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30. Such a table has 11 potential columns (0 to 10). But when a disease was rare sometimes only the first two columns, or even the first only, had nonzero entries; in such cases we used $100X_{ij}$ or, for one disease $30X_{ij}$. Once several columns were present, the results were insensitive to the degree of multiplication.
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Opiate Receptor Distribution in the Cerebral Cortex of the Rhesus Monkey

Abstract. *The distribution of opiate receptors in the cerebral cortex of the rhesus monkey* (Macaca mulatta) *was determined by autoradiographic visualization of [^{3}H]naloxone binding to tissue sections. Naloxone was bound in relatively large amounts to the cortical laminae containing the cell bodies of output neurons, to a varying set of additional laminae in different cortical fields, to fields closer to more primitive types of cortex, and to polysensory cortical fields. From these laminar and areal variations in distribution, it appears that opiate receptors play a role in specific aspects of cortical function.*

Opiates are best known for their analgesic properties, but administration of these compounds results in a constellation of effects. Some of the effects suggest an influence on the cerebral cortex (*1, 2*). While opiate binding levels in broad cortical regions have been described (*3, 4*), no analysis has been made of binding in different cortical laminae or of changes in binding patterns that may occur at the boundaries of cortical fields. We present here an autoradiographic investigation of the laminar and regional distribution of opiate receptors in the cerebral cortex of the rhesus monkey (*5, 6*).

Autoradiographs of [^{3}H]naloxone binding to opiate receptors (*7*) were prepared following incubation of cryostat-sectioned, unfixed, slide-mounted tissue in 2.5 n*M* [^{3}H]naloxone (specific activity, 50 Ci/mmole) and 0.05*M* tris-HCl with 100 m*M* NaCl (*p*H 7.4) at 0°C (*8*). The sections were fixed in formaldehyde vapor after incubation, apposed to tritium-sensitive film, and exposed for 8 weeks at room temperature. The sections were subsequently stained with Thionine for cytoarchitectonic analysis. The ratio of total to nonspecific [^{3}H]naloxone binding was determined to be 9.1:1 by adding unlabeled etorphine (1 μM) to the incubation medium as a competitive blocking ligand. One hemisphere was sectioned in a frontal plane, the other in a parasagittal plane.

Several findings emerged from our analysis. The infragranular layers (*9*) showed relatively high levels of opiate receptor binding throughout most of the neocortex. For example, labeling was heavy in layer VI of the precentral motor cortex (Figs. 1a and 2b) and premotor cortex (not shown). The postcentral somatic sensory areas (Figs. 1a and 2b), the striate visual cortex (Fig. 1), and the peristriate visual cortex (Fig. 1) (*10*) displayed enriched binding in layers V and VI. The primary auditory cortex, the second somatic sensory cortex, and some visual fields (such as the inferotemporal cortex) had high binding levels in layer V, with lower levels in layer VI (Fig. 2a). Many additional fields, especially those in the superior temporal and lateral sulci, also had relatively high levels of binding in infragranular layers (Fig. 1a). Since laminae V and VI contain the cell bodies of the vast majority of corticofugal neurons (*11*), the prevalence of opiate receptors there suggests that opiates may play a role in the control of cortical output.

The influence of opiates on cortical output could be tested directly, since neurons in these layers are identifiable by antidromic activation of corticofugal fibers. It would be of interest to determine, for example, the effect of systemically or locally applied opioid compounds or antagonists on properties of the visual receptive fields of cells in layers V and VI in the monkey's striate visual cortex.

Although the infragranular layers showed relatively high levels of opiate binding in most cortical fields, overall laminar binding patterns varied in different cortical fields (*5*). For example, in the precentral motor cortex, layer I

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showed the highest level of opiate binding and there were areas of less prominent binding in layers III and VI (Figs. 1a and 2b). By contrast, in both the postcentral somatic sensory cortex (Fig. 2b) and the striate visual cortex (Fig. 1), binding in layer I barely exceeded that in the adjacent layer II. In the frontal eye field the highest level of binding was seen in layer III (Fig. 2b). Prominent supragranular binding was also seen in other parts of the frontal lobe (Fig. 3a). In contrast, there was no marked binding in the supragranular layers of the striate visual cortex (Fig. 1a).

