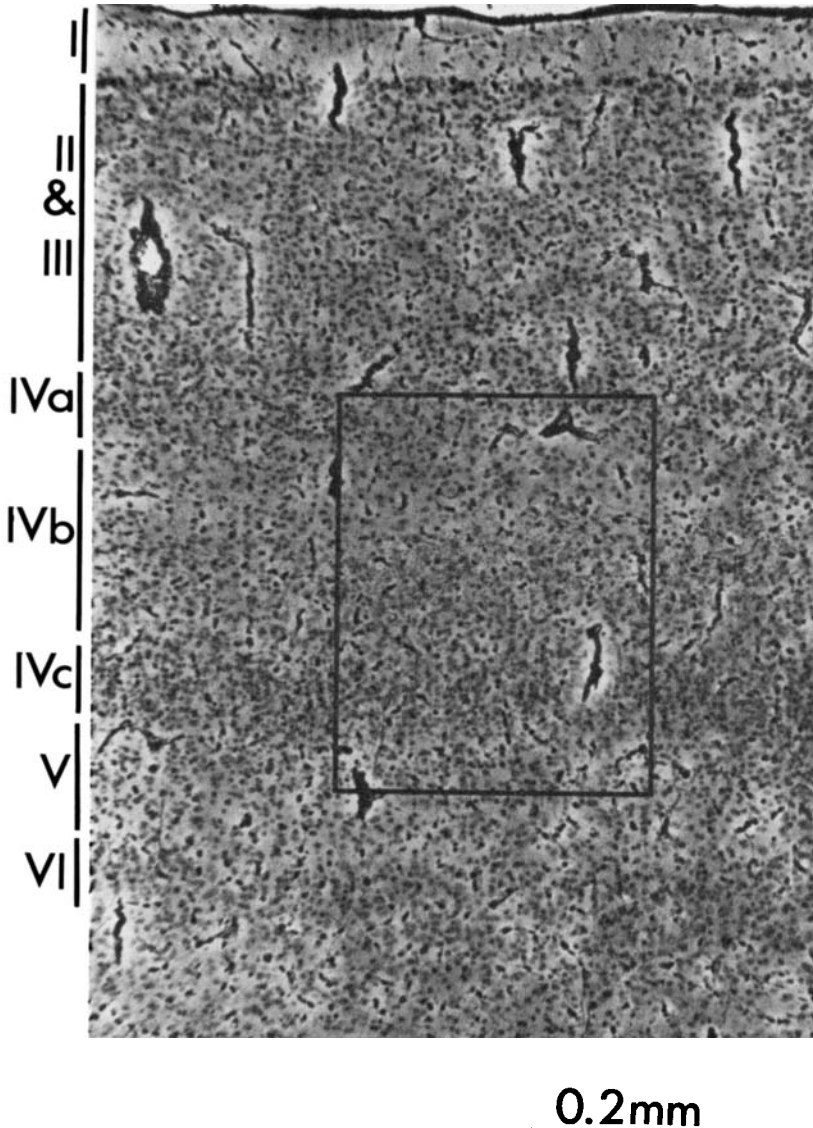


Fig. 6 Low and high-power photographs showing distribution of degenerating terminals following a ventral-layer geniculate lesion (layer 1) in monkey 41. Degenerating terminals are confined to cortical layer IVb in its deeper half, for the most part. Fink-Heimer counter-stained section.

were located in the visual field 9° below the horizontal, and 10° from the vertical midline, and as the electrode advanced these moved out and down. As expected from the known topography, the resulting degeneration appeared in the anterior corner of the mushroom-like buried calcarine cortex, occupying a region of cortex

measuring about $4 \text{ mm} \times 8 \text{ mm}$. Each section showed some six to eight bands of degeneration. In the final reconstruction (fig. 10) the degeneration in layer IVc took the form of a series of more or less distinct parallel stripes, roughly 0.35 mm wide, separated by spaces of roughly the same width. The definition of the stripes is best

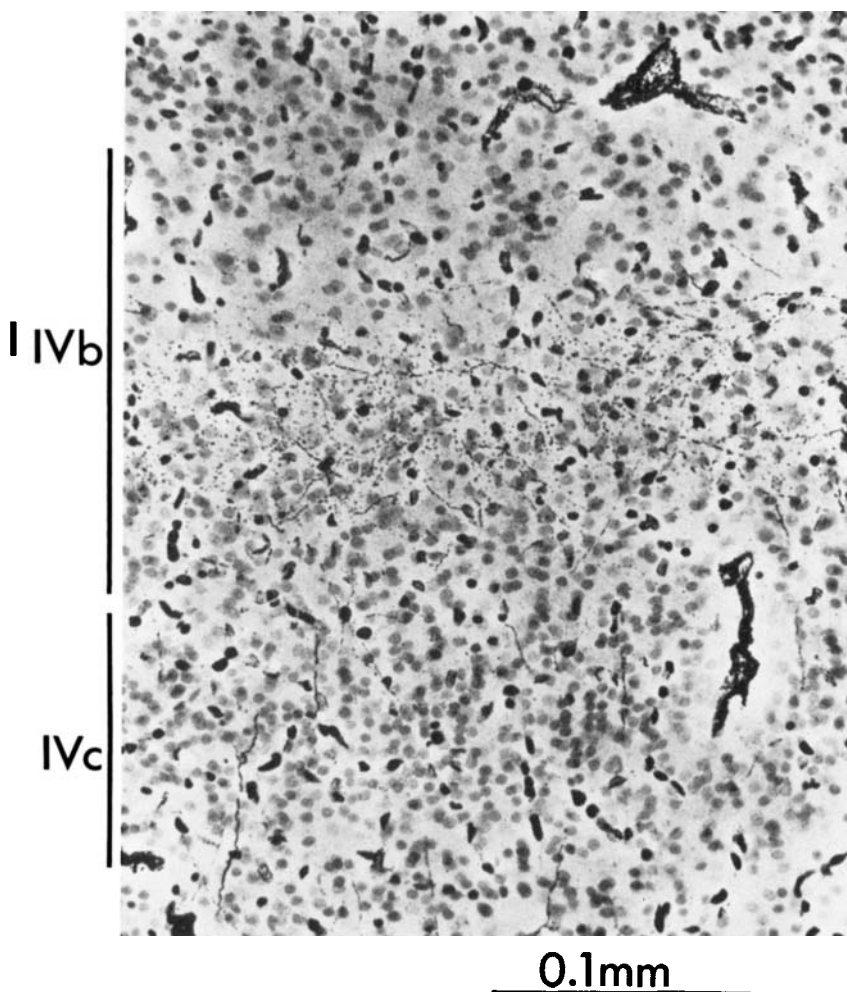


Figure 6B

on the right of the figure (anteriorly) and becomes progressively poorer towards the left of the map. This parallels the abrupt beginning of the degeneration anteriorly and a gradual tapering off posteriorly. In terms of topography, the point of entry of the electrode into the geniculate corresponds to the anterior boundary of the cortical degeneration. It is likely, therefore, that the lesion caught fibers of passage from deeper layers destined for the most posterior part of the degeneration area.

