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A review of lamination in Area 17 of the visual cortex of *Macaca mulatta*

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Summary

This paper develops a concordance of methods for designating laminae in the primate striate cortex. The classic notation schemes of Ramón y Cajal, Brodmann, and von Bonin and four recent modifications are described in words and photomicrographs. The recent trend toward adopting a lamination scheme that effects a division of cells into recognizable layers and at the same time reflects their connections is considered. Since a single, consistent plan for lamination of the visual cortex would facilitate communication among investigators, it is suggested that Brodmann's original scheme be followed as the most generally useful and applicable.

Introduction

In order to co-ordinate the results of anatomical and physiological investigations of the primate visual cortex, it is necessary to agree on a single plan for its lamination. Unfortunately, it is becoming increasingly difficult to correlate the data coming from different laboratories because of the various ways in which cell layers within the striate cortex are identified. The reader who has plunged into the morass of Roman and Arabic numerals, capital and small Latin letters, and Greek subscripts used by different investigators to label the layers, sooner or later makes the disconcerting discovery that any particular cell group may have several designations – or none at all. The intent of this review is to epitomize the most commonly used lamination schemes for Area 17 in the rhesus monkey (*Macaca mulatta*), and thereby to provide a concordance with which to examine the literature more efficiently.

Like other parts of the cerebral cortex, the primary visual cortex is divided into horizontal cell-rich and cell-poor zones. However, the striate cortex is unique in the development of its granular layers, and this is one factor that has produced the present multiplicity

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of lamination schemes. This difficulty is by no means a recent phenomenon. As early as 1925 von Economo and Koskinas published a table comparing eight different schemes that had already been proposed for the primate visual cortex. In 1946, a review by Solnitzky and Harman listed an additional nine. Since then, the number has increased still further.

In this concordance we shall review lamination of the monkey's striate cortex specifically in cell-stained preparations. This method gives approximate information about the shapes of neuronal perikarya, although it leaves undescribed the distribution of their dendrites, and hence the location of most of their synaptic contacts. Despite this drawback, such a cytoarchitectonic pattern is of enormous practical importance. It is, in essence, a descriptive, structural outline of the cortex to which more detailed and specific information on individual neurons and their connections gleaned from other light and electron microscopic methods can be referred. In addition, cell stains provide convenient methods for neurophysiologists to locate electrode tracks and demonstrate histologically the cells and regions from which they have recorded. We shall first briefly describe in words and photomicrographs seven of the more important laminar schemes, and then comment on current trends in their usage.

Schemes of lamination

(1) *Ramón y Cajal*

Studies on the layering of the visual cortex can be traced back to the latter part of the eighteenth century when Gennari described a clearly defined white stria within the human occipital cortex. The first scheme that we shall consider here, however, was proposed in a study of the human visual cortex by Ramón y Cajal (1899). In this work Ramón y Cajal presented an elegant and detailed description of nine different cell layers that he could identify in material stained by the Nissl method:

1. plexiform layer (layer of horizontal cells)
2. layer of small pyramids
3. layer of medium pyramids
4. layer of large stellate cells
5. layer of small stellate cells
6. layer of small pyramids with arcuate axons
7. layer of giant pyramids (solitary cells of Meynert)
8. layer of large pyramids with arcuate and ascending axons
9. layer of triangular and fusiform cells

These layers are indicated on Fig. 1; although this is a photomicrograph of the cortex of *Macaca mulatta*, the applicability of Ramón y Cajal's scheme is immediately apparent.

Ramón y Cajal's scheme, then, was a description based primarily upon the Nissl method, although enlarged by Golgi studies. It was produced as part of his effort to relate structure and function in this particular cortical area. At about the same time that this work was published, 'architectonics' was coming into its own as a branch of neuroanatomy. In this school, attention was turned to parcellation of the brain into regions of specific lamination patterns by use of cell or myelin stains rather than by considering the cellular composition and interneuronal connections in any particular subdivision. The scheme of Ramón y Cajal was only slightly modified by one of the early students of architectonics, Campbell (1905), who merely condensed the four deepest layers into two. But the descriptive work of both of these investigators was overshadowed by that of Brodmann, who became perhaps the most famous proponent of the architectonic school.