Many of the transitions in opiate binding patterns occur at the boundaries of physiologically and cytoarchitectonically defined cortical fields. The opiate binding transition found at the cytoarchitectonic boundary of striate and peristriate visual cortex was noticeably abrupt; binding in layer IV of the peristriate cortex was substantially greater than that in the same layer of the striate cortex (Fig. 1, b and c). The boundary of the precentral motor cortex and the postcentral somatic sensory cortex marked an abrupt change in layer I receptor density (Figs. 1a and 2b). Particularly discrete transitions were observed throughout the hippocampal formation (Fig. 2a). Although not all opiate binding transitions are so discrete and do not always correspond to established cytoarchitectonic boundaries, we believe that opiate receptor patterns can ultimately be used in conjunction with traditional techniques for improved definition of cortical fields.

Progressively higher levels of opiate binding were observed with increasing proximity to the most primitive type of cortex, the allocortex (the pyriform cortex plus the hippocampus). The primary sensory and motor fields [the precentral motor cortex (Figs. 1a and 2b), striate visual cortex (Fig. 1a), postcentral somatic sensory cortex (Figs. 1a and 2b), and primary auditory cortex (Fig. 2a)] had the lowest overall opiate receptor density.

Greater concentrations of opiate receptors were found in neocortical fields lying between the primary fields and those nearest the allocortex. These included the supplementary motor cortex (not shown), the peristriate visual cortex (Fig. 1b), and the second somatic sensory cortex (Fig. 2a). Juxtallocortical fields—those nearest the allocortex—had among the highest concentrations of opiate receptors in the cerebral cortex. Situated dorsomedially near the cingulate sulcus and ventrally near the pyriform cortex, amygdala, and hippocampus, these strikingly receptor-dense limbic fields included the anterior (Fig. 3a) and posterior (Fig. 3, b and c) cingulate fields and the presubicular (Fig. 2a) and parasubicular (Fig. 2a) fields. In the allocortex, the pyriform cortex was labeled comparably to the juxtallocortical fields and the hippocampus was labeled less heavily (Fig. 2a). These findings, along with the high levels of opiate binding in the frontal lobe (Fig. 3a), support the association of opiates with the primate limbic system (*4*, *12*).

The increased labeling with proximity to the allocortex generally agrees with findings for brain homogenates (*3*). It should be noted, however, that in the present autoradiographic study we stressed the laminar peaks of receptor binding within a cortical field rather than averaging the opiate binding over all cortical laminae, as other investigators have done (*3*, *4*).

Cortical fields suggested to be "poly-

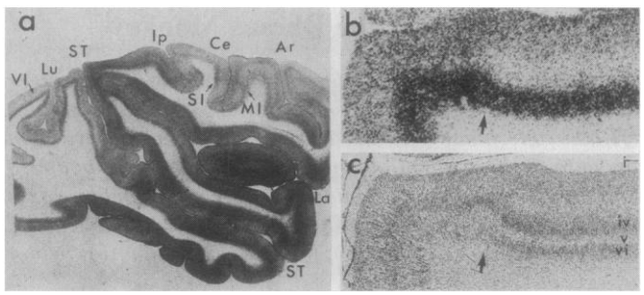

Fig. 1. (a) Representative autoradiograph showing [^{3}H]-naloxone binding in a parasagittal section (×1.0). Rostral is to the right. Darker areas indicate higher levels of opiate binding. Note the wide range of binding levels in different cortical regions. (b) Autoradiograph showing [^{3}H]naloxone binding in striate cortex (right of arrow) and in the peristriate cortex (left of arrow) (×11). (c) Film-exposed section stained with Thionine, showing the correspondence of the opiate binding pattern and cytoarchitecture (×11). Abbreviations: *Ar*, arcuate sulcus; *Ce*, central sulcus; *Ip*, intraparietal sulcus; *La*, lateral sulcus; *Lu*, lunate sulcus; *MI*, precentral motor cortex; *SI*, postcentral somatic sensory cortex; *ST*, superior temporal sulcus; *VI*, striate visual cortex; and *i*, *iv*, *v*, and *vi*, cortical laminae.