The stripes are not entirely independent, but in places are cross-linked to their

neighbors. The original slides were rechecked carefully and it was verified that two neighboring stripes do at times coalesce, and that single stripes in places split to form two. The reciprocal situation, of a stripe being interrupted by coalescence of two interspaces (representing the other eye) was not seen in this experiment but was very common in one of the others (monkey 41, fig. 17).

If destruction confined to one geniculate layer, corresponding to one eye, gives stripes of cortical degeneration separated by equal blank spaces, the assumption is that the blank spaces represent the desti-

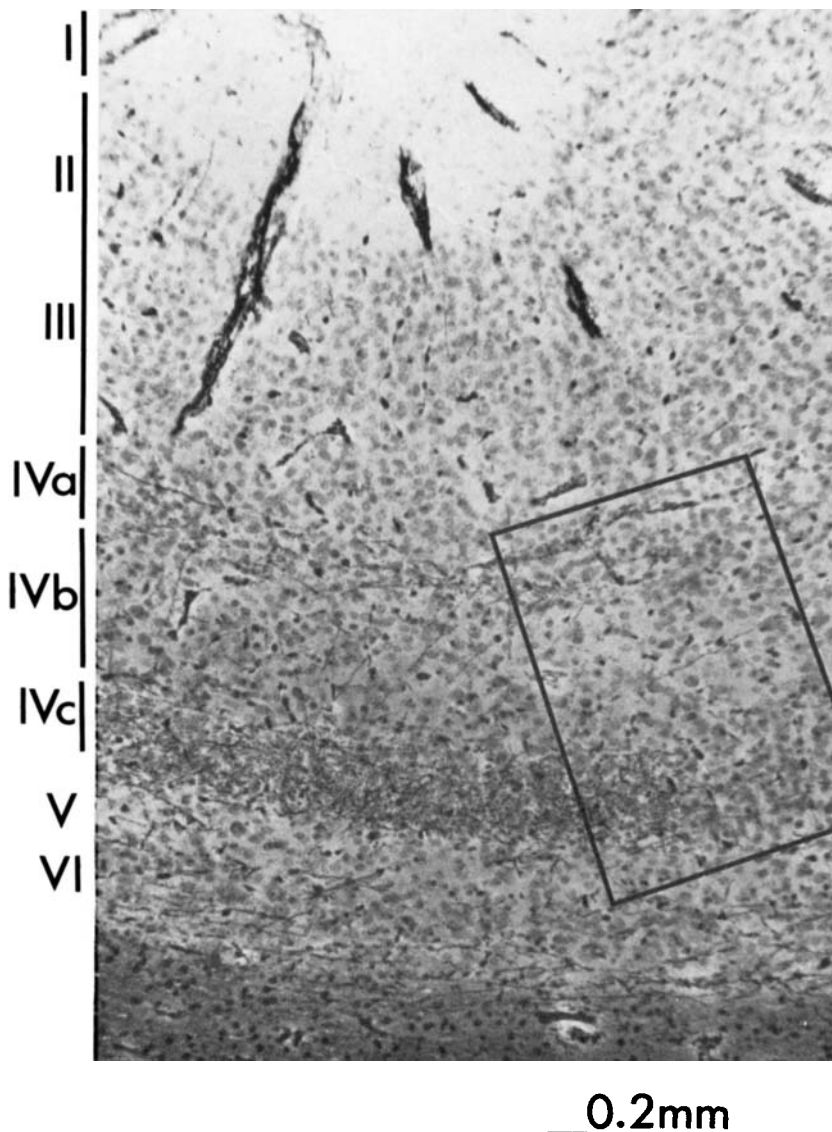


Fig. 7 Terminal degeneration following lesion of a dorsal geniculate layer (layer 6) showing boundary between a band, to the left, and an interband, to the right. Note abruptness of the transition in both the upper and lower tiers of degeneration (layers IVa and IVc), the fact that the transition points lie roughly one above the other. Monkey 12. Fink-Heimer stain.

nation of fibers linked to the other eye. Since the maps from the contralateral half visual field in the different geniculate layers are in exact register a lesion involving layer 6 and layer 5 directly beneath should give a continuous patch of degeneration, rather than a series of stripes. The lesion

in monkey 14 (figs. 11–13) was designed to test this. Here the electrode entered the geniculate in almost the same place as in the previous monkey (12), with the initial receptive fields situated about 8° below the horizontal and 12° out from the mid-line. This time the lesion was extended