(2) *Brodmann*

Apparently Brodmann originally adopted the basic six-layer cortical scheme that had been suggested by Lewis (1878) because it provided useful landmarks with which regional variations in cortical structure could be recognized. The six-layer scheme, then, was at first a working tool. Its advantage was that it generally described most isocortical regions. Its disadvantage was the tendency of some investigators to channel their observations along this rather rigid, preconceived framework and to ignore structural details. Soon, however, Brodmann came to think that his six-layered scheme was based upon an actual embryological event. He believed that all adult cortical layers could be traced back to one of the original six embryological layers, and should be so identified. As we shall see, this is the basis on which Brodmann grouped the apparently doubled inner granular layers and the intervening stripe of Gennari of the visual cortex (IV a, b, c) as a single layer, arguing that they derived from an originally simple internal granular layer.

These embryological concepts were greeted with an enthusiasm that is today rather difficult to understand. The result was the indelible establishment in the literature of Brodmann's schemes for both cortical parcellation and layering. It is fortunate for neuroanatomists that most of Brodmann's theoretical excesses served only to explain rather than to alter his basically accurate morphological description.

Brodmann's description is also of special importance because it was one of the first detailed examinations of the primary visual cortex in the monkey (*Cercopithecus* and *Macaca mulatta*). The layering pattern he distinguished in Nissl material is indicated in Fig. 1 and is given below in a close translation of his classic 1905 paper.

I. *Lamina zonalis* – the narrow cell-free cortical border.

II. *Lamina granularis externa* – very feebly developed and hardly separable from the adjacent pyramidal layer. Fetal brains show this layer best.

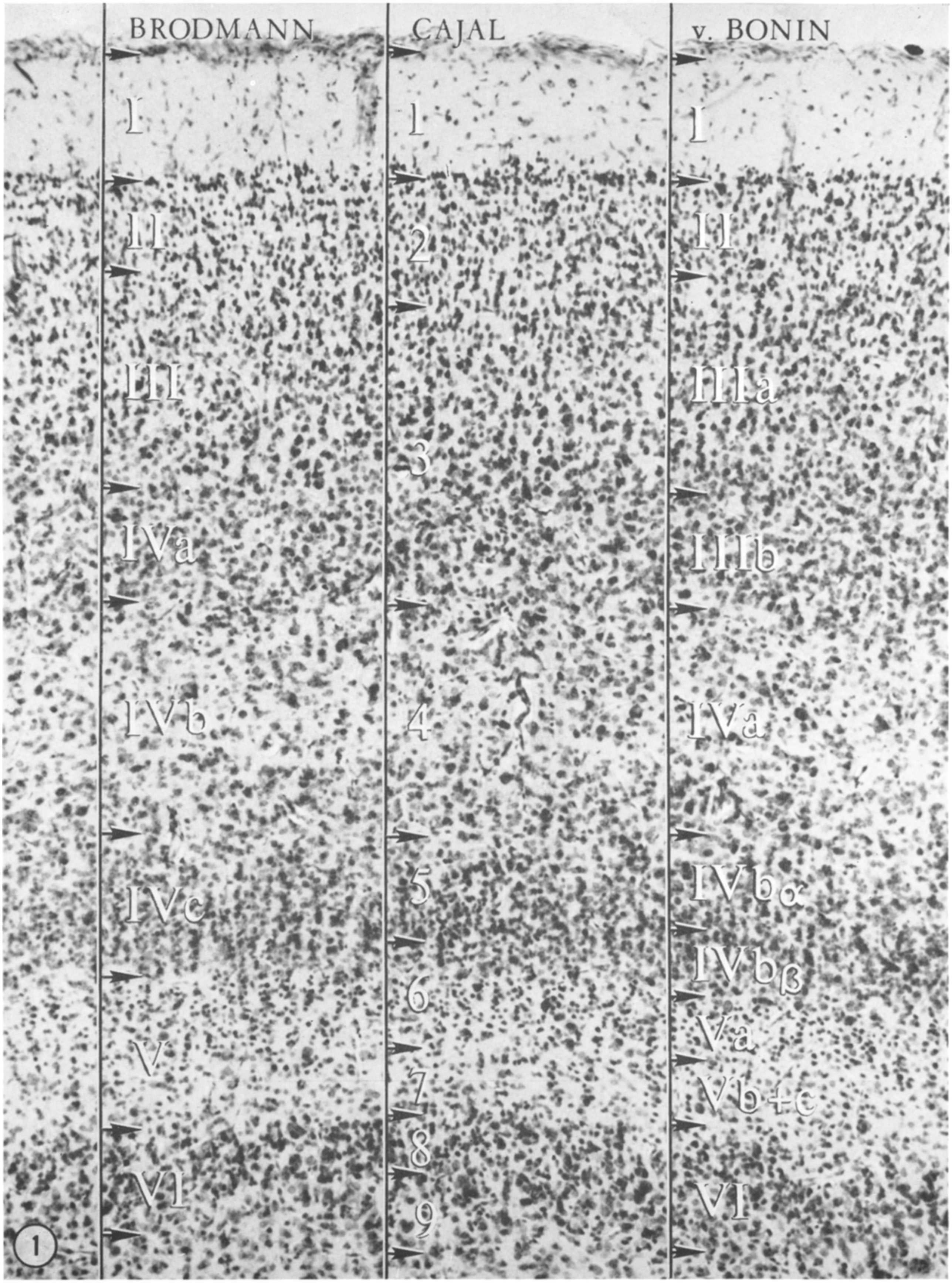
III. *Lamina pyramidalis* – pyramidal cells are located superficially; somewhat larger pyramidal cells are found only in deeper parts.