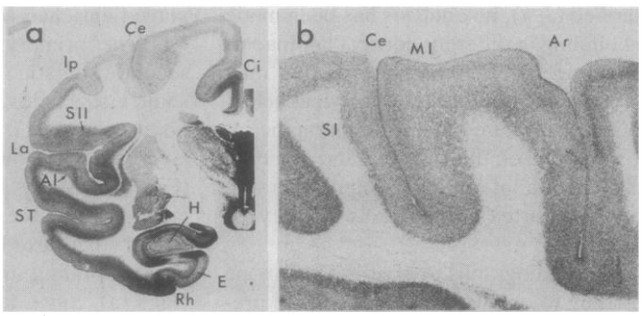

Fig. 2. (a) Autoradiograph showing [^{3}H]naloxone binding in a representative frontal section (×1). Dorsal is at the top and medial is to the right. Note the high levels of opiate binding in juxtallocortical structures dorsomedially (the cingulate cortex) and ventrally and the specific binding patterns in the hippocampal formation (*H*) and the entorhinal cortex (*E*). The superior temporal polysensory cortex is in the dorsal bank of the superior temporal sulcus. *Rh*, rhinal sulcus; *CI*, cingulate sulcus; (b) Autoradiograph of a parasagittal section through the central and arcuate sulci (×3). Rostral is to the right. Note the abrupt opiate binding pattern boundary in the rostral bank of the arcuate sulcus and the difference between layer I binding in the precentral cortex and that in the postcentral cortex (see Fig. 1a). Abbreviations: *AI*, first auditory cortex; *SII*, second somatic sensory cortex.

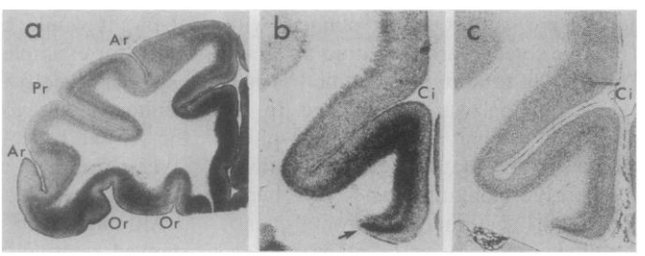

Fig. 3. (a) Autoradiograph showing dense binding of [^{3}H]naloxone to the orbital frontal cortex (between the lateral orbital sulcus and the inferior limb of the arcuate sulcus) and the anterior cingulate cortex (×1.3). Frontal section; dorsal is at the top and medial is to the right. *Pr*, principal sulcus; *Or*, orbital sulcus. (b) Autoradiograph of posterior cingulate cortex (×4). Note the bilaminar opiate binding pattern and its high density relative to that in adjacent cortex. Arrow marks the retrosplenial cortex. (c) Thionine-stained section from (b) (×4).

sensory" on the basis of both corticocortical connectivity and neuronal responses to more than one modality of sensory stimulation (*13*) also showed relatively high levels of [^{3}H]naloxone binding. These fields included the superior temporal polysensory cortex (Fig. 2a), the ventral temporal polysensory cortex (*14*), part of the inferior parietal lobule (*15*), and the orbital frontal cortex (Fig. 3a) (*14*). The ventral temporal and orbital frontal fields had among the highest levels of binding in the cortex.

If increased opiate receptor density indicates greater functional importance, then the laminar and areal patterns of opiate receptors shown by the present investigation indicate that opiates are important in the modulation of specific cortical elements. It appears that opiates may predominantly influence the outflow of cortical fields and those fields involved in polymodal information processing and limbic functions.