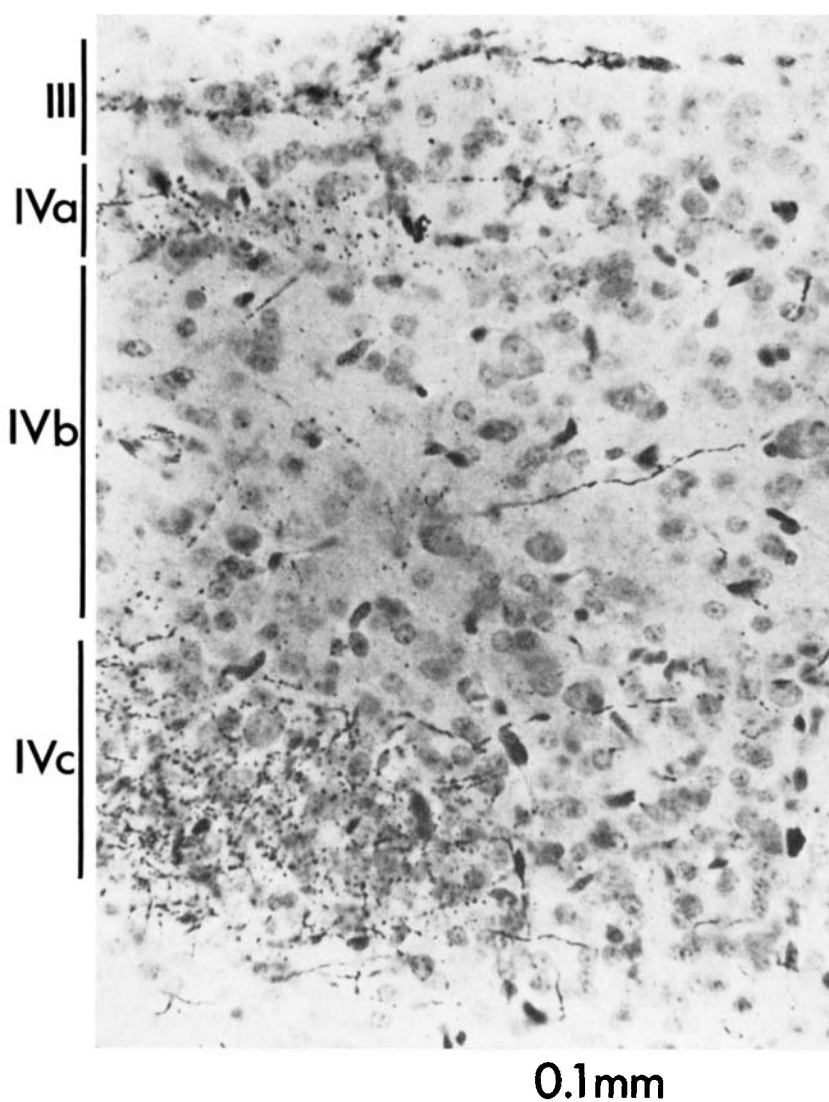


Figure 7B

into layer 5, the final fields being 15° out and 19° down in the visual field. The cortical area showing terminal degeneration was found in almost exactly the same part of area 17, but now in most sections there was a long continuous strip of degeneration in layers IVc and IVa, interrupted only at the two ends. The reconstruction showed a dense elongated central patch of degeneration, with a suggestion of stripes on both sides. We assume that the continuous band of degeneration re-

flects the destruction of geniculate cells lying in the two most dorsal layers along the same radial projection lines, and therefore representing the same region of visual field, whereas the stripes to the upper left and lower right in the figure arise because at the beginning of the lesion the sixth (most dorsal) layer was involved without corresponding involvement of the fifth, and similarly at the end, the fifth was injured without an involvement of the corresponding part of the sixth. Thus a stripe

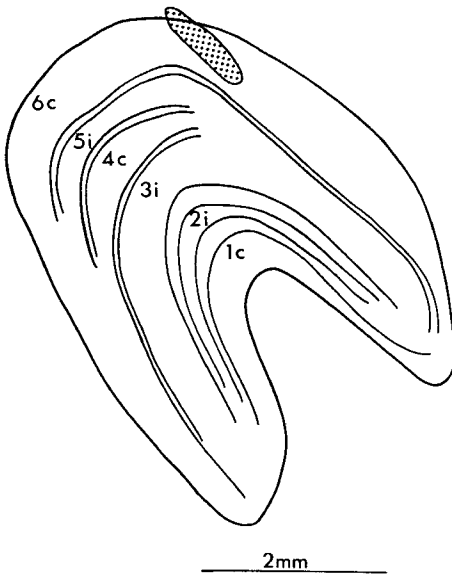


Figure 8A

Fig. 8A Tracing of left lateral geniculate body in monkey 12 to show the extent of the lesion in the most dorsal layer. Coronal section. Left is lateral. c, input from contralateral eye; i, input from ipsilateral eye.

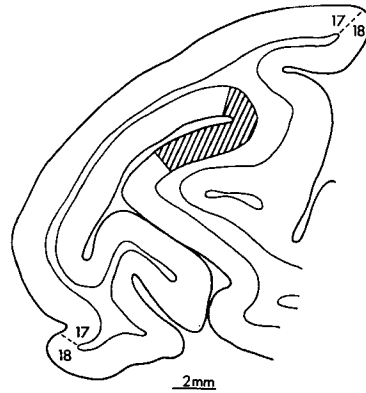


Figure 8B

Fig. 8B Site of degeneration in left striate cortex of some monkey. Parasagittal section about 1 cm from midline, left is posterior. Shading indicates region with degenerating terminals.

beginning in the upper left should continue into an interband in the lower right: unfortunately the method is not good enough, or the stripes themselves are not quite orderly enough, for one to be sure of this, given the size of the dense overlapping region.

It may be worth noting that the direction of the stripes in the first experiment, and the direction suggested by the second, are almost identical. This raises the question of whether the stripes always have the same direction in a given part of the cortex, and whether they bear any constant relationship to the coordinates of the visual field, paralleling the horizontal or vertical meridians, or lying along circles concentric about the fovea, for example. The material we have so far is too scanty and the lesions too widely spread through the visual fields to allow us to answer this.

The results from two other dorsal-layer lesions (monkeys 8, 15) are shown in figures 14 and 15. These were close to, and probably within, the foveal region.

Two ventral layer lesions are illustrated

in figures 16 and 17. The layer-1 lesion in monkey 36 (fig. 16) was in the superior visual-field representation (lateral aspect of geniculate, posterior half of calcarine cortex). That of monkey 41 (fig. 17) was also in the most ventral layer, in the region receiving input from an area 2–3° from the fovea, close to the horizontal meridian. The pattern in this monkey was again striped, in some sense, but here the tendency for interlacing and cross links was very marked, and was seen in both the areas of degeneration and in the spaces between.

We were interested in learning whether there was any obvious relationship between the widths of the bands of degen-

Fig. 9 Enlargement made directly from one parasagittal section through the occipital lobe in the region of degeneration in monkey 12 (fig. 8). (Light areas are dark on the original slide.) The areas showing degeneration have been dotted in. A complete set of photographs such as this was used to make the reconstruction shown in figure 10. Note the pale band at the same level as the upper tier of degeneration (arrows). Fink-Heimer stain.