IV. (a) *Lamina granularis interna superficialis* – stands out in the photographs as a distinct dark cell stripe. At higher magnification many little round cells (so-called granules) can be recognized, apart from larger slender star- and pyramid-shaped cells.

(b) *Lamina (granularis interna) intermedia* – contains the stripe of Gennari in fibre preparations. In cell preparations the layer stands out as a wide, cell-poor band containing single large cells, which arrange themselves here and there in the middle into a somewhat denser

Fig. 1. Nissl-stained section through the striate cortex of *Macaca mulatta*, illustrating the lamination schemes of Ramón y Cajal (1899), Brodmann (1905), and von Bonin (1942). × 145.

Fig. 2. Lamination schemes of Garey (1971, based, in part, on Hassler and Wagner, 1965), Valverde (1971), and Lund (1973). Brodmann's notation is repeated at the left to facilitate comparison. × 145.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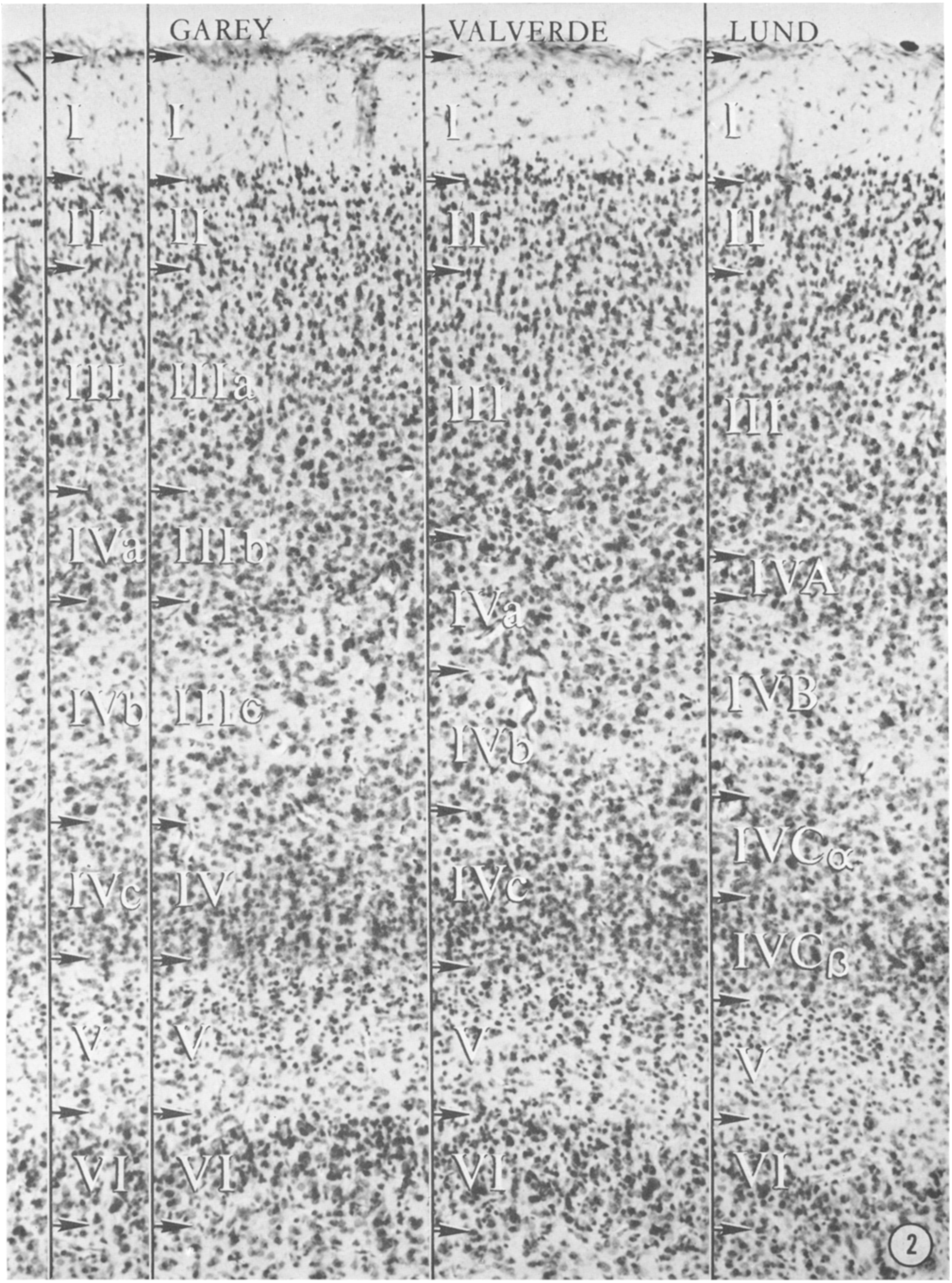

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> cell layer. (In other species, namely *Cebus capucinus*, these large cells of the lamina intermedia form a distinct, compact cell layer in the middle of IVb, so that here one can again make three subdivisions.)
> (c) *Lamina granularis interna profunda* – This is the most cell-rich and, because of this, the darkest, most prominent layer in any cortical cross section. It contains predominantly densely packed granules. With exacting study, particularly with higher magnification or in Bielschowsky preparations, one can also differentiate two layers within this layer – a darker, outer layer composed of granules and large pleomorphic cells, and a light, somewhat thinner, inner layer possessing almost exclusively granules.
>
> In other brains, especially of *Cebus capucinus*, this difference is so significant and conclusive that one can demonstrate two separate layers. However, in the species studied here we ought to retain the layering system set forth for man since this state of things is only hinted at.
>
> V. *Lamina ganglionaris* – the most cell-poor and therefore the lightest layer of Area 17. It contains in its deeper portion (bordering on layer VI) a few scattered enormous pyramidal cells, the so-called solitary cells of Meynert.
>
> VI. *Lamina multiformis* – can be more clearly subdivided than in man into two subdivisions:
> (a) *Lamina triangularis*, a darker outer layer containing mostly larger cells, and
> (b) *Lamina fusiformis*, the lighter cell-poor inner layer, or the true spindle-cell layer, which stands out sharply against the white matter.