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9. The cerebral cortex can be divided into three strata. These are, in order of increasing depth, the supragranular layers (layers I, II, and III), the internal granular layer (layer IV), and the infragranular layers (layers V and VI).
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Retinogeniculate Terminations in Cats: Morphological Differences Between X and Y Cell Axons

Abstract. *We injected horseradish peroxidase into single, physiologically identified, optic tract axons of X and Y cells in cats and studied their termination patterns in the lateral geniculate nucleus. All X cell axons innervate lamina A or A1 in narrow zones, and some sparsely innervate the medial interlaminar nucleus. All Y cell axons have broad terminal zones in laminae A and C (from the contralateral retina) or lamina A1 (if ipsilateral), and most innervate the medial interlaminar nucleus densely.*

The cat's retinogeniculocortical pathways are represented by W, X, and Y cells in the retina and in the lateral geniculate nucleus. These form three parallel, largely independent neural systems that appear to analyze different features of the visual scene (*1*). We know a great deal about physiological differences among these cell classes but little about morphological differences that underlie the physiology. This is because of the difficulty of directly identifying W,

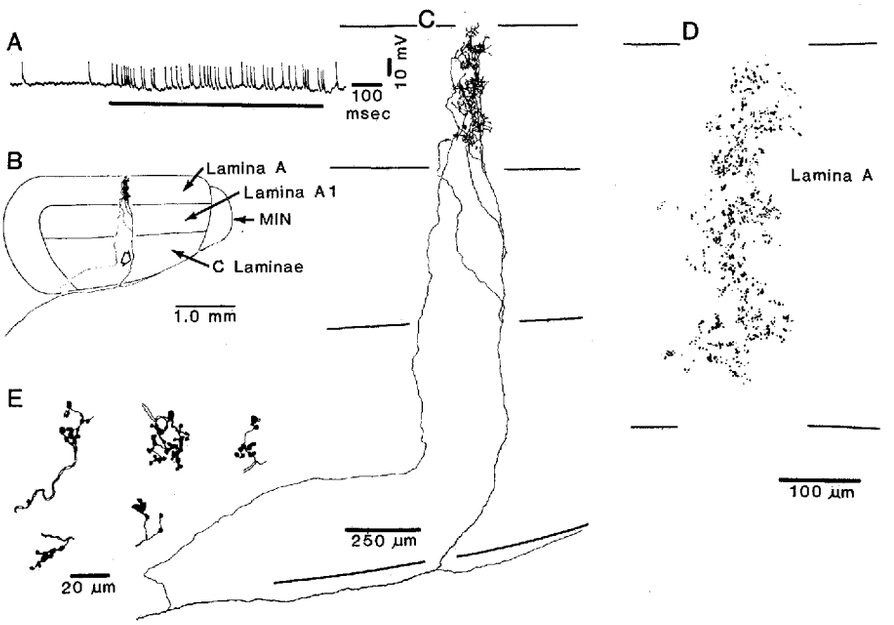

Fig. 1. Data from an X cell axon driven by the right eye (contralateral to the recording site). The axon's receptive field had an ON center of 0.5° diameter located 9° from the vertical meridian and 2° below the horizontal zero parallel of the visual field. The conduction latency from the optic chiasm to the recording and injection site [open arrow in (B)] was 0.9 msec. (A) Intracellular recording. The bar below part of the trace indicates the presence of a small spot of light placed in the receptive field center. Note the sustained response to this stimulus. (B) Drawing of the left lateral geniculate nucleus in the coronal plane with the axon shown. Compressed in this view are 21 consecutive, 100-μm-thick coronal sections. The parent trunk of the axon is 2 μm thick, and its geniculate termination is limited to lamina A. The thin medialward branch continues posteriorly (see text). *MIN*, medial interlaminar nucleus. (C) More detailed drawing of the terminal zone in lamina A. (D) Location and shape of the 793 terminal boutons in lamina A, reconstructed from three consecutive, 100-μm-thick coronal sections. For clarity, the preterminal axon branches are not shown. (E) Morphology of typical terminal bouton arrangements in lamina A. Note both the clustering of the boutons and the relatively homogeneous composition of the medium-sized, spherical type (see text, and compare with Fig. 2E).

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