Figure 9

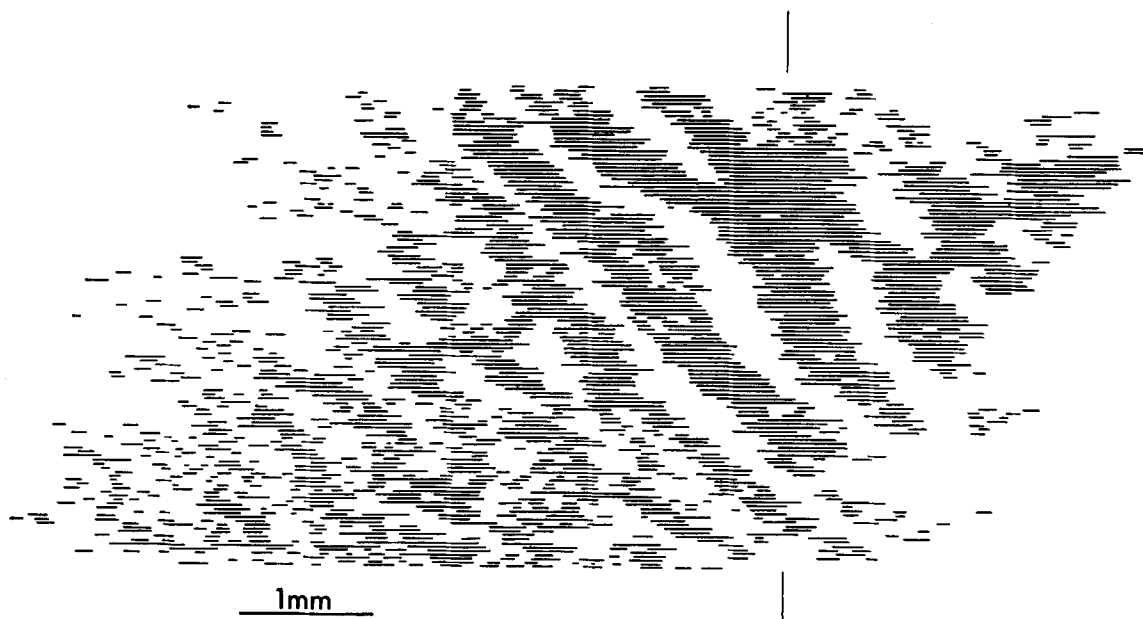


Fig. 10 Reconstruction of region showing terminal degeneration in layer IVc in monkey 12 (see figs. 8, 9). The figure shows a face-on view of the flattened cortex at the level of layer IVc. Each horizontal line segment represents the degeneration in a single band of a single section such as that shown in figure 9. Adjacent $30\ \mu$ -thick sections were plotted on 1 mm graph paper. Curved sections of gyrus were straightened graphically. Anterior is to the right, medial is up. The vertical lines represent the point of sharpest curvature of the gyrus (see fig. 9).

eration, i.e., the period of the alternating stripes, and the distance of the visual-field representation from the fovea. The magnification factor, or degrees of visual field per millimeter of cortex (Daniel and Whitteridge, '61) is well known to be related to distance from fovea, so that our question was the same as asking whether the stripe periodicity was constant in terms of millimeters along cortex, or in terms of degrees of visual field. The apparent period of stripes varied from about 0.5 mm for monkeys 36 and 41, up to 1.2 mm for lesion monkey 8. These measurements are taken from the frozen-section Nauta-degeneration slides, and have not been corrected for shrinkage. It is common experience that shrinkage may be substantial, up to 30% or more, in linear dimensions, and is far from constant from brain to brain or even in the same brain. Furthermore, the process of reconstruction may have led to distortions that could influence stripe width. But from the present material one can say that, at least in order of magni-

tude, the stripe periods were from 0.5 to 1.0 mm or slightly more, and that there was no obvious systematic variation in stripe width over the cortex, certainly none that would be comparable with the variation in magnification factor or in the size of cortical receptive fields. For example, Daniel and Whitteridge ('61, fig. 4) found that in the fovea 1° is represented by about 6 mm of cortex, whereas about 15° from the fovea 1° occupies roughly 0.2–0.3 mm. If the stripe widths had varied by a factor of 20–30 this would surely have been detected in the present study.

DISCUSSION

The findings of this paper are of two different kinds, one having to do with the distribution in the striate cortex of terminals from the magnocellular and parvocellular geniculate layers, the other with the anatomical identification of the ocular-dominance columns and a description of their three-dimensional shape. The first of these represents a step towards under-

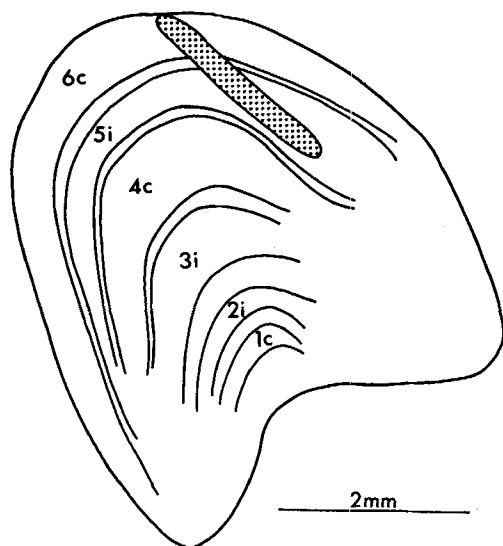


Figure 11A

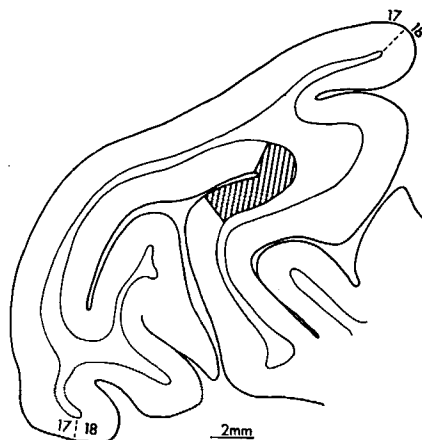


Figure 11B

Fig. 11A Tracing of left lateral geniculate body in monkey 14 to show the extent of the lesion in the two most dorsal layers. Coronal section, left is lateral. Figure 11B Site of degeneration in left striate cortex of same monkey in parasagittal section about 1 cm from mid-line. Left is posterior. Shading indicates region with degenerated terminals.

standing the wiring of the striate cortex, for clearly, not even a rudimentary description can exist if the site of terminations of the afferents is not known to the nearest layer, or if it is not appreciated that the two main subdivisions of the geniculate project to different cortical regions, or if, to take another example, a structure as conspicuous as the line of Gennari is erroneously (and despite the study of Clark and Sunderland, '39) thought to consist largely of afferent fibers. This is not to say that with the present study the input end of the wiring diagram of the striate cortex is by any means solved. Perhaps the most serious gap in our knowledge of area 17's morphology concerns the class of cells upon which the afferents terminate—whether these are stellate or pyramidal cells. This question has been a somewhat vexed one (see Garey and Powell, '71), but recent Golgi studies in the monkey (Valverde, '71; Lund, *in press*) suggest that, after all, the stellate cells are probably the main targets of the input. Certainly, results of the present study, given the dense packing in layer IVc of an almost pure stellate-cell population, provide little encouragement to the

idea that the afferents end primarily on pyramidal cells.