Brodmann's description differs from that of Ramón y Cajal in the regions directly above and below the stria of Gennari (IVb and 4–5, respectively). The single point that has caused the most controversy and confusion is the identification of the layer that Brodmann called IVa, but that Ramón y Cajal considered just a part of the third layer with somewhat smaller, more closely packed cells. The exact boundary that Brodmann placed between his layers III and IV is difficult to determine, and this may have been one factor that subsequently led von Bonin (1942) to question whether that boundary was used merely to designate a change in the laminar clustering pattern of cells, which is visible in Nissl stains, or something more subtle. Von Bonin felt that the functional dignity of a layer was more profoundly affected by its connections with an axonal plexus than by the type of cells it contained. Moreover, like many investigators of his time, he believed that the stria of Gennari was an axon plexus of mostly thalamic origin. Therefore, when certain cells were labelled part of layer IV, it suggested to von Bonin that they were in direct contact with these thalamic afferents. If the same cells were instead included in layer III, this implied to von Bonin that they were not receiving primary thalamic afferents. For von Bonin, then, the key issue in determining the laminar designation for these cells was their relationship to the stria. As will be discussed, he decided that the cells were not in contact with the stria and therefore followed Ramón y Cajal's scheme, rather than Brodmann's, in making them part of layer III. Thus, in his 1942 paper von Bonin explicitly raised the question of whether laminar notation in the striate cortex should be based solely on the clustering patterns of cells that could be seen in cell-stained preparations. This is an important consideration to which we shall later return.

(3) *von Bonin*

Von Bonin (1942) used a combination of Nissl, Bodian, and Golgi methods to examine the striate cortex in a number of primates, including the rhesus monkey. The lamination scheme that he produced for the latter animal was closely related to that of Ramón y Cajal (see Fig. 1), although it was developed by subdivision within a basic six-layer framework. The key differences from Ramón y Cajal included: (1) division of layer III into IIIa and IIIb on the basis of greater cell density and higher number of small Golgi type II cells in the lower IIIb region, and (2) limitation of layer IVa to include only regions of large stellate cells, thus separating it from IVbα and IVbβ. Layer V was subdivided into two parts; solitary pyramids of Meynert are present only in the deepest reaches of Vb+c. The stria of Gennari is located entirely within layer IV. The cells of layer IIIb are not in intimate contact with the stria, nor do they send many dendrites into that plexus.

While there have been numerous other layering schemes proposed for the striate cortex, those of Ramón y Cajal, Brodmann, and von Bonin have probably been the most widely used. Recently, however, the subject has been reopened as new and different types of data have become available through the application of sophisticated modern anatomical and physiological methods. Investigators have attempted to integrate this information into the classic patterns of cortical lamination with varied success. We shall now review four important recent studies in which different laminar schemes have been proposed, and see how they can be compared with those mentioned previously.

(4) *Garey*

In his light and electron microscopic study of the visual cortex Garey (1971) adopted the idea set forth by Hassler and Wagner (1956) that a partly granular band of von Bonin's layer III has falsely been included in von Bonin's layer IV. The basis for this contention appears to be a conviction that by definition layer IV should include very few, if any, pyramidal cells. According to Hassler and Wagner, layer IV should begin with the condensation of small granule cells that Brodmann called IVc, the *lamina granularis interna profunda*. Hassler and Wagner assimilated the lighter layer above this into the third layer, calling it IIIc. Above IIIc begins the cell-rich layer IIIb, which merges without sharp boundary into layer IIIa.

Hassler and Wagner discussed only the controversial III-IV layering. Garey incorporated their ideas, and in addition presented a more detailed description of the entire striate cortex. According to his description (illustrated in Fig. 2) layers I and II consist, respectively, of a molecular layer and a predominantly small pyramidal layer containing a few stellate cells. Layer IIIa contains small and medium pyramids, IIIb larger darker pyramids, and IIIc a reduced number of pyramids interspersed among numerous small stellate cells (granules). Layer IV is a dark band of closely packed large and small stellate cells; layer V is again much lighter, a strip of small pyramidal cells with the solitary pyramids of Meynert on its deep aspect. Layer VI is a dark band composed of deeply staining, medium-sized pyramids. Meynert cells may also be found in its superficial regions. The stria of Gennari is located primarily in IIIc, although it may extend into the superficial part of layer IV.