The finding that the dorsal geniculate layers project to two very distinct regions of layer IV (Hubel and Wiesel, '69) has been noted by Polley ('71) and confirmed by Garey and Powell ('71) both of whom used the Fink-Heimer method. Earlier studies (e.g., Wilson and Cragg, '67) already observed dense degeneration following geniculate lesions, extending superficially as far as layer III (perhaps what we have termed IVa) but the Nauta method did not make it possible to observe two distinct regions of termination. So far there is no hint of the physiological meaning of this two-tiered input. Our previous studies (Hubel and Wiesel, '68) showed the presence of simple cells and strictly monocular responses throughout layer IV. Given the present results, it would be worthwhile to study area 17 looking particularly at responses from the various subdivisions of layer IV. The fact that fibers from the dorsal and ventral layers of the geniculate terminate in different parts of layer IV is also difficult to interpret at present, but it is of potential interest since one knows that these two sets of



Figure 12

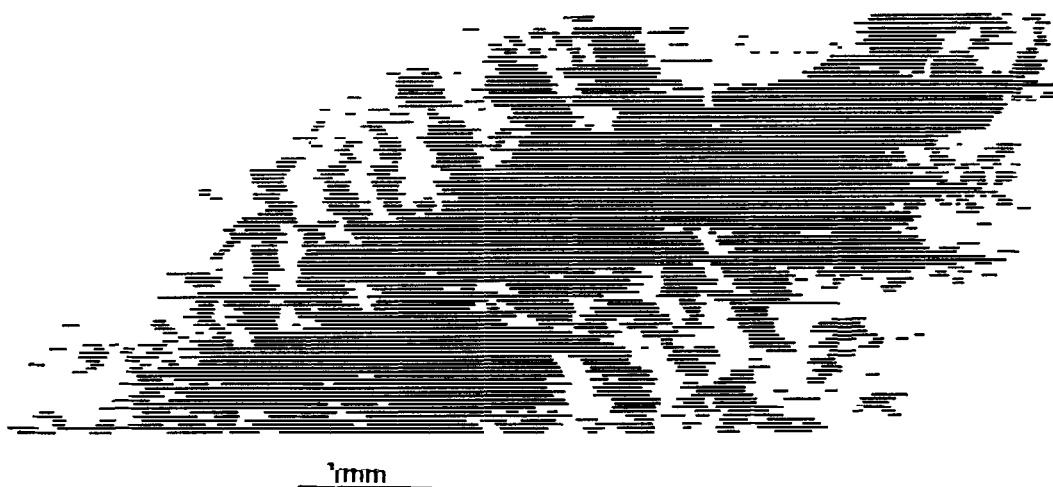


Fig. 13 Reconstruction of region showing terminal degeneration in layer IVc in monkey 14 (see figs. 11, 12). Other conventions as in figure 10.

geniculate layers have very different physiological properties (Wiesel and Hubel, '66). Thus ventral layer cells, on the whole, seem to have less of the color specificity and the variety of receptive-field types that are found in the dorsal group of layers. If one wishes to understand the reasons for the magno-parvo cellular duality in the geniculate, perhaps the best hope is to learn how the information transmitted by the two types of cells is used at higher levels. It thus comes as welcome news that the terminals are not immediately intermixed in the cortex, but are kept to a very large extent separate.

In recording from monkey visual cortex one of the most striking findings has been the vertical subdivisions into ocular-dominance columns. An anatomical demonstration of the corresponding IVth layer left-eye right-eye mosaic not only confirms this observation but also gives some idea of the geometry and degree of regularity of the mosaic. It turns out that the form is a highly regular one, consisting of alternating parallel stripes, with a variable amount of cross linking. The width of the stripes

seems fairly constant at about 0.25–0.5 mm; any variation with position in the cortex was too little to detect, and in any case was certainly far less than the variation in magnification factor. The problem of constancy of stripe direction from animal to animal will be difficult to solve without doing many more experiments of this type. At present we are attempting to evolve a method that will show the stripe pattern over very wide areas of cortex in a single animal.

It is worth stressing that the IVth-layer mosaic brought out by these anatomical methods is only one manifestation of the system of ocular-dominance columns. Each column, as defined physiologically, extends from surface to white matter. In layer IV the cells almost always have fields that are concentrically arranged or simple, and they are almost always strictly monocular. (We have seen exactly one example of a binocularly driven simple cell in the monkey). In upper and lower layers most cells are binocularly influenced, but even here cells favoring a given eye are grouped together, and the grouping occurs in such a way that cells favoring, say, the left eye are directly above and below the IVth layer region monopolized by the left eye. The conclusion that the boundaries between neighboring columns are vertical is based on vertical and oblique microelectrode penetrations, but it receives anatomical

Fig. 12 Enlargement made directly from one parasagittal section through occipital lobe in the region of degeneration in monkey 14 (fig. 11). The areas showing degeneration have been dotted in. A complete set of photographs was used to make the reconstruction shown in figure 13. Note the pale band at the same level as the upper tier of degeneration (arrows). Fink-Heimer stain.

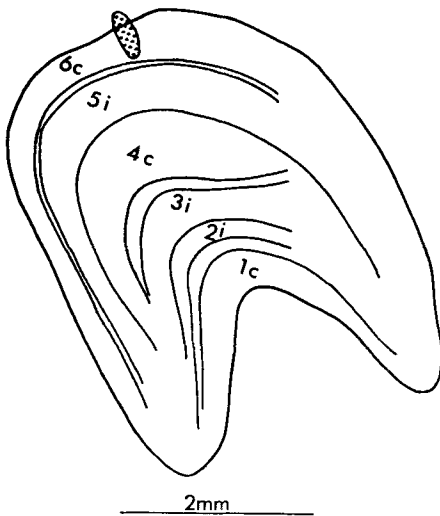


Figure 14A

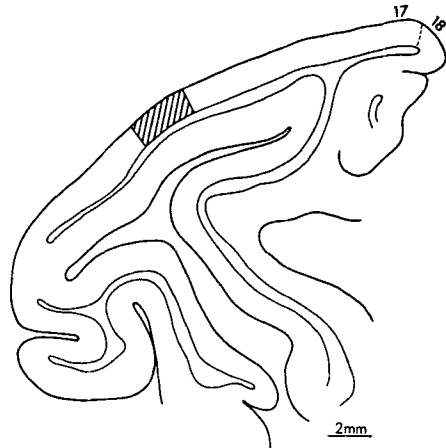


Figure 14B

Fig. 14 Monkey 8. (A) Tracing of left lateral geniculate body to show the extent of a lesion in the most dorsal layer. Coronal section. (B) Site of degeneration in left striate cortex. Parasagittal view about 1.5 cm from midline. (C) Reconstruction of region showing terminal degeneration in layer IVc. Conventions in figure 10.

support from the fact that the upper-tier patches in the present material are directly above and in register with the lower patches except occasionally in regions of high cortical curvature, where it is likely that the planes of section were oblique.

The surprising regularity of the ocular-dominance columns naturally makes one wonder if the orientation columns are similarly regular and long and narrow in cross section. There are some hints that they may be. Long oblique cortical penetrations (e.g., Hubel and Wiesel, '68, fig. 9) have sometimes, though not always, shown a marked regularity, with long sequences of small shifts in orientation all in the same direction clockwise or counter-clockwise. In 1968 we argued that this in itself suggested that the columns might be slab-like in shape. The evidence for this was indirect, though surface mappings had also pointed to the same conclusion (Hubel and Wiesel, '63, fig. 4). The finding that the ocular-dominance columns are slabs would seem to strengthen the possibility that the orientation columns are also. If they are, it would be especially interesting to know whether in horizontal section the stripes are orthogonal to the ocular dominance stripes, or parallel, or have any fixed

relationship. The answer to this may be important, for the input that a binocular complex cell, lying above or below layer IV, receives from two adjacent ocular-dominance columns must at the same time originate from the same orientation column—unless it comes from two similar orientation columns and has to cross over all the intervening ones. The problem is obviously easily solved by having the two systems orthogonal to each other. A diagrammatic example of such an arrangement is given in figure 18.

The two coexisting column systems are of course superimposed upon the two-coordinate mapping of the visual fields. It might reasonably be asked whether a complex cell receiving input from two neighboring ocular-dominance columns would not necessarily, as a consequence, receive its input from two disparate positions on the two retinas. The answer seems to be that the topographic representation does not hold over distances comparable to column widths; in an oblique penetration traversing a single column from one side to the other, no overall drift in receptive-field positions can be discerned against the random variations (Hubel and Wiesel, '62). Even in a penetration that crossed

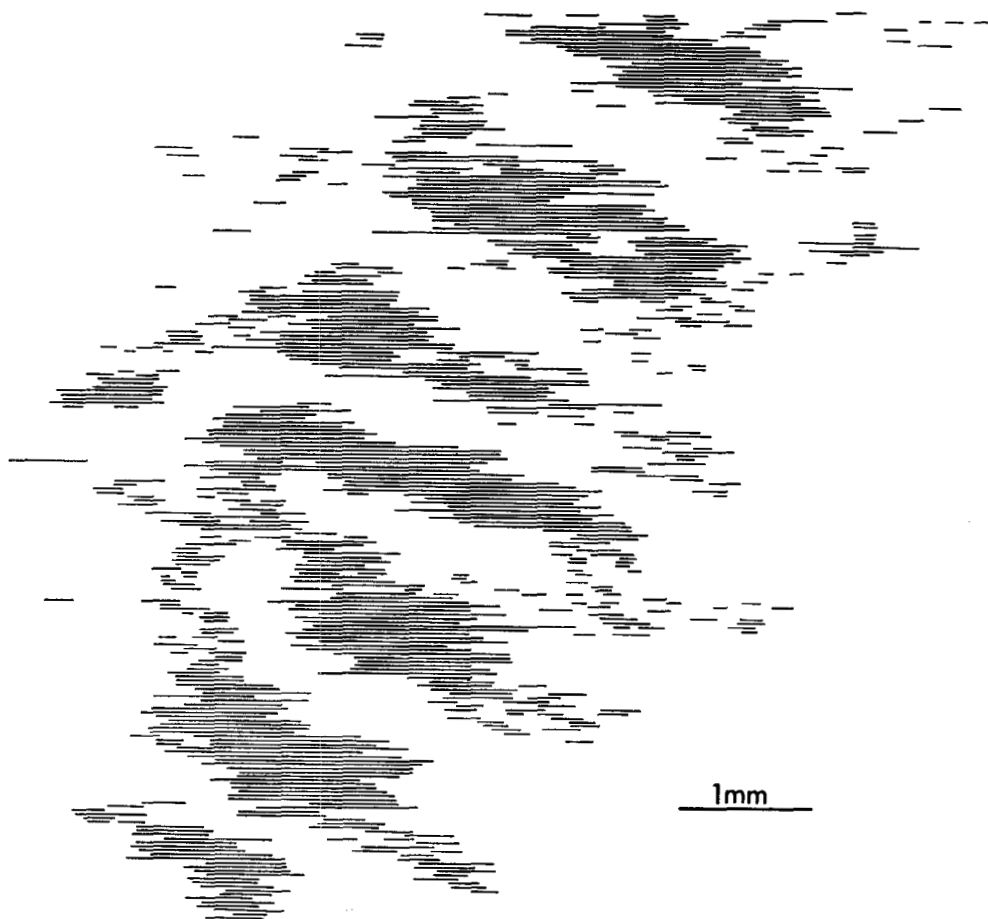


Figure 14C

53 orientation columns (Hubel and Wiesel, '68) there was no detectable change in receptive-field position. The retino-cortical mappings are decidedly not point-to-point, but are region-to-region.

In comparing the results of recordings from striate cortex in cat and monkey, one of the most conspicuous differences has been the sharpness of definition of the ocular-dominance columns. What was such a striking feature in the monkey was only barely detectable in the cat (Hubel and Wiesel, '62, '65). We have repeated the experiments described in the present paper in the cat, and, as might have been predicted from the physiology, find no obvious suggestion of a right-eye left-eye mosaic in layer IV. In cats brought up

from birth with strabismus (Hubel and Wiesel, '65) the relative numbers of binocularly influenced cells drops sharply to about 20% and there is a concomitant strong tendency to grouping of cells according to eye dominance. Our hope was that a mosaic might be demonstrable in these animals by making laminar geniculate lesions, and studies with this objective are now under way, though the results so far have not been very encouraging.

In a previous paper (Hubel and Wiesel, '68) we have drawn attention to the similarity between ocular-dominance columns in the visual cortex, and the "skin" versus "deep" columns originally described by Mountcastle ('57) in the somatosensory cortex. Both are two-fold columnar sys-

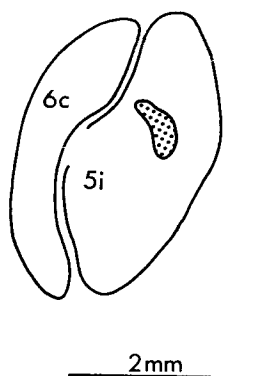


Figure 15A

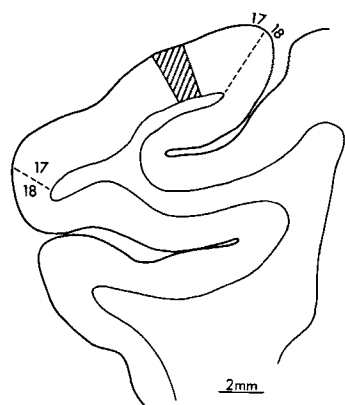


Figure 15B

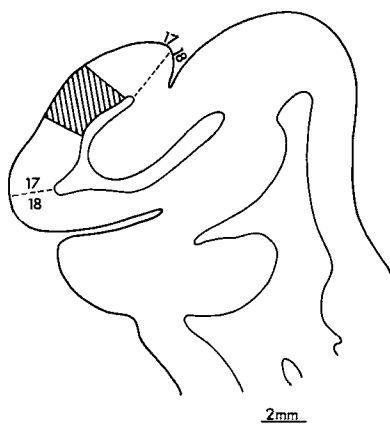


Figure 15C

Fig. 15 Monkey 15. (A) Tracing of left lateral geniculate body to show extent of the lesion in layer 5. Coronal section which passes through geniculate in its most posterior part. (B and C) Two parasagittal section through left striate cortex, very far lateral. Foveal representation. C is a few millimeters lateral to B. (D) Reconstruction of region showing terminal degeneration in layer IVc. Conventions as in figure 10.