(5) *Valverde*

Valverde (1971) presented a Golgi study of the striate cortex in *Macaca mulatta* and

Erythrocebus patas (red monkey) which focused on short-axon cells in layers III to V. While he claimed to have followed the stratification of Brodmann (1905), a careful reading of his paper suggests that this is not strictly true. His descriptions seem to indicate that he has shifted the deep boundaries of layers III and IVa downward. Layer IVb seems to be thinner than Brodmann's original description suggests. Layer IVc, on the other hand, appears to be almost identical to Brodmann's. Both investigators suggest that within IVc a lower sublayer of small cells can be distinguished. Valverde placed the Meynert cells somewhat higher in layer V than Brodmann. Unfortunately, Valverde presented no cell-stained preparations illustrating his laminar pattern, and it is therefore impossible to verify these conclusions directly (Fig. 2 illustrates our interpretation). Further, since Valverde studied material from both the rhesus and the red monkey, it is not clear whether the variation from Brodmann's scheme might represent a species difference.

(6) *Lund*

Lund (1973) also presents a pattern of lamination based upon that of Brodmann. However, the text of her paper and particularly a labelled photomicrograph of a cell-stained preparation suggest several variations which seem to reflect the use of Golgi impregnations (viewed at low magnification) as a basis for determining boundaries of layers. Nissl-stained material was also studied, but in several key instances it is impossible to separate the layers proposed by Lund by this method alone. In Lund's scheme, laminae I and II are as described by Brodmann. The upper border of layer III is not distinct; its lower border according to Lund, is marked by the start of the arborization of axon trunks rising from neurons in the lower cortical layers. Unfortunately this feature is not visible in cell-stained material. Lamina IVA is a narrow strip receiving a direct thalamic projection; its lower border is sharply defined by the start of the horizontal axon plexus of IVB. Layer IVB contains large and medium size stellate cells as well as pyramidal cells. Lund's lamina IVB is distinguished from lamina IVCα by the absence of pyramidal cell bodies in IVCα and by the presence of a thalamic projection. IVCα and β are separated on the basis of the axon projections of so-called spinous stellate cells. In IVCα the axons do not leave layer IV, while in IVCβ these cells project to layer III. The boundaries of Lund's lamina V are demarcated by a dense plexus of horizontally oriented axons. This is lower than Brodmann's layer V and seems, if anything, to correspond to Ramón y Cajal's layer 7. Lamina VI is immediately deep to this plexus. Both layers contain pyramidal cells; layer VI contains some stellate cells as well. Lund's scheme is illustrated in Fig. 2.

(7) *Shkol'nik-Yarros*

Brodmann's scheme has also been adopted by Shkol'nik-Yarros (1971) for *Cercopithecus*. This investigator has retained unaltered Brodmann's original formulation. She has, however, suggested the subdivision of layer IVb into IVbα, containing the large star cells of Ramón y Cajal, small pyramids and stellate cells, and IVbβ, filled with numerous small short-axon cells. Sublayer IVc is richly supplied with small stellate cells and can be further divided into three parts. In layer V Shkol'nik-Yarros has also pointed out the independent sublayer of small pyramids in the upper region.

Recent trends in lamination of the striate cortex

At present there seems to be a trend toward adopting a lamination scheme that both effects a division of cells into recognizable layers and at the same time reflects an important aspect of their wiring. In other words, the identification of layers should, if possible, relate structure and function. According to this line of argument, the key issue in Area 17 would be the site of termination of geniculate afferents. This is not a new consideration. As we have seen, von Bonin had explicitly questioned whether the position of thalamocortical terminals should determine the naming of layers, and decided in the affirmative. However, like many of his contemporaries, von Bonin believed that the stria of Gennari contained the bulk of thalamocortical fibres (and endings), and his layering scheme reflected this belief. The idea that the stria contains primarily afferents coming from the geniculate has persisted in the literature on the visual cortex despite the work of Clark and Sunderland (1939), who undercut the visual cortex and found almost no degeneration within the stria. The recent publication of studies from a number of different laboratories should at last permanently dispel this false impression (Wilson and Cragg, 1967; Hubel and Wiesel, 1969 and 1972; Garey and Powell, 1971; Polley, 1971; Lund, 1973). With the help of modern degeneration techniques, it has been possible to locate geniculocortical terminals accurately and to indicate them on the several layering schemes that have previously been discussed. Here we shall summarize only the key findings of these studies before considering the general issue of utilizing this information in naming cell layers.