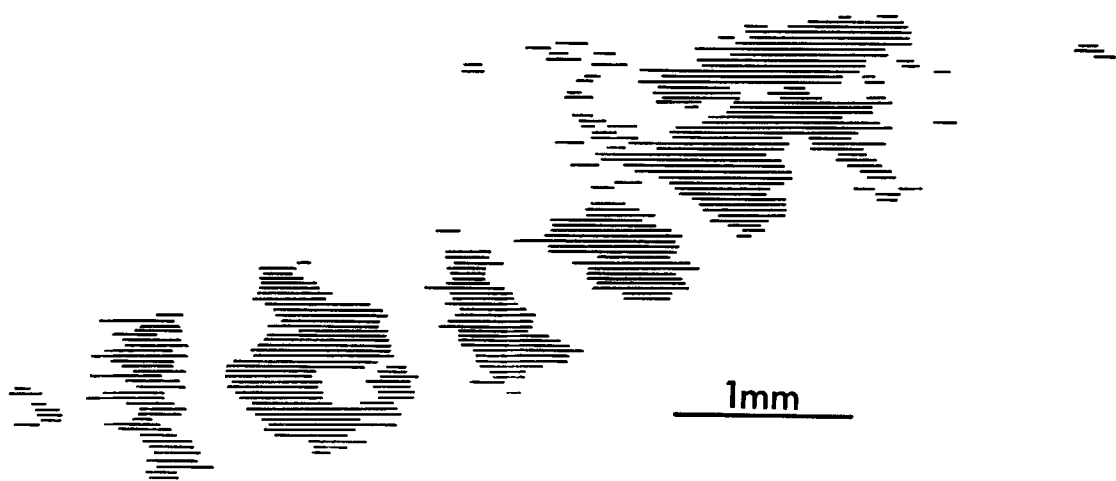


Figure 15D

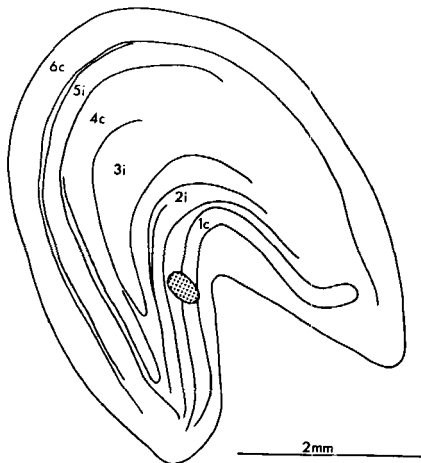


Figure 16A

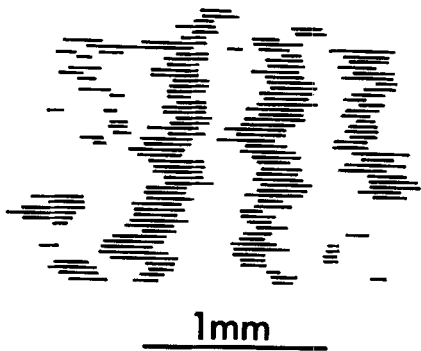


Figure 16C

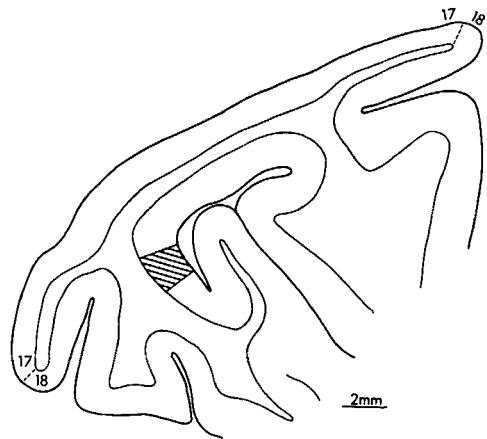


Figure 16B

Fig. 16 Monkey 36. (A) Tracing of left lateral geniculate body from coronal section showing the extent of a lesion in the most ventral layer. (B) Site of degeneration in left striate cortex. Parasagittal section about 10 millimeters from midline. Shading indicates area of degeneration. (C) Reconstruction of region showing terminal degeneration in layer IVb. Conventions as in figure 10.

tems, as opposed to the many-fold orientation columns in area 17; both depend on the distribution of input fibers rather than subsequent intracortical connections. It would be interesting if similar methods could be used to demonstrate the IVth layer mosaic in the somatosensory cortex. That this might be feasible is suggested by the observation of Poggio and Mountcastle ('63) that cells are aggregated in the thalamic ventrobasal complex according to their responsiveness to superficial versus deep stimuli. In a sense, these aggregations may be analogous to the geniculate layers.

It is worth noting that the elegant system of "barrels" described by Woolsey and Van der Loos ('70) in the mouse somatosensory cortex seems to represent a columnar system in which the IVth layer mosaic

is visible by routine staining methods, especially if the cortex is sectioned tangentially. Here each column apparently represents a single whisker of the snout of the mouse, being a part of the two-dimensional cortical topography but nevertheless fulfilling the requirement of discreteness. This is the only case so far where a correlation of columns was observed anatomically before a physiological identification had been made. One wonders, of course, whether cells below and above the barrels represent the site of convergence from several neighboring whiskers.

Finally, the development of these highly regular column systems is worth considering. The ocular-dominance columns are evidently determined by the mode of in-

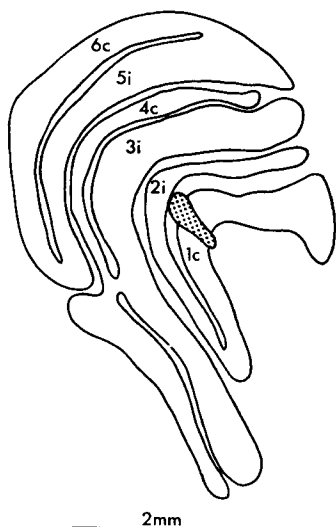


Figure 17A

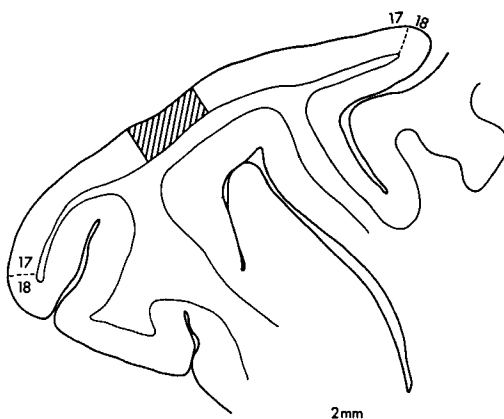


Figure 17B

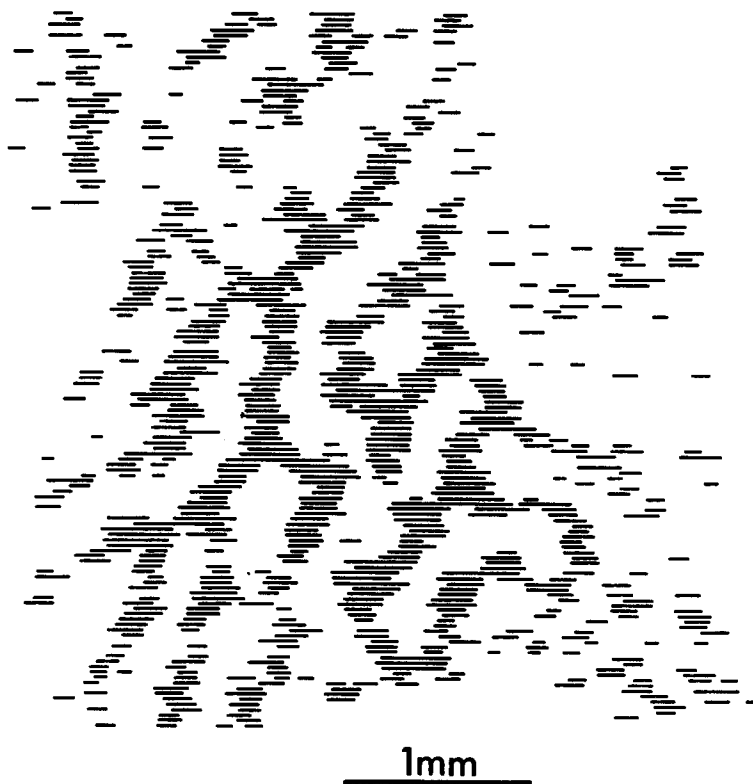


Figure 17C

Fig. 17 Monkey 41. (A) Tracing of left lateral geniculate body from coronal section showing the extent of a lesion in the most ventral layer. (B) Site of degeneration (indicated by shading) in left striate cortex. Parasagittal section about 15 mm from midline. Left is posterior. (C) Reconstruction of region showing terminal degeneration in layer IVb. Conventions as in figure 10.

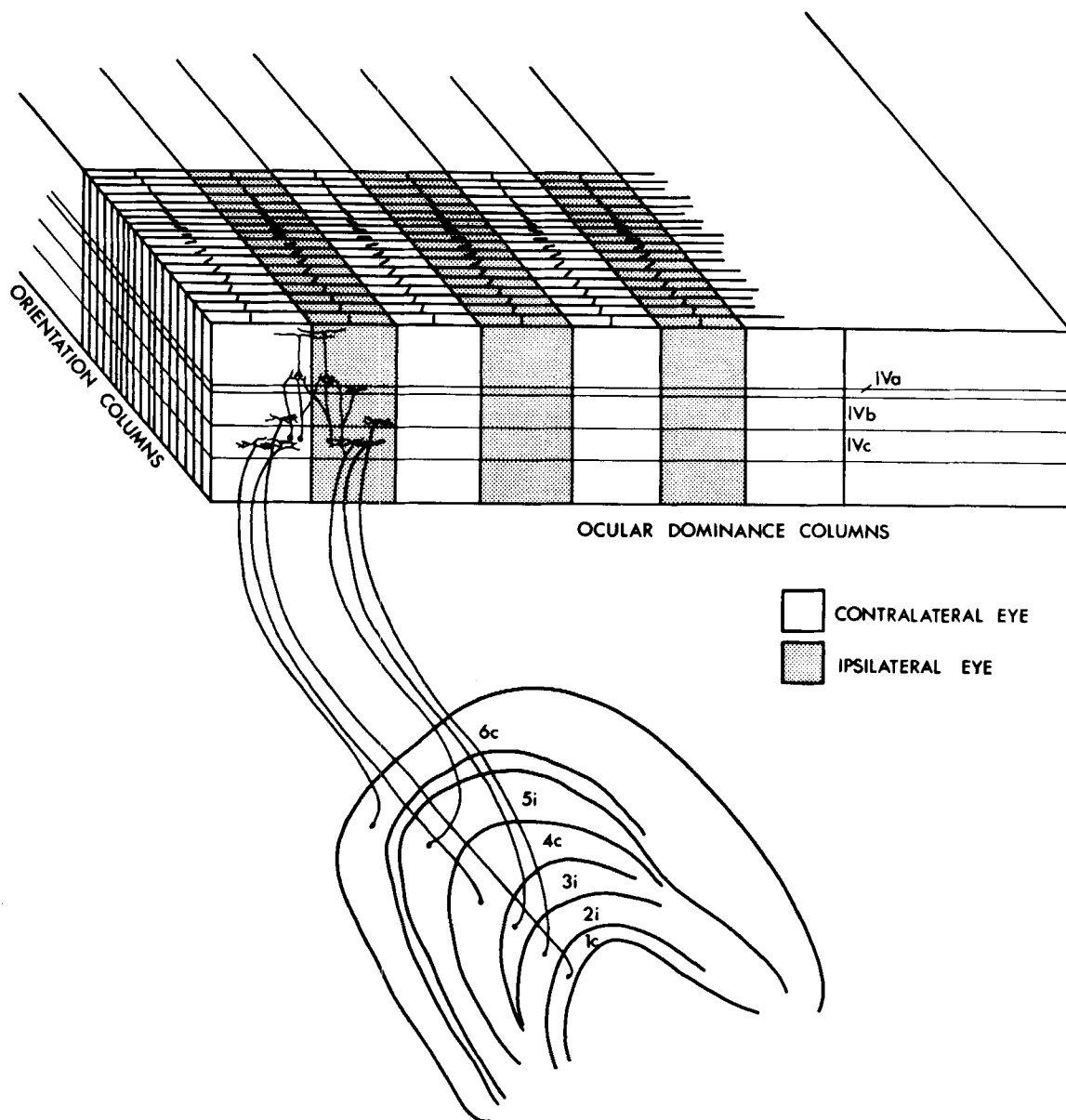


Fig. 18 Diagram showing a possible relationship between ocular-dominance columns and orientation columns assuming the orientation columns are also long narrow parallel slabs, and that their arrangement is very orderly. Note that the width of these orientation slabs is much less than that of the ocular-dominance columns. A complex cell in an upper layer is shown receiving input from two neighboring ocular-dominance columns, but from the same orientation column.

growth of the afferent fibers. The orientation columns, as we have argued before, must be determined by patternings of intracortical connections, perhaps at the first or second synapse. The orientation col-

umns are probably present at birth (Hubel and Wiesel, '63); we have as yet done too few studies of infant monkeys to know whether ocular-dominance columns are also, but it seems very likely that they

are. How such ordered systems can develop innately promises to be a challenging question for the future.

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