In 1967 Wilson and Cragg had noted that degeneration following geniculate lesions in two monkeys was not concentrated in the stria of Gennari. Preterminal degeneration was seen extending to layer 3 (most likely Brodmann's IVa; unfortunately the authors neglect to report which layering scheme they used). More recent studies by Hubel and Wiesel (1969), confirmed by Garey and Powell (1971) and Polley (1971), have demonstrated that after lesions of the *dorsal* layers of the lateral geniculate, two bands of terminal degeneration appear (located in Brodmann's IVa and IVc respectively) which are separated by the intact stria of Gennari. Subsequently Hubel and Wiesel (1972) and Lund (1973) found that the upper band of geniculocortical terminals extends quite high into Brodmann's IVa. In addition, a few axons apparently terminate in layer I. Hubel and Wiesel (1972) have found, on the other hand, that lesions in the *ventral* layers of the geniculate produce degenerating terminals restricted to the lower part of layer IVb of Brodmann, a region below the stria of Gennari but above the terminal zone for fibres from dorsal geniculate layers.

While they formerly espoused von Bonin's scheme (Hubel and Wiesel, 1968, 1969), Hubel and Wiesel (1972) have recently adopted Brodmann's scheme. The justification given is that although it may sometimes be difficult to distinguish layer III from layer IVa, Brodmann's scheme does restrict geniculate afferent endings to a single layer while von Bonin's spread them across both III and IV. Thus Hubel and Wiesel suggest that the choice of the most appropriate lamination pattern may also involve functional considerations. The layering scheme is, after all, but a tool. Hubel and Wiesel imply that today an appropriate use for such a tool is aiding in the correlation of physiological findings with structure. Interestingly, this is not so different from what Brodmann had originally proposed at the turn of the century. He, after all, had adopted his lamination scheme as a working tool, although his goal of cortical parcellation was a somewhat different one.

However, there is also a basic philosophical difference underlying the ideas of Hubel and Wiesel and of Brodmann (see also Lorente de Nó, 1943). While Brodmann was concerned with picking a scheme uniformly applicable to many cortical regions, Hubel and Wiesel have proposed a justification for Brodmann's scheme that is specific to the striate cortex of *Macaca mulatta*.

In sum, Brodmann's scheme incorporating the functional implications suggested by Hubel and Wiesel seems a useful way of notating the lamination of the visual cortex. The notation is purely descriptive and the layering is clearly visible in cell-stained material without reliance on information from the Golgi method. Its only disadvantage seems to be some ambiguity in determining the exact boundary between laminae III and IV. Since a single, consistent plan for the lamination of the cortex would facilitate communication among anatomists and physiologists investigating the detailed architectural and functional organization of the cortex, we suggest that Brodmann's original scheme should be followed as the most generally useful and applicable. It should be understood that the laminations are statistical entities representing laminar clustering patterns of vast numbers of cells. Such patterns are best seen in Nissl preparations of thick sections. Consequently the laminations become a skeleton on which to hang other morphological and functional properties of the cortex, a set of standard co-ordinates. Therefore, investigators should refer their new observations about cortical cells – their dendritic and axonal branching patterns, their afferents and efferents, etc. – to these fixed co-ordinates, rather than shifting or expanding or contracting them according to the latest information. In particular, it would be wise to refrain from subdividing the layers, especially on the basis of Golgi and electron microscopic preparations, until a more comprehensive knowledge of the formal structure of the cortex has been attained.

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